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Meeting abstracts

## Sixteenth Annual Computational Neuroscience Meeting: CNS\*2007

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### INTRODUCTION

#### Computational Neuroscience (CNS\*2007)

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*BMC Neuroscience* 2007, **8**(Suppl 2):1

The international *Computational Neuroscience* meeting (CNS) has been a premier forum for presenting experimental and theoretical results exploring the biology of computation in the nervous system for the last 16 years. The meeting is organized by the *Organization for Computational Neurosciences*, a non-profit organization governed by an international executive committee and board of directors. A separate program committee is responsible for the scientific program of the meeting. Participants at the meeting are from academia and industry. The meeting not only provides a venue for research presentation and discussion by senior scientists but actively offers a forum for promoting and supporting young scientists and students from around the world.

The papers in this supplemental volume were presented at the 16<sup>th</sup> Annual Computational Neuroscience Meeting (CNS\*2007) held in Toronto, Ontario, Canada from Saturday July 7 to Thursday July 12, 2007. The meeting consisted of a welcome reception, three days of oral and poster sessions, an evening harbor cruise and dinner, and two days of workshops. The main meeting was held at 89 Chestnut, a University of Toronto conference facility and the workshops took place at the University of Toronto downtown campus.

Abstracts for the meeting were submitted in early February. Those authors wanting an oral presentation also submitted an extended summary of their work. The abstracts were reviewed by the Program Committee and each extended summary was additionally reviewed and scored by two independent reviewers. In the end 230 papers were accepted for the meeting. The

review comments and scores for the extended summaries were used by the Program Committee to construct the final oral and poster programs.

Abstracts for oral presentations are given first, in order of presentation at the meeting. Abstracts for poster presentations are grouped by topic according to keywords chosen by the authors in their initial submissions. Clearly some papers could fit under multiple topics, so this classification is by no means precise. Nevertheless, these abstracts represent a sampling of some of the exciting work being done today, often by young researchers, in the field of Computational Neuroscience.

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## ORAL PRESENTATIONS

### S1

**Invited talk: Coding strategies for multiscale sensory signals**

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BMC Neuroscience 2007, 8(Suppl 2):S1

There are an increasing number of experimental studies of sensory neural systems devoted to understanding the processing of naturalistic stimuli. Such studies are necessary to reveal the whole spectrum of possible computations accomplished by neural systems. We discuss recent advances in this area in the context of the electric sense, which can be seen as a combination of the visual and auditory senses [1]. This sense is very advantageous for such studies because its input can be well characterized and modeled [2]: modulations of an endogenous electric organ discharge (EOD) carrier caused by objects such as rocks and food, and communication signals between the fish. Especially important is the fact that the anatomy enables electrophysiological recordings through many successive stages of processing.

This talk will briefly review earlier results on coherence shifts, oscillations and bursting in this sense, and present recent results from our experimental/theoretical collaboration. First, in the context of communication, the primary afferent neurons or "electroreceptors" exhibit transitions between synchronized and desynchronized states. The direction of the transition depends on whether the interaction is between fish of the same or opposite sex [3]. The decoding of this effect is performed by pyramidal cells, and depends on the frequency dependence of the synchronous discharges. We also present results showing that the synchronous discharges between afferents selectively encode high frequencies. We then consider the cocktail party problem these animals face, with the goal of discovering the neural solution to this general problem. We address this issue in the context of the detection of slow time scale modulations of the EOD carrier. These slow modulations arise when many fish are in the vicinity of one another. We show that these modulations can be extracted via a Hilbert-type transform, and illustrate the circuitry that enables this computation [4]. Modeling shows that the effect requires strong neuronal nonlinearity, and can under certain circumstances benefit from the presence of noise when a population of neurons is considered [5]. This computation allows parallel transmission of high-frequency signals, as well as the low frequency envelope that results from social interactions.

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### S2

**Dense gap-junction connections support dynamic Turing structures in the cortex**

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 Marcus Wilson<sup>1</sup> and Jamie Sleight<sup>2</sup>

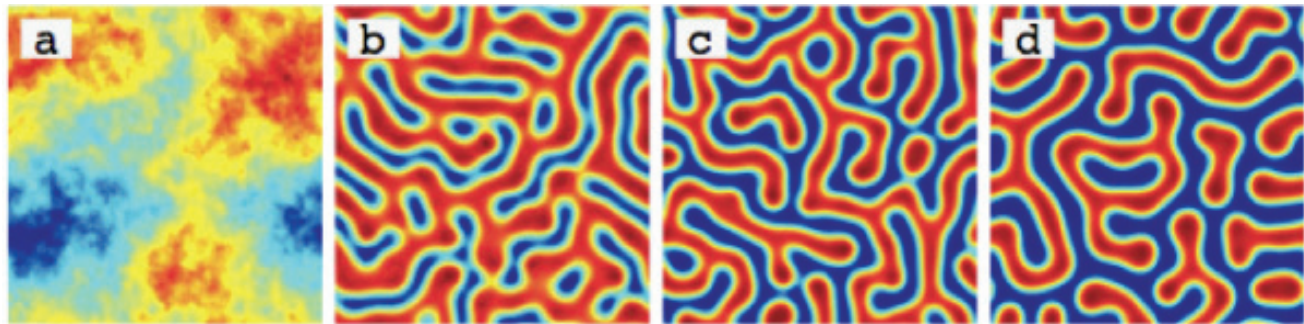
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BMC Neuroscience 2007, 8(Suppl 2):S2

The recent report by Fukuda *et al* [1] provides convincing evidence for dense gap-junction connectivity between inhibitory neurons in the cat visual cortex, each neuron making 60 +/- 12 gap-junction dendritic connections with neurons in both the same and adjoining orientation columns. These resistive connections provide a source of diffusive current to the receiving neuron, supplementing the chemical-synaptic currents

**Figure 1 (abstract S2)**

**Diffusion-induced Turing patterns in a square cortex of side 25 cm.** Panel a shows the case of zero diffusion: the cortex organizes into a diffuse, cloud-like pattern, but fails to generate a Turing structure. Panels b-d show increasing inhibitory diffusion. These cases evolve into stable serpentine Turing patterns containing alternating regions of low-(blue) and high-firing (red) cells.

generated by incoming action-potential spike activity. Fukuda *et al* describe how the gap junctions form a dense and homogeneous electrical coupling of interneurons, and propose that this diffusion-coupled network provides the substrate for synchronization of neuronal populations.

To date, large-scale population-based mathematical models of the cortex have ignored diffusive communication between neurons. Here we augment a well-established mean-field cortical model [2] by incorporating gap-junction-mediated diffusion currents, and we investigate the implications of strong diffusive coupling. The significant result is the model prediction that the 2D cortex can spontaneously generate centimetre-scale Turing structures (spatial patterns), in which regions of high-firing activity are intermixed with regions of low-firing activity (see Fig. 1). Since coupling strength decreases with increases in firing rate, these patterns are expected to exchange contrast on a slow time-scale, with low-firing patches increasing their activity at the expense of high-firing patches. These theoretical predictions are consistent with the slowly fluctuating large-scale brain-activity images detected from the BOLD (blood oxygen-level-dependent) signal [3].

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#### S3

##### **Controlling for spatial variability in single site recordings in an in vitro hippocampal preparation with a spontaneous rhythm**

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BMC Neuroscience 2007, 8(Suppl 2):S3

An important consideration in analyzing the time-frequency rhythms of hippocampal local field potentials is to what extent changes in time of a single site signal actually reflect spatial summation of two wholly separate signals. Signals observed could be the result of the spatial summation of different activities. For example, the duration of activities observed could be due to two shorter durations overlapping. More broadly, it is a source of concern if the hippocampal rhythms do not have well defined spatial properties (preferably fairly homogenous) since a single signal has no control for this variable.

To that end, we examine the behaviour of a spontaneous hippocampal rhythm over time as it varies spatially within an intact whole hippocampus preparation. We also examine the response to a high frequency stimulation protocol of 80 Hz. Using four simultaneous rostral to caudal recordings of two to five minutes, we characterize this changing rhythmic activity according to clustered patterns of activity in its time-frequency distribution. Our data set consists of 40 extracellular recordings. The frequency distribution change in response to stimulation was observed. We calculate the spatial variance of the data for each unit of time. This allows us to link the time-frequency data to a level of spatial variance. The variance of the signal in time was defined to be the variance in the mean frequencies of the signal resultant from partitioning each time-frequency epoch into thirds. That is, a sliding 0.5 second temporal resolution was divided into thirds and the variance in the mean frequencies calculated. The change in the signal in time was then compared to the change in signal in space to determine whether there were any significant correlations.

There is a distinct relationship between the variance among simultaneous rostral caudal recordings and the non-stationarity present in each of those spatially distinct recordings. The peak values nearly follow the  $y = -x$  line. Functional biological rhythms in the hippocampus are commonly both non-stationary and coherent, making this inverse relationship more intuitive. Consider that the hippocampal recording has two components, one of which is



stationary background noise and one of which is the nonstationary signal of interest. Our finding, then, is that the noise is uncorrelated spatially and signal is correlated spatially. In this case, when the signal is low, the non-stationarity would be low and the spatial variance would be high. This is a very useful property for single site recordings because it means that the more physiologically interesting (nonstationary) the recording, the less we need to be concerned that spatial summation is a problem.

#### S4

##### **Synchronization of asynchrony-favoring neurons – wireless clustering**

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BMC Neuroscience 2007, 8(Suppl 2):S4

Paired neurons tend to fire synchronously or asynchronously depending on the membrane potential dynamics. Traditionally, those neurons that favor synchrony are associated with temporal coding, while rate coding is associated with those that favor asynchrony. However, as we show here, the effects of spike-timing-dependent plasticity (STDP) challenge this view. Under STDP, a population of neurons that favors asynchrony appears to self-organize into clusters, each of which exhibits synchronous firing. This paradoxical synchronization within each cluster is possible because STDP selectively disrupts intra-cluster connections, thereby nullifying the asynchrony tendency inherent in neurons. We call this a wireless clustering. When we run the same simulation with neurons that favor synchrony, no cluster-wide synchronization is observed. Instead, these neurons are synchronized globally. Where the impact of a single neuron on other neurons can be as small as 0.5 mV, a cluster of synchronously firing neurons can reliably elicit firing in other neurons, making the cluster the likely unit for information processing in the brain. Therefore, based on this study, asynchrony-favoring neurons appear to contribute to the temporal coding scheme, not synchrony-favoring neurons which exhibit global synchrony which is more common in pathological events like a seizure.

#### S5

##### **Multi input multi output neural population encoding**

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BMC Neuroscience 2007, 8(Suppl 2):S5

A formal mathematical model for representing neural stimuli is presented. The model enables the investigation of stimulus representation by spiking neurons, and provides algorithms that under certain conditions can recover the stimuli with no error, by knowing only the time of the spike trains.

In our model, we assume that  $N$  bandlimited input stimuli approach the dendritic trees of  $M$  spiking neurons. Each stimulus comes to a different branch of each dendritic tree, and each dendritic tree is modeled as a linear time invariant (LTI) filter. The outputs of all dendritic branches are summed together with a background current (bias), and this sum enters the soma of each neuron, which is modeled as an Integrate-and-Fire neuron.

We prove that under certain conditions, it is possible to recover all  $N$  input spike trains, by knowing only the  $M$  spike trains, and provide an algorithm for that purpose. The proof comes from the mathematical theory of frames and the conditions require a minimum average spike density from the neurons and some mild conditions in the impulse responses of the dendritic branches/filters. We illustrate this algorithm with an example that recovers the stimuli when the dendritic branches perform arbitrary but known time-shifts to the signal. This particular example is important as it illustrates how information from sensory neurons that respond with different latencies, can be combined together.

Finally, the model points to the significance of neural population codes, as it shows that data from a single neuron can be misleading in terms of what the input stimulus is. We illustrate this significant observation with an example.

#### S6

##### **Object localization through the lateral line system of fish**

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BMC Neuroscience 2007, 8(Suppl 2):S6

Fish use their lateral-line mechanoreceptive system to analyze water motion around their body. The functional unit of the fish lateral-line system is a neuromast. This is in essence a cupula, a gelatinous protuberance sticking into the water and deflected by local water flow. Deflections stimulate sensory hair cells at the basis of the cupula and in this way generate spikes in the lateral-line nerves. Neuromasts are either free standing on the skin (superficial neuromasts, SN) or in a system of sub epidermal canals (canal neuromasts, CN). It has been shown that SNs are sensitive to constant flow whereas CNs are not. Nobody, however, has ever proposed a mathematical model to relate the water perturbation in the fish environment to the water motion in the canal, the neuromasts displacement, and the spike flow in the afferent nerves. This is what we do here. The CN system consists of canals that are open to the external environment through approximately equidistant pores. Between each pair of pores at the surface one can find one or more neuromasts in the canal. A pressure difference between the pores induces water movement in the canal and hence stimulates the neuromasts. We solve the case of a small sphere oscillating near the body, study the effect of different terms of the hydrodynamics on the pressure map of the fish body and the ensuing neuronal excitation pattern, and show that the maximum and the two points where the pressure difference between two pores vanish suffice to enable a fish to determine the distance to a stimulus. Our theory has been confirmed by recording experiments. It has also been shown that even though a constant flow does increase the firing rate the effect induced by an oscillating dipole and the distance between the zeros can still be measured.

##### **Acknowledgements**

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**S7****Neural coding of natural stimuli: information at sub-millisecond resolution**Ilya Nemenman<sup>1</sup>, Geoffrey D Lewen<sup>2</sup>, William Bialek<sup>3</sup> and Rob R de Ruyter van Steveninck<sup>4</sup><sup>1</sup>Computer, Computational and Statistical Sciences Division, Los Alamos National Laboratory, Los Alamos, NM 87545, USA<sup>2</sup>The Hun School of Princeton, 176 Edgerstoune Road, Princeton, NJ 08540, USA<sup>3</sup>Joseph Henry Laboratories of Physics and Lewis-Sigler Institute for Integrative Genomics, Princeton University, Princeton, NJ 08544, USA<sup>4</sup>Department of Physics, Indiana University, Bloomington, IN 47405, USAE-mail: [nemenman@lanl.gov](mailto:nemenman@lanl.gov)

BMC Neuroscience 2007, 8(Suppl 2):S7

Our knowledge of the sensory world is encoded by neurons in sequences of discrete, identical pulses termed action potentials or spikes. There is persistent controversy about the extent to which the precise timing of these spikes is relevant to the function of the brain. We revisit this issue, using the motion – sensitive neurons of the fly visual system as a test case. New experimental methods allow us to deliver more nearly natural visual stimuli, comparable to those which flies encounter in free, acrobatic flight, and new mathematical methods allow us to draw more reliable conclusions about the information content of neural responses even when the set of possible responses is very large. We find that significant amounts of visual information are represented by details of the spike train at millisecond and sub-millisecond precision, even though the sensory input has a correlation time of ~60 ms; different patterns of spike timing represent distinct motion trajectories, and the absolute timing of spikes points to particular features of these trajectories with high precision. Under these naturalistic conditions, the system's information transmission rate still increases with higher photon flux, even though individual photoreceptors are counting more than one million photons per second. Further, exploiting the relatively slow dynamics of the stimulus, the system removes redundancy and so generates a more efficient neural code.

**S8****Information theoretic bounds on the effectiveness of neural prosthetics**

Ilan N Goodman and Don H Johnson

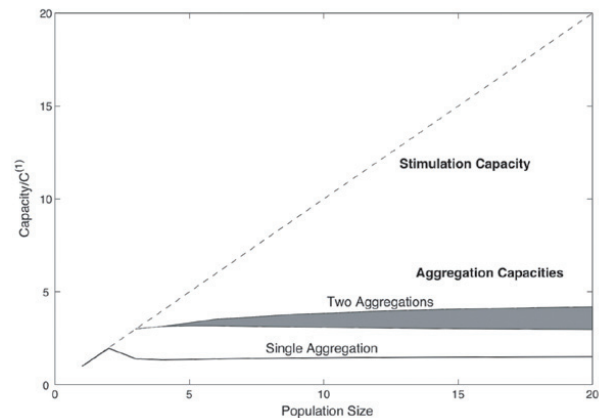
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Capacity defines the ultimate fidelity limits of information transmission by any system, be it conveyed by digital, analog or spike train signals. Rate-distortion theory shows that regardless of how error is defined, any system having a smaller capacity than another must result in larger estimation errors. For example, this theory shows that, for bandlimited Gaussian stimuli, the smallest possible mean-squared error decays exponentially with capacity. Since a single neuron's capacity is proportional to peak spike rate,  $\varepsilon_{\min}^2 \propto \exp\{-\lambda_{\max}/eW\}$  ( $W$  is the stimulus bandwidth).

In previous work, we derived the capacity of parallel Poisson process channels, which allows us to study the relative

**Figure 1 (abstract S8)**

Capacity as a function of neural population size.

effectiveness of neural population structures. Here, we elaborate those results for two models of neural prosthetics: (1) electrical stimulation systems such as cochlear implants and (2) neural control systems that use surface or gross potentials to control movements of limb prostheses. We show that for the electrical stimulation case, the capacity is proportional to the size of the population being stimulated, regardless of whether the stimulus drives the entire population or whether individual neurons are independently stimulated (fig 1). In this case, gross stimulation theoretically suffices. In contrast, neural control systems using gross recordings have a far smaller capacity. If a single potential represents the aggregate population activity, we found that capacity does not increase with population size, but instead saturates at a value less than the capacity provided by using the individual outputs of two neurons to derive the control signal. If two gross potential measurements are made, assumed here to represent overlapping subpopulations, capacity is larger than in the single-potential case but still saturates with increasing population size.

We conclude that stimulation prosthetics face no fundamental barriers to being effective. Neural control systems do, however. This fundamental limitation can be overcome by using spike sorting (teasing apart the gross potential into its constituents) and/or by using feedback, which has been shown to increase capacity.

**S9****Invited talk: What can brain imaging add to neuronal and network representations of pain and attention?**Karen D Davis<sup>1,2</sup><sup>1</sup>Department of Surgery, Institute of Medical Science, University of Toronto, Toronto, Ontario, Canada<sup>2</sup>Division of Brain, Imaging and Behaviour Systems, Toronto Western Research Institute, Toronto, Ontario, CanadaE-mail: [kdavis@uhnres.utoronto.ca](mailto:kdavis@uhnres.utoronto.ca)

BMC Neuroscience 2007, 8(Suppl 2):S9

Classic electrophysiological studies laid the groundwork for our understanding of pain mechanisms and the impact of attentional factors. However, with the advent of neuroimaging technologies

such as functional MRI, brain mechanism associated with the multidimensional aspects of human pain perception can now be mapped. Our lab is developing models of specific qualities (percept-related fMRI) of the pain experience, how they are impacted by attentional and individual factors in both healthy individuals and chronic pain states. Such models are also informed by single cell electrophysiological recordings in the human brain, and network models of pain and attention we are developing from multivariate analyses. This presentation will provide an overview of these studies.

## S10

### Recollection and imagination in a functional model of visual cortex

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BMC Neuroscience 2007, 8(Suppl 2):S10

In [1] we have presented a model of signal flow in functional cortical columns, across the six cortical layers and between several cortical areas. We showed how the columnar subsystems interact to predict and recognize stimuli in terms of locally stored knowledge. In this model, columnar communication integrated bottom-up signals with internally generated top-down signals to describe the stimulus consistently across all cortical areas. Here we extend this model to demonstrate that the same setup of intercommunicating columns can use the stored knowledge to integrate a pre-activation on the highest level with the bottom-up recognition process. Given only coarse or invariant top-down activation, the model can (i) guide and support the recognition of noisy or ambiguous stimuli, and (ii) recall known objects, at the highest level of detail, by creating specific neural activations across all cortical areas. The second process corresponds to recollection or mental imagery, in which the brain internally creates a percept without a physical stimulus.

The top-down pre-activation supports recognition of a stimulus in several ways. (1) If the stimulus is noisy and could not be recognized in the pure bottom-up-driven mode, the pre-activation of the highest area supports weak bottom-up activations that are consistent with the top-down signal, and stabilizes recognition of the stimulus. (2) If the stimulus is ambiguous and did not lead to a stable pattern of activity, because no consistent description across all levels could be found, pre-activation of one of the alternative objects (words) in the highest area stabilizes the recognition of this object, and marks the other parts of the stimulus as errors. In both cases, the dynamics of the interacting neural subsystems promotes the top-down influence across all model areas. (3) If the physical stimulus is unspecific or missing, the top-down activation shapes the diffuse bottom-up activation towards recognition of the respective object. Because the dynamics of the interacting neural subsystems strives towards consistent neural activity on all cortical levels, it (re-)creates a detailed and specific mental image of the recalled object.

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## S11

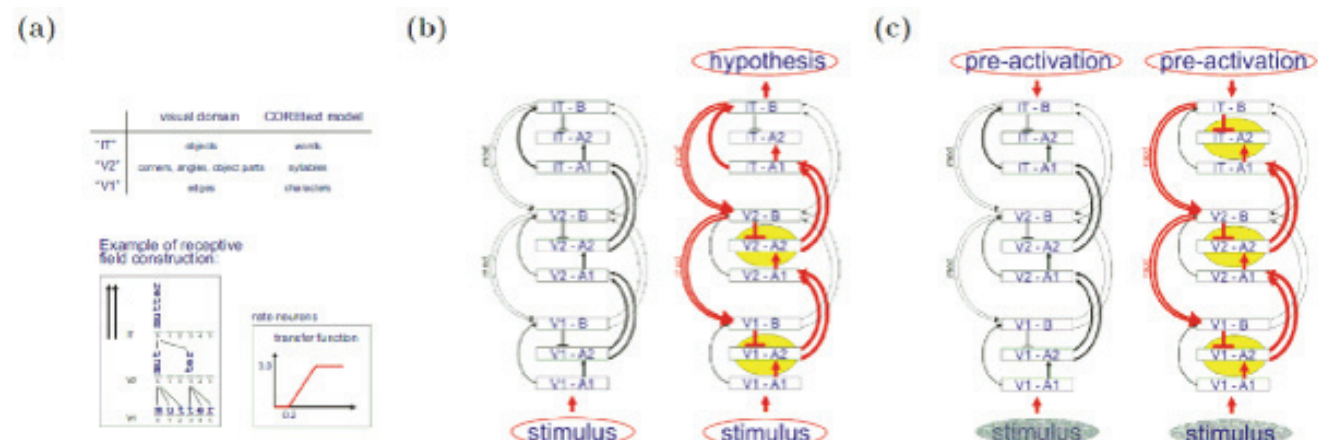
### The study of nonlocal neural populations involving two neuron types and the effect of propofol

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The work derives a neural population model, which considers excitatory and inhibitory synapses as well as excitatory and inhibitory neurons. Then the spatio-temporal dynamics of the

Figure 1 (abstract S10)



Recognition and recall in the COREtext model. (a), characters, syllables, and words in the COREtext model correspond to edges, parts, and objects in the visual system; (b), bottom-up mode (recognition); (c), top-down mode (recall).

neural population is studied subject to the increase of the inhibitory synaptic decay rate. This study is motivated by the effect of the anaesthetic propofol, which increases the inhibitory synaptic decay rate with increased blood concentration and may yield loss of consciousness. We find regimes of stationary multistability and stability criteria for the stationary states. It turns out that the increase and subsequent decrease of propofol yields saddle-node bifurcations in a hysteresis loop.

## S12

### Non-renewal Markov models for spike-frequency adapting neural ensembles

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We present a continuous Markov process model for spike-frequency adapting neural ensembles which synthesizes existing mean-adaptation approaches and inhomogeneous renewal theory. Unlike renewal theory, the Markov process can account for interspike interval correlations, and an expression for the first-order interspike interval correlation is derived. The Markov process in two dimensions is shown to accurately capture the firing-rate dynamics and interspike interval correlations of a spike-frequency adapting and relative refractory conductance-based integrate-and-fire neuron driven by Poisson spike trains. Using the Master equation for the proposed process, the assumptions of the standard mean-adaptation approach are clarified, and a mean+variance adaptation theory is derived which corrects the mean-adaptation firing-rate predictions for the biologically parameterized integrate-and-fire neuron model considered. An exact recipe for generating inhomogeneous realizations of the proposed Markov process is given.

## S13

### Efficient supervised learning in networks with binary synapses

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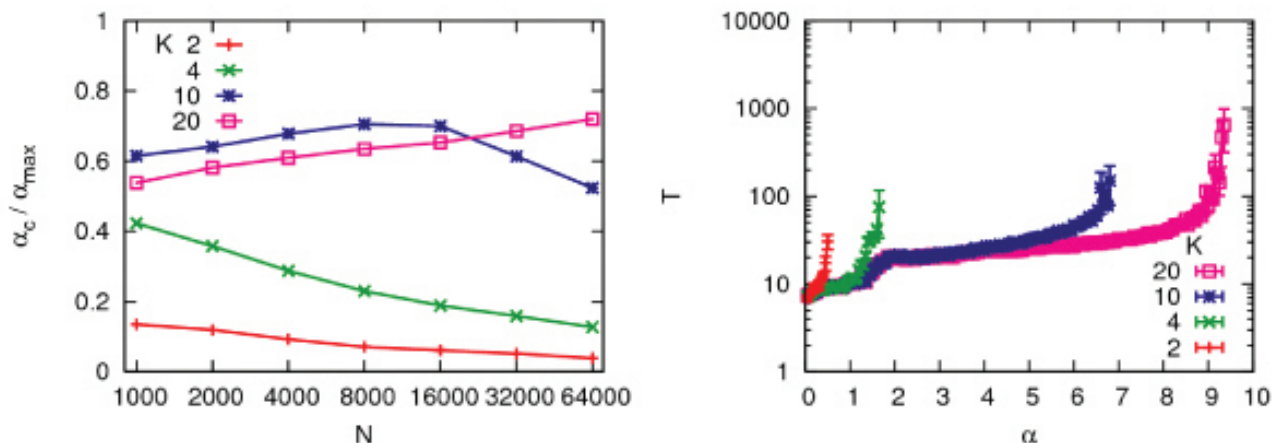
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Recent experiments [1, 2] have suggested single synapses could be similar to noisy binary switches. Binary synapses would have the advantage of robustness to noise and hence could preserve memory over longer time scales compared to analog systems. Learning in systems with discrete synapses is known to be a computationally hard problem. We developed and studied a neurobiologically plausible on-line learning algorithm that is derived from Belief Propagation algorithms. This algorithm performs remarkably well in a model neuron with  $N$  binary synapses, and a discrete number of 'hidden' states per synapse, that has to learn a random classification problem. Such a system is able to learn a number of associations which is close to the information theoretic limit, in a time which is sub-linear in system size, corresponding to very few presentations of each pattern. Furthermore, performance is optimal for a finite number of hidden states, that scales as  $N^{1/2}$  for dense coding, but is much lower ( $\sim 10$ ) for sparse coding (see Figure 1). This is to our knowledge the first on-line algorithm that is able to achieve efficiently a finite capacity (number of patterns learned per synapse) with binary synapses.

The algorithm is similar to the standard 'perceptron' learning algorithm, but with an additional rule for synaptic transitions which occur only if a currently presented pattern is 'barely correct' (that is, a single synaptic flip would have caused an error).

Figure 1 (abstract S13)



**Learning capacity and learning time.** (left) achieved capacity vs. the number of synapses  $N$ , with different numbers of hidden states, in the sparse coding case: the algorithm can achieve up to 70% of the maximal theoretical capacity at  $N \sim 10000$  with 10 hidden states; (right) average learning time (number of presentations per pattern) versus number of patterns to be learned, for  $N = 64000$ : less than 100 presentations are required up to the critical point where learning fails.



In this case, the synaptic changes are meta-plastic only (change in hidden states and not in actual synaptic state), and go towards stabilizing the synapse in its current state. This rule is crucial to the algorithm's performance, and we suggest that it is sufficiently simple to be easily implemented by neurobiological systems.

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#### S14

##### **A model for structural plasticity in neocortical associative networks trained by the hippocampus**

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The hippocampal formation plays a crucial role in organizing cortical long-term memory. It is believed that the hippocampus is capable of fast (one-shot) learning of new episodic information followed by extensive time periods where corresponding neocortical representations are trained and “compressed” [1]. Here, compression usually refers to processes such as chunking spatially and temporally distributed activity patterns. We take the complementary approach and optimize the synaptic network by structural plasticity, e.g., replacing unused synapses, thereby making full use of the potential connectivity [2].

We apply the frameworks of structural plasticity and hippocampus-induced learning to the training of neocortical associative networks [3]. Associative networks such as the Hopfield or Willshaw model are at the heart of many cortex theories and have been analyzed for a long time with respect to information storage capacity and plausible retrieval strategies [3, 4]. For example, it is well known that a completely connected network can store about 0.7 bits per synapse. However, for incompletely connected networks the capacity per synapse can be massively reduced or even vanish, depending on the retrieval algorithm [4]. In this work we analyze how structural processes and synaptic consolidation [5] during hippocampal training can improve the performance of neocortical associative networks by emulating full (or increased) synaptic connectivity. In our model the hippocampus can store a set of activity patterns by one-shot learning. Then the hippocampus trains the neocortex by repeatedly replaying the patterns in a sequence. The synapses of the neocortical network are consolidated depending on Hebbian learning. In each time step a fraction of the unconsolidated synapses are removed and replaced by the same number of new synapses at random locations thereby maintaining total connectivity. We show that this procedure can massively increase the synaptic capacity of a cortical macrocolumn (factor 10–20 or even up to factor 200 for pattern capacity). In a second step we analyze the model with respect to the time (or

number of repetitions) necessary to increase effective connectivity from base level to a desired level. The analysis shows that acceptable training time requires a certain fraction of unconsolidated synapses to keep the network plastic.

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#### S15

##### **Solving the distal reward problem through linkage of STDP and dopamine signaling**

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Learning the associations between cues and rewards (classical or Pavlovian conditioning) or between cues, actions, and rewards (instrumental or operant conditioning) involves reinforcement of neuronal activity by rewards or punishments. Typically, the reward comes seconds after reward-predicting cues or reward-triggering actions, creating an explanatory conundrum known in the behavioral literature as the *distal reward problem* and in the reinforcement learning literature as the *credit assignment problem*. Indeed, how does the animal know which of the many cues and actions preceding the reward should be credited for the reward? In neural terms, in which sensory cues and motor actions correspond to neuronal firings, *how does the brain know what firing patterns, out of an unlimited repertoire of all possible patterns, are responsible for the reward if the patterns are no longer there when the reward arrives?* How does it know which spikes of which neurons result in the reward if many neurons fire during the waiting period to the reward? Finally, how does the common reinforcement signal in the form of the neuromodulator dopamine (DA) influence the right synapses at the right time, if DA is released globally to many synapses? Here, I show how the credit assignment problem could be solved in a network of cortical spiking neurons with DA-modulated plasticity.

The model is based on the experimental findings that DA modulates synaptic plasticity by enhancing long-term potentiation (LTP) and long-term depression (LTD): For example, in hippocampus, dopamine D1 receptor agonists enhance tetanus-induced LTP, but the effect disappears if the agonist arrives at the synapses 15–25 seconds after the tetanus, thereby suggesting the existence of a short window of opportunity for the enhancement. My major hypothesis is that DA acts the same way on the spike-timing dependent synaptic plasticity (STDP). That is, a particular order of firing induces a synaptic change (positive or negative), which is enhanced if extracellular DA is present during the critical window of a few seconds.



I show that DA modulation of STDP has a built-in property of instrumental conditioning: It can reinforce firing patterns occurring on a millisecond time scale even when they are followed by rewards that are delayed by seconds. This property relies on the existence of slow synaptic processes that act as “synaptic eligibility traces” or “synaptic tags”. These processes are triggered by nearly-coincident spiking patterns, but due to a short temporal window of STDP, they are not affected by random firing during the waiting period to the reward. This “insensitivity” of the synaptic tags to the random ongoing activity during the waiting period is the key feature that distinguishes my approach from previous studies, which require that the network be quiet during the waiting period or that the patterns are preserved as a sustained response. I also discuss why *this mechanism works only when precise firing patterns are embedded into the sea of noise* and why it fails in the mean firing rate models. I also present a spiking network implementation of the most important aspect of the temporal difference (TD) reinforcement learning rule – the shift of reward-triggered release of DA from unconditional stimuli to reward-predicting conditional stimuli.

This study emphasizes the importance of precise firing patterns in brain dynamics and suggests how a global diffusive reinforcement signal in the form of DA can selectively influence the right synapses at the right time. The model provides a testable prediction on the action of DA on STDP, which will be tested by G. Bi (Pittsburgh University) and R. Froemke (UCSF) (personal communications).

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#### S16

##### **Spike timing dependent plasticity implements reinforcement learning**

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An explanatory model is developed to show how synaptic learning mechanisms modeled through spike-timing dependent plasticity (STDP) can result in longer term adaptations consistent with reinforcement learning models. In particular, the reinforcement learning model known as temporal difference (TD) learning has been used to model neuronal behavior in the orbitofrontal cortex (OFC) and ventral tegmental area (VTA) of macaque monkey during reinforcement learning. While some research has observed, empirically, a connection between STDP and TD there is as yet no explanatory model directly connecting TD to STDP. Through analysis of the STDP rule, the connection between STDP and TD is explained. We further show that an STDP learning rule drives the spike probability of reward predicting neurons to a stable equilibrium. The equilibrium solution has an increasing slope where the steepness of the slope predicts the probability of the reward. This connection

begins to shed light into more recent data gathered from VTA and OFC which are not well modeled by TD. We suggest that STDP provides the underlying mechanism for explaining reinforcement learning and other higher level perceptual and cognitive function.

#### S17

##### **Supervision of motor cortex by basal ganglia**

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Each somatic motor cortical area receives input from non-motor cortical areas and from the basal ganglia. Each area projects to all of the other areas, and each area also projects directly to the spinal cord. There is a limited understanding of how these different motor areas interact, and how mappings from cognitive goals to coordinated motor behaviour are established. The role of the basal ganglia afferents is also enigmatic. While the basal ganglia sometimes have a profound influence on movement, the ablation of their output nuclei does not cause striking motor symptoms. We present the hypothesis that the basal ganglia obtain rough sketches of effective motor patterns via reinforcement learning, and that they subsequently drive the cortex in these patterns, such that the patterns are gradually transferred to the cortex via supervised learning. Such a transfer mechanism may account for a number of phenomena including: 1) the way in which activity migrates between structures as expertise develops in some motor tasks; 2) the subtlety of motor symptoms following ablation of basal ganglia output nuclei (as opposed to the striking motor symptoms of basal ganglia diseases); and 3) changes in motor cortical maps in Parkinson's disease. The feasibility of this mechanism is tested with a cortico-basal ganglia model. The model produces appropriate motor patterns given sensory and goal-related inputs, and produces progressively more sophisticated patterns of movement as it matures. On the basis of this model, we predict that patients should have difficulty learning novel, complex movement patterns following ablation of basal ganglia output nuclei.

#### S18

##### **Invited talk: The role of spontaneous activity in sensory processing**

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Spontaneous, background activity in sensory areas is often similar in both magnitude and form to evoked responses. Embedding responses evoked by sensory stimuli in such strong and complex background activity seems like a confusing way to represent information about the outside world. However, modeling studies indicate that, contrary to intuition, information about sensory stimuli may be better conveyed by a network displaying chaotic background activity than in a network without spontaneous activity.

**S19****Activity-homeostasis preserves synaptic plasticity in Purkinje cell but calcium is not the activity-sensor**Pablo Achard<sup>1</sup> and Erik De Schutter<sup>1,2</sup><sup>1</sup>Theoretical Neurobiology, University of Antwerp, Belgium<sup>2</sup>Computational Neuroscience Unit, Okinawa Institute of Science and Technology, Onna-Son, JapanE-mail: [pablo@tnb.ua.ac.be](mailto:pablo@tnb.ua.ac.be)

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Activity homeostasis designates bio-mechanisms that regulate the activity of a neuron through the dynamic expression of ion channels or synapses [1]. We have recently shown [2] that it is possible to reproduce the complex activity of a Purkinje cell (PC) with very different combinations of ionic channel maximum conductances. However, if the global effect of homeostasis is starting to be understood, the detail of its machinery remains unknown. Some models [3, 4] have hypothesized that one such mechanism could work via the regulation of the average cytoplasmic calcium concentration. While this hypothesis is attractive for rhythm generating neurons, it raises many questions for PCs since in these neurons calcium is supposed to play a very important role in long-term memory [5]. To address this question, we generate 81 PC models, all having a similar electrophysiological activity and all different enough from each other in their conductance set. We demonstrate that, while the somatic membrane voltage is stable during complex spikes, the somatic calcium behavior is very variable from cell to cell, in agreement with experimental results [6]. Therefore calcium is a weak candidate for being an activity-sensor in this cell. Conversely, we show that the calcium signal in the spiny dendrites is very robust. To further test whether long-term depression (LTD) mechanisms are preserved for these different models, we use a PC spine model of calcium signal transduction pathways [7]. In all our models, conjunctive parallel fibers-climbing fiber activation leads to a sustained calcium release from internal stores, hence LTD induction is preserved.

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**S20****Sensitivity analysis enables comparison of how realistic morphology and other intrinsic properties influence neuronal firing**Christina M Weaver<sup>1,2,3</sup>, Georgi Gamkrelidze<sup>2,3,4</sup>, Robert Baker<sup>4</sup> and Susan L Wearne<sup>1,2,3</sup><sup>1</sup>Laboratory of Biomathematics, Mount Sinai School of Medicine, New York, NY 10029, USA<sup>2</sup>Computational Neurobiology and Imaging Center, Mount Sinai School of Medicine, New York, NY 10029, USA<sup>3</sup>Department of Neuroscience, Mount Sinai School of Medicine, New York, NY 10029, USA<sup>4</sup>Department of Physiology and Neuroscience, New York University Medical School, New York, NY 10016, USAE-mail: [christina.weaver@mssm.edu](mailto:christina.weaver@mssm.edu)

BMC Neuroscience 2007, 8(Suppl 2):S20

Several studies have shown that dendritic morphology and spatial distributions of active ion channels contribute significantly to neuronal firing dynamics and signal processing, however the relative importance and interactions between these mechanisms are not well understood. Within computational models these intrinsic properties are represented by parameters with different units and magnitudes that interact nonlinearly to simulate experimentally observed behaviors. Mathematical sensitivity analysis provides a tool to assess how strongly these parameters influence model output. For a given model neuron, the normalized sensitivity coefficient ('sensitivity') of its output to a particular parameter describes the percentage change in its output for a one percent increase in that parameter. The sensitivity magnitude indicates how much the measured output changes under the perturbation, while its sign indicates whether the output increases or decreases. One such sensitivity can be computed to each parameter; its sign and magnitude may vary for models represented by different points in a space defined by morphologic, active membrane, and passive cable parameters.

We perform this sensitivity analysis on a compartmental model comprising a soma and cylindrical active dendrite, with output measured by firing rates under current injections and by firing rate gain. Across the parameter space, sensitivity of these output variables to perturbations of dendritic length, diameter and surface area was compared with sensitivity to active and passive conductance parameters. For spontaneous firing rate, sensitivity increased most with increasing levels of persistent sodium and A-type potassium conductance, whereas for gain, sensitivity increased most as high-threshold calcium conductance decreased. Particularly in regions of space with slow calcium removal from the cytoplasm in the model cells, sensitivities of firing rates and gain to dendritic diameter and surface area were greater than to almost all active parameters. The sensitivity analysis was extended to a model neuron from the precerebellar nucleus Area II of goldfish. Area II neurons are necessary for eye velocity storage, a mechanism that displays persistent activity after extinguishing visual or vestibular stimuli. Parameter optimization identified sets of active and passive model parameters consistent with Area II electrophysiology for a morphology obtained *in vivo* and traced in 3D. Sensitivities to perturbations of dendritic length, diameter and surface area were

compared with those of active and passive parameters. These data indicate that, as in the simple model, there are regions of parameter space where dendritic morphology influences firing rate and gain more strongly than active conductances or passive cable parameters.

#### Acknowledgements

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#### S21

##### Specificity of synaptic connections formed during development of a functioning neuronal network

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When neuronal circuits develop, do cellular recognition processes ensure that only specific, "correct" synaptic connections form? To assess this question we have examined synaptic connections between neurons in the developing spinal cord of the hatchling frog tadpole when neuronal circuits for reflexes and swimming are functioning. We made electrical recordings from 500 pairs of neurons to determine synaptic contact probabilities between 7 different neuron types. Overall, the results from paired recordings reveal very widespread connectivity. Where evidence is available, neurons with dendrites receive synapses from all other neuron classes.

We then examined the anatomical distributions of the axons and dendrites of these 7 types of neuron, more precisely their dorsoventral positions. This allowed us to calculate the probabilities that axons would contact dendrites and therefore be able to form synaptic connections. When contact probabilities determined from anatomy were compared to synapse probabilities determined directly by electrical recording, the two were significantly correlated.

These results suggested that synapse formation may not depend on specific recognition between axons and "correct" dendrites. To test if rules based simply on contact probabilities could lead to functioning spinal networks, we made physiological models of spinal neurons, based on the Hodgkin-Huxley neuron model, and connected them using the contact probabilities we had determined. Networks created

in this fashion turned out to be quite reliable: the majority produced swimming. Purely random networks, with the same overall degree of connectivity, were much less successful in producing swimming, even when preserving the sensory pathway from the probabilistic rules. Simple rules controlling axon growth may determine the initial connections made as the nervous system develops. Our detailed analysis implies that cellular recognition to specify correct connections may be unnecessary for the formation of pioneer functional networks.

#### S22

##### Phase response curve analysis of a morphologically realistic globus pallidus neuron model reveals a distal dendritic mechanism for synchronization

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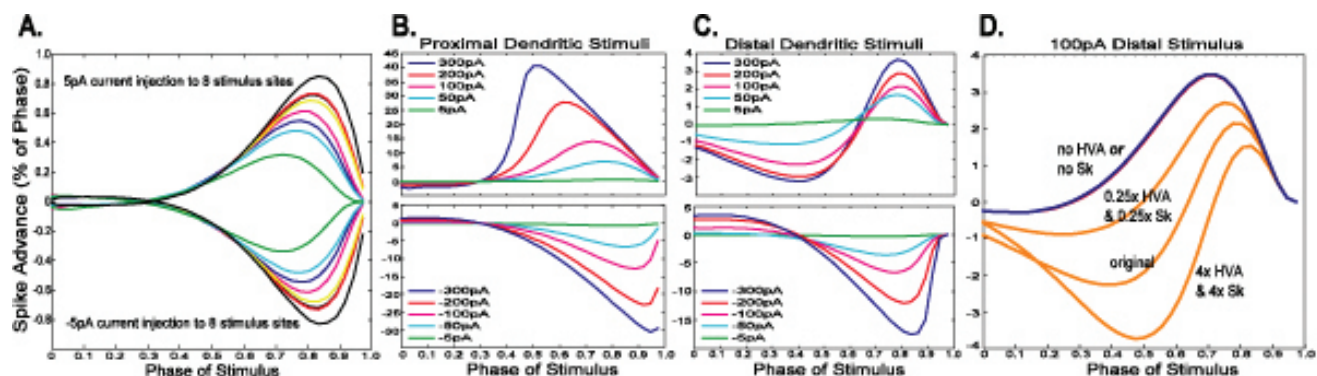
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**Background:** Phase-locked bursting and oscillations in low frequency bands between the subthalamic nucleus (STN) and the globus pallidus (GP) are key features of the pathophysiology of Parkinson's disease (PD). These dynamics may reflect susceptibility of the basal ganglia (BG) to entrainment with cortical oscillations or could also be a consequence of enhanced reciprocal STN-GP coupling under conditions of dopamine depletion.

Phase response analysis is an efficient method of characterizing the tendency of single neurons to entrain to periodic input, and to predict the tendency of connected networks to synchronize. A phase response curve (PRC) describes the dependency of shifts in spike timing that result from weak inputs on the timing of inputs within the ongoing inter-spike interval (ISI). If, independent of stimulus phase, a depolarizing input causes an advance of the next spike, the PRC will be composed purely of positive values (a Type I PRC). A Type II PRC contains both positive and negative regions, indicating that a depolarizing input can cause either an advance or delay of the next spike depending on when within the ISI it occurs. Type II PRCs favor synchronization in connected neuronal populations.

**Methods and results:** To investigate the phase response properties of GP neurons, we applied simulated current

Figure 1 (abstract S22)



Phase response curves. **A.** PRCs for weak stimuli. **B.** PRCs for proximal stimuli of different amplitudes. **C.** PRCs for distal stimuli of different amplitudes. **D.** PRCs for distal stimuli when HVA and/or SK have been varied.



injections and synaptic inputs to a morphologically realistic 585 compartment GP neuron model containing 9 voltage-gated conductances. Stimuli were delivered to one of seven dendritic locations or the soma to determine whether the input site affects significantly the shape of resultant PRCs. When inputs were small ( $\pm 5$  pA current injections or equivalent synaptic strengths) PRCs from all eight locations were Type I, and excitatory and inhibitory PRCs were symmetric across zero. (Fig. 1A.) More distal stimulus locations yielded PRCs with increasingly attenuated and left-shifted peaks.

For distal dendritic sites, larger excitatory stimuli resulted in Type II PRCs. (Fig. 1C.) To uncover the mechanism of this stimulus-amplitude-dependent transition between Type I and Type II PRCs, we analyzed differences in distal dendritic currents between control and stimulated conditions. We found that larger stimuli caused increased outward  $K^+$  flow through the  $Ca^{++}$  activated SK channel, and hypothesized that large stimuli delivered to small distal compartments (with high input resistance) activate the high-voltage  $Ca^{++}$  channel (HVA) which in turn activates SK. When we locally up- or down-regulated HVA and SK in tandem, the degree of Type II character was correspondingly increased or decreased, and the complete removal of either HVA or SK from the dendrite yielded identical Type I PRCs. (Fig. 1D.)

**Conclusion:** Our findings confirm previous work demonstrating PRC attenuation and left-shifting when weak stimuli are applied at increasing distance from the soma. In addition, by using realistic synaptic input, and analyzing evoked active conductances in spatially distinct regions of a realistic model, we characterize a mechanism in distal dendrites for Type II phase response dynamics. As network synchronization is observed in PD but not normal conditions, our findings suggest the hypothesis that GP neurons in PD may receive enhanced distal dendritic excitation and/or show an upregulation of SK conductance.

## S23

### Reconciling models of surround modulation and V1 feature map development

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The cerebral cortex of mammals is organized as a set of topographic maps, forming sensory and motor areas such as those in the visual, auditory, and somatosensory systems. Understanding how these maps develop and whether they have any functional significance is critical for understanding cortical processing.

The prototypical example of topographic feature maps is the map of orientation preference in primary visual cortex (V1). Models of V1 orientation map development have been very successful in reproducing the features of biological maps. The majority of these models are based on a principle of "Mexican-hat" connectivity i.e. short-range excitatory and long-range inhibitory connections between neurons (e.g. [1]).

However, experimental data is in striking disagreement with this principle. There is a consensus that long-range connections between V1 neurons are excitatory [2]. Moreover, models with

long-range excitatory connections are able to account for a wide range of experimental data from adult V1, such as surround modulation (e.g. [3]). Models of orientation map development are thus based on a connectivity which is precisely opposite to that suggested by a mounting body of experimental and computational evidence.

It is not yet clear if the circuits used in surround modulation models are consistent with the development of orientation maps. It is also important to consider how the topographic organization of orientation preference may affect surround modulation. Since cortical circuitry is intimately tied to topographic organization, it is likely that surround modulation properties differ depending on the position of a cell within the orientation map.

In order to address the above issues, we have developed the first model that is consistent with current models of surround modulation, yet also reproduces the features of successful developmental models of topographic map formation. The model consists of sheets of firing-rate-based units that represent the retina, LGN, excitatory, and inhibitory neurons in V1. An activity-driven Hebbian learning mechanism results in the adjustment of afferent (retina to V1) and long-range lateral connection weights (within V1), leading to the development of orientation selectivity organized smoothly in a realistic orientation map.

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## S24

### Modeling self-organizing tri-chromatic color selective regions in primary visual cortex

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How does the brain represent and process color in the primary visual cortex (V1)? Experimental evidence from macaque monkey suggests that cells selective for color are organized into small, spatially separated blobs in V1. This organization is strikingly different from that of orientation and ocular dominance maps, which consist of large, spatially contiguous patterns.

In this paper, a self-organizing tri-chromatic model of V1 is constructed using natural color image input. Neurons in the modeled V1 are initially unselective, and develop multi-lobed



ON/OFF receptive fields through Hebbian learning of retinal responses to visual patterns. The model develops realistic color-selective receptive fields, color maps, ocular dominance columns, and orientation maps. Color-selective blobs are located inside ocular dominance columns, and lateral connections link cells with similar orientation preferences, matching previous experimental results. Further, the model makes a number of predictions for future experiments, including:

1. The color map has three types of color-selective blobs and a unique cortical activation pattern exists for each of the pure color hues.
2. The usual blob-like organization for color emerges as long as the training images have a higher brightness contour gradient compared to the hue contour gradient, and the inputs are highly correlated between the eyes. Otherwise the color blobs regularly extend across borders of ocular dominance stripes (contrary to macaque results).
3. Neurons in areas where red and green patches are near each other respond to both red and green, causing them to maximally prefer yellow, even though there are no yellow photoreceptors in the retina.
4. Cells selective for color connect to other cells with similar chromatic preferences: Blue-selective neurons connect to blue selective neurons, red-selective to other red-selective neurons, and so forth.

Thus the model replicates the known data on the organization of color selectivity in V1, gives a detailed explanation for how this structure develops and functions, and provides concrete predictions that can be tested in future experiments. These findings suggest that a single self-organizing system may underlie the development of orientation selectivity, eye preference, color selectivity, and lateral connectivity in the primary visual cortex.

## S25

### A neurocomputational model of temporal processing: evidence from sequence experiments

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Our world changes both in space and time, and our brain faces the challenge to cope with these changes in both dimensions. While substantial progress has been made on the way to understanding the neural substrate of e.g., spatial vision or sound localization, "the field of temporal processing is still at its infancy" [1]. There are many models of the neural substrate of this ability, but it is not easy to decide which model to use based on purely neuronal data. Psychophysical research on temporal processing makes it possible to formulate constraints on neuronal models.

We conducted a series of human experiments to study temporal variability under various conditions. Participants were presented with a sequence of identical intervals, containing a single interval which differed from the others by a small amount  $X$  at a random position. After the presentation, they had to judge the sequence

as an even or an uneven rhythm. The minimal value of  $X$  for which the sequence was reliably judged as "uneven" was used as a measure for temporal variability. We found that this measure varies considerably with its position in the sequence. Thus, we could rule out a class of models that do not predict an adaptation effect. Furthermore, the mean threshold increases with the duration of the standard intervals, consistent with former results. In a subsequent experiment, we could show that variability does not depend on the total length of the sequence. This implies that the sequence is not processed as a whole and that effects of interval duration and sequence context can be separated into different processing stages.

We propose a computational model for the first stage. While it was long believed that timing errors increase linearly with the interval to be processed (Weber's law) [2], recent experiments show that for longer and shorter intervals, deviations from linearity occur [3]. Our model provides an explanation for both Weber's law and its deviations. It consists of a group of synfire chains, layered networks that are able to transmit a wave of neural activity through its layers with high temporal precision. These networks are able to convert temporal information into a quasi-spatial code. In a single chain, timing errors increase only with the square root of the interval length. We show that the experimentally observed error course results as the optimal solution from competition among several synfire chains with different transmission speeds.

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## S26

### Stimulus encoding and correlates with behavior in area MT of visual cortex is dependent on spike phase

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How is the activity of neurons in the sensory areas of cortex related to our perceptual abilities? Past studies have suggested that sensory neurons that best encode a visual stimulus are also more influential in forming the perception of the stimulus. We wanted to know if this relationship also extended to individual action potentials. If some spikes encode the stimulus better than others, then would these same spikes have more weight in supporting the perceptual behavior?

To address this question, data from a past motion detection experiment was analyzed [1]. In this study, two monkeys were trained to detect the onset of coherent motion in a random dot patch that initially contained 0% coherent motion. The coherent motion signal occurred at a random time and the animals were rewarded for responding within a 750 ms window. Extracellular recordings were made from single neurons in the Middle Temporal (MT) area. The random dot patch overlapped the

receptive field of the neuron and the coherent motion was matched to the neuron's preferred direction and speed. Importantly, the position of the random dots was only updated once every 27 ms. Because of the slow motion update rate, the neural activity of many of the MT neurons oscillated at the same frequency as the motion updates. It was these oscillations that allowed us to ask if some spikes were more influential than others by measuring how sensory and choice related information varied as a function of the phase of the oscillation. To determine whether some spikes encoded the stimulus better than others, we examined the difference between spikes on the rising phase of the oscillation (from the trough to the peak) compared to spikes on the falling phase (peak to trough). Using the spike-triggered average of the motion stimulus, we found that spikes did not equally represent sensory information. Spikes occurring during the rising phase of the stimulus-induced oscillation encoded stronger motion than spikes occurring during the falling phase. Importantly, the same spikes that encoded stronger motion were also more correlated with the animal's behavioral performance and reaction time. This suggests that the spikes carrying the most reliable task related information are more strongly linked to the behavioral decision. In addition, these results support the hypothesis that phase could be used as a possible encoding scheme during neuronal oscillations.

#### Acknowledgements

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## POSTER PRESENTATIONS

### P1

**Using NeuroML and neuroConstruct to build neuronal network models for multiple simulators**  
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Increased use of biologically detailed cellular and network models by the wider neuroscience community is hampered by the variety of simulation platforms and programming languages used to create these models. While experimentalists and theoreticians share common concepts for describing these physiological phenomena a framework for specifying models is not in common use. The Neural Open Markup Language project, NeuroML [1, 2] <http://www.neuroml.org>, is an international, collaborative initiative to develop standards to facilitate exchange and encourage greater accessibility of models of neuronal systems.

The standards, which are specified in XML (eXtensible Markup Language), are arranged in Levels, with each subsequent Level increasing the scope of the standards. Level 1 concentrates on

neuroanatomical information (MorphML [2, 3]) and metadata. Level 2 allows for the specification of detailed conductance based cell models with realistic channel and synaptic mechanisms specified in ChannelML. Level 3 (NetworkML) describes networks of these cells arranged and connected in three dimensions.

One application which uses these standards is neuroConstruct, which has a graphical interface for building and visualizing detailed 3D network models. neuroConstruct allows the automatic generation of script files for the GENESIS and NEURON simulators, and can be used for replaying and analyzing simulated cell and network behavior. Examples of cell and network models from multiple brain areas will be demonstrated on these two simulators, as will a preliminary implementation of automatic generation of scripts for execution in parallel computing environments.

The combination of these technologies allows the development of more detailed large scale neuronal network models while managing the huge complexity associated with these systems. The latest version of the NeuroML specifications is available at <http://www.morphml.org:8080/NeuroMLValidator> and neuroConstruct is freely available by contacting: [p.gleeson@ucl.ac.uk](mailto:p.gleeson@ucl.ac.uk).

#### Acknowledgements

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### P2

**PyNN: towards a universal neural simulator API in Python**

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Trends in programming language development and adoption point to Python as the high-level systems integration language of choice. Python leverages a vast developer-base external to the neuroscience community, and promises leaps in simulation complexity and maintainability to any neural simulator that adopts it. PyNN <http://pynn.gforge.inria.fr/> strives to provide a uniform application programming interface (API) across neural simulators. Presently NEURON and NEST are supported, and

support for other simulators and neuromorphic VLSI hardware is under development.

With PyNN it is possible to write a simulation script once and run it without modification on any supported simulator. It is also possible to write a script that uses capabilities specific to a single simulator. While this sacrifices simulator-independence, it adds flexibility, and can be a useful step in porting models between simulators. The design goals of PyNN include allowing access to low-level details of a simulation where necessary, while providing the capability to model at a high level of abstraction, with concomitant gains in development speed and simulation maintainability.

Another of our aims with PyNN is to increase the productivity of neuroscience modeling, by making it faster to develop models *de novo*, by promoting code sharing and reuse across simulator communities, and by making it much easier to debug, test and validate simulations by running them on more than one simulator. Modelers would then become free to devote more software development effort to innovation, building on the simulator core with new tools such as network topology databases, stimulus programming, analysis and visualization tools, and simulation accounting. The resulting, community-developed 'meta-simulator' system would then represent a powerful tool for overcoming the so-called *complexity bottleneck* that is presently a major roadblock for neural modeling.

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### P3

#### Modeling a single dendritic compartment using Neurospaces and GENESIS-3

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**Modeling a single dendritic compartment:** The standard technical approach to realistic modeling of single neurons involves dividing the cell and especially its dendrites into a series of compartments assumed to be effectively isopotential. During simulation a single membrane voltage is calculated for each of these compartments. Recent cerebellar network and Purkinje cell single cell modeling efforts in our laboratory have suggested, however, that membrane dynamics may depend on a finer level of control of membrane voltage within the dendrite [1]. Accordingly, we have now identified the precise dendritic geometries and positions of excitatory and inhibitory synapses using serial electron microscopy. This paper describes our efforts to construct an electrical/chemical model of the resulting fully reconstructed segments ranging from 5 to 10 microns in length.

**Technical challenges:** Modeling these small dendritic segments realistically poses several technical challenges. Beyond issues of how to represent space, the project is also inherently multiscale, as the behavior of segments must be interpreted in the context of the larger compartmental simulation of the dendrite, and second, at a finer scale, molecular and cellular processes (Ca diffusion for example), also come into play.

**Completing the software tool chain:** This project is being undertaken in the context of two ongoing computational software development projects, the GENESIS 3.0 project and Neurospaces. GENESIS 3.0 is a major redevelopment effort focused on the development of a state of the art Graphical User Interface and Database structure for the GENESIS project. The Neurospaces project <http://www.neurospaces.org> involves the development and elaboration of a new open, modular framework for essential tools used in computational simulations in biology, and defines the hooks required for collaborative software components, that work on the same modeling project. This poster will describe the latest tools of the Neurospaces project in the context of our efforts to simulate small segments of the Purkinje cell dendrite. As an example, we have developed algorithms to slice the volume obtained from serial EM into small cylinders intended for simulation. The cylinders can be visualized, validated and compared with the original volume. The compartmental solver Heccer, also part of the Neurospaces project, simulates the model, using the spatial and temporal precision appropriate for these fine scale models.

**Conclusion:** The tools developed in the context of this project, give a detailed insight in the level of control of inhibition and excitation on membrane dynamics in a small dendritic segment of a Purkinje cell. Additionally, in the context of larger compartmental simulations of the entire dendritic tree, the interpretation of the effect of these dynamics on dendritic signal processing is likely to have important functional consequences for the regulation of dendritic dynamics in the Purkinje cell.

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### P4

#### The GENESIS 3.0 Project: a universal graphical user interface and database for research, collaboration, and education in computational neuroscience

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**Background:** The General Neural Simulation System (GENESIS) was first released for general use in 1988 as part of the first Methods in Computational Neuroscience Meeting at the Marine Biological Laboratory in Woods Hole, Mass. Since its release 19 years ago, GENESIS has provided one of the foundations for the ongoing course in Woods Hole, as well as courses offered by the European Union, courses in Mexico, Brazil, and India and soon in Japan. At last count GENESIS has also provided support for courses in at least 49 universities around the world where it has been used both as an instruction tool in realistic modeling of the nervous system, and as a simulation based tool for neurobiological education in general. The Book of GENESIS [1], which was designed to support both computational and

neurobiological instruction has sold more than 6000 copies worldwide. This substantial support for the use of GENESIS in instruction has also provided the base for extensive and growing use of this software system in biological research providing the foundation for literally hundreds of peer reviewed scientific papers.

From the outset, the design of GENESIS has been premised on the assumption that advancement in understanding neural function requires the ability to build computer models based on the actual anatomy and physiology of the nervous system itself [2]. GENESIS was the first broad scale modeling system in computational biology to encourage modelers to continue to develop and share model features and components. At the same time, the GENESIS project was involved in proposed technological standardization efforts for testing simulation performance and sharing of neuronal models (the Rall packs and NeuroML).

**GENESIS 3.0 and the future:** With the growing interest and involvement of both neurobiologists and technologists in computational neuroscience, it became clear a number of years ago that it made sense to restructure and reshape the GENESIS simulator project. While version 1 of GENESIS and the upgraded version 2 were both self contained modeling systems, the decision has been made to compartmentalize the software architecture in order to ease external contributions, and even more importantly, for enhanced interfacing capabilities with other neuroscience software tools and databases. The technical motivation for this decision is easily appreciated in the context of recent general advancements in gluing languages (e.g. Swig and Python) and interfacing languages (e.g. SOAP), as well as the level of maturity of model exchange languages (e.g. NeuroML), and meta data exchange formats (e.g. BrainML).

More specifically, the CBI (Computational Biology Initiative) simulator architecture, recently developed in our lab as the context for GENESIS 3.0 development, is an open framework that provides a general and necessary context for the GENESIS project to proceed. It will also allow the project to focus on the user needs to conceive, organize, execute, and evaluate simulations, as well as on the development of new tools to support simulation based education, collaboration, and publication. By doing so, GENESIS 3.0 will no longer include parsers, script interpreters, run time schedulers, numerical engines, or other components necessary to actually run simulations. Instead, GENESIS 3.0 is being developed with the necessary interfaces that will, in principle, allow any simulation system to use its features. At present GENESIS 3.0 is being developed in collaboration with two simulation tool development projects, "MOOSE" under development by Upinder Bhalla in Bangalore India, and "Neurospaces" under development by Hugo Cornelis in San Antonio, Texas. This poster will describe both the GENESIS 3 project, the overall structure of the CBI framework, and how these efforts support both the development of MOOSE (by Dr. Bhalla), and Neurospaces (by Dr. Cornelis).

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#### P5

#### Neurofitter: a parameter tuning package for a wide range of electrophysiological neuron models

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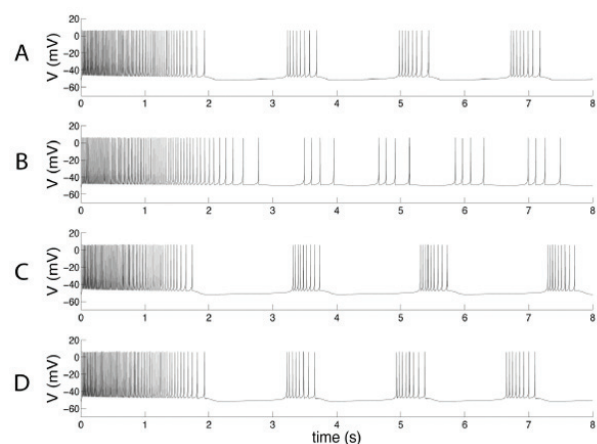
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One of the major tasks of a neuroscientist who is developing a neuron model is to find suitable values for all the parameters of the model. This is, in general, a very complex job that can take a lot of time and that requires a lot of know-how when the parameter tuning is done by hand. We have developed a software tool called Neurofitter that can be used to automate the process of parameter searching for neuron models. The user has to provide time series data recorded during an experiment in the form of traces. Neurofitter will then run the computer model several times with different sets of values for the model parameters and will compare model output traces with the experimental data traces using the phase-plane trajectory method [1]. This way Neurofitter maps every set of parameters values onto a fitness value that shows how well a model is able to reproduce the experimental data. This transforms the search for optimal parameters into a problem that can be solved with general optimization algorithms. The algorithms used by Neurofitter include Evolutionary Strategies, Particle Swarm Optimization and Mesh Adaptive Search. We will show some results obtained using the method to fit a single compartmental

Figure 1 (abstract P5)



**Voltage traces showing output of a simple single-compartmental model of a rhythm generating neuron in the pre-Bötzinger complex [3]. A.** Reference traces used to fit the model to. **B.** A trace showing the output generated by increasing the persistent sodium current conductance by only 20% compared to the original data. **C.** Result obtained after automatic parameter fitting using Evolutionary Strategies **D.** Result found by a Mesh Adaptive Search that started with the best result obtained using Evolutionary Strategies.



model, a simple network model and a complicated model of a Purkinje cell [2]. The source code can be freely downloaded from Sourceforge <http://neurofitter.sourceforge.net>

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#### P6

##### Fully implicit parallel simulation of single neurons

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When tree topology matrices are divided into subtrees where each subtree is on a different cpu and with the constraint that other subtrees are not connected to a given subtree at more than two distinct points (defining a backbone path on that subtree), the entire system remains amenable to direct gaussian elimination. The complexity increase is twice the number of divisions and four times the number of multiplications normally required along the backbones due to the necessity, during the triangularization phase, of transforming the tridiagonal backbone into an N topology matrix. In addition, each subtree is required to send its root diagonal and right hand side element, or, in the case of a subtree with a backbone, the  $2 \times 2$  matrix and right hand sides of the backbone end points, to one of the cpus where that information is added together to form a reduced tree matrix of rank equal to the number of split points on the cell. The reduced tree matrix equation is solved, giving the voltages at the split points, and this information is sent back to the appropriate subtrees on the other cpus. Those subtrees with backbones can then use the N topology to quickly compute the voltages along the backbone and everyone can complete the back substitution phase of their gaussian elimination. Accuracy is the same as with standard gaussian elimination on a single cpu and any quantitative differences are attributed to accumulated round off error due to different ordering of subtrees containing backbones.

With this method, it is often feasible to divide a 3-d reconstructed neuron model into a dozen or so pieces and experience almost linear speedup. We have used the method for purposes of load balance in network simulations when some cells are very much larger than the average cell and there are more cpus than cells. The method is available in the current standard distribution of the NEURON simulation environment.

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#### P7

##### Just-in-time connectivity for very large neuronal networks

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Memory storage remains a limitation when running very large neuronal networks (VLNN). With number of neurons  $n$ , connectivity storage grows as  $n^2$ . With connectivity densities of 0.1–10%,  $1e6$  neurons will require  $1e9$ – $1e11$  synapses. A single connection requires at least an associated weight and delay as well as additional pointers or offsets to store the connectivity matrix. Conservatively, this will require 10 bytes (e.g., 2 floats and 2 chars) which will then bring the total synaptic memory load to 10 GB–1 TB. The former value may be barely executable on a single large machine.

We have exploited an algorithmic space-time trade-off to build large event-driven artificial-cell simulations in the NEURON simulator by utilizing just-in-time connections (JITCONs) that are generated at the time of presynaptic cell spiking. JITCON utilizes a presynaptic-cell-specific random-number-generator seed based on presynaptic-cell serial number that permits it to generate a list of postsynaptic cell targets on the fly, and seeds based on a multiple of presynaptic-cell and postsynaptic-cell serial numbers for generating weights.

We have utilized the JITCON algorithm to readily run simulations of  $>2e6$  neurons. These simulations include a moderate level of cellular detail with AMPA, NMDA, GABA<sub>A</sub> and GABA<sub>B</sub> synapses, as well as multiple intrinsic properties such as bursting, depolarization blockade and an afterhyperpolarizing “channel.” Note that these are event-driven simulations and therefore do not utilize continuously integrated compartmental neurons. Since these simulations are event-driven, there is no overhead unless there is activity: simulation time varies widely depending on the level of network activity. An active network of  $1.2e5$  cells with  $>8.9e6$  synapses, generating  $>1.1e7$  spikes in 1 s simulation time, took 32.3 minutes to run on a 2.4 GHz AMD Opteron processor. Large, active simulations still develop space problems due to the need for a variable-size queue to accommodate varying delivery delays. This limitation is minimized by restrictions on the range and variability of permitted delays. We have begun to explore algorithms that permit a nuanced approach to the space-time trade-off. We permit individual presynaptic cells to store their list of postsynaptic targets in a compressed format. This additional storage can be turned on or off on a per-cell basis. We will explore making this storage dynamic so that a cell can maintain its connectivity list during a period of high activity and then return the memory when its activity is reduced. An additional direction for future development will be the incorporation of an entire encapsulated artificial-cell network as an independent piece of a compiled code (a mod file in NEURON). Such a network module could then be plugged in to other network modules or to a more detailed network that used compartmental models or compartmental/artificial cell hybrids, running in the main NEURON simulator. Running such

simulations on parallel supercomputers will permit execution of very-VLNNs of order 100 million neurons.

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#### P8

##### Open source simulation of the pyloric network

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**Background:** The pyloric network (Figure 1) is part of the stomatogastric ganglion (STG) of crustaceans [1]. The network is a central pattern generator (CPG) that drives the muscles of the pylorus, which is a food filtering organ within the gastric system of these animals. The pyloric network is one of the most researched neural circuits and many details of it are known, including types and numbers of participating cells, connections between these cells, transmitters, receptors and neuron-modulators used by cells within the network [1]. Consequently, this network is an ideal candidate to develop detailed network simulations of neural systems.

Simulations of the pyloric network have been developed since the 1970s [1]. However, these simulations do not include many of the known details about the pyloric network, and produce a behaviour that resembles at high level the behaviour of the biological network, but ignores the behavioural details. These earlier simulations are also application specific, and cannot be easily modified and re-used by researchers.

**Methods and results:** We present here a new open source simulation of the pyloric network. The simulation is developed using the Neuron simulation language [2]. Each neuron is simulated using four compartments: soma, primary neurite, axon, dendrite. The primary neurite is connected to all three other compartments. The connections are implemented by linking the axon outputs of neurons to the corresponding dendrite inputs of other neurons. The effects of neuromodulation are implemented in form of changing characteristics of neural connections in response to changes in the values of a multi-dimensional modulation state

variable (i.e. each component of the vector indicates the presence and concentration of a neuromodulator, the components being labeled by the corresponding modulator). The values of parameters for the neural compartments are set using the STG neuron database developed by Prinz et al [3]. To determine the right setting of parameters for each cell type we used the simulator attached to STG neuron database [3] to check that the output of our model neurons matches the output of modeled neurons.

**Conclusion:** Our simulation is developed as open source software, allowing other users to download the source code and modify it. In this way other researchers may use this detailed simulation of the pyloric network to check experimental assumptions and also possibly to develop simulations of other related networks (e.g. gastric mill network).

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#### P9

##### Simulating large and heterogeneous networks of spiking neurons with SpiNet

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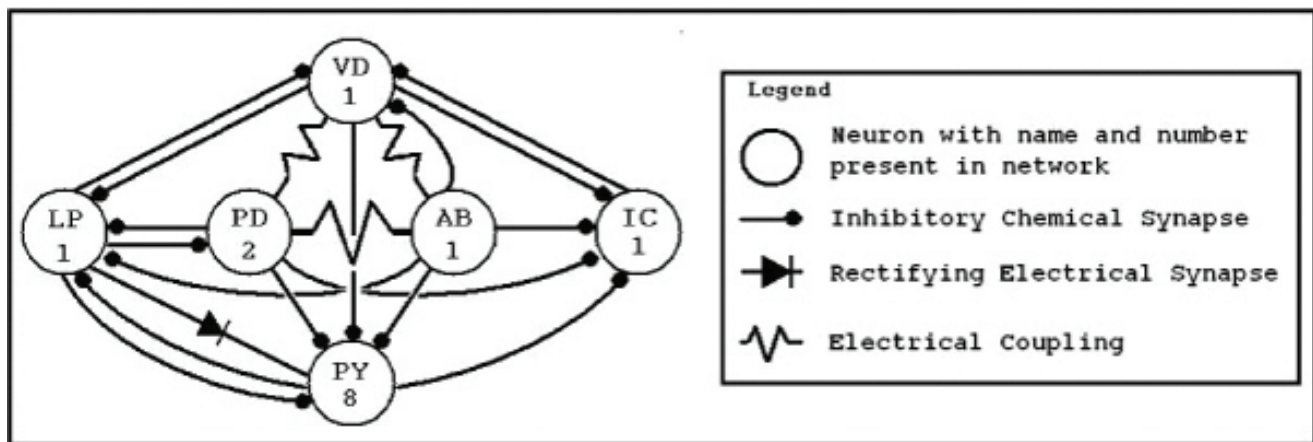
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SpiNet is a novel simulation environment for building and analyzing large networks of spiking neurons. Heterogeneous networks with complex architectures can be easily built and simulated without detailed knowledge of a particular programming language or script

Figure 1 (abstract P8)



A diagram of the pyloric network. The diagram shows the participating neurons, their numbers and the connections between these neurons.

language interpreter. SpiNet is composed of two components: a simulation engine, written in C programming language for performance purposes, and SpiNet network builder tool, or simply NetBuilder, written in Matlab for expansibility purposes. The NetBuilder tool provides a flexible and efficient graphical interface allowing the user to easily define and set all the main network model properties. The NetBuilder creates the network model files which can then be simulated with the simulation engine. Neurons are modeled as integrate-and-fire units with dual exponential synaptic conductances and the simulation engine uses a second order Runge-Kutta method with a linear interpolant to find spike times and recalibrate post-spike potentials. The engine is capable of handling a vast number of properties including dynamical synapses, long-term plasticity, stochastic activity, detailed 3-dimensional architecture, external stimuli, among others. SpiNet does not incorporate data analysis tools but provides several channels to export simulation results for off-line analysis by specialized data analysis software. An OpenGL graphical engine is integrated into the simulation environment providing visual information of the model dynamics. SpiNet is far from being as complete and feature rich as NEST, Neuron or Genesis, but has the benefit of facilitating the process of building and simulating heterogeneous network models: it is fast and easy to add new neuron populations, change connectivity properties or assign different types of synaptic plasticity without having to edit or write lines of code; all changes are done within NetBuilder GUI. SpiNet is therefore a valuable tool when analyzing large heterogeneous models where many modifications have to be done in order to better understand the contributions of the different functional components involved.

## P10

### Verifying the biological relevance of a neuromorphic hardware device

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BMC Neuroscience 2007, 8(Suppl 2):P10

**Background:** Within the FACETS research project, a neuromorphic mixed-signal VLSI device was created [1]. It was designed to exhibit a linear correspondence with an I&F neuron model, including synaptic plasticity and short-term synaptic dynamics. It operates with a speedup factor of around  $10^5$

compared to biological real time. Utilizing the existing prototype, networks of up to 384 neurons and the temporal evolution of the weights of  $10^5$  synapses under STDP can be modeled.

**Methods:** We developed a software framework which allows a unified access to both the hardware system and the pure software neuro-simulator NEST, providing the possibility to verify that the chip can be operated in a biologically realistic regime. From within a single software scope, we can compare and post-process results obtained from both systems, based on identical input and network setups.

**Results:** We present experiments that illustrate the status of hardware neuron model verification by comparing its dynamics to NEST simulations. Exemplarily, Figure 1 shows the linear correspondence between the hardware and the software neuron model.

**Conclusion:** To establish neuromorphic hardware as a valuable tool for neuroscience, its biological correctness has to be proven. We provide a tool for the direct comparison of a specific hardware system and a simulation software. Our experimental data illustrates the functionality of the hardware and shows its biological relevance. The resulting uniform software interface will allow modelers to port existing network models to the hardware system with minimal effort.

### Acknowledgements

This work is supported by the European Union under the grant no. IST-2005-15879 (FACETS).

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## P11

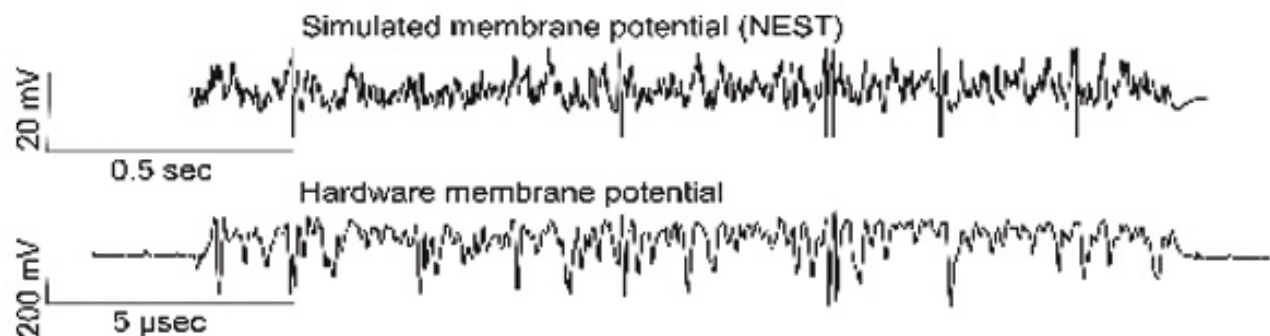
### NeuroBlast: a 3D spatial homology search tool for gene expression

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BMC Neuroscience 2007, 8(Suppl 2):P11

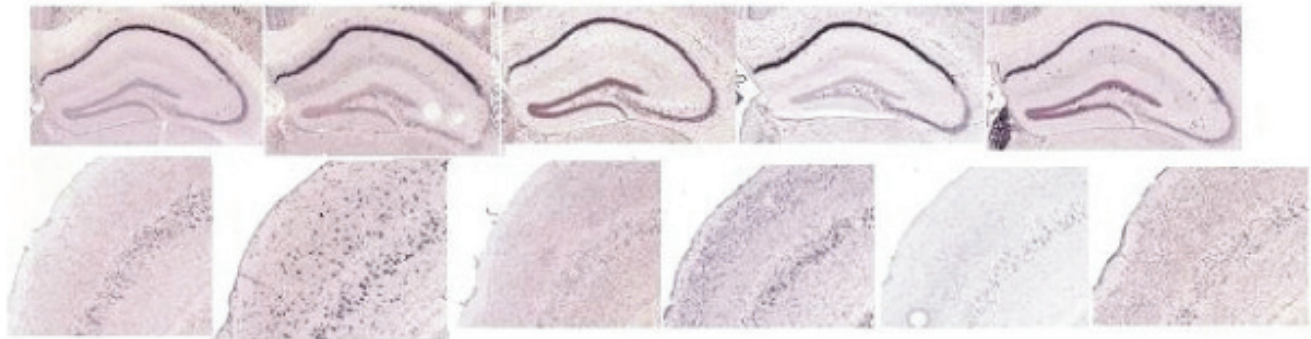
**Background:** Finding genes with a similar spatial expression pattern as a known gene could potentially reveal novel or

Figure 1 (abstract P10)



The membrane potentials of a single neuron under Poisson process input. The upper one has been simulated using NEST, the lower one is a digitization of the analog voltage trace of the neuromorphic hardware.



**Figure 1 (abstract P11)**

Search result examples.

unknown genes involved in similar processes or pathways. The Allen Brain Atlas (ABA) [1] is an effort to produce a genome-wide mapping of the gene expression in the adult C57BL/6J mouse brain. To date, more than 21,000 genes have been assayed using a high-throughput in situ hybridization (ISH) platform and the resulting image data is publicly available at <http://brain-map.org>. A major goal of the ABA project is to employ image analysis techniques to search the ABA data for particular expression patterns such as spatial gene expression homologues.

**Methods:** Each ISH image series is processed through an automated anatomic mapping pipeline with the goal of determining expression sites and the spatial localization of these sites with respect to a 3D reference brain. Expression statistics is then aggregated with respect to individual  $200\ \mu\text{m}^3$  cubes in reference space thereby reducing data complexity from  $> 2 \times 10^8$  pixels per series to  $\sim 2.5 \times 10^4$  cubes. Since every image series is spatially mapped with accurate registration to the same 3D reference space, we can compare expression statistics on a global scale in approximately the same  $200\ \mu\text{m}^3$  spatial extent for all series. The most straightforward approach to finding spatial homologues is to compute the similarity between  $200\ \mu\text{m}^3$  grid statistics of two genes. We conducted a pilot study computing the Pearson similarity score between every pair of over 4200 coronal series images. Two example searches are shown in Figure 1 with the initial seed gene shown in the left most panel: *Nov* (row 1) showing differential expression in CA1 of the hippocampus and *Etv1* (row 2) with enriched expression in layer 5.

**Conclusion:** We presented the functionality of NeuroBlast, a spatial search tool for finding genes with similar expression patterns within the ABA dataset. Preliminary testing of our pilot study has demonstrated efficacy of searches over different expression patterns and domain of interest. A comprehensive version of NeuroBlast spanning the entire ABA data will be publicly available in 2007.

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#### P12

##### **Role of the semi-lunar process in locust jumping**

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The biomechanical and neural components that underlie locust jumping have been extensively studied [1, 2, 3, 4]. Previous research suggested that energy for the jump is stored primarily in the extensor apodeme and in the semi-lunar process (SLP) [5], a thickened band of cuticle at the distal end of the tibia. As it has thus far proven impossible to experimentally alter the SLP without rendering a locust unable to jump, it has not been possible to test whether the energy stored in the SLP has a significant impact on the jump, or how that energy is applied during the jump.

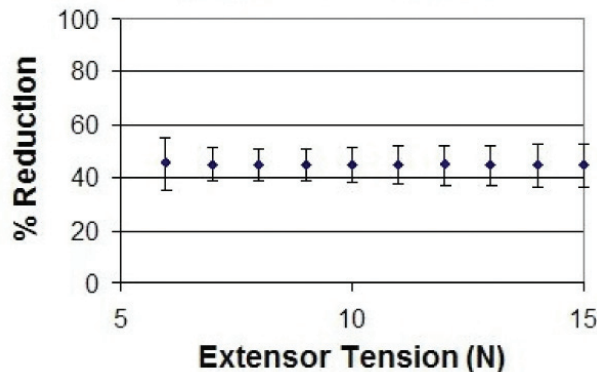
To address problems such as this we have developed a software toolkit, AnimatLab, which allows researchers to build and test virtual organisms. We used this software to build a virtual locust, and then asked how the SLP is utilized during jumping, and how manipulation or removal of the virtual SLP influences jump dynamics (figures 1 and 2). The results show that without the SLP the jump distance was reduced by almost half. Further, the simulations were also able to show that loss of the SLP had a significant impact on the final phase of the jump impulse which prevented the full extension of the tibia against the ground. Power for the jump during the initial phase was almost identical between the two cases, but without the SLP the power peaked early and there was a significant difference in the power for the late phase of the jump.

#### Acknowledgements

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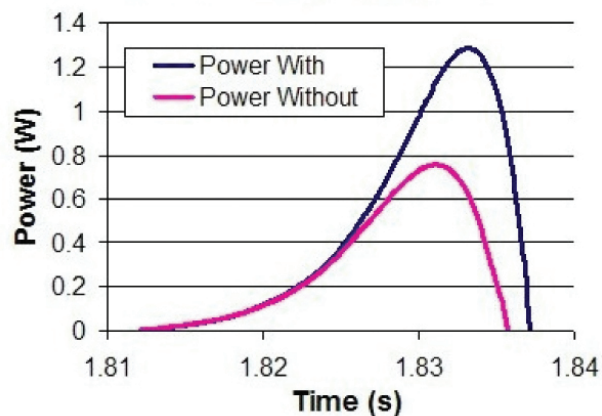


Figure 1 (abstract P12)



**Percentage reduction in jump distance without semilunar process.** Loss of the SLP reduced the distance jumped by approximately 45% across the entire range of extensor tensions tested. Each point is  $n = 20$ .

Figure 2 (abstract P12)



**Power during jump impulse.** The power during the early phase of the jump is almost identical, but without the SLP it peaks early and the power from the late phase of the jump is almost entirely missing. This has a significant impact on the jump distance.

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#### P13

##### **iBrain: a simulation and visualization tool for activation of brain areas on a realistic 3D brain image**

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**Introduction:** Many computer models have been developed to simulate a neuron, neural networks, and activation of brain areas aimed at the elucidation of mechanisms of brain functions. In this track there is one clear direction of modeling from a single cell to the whole brain [1]. We developed a simulation and visualization tool, “iBrain”, by which we could construct, simulate and visualize a model of the transition of brain activation on a realistic brain anatomical atlas.

**Methods:** The modeling and simulation parts were constructed by modifying the software tool for a biological cell, “A-Cell”. Users can construct a Brodmann area-level model through A-Cell like GUI. The simulation algorithm is the same as that in A-Cell. In the visualization part, an anatomical atlas of human brain was constructed from the data of “Talairach Daemon Client” superimposing them on the human brain MRI volume of “ICBM template” from LONI. This allows users to see the shape and position of various anatomical regions of the brain from mm to hemisphere resolution in the realistic 3D brain (Fig. 1). The activation patterns calculated in the simulation are visualized on this brain image.

**Results:** To test the simulator, we tried to reproduce the activation patterns of a human’s word processing which were measured by MEG (magneto-encephalogram). The reproduced patterns were roughly matched to the patterns from the experiment and we could see them visually on the iBrain.

**Conclusion:** Simulation and visualization of spatio-temporal activation of brain areas on a realistic 3D brain image can be realized by iBrain. We believe this software can help us to understand the brain function at macroscopic level.

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#### P14

##### **A large-scale neurocomputational model of emotional decision making**

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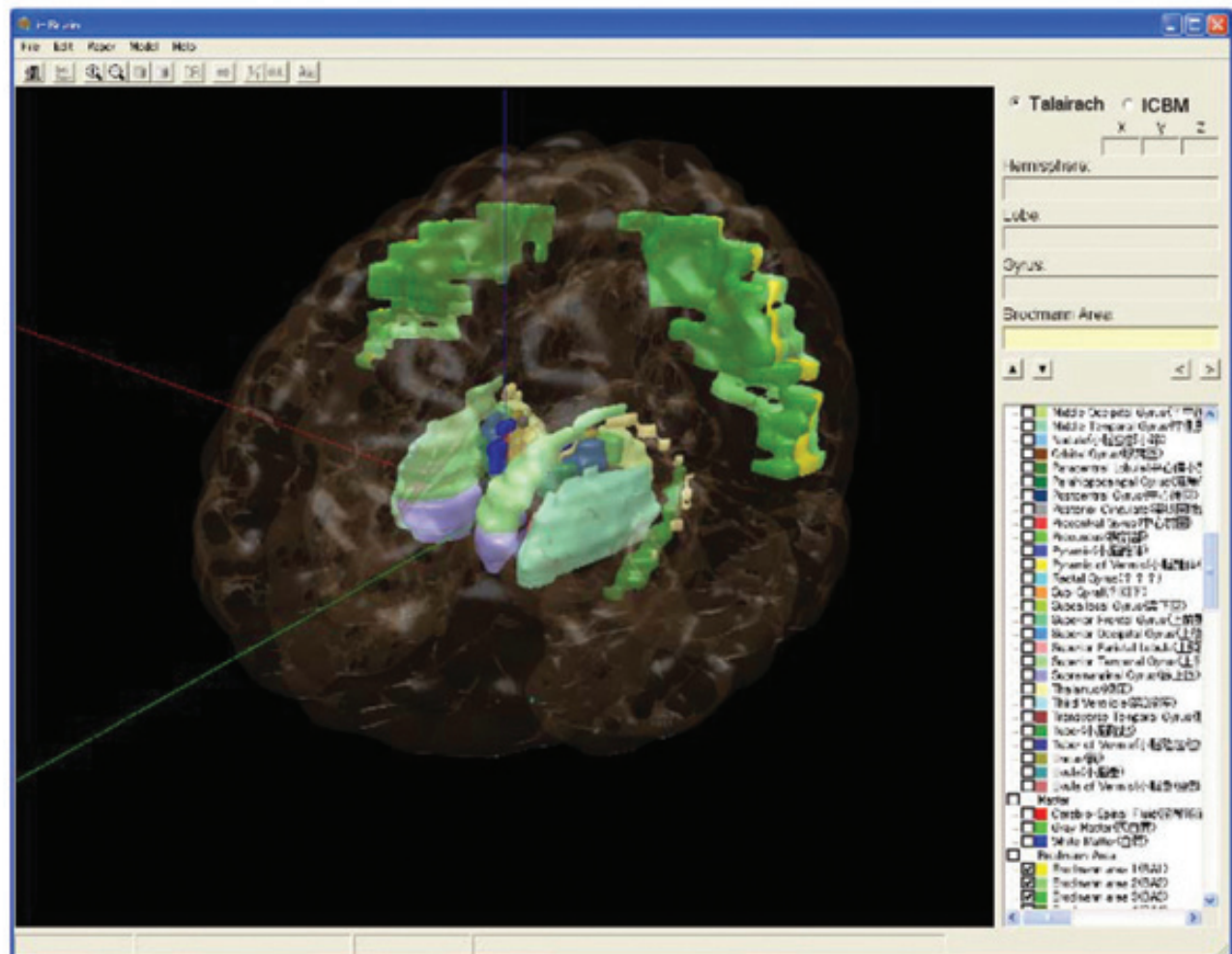
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BMC Neuroscience 2007, 8(Suppl 2):P14

There is growing interest in exploring the neurological activity underlying valuation and decision making. Recent findings have

**Figure 1 (abstract P13)**

An example of Brodmann area display in "iBrain".

greatly enriched behavioral investigations of the psychology of preference and choice by revealing the specific biological substrates of reward encoding, trust, risky choice, and other relevant phenomena. Neurocomputational modeling allows for precise integrations of empirical findings into detailed mechanisms for how specific brain operations can produce complex cognitions and behaviors. We present a biologically realistic spiking neural model of affective choice and judgment that demonstrates this important explanatory role for computational neuroscience.

Our model proposes a fundamental interplay between an emotional arousal state encoded by the amygdala and judgments of reward value and valuation changes computed in orbitofrontal cortex. Inspired by findings from attention research, we model a multiplicative modulation of reward valuation by affective arousal, whereby highly emotive events or contexts cause an amplification of positive or negative subjective judgments. This modulated signal feeds into interacting opponent systems for computing positive and negative reward prediction errors, which we have respectively encoded through dopaminergic and

serotonergic activity. The degree to which an obtained outcome was positively or negatively unexpected induces activity in our modeled anterior cingulate and dorsolateral prefrontal cortical areas regarding the behavioral relevance of the outcome, with negative surprises indicating current behavior may need to be modified. A consolidation of encoded valuation, saliency and relative surprise is proposed to drive the planning of stimulus-appropriate behavior. Finally, information regarding behavioral saliency and prediction error feeds back to modulate emotional arousal level itself. These modeled mechanisms help to explain several important findings of behavioral decision research.

In particular, the model provides a rigorous biological account of prospect theoretic loss aversion by encoding an asymmetric influence of the effects of positive and negative outcomes on emotional arousal, which produces disparities in subjective valuations of equivalent losses and gains. Mechanisms for relative valuations and neural firing saturation effects in orbitofrontal cortex further contribute to an explanation of the shape of the observed value function from prospect theory. The model also suggests multiple distinct neurological mechanisms by which

information framing may affect choices, including ones involving anticipated pleasure. This allows for the proposal of a detailed neural basis for observed interactions between affect, prior expectations and counterfactual comparisons considered at the behavioral level in decision affect theory. Simulations of these important emotional decision phenomena lend support to the specific mechanisms of cognitive-affective interaction implemented in our model, and show the valuable role computational neuroscience can play in developing richer and more complete explanations in cognitive psychology.

## P15

### Spatial attention in V4: a biophysical model

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It has been shown that directing attention towards a location inside the receptive field of a V4 neuron induces an increase in the stimulus response of the neuron, in the local field potential power within the gamma frequency range and also an increase of phase-locking. When two stimuli are presented in the receptive field of the same neuron, the two compete and the neuron's response is in between the responses to each stimulus presented alone. Attention to the location of one of the stimuli is found to bias this competition, favouring this stimulus. The top down attentional signal presumably comes from prefrontal areas. In one of these areas, the frontal eye field, the neural activity has been shown to be linked with the activity in V4 and to be able to induce the attentional effects seen in V4. Despite these experimental results, the basic mechanisms underlying competition and attention are still not well understood.

We introduce a biophysical model of V4 to study this problem. The model consists on a network of pyramidal neurons and interneurons, connected via realistic synapses and receiving stimulus inputs from area V2 and feedback attentional inputs. We study parameters roles (like the synaptic conductances) on the network dynamics and find values for which the *in vivo* type of dynamics is reproduced. In presence of two stimuli, the model results show that they compete. Applying an attentional signal towards one stimulus is found to induce the observed attentional effects. Interneurons are found to play an important role in both phenomena. These network results extend our previous conclusions regarding competition and attention but which were at the neuronal level.

## P16

### Constraining neural microcircuits with surrogate physiological data and genetic algorithms

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**Background:** Biophysically detailed bottom-up approaches to modelling neural networks have previously used simulated annealing, gradient-descent or ad-hoc algorithms to constrain the many free parameters [1]. This study explores the use of genetic algorithms to automatically search for a known configuration using extracellular spike recordings or intracellular voltage data. Surrogate data on neural responses is generated and the ability of the algorithms to find the (known) neural parameters is assessed.

**Materials and methods:** Four cell subtypes, in a known microcircuit of the mammalian cochlear nucleus [2], are simulated in a network with 60 frequency channels of auditory input. Each cell received a 'tonotopic' projection of auditory nerve fibres, simulated using a phenomenological auditory nerve model response to a 60 dB SPL notch noise stimuli. Single compartment Hodgkin-Huxley neurons and conductance synapses were implemented in NEURON. Detailed equations for the active voltage-dependant currents  $I_{Na}$ ,  $I_{KHT}$ ,  $I_{KLT}$ ,  $I_{KA}$  and  $I_h$ , were derived from *in vitro* studies of cochlear nucleus cells [3]. Using genetic algorithm optimisation, four cost functions using identical input stimuli were investigated. The cost functions calculated error in either: (i) absolute spike times, (ii) peri-stimulus time histograms, (iii) cumulative spike counts, or (iv) average intracellular voltages for each cell in the network. Network parameters controlling the number, weight and distribution of the synaptic connections were used in the optimisation, but these could easily be extended to incorporate other cell properties. In all, 30 parameters controlling 10 synaptic connections were converted to a GA binary string.

**Results:** Each cost function was allowed to run for  $2 \times 200$  generations of the GA, after which a best solution was determined. Normalisation of the results was difficult due to the different scale of scores produced by the cost functions and the different binary resolutions of the parameters. Table 1 shows the performance of the cost function as judged by the best solutions. The average intracellular voltage obtained the best solution as determined by the parametric mean error relative to the target parameters, although each of the cost functions were able to converge successfully to a solution that

**Table 1 (abstract P16) Genetic Algorithm Cost Function Performance**

% Diff	<sup>1</sup> Best GA Score	Mean Top 100 <sup>2</sup>
Spike Times	31.08	32.8 (5.5)
PSTH	30.13	31.3 (7.1)
CSC	29.41	32.2 (12.3)
IV	23.17	28.2 (14.7)

<sup>1</sup> Percentage difference between target values and best GA solution, normalised for each parameter. <sup>2</sup> Mean (stdev) of each the top 100 GA scores (per parameter).

was within 30% of the target values. Cost function parameter sensitivity was a key factor, since some parameters were visibly under constrained. Sensitivity analysis was also performed for each parameter in the search space around the target.

**Conclusion:** Success of the GA optimization was affected by intrinsic noise in the neural model and depended on the sensitivity of the cost function to changes in each parameter. The results have shown the potential of genetic algorithms to constrain the underlying synaptic parameters of BNNs from any of the chosen sources of physiological data. More work is needed to assess the impact of reducing the amount of information available to the cost function and setting confidence limits for each parameter.

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#### P17

##### State-dependence of sensory-evoked responses in neocortex

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The neocortex typically operates in one of two states. The activated (desynchronized) state, typical of alert wakefulness and REM sleep, is characterized by a high-frequency, low amplitude local field potential (LFP). The inactivated (synchronized) state exhibits high low-frequency power, and spontaneous transitions between UP states of widespread depolarization and spiking, and DOWN states of generalized silence.

Cortical responses to sensory stimuli exhibit enormous trial-to-trial variability, much of which is state-dependent. This presents a problem for averaging in order to find the “typical” response. One solution is to classify trials (repeated presentations of the same stimulus) into categories depending on the cortical state at the time of the stimulus (activated vs. inactivated, UP vs. DOWN, etc.). In this work, we are more interested in understanding how the intrinsic dynamics associated to different states controls population activity.

We investigated the state-dependence of sensory-evoked responses using a dynamical systems approach. Cortical LFPs and population spike trains were recorded from the auditory cortex of urethane-anesthetized rats using multi-site silicon microelectrodes. 5 ms noise click stimuli were presented, and intervals of silence were used to investigate spontaneous activity. Activated states were induced by electrical stimulation of the pendunculo-pontine tegmental nucleus (PPT).

We quantified the strength of “initial” and “persistent” network responses using multiple unit activity (MUA). In the activated

state, initial responses were more or less consistent, whereas persistent network activity merely reflected a return to baseline. In contrast, the inactivated state exhibited greater variability in initial responses, and persistent activity that often reflected transitions between UP and DOWN states. We found that a “past activity” variable, which summarizes recent network activity, is highly correlated to persistent network activity after a stimulus presentation. In the activated state, the correlation was strongly positive, whereas in the inactivated state, the correlation was strongly negative.

By viewing the MUA as the output of a dynamical system driven by external sensory stimuli, we constructed a simple nonlinear model that captures the essential dynamic differences between the activated and inactivated states, and explains much of the trial-to-trial variability of sensory-evoked responses. By fitting the model to data, we were able to determine the phase diagram associated to each kind of activity, and the bifurcation that transitions from activated to inactivated state. Furthermore, using the model we made predictions for initial and persistent responses that were better than those using past activity alone.

#### Acknowledgements

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#### P18

##### Stability of splay states for pulse-coupled neuronal networks: finite size versus finite pulse-width effects

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The dynamics of collective states observed in globally coupled neuronal networks is still an open problem. In particular, although it is claimed that the periodic firing state (“splay state”) is stable only for excitatory coupling [1], counterexamples have been found for inhibitory coupling as well [2]. Moreover, the stability of the splay states has been analyzed only in the mean field limit [1, 3, 4]. Our aim is to investigate simultaneously, for a pulse-coupled network of leaky integrate-and-fire neurons, the effect of the number N of neurons as well as of the pulse-width of the post-synaptic potentials. Finite-N networks can be studied by suitably modifying the map-like formalism [5, 6] usually adopted to implement numerically the model. As a result, we find that the stability of the splay state depends crucially on a parameter that is proportional to the width of the delivered pulses rescaled to the average interspike interval. More precisely, we show that the Floquet spectrum of eigenvalues is made of two components, one of which coincides with that one predicted by the mean-field analysis [1]. Depending on the value of the relevant parameter, the second component may be responsible for the occurrence of instabilities which in turn suggest the failure of the continuum limit approximation. Finally, for sufficiently small pulse-width we observe that the splay state can be stable even for inhibitory coupling.



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## P19

### Analysis of coupled decision-making modules for multisensory integration

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We were interested in how two coupled decision-making modules behave. This is for example interesting in multisensory integration, in which both auditory and visual precepts have to be integrated into one common percept. We used a biophysically realistic neural model consisting of integrate-and-fire neurons with detailed synaptic channels. We studied the influence of the strength of the cross-connection between the two decision-making modules on the performance of the model. The performance was assessed by how often the system can correctly extract the stimulus even though just weak input was applied. We found that the optimal performance of the coupled modules is achieved by a certain cross-connection strength, which is independent of the amplitude of the stimulus input. This means that once an optimal cross-connection has been learned it can be used for all types of stimulus inputs to achieve an optimal performance. We also present the mechanism, which is responsible for this improvement: Inconsistent constellations in the two modules converge to the correct response. We could also simulate the law of inverse effectiveness in our model. We related the strength of the input bias to the multisensory integration index and found an inversely correlated relationship such as observed in experimental data [1]. We also investigated a three-module architecture, in which two primary sensory areas like the auditory and the visual one are connected by a third, integrating module. The 3<sup>rd</sup> module could correspond to higher processing areas such as the STS, which mediates between the two primary sensory areas. We show that there are similar dynamics as in the two-module case, although the necessary coupling strength between the modules is increased. The coupling is more indirect than in the two-module case. We conclude that decision-making modules can be coupled to increase performance compared to single decision-making module.

## Acknowledgements

The study has been supported by the Volkswagen Foundation.

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## P20

### Network reconstruction in the presence of unmeasured neurons

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We present a method to determine whether a correlation in the spikes of two neurons is due to a causal connection between the neurons or due to common input originating from unmeasured neurons. The distinction is based on a point-process model of how a neuron's spiking probability can depend on both its own spiking history and a stimulus (or other external variables). Although the results depend on selecting a parametric model that captures essential features of the neural response, a large class of models can be used with the network analysis. Hence, the analysis could be applied to probe circuitry in a large range of neuronal systems.

## P21

### The complex world of the small brain

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Since Stanley Milgram's "six degrees of separation", the interest in the topological structure of network graphs and implications for their functional role experienced a dramatic surge. 40 years later, small-world and scale-free properties, with the latter being generally viewed as a crucial prerequisite for complex dynamical behaviours, are identified as a unifying feature of many real-world networks. However, the study and characterisation of complexity at the level of neuronal populations such as cortical microcircuits, large-scale functional networks or, ultimately, the whole brain still remains a technically and mathematically difficult and, therefore, widely unsolved task. Moreover, recent research shows that small-world and scale-free connectivity are just two out of a vast plethora of applicable graph-theoretical measures to yield a more accurate characterisation of the networks structural or functional properties.

In this contribution we provide a detailed comparative characterisation of publicly available brain networks. The latter include structural areal connectivity graphs from the cat cortex, macaque and macaque visual cortex, as well as cellular networks of *C. elegans* and corresponding subnetworks formed by chemical synapses and gap junctions only. Graph theoretical tools applied include node degree and correlation, edge distance, clustering and cycle, entropy, hierarchical, centrality, spectral and complexity measures, as well as the study of

subgraphs and fractal properties. Moreover, extensions of these measures incorporating weight and spatial information are proposed and applied to graphs where such data were available. Our analysis shows that, first, in agreement with numerous previous studies, all investigated systems exhibit small-world properties (i.e. small average geodesic distance and high clustering coefficient) when relational graphs are considered. Second, for many other measures, marked differences (e.g. for efficiency and vulnerability) between the investigated networks were found, thus revealing a rich universe of structural qualities. We argue that the latter forces a re-evaluation of the question about structural prerequisites for functionally complex dynamical behaviours. Third, the incorporation of weight and spatial information qualitatively alters some conclusions drawn from the analysis of corresponding relational graphs, thus arguing for a careful re-evaluation of real-world networks in the context weighted and spatial graph theory.

In summary, our study suggests that a deeper understanding of the functional dynamics and role, and possible differences in the latter, of neural and brain networks necessitate their detailed structural characterisation beyond small-world and scale-free qualities. Moreover, a detailed graph-theoretical characterisation of structural and functional brain networks will allow to constraint developmental mechanisms which lead to the preference of specific network topologies over others. Finally, studying structural and functional patterns on the global scale with the full weight of graph theory could provide an alternative way to argue for complexity as an emergent quality of brain networks which goes beyond a pure description of the wealth of structural and functional properties observed in isolated neural systems.

## P22

### Image-based configuration and interaction for large neural network simulations

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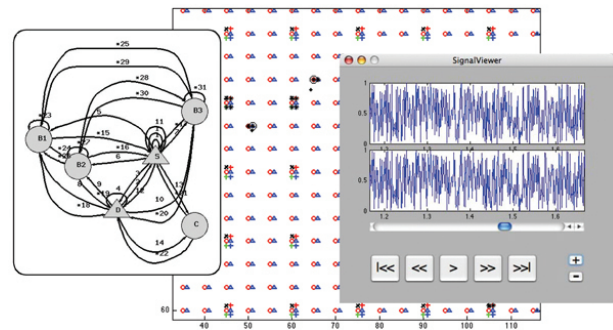
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**Background:** Large neural network simulations are becoming more complex to set up. They require modeling at multiple scales, include the effects of many interacting physical processes, encompass greater detail, and consume greater computational resources. The drive to solve problems that rely on increasingly complex codes will soon land us in the realm of petascale computing. How will we manage such simulations, configure them, and accurately aim them at the problems we're trying to solve? Simulation is an increasingly expensive process, with each run providing data to inform configuration and targeting of subsequent runs. Hence, it is vital to configure and execute simulations efficiently in order to minimize time spent on the computer cycles as well as time spent interpreting simulation results and designing follow-up experiments. We are developing a framework for interacting with and configuring large simulations using image-based interfaces generated automatically from the simulation source code.

Figure 1 (abstract P22)



Framework for interacting with large simulations.

Figure 1 shows a working prototype of some of the key components of the interactive framework. The diagram at the left is an automatically generated view of the probabilistic wiring diagram showing excitatory (\*) and inhibitory connections between pyramidal, basket, and chandelier cell types. The central image is an automatically generated physical layout of a portion of the neurons in a larger patch of the neocortex simulation. Circles, triangles, pluses, and exes correspond to superficial and deep pyramidal, basket, and chandelier cells. The mouse has been used to select two cells in the subpatch, which caused the signal viewer shown on the right to launch (not wired to a live simulation in this prototype).

**Conclusion:** The goal of the project is to create an interface to supercomputing platforms that will enable scientists to directly engage the live simulation during its critical setup and initial phases and at later times for monitoring and redirecting. This capability will enable rapid intuition building and will improve scientists' effectiveness in deploying productive, well-targeted experiments across research domains.

### Acknowledgements

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## P23

### Simulated-annealing as a tool to identify parameter values associated with epileptiform activity in single-neuron and network compartmental models

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**Background:** Automated parameter search algorithms, such as simulated annealing, seek to tune a model's parameters to reproduce important features of a target data set. A match function compares the model and target data to generate a goodness of fit and is crucial because it reflects which target features are considered of interest. Previous work has shown

the effectiveness of combining simulated annealing with time-domain match functions (e.g., spike timing and least mean square (LMS) of membrane potentials) to tune a compartmental model of a cortical pyramidal cell [1].

**Methods:** Here, we assessed the applicability of LMS and spike timing match functions to single-cell and cortical network targets displaying epileptiform activity. To accommodate the more time-variable nature of network activity, we also included frequency-domain (e.g., raw and banded power spectra) match functions with the goal of determining their relative efficacy in identifying and constraining the model parameters important for generating epileptiform discharges.

**Results:** The results of two representative cases are depicted in Figure 1. Figure 1a shows a bursting single-cell model target and a representative best-match found using an LMS match function; the parameter domain subject to search varied over a factor of 2 about the target value. Runs using larger domains, more parameters, and other match functions, such as spike timing, indicate that, for this target, the fraction of reasonable matches as a function of search domain scales most poorly for LMS. Figure 1b shows the LMS match function applied to a network model. This search restricted the domain to exclude the correct value of one of the parameters to simulate a real target in which parameters are not known *a priori* and may be situated outside the searchable domain. Encouragingly, the search found the value at the boundary of the allowable space, closest to the excluded target value.

**Conclusion:** Both our single-cell and network search results demonstrate the feasibility of using simulated annealing to identify parameters underlying behaviors related to epileptiform bursting activity. In real intracellular target traces, lack of knowledge about target parameter values may necessitate larger searchable spaces, for which LMS appears to be suboptimal compared to other match functions such as spike timing. If the searchable space is poorly chosen, so that the true parameters are excluded, then the search algorithm often indicates the situation by finding parameters at the edge of the searchable space, even for relatively complex network models as illustrated by Figure 1b. We note anecdotally that, at least in our models, it is easy to determine by inspection whether the automated searches have settled on a reasonable match, which makes them

useful tools for selecting interesting areas of parameter space even when they do not provide exact matches to the targets.

#### Acknowledgements

This work was supported in part by the Falk Foundation, the Linn family, and the U.S. Department of Energy under Contract DE-AC02-06CH11357.

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#### P24

#### Transmission of spiking-rate information through layered networks: the role of recurrent and feedback connections

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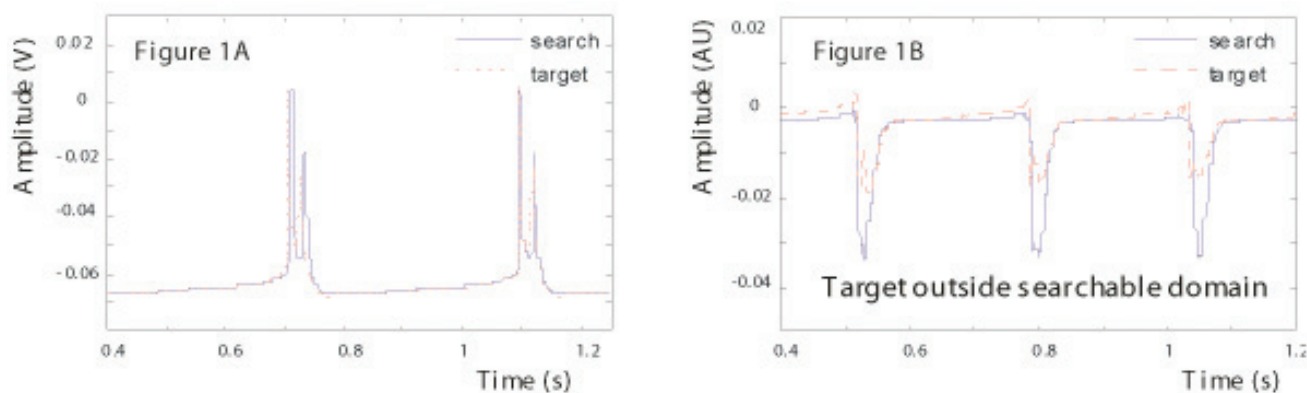
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**Background:** It is a widely accepted tenant that one of the means by which the nervous system and brain encodes information about external stimuli is via the spiking-rate of neurons. Such a spiking-rate code necessitates the transmission of an elevated spiking-rate through successive neurons in a structured network, such as occurs in the auditory and visual pathways. Recent studies, however, have raised serious questions about our understanding of the propagation of such spiking-rate information through structured networks. In networks consisting of successive layers of integrate-and-fire neurons with conductance synapses with feed-forward of information from one layer to the next, it has been found that the mean spiking-rate in deep layers is essentially independent of the input spiking-rate [1]. The neurons within each layer tend to synchronize with each other, resulting in a synchronous volley of action potentials through successive layers, reminiscent of synfire chains. The average spiking-rate in deeper layers either decays to zero or

Figure 1 (abstract P23)



LMS match function results.

reaches a stable fixed-point, depending upon the model parameters. This behaviour was also observed in an *in vitro* study using a dynamic patch clamp [2].

**Methods:** A network consisting of many layers of neurons is analysed using both analytical and computational techniques. Within each layer the neurons (both excitatory and inhibitory) are recurrently connected. Adjacent layers are connected to each other through both feed-forward and feedback excitatory connections. The neurons receive *specific* (or *driving*) excitatory synaptic input from inputs in the previous layer and *non-specific* (or *background*) excitatory inputs from neurons outside the layered network. Both Poisson neurons and integrate-and-fire neurons with conductance synapses are analysed [3]. The fixed-point behaviour of the transmission of spiking-rate information is analysed analytically. Dynamical aspects of the behaviour are analysed computationally.

**Results:** It is found that, with a sufficient level of recurrent excitation and background input, the response of the neurons within a layer to input that is external to the layer can be described as a threshold-linear function to a very good approximation over a wide range of input intensities. Activity-dependent synaptic scaling is used to determine the effective gain of the threshold-linear response. The conditions under which spiking-rate information can be reliably transmitted through successive layers are deduced using a fixed-point analysis and are found to depend upon the relative amounts of excitatory feed-forward and feedback input between layers.

**Conclusion:** It is found that there is a set of *privileged* neural parameters allow the propagation of spiking-rate information through deep layered networks and that this set of parameters can arise naturally as a result of simple well-founded principles. This represents a significant result demonstrating that the propagation of spiking-rate information can be achieved when the feedback and recurrent connections, that were absent in previous feed-forward layered models, are incorporated. Also, in contrast to feed-forward models, there is in the present model a clear rationale for the privileged sets of neural parameters that allow the transmission of spiking-rate information.

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#### P25

##### A population density framework that captures interneuronal correlations

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We have developed a population density framework that captures correlations between any pair of neurons in the

population. We model each population of integrate-and-fire neurons as receiving input in the form of correlated Poisson processes. The evolution equation for the probability density of any pair of neurons within the population is a multivariate integro-differential equation which we solve numerically. We demonstrate the numerical method and compare the numerical solutions with Monte-Carlo simulations. Traditional population density approaches assume all neurons within a population are independent. However, correlations that are missed by these approaches can significantly alter network dynamics. Hence, the correlated population density method developed here could provide a framework to analyze how correlations propagate through networks and could be a computationally efficient method to accurately simulate large scale networks.

#### P26

##### Testing for higher-order correlations in massively parallel spike trains

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The cell assembly hypothesis [1] postulates dynamically interacting groups of neurons as building blocks of cortical information processing. Synchronized spiking across large neuronal groups was later suggested as a potential signature for active assemblies [2], resulting in specific higher-order correlations among assembly members. Mathematical concepts for the treatment of higher-order correlations in massively parallel spike trains have been suggested in the past, but, due to constraints of insufficient sample sizes, estimation of higher-order parameters from recorded data poses serious problems [3]. As a consequence, most attempts to detect active cell assemblies resort to pairwise interactions. However, pairwise approaches do not imply the presence of higher-order effects in large neuronal populations and are not sensitive for sparse synchronous events [4]. The limited experimental evidence in favor of the cell assembly hypothesis must to a large extent be assigned to the lack of suitable analysis tools [5]. Massively parallel extracellular recordings, in contrast, are nowadays widely available.

Here we present a novel procedure that allows us to detect higher-order correlations in binned (filtered) multi-unit spike trains. Based on estimates of only a few low-order cumulants of such signals we can devise a test for the presence of higher-order correlations in the observed neuronal population. The method circumvents the need to estimate large numbers of higher-order parameters and, therefore, is less susceptible than previous approaches to the problems associated with limited sample sizes from *in vivo* recordings [3, 4]. The method was tested for correlated Poisson processes where correlations of various orders were induced by 'inserting' appropriate patterns of near-synchronous spikes [6]. When applied to simulated data,



the test was found to be surprisingly sensitive, even for cases where the effect of the higher-order patterns on pairwise correlation coefficients  $c$  were negligible (in the range of  $c \sim 0.01$ , see [4]).

We present our test for rectangular filters that mimic the binning and/or counting that is usually applied to extracellular spike recordings. We discuss applications with other types of filters that could make the proposed test applicable for other signal types, e.g. intracellular membrane potentials. Furthermore, the sensitivity and reliability of the new method for data, where the Poisson assumptions are not strictly satisfied, is critically discussed.

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## P27

### Neural mechanism for temporal integration of the fluctuating component of an external input

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Temporal integration of information plays a crucial role in a variety of cognitive processes, such as sensory discrimination, decision-making or interval timing. However, neural mechanisms of this computation remain to be elucidated. In previous models of temporal integration by recurrent neuronal networks [1] or by single cells [2], neurons integrate a constant external input. Recent lines of evidence, however, suggest that activity of in vivo cortical neurons is driven by noisy, balanced excitation and inhibition [3, 4]. Here we propose a recurrent neural-network model that integrates a noisy external input. We show that the temporal integration in this network is more accurate when it integrates the fluctuating component of this input rather than the mean value.

We consider a uniform recurrent network of  $N$  excitatory leaky integrate-and-fire neurons. All the neurons are initially in the resting state ('off' state); if a neuron discharges a spike, it moves to another state ('on' state) where constant depolarizing current is active, which promotes regenerative spike discharges. Each neuron receives an external input that consists of excitatory and inhibitory bombardments, which generates a

rapidly varying postsynaptic current  $I(t) = \mu + \sigma\xi(t)$ . Here  $\mu$  and  $\sigma^2$  are the mean and the variance of this current, respectively;  $\xi$  denotes fluctuation with zero mean, which is approximated by Gaussian white noise.

It is analytically or numerically shown that, if the strength of recurrent connection is properly tuned, the number of neurons in the 'on' state, say  $n$ , grows with time at an exact-constant rate. When  $\sigma^2$  is varied while  $\mu$  is constant, the constant growth is kept, with its rate scaling linearly with  $\sigma^2$ . In contrast, the constant growth is not kept when  $\mu$  is varied while  $\sigma^2$  is constant. These results indicate that  $n$  represents temporal integration of the variance but not the mean of an external input. We further propose that  $n$  is decoded by the firing rate of a downstream neuron that has afferent inputs from the recurrent network, which are mediated by NMDA current.

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## P28

### The role of glia in seizures

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**Summary:** We present an ionic current model, composed of Hodgkin-Huxley type neurons and glia designed to investigate the role of potassium in the generation and evolution of neuronal network instabilities leading to seizures. We show that such networks reproduce seizure-like activity if glial cells fail to maintain the proper extracellular  $K^+$  concentration.

**Methods:** Our neuronal network model combines the Hodgkin-Huxley type of formalism for the neuronal currents with a model for the dynamics of extra and intracellular  $K^+$  concentration controlled by a glial network. The equations for the ionic currents are adopted from the model in ref. [1]. The extra and intracellular  $K^+$  concentrations are calculated based on various  $K^+$  currents.

**Results:** We investigate the instability in cortical networks by studying two interacting one-dimensional networks consisting of 100 pyramidal cells and 100 interneurons. The network exhibits persistent and spatially confined activity in a parameter range

where inhibition is balanced by excitation. We then find various physiologic conditions under which a network displaying a stable persistent activity can switch to seizure like states.

**Conclusion:** The main finding of our study is that the network activity packet is stable provided that (1) the excitable synaptic strength is not very high; (2) the extracellular potassium concentration is low enough to be well in the physiological range (i.e. the glial network is functioning efficiently); and (3) perturbations to the network are not very strong.

#### Acknowledgements

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#### P29

##### Event-driven mathematical framework for noisy integrate-and-fire neuron networks: spike trains statistics via stochastic calculus, network analysis inspired by queuing theory and an event-driven simulator

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**Motivation:** The dynamics of neural networks in the brain is greatly influenced by noise. In the nervous system, sources of noise are everywhere (in the stimulus, in the uncorrelated activity, in the synapses, in the channels), and the emergent phenomena related to these random events such as spontaneous spiking and random collective behaviours are of special importance in the study of the neural code.

Usually, networks of integrate-and-fire neurons with a noisy external drive are studied using the Fokker-Planck equation [1]. Under the assumption of sparse random connectivity, it has been shown that the network dynamics can be in one of two regimes, depending on the parameters: a desynchronized stationary regime, and a weakly synchronized oscillatory regime. However, this approach does not seem to be fully satisfactory because it cannot be easily applied to more general neuron models.

**Mathematical approach: bridging neuroscience and communication networks theory:** We propose a framework inspired by the communication network theory to study this type of networks. In contrast with classical analysis (considering the membrane potential of the cells), we consider an event-based description of the network and define a Markov process related to the times of the spikes, the *countdown process*. We show that this biologically inspired model is formally equivalent to a class of stochastic networks studied in the field of probability theory [2, 3]. Our work consists in generalizing the results obtained in this field to the more intricate biologically-inspired model, and address new questions of special interest for the biological applications under this framework.

**Spike train statistics:** In this model, the probability law of the time of the first spike is a fundamental parameter, hence we

need to characterize the spike trains statistics as fast and accurately as possible. To this aim, we review and extend some methods coming from stochastic analysis. For instance we show that for classical integrate-and-fire models, the problem reduces to finding the hitting time of a curve by the Brownian motion, using the Dubins-Schwarz' theorem of local martingales representation.

**Event-driven stochastic simulator:** This approach leads to a natural event-driven simulation strategy we implemented by extending the software Mvaspike[4]. We show some simulation results illustrating transient behaviours of the network.

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#### P30

##### A general, flexible decision model, applied to visual search

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To survive, an organism must pursue multiple goals and switch between them at appropriate times. Generating such behavioral flexibility is an extremely important brain function, yet little is known about how a network of neurons can pursue different goals at different times. A network's behavior can only change with an organism's goals if it receives information about those goals as input. Thus, network responses must depend jointly on both current stimuli and current goals. How are these sources of information combined to generate behavior? And, given those combinations, how can different decision criteria be implemented depending on the task at hand?

Here we present a plausible network model for visual search that exhibits different decision criteria depending on the current goal. The network accurately performs several different search tasks based on the same stimulus set, and is capable of switching between tasks without retraining.

The model consists of three layers, each directly inspired by cortical neurobiology: (1) A layer of input or sensory neurons whose responses to stimuli are gain-modulated depending on current goals. Such gain modulation implies that sensory and

goal-dependent information are combined nonlinearly, as documented in various experiments, but the exact form of this nonlinearity is not crucial. (2) A randomly connected layer of non-linear neurons that acts as a reservoir computer. As in a liquid-state machine, this layer is capable of generating widely different response patterns. (3) A standard race-to-threshold decision model containing two competing neural populations. These are used to indicate the system's decision, whether a target is present or absent in the display, depending on which population reaches a threshold first.

We illustrate the model's performance in a series of visual search tasks for which human behavioral data are available. We show that a single fixed network can perform all of these tasks correctly, qualitatively reproducing eight sets of experimental observations:

1. Variations in reaction times due to the number of displayed distractors (set size effects).
2. Differences in reaction times between conjunction and single-feature (or pop-out) searches.
3. Differences in reaction times between target-absent and target-present displays.
4. Reaction-time dependencies on the similarity between distractors and targets.
5. Search asymmetries; that is, differences in reaction-time curves when target and distractor objects are exchanged.
6. The redundant targets effect; that is, decreased reaction times as the number of targets present increases.
7. The ability to perform both singleton search (search for an object that stands out in some way) and directed-object search (search for a specific object).
8. Similar reaction-time curves for search in standard, static displays and in dynamic displays, in which the positions of all objects change randomly with a certain frequency.

The last point is particularly significant because other models predict large differences in reaction times between static and dynamic conditions, whereas ours does not. We also show that the model is robust to noise, and can perform either with perfect accuracy or exhibit behaviorally realistic error rates, depending on noise and training parameters.

Our model demonstrates that three key properties of cortical neurons – gain-modulation, recurrent connectivity, and race-to-threshold dynamics – can be combined to generate a powerful and flexible decision-making model. We suggest that these features, which are successful at replicating many aspects of visual search, may be combined in a similar manner to generate goal-dependent decisions in many other circumstances.

### P31

#### **Non-additive coupling enables stable propagation of synchronous spiking in purely random networks**

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Precise timing of spikes and synchronization in the millisecond range has been experimentally observed in different neuronal

systems. Their occurrence correlates with external stimuli and is thus considered a key feature of neural computation. The dynamical origin of precise and coordinated spike timing, however, is not well understood. Here we show in a modeling study that synchronous spiking activity of subgroups can persist and propagate in purely random networks if we take into account the non-additive nature of dendritic input integration that was recently uncovered experimentally. We find a transition to stable propagation of synchronized spiking: For additive coupling and at low strength of non-additivity, synchronous spiking dies out; above a critical strength, stable propagation of a group of synchronized spikes becomes possible. We derive a map giving the average future size of a synchronous group in terms of the current group size. For networks with homogeneous parameters the map can be obtained analytically and reveals that the discontinuous transition found is due to a tangent bifurcation at a critical strength of non-additivity. We discuss the mechanism underlying this transition and its consequences for networks with inhomogeneous parameters and additional external noise. Prominent 'synfire-chain' models for the stable propagation of synchronous activity in cortical networks require the existence of feed-forward structures that are superimposed on otherwise randomly connected local cortical circuits. It is unclear, however, whether feed-forward structures actually exist in such local circuits. Our study suggests that additional structural features of the network connectivity may not be required for the propagation of synchronous spiking activity if synaptic interactions exhibit non-additive dendritic integration.

### P32

#### **A second-order maximum entropy model predicts correlated network states, but not their evolution over time**

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Highly correlated network states are often seen in multi-electrode data, yet are predicted to be rare by independent models. What can account for the abundance of these multi-neuron firing patterns? Recent work [1, 2] has shown that it is possible to predict over 90% of highly correlated network states, even when correlations between neuron pairs are weak. To make these predictions, both groups used a maximum entropy model that fit only the firing rates and the pairwise correlations (a second-order maximum entropy model), and which was maximally uncommitted about all other model features. This new work raises several questions. First, how general are these results? Both previous reports largely used retinal data. Could this maximum entropy approach also succeed when applied to cortical slices? Although the original model explained correlations among spikes, could it also be used to explain the abundance of correlated states of local field potentials (LFPs)? A second issue concerns the abundance of

correlated states over time. Can a second-order maximum entropy model predict sequences of correlated states?

To examine the generality of this approach, we applied a second-order maximum entropy model to a variety of in vitro cortical networks, including acute slices from rat ( $n = 3$ ) and human epileptic tissue ( $n = 1$ ), as well as organotypic ( $n = 3$ ) and dissociated cultures ( $n = 3$ ) from rat.

We explored its effectiveness in predicting correlated states of both spikes and LFPs at one time point. On average, the model accounted for  $90 \pm 6\%$  (mean  $\pm$  s.d.) of the available multi-information, in good agreement with previous studies. In all cases, the maximum entropy model significantly outperformed an independent model, demonstrating its effectiveness in explaining correlated states in cortical spikes and LFPs at one time point. We also explored how well the maximum entropy model predicted sequences of correlated states over time. Here, the model often failed to account for the observed sequence lengths. In 8/10 preparations, the distribution of observed sequences was significantly longer ( $p = 0.003$ ). We conclude that a second-order maximum entropy model can predict correlated states, but not their evolution over time. This suggests that higher-order maximum entropy models incorporating temporal interactions will be needed to account for the sequences of correlated states that are often observed in the data.

#### Acknowledgements

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#### P33

##### Storage and recall in the CA1 microcircuit of the hippocampus: a biophysical model

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It has been suggested that the hippocampal theta rhythm can contribute to memory formation by separating encoding and retrieval of memories into different functional cycles [1]. Herein, we investigate via computer simulations the mechanisms by which storage of spatio-temporal input patterns is achieved by the CA1 microcircuitry. A model of the CA1 microcircuitry is presented using biophysical representations of its major cell types including pyramidal cells and three types of inhibitory interneurons: basket cells, chandelier cells and bistratified cells. Inputs to the network come from the medial septum, entorhinal cortex and CA3 Schaffer collaterals. Patterns of CA3 input are stored via an STDP-type learning rule on the pyramidal cell

target synapses. The other inputs provide context and timing information. The model simulates accurately the timing of firing of different hippocampal cell types relative to the theta rhythm and proposes functional roles for the different classes of inhibitory interneurons in the storage and recall of input patterns.

#### Acknowledgements

This work is funded by an EPSRC project grant to BG and SC.

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#### P34

##### Mechanisms of carbachol oscillations

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Carbachol (CCh) is a cholinergic agonist that causes spontaneous theta frequency oscillations in the entorhinal cortex and hippocampus. To better understand the mechanism by which these oscillations are generated, we measured the effect of CCh on phase response curves from pyramidal neurons and stellate cells in the entorhinal cortex. Based on the measurements, it was predicted that CCh would facilitate synchronization of a network of pyramidal neurons but would have little or even a desynchronizing effect on stellate cells. The pyramidal cell results were then confirmed by coupling pairs of pyramidal neurons using the dynamic clamp and measuring their synchrony in control and CCh conditions.

#### P35

##### The balance of synaptic conductances in shaping hippocampal population rhythms

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A central feature of the hippocampus is its rich tapestry of population oscillations as revealed by electroencephalographic (EEG) recordings. These myriad forms of population activities are related to various behavioural states. For example, during



slow wave sleep and awake immobility, the rodent hippocampus exhibits two dominant EEG rhythms, irregular activities with dominant frequencies of 2–3 Hz and intermittent sharp waves. These EEG activities have been implicated in memory-related signal processes. As these population activities primarily rely on CA3 network activities, a sound knowledge regarding the balance between excitatory and inhibitory activities in the CA3 circuit is the key to understanding their generation.

Using thick slices of adult mice, we have produced an in vitro model that is capable of exhibiting either spontaneous rhythmic field potentials (SRFPs, 1–4 Hz) alone or SRFPs together with sharp wave like events [1, 2]. We study the balance of synaptic conductances that may underlie these population activities. Our approach is to use the VmD method [3] to investigate the excitation/inhibition balance in individual hippocampal CA3 neurons.

Our results show that 1.) there is a global inhibitory dominance for all the neurons in slices exhibiting SRFPs alone and with sharp wave like events, in accordance with the fact that the SRFPs are inhibitory in nature. 2.) The inhibitory hegemony lessens by a significant degree for neurons in the slices having both sharp wave like events and SRFPs. This sheds light on the importance of increased excitatory inputs in sharp wave generation. 3.) There is a significant disparity in excitation/inhibition balance between pyramidal cells and interneurons, with the pyramidal cells generally receiving a lower ratio of inhibitory inputs. This difference in excitation/inhibition balance probably underscores the possible inhomogeneity of the neural network. These results provide insights not only on the balance of synaptic conductances conducive to hippocampal rhythm generation, but also on the prospective wirings of the structure itself. These insights can in turn be used to constrain computational network models that simulate rhythm generation in the hippocampus.

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#### P36

##### **A large-scale realistic model of VI exhibiting orientation selectivity diversity and laminar dependence**

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**Background:** An important question regarding orientation selectivity (OS) in the primary visual cortex (VI) is to know how

OS varies among different VI neural populations and throughout VI layers [1, 2]. In this work we present a large-scale model highly constrained by physiology and anatomy and use it to address these questions.

**Methods:** The model corresponds to 4 mm<sup>2</sup> of cortical area in a 10:1 scale. It is composed of 59,821 cells arranged into six layers (L1, L2/3, L4B, L4C<sub>α</sub>, L5 and L6) representing the M pathway. Six different HH-type neuron models were constructed to simulate six different cell classes: late spiking, non-late spiking, fast spiking, regular spiking, chattering, and bursting neurons. These neurons were distributed in the six layers in a realistic way with short- and long-range intra-laminar connections as well as inter-laminar connections. Thalamic inputs are delivered to all excitatory cells in layers 4C<sub>α</sub> and 6. Activation of a cortical cell is modeled by a convolution of a sinusoidal drifting grating with a Gabor function. Neural OS profile was determined via circular variance and half-height bandwidth of its tuning curve.

**Results:** Neurons in the model show a diversity of OS consistent with experimental data (see Figure 1).

**Conclusion:** Results suggest that the diversity in OS observed across cortical layers is at least partially due to heterogeneity in cellular electrophysiology and circuitry properties.

#### Acknowledgements

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#### P37

##### **A model for the rat exploratory behavior in the elevated plus-maze**

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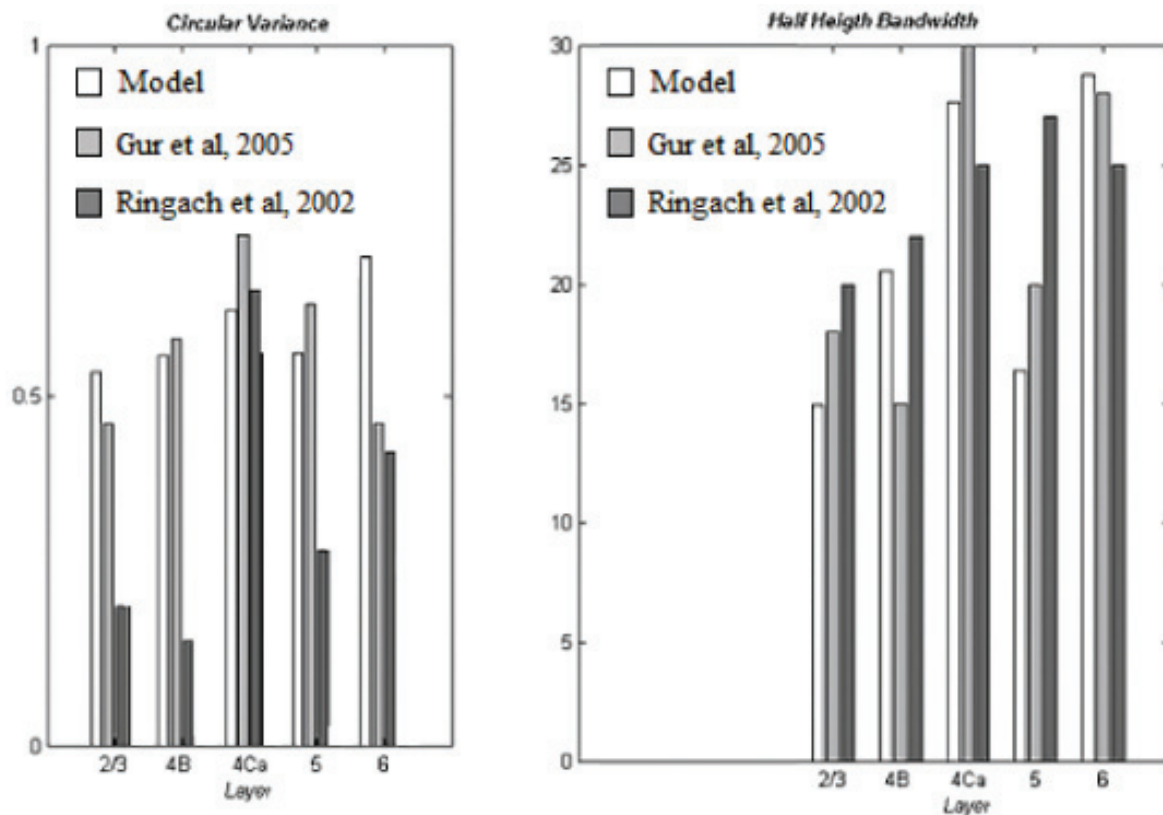
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**Background:** The elevated plus-maze (EPM) is a standard animal model of fear/anxiety in which the rodent is initially placed at the center of an elevated four-arm maze in which two arms are open and two are enclosed by walls. The anxiety-related behavior comes from the conflict between staying in a safe place (the enclosed arms) and exploring a potentially dangerous environment (the open arms). The rat's anxiety level

Figure 1 (abstract P36)



Comparison of the OS profile shown by the model with experimental results.

in the EPM is characterized by two main measures, namely the number of times the animal enters each kind of arm and the time spent in each kind of arm. In this work we present a modified version of an earlier model [1] for rat exploratory behavior based on competition between motivation and aversion and compare the simulation results with experimental data for real rats [2].

**Methods:** The model is a network based on the structure of a plus-maze divided into squares of equal size, five per arm and a central one [1]. Each network unit corresponds to a specific square and the connections, only between closest neighbors, represent the possible adjacent squares where a virtual rat could go. The exploratory behavior is modeled by a matrix of network weights  $w_{ij}$  whose elements represent the rat's tendency for exploring square  $i$  from square  $j$ . This matrix is given by  $w_{ij} = M_{ij} - A_{ij}$ , where  $M_{ij}$  is the animal's motivation to explore square  $i$  from square  $j$  and  $A_{ij}$  is its aversion to move to square  $i$  from square  $j$ . This equation was kept from the original model but here the equations that model the way the matrices  $M_{ij}$  and  $A_{ij}$  depend on the number of times  $N_{ij}$  the virtual rat moves from square  $j$  to square  $i$  were modified to  $M_{ij} = M/(\mu + N_{ij}^{\beta_i})$  and  $A_{ij} = A/(\nu + N_{ij}^{\alpha_i})$ , where  $M$  and  $A$  are constants which have the same values for all virtual rats and determine, respectively, the initial values of motivation and anxiety,  $\mu$  and  $\nu$  are parameters that vary from virtual rat to virtual rat determining their individual differences and  $\alpha_i$  and  $\beta_i$

are positive exponents which determine how motivation and anxiety respectively decay with  $N_{ij}$ . The exponent  $\alpha_i$  can have two different values, one when square  $i$  represents a place inside an open arm, which we will call  $\alpha_{io}$ , and the other when  $i$  represents any other square of the EPM, which we will call  $\alpha_{ia}$ . The exponent  $\beta_i$  also can have two different values, one when square  $i$  represents a place inside a closed arm, which we will call  $\beta_{ic}$ , and the other when  $i$  represents any other place of the EPM, which we will call  $\beta_{ia}$ . The values of the parameters were determined by an exhaustive search using genetic algorithms with a fitness function which combines the two anxiety measures mentioned above.

**Results:** The results of the simulations agree well with experimental data from our lab [2]. The time spent in the arms and the number of entries into them by the virtual rat are similar to the same measures exhibited by real rats.

**Conclusion:** The modified model is capable of replicating the rat exploratory behavior in the EPM. The major weakness of the model is its large number of parameters, which turns its interpretation in a biological or cognitive context difficult. In spite of this, the model can be considered as a first step for a theoretical understanding of the basis of rodent exploratory behavior.

#### Acknowledgements

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## P38

### Modelling selective attention with Hodgkin-Huxley neurons

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**Background:** We develop a large-scale brain-inspired model of selective visual attention, which is a generalization of our previous developments [1, 2]. The global architecture of the model includes a Map Representation Module for feature detection, an Invariant Representation Module for visual scene representation and competition among objects, and a Central Assembly Module for top-down control of attention focus.

**Map Representation Module (MRM):** The input image is projected to the MRM which includes several submodules for representation of the pixel's hue, brightness, and some other visual features such as orientation and contrast; each of these submodules uses a cubic architecture. Each representation cube contains several vertical layers, and each layer is a grid of Hodgkin-Huxley neurons. There is one-to-one correspondence between input image pixels and pixels in a layer of a representation cube. Object features are passed to the Invariant Representation Module.

**Invariant Representation Module (IRM):** At the second stage of image processing, an invariant representation with respect to position, size, and rotation is created. This representation enables the organization of a competition among different objects which reflects bottom-up selective attention. Each object is represented by a group of excitatory locally coupled Hodgkin-Huxley neurons. Different groups inhibit each other until only one remains active, representing the selected object. Neurons are operating near the Andronov-Hopf bifurcation. Each neuron has an independent source of noise to produce either sparse spiking or coherence resonance [3]. The onset frequency can be trained through intrinsic plasticity, which has recently been observed in experiments [4].

**Central Assembly Module (CAM):** The CAM is modelled by a group of Hodgkin-Huxley neurons which also operate near the Andronov-Hopf bifurcation. The CAM controls the dynamics of neuronal groups representing objects in the IRM and modulates its behaviour to realize the top-down attention effect.

Simulations show that the system sequentially forms an attention focus selecting the most salient object (in this case we consider the size and brightness of the object). CAM modulation enables control of a scan-path where the focus of attention moves. The system also demonstrates a competition between attention energy and external disturbance, comparable

with phenomena observed in psychological experiments, such as Garner effect and Stroop effect.

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## P39

### Attentional modulation in a two-layer system

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Experimental works have shown that the attentional modulation of firing rates increases along the visual pathway. It has also been shown that attention modulates the gamma-frequency synchronisation. In electrophysiological experiments, these modulations have been found in layer V4 [1] but not in layer V1 [2]. In this modelling work, we study how selective attention modulates neuronal activity in different layers of the visual system. We use a two-layer model of integrate-and-fire neurons, modelling attention as an external input biasing the competition. We study the influence of the attentional bias on both the modulation of the firing rates and the gamma frequency synchronisation in both layers. We show that the gamma frequency synchronisation is much higher in the upper layer (V4) than in the lower layer (V1). In addition, the modulation of the synchronisation is generally stronger in the higher layer. Our findings are thus consistent with an increase of the gamma frequency modulation along the visual pathway. This might explain the different findings in [1] and [2], as they measured from different layers in the visual system. We also analyse attentional modulations as a function of the connection strength between the two layers. Our results show that depending on the connection strength, either the rate modulation or the gamma frequency modulation is stronger, suggesting that both play an active role in the encoding of attention.

## Acknowledgements

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**P40****Chopper unit responses to amplitude-modulated tones: does stochastic mode-locking theory allow a more accurate characterisation of observed temporal structure?**

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Responses to amplitude-modulated pure tones have been used extensively to assess temporal properties of neurons across the auditory system. The synchronisation to the modulation frequency has mostly been measured by an index called vector strength. This index is based on the distribution of spikes along the period of modulation. One obtains a low value when the spikes occur evenly across the period and a high value when they are sharply distributed around a single time. In the ventral cochlear nucleus, chopper units have been found to show band-pass temporal responses at high sound pressure level and low-pass temporal responses at low level [1]. However, the fine structure of the responses remains uncharacterised.

Here, we show that data obtained from chopper neurons in response to amplitude-modulated tone exhibit more complex synchronised discharge patterns, reminiscent of mode-locked states. These responses can be organised around an Arnol'd tongue structure of a periodically forced model accounting for the sub-threshold properties of the T-multipolar cells. Numerical simulations of a stochastic version of this integrate-and-fire model give response patterns similar to the one observed experimentally. Thus, the results tend to show that care should be taken when considering the temporal properties of a neuron only on the basis of its vector strength.

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**P41****Enhanced measured synchronization of unsynchronized sources: significance for brain recordings**

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The analysis of synchronization, particularly phase locking, is being increasingly used in neuroscience to explore coordinated brain activity. The application of this methodology to magnetoencephalographic (MEG) and electroencephalographic (EEG) recordings would seem promising because these two recording techniques have great temporal resolution. However, current methods of synchronization analysis applied to raw MEG/EEG

data may not be as physiologically sound as previously thought. In this work we present a model of brain activity based on random current dipoles that reproduces the main characteristics observed in measurements of real data synchronization, even when no synchronized activity is taking place among the sources. In particular, we show that the enhanced local synchronization, previously described in some studies of epileptic seizures, may result from the activity of only a few unsynchronized sources.

**P42****Zero-lag long-range synchronization of Hodgkin-Huxley neurons is enhanced by dynamical relaying**

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**Background:** The synchrony hypothesis postulates that precise temporal synchronization of different pools of neurons conveys information that is not contained in their firing rates. The synchrony hypothesis had been supported by experimental findings demonstrating that millisecond precise synchrony of neuronal oscillations across well separated brain regions plays an essential role in visual perception and other higher cognitive tasks [1]. Albeit, more evidence is being accumulated in favour of its role as a binding mechanism of distributed neural responses, the physical and anatomical substrate for such a dynamic and precise synchrony, especially zero-lag even in the presence of non-negligible delays, remains unclear [2].

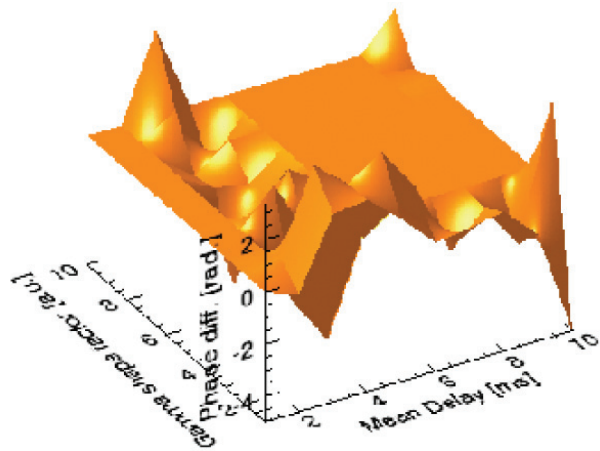
Here we propose a simple network motif that naturally accounts for zero-lag synchronization for a wide range of temporal delays [3]. We demonstrate that zero-lag synchronization between two distant neurons or neural populations can be achieved by relaying the dynamics via a third mediating single neuron or population.

**Methods:** We simulated the dynamics of two Hodgkin-Huxley neurons that interact with each other via an intermediate third neuron. The synaptic coupling was mediated through  $\alpha$ -functions. Individual temporal delays of the arrival of pre-synaptic potentials were modelled by a gamma distribution. The strength of the synchronization and the phase-difference between each individual pairs were derived by cross-correlation of the membrane potentials.

**Results:** In the regular spiking regime the two outer neurons consistently synchronize with zero phase lag irrespective of the initial conditions. This robust zero-lag synchronization naturally arises as a consequence of the relay and redistribution of the dynamics performed by the central neuron. This result is independent on whether the coupling is excitatory or inhibitory and can be maintained for arbitrarily long time delays (see Fig. 1).

**Conclusion:** We have presented a simple and extremely robust network motif able to account for the isochronous



**Figure 1 (abstract P42)**

Phase difference between the outer neurons as a function of the mean delay and shape factor of the axonal delays distribution.

synchronization of distant neural elements in a natural way. As opposed to other possible mechanisms of neural synchronization, neither inhibitory coupling, gap junctions nor precise tuning of morphological parameters are required to obtain zero-lag synchronized neuronal oscillation.

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#### P43

##### **Theory of spike correlations: a formal description of input and output correlations in spiking neurons**

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BMC Neuroscience 2007, 8(Suppl 2):P43

Spike correlations between neurons are ubiquitous in cortex, but their role is at present not understood. Here we describe the firing response of a leaky integrate-and-fire neuron when it receives a temporarily correlated input generated by pre-synaptic correlated neuronal populations. Input correlations are characterized in terms of the firing rates, Fano factors, correlation coefficients and correlation time scale of the neurons driving the target neuron. It has been shown [1] that the sum of the pre-synaptic spike trains cannot be well described by a Poisson process. In fact, the total current has a non-trivial two-point correlation function described by two main parameters: the correlation time scale (how precise the input correlations are in time), and the correlation magnitude (how strong they are). Therefore, the total current generated by

the input spike trains cannot be approximated by a white noise Gaussian process in the diffusion limit. Instead, the total current is replaced by a colored Gaussian process with the same mean and two-point correlation function, leading to the formulation of the problem in terms of a Fokker-Planck equation. Solutions of the output firing rate are found in the limit of short and long correlations time scales. The solutions described here expand and improve our previous results [1] by presenting new analytical expressions for the output firing rate for general IF neurons, extending the validity of the results for arbitrarily large correlation magnitude, and by describing the differential effect of correlations on the mean driven or noise dominated firing regimes. In addition, we also study the correlated output spike trains of two neurons receiving independent as well as common sources of Gaussian noise. This formalism [2] describes analytically the Fano factor of the output spike count, the output auto-correlation function and output cross-correlation function of the spiking response of a pair of neurons. These results open the door to the study of spike correlations in neuronal networks and their role in neural processing and information transmission.

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#### P44

##### **Resonant responses to variance modulation in stochastic integrate-and-fire neurons**

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In the stochastic integrate-and-fire (SIF) model, the distribution of membrane potentials is subject to drift, due to the mean input current, and diffusion, due to input variance; the firing rate is determined as the instantaneous probability of crossing threshold. Previous research has shown that when the drift term dominates, the SIF acts like a neural resonator, amplifying fluctuations in the mean input at multiples of the neuron's steady-state firing frequency. Here we show that the SIF also displays two distinct resonances to fluctuations in the input variance. Similar to the resonance for mean input fluctuations, the first "drift resonance" occurs near the steady-state firing frequency and is found only in the drift dominated (regular firing) regime. However, the peak of this resonance occurs at frequencies slightly higher than the steady-state firing frequency. The second "variance resonance" differs significantly from the drift resonance and predominates in the variance dominated (random firing) regime. This resonance has a broader frequency range and peaks at frequencies an order of magnitude greater than the underlying steady-state firing frequency of the neuron.

Because oscillatory input that synchronously activates excitatory and inhibitory neurons is expected to generate disynaptic input modulations of the variance and not necessarily the mean, the variance resonance may play a significant role in modulating oscillatory activity in circuits with a balance of excitation and inhibition.

#### P45

##### **Synchronization of interhippocampal ripple events (80–200 Hz) by long-projection inhibitory neurons**

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Network oscillations between the two hippocampi are highly synchronized. Synchronized theta is believed to be the result of the common input from the septal region, whereas the mechanism of the ripple synchronization is not well understood. It was previously demonstrated using partial coherence analysis that the "coupling" between the two CA1 regions of hippocampi during theta oscillations is stronger than that between the individual layers of the same hippocampus.

Hippocampal sharp wave-ripple complexes occur during slow-wave sleep and awake immobility and are thought to be important for memory consolidation. The delay between simultaneously recorded ripple events from the two hippocampi is remarkably short (1–2 ms). This observation suggests that some sort of fast communication mechanism should connect the two hippocampi. We demonstrate that the simultaneously occurring ripple events in the two hippocampi are highly coherent. This observation suggests an important role of the commissural projections in interhemispheric network synchronization. Using various anatomical methods we demonstrate that a subset of inhibitory neurons (NPY-expressing cells), located in the CA1, CA3 area and dentate gyrus, extensively project not only to the contralateral hippocampus, but also to the septal region. We use model simulations to determine to what extent and under which conditions the highly synchronous ripple events can be produced by long-range intra- and interhippocampal inhibitory projections.

#### P46

##### **Synchronization, multistability and clustering: How useful are predictions from phase models?**

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We consider a model of a network of hippocampal interneurons based on the work of Wang and Buzsáki. We construct a phase

model representation of the network, and show that this model can give reasonably accurate quantitative information, such as the size of basins of attraction and the maximum heterogeneity permissible in the inherent frequencies of the neurons before synchrony is lost. We show that predictions of existence and stability of the synchronous solution from a two cell network carry over to N-cell networks, either exactly or in the limit of large N.

#### P47

##### **The axonal plexus: a description of the behavior of a network of neurons connected by gap junctions**

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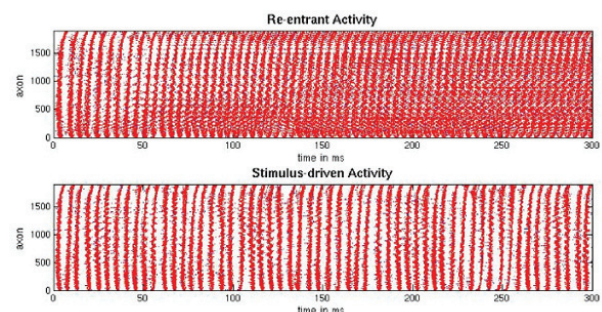
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Putative gap junctions between pyramidal axons have been reported in the hippocampus as well as the neocortex. These gap junctions are indicated in very fast oscillations (VFOs, > 80 Hz) in slow-wave sleep as well as in seizures. They could also play a role in gamma oscillations (30–80 Hz) in the hippocampus and other areas. Computational modeling studies have yielded results consistent with these hypotheses [1, 2, 3].

We explore, in greater detail than in previous studies, the parameter dependence of the dynamics of a random neuronal network with axo-axonal gap junctions. First, we analyze propagation through a network of axons (without somata and dendrites). We vary excitation levels and gap junction conductances, and study regimes of disorderly behavior, stimulus-driven VFOs, and re-entrant VFOs (that is, VFOs that persist after the stimulus is removed). We also show examples of spontaneous (noise-driven) toggling of the network between qualitatively different oscillatory regimes. Second, we add intrinsically bursting somata, and analyze the behavior of the resulting system in light of our study of the isolated axonal plexus. Finally, we discuss links between gap junction dependent activity in the axonal plexus, very fast oscillations, and gamma oscillations.

**Figure 1 (abstract P47)**



**An example of re-entrant VFOs vs. stimulus-driven VFOs.** Each red dot stands for when an axon spiked. Notice the similarity between each wave of activity for the re-entrant VFOs, while each wave is unique for the stimulus-driven VFOs.

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## P48

### Determining the effect of the A-current on the activity phase of a follower neuron in an inhibitory network

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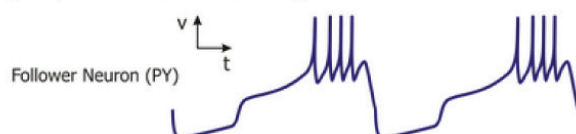
**Background:** The A-current is a transient outward potassium current that is present in most vertebrate and invertebrate neurons. When a neuron is subject to a strong inhibitory synapse, the activity time following the rebound from inhibition can be set by the conductance and kinetics of the A-current. As such, the A-current plays an important role determining the activity phase of neurons in rhythmic networks that involve inhibitory synapses. The precise influence of the A-current in setting the activity of neurons depends on its interaction with the inhibitory synaptic inputs and with other intrinsic properties of the neuron. We examine the role of the A-current in determining the phase of activity of a follower neuron in a rhythmic inhibitory network. Our modeling results are compared with the activity of the follower pyloric constrictor (PY)

neurons in the rhythmically active crustacean pyloric network (Fig 1a). We examine the role of the A-current in a Morris-Lecar (ML) model plus an A-current with instantaneous activation kinetics, resulting in a 3D model with 2 variables ( $v$  and  $w$ ) from the ML system and one variable  $h$  describing A-current inactivation. The response of the model to an inhibitory input from a square-wave presynaptic voltage is shown in Fig 1b.

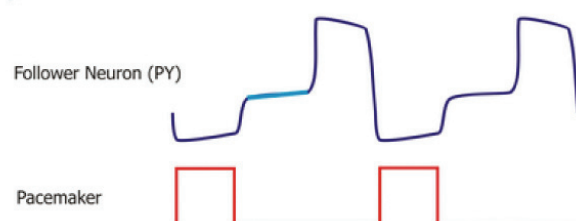
**Results:** We examine the behavior of the model neuron in response to a periodic inhibitory input. After release from inhibition, the membrane potential moves to a "middle state" (light blue line in Fig 1b) where the A-current becomes activated. At this point, the trajectory encounters three possibilities: jumping to the active state, jumping back to the inactive state or staying in the middle state. Using phase plane analysis, we find that the outcome is determined by several factors: the shapes of the ML  $w$ -nullcline ( $w_\infty$ ) and the steady-state activation curve  $m_\infty$  of the A-current, the time constants  $\tau_w$  and  $\tau_h$ , and the inactive duration of the pacemaker. In the  $v$ - $w$  phase plane (Fig 2), the  $v$ -nullcline has a quintic shape in the presence of the A-current and the middle branch represents the middle state in Fig 1. When the trajectory reaches the middle branch, it moves toward the stable fixed point (FP) at a rate determined by the  $\tau_w$ . Meanwhile, the lower knee (LK) of the middle branch moves up as the A-current inactivates ( $h$  decreases). If the trajectory encounters LK (resp. upper knee-UK), it jumps to the active (resp. inactive) state. If the trajectory does not reach LK or UK before the next inhibition phase, it will remain on the middle branch. In the case of Fig 2, FP is located below UK due to the steepness of the  $w$ -nullcline and therefore the trajectory can only jump to the right branch or remain in the middle branch. However, if FP is higher than UK (in the  $w$  direction), it is possible for the trajectory to jump to the left branch if it reaches UK. By following the trajectory in the slow manifold ( $w$ - $h$  phase plane on the middle branch) we

Figure 1 (abstract P48)

#### (a) Experimental Recording

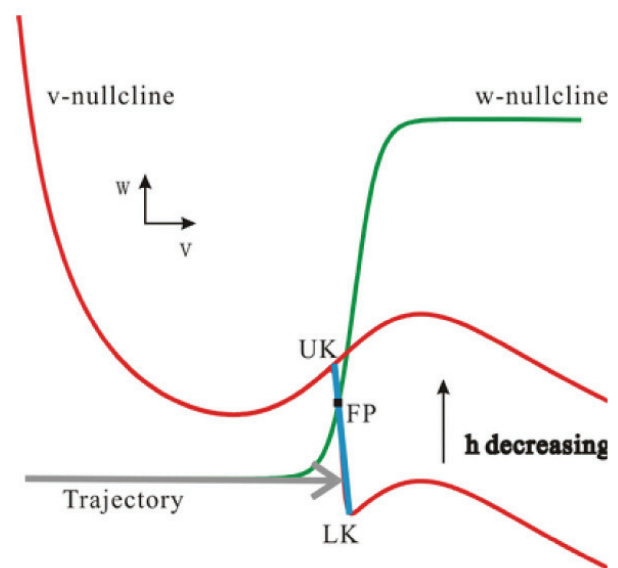


#### (b) Model

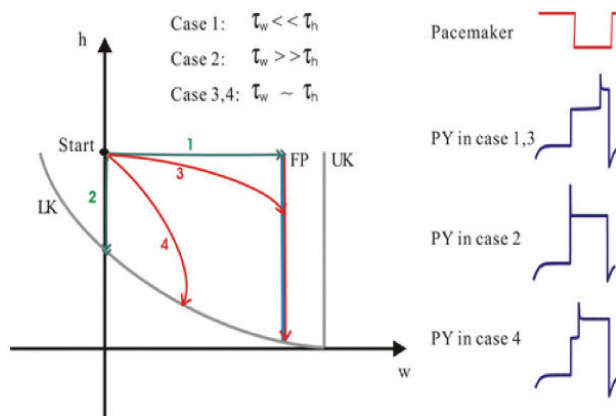


Delay to activity in the follower neuron following inhibition.

Figure 2 (abstract P48)



Fast-slow phase-plane dynamics demonstrating the effect of the A current inactivation.

**Figure 3 (abstract P48)**

The trajectory in the slow phase space.

can determine its fate before the arrival of the next inhibition (Fig. 3). Our results show that, depending on the parameters mentioned, the effect of the A-current can be quite complex and non-intuitive. In particular, for large maximal conductance, the A-current may prevent the neuron from returning to its inactive state even when inhibited.

**Conclusion:** We are able to predict the effect of the A-current on setting the activity phase of an oscillatory neuron as a function of the shapes of  $w_\infty$  and  $m_\infty$ , the values of  $\tau_w$  and  $\tau_h$ , and the inactive duration of the pacemaker.

#### Acknowledgements

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#### P49

##### Model of the regulation of *Drosophila* flight by mechanosensory feedback

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The aim of this theoretical work is to understand how the fruit fly uses sensory input from wings and other structures to be able to quickly maneuver during flight. We capture in the model the qualitative features of flight dynamics that depend on the mechanosensory feedback.

To describe mechano-transduction in the campaniform sensillum, we use a leaky integrate-and-fire neural model. Its excitatory conductance is dependent on strain, corresponding to a mechanically gated ion channel. The parameters of this first part of the model were fixed with the help of previously published physiological data on campaniform receptors, as well as the closely related bristle sensillae.

In a second part of the model we study how the mechanosensory information is used in flight control. The output of mechanoreceptors is coupled to a dynamical model of the activation of control muscles and its effect on the wing motion. As the mechanics of the wing hinge and its reconfiguration by the action of control muscles is not known in detail, we adopt a

highly simplified description of the system. In this part of the model, a nonlinear oscillator, representing the indirect power muscles, is coupled to two linear mechanical subsystems, representing the wing, the sclerites, and the direct control muscles on the left and right sides. Sensory input perturbs the dynamics of the system by altering parameters of the linear subsystems. Motivated by the experimental data of Tu and Dickinson [1], we take the stiffness of the control muscle to depend on the timing of the mechanosensory spike in the previous wingbeat cycle.

Our goal is to capture the dynamics of a saccade, a fast maneuver in the yaw plane. In the model, the saccade is initiated by a strong transient perturbation on the left or right side. (In experiment, this is usually a consequence of an optical stimulus). The saccade then continues until the left and right subsystems are fully phase- and amplitude-synchronized. The synchronization dynamics is driven by the coupling of the left and right subsystems through the nonlinear oscillator, as well as by ipsilateral and contralateral mechanosensory feedback. We analyze the characteristic features of synchronization through these distinct neural and muscular mechanisms, and we compare the predicted courses of a saccade to experimental recordings.

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#### P50

##### How specific is synchronous neuronal firing?

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**Background:** Synchronous neuronal firing has been discussed as a potential neuronal code. For testing first, if synchronous firing exists, second if it is modulated by the behaviour, and third if it is not by chance, a large set of tools has been developed. However, to test whether synchronous neuronal firing is really involved in information processing one needs a direct comparison of the amount of synchronous firing for different factors like experimental or behavioural conditions. To this end we present an extended version of a previously published method NeuroXidence [1], which tests, based on a bi- and multivariate test design, whether the amount of synchronous firing above the chance level is different for different factors.

**Methods:** In order to make a spike rate correction of an observed amount of joint-spike-event (JSE), we define two time scales: 1.  $\tau_c$ , which defines the fine-temporal cross-structure of interest and is equal to the assumed temporal extension of JSE (~5 ms), 2.  $\tau_r$ , which is  $\eta$  times slower than  $\tau_c$  and equal to a lower bound of rate changes ( $\tau_r = \eta^* \tau_c, \eta \sim 5$ ). Using  $\tau_c$  and  $\tau_r$  the chance amount of JSE is derived based on surrogate data. The latter is generated by random jittering of all spikes in each individual original spike train by an amount smaller than  $\tau_r$ . Hence, jittering destroys the fine-temporal cross-structure but



maintains any other properties of each spike train like the full auto-structure and rate co-variation. Next we compute for each trial ( $m$ ) and each factor ( $i$ ) the difference between the amount of JSE in the original and jittered spike train  $\Delta f^{m,i}$ . To assess if  $\Delta f^{m,i}$  is different for different factors, we use a bi- and multivariate test (Mann-Whitney, Kruskal-Wallis).

**Results:** We demonstrate based on toy data that the bi- and multivariate version of NeuroXidence is a conservative and reliable method for detecting modulations in the synchronous firing across different experimental factors. To this end we used various scenarios that had been discussed to induce false positives like rate changes and rate co-variations, low rates and different forms of renewal processes. Furthermore we show results based on simultaneous recordings from awake monkeys performing a short term memory paradigm, that modulations of synchronous firing are correlated to behavior and task conditions.

#### Acknowledgements

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#### P51

##### Opposite role of slow and fast GABAergic inhibition in synchronization and spike timing precision

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**Background:** The firing rate of projection neurons in the insect antennal lobe (AL) increases in presence of picrotoxin (GABA-A antagonist) or CGP54626 (GABA-B antagonist), hence demonstrating the existence of both slow and fast GABAergic inhibition [1]. Fast GABA-A inhibition is known to play a key role in synchronization and spike timing precision. Field potential oscillations and neural synchronization are indeed disrupted when the fast GABAergic synapses are pharmacologically blocked. The role of slow GABA-B inhibition is, however, unclear. On the one hand, spike timing precision increases following in vitro injection of hyperpolarizing current pulses, and higher precision is obtained for pulses of longer duration (see Fig. 4 in [2]). Thus, in vitro experimental data suggest that slow inhibition may enhance spike timing precision and synchronization. On the other hand, in vivo experimental data just show the opposite as spike timing precision increases, instead of decreasing as expected, when the slow inhibition is pharmacologically blocked (see Fig. 4 in [1]). To understand this paradox, we have built a computational model of the insect AL.

**Methods:** Based on previous work [3], our AL model is a network of quadratic integrate-and-fire (theta) neurons coupled with slow (determined by GABA-B receptors) and fast (determined by GABA-A receptors) inhibitory synapses. In this study, we consider a probability of synaptic failure ( $p = 0.5$ ) and three patterns of connectivity: global (all-to-all connections), heterogeneous (random connections with 0.5 probability) and homogeneous (random connections but with the same number of synaptic inputs per cell).

**Results:** Tight synchronization and precise spike timing are obtained (i) when the connectivity is global or homogeneous and the neurons are coupled by fast and slow inhibition without synaptic failure, or (ii) when the neurons are connected by fast inhibition alone, irrespective of the pattern of connectivity and the presence or not of synaptic failure. Asynchronous state and imprecise spike timing are obtained with slow inhibition (i) when the connectivity is heterogeneous or (ii) when the connectivity is global or homogeneous and with synaptic failure.

**Conclusion:** Our results predict that loss of synchronization is attributable to variance in the number of received slow inhibitory synaptic events (whereas fast inhibition is robust to such variability). This variance comes from heterogeneous connectivity or from the presence of synaptic failure, both of them being likely to occur in vivo [1]. In contrast, in vitro injection of hyperpolarizing current pulses, as done in [2], does not present such a variability which explains the apparent contradiction between in vivo and in vitro experimental data.

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#### P52

##### Inferring neural connectivity from multiple spike trains

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BMC Neuroscience 2007, 8(Suppl 2):P52

Recently the temporal coding based on spike timing is one of the hot issues in neuroscience. In the neural network, spike timing depends on the external stimulus and also on the internal network structure. In this study, we propose a method of inferring network connectivity from multiple spike trains. It is based on the phase model description of the spike trains. A continuous phase variable is introduced for each of the spike trains by assigning  $2\pi$  phase for each of the spike intervals and by the linear interpolation. The relative strength of the mutual dependence allows us to estimate the relative strength of the coupling as well as the type of coupling. We report the results of our test on the coupled neural network model and also on the electronic circuit experiment. When compared with the conventional method based on the cross-correlogram, the proposed method is much more effective in estimating the network connectivity. At the same time, the measurement of the effective coupling allows us to estimate the type of coupling.

**P53****Feedback modulation of intrinsic firing dynamics restores feature detection in electrosensory processing**W Hamish Mehaffey<sup>1</sup>, Leonard Maler<sup>2</sup>  
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BMC Neuroscience 2007, 8(Suppl 2):P53

Neurons are almost invariably embedded in complex feedback networks. In order to study the feedback regulation of individual neurons and their ability to accurately code sensory information we chose to examine a simple, well understood feedback network. Specifically, we examine here a simple network based on the known neuroanatomical substrates underlying sensory processing in the weakly electric fish *Apteronotus leptorhynchus*. We consider here a network of 100 biophysically plausible model neurons, embedded in an inhibitory closed loop consisting of GABA<sub>A</sub> and GABA<sub>B</sub> mediated conductances. We have shown previously an interaction between the GABA<sub>B</sub> portion of this inhibitory feedback and the burst dynamics intrinsic to ELL pyramidal cells. By including the intrinsic bursting dynamics we are able to replicate specific *in vivo* results relating to the regulation of bursting by this feedback network, and able to examine the regulation of sensory coding by this feedback. The GABA<sub>A</sub> component of the inhibition is able to create a network mediated oscillation, which significantly deteriorates coding. The GABA<sub>B</sub> component, while unable to ameliorate the interference of the network oscillation, is able to restore the feature detection properties of the individual units such that the ability to accurately detect burst stimuli is improved. This may represent a mechanism for improving the detection of prey-like stimuli in the presence of conspecifics.

**P54****Resonance of coefficient of variation induced by rebound currents for stochastic inhibitory inputs**

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We study a Hodgkin-Huxley type neuron model describing the firing properties of an endogenously oscillating subthalamic neuron [1] incorporating a low-voltage activated (T-type) calcium current when the cell is affected by random alpha function inhibitory inputs (frequency,  $\lambda$ ). The postinhibitory rebound current (parameterized by its maximal conductance,  $G_T$ ) caused by the brief inputs can induce output spikes in response to two or more coincident arrivals or even a single strong enough inhibitory arrival [2]. Thus the output firing sequence becomes random, while the firing rate increases with  $\lambda$ . For small  $G_T$ , the coefficient of variation (CV) of the output spike sequence also increases with  $\lambda$ , but when the rebound is strong, the CV exhibits an unexpected and prominent local

maximum at a preferred input frequency. At the preferred frequency, the firing rate has a maximum slope. Weaker input amplitudes can increase the preferred frequency, but the cell's firing rate, at the preferred  $\lambda$ , is independent of the input strength. This phenomenon may be useful in characterizing and identifying cells [3] that receive complex pattern of inhibitory inputs like those in subthalamic nucleus with T-type calcium currents [4].

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**P55****Phase response curves in the characterization of epileptiform activity**Jose Luis Perez Velazquez<sup>1,2</sup>, Luis Garcia Dominguez<sup>1,2</sup>, Stewart Lo<sup>1,2</sup>, Roberto Fernández Galán<sup>3</sup> and Ramon Guevara Erra<sup>1,2</sup><sup>1</sup>Department of Paediatrics and Institute of Medical Science, University of Toronto, Canada<sup>2</sup>Brain and Behaviour Programme and Division of Neurology, Hospital for Sick Children Toronto, Canada<sup>3</sup>Department of Biology, Carnegie Mellon University and Center for the Neural Basis of Cognition, Pittsburgh, USAE-mail: [jose-luis.perez-velazquez@sickkids.ca](mailto:jose-luis.perez-velazquez@sickkids.ca)

BMC Neuroscience 2007, 8(Suppl 2):P55

Oscillatory coordinated cellular activity is a major characteristic of nervous system function. Recent years have witnessed a surge of interest in the concept that synchronized activity in brain cellular networks plays a crucial role in information processing and behavioural responses. However, adequate frameworks to understand the relation between brain function and behaviour are still underdeveloped. Coupled oscillator theory offers unique avenues to address these questions, as most of the nervous systems can be considered fields of oscillators coupled in different ways. In this study, we focus on the characterization of the dynamics of epileptiform activity, based on some seizures that manifest themselves with very periodic rhythmic activity, termed absence seizures. Taking advantage of this long-lasting periodic activity, our approach consists in obtaining experimentally the phase response curves (PRC), which describe the alteration of the phase due to an input at each point of the cycle, and incorporating these into models of coupled oscillators. To this end, we use a rat model of absence seizures that results from injection with gamma-hydroxybutyric acid (GHB). As a result, very rhythmic synchronized spike-and-wave (SWD) discharges occur in the neocortex and thalamus. Intracerebral recordings are obtained using bipolar electrodes inserted into

the cortex and thalamus. Of 42 rats recorded, 17 were used to estimate the PRC. PRCs were obtained by stimulating either the thalamus or the cortex, and evaluating the alteration (advance or delay) of the oscillation in the cortex or thalamus, respectively. The electrical stimuli used were the minimal that allowed an identification of the stimulating artefact, so that the phase of the stimulation could be calculated, and did not alter profoundly the oscillation. In addition, larger stimulations were tested for their ability to halt the SWD. Only brief (~1 second) stopping (desynchronization) of the SWD was observed in some cases (55%) at large stimulation intensities, phenomenon for which no specific phase of the perturbation was noted. Because these rats have a very low threshold for triggering a SWD, we estimated the instantaneous phase at which a single pulse triggered a seizure, phenomenon which occurred in ~53% of stimulations. Just like in the above case of seizure abortion, no particular instantaneous phase was noted in the pulses that triggered a SWD.

The experimentally obtained PRCs, for the cortex (in response to thalamic stimulation) and thalamus (cortical stimulation) were approximated by a polynomial as well as by a few terms of the Fourier expansion. In our case, these PRCs represent the interaction function between the two oscillators involved in the SWDs: cortex and thalamus. Incorporating these functions into a system of two coupled differential equations representing the time evolution of the respective phases, we are determining the phase preferences of the stationary states and their stability, and these results from the model are compared with the experimental recordings.

## P56

### Customization of coherence analysis by relaxing its iso-frequency constraint

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Coherence analysis is a tool to probe the functional connectivity of two neural oscillators through studying the two signals recorded from them. A sliding window cuts the two signals into a number of corresponding epochs. The power of any given frequency in the two signals can be expressed as a pair of multidimensional vectors. The number of dimensions is equal to the number of the epochs. Coherence of the two signals at that given frequency is calculated as the squared cosine of the angle between these two multidimensional vectors. This style of calculation of coherence is based on the presumption that the functional connectivity of the two oscillators would be demonstrated as simultaneous, linearly correlated wax and wane in the power of oscillation in identical frequencies; but many connected neural oscillators do not exhibit this behavior. An example is the circuitry of Globus Pallidus internus (GPi), thalamocortical relay nucleus (TC), and thalamic reticular nucleus (RE). In this circuit, a four Hz burst activity in GPi

triggers an eight Hz burst in TC under the effect of RE. Therefore, GPi and TC are functionally connected but not in identical frequencies and this aspect of their connectivity can not be demonstrated by the conventional coherence analysis. The present study suggests a customized version of coherence in which the calculation of coherence can be extrapolated to the vectors representing powers of non identical frequencies in the two signals. This extrapolation has been tested on a model of GPi-TC-RE and a peak in the customized coherence between the vector of 4 Hz activity of GPi and the vector of 8 Hz activity of TC has been demonstrated.

## P57

### Stochastic synchrony of neuronal oscillators: a Fokker-Planck study with the finite-element method

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The interest in stochastic processes has increased remarkably in the last few years, in part motivated by the investigation of the constructive role of noise in many biological systems. A quantitative description of these phenomena often requires the solution of complicated Fokker-Planck equations (FPE). Here, we apply an efficient approach from computational engineering, the finite-element method, to numerically solve the Fokker-Planck equation in two dimensions. This approach permits us to find the solution to complicated stochastic problems. We illustrate our method by studying the stochastic synchronization of neuronal oscillators, a phenomenon that has attracted considerable attention in neuroscience recently. In particular, we show that resonators (type II neural oscillators) respond and synchronize more reliably when provided correlated stochastic inputs than do integrators (type I neural oscillators). This result is consistent with recent experimental and computational work.

## P58

### Spike timing dependent plasticity promotes synchrony in inhibitory networks in presence of heterogeneity and noise

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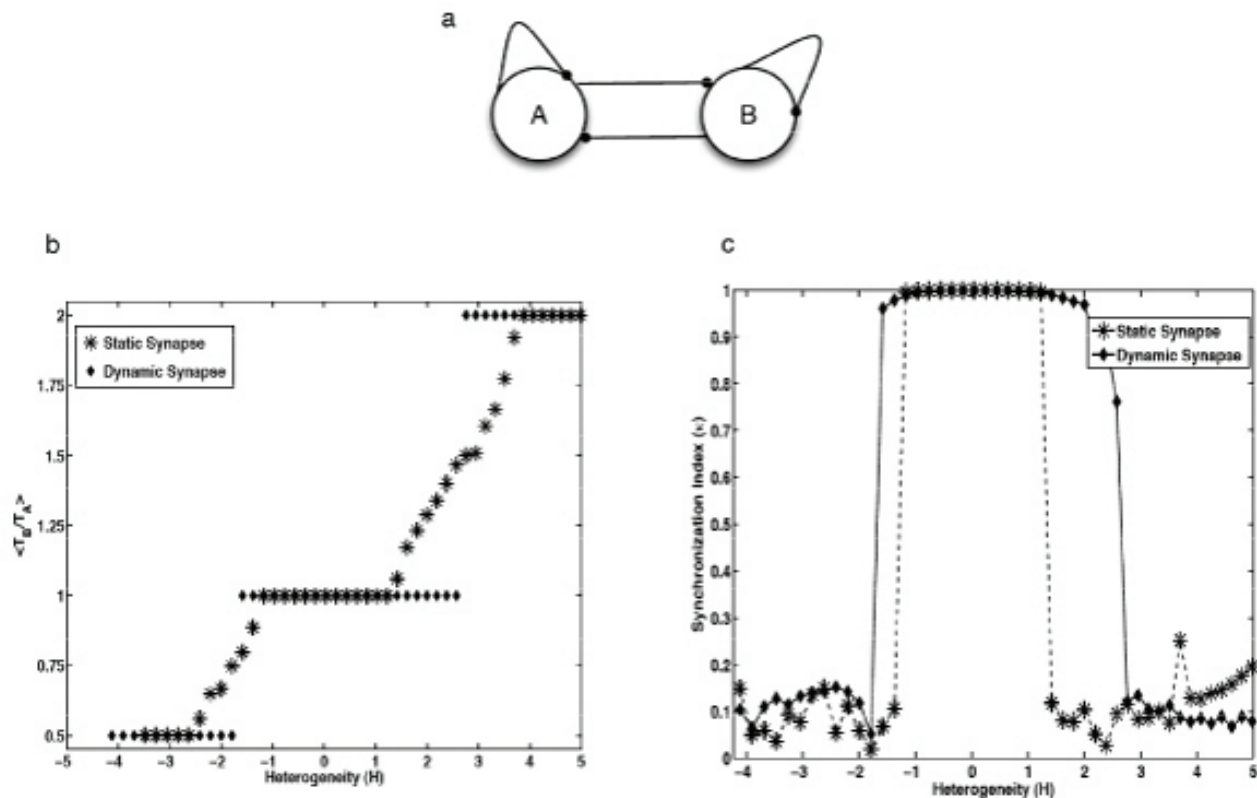
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**Introduction:** Recently a novel form of spike timing dependent plasticity (STDP) was observed in GABAergic synaptic

**Figure 1 (abstract P58)**

**Example demonstrating the enhancement in synchronization of mutually coupled interneurons through spike timing dependent plasticity on inhibitory synapses.** (a) Schematic diagram of reciprocally connected interneurons with self-inhibition. (b) The ratio of average firing period of the two neurons is plotted as function of heterogeneity in intrinsic firing frequency of each neuron. The ratio (diamond) represents a dynamic synapse, where STDP modulates the synaptic strength between the coupled neurons. The ratio (star) represents the situation when the synaptic strength is static. (c) The synchronization index is plotted as function of heterogeneity H for the two cases discussed in (b).

couplings in layer II of the entorhinal cortex. Depending on the relative timing of pre-synaptic input at time  $t_{pre}$  and postsynaptic excitation at time  $t_{post}$  the synapse is strengthened ( $\Delta t = t_{post} - t_{pre} > 0$ ) or weakened ( $\Delta t < 0$ ). Because the observed effect is the largest at  $\pm 10$  ms, the operational dynamic range of the observed STDP rule lies in the higher gamma frequency band ( $> 40$  Hz), a frequency range important for several vital neuronal tasks. In this work we study the influence of this novel STDP of inhibitory synapses on the synchronization of two mutually coupled interneurons (MCI) in the presence of heterogeneity and noise. We demonstrate analytically how this synchronization is brought about by defining the spike response curve (SRC), which measures the nonlinear response of neuron to pre-synaptic input. We present simulation results to demonstrate how the unique features of the STDP increase the robustness of synchronization even in the presence of heterogeneity and noise.

**Results:** See Figure 1.

**Conclusion:** STDP of inhibitory synapses promotes synchrony between two mutually coupled interneurons thereby making it more robust against intrinsic heterogeneity in firing frequency of the coupled neurons.

## P59

### Phase-locking in electrically coupled spiking neurons: the influence of intrinsic properties of neurons

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Electrical coupling between groups of inhibitory interneurons appears to be ubiquitous in the cortex. Because inhibitory interneurons are thought to play a fundamental role in generating cortical oscillations, phase-locking dynamics of electrical coupled interneurons has received considerable interest. A recent experimental study showed that electrically coupled neocortical interneurons have the ability to robustly synchronize over a broad range of frequencies and an inability to phase-lock in anti-phase [1]. How electrical coupling interacts with the intrinsic properties of neurons to generate stable phase-locked states remains unclear. Using the theory of weakly coupled oscillators and phase-response curves (PRC) from both



real and model interneurons, I identify some of the intrinsic properties of neurons that determine the stability of phase-locked states and describe the underlying dynamical mechanisms. In the real and model interneurons that are examined, wide spikes and shallow action potential afterhyperpolarizations promote synchronous behavior; however, this property depends critically on the shape of the PRC. I discuss the combinations of PRC shapes and membrane potential time-courses required for stable synchrony and for stable anti-phase activity. I then use these results as a framework to examine how specific ionic conductances alter stability of phase-locked states.

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#### P60

##### **Eyeblinking dynamics underlying decision-making and responses in Stroop Task**

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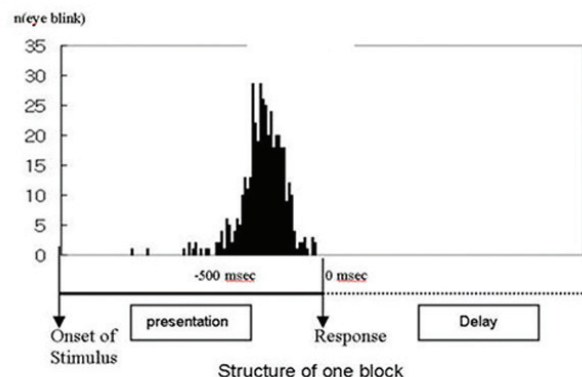
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BMC Neuroscience 2007, 8(Suppl 2):P60

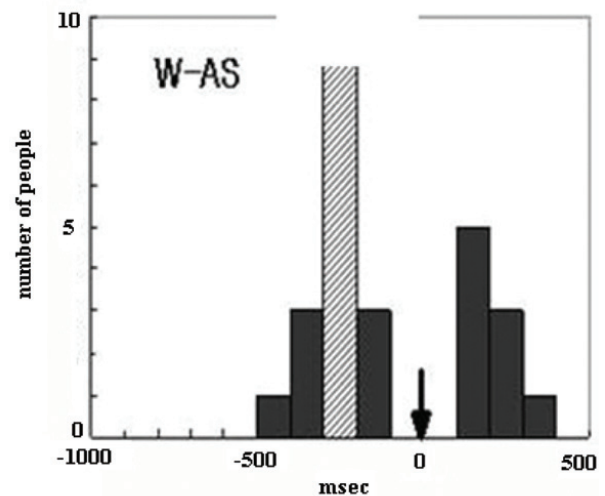
**Background and methods:** The aim of this study was to investigate whether eyeblinking is associated with cognitive process or not by examining the temporal correlation between eyeblink timing and decision-making and vocal response timing in Stroop task. 32 subjects performed the auditory and visual stroop tasks and their eyeblinks were recorded using EMG monitor systems during color naming and word reading in Stroop task.

**Figure 1 (abstract P60)**



**The temporal association between eyeblinks and response time measured from all blocks (total = 480) in a subject.** The average duration for each block was 2,100 msec and the duration between vocal response and stimulus presentation was 500-1,300 msec. The time of occurrence of the successive stimulus after the response was 1,200 msec.

**Figure 2 (abstract P60)**



**The eyeblinking types can be divided into subgroups based on the mean of eyeblink and response for all subjects (n = 32) (W: Word Reading, AS: Auditory Stroop).** '0' indicates the response timing and the bin with oblique lines represents 9 subjects that have a mean value between eye blink and response time of -300 to -200 msec in the corresponding block (total = 120, (-) means eye blink occurs before the response).

**Results and discussion:** The main results are graphically presented in Figure 1 and 2: we found a 100–200 ms delayed synchrony between eyeblink and response timing, indicating that eyeblinks induce the vocal response. A similar association was found in the auditory Stroop task, indicating that eyeblinks were closely related to the cognitive processes rather than visual stimulation. However, the length and difficulty of the stimuli were not correlated with eyeblinks. This study suggests that eyeblink may get involved in mode shifting from decision-making to response.

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#### P61

##### **Dynamical evolution of spatiotemporal patterns in mammalian middle cortex**

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BMC Neuroscience 2007, 8(Suppl 2):P61

**Background:** Neural systems think through patterns of activity. We have recently discovered that in an isotropic preparation of tangential slices of the middle cortical layers of mammalian brain, spontaneously organizing episodes of activity

demonstrate a dynamical evolution: such episodes initiate with irregular and chaotic wave activity, followed by the frequent emergence of plane and spiral waves, and terminate with the recurrence of irregular wave patterns [1].

**Methods:** We have employed techniques drawn from experimental fluid dynamics to better understand these phenomena. In voltage sensitive dye imaging from fields of neurons, we applied an empirical eigenfunction approach, using singular value decomposition (SVD) in both amplitude and spatial frequency domain.

**Results:** The temporal structure of such modes emphasize the crystalline nature of the brain lattice – neurons are fixed in space, and 'wave' activity is a function of the phase relationships of the firing neurons. Calculating the effective dimensionality as in [2] we find that the dynamics tend to concentrate into a small number of dominant coherent modes as these episodes organize, and then disseminate onto a larger number of modes prior to termination. For modes composed of voltage amplitude or spatial frequency, the dynamics of these phenomena show a monotonic and significant decrease in dimension during the middle of the events (ANOVA: amplitude,  $F = 1950$ ,  $p < 0.00001$ ; frequency,  $F = 2058$ ,  $p < 0.00001$ ), and post-hoc Tukey multiple comparison testing confirms that there is a significant decrease in dimensionality during the middle of these episodes.

**Conclusion:** This analysis demonstrates that a key factor in this dimensional evolution is not the appearance of qualitative spirals or plane waves, but rather depends on more subtle features within the interactions of these neurons. Further work to define the relevant order parameters that control the evolution of these spatiotemporal dynamics will lead to a better understanding of cortical information processing.

#### Acknowledgements

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#### P62

##### Mesoscopic model of balanced neuron networks using a Master equation formalism

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Cortical activity in awake animals manifests highly complex behaviour [1]. It is during this regime that the main computational tasks are performed and no model is yet able to explain how this complex dynamics is exploited to provide a fast and accurate information processing. However, many efforts have been devoted to the study of how such activity emerges.

Balanced networks have been introduced as a possible model to generate dynamical states similar to the biological ones [2]. The stability of such states was studied for current-based Integrate-And-Fire (IAF) neurons with respect to external input and excitatory-inhibitory synaptic strength ratio [3]. In particular, stable asynchronous irregular (AI) states with a relatively low level of activity have been obtained. Recently, AI states have

been observed in balanced networks of conductance-based IAF neurons with self-sustained activity [4].

However, no simple description of the network activity dynamics has been developed yet. First-order mean-field approximation fails to describe these networks because of their inherent dynamics which rely dramatically on activity fluctuations. Moreover, the thermodynamic limit is usually performed for randomly connected networks despite the lack of biological relevance.

We introduce here a new framework in which network dynamics as well as inherent neuron behaviour is taken into account. We aim to obtain a reduced description of mesoscopic balanced networks where finite size effects are not neglected. The model is intended to describe AI states far from critical boundaries where long-term behaviours appear. Furthermore, we set the spatial and temporal scales of the model by using biological data. Using the master equation formalism, we derive a second-order mean-field set of ordinary differential equations. The transition matrix necessary in the master equation context is computed based on the Fokker-Plank approach. Conductance-based as well as current-based IAF neurons are constructed. The kernel of this formalism lays in the way activity micro-fluctuations are modelled. We discuss different possibilities and considerations in regard to this question.

This model provides at the same time an extracellular and a sub-threshold description of finite size neuron networks. Once the couplings will be adjusted, it will be possible to build a large-scale model of cortical area with specific architectures, where the fundamental unit is the randomly connected network. We further discuss the possibility to compare large-scale behaviour observed in voltage-sensitive dyes experiments with our model.

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#### P63

##### Cross-correlation based methods for estimating the functional connectivity in cortical networks

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**Introduction:** Identification of the causal relationships between pairs of neurons plays an important role in the study

of synaptic interactions within the nervous system at the population level. The simplest approach uses the cross-correlation function between pairs of spike trains. However, cross-correlograms cannot tell whether the observed peaks or troughs in the correlation function derive from either direct or indirect connections, or result from a common input. This limitation can be partly overcome with the notion of partial correlation or conditional firing probability [1, 2].

**Methods:** Dissociated cortical neurons were obtained from rat embryos and plated into high-density microelectrode arrays (MEAs). Functional connectivity is estimated using cross-correlation based techniques and partial-correlation. To determine a connection, and also its strength, between two electrodes we calculated the area under the highest peak near to zero. Its latency determines the direction in the transmission of information.

**Results:** Cross-correlation based methods measure the direction of a possible connection between a pair of electrodes meanwhile, partial correlation comes out not only with direction but also eliminates indirect connections and gives the real strength between two channels. However, partialization presents some limitations when the number of neurons and connectivity of the network increases. Depending on how big is the network, partial correlation can show unreliable results or even breakdown in the identification of synaptic connections. In this work, we analyzed data obtained from cortical cultures coupled to high-density MEAs and we compared cross-correlation based techniques with partial-correlation analysis.

**Discussion:** Cross-correlation based methods are useful tools to estimate functional connectivity at the population level. Standard cross-correlation is applied just between pairs of electrodes and does not consider the entire network. It is the simplest method to infer about functional connectivity and obtain a general overview of the network map. On the other hand, partial correlation gives more details about the connectivity. Both methods can be used to study the development of the network or changes in the network behavior after electrical and/or chemical stimulation.

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## P64

### Modeling and experiments of small neuronal networks coupled to micro-electrode arrays

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BMC Neuroscience 2007, 8(Suppl 2):P64

**Introduction:** The use of neuronal cultures coupled to Micro-Electrode Array (MEA) is becoming a widely used and

recognized experimental model for studying basic properties of information processing in neuronal systems. On the other hand few models of interconnected neurons are used in conjunction with such devices [1].

In this work, we present a simplified neuronal network made of 60 neurons randomly and synaptically connected. Each neuron is coupled to a microelectrode position, and the network is mapped to reflect the number of recording sites in a MEA. Indeed, the actual number of neurons and connections forming the biological network is much more than those constituting the simplified modeled network. Nevertheless, the simulated architecture is able to account for the neuronal dynamics measured by means of the 60 recording channels. Comparing the model with experimental results, it turned out that the overall dynamics of such large networks can be captured by a reduced (small) neuronal network with proper connectivity. In fact, in actual measurements, we are sampling from a small fraction of the neurons constituting the network and it seems that the behavior of such networks can be replicated by few representatives of them. Additionally, our approach can be also conveniently utilized when dealing with low-density patterned networks or interconnected sub-populations [2].

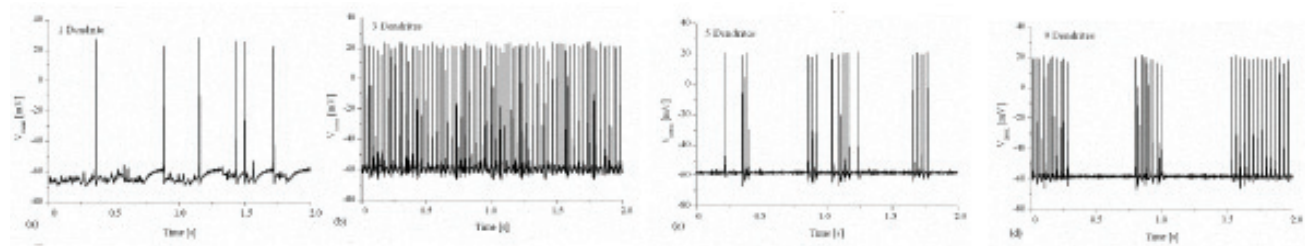
**Materials and methods:** All the simulations were carried out by using the software NEURON and the results were compared to the experimental data obtained in our laboratories. Cultured cortical neurons from rat embryos (E18) were plated over MEAs (from Multi Channel Systems, Reutlingen, Germany). The post-processing analysis both for the simulated and experimental data was performed by custom developed software [3].

**Results:** We developed a model of a bursting neuronal network by using neurons characterized by Hodgkin-Huxley and passive channels that, in their isolated form, exhibit spiking activity. We showed that by changing the complexity of the dendritic arborization and the degree of connectivity of the network (percentage of inhibitory and excitatory synapses), it is possible to switch from a *network spiking activity* to a *network bursting activity*, typical of the mature cortical neuron cultures. The simulated spike trains of one of the sixty neurons of the network, as a function of the morphology of the dendritic tree, are shown in Figure 1. It is evident that in the situation shown in Figure 1a (one dendrite per neuron), a low electrical activity was recorded: that suggests the network activity seems to be ruled by isolated spikes. An increase in the number of dendrites makes the behavior of the network change dramatically: with three dendrites per neuron, the network exhibits tonic activity (Figure 1b) with a high firing rate. At a further increase in the number of dendrites (five or nine), clusters of spikes (bursts) spaced out by silent periods were obtained (Figure 1c and 1d).

**Conclusion:** A simple model of a small-scale network coupled to MEAs is presented. Interestingly enough, network bursting behavior using a biophysical neuron model and proper geometry and connectivity is obtained by using spiking neurons. The model is able to capture the overall dynamic of the network with a reduced number of neurons demonstrating uniform spatial behavior and redundancy in such *in vitro* randomly cultured neuronal systems.

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**Figure 1 (abstract P64)**

NEURON simulations of the spontaneous activity of one neuron of the network as a function of the dendritic arborization.

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## P65

### The representational capacity of cortical tissue

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The ability to make distinctions is one of the fundamental capacities underlying cognition, from perception through abstract (categorical) thought. The distinctions a cognitive system is capable of making, should be manifested in its neural activity. Given a set of distinctions, the natural question that arises is whether this imposes constraints on the activity spaces which could embed such a set. We hypothesize that an activity space can embed a given set of distinctions only if its structure corresponds in some sense to the set of distinctions (that is it does not cause collapse of distinctions or undue elaborations within domains or clusters). Thus, we reason that the homology of an activity space approximates the rough structure of the underlying set of distinctions that is realized by the system's activity. Therefore, we refer to the structure of a given activity space as its representational capacity.

Thus we hypothesize that there will be a disparity in representational capacity between different states of arousal (for example wakefulness as compared to sleep). In other words, that the structure of activity spaces becomes progressively more complex as arousal increases. To test this hypothesis we analyzed voltage sensitive dye imaging [1] data obtained from the primary visual cortex of behaving primates:

1) Instances of activity were registered at different states of vigilance (anesthesia/closed eyes/visual stimulation). We conjecture that what constitutes a state in terms of activity is

similarity (invariance) in the structure of instances of activity. Thus, real (structure sensitive) functions could be utilized to classify activity according to state.

2) The level sets of the typical value corresponding to a state were calculated explicitly within a boundary of from the set of measurements.

3) Finally, the persistent Betty numbers of such level sets, which give the rank of the corresponding homology groups, and the corresponding statistics were computed following [2, 3, 4, 5]. Indeed, it was found that activity is an invariant of state – activity becomes less random, more regularly distributed in space and time, more correlated, and has typical distribution of spectral energy in specific spatial-temporal bands, as arousal increases. These phenomena are very robust and thus allow not only perfect classification of activity according to state, but also noticeable confidence margins. Moreover the representational capacity of the imaged cortical tissue increased with arousal – that is the structure of activity space tends to be more complex as arousal increases.

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## P66

### Dependent multivariate diffusion models and related point process models of ensemble spiking neurons

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The first-passage time of a diffusion process through a constant or variable boundary has been the focus of many stochastic



models of neuronal membrane potential dynamics. Diffusion processes have been used extensively to model a latent process that may only be observable through consequent renewal point process events. The mathematical relationship between inter-spike intervals and the first-passage time of simple diffusion models is well-known, however this relationship becomes increasingly more complex as the diffusion models become more physiologically realistic, and when multivariate diffusion processes are no longer considered to be independent. The probability density of a diffusing particle position at a particular point in time  $P(x, t)$  as defined by the Fokker-Planck equation can be solved, under suitable conditions, using the method of images. We show how the method of images can be extended to a multivariate probability density constructed from marginal densities modeling simple individual spiking neurons using a copula construction that factors out the correlated (dependent) noise structure. This in turn provides a straightforward method for estimating multivariate spike survival and hazard functions from simultaneously recorded single unit activity and, indirectly, the ensemble neuron diffusion noise dependence. The analytical approach is supported by simulated Wiener processes with drift and applied to simultaneous single unit recordings from Heschl's gyrus in awake human subjects. Extensions of this approach to more physiologically realistic diffusion models such as the Ornstein-Uhlenbeck and Feller processes will be discussed.

## P67

### Storage capacity of a superposition of synfire chains using conductance-based integrate-and-fire neurons

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**Background:** It has been proposed that the cortex could be a random superposition of synfire chains, in which waves propagating on the synfire chains account for the majority of the 5 Hz background activity observed in cortex [1]. This proposal is an alternative to other recent models that treat background activity as the stochastic firing of neurons in response to recurrent and external input in a sparse random network [2]. Here we study the synfire superposition model using a leaky integrate-and-fire spiking neuron with conductance-based synapses, along with the incorporation of inhibitory neurons into the chains, to establish whether the model is feasible and consistent with observed neurophysiology.

**Methods:** Storage capacity is analysed in terms of two constraints: spurious spiking rate stability and synfire wave propagation stability. An expression for the (spurious) spiking rate in response to excitatory and inhibitory background input has been obtained using a diffusion approximation [3]. A low spiking rate is achievable with high rates of background input in the regime where the mean of the fluctuating membrane potential is positioned sufficiently below the firing threshold. In this regime, a linear relationship between background input and spurious spiking rate is found. We use this to obtain a limit on the amount of connectivity available to store synfire links such that the

network state of low spurious spiking rate remains stable and below the spiking rate due to synfire waves. For a given level of background activity (5 Hz) this equates to a limit on background input. Next, the minimum pool size for stable wave propagation is obtained for a given level of background input, via single-neuron simulations that determine the probability of firing in response to synfire wave input. This is done for plausible settings of three independent background input parameters (excitatory synaptic conductance, ratio of excitatory to inhibitory input connectivity per neuron, and number of standard deviations of mean potential below threshold). Simulations of wave propagation on synfire chains of varying pool size in the presence of varying levels of background input are used to verify the validity of the minimum pool size calculation. The optimal storage capacity is then found by minimising pool size and maximising connectivity subject to the two constraints.

**Results:** The minimum pool size for wave transmission as a function of background input as obtained by single-neuron simulations was in close agreement with the corresponding synfire chain simulations. High storage capacities in which the number of synfire pools exceeds the number of neurons in the network were found for plausible parameter choices. Cortically realistic levels of reinforced connectivity ( $2 \times 10^3$ – $2 \times 10^4$  excitatory inputs per neuron) were also found. Storage was found to be optimised by a mean membrane potential positioned about 3.5–3.8 standard deviations below threshold.

**Discussion:** The optimal position of the mean membrane potential is due to a trade-off between stability of wave propagation and stability of spurious firing, and is located only a few millivolts below threshold, in accordance with *in vivo* observations [4]. This implies an advantage for conductance-based over current-based synapses in the synfire superposition model: in the latter a much larger standard deviation is found for the same background input level [2] implying a much less favourable trade-off for synfire chain storage.

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## P68

### Bumps and waves in a two-dimensional multilayer neural field model

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**Background:** Neural field models of firing rate activity have played a major role in developing an understanding of the

dynamics of neural tissues [1]. They can be used to model extrinsic optical imaging signals and understand how different neuronal layers contribute to them. A two-dimensional, multi-population approach is therefore required. At a higher level of detail, biological data on horizontal cortical connectivity must be well taken into account. Finally, the spatial resolution of extrinsic optical imaging and biological connectivity studies involving patches of neurons [2, 3] suggest a mesoscopic neural mass approach.

**Methods:** We model a cortical area as a two-dimensional neural field composed of one excitatory and one inhibitory layer of neural masses. It is governed by a four-dimensional integro-differential system that we write as the sum of two terms. The first term is linear and describes the synaptic integration made by the neural masses. The second term is the input feeding a neural mass at a given point of the field. It sums up the contributions of all neural masses in the field by a weighted integral of their instantaneous firing rates. This is done through kernels that include both quantitative ("In which proportion do different types of neurons connect to each other?") and spatial ("How are these connections distributed on the cortical surface?") information between each pair of neuronal types. Neural masses are described by two average variables: the average membrane potential (dendritic compartment) and the average firing rate (axonal compartment), which is obtained from the potential by a Heaviside transformation.

**Results:** We have considered translation invariant, rotationally symmetric connectivity kernels and looked for rotationally symmetric bumps and pulses solutions [1, 4]. For both problems, the analysis falls in two parts: find solutions and check their stability. In the case of stationary bump solutions, expressing connectivities in terms of Bessel functions leads to closed forms depending on the parameters of the model. But not all these solutions are actual bumps and we need sufficient conditions to characterize acceptable bump radii according to other parameters values. A first step is made by writing several local necessary conditions, e.g., the solution must be equal to the threshold of its Heaviside voltage-to-rate transformation on the boundaries of the bump. The same problem arises for traveling pulses solutions. We then check the stability of bumps and pulses solutions to a family of perturbations with separated polar coordinates by reducing the analysis to an eigenvalue problem. Technical computations lead to implicit formulas for the eigenvalues. In the case of bumps it takes the simple form of a second order polynomial.

**Conclusion:** The model we have proposed extends previous related work [1, 4] in two directions: we can deal with several populations of neural masses and perform the model analysis in the framework of a 2D continuum as opposed to 1D. Our analysis raises several interesting biological questions related to connectivity functions that may be answered using optical imaging.

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**tory and inhibitory lateral connections in the visual cortex of the cat.** *Cerebral Cortex* 1997, **7**:605–618.

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## P69

### Relationship between synaptic and functional connections of a local cortical network model

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Synaptic connectivity must have a significant impact on the dynamical behavior of neuronal networks and neural information processing. However, not much is known about the relation between neuronal activity and synaptic connectivity except for networks with simple connectivity, such as all-to-all or random connections. To clarify the issue, we first constructed a computational model of a local cortical network with realistic neuron models and systematically varied synaptic connections in a paradigm of the "small-world" network. Numerical simulations with the model showed spike activities depended on the network topology as well as the strengths of synaptic connections. In particular, the degree of pairwise spike synchrony, spatially distributed, characterizes the network connectivity. Therefore, we next tried to estimate the underlying synaptic structure based on spike data evoked by the model network. We defined functional connections with a measure of the pairwise spike synchrony, the coherence index, to discuss how the topology of the functional connections is related to that of synaptic connections.

## P70

### Single and multiple-spikes traveling wave solutions in integrate and fire neural networks

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We investigate the propagation of the traveling wave fronts in a one-dimensional integrate-and-fire network of synaptically coupled neurons for the case of one, two and multiple spike waves. We use an integro-differential equation characterizing the evolution of the firing times as a function of spatial position to determine the relationship between the speed of the propagating wave and its acceleration. We use the evolution equation to show that for a network of neurons with exponential synaptic connectivity and instantly rising, then

exponentially decaying synapses, the evolution of the propagation is fully determined by the instantaneous speed of the traveling wave front. In this case the history of the firing map determines the initial speed of the transient propagation; the acceleration however depends only on the instantaneous speed, thus greatly simplifying the understanding of the network dynamics. This allows for a clear understanding of the conditions required for propagation failure, as well as of the mechanisms by which sustained transient propagation evolves towards the stable constant-speed traveling wave solution. Expanding the equation for the two and multiple wave cases yields further insight on the mechanisms by which sustained transient propagation evolves towards the stable constant-speed traveling wave solutions. In addition, we show that the wave speed and interspike intervals of the asymptotically stable state depend mainly on the interaction between a few successive wavefronts. It then follows that a unique asymptotical solution is selected from an infinite number of theoretically possible solutions and that this solution is independent of the initial conditions in the neural network.

## P71

### Emergence of reliable spike patterns in models of CA1 cells contacted by unreliable synapses

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Excitatory synapses onto CA1 pyramidal cells fail four times out of five on average, yet the firing of CA1 neuron is elicited at specific phases of the EEG theta cycle with a high degree of precision when a rat is traversing a place field.

We use a multicompartmental biophysical model of several reconstructed CA1 cells, and a model of a stochastic glutamatergic synapse that includes facilitation and depression to study the conditions and properties for reliable and precise CA1 firing. The model of the synapse is tightly constrained by experimental data obtained with minimal stimulations in vitro. Synapses are presynaptically stimulated with CA3/entorhinal spike trains that have been recorded in vivo in the behaving rat. We report that under those conditions, CA1 pyramidal cells are capable of generating precise spike patterns that are theta-modulated. The precise timing of the pattern depends mainly on either the recruitment of high initial probability synapses, or on the recruitment of weaker perisomatic synapses receiving fast bursts of 1–3 presynaptic action potentials. The patterns generated are robust to noise, and contain a marked theta-frequency component, even though the input spikes are not coherent at any particular frequency. We also report that spike patterns may include gamma-like frequency components in part due to the synaptic dynamics, and to the presence of fast bursts in the presynaptic inputs.

We conclude that even though afferent synapses are unreliable, CA1 pyramidal cells are able to generate precisely timed

patterns of spiking that mimic those that are reported in vivo. Our model further predicts that about 400 presynaptic cells are involved in the firing of a single CA1 pyramidal cell when the rat traverses a place field.

## P72

### Principal dynamic mode analysis of hippocampal neuronal networks

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**Background:** Principal dynamic modes (PDMs) are a primary set of basis functions that describes the dynamics of the system. By using PDMs, we attempt to show the differences between the dynamics of the epileptic neuronal network and the normal (non-epileptic) neuronal network.

**Methods:** The input-output data required for training and modeling was acquired from acute slices of the rat hippocampus. A seizure-like state was induced by perfusion with low  $Mg^{2+}$  artificial cerebrospinal fluid. Gaussian white-noise (GWN) was applied as input to CA3 pyramidal neuron and the output was measured from the same CA3 pyramidal neuron. PDMs were computed using the Laguerre expansion technique.

**Discussion:** Computed PDMs of the normal neuronal network confirmed that the two classical modes, integrative and differential modes, are the most dominant modes of the hippocampal neuronal network. As well, higher order modes which are higher in frequency exist and are essential in characterizing the network. In epileptic neuronal network, these higher frequency modes become more dominant over the integrative and differential modes. In addition, the length of memory required to optimally compute the PDMs were increased in epileptic network from the normal network. This suggests changes in the synaptic connections in the epileptic hippocampal network from the normal network.

## P73

### Modelling gap junctions in a neural field model

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We study a nonlinear, one-dimensional neural field model based upon a partial integro-differential equation, that is used to model spatial patterns in working memory. Through the application of Fourier transforms to the PIDE, steady states of spatially localised areas of high activity can be represented by solutions of a fourth order ODE. Recent research has shown a high density of gap junctions in areas of the brain that experience epileptic events. We extend the model by including a diffusion-like term to model gap junctions and derive a sixth order ODE which we use to investigate changes in the dynamics of spatially localised solutions. We find that symmetric homoclinic orbits to a zero steady state exist for a wide area of parameter space. Numerical work shows families of solutions are destroyed as the strength of the term modelling gap junctions increases.



**P74****Realistic synaptic inputs applied to coupled oscillator model of the dopamine neuron**

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Midbrain dopamine neurons are involved in motivation and the control of movement, and have been implicated in various pathologies such as Parkinson's disease, schizophrenia and drug abuse. Dopamine neurons in the presence of their afferent inputs *in vivo* can exhibit one of several firing modes: silence, regular single-spike firing, irregular single-spike firing, and bursting. Bursts in dopamine neurons are thought to convey the reward prediction and salience signals. Dopamine neurons in a slice preparation fire spontaneously in a regular, pacemaker-like manner at a low frequency (~2–3 Hz). This regular firing appears to be driven by a subthreshold oscillation caused by interaction of a low voltage threshold, noninactivating  $\text{Ca}^{2+}$  current and a  $\text{Ca}^{2+}$ -activated small conductance  $\text{K}^+$  current. Somatic injection of depolarizing bias current can increase the frequency of sustained firing only up to 10 Hz before the neurons go into depolarization block. Bursts observed *in vivo* have higher instantaneous frequencies. Two theories have been advanced for how higher frequencies are achieved *in vivo*. One is that during pacemaking, the natural frequencies of the soma and proximal dendrites drive the subthreshold oscillation, whereas during bursting the NMDA input to the dendrites amplifies the current associated with the distal dendritic oscillation, and drives the soma, resulting in high-frequency spiking. The other hypothesis is that the rapidly varying synaptic input (particularly the AMPA component) is not equivalent to a constant depolarizing pulse but this rapid variation can drive faster spiking that can be observed in response to a constant pulse. We have constructed a realistic multicompartmental model to test the contribution of intrinsic and synaptic currents in the dendrites to the firing pattern. The oscillatory dendrites regularize the firing pattern, decrease the frequency compared to a model in which the subthreshold oscillation is confined to the soma, and contribute to grouping of spikes into bursts.

**P75****A self-adaptive burst-detection algorithm**

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A self-adaptive, time-scale invariant single-unit spike train analysis technique is introduced to detect burst firings in neurons. This burst-detection method is an adaptive algorithm that uses the characteristic firing patterns statistics within and between bursts to identify the inter-burst period, intra-burst period and burst duration. Bursts in this self-adaptive method are identified when the inter-burst periods (interspike intervals

between bursts) exceed a threshold for the intra-burst periods (the sum of interspike intervals within a burst). Iterative use of this algorithm can also be used for the detection of finer structure of bursts, i.e., micro-bursts within a macro-burst, independent of the time-scale. By iterative-use of timing statistics of the spike train, this burst-detection technique can identify bursts not only self-adaptively but also independent of the time-scale of the burst-firing pattern. This auto-adaptive algorithm provides a time-scale invariant automated method for micro-burst within a macro-burst when applied iteratively. It succeeds to detect various micro-bursts with minimal *ad hoc* assumptions or criteria about the specific structure of the burst-firing patterns in neurons.

**P76****Revisiting time discretisation of spiking network models**

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A link is built between a biologically plausible generalized integrate and fire (GIF) neuron model with conductance-based dynamics [1] and a discrete time neural network model with spiking neurons [2], for which rigorous results on the spontaneous dynamics has been obtained. More precisely the following has been shown.

- i) Occurrence of periodic orbits is the generic regime of activity, with a bounded period in the presence of spike-time dependence plasticity, and arbitrary large periods at the edge of chaos (such regime is indistinguishable from chaos in numerical experiments, explaining what is obtained in [2]),
- ii) the dynamics of membrane potential has a one to one correspondence with sequences of spikes patterns ("raster plots"). This allows a better insight into the possible neural coding in such a network and provides a deep understanding, at the network level, of the system behavior. Moreover, though the dynamics is generically periodic, it has a weak form of initial conditions sensitivity due to the presence of the sharp spiking threshold [3]. A step further, constructive conditions are derived, allowing to properly implement visual functions on such networks [4].

**Figure 1 (abstract P76)**



A view of the numerical experiments software platform raster-plot output, considering either a generic fully connected network or, here, a retinotopic network related to visual functions (top-left: 2D instantaneous spiking activity).



The time discretisation has been carefully conducted avoiding usual bias induced by e.g. Euler methods and taking into account a rather complex GIF model for which the usual arbitrary discontinuities are discussed in detail. The effects of the discretisation approximation have been analytically and experimentally analyzed, in detail.

#### Acknowledgements

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#### P77

##### Structure of the neuronal interactions underlying human contour integration

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Contour integration is believed to be an important step in human image processing and object recognition, and has been shown to be performed very efficiently by the visual system. However, its neuronal mechanisms are still not well understood. Most contour integration models propose lateral connections between distant orientation columns of similar orientation preference for establishing a so-called 'association field', which links colinearly aligned edge elements into a single contour. However, these models differ both in their dynamics and structure. In some models, afferent input from visual stimuli and lateral input are summed up, in other models these quantities are multiplied. In addition, one finds different assumptions on the range, geometry, and symmetry of the lateral connectivity. It is often assumed that long-range horizontal interactions in V1 serve as the neuronal substrate for the association field. Probabilistic models require unidirectional lateral interactions, linking orientation columns in only one direction, in order to get optimal contour detection performance. In contrast, experimental findings in monkeys rather suggest isotropic connections, spreading symmetrically into all directions from an orientation column.

In order to analyze the range and symmetry of lateral interactions underlying contour integration in the human brain, we compared simulations of multiplicative and additive model dynamics with psychophysical contour detection data. For these investigations

we used stimuli generated from association fields with different geometries. As expected, models detect contours exceedingly well when using the same association field for contour generation and contour detection. However, analyzing the correlations between human behavior and model prediction on a trial-by-trial basis showed that human behavior is reproduced best, when using the same association field for all contour geometries. Furthermore it turned out that a bidirectional association field reaching only to the nearest neighboring edge elements can not explain the correlations found among the responses of different subjects, while a single unidirectional association field can do so. However, when assuming connections up to the next to-nearest-neighbor elements, a bidirectional association field also explains the correlations between human subjects.

The stimuli were designed such that the distance between two neighboring elements lies within the range of long-range connections found in V1. Hence our results allow two possible conclusions: If contour integration relies on horizontal interactions of the spatial range like in V1, a so far unknown unidirectional linking mechanism between neuronal columns is required. If such a unidirectional mechanism does not exist, our results suggest that contour integration is based on interactions on a larger spatial scale as found in higher cortical areas.

#### P78

##### Maximum alternation rate in bi-stable perception occurs at equidominance: experiments and modeling

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We present ambiguous stimuli, such as a pair of superimposed gratings exhibiting bi-stable depth ordering and binocular rivalry stimulus, to human subjects and measure the amount of time each of the two possible percepts dominates the other. Parameters of the stimuli are manipulated in order to strengthen gradually one of the percepts compared to the other, that is, to increase the fraction of time that this percept is dominant. For some choice of the parameters, the two percepts become equidominant: they dominate for the same fraction of time, or, equivalently, their mean dominance durations are the same. When the parameter which controls the strength of the percepts is varied from the equidominance value, its effect on the mean dominance duration for each percept is not the same. For the percept which becomes stronger, the mean dominance duration increases greatly in comparison to its value at equidominance, while for the percept which becomes weaker, the mean dominance duration is only slightly reduced. This result implies that as a function of the parameter that controls percept strength, the alternation rate between the two interpretations reaches a maximum at the equidominance point. We show that these features naturally arise in a bi-stable energy-based attractor model [1] where parameter manipulations produce symmetrical deformations of the energy landscape. Based on this formalism, we construct a two-population

rate-based model with divisively normalized inputs, which produces behavior qualitatively similar to the one observed experimentally. A general class of neuronal competition models which describe rivalry during ambiguous stimulus presentation [2, 3] exhibits the described behavior as well, as long as divisively normalized inputs are introduced. We calculate the entropy of a binary system in which probabilities are equal to the fraction of dominance of each state and show that it correlates with the alternation rate between the states in both experiments and models, suggesting that the alternation rate is a reflection of the uncertainty present in the system due to ambiguous stimulation.

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#### P79

##### Measuring spike train synchrony and reliability

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Estimating the degree of synchrony or reliability between two or more spike trains is a frequent task in both experimental and computational neuroscience. In recent years, many different methods have been proposed that typically compare the timing of spikes on a certain time scale to be fixed beforehand. In this study [1], we propose the ISI-distance, a simple complementary approach that extracts information from the interspike intervals by evaluating the ratio of the instantaneous frequencies. The method is parameter free, time scale independent and easy to visualize as illustrated by an application to real neuronal spike trains obtained in vitro from rat slices (cf. [2]). We compare the method with six existing approaches (two spike train metrics [3, 4], a correlation measure [2, 5], a similarity measure [6], and event synchronization [7]) using spike trains extracted from a simulated Hindmarsh-Rose network [8]. In this comparison the ISI-distance performs as well as the best time-scale-optimized measure based on spike timing, without requiring an externally determined time scale for interaction or comparison.

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#### P80

##### Slow potassium dynamics and seizure evolution

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Seizures involve dynamics on a wide range of temporal scales, from spike times on the order of milliseconds to the large depolarizations seen in single cells that can last several tens of seconds. At the longest time scales, these events modify the cellular environment, altering oxygen, potassium, sodium and other electrolyte concentrations to produce a durable but transient modification of the network dynamics. In order to investigate these slow dynamics we have developed a highly simplified model that monitors the changes in ionic concentrations in and around highly active cells, while disregarding the fast dynamics responsible for action potential generation. We model the time-dependent potassium concentration in and around a cell resulting from flow through voltage-gated channels, pumps, and the surrounding glial network. The flow through voltage-gated channels is determined by time-averaging simulated potassium currents in a Hodgkin-Huxley conductance-based neuron. The current is a function of both intra- and extracellular potassium concentrations and responds to changes in the concentration gradient over a duration that is long compared to the time associated with spiking events. On the other hand, this response time, which can be as slow as a fraction of a second, is still short compared to the lifetime of a network seizure and can be considered instantaneous. Therefore we disregard the response time and approximate the model as a pair of

differential equations which are amenable to a complete phase plane analysis. We report on the results of this phase plane analysis and show comparisons with results from *in vitro* experiments.

## P81

### Structural factors leading to changes in persistent activity following focal-trauma and neurodegeneration

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Considerable research efforts have focused on the molecular mechanisms of epilepsy following trauma and neurodegeneration. In contrast to this cell-centric approach, we present a range of computational network models demonstrating that architectural factors may be critical to understanding seizure susceptibility and other changes in neural dynamics.

The models consisted of large recurrent networks of up to 10,000 spiking neurons that included both inhibitory and excitatory populations with inter-layer and columnar intra-layer connectivity. Layers were toroidal so that initial networks were homogeneous and without edges. We examined the effects of both localized and diffuse cell deletions. In the first case cells were removed at adjacent locations to emulate focal trauma. In the case of diffuse cell deletion we randomly deleted cells throughout the network. In both types of simulations, the properties of remaining cells were held constant in order to establish that changes in dynamics were indeed network-level effects and that the alterations in connectivity were the critical factor in any threshold change.

Simulations in the focal model confirmed that confined alterations in structure were sufficient to change the threshold of an entire network. We found that the lesion site acted both as an initiation point of oscillatory activity as well as a locus that increased the probability that existing waves will continue propagating. The localized deletions models thus demonstrate the possibility that structural factors may be sufficient to account for the focal activity seen in early post-traumatic epilepsy.

The diffuse cell deletions correspond to changes following cell death in aging and neurodegenerative conditions. Here we found that high levels of diffuse deletions (70–90%), representing extensive cell death, resulted in activity settling to repetitive patterns (limit-cycle oscillations). The changes in activity seen in these diffuse lesion models may thus help explain the increased incidence of epilepsy with aging. That is, such seizures may be caused by structural network changes due to age-related cell death rather than pathology in surviving cell properties.

Interestingly, the heterogeneity of connectivity that accompanied lower levels of diffuse deletions (40%) actually encouraged complex persistent activity often associated with healthy cognitive processing suggesting that heterogeneity in structure may play an important

role in initiating and maintaining such activity. It is also notable that shifts in population dynamics took place independently of changes to inhibitory-excitatory balance and did not require complex connectivity assumptions (e.g., small-world networks). That is, the propensity for activity to persist could be varied by structural changes as simple as random deletions.

The findings suggest that structural considerations may be fundamental to our understanding of trauma and age-related epileptogenesis and that we may need to look beyond intrinsic cell properties or inhibitory-excitatory balance in order to identify potential therapies.

## P82

### A simple model of cued T-Maze learning based on basal ganglia anatomy and sequence replay

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I present a simple firing rate neural network model describing how a rat may learn to navigate a cued rewarded T-Maze. The model is based on a realistic approximation to the Basal Ganglia dopaminergic system anatomy including the 'Go' and 'No-Go' channels which project to the thalamus and substantia nigra and their differential feedback modulation by D1 and D2 dopamine receptors at the cortical-striatal synapses. The model includes an input from association layers in cortex or hippocampus where experienced sequences are replayed when the rat finds the reward location, as recently described by Foster and Wilson [1]. The sequence replay creates *task* and *expert* MSN neurons in the striatum with spatial response characteristics similar to those reported by Barnes et al [2] in dorsal striatum and Mulder et al [3] in ventral striatum. The system is able to produce expert neurons in striatum which specifically respond to cues and actions with strengths which reflects the reward predictabilities of the associated cues and actions. Such response modulation by reward predictability is well known in striatum [4]. In addition a simple action selection system is implemented so that the system is able to make a transition from a random choice 'exploratory' phase to a 'goal directed' phase as the learning proceeds. Some behavioural characteristics of the T-Maze learning are thereby reproduced.

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**P83****Shaping of STDP curve by interneuron and  $\text{Ca}^{2+}$  dynamics**

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Spike-timing-dependent-plasticity (STDP)[1, 2] is a special form of Hebbian learning [3] where the relative timing of post- and presynaptic activity determines the change in synaptic weight. More familiarly, the postsynaptic and presynaptic activity correspond respectively to the derivative of the membrane potential  $V_m$  and the NMDA channel activation [4]. We present a model where the postsynaptic activity is modelled by the derivative of the  $\text{Ca}^{2+}$  concentration. Using a model of a pyramidal cell, attached interneuron and detailed  $\text{Ca}^{2+}$  dynamics, we show that the classical STDP curve is greatly altered, in particular, that long term depression (LTD) is markedly reduced [5] while LTP remains close to the original expected weight-change curve. In addition to this we have shown that by reducing the NMDA activity in the circuit model there is a noticeable change in the LTD/LTP magnitude in the STDP weight-change curve. This modification causes two effects; it reduces plasticity in the excitatory neuron but also reduces inhibition on the excitatory neuron. Therefore we show that by decreasing NMDA activity there is a clear reduction in LTD and LTP. This appears much like the "classical" STDP curve albeit scaled down in ratio to the reduced NMDA activity. In this study we have shown that the inhibitory interneuron reduces the LTD part of the STDP weight change curve. The more inhibition seen, the less LTD in the excitatory neuron. Thus, a hypofunction of inhibitory neurons will lead to more LTD in cortical structures and ultimately to less cortical activity. This hypofunction could be a possible mechanism of how administration of the NMDA antagonist PCP causes cortical hypoactivity[6] after a time lapse of a few days, and is already a topic of interest in the research of schizophrenia.

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**P84****Activity-dependent scaling of excitability and its influence on spike timing dependent plasticity**

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Neurons show plasticity in neuronal and synaptic properties due to development and/or learning, affecting both the input levels to the neuron as well as the neural excitability. However, neurons have a limited dynamic range, i.e. the range over which they are sensitive to the input and are not in either a quiescent or a saturated activity state. This suggests neurons possess control mechanisms that match neural excitability and synaptic input levels. Recent experimental studies suggest that neurons indeed show a homeostatic scaling of excitability (HSE) by sensing activity levels and adapting the neural excitability via regulation of specific membrane conductance densities. The maintenance of sensitivity to synaptic input is also central to learning processes. In one form of learning it has been demonstrated that synaptic modification depends on the exact timing of presynaptic inputs and postsynaptic spikes. The performance of this spike timing dependent plasticity (STDP) is expected to be affected by a decrease in the sensitivity of the neuron to its input. At the one hand this suggests an important role for HSE in the functioning of STDP, at the other hand it leads to the question whether HSE could interfere with the learning of input patterns via STDP. Here, we address these issues by using both mathematical analysis and numerical simulations of a neuron that shows HSE and that receives input from synapses showing STDP. Based on experimental results, HSE is implemented as activity-dependent shifts of the input-output function. We use the multiplicative formulation of STDP in which the changes in synaptic strength depend on the synaptic strength itself. We show that while background input levels vary greatly, HSE keeps the neuron within its dynamic range and does not affect the synaptic weight distribution. HSE can also easily compensate for variations in the shape of the STDP learning window and maintain the sensitivity to correlations in the input. However, in neurons without HSE, the sensitivity to correlations in the input depends strongly on the various parameters. The effects of HSE are further explored by examining the neuron response to input patterns. We show that when neural excitability is controlled by HSE, STDP leads to changes of the synaptic weights as a function of the properties of the input pattern, i.e. the number of inputs forming the pattern and the strength of the correlation within the pattern. Learning of a pattern increases the probability of it generating a postsynaptic spike, depending on the properties of the pattern. HSE makes the effect of learning input patterns almost independent of the background levels. The results suggest HSE



does not interfere with STDP and that HSE has a central role in maintaining the learning capabilities of the neuron in its highly plastic environment.

### P85

#### Rate and timing dependent plasticity in a biophysical model of synaptic plasticity

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Activity dependent synaptic plasticity is typically induced by delivering a large number (~1000) of highly regular electrical stimuli, designed to saturate the synaptic strengths. However, natural spike trains typically contain a small number of spikes with variable regularity. We investigate how spike patterns with physiologically realistic spike counts generate plasticity using a standard, biophysical model of calcium-dependent plasticity. We find that for physiological spike patterns, there exists a resonant frequency ( $f_{max}$ ) that induces maximal firing rate dependent potentiation and periodic stimuli produce substantially more plasticity than aperiodic ones. Frequency dependent facilitation (depression) of the synapses does not affect the  $f_{max}$  but increases (decreases) the amount of plasticity; relative change in the amount of plasticity varies with number of spikes. The model combines the rate dependent plasticity with spike timing dependent plasticity (STDP) and shows that the direction of STDP depends both on the number of postsynaptic spikes that a single presynaptic spike is paired with and on the frequency of postsynaptic discharge. We discuss experimental tests of these results, and their functional significance for learning under natural, dynamical conditions.

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### P86

#### Spike-timing-dependent plasticity and temporal input statistics

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A lot of research has recently focused on possible functional interpretations of the peculiar dependence of synaptic plasticity on the relative timing of pre- and post-synaptic spikes. Here we use a linear Poisson neuron to analytically examine how the temporal statistics of the input signals influence the distribution of the synaptic weights. The analysis shows that the outcome of learning is not determined by the shape of the learning window alone, but rather by the convolution of the learning window with the shape of the excitatory post-synaptic potential (EPSP), subsequently referred to as the effective learning window. This indicates that very different learning windows may have the

same functional role depending on the shape of the EPSP. Moreover, it offers a new interpretation of the commonly observed asymmetry of the learning window of spike-timing-dependent plasticity (STDP) as a mechanism for inverting neuronal low-pass filtering as invoked by the EPSP.

For reversible input statistics, the learning rule shows a preference for certain frequency ranges in the input signals. If the symmetric component of the effective learning window has the form of a low-pass filter, STDP focuses on low-frequency components of the input signals, i.e., components that vary slowly relative to intrinsic time scales given by the learning window and the EPSP. This is in line with several learning paradigms that have been proposed as mechanisms for learning invariant sensory representations and for the self-organized formation of visual receptive fields. Moreover, in case the EPSP is short, the effective learning window acts as a band pass filter, leading to the speculation that there could be a connection between cortical rhythms and STDP learning.

Interestingly, it turns out that irreversible input statistics, e.g., causal dependencies between the input signals, tend to destabilize the weight distribution and favor oscillating weights. This observation challenges the interpretation of the asymmetric learning window as a causality detector.

### P87

#### Coincident excitatory and inhibitory spike-timing dependent plasticity potentiates pyramidal neurons

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Spike-timing dependent plasticity (STDP) has been demonstrated separately at both glutamatergic and GABAergic synapses, however the result of both of these synapses undergoing STDP simultaneously has not been examined. Here we investigate how simultaneous STDP of excitatory and inhibitory synapses onto CA1 pyramidal cells alters their probability and timing of spike generation, thus regulating the output of the hippocampus. Using a multi-compartment model of a CA1 pyramidal neuron with excitatory and inhibitory synapses modeled onto the proximal dendrites, we demonstrate that when these synapses are modified by positive coincident (+10 ms) spike-timing dependent rules there is an increase in both the probability of generating an action potential and a decrease in the latency from synaptic input to spiking. Modifying both excitatory and inhibitory synapses with a negative coincident (-10 ms) spike-timing rules decreases pyramidal cell spiking less than if excitatory synapses were modified alone. When excitatory and inhibitory synapses undergo positive coincident spike-timing dependent synaptic plasticity, in the presence of a theta rhythm, there is a decrease in the interval between synaptic input and spiking which advances the spike forward on the theta cycle. Thus simultaneous modification of excitatory and inhibitory synapses alters the probability of spike generation and the precision of spike-timing within the hippocampus.

**P88****How bursting and tonic dopaminergic activity generates LTP and LTD**Adedoyin Thompson<sup>1</sup>, Bernd Porr<sup>1</sup>, Alice Egerton<sup>2</sup> and Florentin Wörgöter<sup>2</sup><sup>1</sup>Department of Electronics and Electrical Engineering, University of Glasgow, Glasgow, G12 8LT, UK<sup>2</sup>Bernstein Center for Computational Neuroscience, University of Göttingen, Göttingen, Germany

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Dopaminergic activity has commonly been interpreted as an error signal in which an increased activity codes a positive error [1] i.e. long term potentiation (LTP), and a decrease in dopamine concentration codes a negative error [1] i.e. long term depression (LTD). Recent experimental evidence in the cortical and sub-cortical areas of the brain [2], propose a different method of generating LTP or LTD by dopaminergic activity. It is suggested that LTP or LTD are controlled not by the quantity, but by the rate of the dopaminergic activity. A model of the sub-cortical nuclei of the limbic system has been shown to implement a process in which learning and reverse learning of reward stimulus associations can be achieved. The following nuclei are implemented: The nucleus accumbens (NAcc), with its sub units NAcc shell and NAcc core and the ventral tegmental area (VTA), which provides a Dopamine (DA) input to the Nacc. During learning, bursting dopaminergic activity will dominate and cause LTP, whereas during reverse learning, tonic dopaminergic activity will cause LTD. This new coding of dopaminergic activity has been implemented in the limbic system circuitry and has successfully been shown to implement a process in which learning and reverse learning of reward stimulus associations can be achieved.

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**P89****Tinnitus-related hyperactivity through homeostatic plasticity in the auditory pathway**Roland Schaette<sup>1,2</sup> and Richard Kempster<sup>1,2,3</sup><sup>1</sup>Institute for Theoretical Biology, Humboldt-Universität zu Berlin, Germany<sup>2</sup>Bernstein Center for Computational Neuroscience, Berlin, Germany<sup>3</sup>Neuroscience Research Center, Charité Berlin, Germany

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Hearing loss through acoustic trauma or administration of ototoxic drugs leads to the development of increased spontaneous firing rates (hyperactivity) in neurons of the auditory pathway. Hyperactivity in the first processing stage, the dorsal cochlear nucleus (DCN), is correlated to behavioral signs of tinnitus, and the distribution of hyperactivity along the tonotopic axis of the DCN corresponds to the patterns of cochlear damage. Recently, we have proposed that the development of

hyperactivity after hearing loss is a consequence of activity stabilization through homeostatic plasticity [1].

We now include inhibitory interneurons in our model to reproduce the basic neuronal circuit of the DCN where projection neurons (PNs) are inhibited by type-II and wide-band inhibitory units. By altering the strengths of the inhibitory connections, we can tune the PN responses to resemble the response characteristics of DCN principal cells like type-III and type-IV responses. We then analyze how the activity of the model neurons is changed by hearing loss through different kinds of cochlear damage. After hearing loss, the mean activity of the model neurons depends on the severity of cochlear damage and the strengths of excitation and inhibition.

In our model, homeostatic plasticity stabilizes the mean firing rate of the PNs by scaling the strengths of excitatory and inhibitory synapses, which also influences the spontaneous firing rate. After hearing loss and homeostasis, the spontaneous firing rate of PNs depends on the type and severity of cochlear damage and on the ratio of the mean to the spontaneous firing rate before hearing loss. Only those PN types where excitation dominates over inhibition become hyperactive. We observe hyperactivity in type-III and type-IV-T PNs, but not in type-IV PNs whose mean rate is close to the spontaneous rate.

Finally, we apply our model to data from tinnitus patients [2] and predict changes in spontaneous firing rates of auditory neurons from the patients' audiograms. Estimates of tinnitus pitch based on the hyperactivity patterns in the model DCN are consistent with observed tinnitus pitch. We conclude that hyperactivity through the action of homeostatic plasticity after hearing loss may be the basis for a tinnitus sensation.

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**P90****Information transmission by synapses with short-term synaptic plasticity**Dmitri Bibitchkov<sup>1,2</sup>, Jin Bao<sup>1</sup> and Erwin Neher<sup>1,2</sup><sup>1</sup>Department of Membrane Biophysics, Max-Planck Institute for Biophysical Chemistry, Göttingen, Germany<sup>2</sup>Bernstein Center for Computational Neuroscience, Göttingen, Germany

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Synapses in the nervous system show dynamic behaviour in the transmission of signals from pre- to postsynaptic neuron. The postsynaptic response can decrease (short-term synaptic depression) or increase (short-term synaptic facilitation) during repeated stimulation. In this study, we formulate the theoretical description of the short-term synaptic plasticity in the calyx of Held and analyze the role of the observed dynamics for the processing of sensory information. Patch-clamp recordings of the pre- and postsynaptic elements of the calyx of Held were performed in rat brainstem slices. Experimental data suggest that the dominating dynamic property of this synapse is synaptic depression, originating from the

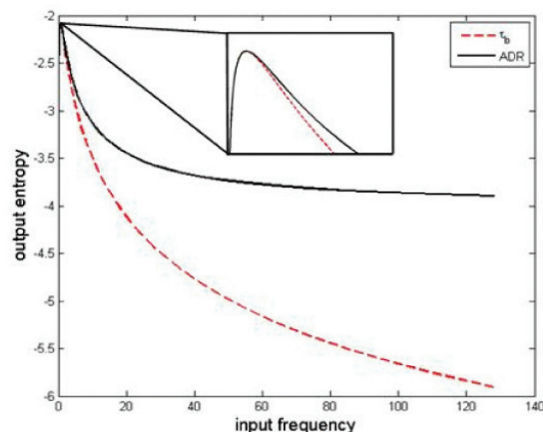
depletion of a vesicle pool by a constant factor with subsequent recovery. The data indicate that the dynamics of recovery cannot be described on a single time scale [1]. The synaptic dynamics can either be modelled as a process with activity-dependent recovery rate [2] or as originating from two releasable pools operating on different time scales [3].

We compared the performance of two models in terms of goodness of fit to the electrophysiological data. While the dynamics of responses during regular spike trains could be well described by both models, the data on the recovery after the spike trains favour the activity dependent recovery model. Using the models based on the experimental data we analyzed the properties of the synapse from the perspective of information theory. From this point of view, a synapse can be seen as a device transmitting information from sender (a presynaptic cell) to receiver (a postsynaptic cell) and transforming singular input events (spikes) into analogue outputs (post synaptic potentials). We calculated the mutual information between presynaptic spike trains and (predicted) postsynaptic responses. We analytically estimated and numerically calculated optimal stimulation conditions (e.g. an optimal frequency range) for temporal information coding for a given set of synaptic parameters. The results show that, when compared to synapses with fixed recovery rates, activity-dependent recovery extends the frequency range, in which the information about the interspike intervals is coded by synaptic responses (see Figure 1). Interestingly, the effective recovery rate as a function of stimulation frequency, estimated from the experimental data, qualitatively agrees with the optimal recovery rate obtained via information theory. We suggest that the activity-dependent recovery can serve as a mechanism for adaptation of synaptic properties to the input statistics and optimization of transfer of relevant information through a synapse.

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**Figure 1 (abstract P90)**



**Information contained in postsynaptic responses of a deterministic depressing synapse about the interspike intervals plotted as function of presynaptic firing frequency.** Solid line: synapse with activity-dependent recovery rate, dashed line: a synapse with a constant recovery time  $t_b$ .

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#### P91

##### **A model of activity-dependent changes in dendritic spine density and spine structure**

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Recent evidence indicates that the morphology and density of dendritic spines are regulated during synaptic plasticity. See for instance a review by [1]. High-frequency stimuli that induce long-term potentiation (LTP) have been associated with increases in the number and size of spines. In contrast, low-frequency stimuli that induce long-term depression (LTD) are associated with decreases in the number and size of spines. Decreases in spine density also occur due to excitotoxicity associated with very high levels of activity such as during seizures.

In this work, we extend previous modeling studies [2] by combining a model for activity-dependent spine density with one for calcium-mediated spine stem restructuring. The model is based on the standard dimensionless cable equation for the changes in membrane potential in a passive dendrite. An additional equation characterizes the activity-dependent changes in spine density along the dendrite. For this continuum model, a typical Hodgkin-Huxley type current balance equation represents the change in membrane potential in an isopotential compartment representing a spine head. Both the cable equation and the current balance equation rely on the spine stem current to represent current flow between the spines and the dendrite. The model also includes equations for activity-dependent changes in the calcium concentration in spines as well as changes in spine stem resistance that depend on the level of calcium in an individual spine. The calcium-mediated changes in spine density and spine stem resistance are based on a conceptual model proposed by Segal et al. [1] where low calcium concentrations lead to spine shrinkage and pruning, an increase in calcium concentration leads to spine elongation and formation of new spines, and significantly higher values cause spine shrinkage and pruning.

We use computational studies to investigate the changes in spine density and structure for differing synaptic inputs and demonstrate the effects of these changes on the input-output properties of the dendritic branch. Moderate amounts of high-

frequency synaptic activation to dendritic spines cause an increase in spine stem resistance, which is correlated with spine stem elongation. In addition, the spine density increases both inside and outside the input region. The model is formulated so that this LTP-inducing stimulus eventually leads to structural stability. In contrast, a prolonged low-frequency stimulation paradigm that would typically induce LTD results in a decrease in stem resistance (correlated with spine shortening) and an eventual decrease in spine density.

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## P92

### Spatiotemporal dynamics of calcium and calmodulin at the spine

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Calcium levels in spines play a significant role in determining the sign and magnitude of synaptic plasticity. Recent experiments using calcium sensitive dyes have allowed measurements of calcium transients in whole spines, however experimental resolution does not allow imaging of the spatial distribution of calcium within the spine [1, 2, 5]. Calcium can activate Calcineurin or bind to CaM and consequently activate CaMKII which is key mediator of synaptic plasticity. A main source of calcium influx into the spine is from the NMDA receptors. There are four different subtypes of obligatory NR2 subunits of NMDA receptors, NR2A/B/C/D. In the mature cortex the majority of the synaptic NMDA receptors are constituted by NR1/NR2A and in the immature cortex by NR1/NR2B. Experiments have shown that the subunit composition of NMDA receptors has an influence on the sign of synaptic plasticity, but different experiments resulted in different and possibly conflicting results [3, 4]. NR2B has slower kinetics and higher affinity for Glutamate than that of NR2A. In addition NR2B receptors have a binding site for CaMKII.

For the study of the spatiotemporal dynamics of Calcium and Calmodulin we implemented a compartmental model of the spine head including the neck. We also simulated an intrinsic calcium buffer and calcium pumps on the surface of the spine. Calcium pumps and as well as NMDA receptors were simulated by Markov models [7]. Using this model we observe the spatiotemporal distribution of calcium and calcium-calmodulin transients. We find that the calcium pumps as well as the geometry of the neck affects the spatiotemporal dynamics of

calcium and consequently of calmodulin, and that different NMDA receptor subunits differentially affect this distribution. Finally, in the past it has been shown that stochasticity of calcium transients can affect plasticity rules [6]. We hypothesize that the main source of stochasticity of calcium transients at the spine arises from the stochasticity of NMDA receptor opening and presynaptic release. We investigate the validity of our hypothesis using a stochastic model for the spine. In that way we compare the calcium and calmodulin dynamics of the stochastic model with those of deterministic and hybrid models.

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## P93

### An efficient $\text{Ca}^{2+}$ based plasticity rule with combined $\text{Ca}^{2+}$ sources

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A number of research groups have proposed generative,  $\text{Ca}^{2+}$  based plasticity models in recent years. Such rules are based on the premise that moderate, above-basal levels of post-synaptic  $\text{Ca}^{2+}$  lead to long term depression (LTD) and that high levels lead to long term potentiation (LTP). We present such a rule and discuss its assumptions and implications.

Our rule has similarities with two models in [1] in that  $\text{Ca}^{2+}$  may enter the post-synaptic density (PSD) through voltage gated channels  $\text{Ca}_v^{2+}(\text{V})$  and NMDA receptor (NMDAR) mediated channels  $\text{Ca}_r^{2+}(\text{V}, \text{NMDA})$ . Unlike Model 1 in their study and the model of the Shouval group [2], our model achieves spike time dependent LTD without the requirement that back-propagating



action potentials (BAP's) have a long tail. Thus, we do not assume this tail is sufficient to expel  $Mg^{2+}$  from glutamate-bound NMDAR's. In our model, LTP and LTD processes are compounded while  $Ca^{2+}$  exceeds LTP and LTD thresholds respectively. We do not use a specific function of peak  $Ca^{2+}$  or the time-integral of pre- and post-synaptic interactions.

The simple formulation of our model makes fewer assumptions about the underlying biology of NMDAR-dependent plasticity than the models in [1] and [2], but our simulations of spike-time dependent plasticity (STDP) experiments show similar output to theirs. For *post-before-pre* spike pairings, depression is graded because the respective time courses of  $Ca^{2+}$  and NMDAR-activation are sufficiently long to interact with one another.  $Ca^{2+}(V)$  is spatially non-specific because it is driven by the BAP, but NMDAR's provide an indicator of pre-synaptic plasticity that interacts with this  $Ca^{2+}$  source. We use NMDAR's in this role for convenience, as other molecules could serve this purpose. This mechanism is similar to Model 2 in [1] where the two  $Ca^{2+}$  sources are separate. Here, the  $Ca^{2+}$  sources are combined to exceed the LTP threshold, resulting in the much-debated LTD window at long-latency *pre-before-post* pairings. Our model points to several mechanisms for experimental study. For instance, spatially non-specific  $Ca^{2+}(V)$  must integrate with  $Ca^{2+}(V, NMDA)$  in the PSD very quickly to produce LTP. Alternatives to rapid integration at the PSD include the possibility that plasticity-inducing processes determine the relative levels of  $Ca^{2+}$  inside and outside the PSD, that  $Ca^{2+}(V, NMDA)$  exceeds  $Ca^{2+}(V)$  by some margin, or that  $Ca^{2+}$ -dependent release from internal stores plays a role in this regard.

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#### P94

##### Induction and binary expression of LTP/LTD in a minimal model of the CaMKII system

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The calcium/calmodulin-dependent protein kinase II (CaMKII) plays a key role in the induction of long-term post-synaptic modifications following synaptic activation. Experiments suggest that these long-term synaptic changes are all-or none switch-like events between discrete states [1]. The biochemical network involving CaMKII and its regulating protein signaling cascade has been hypothesized to durably maintain the evoked synaptic state in the form of a bistable switch [2, 3]. However, it is still unclear whether different experimental LTP/LTD protocols lead to corresponding transitions between the two states in models of such a network. Furthermore, the biochemical mechanisms and signaling cascades giving rise to the non-linearities exhibited during LTP/LTD induction remain elusive.

Starting from a detailed biochemical model, a minimal model describing the CaMKII phosphorylation (activation) level is presented which preserves the features of a comprehensive description. CaMKII autophosphorylation is governed by calcium/calmodulin binding and is a highly cooperative process. CaMKII dephosphorylation is mediated by protein phosphatase I whose activity is indirectly regulated by a calcium-dependent balance of kinase (protein kinase A) and phosphatase (calcineurin) activity. These two competing effects are implemented via phosphorylation- and dephosphorylation rates changing the CaMKII phosphorylation level and are realized as simple step functions activating above different calcium levels.

The model retains previous results [2, 3], two stable states of CaMKII phosphorylation exist at resting intracellular calcium concentrations. With an appropriate positioning of the de-/phosphorylation thresholds, high calcium transients can switch the system from the weakly-(DOWN) to the highly-phosphorylated (UP) state of the CaMKII (similar to a LTP event) and intermediate  $Ca^{2+}$  concentrations can lead to switching from the UP to the DOWN state (similar to a LTD event). As a basic principle, this can be achieved if the CaMKII dephosphorylation activates at lower  $Ca^{2+}$  levels than phosphorylation. This simple approach allows us to address whether or not a read-out system using the calcium level as the sole input signal can account for the non-linearities exhibited during LTP/LTD induction. It is shown that this simple realization of the CaMKII system can qualitatively reproduce experimental plasticity results in response to spike-timing dependent plasticity (STDP) protocols (spike-pairs and -triplets), pre-synaptic stimulation protocols and pairing protocols. Our investigations show that a minimal model of the CaMKII protein network can account for both induction (through LTP/LTD-like transitions) and storage (due to its bistability) of synaptic changes. However, we suggest that the dynamics of the global calcium time course play a crucial role for the sign of synaptic changes alongside the crosstalk between signaling cascades that include the one considered here.

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#### P95

##### A computational approach to dendritic spine motility with calcium signaling by the immersed boundary method with advection-electrodiffusion

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Dendritic spines are small protrusions from the dendritic branches of neurons. Influenced by internal and external signals

and forces, even adult spines are not static but dynamically move. In this paper, we consider actomyosin-based spine motility with calcium signaling. The simulation begins with influx of calcium ions through glutamate receptors. Calcium Induced Calcium Release (CICR) with IP<sub>3</sub> (inositol-1,4,5-trisphosphate) dynamics is also considered. The sensitivity of elasticity of actomyosin network is assumed to follow a Hill-type function of Ca<sup>2+</sup> concentration. Several combinations in size of spine head and neck, physiology of Endoplasmic Reticulum (ER), and distribution of receptor/channels/exchangers are considered. Different functions of a spine as absorber, pumper and/or diffuser are observed. The computational framework used for these studies is the immersed boundary method with advection-electrodiffusion.

## P96

### Long term maintenance of synaptic plasticity via CPEB mediated local translation control at synapses

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The persistent change in synaptic efficacy, which is a basis of long term memory and learning, depends on synthesis of new proteins. The phenomenon of late long-term potentiation (L-LTP), the persistent activity dependent enhancement of synaptic efficacies, is protein synthesis dependent. The main objective of this work is to explore a possible link between activity dependent temporal and spatial regulation of gene expression and life long stability of some memories despite the rapid turnover of their molecular substrates. This work is motivated by the following three experimental observations. 1. L-LTP requires new protein synthesis but not new mRNAs [1, 2]. 2. Some local mRNAs encode proteins which regulate the synaptic functions e.g.,  $\alpha$ CaMKII-mRNA encodes the  $\alpha$ CaMKII, which has crucial role in activity induced L-LTP [3, 4, 5]. 3. Almost all the components of translational machinery are constitutively localized in dendrites [6, 7, 8]. Here, we propose a hypothesis that a molecular loop between a kinase and a translation regulation factor acts as a bistable switch to stabilize activity induced synaptic plasticity over long periods of time. We implement one possible instantiation of such a loop; an  $\alpha$ CaMKII-CPEB molecular pair. Our proposed model of translation regulation is based on  $\alpha$ CaMKII induced phosphorylation of CPEB at synapses which can trigger the cytoplasmic polyadenylation initiated translation of  $\alpha$ CaMKII-mRNA at synapses in CPE dependent manner. We show that  $\alpha$ CaMKII-CPEB loop can operate as a bistable switch. Our results imply that L-LTP should produce a significant change in the total amount of  $\alpha$ CaMKII at potentiated synapses, but that the fraction of phosphorylated  $\alpha$ CaMKII only moderately changes. By carrying out bifurcation analysis we identify the key parameters that determine whether the system is in a bistable region, this could indicate the key parameters that should be measured experimentally. We also demonstrate that a partial block of  $\alpha$ CaMKII translation in the induction phase of L-LTP can block L-LTP, but a partial block of translation in the maintenance phase might not block L-LTP. Our results provide a possible explanation for why the application of protein synthesis inhibitors

at the induction and maintenance phases of L-LTP can have a very different outcome. This proposed molecular switch, based on translation initiated by phosphorylation, provides the mechanistic basis both for persistency and input specificity during L-LTP.

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## P97

### Maintaining phase of the tri-phasic crab pyloric rhythm

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**Introduction:** Synaptic depression is a type of short-term plasticity that is observed in many rhythmically active networks [1]. We examine the role that synaptic depression plays in determining the phase of a group of neurons of the crab stomatogastric nervous system. We mathematically construct and analyze a model network consisting of an oscillator neuron that inhibits two follower neurons. We show that constant phase maintenance can be achieved solely through the interplay

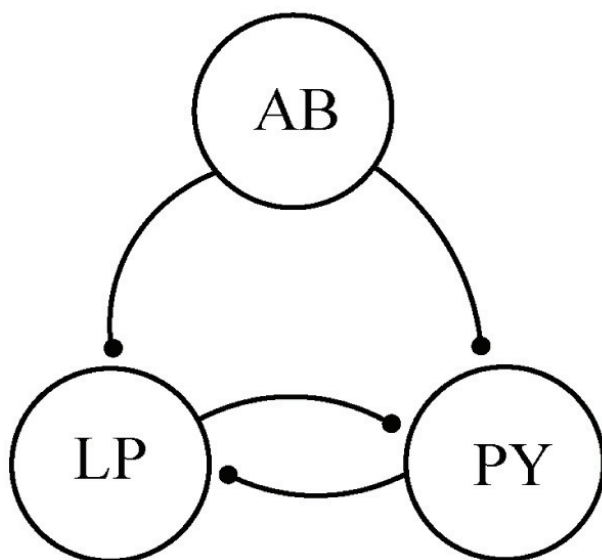
of the two follower neurons due to the depressive nature of their synaptic connectivity.

**Model:** The network we are studying is comprised of three neurons, AB, LP, and PY. AB is the pacemaker neuron of the pyloric network while LP and PY are the follower neurons. The activity of these neurons is modeled using Morris-Lecar type first order differential equations. LP and PY receive synaptic inputs from one another and from AB; see figure 1. The synapses are depressing and inhibitory meaning that the strength of the synapse weakens while the pre-synaptic neuron is active. The set of equations used to model this network is similar in form to that of [2].

**Results and conclusion:** To understand the effect of the depressing synapses between LP and PY, we derived a set of equations that allows us to determine the time at which LP and PY enter their active states relative to when AB enters its active state. This then allowed us to determine which parameters most significantly contribute to the phase of LP,  $\Phi_{LP}$ , and the phase of PY,  $\Phi_{PY}$ . We found that reciprocal inhibition between LP and PY leads to better phase maintenance than when AB is the sole input to these neurons. This occurs because when the reciprocal inhibition is present,  $\Phi_{LP}$  and  $\Phi_{PY}$  are determined mostly by the synaptic properties rather than by their membrane kinetics. In addition, we found that when the input from the oscillator neuron AB is not depressing, the connectivity between LP and PY is in fact able to produce phase maintenance. The essential property necessary to produce this phase maintenance is for the synapses to increasingly recover from the synaptic depression as the period increases. However, phase maintenance is optimal when the synapse from AB is depressing. Furthermore, these analytic results can be compared to experimental data and can be used to make predictions about the biological network in the absence of synaptic depression from the group pacemaker.

#### Acknowledgements

**Figure 1 (abstract P97)**



Crab pyloric network.

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#### P98

##### Modeling TRPC1 mediated slow EPSPs in cerebellar Purkinje cells

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**Background:** Synaptic plasticity in granule cell (GC) inputs to Purkinje cells (PCs) has been a major and ongoing subject of experimental investigation ever since the publication of the Marr/Albus hypothesis of cerebellar learning. It is known that this synaptic plasticity may very well be associated with a slow EPSP through metabotropic glutamate receptors (mGluR) which have been demonstrated to be central to mechanisms for synaptic change in the cerebellum. In PCs, mGluR1 has been studied more thoroughly than any other mGluRs. This excitatory action is through a mixed channel which has inward and outward components. This cation channel has also recently been identified as a transient receptor potential channel 1 (TRPC1, [5]) which can apparently be involved in the prolonged PC responses known as slow EPSPs. This report describes the first effort to model the kinetic effects of these interactions at cellular, channel and subcellular biochemical levels in PCs. This effort is the first stage in constructing an eventual kinetic model of long term plasticity including LTD based on experimental data.

**Methods: Experiment:** Sprague-Dawley rats (14-31 days old, Charles River) were used to prepare cerebellar cortical slices cut 350  $\mu$ m thick in coronal sections. Slices were incubated at either 30°C or room temperature in oxygenated ACSF following standard procedures. Stimulation was delivered using glass electrodes prepared from theta tubes, using a stimulus isolater set to provide stimulation intensity between 5-100  $\mu$ A and with a 2 ms duration. To generate slow EPSPs, five pulses of train stimulation at 100 Hz were given in the molecular layer (ML). In order to study the slow EPSPs that have been shown to result from stimulating GC axons, in some experiments, the ionotropic glutamate receptor antagonist, 2,3-dioxo-6-nitro-1,2,3,4-tetrahydro-benzoquinoline-7-sulfonamide (NBQX, 5  $\mu$ M) was used to block fast EPSPs. After the fast EPSP is blocked, the amplitude of sEPSPs is stimulation intensity dependent and saturated after it reaches 30  $\mu$ A.

**Computational simulations:** Genesis 2.3 was used to simulate the TRPC1 mediated sEPSP. The model was implemented using two distinct parts. The first involved

modeling one dendritic segment, a spine neck, and a spine head. Averaged values from electron microscopic data were used for the dimension of each compartment [4]. The second part was created by Kinetikit under the path/kinetics to model the chemical reactions between glutamate binding, mGluR receptors and the  $G\alpha_q$ -activated TRPC1 channels. The kinetics model was modified from Bhalla and Iyengar [1]. The activation of TRPC1 channels is simulated in the spine head. Upon stimulation, there is an increase in synaptic glutamate concentration. This increase in glutamate concentration activates mGluR receptors which, in turn, increases the amount of GTP-bound G protein. These activated G proteins will activate TRPC1 receptors. In the second modeling step, local model was applied to the whole PC dendritic tree using the whole cell model [2, 3].

**Results:** Voltage clamp data suggested that the current through the TRPC1 channel can result in a somatic response as large as 80 pA. The value can be used together with the time course to guide the simulation in both local and full models. In the local model, about 10 mV voltage response can be generated in the dendritic compartment as a consequence of a 1.5 pA current through the channel of TRPC1. In the full model, the membrane potential is hyperpolarized before the synaptic inputs were delivered at 200 ms. However, a sEPSP similar with the one in the local model was evoked. Since the base line shift was not in the local model, this change must result from the inclusion of the mGluR related processes in spines. Surprisingly, the hyperpolarization continues even after the sEPSP ended around 2 sec. This unexpected phenomenon requires further study. Once the base line is stabilized, the channel kinetics of TRPC1 as tuned so that the somal peak current and time course matched experimental data.

**Conclusion:** The TRPC1 mediated sEPSP is successfully simulated in the local model. An interaction was observed between the kinetic biochemical models and the electrical response of the full PC model that was unexpected and is now under further study. It is likely that a more realistic model is needed to accurately simulate this sEPSP. The current work is the first step towards modeling the long term plasticity in PC synapses which have important implications for cerebellar function.

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#### P99

##### Frequency filtering of vestibular signals by synaptic transmission in brainstem slices

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Frequency-modulated (FM) signals are present in neural systems that are characterized by high discharge rates and continuously-varying stimulus parameters, such as the vestibular system. In the medial vestibular nucleus (MVN) a rate code is used to encode the speed of head rotation and the modulating frequency is equal to the rotation frequency. During rotation in the 1–10 Hz range, many neurons in the medial vestibular nucleus (MVN) have frequency-dependent responses. The role of synaptic processes such as summation and short-term plasticity in the frequency dependence of MVN responses has not been established. Vestibular afferents to the MVN are tonically active in the range of 100 spikes/s, modulated in proportion to head velocity. We asked whether this velocity signal is filtered by synaptic transmission in the brainstem. We found short-term depression and summation of the evoked EPSPs in nearly all MVN cells. Responses to FM pulse trains were dominated by summation of EPSPs, so that membrane potential was approximately sinusoidal during continuous FM stimulation. Responses were highly dependent on the modulating frequency. In the presence of GABA antagonists, postsynaptic potential showed a variety of frequency responses. Long-lasting EPSPs were associated with low-pass filtering of the modulating signal. Short EPSPs were associated with high-pass filtering. Short-term depression resulted in distortion of the sinusoidal response. Modeling using depression and recovery duplicated the form of the responses but failed to simulate the frequency response. We conclude that synaptic transmission between primary afferents and MVN neurons may contribute to frequency filtering in the vestibular pathway.

#### P100

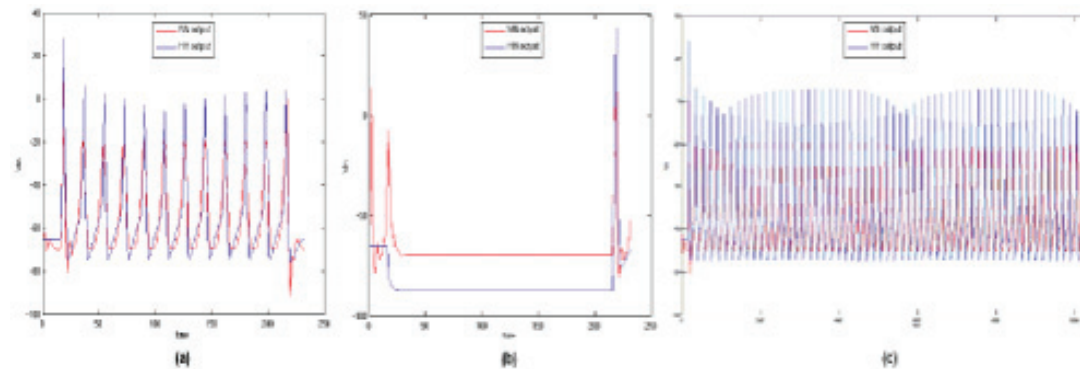
##### Extracting the dynamics of the Hodgkin-Huxley model using recurrent neural networks

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**Overview:** A single biological neuron is able to perform complex computations that are highly nonlinear in nature, adaptive, and superior to the perceptron model. A neuron is essentially a nonlinear dynamical system. Its state depends on the interactions among its previous states, its intrinsic properties, and the synaptic input it receives. Some of these factors are included in Hodgkin-Huxley (HH) model, which describes the ionic mechanisms involved in the generation of an action potential. This paper proposes training of an artificial neural



**Figure 1 (abstract P100)**

Output of the LRN trained with 232 ms of data on a positive step current, tested on (a) the training data, (b) novel test data that consists of a negative step current, (c) 800 ms of previously unseen data that follow the 232 ms of training data.

network to identify and model the physiological properties of a biological neuron, and mimic its input-output mapping. An HH simulator was implemented to generate the training data. The proposed model was able to mimic and predict the dynamic behavior of the HH simulator under novel stimulation conditions; hence, it can be used to extract the dynamics (*in vivo* or *in vitro*) of a neuron without any prior knowledge of its physiology. Such a model can in turn be used as a tool for controlling a neuron in order to study its dynamics for further analysis.

**Methods and results:** To test whether artificial neural networks were able to learn the dynamic behavior of the HH model, four properties of the model were used as testing criteria: thresholding, periodic firing, refractory period, and anode break action potential. Three different neural network architectures were explored: parallel and series-parallel non-linear autoregressive models with exogenous inputs (NARX [1, 2]) and layer-recurrent networks (LRN [3]). All three architectures were able to mimic the behavior of the HH model, provided that they had been trained previously on a similar input. However, among them LRN was the only one that was able to generalize to novel stimuli (Figure 1b). Furthermore, when tested for long-term prediction, LRN outperformed other network architectures by predicting the output for an extra 800 time steps for a positive step signal, although it was trained only once for duration of 232 ms (Figure 1c).

**Conclusion:** This paper shows that ANNs can learn to behave like the Hodgkin-Huxley model of a biological membrane. In the future it should be possible to apply this approach to modeling biological neurons *in vitro*. The main advantage of this approach is that it does not require any prior knowledge of the physiological properties of the neuron. After training is completed, the neural process is encoded within the weights of the ANN used to model the neuron. Several ANN architectures were tested in this task, with the recurrency in the LRN architecture proving to be the best. Online modeling using ANNs can provide the necessary tools for capturing the dynamical state of a biological neuron, simulate its output for further analysis, and may provide a more powerful dynamic clamp and online control. Such mechanisms should prove valuable in understanding the behavior of biological neurons in the future.

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## P101

### Two-compartment models of spasticity in spinal motor neurons following spinal cord injury

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Spasticity is characterized by hyperreflexia, clonus and hypertonic musculature and is an impediment to functional locomotor recovery after spinal cord injury (SCI). It is known that the structure and biophysical properties of motoneurons are altered following SCI; however, the physiological mechanisms underlying spasticity are not well understood. Under control conditions motoneurons can produce plateau potentials, which are sustained depolarizations triggered by brief synaptic inputs. These plateau potentials are mediated by L-type calcium currents and are known to cause bistable behavior in the motoneurons of brain-stem intact animals and humans. This bistable behavior endows motoneurons with a mechanism for translating short lasting synaptic inputs into long lasting motor output [1]. During the acute stage following SCI, rat motoneurons lose the endogenous ability to generate plateau potentials but at chronic stages the plateau potentials reappear [2]. Voltage gated persistent sodium and calcium currents (PICs) have been identified as the cause of plateau potentials in the chronic stage following SCI [3]. In the presence of PICs, a brief stimulus can produce self sustained firing.

**Table 1 (abstract P101) Motoneuron model currents.**

Motoneuron	Soma Channels	Dendritic Channels
Control	$I_{Na}$ , $I_{K-dr}$ , $I_{Ca-N}$ , $I_{K(Ca)}$ , $I_{Leak}$	$I_{Ca-N}$ , $I_{Ca-L}$ , $I_{K(Ca)}$ , $I_{Leak}$
Acute	$I_{Na}$ , $I_{K-dr}$ , $I_{Ca-N}$ , $I_{K(Ca)}$ , $I_{Leak}$	$I_{Ca-N}$ , $I_{K(Ca)}$ , $I_{Leak}$
Chronic	$I_{Na}$ , $I_{K-dr}$ , $I_{Ca-N}$ , $I_{K(Ca)}$ , $I_{Leak}$	$I_{Ca-N}$ , $I_{Ca-P}$ , $I_{Na-P}$ , $I_{K(Ca)}$ , $I_{Leak}$

Two-compartment models with Hodgkin-Huxley type channel kinetics were constructed to mimic motoneuron dynamics for the control case and for the acute and chronic stages following SCI. Table 1 shows the channels used in constructing the motoneuron models.

Experimental data for injected ramp currents and injected pulse currents were used to constrain the model parameters [2]. Computational studies were used to systematically investigate the mechanisms underlying the generation of plateau potentials and the firing properties in the three cases including: the influences of the specific ionic currents, the coupling strength between the somatic and dendritic compartments, and the relative sizes of the two compartments.

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#### P102

##### Broadband coding with dynamic synapses

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Short-term synaptic plasticity (STP) comprises facilitation and depression processes. Although STP can alter the mean value and spectral statistics of the effective input to a neuron from presynaptic spike trains, its functional roles are not clear. In a steady state condition, synaptic depression is generally considered to provide low-pass filtering of inputs, with facilitation providing high-pass filtering. Here, we consider the general case of a model neuron receiving inputs from a population of independent Poissonian spike trains, and show using both analytical results and simulations that dynamic synapses can add or remove (depending on synaptic parameters) spectral power at low frequencies. The implications of these findings are demonstrated when a band-limited-noise rate modulation of the Poissonian spike trains is considered. Information transmission, as measured by the spectral coherence between the rate modulation and synaptic input, does not depend on frequency. This effect is also observed for the coherence between the rate modulation and the membrane voltage of the postsynaptic neuron. In contrast to the prevalent view, in terms of

information transmission, synaptic dynamics provide no low- or high-pass filtering of the input under steady-state conditions. Despite the lack of dependence on frequency, there is a balance between facilitation and depression that optimizes total information transmission and this balance can be modulated by a parameter associated with some forms of long-term plasticity.

#### P103

##### A network model that can learn reward timing using reinforced expression of synaptic plasticity

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Recent experimental results indicate that cells within the primary visual cortex can learn to predict the time of rewards associated with visual cues [1]. In this work, different visual cues were paired with rewards at specific temporal offsets. Before training, neurons in visual cortex were active only during the duration of the visual cue. After sufficient training neurons developed persistent activity for a time period correlated with the timing of reward.

Recurrent connections in a neural network can be constructed to set a desired network time constant that is different from the time constants of the constituent neurons. However, it is not known how such a network can learn the appropriate recurrent weights. A plasticity model that is able to accomplish this must be sensitive to the timing of reward events that, at least initially, occur seconds after the activity in the network returns to its basal level. In order to learn the appropriate dynamics, this network needs to solve a temporal credit assignment problem. In our model plasticity is an ongoing process changing the recurrent synaptic weights as a function of their activity; in the absence of a reward signal this plasticity rapidly decays. External reward signals allow permanent expression of preceding plasticity events, reinforcing only those which predict the reward. As a result, the network dynamics are altered and it develops time constants correlated with the timing of different rewards. As in other reinforcement learning models the reward signal is inhibited by the network activity to produce a stable activity pattern.

We have implemented these ideas in both abstract passive integrator networks and in more realistic integrate and fire networks and obtained results that are qualitatively similar to the experimental results. Further, we examine the implications of different possible biophysical mechanisms and propose experiments to test which specific mechanism are involved.

Support: NSF CRCNS grant number 0515285.

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**P104****Modeling morphological changes in spinal motoneurons following spinal cord injury to explore changes in electrical behavior**Joe W Graham<sup>1,2</sup> and Ranu Jung<sup>1,2</sup><sup>1</sup>Harrington Department of Bioengineering, Arizona State University, Tempe, AZ 85287, USA<sup>2</sup>Center for Adaptive Neural Systems, The Biodesign Institute at Arizona State University, Tempe, AZ 85287, USA  
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**Background:** Following a contusion injury to the spinal cord (SCI), motoneurons below the level of injury undergo significant morphological and behavioral changes. Compared with uninjured controls, SCI motoneurons have a larger soma, fewer and thicker primary dendrites, and less dendritic branching [1]. Behaviorally, SCI motoneurons are more excitable and exhibit altered rhythmic firing and reflex properties [2]. While neuronal morphology and neuronal excitability are linked, to date it is not clear to what extent the morphological changes in motoneurons following SCI are responsible for the altered electrical behavior.

**Methods:** Using the program L-Neuron, two groups (control and SCI) of five morphologically realistic virtual motoneurons were created. L-Neuron “grows” compartmental neuronal models based on a stochastic selection of values from morphological parameter distributions from the literature [3]. The SCI motoneuron input parameters were identical to the control parameters except: mean soma diameter was increased by 18%, mean number of primary dendrites was decreased by 22% and mean primary dendrite diameter was increased by 20% as seen experimentally following SCI in [1]. Morphology of the neurons was then explored using L-Measure [3] and the models were converted into GENESIS format to explore their electrical behavior.

**Results:** The differences in the input morphological parameters resulted in differences in several “emergent” morphological parameters of the virtual motoneuron groups which were also seen experimentally, including: a decrease in maximum dendritic branch order and in the total number of dendritic bifurcations in the SCI motoneurons. Preliminary exploration of the different morphologies in GENESIS indicates that the differences in electrical behavior can be partially accounted for by the changes in morphology.

**Conclusion:** Changes in motoneuron morphology are likely to contribute to changes in motoneuron electrical behavior following SCI. Further exploration and quantification of the role of morphological change in altering electrical behavior will allow a better understanding of the interplay between form and function in motoneurons.

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**P105****Selective neural activation by field sculpting: results from a new computer model for spinal cord stimulation**

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BMC Neuroscience 2007, 8(Suppl 2):P105

**Background:** Technical advancement in computational models can provide not only theoretical tools to improve understanding of the mechanism of electrical stimulation, but also evaluations of new stimulation technologies, such as novel electrode designs, optimal polarity configurations, and stimulation pulse waveforms for neurostimulators.

We report on our development and use of a new computer model [1] to study the effect of various electrode configurations on activation of dorsal column (DC) and dorsal root (DR) neurons in spinal cord stimulation (SCS).

**Method:** A volume conductor model of a low-thoracic spinal cord with single and multiple epidurally-positioned cylindrical percutaneous leads was created using the finite element model tool ANSYS from which the electric field was calculated. The electric field results were then coupled with the NEURON simulator to determine the activated region of spinal cord DC and DR fibers [2]. DC and DR fiber models were adopted from double-cable axon model [3] with various fiber sizes (5.7–15 um diameter).

Using the model, we studied the capability to “sculpt” the electric field using constant current pulse delivery fractionalized across various contacts from multiple leads.

**Results:** In a longitudinal tripolar configuration (anodes placed rostro-caudally around a cathode), a single percutaneous lead on midline had deeper penetration of DC fibers than similar polarity configurations on multiple leads. In contrast, dual leads had mediolateral steering capability to selectively stimulate left vs. right DC fibers. For three leads placed in a symmetric, parallel mediolateral arrangement, anodes can be placed laterally to the cathode with a variable anode-cathode separation and still prevent DR fibers from being stimulated by cathode.

**Conclusion:** Our computational model was able to quantify and provide visualizations of the volumes of activated spinal cord fibers for multiple lead orientations and contact polarities. The ability to determine the neural selectivity of a given electrode configuration and fractionalization of current can provide insight into the therapeutic possibilities of lead placement and programming in SCS.

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**P106****Development of place cells by a simple model in a closed loop context**Tomas Kulvicius<sup>1,2</sup>, Minija Tamosiunaite<sup>2</sup>  
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BMC Neuroscience 2007, 8(Suppl 2):P106

**Introduction:** Experiments on rats show that visual cues play an important role in the formation of place cells. Nevertheless, rats also rely on other allothetic non-visual stimuli such as auditory, olfactory and somatosensory stimuli. Most researchers have seen navigation in the dark as evidence for the importance of path integration as an additional input to place cells. Many place cell models have been developed by combining visual and self motion (path integration) information. However, Save et al. have shown that olfactory cues rather than self-motion information have been used to stabilize the place fields (PF) of rats in the dark [1]. Based on these findings we model place cells by combining visual and olfactory information in a feed-forward network. We also analyze the influence of the directionality of place cells on a goal navigation task.

**Methods:** In a model we develop place cells from external visual and olfactory cues. Sensory inputs as well as place cells are affected whenever the rat navigates in the environment, thus closing the loop. We use a fully connected feed-forward network to create place cells where initially random connection weights  $W$  are used. Features  $X$  derived from visual and olfactory cues are fed to the input layer and the best matching unit (BMU) is found at each time step according to minimal Euclidian distance. We update weights of the BMU by  $W_{t+1}^i = W_t^i + \mu(X_t - W_t^i)$ , where  $\mu$  is a learning rate,  $\mu \ll 1$ . The firing rate of place cells is calculated as the following:  $r_t^i = \exp(-||X_t - W_t^i||^2 / 2\sigma^2)$ , where  $\sigma$  defines the size of the place field. Obtained PFs are used for goal navigation where the model rat had to find the food source by ways of the Q-learning algorithm.

**Results:** An example of PFs is shown in Fig. 1A and we observed that less directional cells were obtained by using visual and olfactory cues as compared to the case where vision alone was used (~13% vs. ~38%). We have also obtained that use of olfactory information increases performance in a goal navigation task where the model rat finds the food source faster if in addition to the visual information olfactory cues are used (see panel B).

**Conclusion:** In this study we have shown that formation of place fields by combining visual and olfactory cues and goal navigation by ways of simple model is possible in a closed loop context. We also emphasize the contribution and benefit of olfactory cues in a goal navigation task.

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**P107****Gating effects along mitral cell lateral dendrites**Thomas McTavish, Larry Hunter, Nathan Schoppa  
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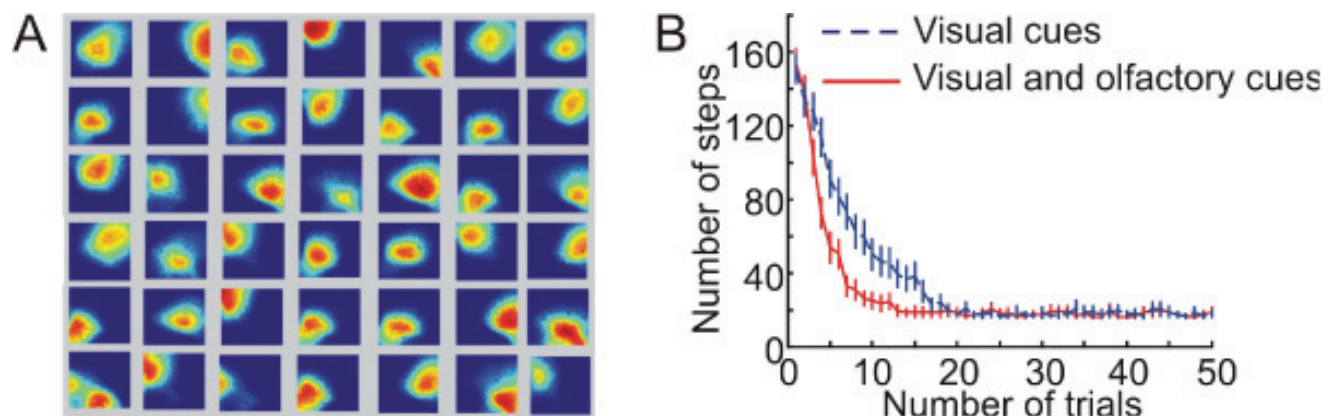
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**Background:** It is generally thought that granule-mitral cell synapses in the olfactory bulb function to inhibit mitral cell firing, and that this inhibition can underlie such functionally important phenomena as lateral inhibition and synchronization [1]. Recent electrophysiology [2] and imaging [3] studies indicate that the location of the dendrodendritic synapse must be close to the soma to impact the mitral cell's firing.

**Materials and methods:** Our objective was to survey the effect of dendrodendritic synapses on firing of pairs of mitral cells sharing a granule cell using a standard, computational mitral cell model [4].

**Results:** We show that depending on the location of the dendrodendritic synapses along the mitral cell lateral dendrite,

**Figure 1 (abstract P106)****(A)** Example of place fields. **(B)** Average number of steps against number of trials needed to find a goal in 100 experiments.



three types of inhibitory effects can be described between mitral cell pairs: 1) A "bidirectional gate" arises when the granule cell induces a discernible inhibitory response in both mitral cell somas. 2) A "unidirectional gate" occurs when the granule cell induces a discernible inhibitory response in only one mitral cell soma. 3) An "inconsequential gate" occurs when the granule cell does not induce a discernible inhibitory response in either mitral cell soma.

**Conclusion:** Preliminary results indicate that most of the lateral dendrite contains unidirectional or inconsequential gates. This is important as most olfactory bulb models effectively treat the mitral-granule dendrodendritic synapse as a bidirectional gate and may need to account for other gating behaviors created by considering the spatial extent of dendrodendritic synapses.

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#### PI08

##### Systematic mapping of neural function to morphology

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The dendrites of neurons in animal brains display a wide variety of shapes and branching patterns both across different animal species as well across different brain structures and cell types within each species. This diversity of dendritic shapes presumably parallels the diversity of dendritic computational functions. Although some function – structure relationships are understood, there is no general insight in how dendritic functions, such as the integration of synaptic signals, are fulfilled differently by different dendritic morphologies. We have previously developed two methods for finding dendritic structures optimized for a given computational function ([1] and [2]). Both methods implement a recursive algorithm that represents dendritic morphology in a compact manner, by an L-System as in [3]. Then, Genetic Algorithms (GAs) are used to find L-Systems [2] or its parameters [1] so that the resulting dendritic morphology fulfills a certain computational function chosen by the user. Dendritic function was assessed using multi-compartmental models using NEURON [4].

We have previously shown that this method can reliably find dendrites that sum synaptic potentials linearly [1, 2] or react

preferentially to one temporal order of synaptic inputs [1]. Here, we first improved this method in order to generate more realistic neural morphologies. Then we used it to systematically explore the mapping of dendritic function to structure. In particular, we investigated the trends in dendritic shapes when neurons were optimized to react preferentially to the temporal order of synaptic inputs, with a range of interval times ( $\Delta t = 2, 4, 8, 16, 32, 64$  ms). As previously observed, the optimized neurons had two sets of dendrites carrying the synapses activated 1<sup>st</sup> and 2<sup>nd</sup> in the preferred temporal order. A systematic, but non-linear, trend emerged in the properties of the two sets of dendrites in the electrotonic length, number of synapses and differential filter properties when  $\Delta t$  was varied. We have thus established a mapping from one axis of function space onto the space of dendritic morphologies.

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#### PI09

##### The Blue Brain Project: building the neocortical column

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The Blue Brain Project is an attempt to reverse-engineer and model the neocortical column, to explore how it functions and to serve as a tool for neuroscientists and medical researchers. The project integrates physiological experimental databases, analysis tools, modeling applications, simulation software and 3D interactive visualization to provide a rich environment for the systematic study and calibration of the model to experimental data. To construct the column, electrical models of neurons are first generated from a combination of gene expression, ion channel, cell morphology and electrophysiological data. These models are then placed according to physiological data that constrains the volume constraints, composition and connectivity of the cortical microcircuit. Finally the column is simulated and calibrated in an iterative process to integrate multiple levels of experimental data. This process provides a data-driven modeling framework for large-scale realistic simulations that incorporates many levels of physiological detail and can be extended to capture a wide range of experimentally-observed phenomena.

**PI10****The Blue Brain Project: calibrating the neocortical column**

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The Blue Brain Project is an attempt to reverse-engineer and model the neocortical column, to explore how it functions and to serve as a tool for neuroscientists and medical researchers. In order to achieve the goal of automatically fitting models to the latest data from clearly defined sources, a series of calibration steps have been developed. Each calibration step includes a physiological database, analysis technique and comparison to model data. All data is scored for completeness and quality. The aspects of the neocortical model for which calibration steps have been implemented are: the volume and composition of the column, ion channels, single cell electrical behavior, morphology repair and cloning, synaptic properties, short- and long-term plasticity, synaptic integration, polysynaptic loops, touch detection, structural and functional connectivity and emergent phenomena. The result of the calibration process is a score indicating the overall precision and quality of the fit. This system provides a means to identify those areas which require additional biological data as well as those areas where the model is biologically accurate or in need of refinement. The calibration process will continue to develop, as further biological details become known, and guide the refinement of the neocortical column model.

**PI11****Physical interactions between D1 and NMDA receptors as a possible inhibitory mechanism to avoid excessive NMDA currents**

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Coactivation of N-methyl-D-aspartate (NMDA) and dopamine (DA) receptors generates a potentially feed-forward system that could lead to excessive NMDA currents [1]. Through second messenger systems, activation of NMDA receptors increases the presence of the D1 subtype of DA receptors in dendritic spines in striatum [2]. Likewise, activation of D1 receptors increases the number of NMDA receptors in synaptic regions in striatum [3, 4]. Given the potential contribution of NMDA receptor activation to apoptosis, there must be some mechanism to limit the expression of NMDA currents. This mechanism is not yet currently known, however. Cepeda and Levine [1] have suggested that physical interactions may serve as a limiting mechanism to this positive feedback system. It is known that

physical interactions between D1 and NMDA receptors may lead to formation of D1/NMDA complexes and may inhibit NMDA currents [5]. We use both dynamical systems and agent-based modeling techniques to investigate whether such physical interactions are sufficient to generate a stable fixed point for NMDA current levels or, more generally, to bound NMDA currents.

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**PI12****Computational simulations of dopaminergic varicosities suggest two sources of DOPAC rather than two populations of dopamine storage vesicles**

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BMC Neuroscience 2007, 8(Suppl 2):PI12

Results from several different experimental paradigms have been interpreted as supporting the concept that two populations of dopamine storage vesicles exist in the nerve terminals of dopaminergic neurons. The goal of this work is to develop a computer simulation model of a dopaminergic varicosity that provides a plausible quantitative description of these populations and a possible set of rules for dopamine movement between two populations of vesicles. We first looked at how well a one compartment model provides accurate simulations of published experimental data. The model allocates dopamine among three compartments: vesicles, cytosol, and extracellular. Dopamine moves from vesicles to extracellular (exocytosis), extracellular to cytosol (dopamine transporter), and from cytosol to vesicles (vesicular monoamine transporter). Synthesis of new dopamine molecules occurs in the cytosolic compartment, with new dopamine entering that compartment. Metabolism of dopamine also occurs in the cytosolic compartment, with a fraction of the dopamine in that compartment being metabolized to DOPAC. With appropriate values for all rate constants, this model successfully explains all data purportedly

supporting two populations of storage vesicles in paradigms that stimulate dopaminergic neurons at rates much faster than physiological. However, this model does not explain other data that support the two populations of vesicles concept. Models with two storage vesicle compartments were evaluated for ability to explain these data; however, none were successful. An alternate model was developed from the one storage compartment model but with the addition that the dopamine synthetic process has a branch point where newly synthesized dopamine is either secreted to the extracellular space or converted to DOPAC, which is deposited into the cytosolic compartment. This model successfully explains data regarding the specific activity of dopamine and metabolites after injection of labeled tyrosine into the varicosity, dopamine metabolite kinetics after inhibition of dopamine synthesis, and preferential secretion of newly synthesized dopamine. Thus, our model suggests that dopaminergic varicosities have two sources of DOPAC, one likely associated with mitochondria and the other associated with the dopamine synthetic complex.

### P113

#### Computational model of a modulatory cell type in the feeding network of the snail, *Lymnaea stagnalis*

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**Introduction:** Realistic mathematical models of single neurons are significant in assessing the contribution of specific ionic

conductances to neuronal excitability. This study presents a detailed computational model of the Cerebral Giant Cells (CGCs), a pair of serotonergic neurons in the feeding network of *Lymnaea stagnalis*, which are critical for the expression of motor behaviour (feeding) and the formation of long-term memory.

**Methods:** First, we fitted a single-compartment, Hodgkin-Huxley model of the CGCs to two-electrode voltage- and current-clamp data [1] using a combination of linear and non-linear least-square fitting techniques. Then, we selectively blocked each ionic current to assess its role in the model, thus mimicking the application of pharmacological agents in the biological neuron.

**Results:** The model replicates accurately the shape of the action potentials and the tonic firing (~0.74 Hz) of the biological neuron (Fig. 1A). A persistent sodium current  $I_{NaP}$  and a transient low-threshold calcium current  $I_{LVA}$  keep the neuron spontaneously active (Fig. 1Bi, ii). A transient potassium current  $I_A$  regulates the interspike interval, while a transient high-threshold calcium current  $I_{HVA}$  increases the duration of each spike (Fig. 1Biii, iv). Transient sodium and delayed rectifier potassium currents are responsible for the depolarizing and repolarizing phases of the action potential, as in the classical Hodgkin-Huxley model. The available experimental data [1] are in agreement with these conclusions.

**Conclusion:** The model we have developed here provides an accurate description of the CGCs at the biophysical level and it is a useful tool for studying the electrical properties of these important modulatory neurons.

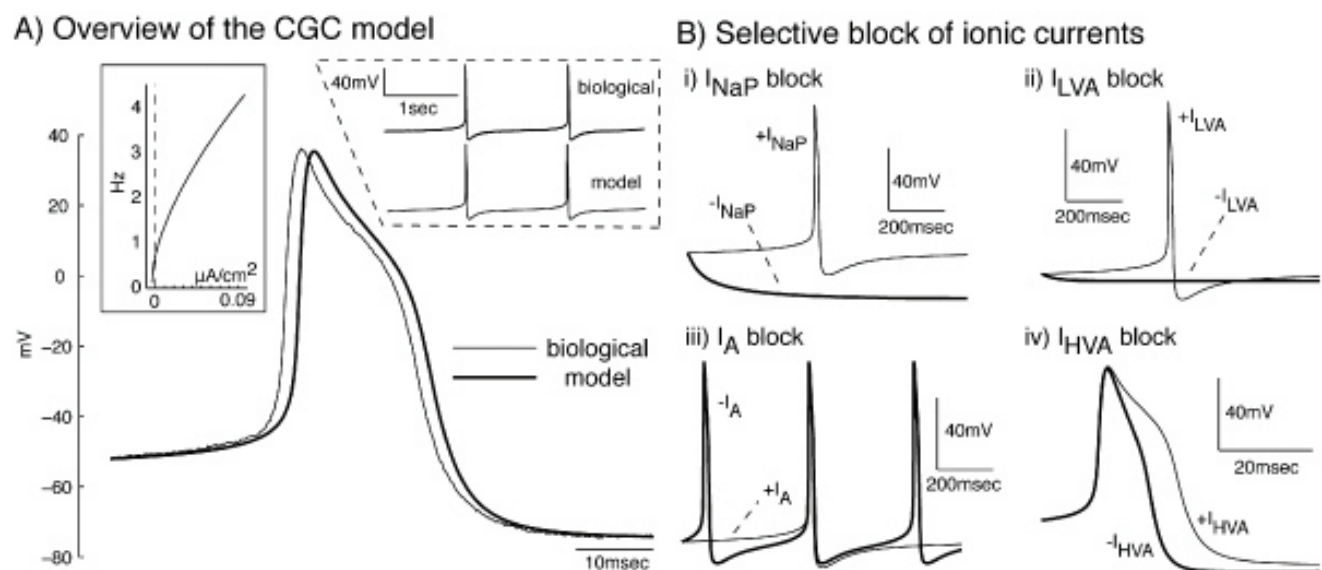
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Figure 1 (abstract P113)



**Overview of the CGCs model and the contribution of specific currents to neuronal excitability.** In A, the model has been shifted to the right by 2 msec compared to the biological action potential.

**P114****Sodium gating capacitance and the optimization of the squid giant axon for metabolic energy usage**

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BMC Neuroscience 2007, 8(Suppl 2):P114

**Background:** In previous work [1, 2], we observed that the ionic fluxes during an action potential (AP) in the squid giant axon can be divided into three functionally separate components. Of these, the component responsible for the depolarizing phase of the AP, and hence its velocity, attains a minimum as a function of the ion channel densities and the axon diameter very near the experimental values of these parameters when the AP velocity is constrained to be at a single value. Since the ion channel fluxes are proportional to the metabolic energy consumption via the ATPase  $\text{Na}^+/\text{K}^+$  exchanger, this suggests that evolution, subject to an external constraint on AP velocity, has optimized ion channel densities and axon diameters for the energy associated with the velocity. The energy minimum is close to, although not identical with, a similar minimum in the total membrane capacitance. The total capacitance consists of the intrinsic membrane capacitance (about  $0.88 \mu\text{F}/\text{cm}^2$ ) and a term proportional to the active  $\text{Na}^+$  channel density (about  $1 \text{ nF}/\text{mS}$  of  $\text{Na}^+$ ), the so-called sodium "gating capacitance," which arises from movements of charged segments of the  $\text{Na}^+$  protein during conformational changes. In the present work, we investigate and resolve the discrepancy in the locations of the energy and membrane capacitance minima.

**Methods:** The Hodgkin-Huxley squid giant axon model was simulated using NEURON and NMODL. The axon diameter and the ion channel densities were taken as two independent parameters, with the channel densities (consisting of voltage-gated  $\text{Na}^+$ , voltage-gated  $\text{K}^+$ , and nonspecific leak channels) varied by a common factor and parameterized by the maximum sodium conductance. Note that this also necessitated varying the sodium gating capacitance by this factor. Constraining the

velocity to be at a single value, we determined how the shape and height of the action potential varied along the resulting isovelocity curve.

**Results:** Our results are summarized in Figure 1. All quantities are plotted on the 21.2 m/s isovelocity curve in axon diameter-channel density phase space. The amount of charge per unit axial length on the membrane capacitor at the peak of the action potential is  $q_p = c_m V_m^{\text{peak}}$ , where  $c_m$  is the total membrane capacitance per unit axial length. This charge is approximately equal to the total depolarizing charge crossing the membrane during the action potential, and hence is proportional to the metabolic energy. Since  $V_m^{\text{peak}}$  increases with the ion channel densities, values of  $c_m$  further to the right are more heavily weighted in the product  $c_m V_m^{\text{peak}}$ . This causes the minimum in the charge and energy curves to be further to the left than in the  $c_m$  curve alone.

**Conclusion:** The discrepancy between the locations of the energy and capacitance minima is resolved by considering the amount of charge placed on the membrane capacitor at the peak of the action potential. The AP peak-height rises with the ion channel densities, and therefore, the ion flux per unit membrane surface area across the membrane and the associated metabolic energy also increase. When this increase is taken into account, the location of the net charge minimum is at the same channel densities as the depolarizing energy minimum. This also illustrates that energy, rather than capacitance, is what evolution has minimized.

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**P115****A computational study of factors in the evolution of myelin**

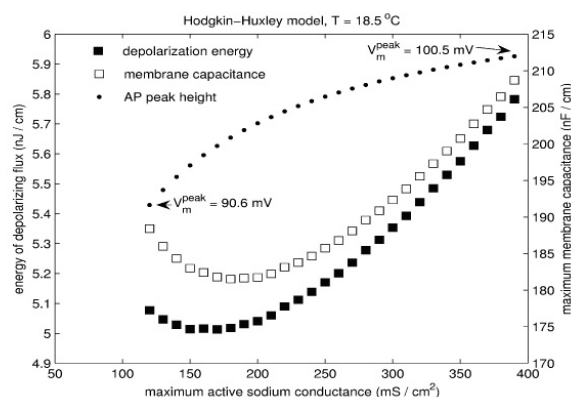
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Myelin is a multilayered, lipid-rich coating of axons that increases the conduction velocity of nerve impulses, contributes to compact nervous systems, and reduces metabolic costs of neural activity. Although usually thought of as a vertebrate adaptation, functionally identical myelin sheaths have evolved in several invertebrate lines. To gain insight into the possible factors in its evolution in the different lines, we undertook a modeling study of different configurations of myelin ensheathment and its physiological parameters. Based on the hypothesis that increased impulse conduction velocity provides a selective advantage that drives the evolution of myelin, we focused on parameters that speed nerve conduction. The myelin sheath was modeled with several levels of complexity using the NEURON simulator, ranging from approximating the effect of myelination by changing the specific capacitance ( $C_m$ ) of a uniform cylindrical axon to a double cable model that represented the axon and

**Figure 1 (abstract P114)**

Action potential peak height, depolarization energy and membrane capacitance as functions of sodium conductance.



myelin sheath separately using NEURON's extracellular mechanism. Simulations were performed on a sequence of plausible intermediate stages of myelin evolution from the apposition of membrane from adjacent glial cells to a single layer of myelin surrounding the axon to multiple myelin wraps with well-organized nodes. At each stage the effects of the model parameters on conduction velocity were assessed. We found that a relatively small amount of myelination, even partial coverage by a single layer of glial membrane, produced a substantial increase in conduction velocity. For example, the addition of one myelin wrap (2 membranes) to a small (2 micron) diameter axon resulted in a 70% increase in conduction velocity, suggesting that a substantial advantage of myelin could be available to the earliest stages in myelin evolution. For the double cable model, conduction velocity increased more rapidly with increasing myelin wraps for larger diameter axons. This suggests that in the transition to a myelinated nervous system, it is large diameter axons that become myelinated first.

#### Acknowledgements

This study was supported by NSF OCE 04-51376 and by grants to the Békésy Laboratory of Neurobiology from the Cades Foundation.

#### P116

#### Differences in biophysical properties of nucleus accumbens medium spiny neurons emerging from inactivation of inward rectifying potassium currents

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BMC Neuroscience 2007, 8(Suppl 2):P116

**Background:** Nucleus accumbens medium spiny neurons display a two state membrane potential controlled by active channels and synaptic input. Inward rectifying potassium ( $K_{IR}$ ) channels play a major role in maintaining one of the states, the

hyperpolarized down state. The  $K_{IR}$  currents in 60% of these neurons are non-inactivating whereas in the remaining, they inactivate [1]. The significance of this difference is unknown. We describe a computational study comparing the biophysical properties of medium spiny neurons possessing these two types of currents.

**Methods:** Two medium spiny neuron cells were modeled using NEURON, one equipped with non-inactivating  $K_{IR}$  currents (henceforth, "Cell A") and the other with inactivating  $K_{IR}$  currents (henceforth "Cell B") and their behaviors were compared in response to current injection inputs.

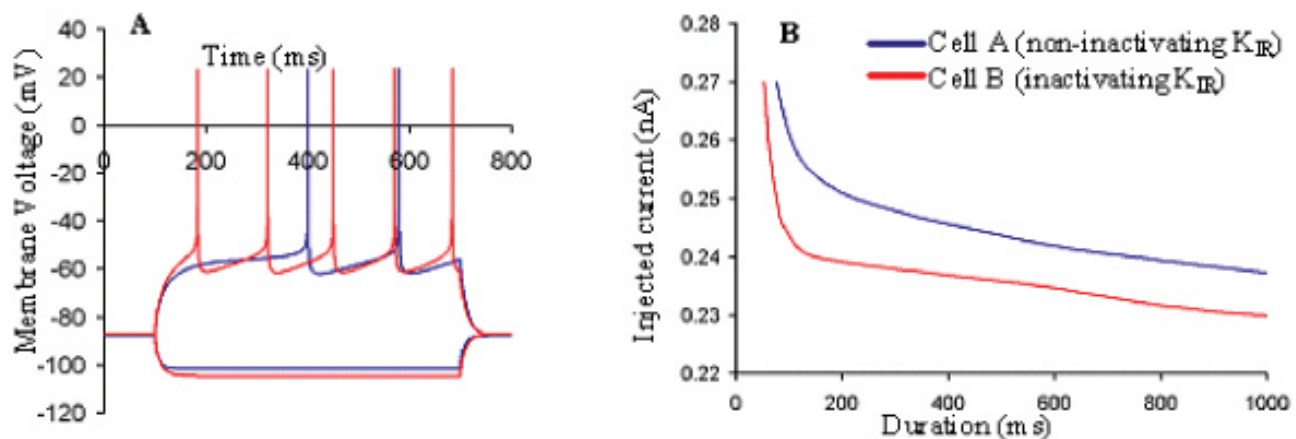
**Results:** It was observed that these two kinds of cells were different in several notable ways. For instance, Cell B when compared with Cell A (i) had a resting potential higher by +0.6 mV; (ii) had a higher frequency of firing for the same injected current (Figure 1A); (iii) hyperpolarized more for the same injected negative current (Figure 1A); (iv) reached firing threshold with smaller injected currents; (v) had higher average inter-spike interval (by up to 15%) with the first spike occurring up to 32% earlier for injected currents matched for firing frequency; (vi) showed noticeable differences in strength-duration curves (Figure 1B), injected current vs spike frequency curves and voltage-current relationships.

**Conclusion:** These results show that clear biophysical differences in the properties of medium spiny neurons can emerge owing to the presence of inactivation in  $K_{IR}$  channels and indicate that these differences can influence state transitions driven by cortical and hippocampal excitatory inputs. They also suggest that the two types of neurons expressing the different types of  $K_{IR}$  channels may have computationally different functions.

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Figure 1 (abstract P116)



**Comparison of Cell A with Cell B. (A)** Membrane response to injected currents of 0.248 and -0.2 nA. **(B)** The strength-duration curves of the cells show a significant difference in trend.

**PI17****Comparison of match functions applied to records with trains of action potentials**Jose Ambros-Ingerson<sup>1</sup>, Lawrence M Grover<sup>2</sup> and William R Holmes<sup>1</sup><sup>1</sup>Dept of Biological Sciences, Ohio University, Athens, OH 45701, USA<sup>2</sup>Dept of Pharmacology, Physiology and Toxicology, Marshall University School of Medicine, Huntington, WV 25755, USA  
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BMC Neuroscience 2007, 8(Suppl 2):PI17

Any attempt to construct a realistic computational model of a neuron has to face the difficult problem of assigning values to a large number of parameters. The parameter value ranges obtained experimentally are often insufficient to constrain the behavior of a model; parameter values are frequently encountered that are within experimental estimates but result in vastly dissimilar outputs.

Finding parameter values to make the model match complete experimental waveforms may address the failure of direct parameter estimates to sufficiently constrain parameter values. Automated optimization techniques can be used with this approach provided appropriate target match functions are available. However, a sum of squared differences comparison between traces with trains of action potentials suffers from their narrow shape and subtle variation in peak times.

To address this issue we developed a novel match function that uses the time-points of action potentials as fiducial points. We tested its performance using a set of patch-clamp 500 ms depolarizing (+800 pA) current pulse recordings from hippocampal CA1 pyramidal cells, using a criteria based on the notion that traces from the same cell should be closer to each other than to those from other cells.

We found that fiducial-point matching realized our criteria and also outperformed other published methods, such as those based on spike times and on voltage-gradient phase planes. Thus, based on fiducial-point scores, CA1 pyramidal cell responses from one cell can be systematically differentiated from those of other cells.

**Acknowledgements**

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**PI18****5HT neuromodulation of hippocampal pyramidal cells: effects of increased  $I_h$  on cell excitability**Anne Lippert<sup>1</sup> and Victoria Booth<sup>2</sup><sup>1</sup>Committee on Computational Neuroscience, University of Chicago, Chicago, IL 60637, USA<sup>2</sup>Departments of Mathematics and Anesthesiology, University of Michigan, Ann Arbor, MI 48109, USA  
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BMC Neuroscience 2007, 8(Suppl 2):PI18

**Background:** During waking, serotonin (5HT) levels in the hippocampus are high but during REM sleep hippocampal 5HT levels drop so low that it is virtually absent. We investigate how differing levels of 5HT affect the properties of hippocampal pyramidal cells through analysis of biophysical models of CA1 pyramidal neurons. Studies in the hippocampal slice show that 5HT increases  $I_h$ , the hyperpolarization-activated current, by

affecting its maximal conductance and its half-activation voltage [1]. In hippocampal pyramidal cells,  $I_h$  has been shown to have a normalizing influence on the temporal summation of dendritic synaptic inputs [2] that has been analyzed in modeling studies where  $I_h$  was the only active conductance in the model cell membrane [3, 4, 5]. Recently, dopaminergic neuromodulation of  $I_h$  has been shown to influence excitability of pyramidal cells in the entorhinal cortex [6]. While the action of dopamine on the kinetics of  $I_h$  was not determined in these cells, dopamine had the general effect of increasing  $I_h$  which resulted in a decrease of excitability. We consider how the specific 5HT modulation of  $I_h$  affects cell excitability in model hippocampal pyramidal neurons. Our analysis pays particular attention to rectifying the well-known depolarizing effects of  $I_h$  on resting potential with its inhibitory effect on excitability.

**Methods:** To concentrate on the interaction of  $I_h$  with spike generating currents, we constructed a single compartment model neuron that contains biophysically accurate  $Na^+$ ,  $K^+$ -delayed rectifier and  $h$  currents with parameters set to replicate CA1 pyramidal cell subthreshold and firing behaviors [4]. We also constructed a simplified single compartment model that includes  $I_h$  and the Morris-Lecar model equations for spike generating currents in order to analyze  $I_h$  effects on cell firing using phase plane techniques. In these models, we simulate the changes to  $I_h$  that the slice studies indicate occur when 5HT is present.

**Results:** Preliminary simulations using both the biophysical and simplified models show that neuronal excitability decreases with increased  $I_h$ . However, there is a voltage-dependence of the effects of increased  $I_h$ : if cell voltage is held around -70 mV and a current pulse is given, excitability decreases but if cell voltage is held around -50 mV when the pulse is given, excitability increases. We also investigate how the changes to  $I_h$  due to variations in serotonin level affect the cell response to a stimulus.

**Conclusion:** While the rectifying effects of  $I_h$  on resting potential are well understood, we concentrate on understanding the interaction of  $I_h$  with spiking currents and its nonintuitive effects on cell excitability. 5HT modulation of  $I_h$  suggests that excitability and, hence, synaptic processing in hippocampal pyramidal cells may change in different behavioral states such as waking and REM sleep. Understanding this change in neuronal processing during waking hippocampal activity which is involved in memory formation and during reactivation firing in REM sleep may lead to insight into the role of REM sleep in learning and memory.

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## P119

### A dynamical system analysis of the adaptive spike threshold

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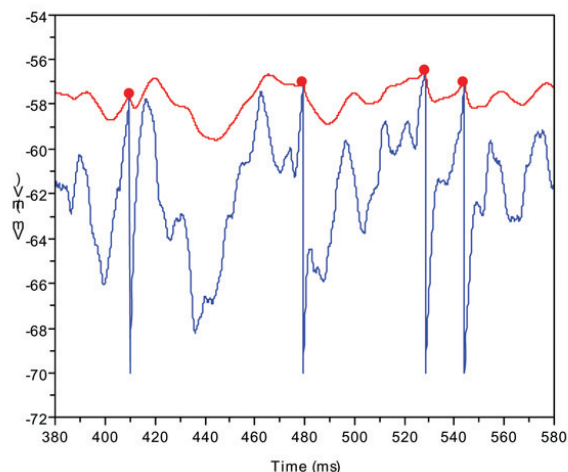
BMC Neuroscience 2007, 8(Suppl 2):P119

Recent *in vivo* experiments have revealed that the action potential threshold depends on the rate of depolarization just preceding the spike. This phenomenon can be reproduced in the Hodgkin-Huxley model. We analyzed spike initiation in the (V, h) phase space, where h is the sodium inactivation variable, and found that the dynamical system exhibits a saddle equilibrium, whose stable manifold is the curve of the threshold. We derived an equation of this manifold, which relates the threshold to the sodium inactivation variable. It leads to a differential equation of the threshold depending on the membrane potential, which translates into an integrate-and-fire model with an adaptive threshold. The model accounts well for the variability of threshold and the slope-threshold relationship. See figure 1.

#### Acknowledgements

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**Figure 1 (abstract P119)**



**Sample trace of a noise-driven integrate-and-fire model with adaptive threshold.** Blue: membrane potential, red: spike threshold.

## P120

### Cell-field interaction arising from tissue inhomogeneity determines electric stimulation efficiency

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**Background:** Electrical stimulation of neuronal tissue has been widely used in laboratory research and in the treatment of neurological diseases such as Parkinson's disease, essential tremor and dystonia. During stimulation, cells are polarized by the electrically-induced transmembrane potential, and the electric field is re-distributed by the presence of the cell. Previous studies have separately studied each aspect of this interaction. The electrically-induced transmembrane potential has been computed by various modeling works with various cell shapes, cell-field orientations, and field designs. The electrical field distribution has also been extensively studied. How do cell-field interactions influence the efficiency of electrical stimulation? To answer this question, we have developed a simple spherical cell model under uniform DC electrical field stimulation.

**Materials and methods:** We computed the potentials in the extracellular medium, along the membrane (transmembrane potential) and the cytoplasm by solving Laplace's equation with appropriate boundary conditions. The electrical field distributions in all regions were calculated as  $\vec{E} = -\nabla V$ , where V is the potential.

**Results:** 1. The membrane is regionally polarized by the electrical field.

2. The extracellular electrical field is perturbed by the presence of the cell. The transmembrane electrical field is amplified by the low-conductive membrane. The intracellular electrical field is partially shielded by the membrane.

3. Correlation between the transmembrane potential and the electrical field is a complex function of the cell geometrical and electrical properties, suggesting the two are not replaceable in considering the efficiency of electric stimulation.

**Conclusion:** 1. The electrically evoked transmembrane potential not only depends on parameters that define the field, but also depend on the electrical properties of the tissue, suggesting that tissue inhomogeneity play a critical role for the efficiency of stimulation.

2. The model cell perturbs the extracellular electrical field, suggesting possible "secondary" effects from neighboring cells. The model cell also shields the intracellular electrical field, suggesting that the cell membrane plays a role in protecting internal organelles against electrical exposure.

3. The presence of complicated interactions between the cell and the electrical field suggest they should be considered simultaneously in future modeling work. Specifically, it is important to consider the reciprocal effects of the neuron to the extracellular field distribution.

**P121****Predicting neuronal activity with an adaptive exponential integrate-and-fire model**

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BMC Neuroscience 2007, 8(Suppl 2):P121

An adaptive Exponential Integrate-and-Fire (aEIF) model [1] was used to predict activity of cortical neurons. This model is a leaky Integrate-and-Fire which has in the voltage equation an additional exponential term [2] describing early activation of voltage-gated channels combined with a second variable introduced in the model to allow for subthreshold and spike frequency adaptation [3].

Previously, we used the aEIF model to predict the membrane potential of pyramidal neurons under random current injection [4]. Moreover, similarly to the Izhikevich model [3], we know that the model can mimic more complicated firing patterns, that is, the model can reproduce spike trains of a detailed conductance-based model under standard electrophysiological paradigms [1]. Here, we reproduce several firing patterns of mainly interneurons from the EPFL microcircuit database [5]. The aEIF model was used to reproduce the firing pattern of the different electric classes of neurons under standard electrophysiological input regime. We studied nine classes among which Delayed Initiation Spiking, Burst Spiking, Fast Adapting or Non-Adapting Spiking [6] and compared simulation of the aEIF model (with 9 parameters) to a Hodgkin-and-Huxley model with 6 different ion channels. Moreover, we wondered whether the model can be fitted directly to experimental data. We successfully fitted the aEIF model to recordings of a Layer-II-III cells with different firing properties.

In summary, we found different areas of the parameter space corresponding to these specific classes. That is, the aEIF model includes an additional mechanism that can be tuned to model spike-frequency adaptation as well as burst activity. The exponential term allows one to model specific behaviors such as delayed spike initiation and offers flexibility at the level of the threshold mechanism. At the moment a large part of the tuning is done manually. However, once our automatic parameter fitting procedure is in place, we expect that clustering in parameter space could contribute to an automatic neuron classification.

**Acknowledgements**

This work has been supported by the European grant FACETS.

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**P122****Converting a globus pallidus neuron model from 585 to 6 compartments using an evolutionary algorithm**

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BMC Neuroscience 2007, 8(Suppl 2):P122

**Background:** Biologically realistic neuron models are useful tools for understanding the behavior and mechanisms of neurons, but they are computationally expensive due to their fine granularity. This makes them unattractive for use in network simulations and generally leads to their replacement by simpler “integrate and fire” or black box models which are computationally cheaper, but further removed from biology. An attractive alternative is to replace a biologically realistic model with a ‘reduced’ version containing fewer compartments. This reduced model should largely preserve biological realism while limiting complexity and computational cost.

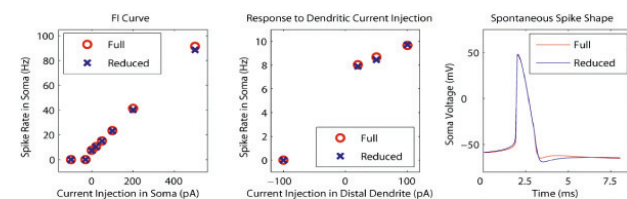
**Methods and results:** We present a 6 compartment ‘reduced’ model which preserves the electrotonic surface area distribution of a morphologically realistic 585 compartment globus pallidus ‘full’ model previously developed in the Jaeger Lab. Using an evolutionary algorithm, we searched the parameter space of the reduced model for values of  $R_m$ ,  $R_a$ , and  $C_m$  which yield close matches to the passive properties of the full model. The passive fitness function is based on varying levels of current injection, at different locations, with different frequencies. Once our search was complete, we chose the values of  $R_m$ ,  $R_a$ , and  $C_m$  that yield the best match with the passive properties of the full model. To match the active properties of the full model, we used an evolutionary algorithm to search the parameter space consisting of the various conductances shown in Table 1, along with their relative somatic and dendritic distributions. Our fitness function compares the FI curve, response to dendritic current injection, and various measures of spike shape. We tested approximately 120,000 different parameter sets, and the best (of many good fits) is shown in Table 1 and Figure 1. The fit between the full and reduced models is extremely good for the measures tested, with the exception of the afterhyperpolarization; we suggest that this may be due to differences in axial resistance. Further characterization of the parameter space is in progress.



**Table 1 (abstract P122)** Parameter sets which yield good matches to the full model.

Param Set	NaF	NaP	Kv2	Kv3	Kv4	KCNQ	SK	Ca_HVA	IH
Full Model	350	1.015	1	11.25	20	2	4	0.3	0.2
Reduced Model	303.49	1.26	1.92	8.48	27.13	2.38	2.79	0.91	0.33

Units of conductance are in  $S/m^2$ . {NaF, NaP} fast, persistent sodium; {Kv2, Kv3, Kv4, KCNQ} voltage gated K<sup>+</sup> channel families; {SK} calcium-activated K<sup>+</sup>; {Ca\_HVA} L-Type calcium; {IH} hyperpolarization activated current

**Figure 1 (abstract P122)**

**Fit results.** Full is the output trace from the full model, and Reduced is the output trace from the reduced model.

### P123

#### Characterizing the heterogeneity of globus pallidus neuron behavior by comparing a real neuron database with model databases of varying conductance parameters

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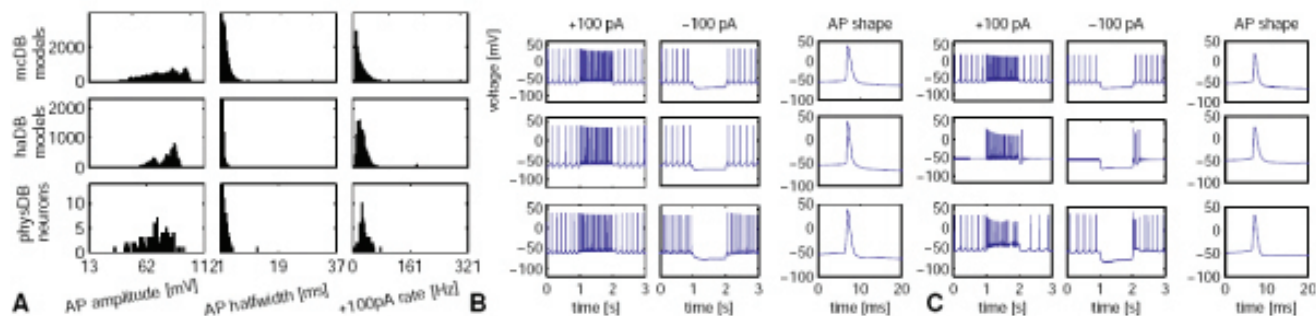
**Background:** The function of brain networks is highly dependent on the dynamical properties of single neurons, whose activity ranges from complex spontaneous activity patterns such as oscillations and bursting, to a variety of

synaptic response patterns serving functions such as coincidence detection or rebound firing. These dynamical properties vary in time through modulation and plasticity, and are also heterogeneous across individual neurons of the same type. Commonly, neurons show two to five-fold variability in the density of voltage-gated conductances, which accounts for large variations in dynamical behavior.

The globus pallidus (GP) is dominated by a single morphological type of GABAergic projection neuron, which shows patterns of spiking ranging from strongly bursting to more regularly firing in vivo. The activity of different neurons is uncorrelated in normal animals, but in Parkinsonian states, activity switches to synchronous bursting. The degree to which single neuron properties contribute to the diseased activity pattern has not been addressed.

We study the composition of intrinsic properties that yields the electrophysiology recorded from rat GP neurons in slice. The GP population provides heterogeneous electrophysiology that can be addressed by modeling. Finding intrinsic properties of GP neurons and their distribution is a crucial step in understanding larger-scale phenomena such as network oscillations and inter-nuclei synchronization.

**Methods:** We use the PANDORA Matlab Toolbox to automatically determine electrophysiologic measures of real and model GP neurons from voltage traces. These measures are collected in databases (DBs), allowing quantitative comparisons between neurons (e.g., between model and real neurons). The physiology DB (physDB) contains recordings from 146 real GP neurons. The model DBs contain variations of our GP model that consists of 500 – 600 compartments in three different morphological reconstructions, where each compartment has 9 conductances. Each conductance can be scaled using a maximal conductance parameter, and its dynamics are governed by activation, inactivation and time constant curve parameters. In earlier work, we analyzed a ~100,000-model DB by varying the maximal value of the model's nine conductances (mcDB). In the present study, we compare earlier results with a model DB obtained by varying the half-activation voltage parameter of selected conductance activation and inactivation curves (haDB). We used a brute-force approach to scan the entire parameter space to identify all regions that give physiologically realistic models and understand parameter effects throughout the

**Figure 1 (abstract P123)**

Matching real and model neuron traces. **(A)** Action potential (AP) amplitude, width, and firing rate measure distributions from the two model neuron DBs are similar and match distributions from real neurons. **(B)** Raw traces of matching real and model neurons. **(C)** A model in the haDB is superior in matching AP amplitude decay.

specified range. mcDB was obtained by choosing 3 – 4 levels of each of the nine maximal conductances in a geometric scale, whereas haDB was obtained by shifting the curve half-activations by  $\pm 5$  mV. The measures of models in both model DBs are matched against the measures of neurons in physDB. Each model DB is evaluated for its quality of representing the electrophysiological heterogeneity found in real GP neurons.

**Results and conclusion:** Preliminary analyses revealed that distribution of model measures obtained by shifting the half-activation and by varying maximal conductance were similar (Fig. 1A), and both manipulations provided good matches to the electrophysiological characteristics of the recorded GP neurons (Fig. 1B). A formal analysis of the relationship between the conductance and half-activation parameters was consistent with the view that these parameters cause common effects within limited ranges of membrane voltage. We found specific cases where each manipulation had its advantages in obtaining realistic behavior (Fig. 1C). We conclude that it is equally possible that GP heterogeneity is caused by a continuous distribution of either maximal conductance (ion channel density) or half-activation curve shifts (change in ion channel voltage-sensor sites).

## P124

### A computer model of EPSP time integral modulation by the spatial distribution of dendritic voltage-dependent channels at a realistic $\alpha$ -motoneuron

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**Introduction:** Neuronal dendrites contain thousands of synaptic inputs and are the first phase for signal processing. The activation of dendritic voltage dependent currents modulates the amplitude and time course of synaptic inputs, thus when the synaptic potential finally reaches the soma, it is a highly transformed version of the original input. In a previous publication [1] we simulated the effect of inhibition on the EPSP peak under various conditions of voltage dependent channel activation. In the present study we analyze the effects of similar conditions on EPSP time integral and its inhibition, since this parameter is also important in determining the firing pattern of a neuron.

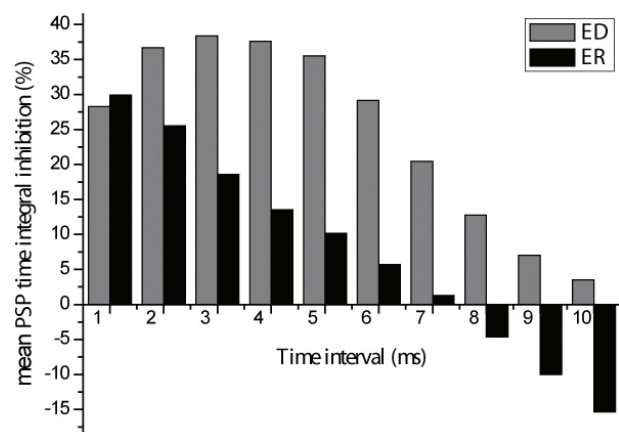
**Methods:** Modeling of excitation (glutamatergic) and inhibition (glycinergic) of morphologically and physiologically characterized triceps sarea MN 43 was executed by a NEURON simulator. Two types of active channel (sodium and potassium) distributions were tested: 1. Exponential decay (ED), where high conductance density, located proximal to the soma, decays exponentially away from the soma, and 2. Exponential rise (ER), where proximal low conductance density increases exponentially with the distance. For each model, out of a total of 11 dendrites, we ran simulations with 2, 4, 6, and 8 active dendrites, while the other dendrites remained passive. In each case, we

executed 10 runs of randomly selected dendrites. Densities of the sodium conductance ( $g_{Na\_step}$ ) were varied relative to the type of conductance distribution, between a minimum and a maximum value in order to attain equal total conductance, G (S, Siemens) in order to be able to compare the results of the ER and ED models. In our model, the soma and the axon remained passive and so the impact of dendritic-voltage dependent channels on the EPSP time integral (ETI) and on the efficacy of its depolarizing recurrent inhibition could be distinguished. In all simulations the excitatory synapses were activated after the inhibitory ones at various time intervals.

**Results:** ETI was dependent on the model of voltage dependent channels distribution and the density of the channels ( $g_{Na\_step}$ ). However the effects were in an opposite manner: in the ED model gradually enhancing the  $g_{Na\_step}$  (and thus G) increased the ETI (in a range of 62–83 mV.ms), whereas in the ER model the inverse relation was observed (in a range of 60–15 mV.ms). When slightly depolarizing inhibition is applied, the averaged inhibition of the PSP (EPSP+IPSP) time integral (PTI) was larger at all time intervals in the ED model than that in the ER model (Fig 1). The relation between the PTI inhibition in the ED and ER models and the  $g_{Na\_step}$  in single runs was similar to the one described above for ETI; namely large  $g_{Na\_step}$  increased the PTI inhibition in the ED model while the opposite was observed for the ER model. In the ER model, at large time intervals (no shunt) the depolarizing inhibition even enhanced the PTI relative to the ETI (Fig 1).

**Discussion:** We conclude that the distribution of voltage dependent channels determines the ETI and its inhibition; the ED model being more effective in producing larger inhibition of the PTI. A possible explanation for this result could be the following mechanism: At the synaptic input location the EPSP amplitude is certainly larger than its amplitude near the soma. Therefore, since the ER model contains a high active conductance density near these synaptic boutons, the EPSP was augmented to a pseudo action potential. However in the ED model, amplifying the EPSP proximal to the soma by voltage

Figure 1 (abstract P124)



The mean PTI inhibition ( $n = 200$ ) as a function of time interval. At all time intervals the inhibition of PTI in the ED model is larger than in the ER model. Note that negative PTI inhibition means excitation (at the 22, 27, 32 ms time intervals).

dependent channels produced a subthreshold response. A subthreshold ETI is significantly less depressed by the active potassium currents than supra-threshold ETI. However, inhibition of the supra-threshold response is less effective than of the sub-threshold response. In sum, the ED model could support larger ETI inhibition.

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#### P125

##### **Investigation of bifurcation properties of a model of myotonia caused by incomplete inactivation of sodium channels in skeletal muscle fibers**

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Muscle fibers from people suffering a myotonia condition generate trains of action potentials when extracellular potassium to the fiber is elevated. In milder cases of myotonia this leads to muscle stiffness, while in more severe cases the muscle can experience partial paralysis. The pathological features arise mainly from mutations of the sodium channel that causes a partial loss of inactivation. These features can be simulated in rat skeletal muscle by applying a toxin (anemonia toxin ATX II) in vitro to the muscle. Cannon, et al [1] formulated a two-compartment model representing the sarcolemma and t-tubule system of a skeletal muscle fiber, employing Hodgkin-Huxley type dynamics, with parameter values of mammalian muscle at room temperature, and compared its behavior to ATX II-affected rat muscle. A parameter,  $f$ , representing the fraction of sodium channels in the sarcolemma with defective inactivation dynamics could be adjusted to simulate normal, myotonic, and paralysis features in the muscle. To better understand features of their 9 equation model, we first reduced the model to considering just the t-tubule potential and potassium activation dynamics, depending on the parameter  $f$  and extracellular potassium concentration  $K_t$ . Over the physiological range in  $f$ ,  $K_t$  space we obtain regions of multiple equilibrium states, and their bifurcation properties, mostly saddle-node and Hopf bifurcations, and identify the onset of large limit cycle behavior representing post-stimulus repetitive discharging. Because coldness can bring on the episodic symptoms, we then examine the sensitivity of the model to temperature, as well as with other parameters. The reduced model is too simple to produce paralytic effects, so we consider other interactions of Cannon's two-compartment model formulation. This study is

preliminary in that more dynamics is slowly being incorporated into the model study, including spatial effects.

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#### P126

##### **Activity-dependent gating of lateral inhibition by correlated mitral cell activity in the mouse main olfactory bulb**

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Excitatory mitral and tufted cells (M/Ts) provide the primary output of the mouse main olfactory bulb (MOB). M/Ts provide excitatory input to and receive inhibitory input from GCs via the dendrodendritic synaptic connections. These circuits provide both recurrent and lateral inhibition among M/Ts. However, given the large area spanned by M/T secondary dendrites as well as the lack of evidence for a clear correlation between the proximity of M/Ts and their odor response profiles, we asked what mechanism could provide for specific and useful lateral inhibitory connectivity? To address this question we conducted whole-cell patch clamp recordings of pairs of M/Ts in the MOB. Current steps (400 ms, 0–1200 pA) were injected into one of the paired cells (Cell A). We then compared the firing rate of Cell A when it was stimulated alone vs. when it was stimulated during simultaneous activation of a second M/T (Cell B) at approximately 80 Hz. We found that activity of Cell B significantly reduced the firing rate of Cell A only when Cell A was firing at frequencies between 35 and 110 Hz (19%/17 Hz peak reduction,  $n = 16$  pairs,  $p < 0.05$ ). This effect, which we call activity-dependent lateral inhibition, is presumably due to activation of GCs correlated M/T cell activity and subsequent saturation of GC output. Furthermore, activation of larger populations of presynaptic M/Ts via extracellular stimulation in the glomerular layer produced similar activity-dependent lateral inhibition but of higher magnitude and occurring at lower frequencies (25% peak reduction between postsynaptic firing rates between 25 and 65 Hz,  $n = 8$ ,  $p < 0.05$ ). We then implemented this physiologically characterized mechanism in a network model with all-to-all connectivity. Results show that initially correlated patterns of activity are decorrelated in a spatially independent manner using this activity-dependent mechanism. These results suggest that the magnitude of inhibition received by M/Ts is dynamically determined based on the pattern of activity within the bulb and can be used to decorrelate similar input patterns, enhancing odor discrimination. Supported by R01 – DC005798.

**P127****Dendritic transmitter release and analog computation in mitral cells**Jason B Castro<sup>1,2</sup> and Nathaniel N Urban<sup>1,2,3</sup><sup>1</sup>Center for Neuroscience, University of Pittsburgh, Pittsburgh, PA 15213, USA<sup>2</sup>Center for the Neural Basis of Cognition, Carnegie Mellon University, Pittsburgh PA 15216, USA<sup>3</sup>Department of Biological Sciences, Carnegie Mellon University, Pittsburgh PA 15216, USA  
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Mitral cells of the accessory olfactory bulb contain between 2–10 principal dendrites, each of which terminates in a densely branched tuft contained in the glomerular layer. This multi-tufted morphology has led to the proposal that tufts may serve as local subthreshold processing stations that function independently of one another and in relative isolation from the soma. Consistent with this, we have found that focal synaptic stimulation of individual tufts results in regenerative calcium spikes restricted to the tuft ( $n = 7$ ). In addition, tufts are closely associated with local interneurons called periglomerular (PG) cells, with which they form reciprocal dendrodendritic synapses. In experiments in which mitral cells were patched and filled with the calcium indicator Calcium Orange, we found a strong covariation between tuft calcium influx and inhibition received by mitral cells ( $n = 8$ ), suggesting that tufts may self regulate their excitability via subthreshold synaptic mechanisms. To test this more directly, we first patched mitral cells with normal internal and evoked inhibition by activation of tuft spikes via afferent inputs. We then repatched with internal containing 1 mM BAPTA to buffer intracellular calcium concentration, which should reduce release from the mitral cell ( $n = 5$ ). The magnitude of inhibition received by the mitral cell decreased by  $75\% \pm 27\%$  within 2 minutes of BAPTA repatch. In a final set of experiments, we performed paired recordings of mitral and PG cells and found that synaptically evoked tuft calcium transients were highly correlated with the amplitude of EPSPs recorded in PG cells. Moreover, the synaptic input to PG cells was reduced by hyperpolarizing the mitral cell.

The above data motivate a model of synaptic integration in AOB mitral cells in which each tuft acts as an independent processing station capable of providing synaptic output to local interneurons. We are currently exploring the computational consequences of this phenomenon by modeling AOB mitral cells as binary classifiers and exploring how dendritic transmitter release contributes to their ability to discriminate among analog patterns.

**P128****Effect of T-channel distribution on firing pattern of the thalamocortical cell**Reza Zomorodi<sup>1,2</sup>, Helmut Kroger<sup>1</sup> and Igor Timofeev<sup>2</sup><sup>1</sup>Physics Department, Laval University, Quebec, Canada<sup>2</sup>Anatomy and Physiology Department, Laval University, Quebec, CanadaE-mail: [rzomor@phy.ulaval.ca](mailto:rzomor@phy.ulaval.ca)

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The low-threshold calcium current ( $I_T$ ) underlies burst generation in thalamocortical (TC) relay cells and plays a central role in

the genesis of synchronized oscillations by thalamic circuits. Ascending and descending inputs to thalamic relay cells arrive on the dendritic tree, thus the study of synaptic integration in model cells requires simulations incorporating the electrically active properties of the dendritic tree. We developed a 3-compartment model of a thalamocortical cell to consider effects of dendritic currents on the response of the cell. First, we attribute uniform T-channel distribution for all compartments in the model, then we find a threshold value of channel permeability,  $P_{Ca} = 1.56e-4$  (cm/sec) that enables generation of a low-threshold calcium spike (LTS). By multiplying the permeability of each section by its area we estimated the threshold number of channels necessary to reproduce an LTS. While we kept the total number of channels constant, we attributed different calcium permeability to the different compartments. Our simulations show, independent of the  $Ca^{2+}$  channel distribution, for a total channel number below the threshold value that the cell gives a passive response and above the threshold, the model reproduces the LTS spike. In a small range below the threshold the difference between uniform and non uniform distributions becomes visible. In the range of 1–2% below threshold a uniform distribution of T-channels produces a passive response while a non-uniform distribution reproduces an LTS response. A comparison with experimental data of firing patterns and the I-V curve of the T-current shows a non-uniform distribution with higher density in sections near the soma better represents the experimental data. However, the geometry of the I-V-curve of the T-current strongly depends on the quality of the voltage clamp. Depending on the electrode resistance, the maximum of the I-V-curve can change from (6 nA, -60 mV) to (3 nA, -40 mV). In addition we investigated the influence of the cell size on firing patterns. The model shows that with the same number of channels, the frequency of tonic firing increases with a decrease in the cell size, while the LTS response increases with an increase in cell size.

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**P129****The effects of modulatory systems in sensory thalamic nuclei**

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Thalamic relay cells receive two types of afferents: **drivers**, considered responsible for relay cells' receptive field properties, and **modulators**, thought not to contribute significantly to the receptive field properties, but, rather, to modulate thalamic relay properties. Modulators often work by slowly modifying the resting potential of the cell and thus determining the mode of response: if sufficiently depolarized, tonic (more linear) or if sufficiently hyperpolarized, burst (highly non-linear but capable of larger signal to noise ratios and cortical activation).

Thalamic drivers have two origins. Some relay cells receive their drivers from subcortical areas, including those in the lateral geniculate nucleus (LGN), the ventral posterior nucleus (VP), and the ventral portion of the medial geniculate body (MGBv). These have been called **first order relays (FO)** since this is



the first time that a particular information type is relayed to cortex. Other relay cells receive drivers from layer 5 of cortex, including those in the lateral posterior nucleus (LP), the posterior medial nucleus (POm), and the dorsal portion of the medial geniculate body (MGBd). These are known as **higher order relays (HO)**. Both FO and HO relays receive modulatory inputs, mainly from brainstem areas (e.g., cholinergic input from the parabrachial region, noradrenergic input from locus coeruleus, serotonergic input from the dorsal raphe nucleus, etc) and from layer 6 of cortex.

We sought to determine the effects of modulators in the two types of relays, using current and voltage clamp recordings of rat (P12–P18) thalamic cells in the whole-cell, patch-clamp configuration. We bath-applied general agonists for muscarinic and serotonergic receptors and determined their effects on relay cells of six sensory nuclei, three FO relays (LGN, VP, and MGBv) and three HO relays (LP, POm, and MGBd).

We have recently shown that cholinergic input (by activating muscarinic M2 receptors) hyperpolarizes about 17% of the HO relay cells, whereas it depolarizes all FO relay cells through M1 and possibly M3 receptors. Preliminary results suggest that serotonergic inputs also have differential effects in FO and HO relays: 3 out of 5 cells recorded in LP are depolarized by serotonin whereas all 4 cells from VP and LGN are depolarized. Furthermore, we are finding that HO and FO cells differ in their response properties. HO cells are more likely (60% of cells vs. 25% in FO; N = 23) to show spike frequency adaptation, which is also stronger than in FO cells. Activation of muscarinic receptors modifies the response properties of some HO cells, largely reducing the spike frequency adaptation.

Our results indicate that modulatory influences are different in thalamic nuclei that process information of cortical and non-cortical origin. They suggest that HO nuclei are more likely to be hyperpolarized when brainstem centers are active (waking, attention), therefore being more likely to respond to cortical inputs in the non-linear burst mode.

### P130 Supralinear reliability of cortical spiking from synchronous thalamic inputs

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Thalamic and cortical VI layer 4 neurons are capable of firing highly reliably and precisely upon repeated presentations of the same visual stimulus to the retina. To compare candidate causal mechanisms of spike-time reliability, a reconstructed multi-compartment spiny stellate cell model with dynamic stochastic synapses was given varying synaptic inputs. We found reliability was primarily influenced by the number of synapses that fired synchronously during events (synchrony magnitude), which exhibits a supralinear relation; rather than by the rate of synchronous firing events (event rate) or synaptic strength, which exhibits comparatively more linear relations, even in the absence of voltage dependent conductances. Supralinear reliability highlights the efficacy of synchronous but weak synapses in

driving output spiking, and may have implications for neural synchronicity within and between cortical areas.

### P131

#### Features of network oscillations in data from single-channel neuronal recording

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We present a new algorithm for analysis of neuronal data from single-channel time-series. Using a novel view of stochastic geometry to obtain a realistic model of nonlinear oscillatory systems, we extract traces of multiple oscillations from single-electrode extracellular recordings obtained from a representative neuron. Empiric data from neuronal recording has supported the observation that oscillations are prevalent in dynamics of the brain [1]. The literature on mathematical and computational modeling of neuronal networks of coupled oscillators is rich and includes numerous examples of successful explanations of experimental data. A number of mathematical approaches to model oscillatory networks of neurons take a deterministic approach to modeling the dynamics of such sophisticated complex biological systems where noise is added, if at all, as a test of stability of the system and its behavior under small perturbations. There are possible situations where the dynamics of the system depends fundamentally on the actual non-stationary statistics and the transient nature of “noise” in the system. The most natural mathematical theories in this context involve nonlinear dynamics and probability theory, which has been the subject of research in describing networks as well as individual neurons. The key theory that enables us to achieve a mathematically rigorous synergy between an ideal geometric theory and the biological reality is a recent merging of stochastic analysis and ergodic theory, known as the theory of Random Dynamical Systems (RDS) whose systematic foundations are laid out in the seminal work of L. Arnold [2]. The far-reaching ideas of RDS require a demanding technical mastery of stochastic analysis and ergodic. Our geometric and topological view will illustrate some of the remarkable theoretical and numerical achievements that RDS offers for biologically realistic modeling of nonlinear dynamics, while at the same time, it illuminates the ideas behind its algorithmic development.

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**P132****Patterns recognition in the ECoG data of auditory evoked response**

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We study the evoked potential of the local neuronal circuits of the left temporal lobe surrounding the auditory cortex in response to two types of simple auditory stimuli. We wish to gain deeper insight into the systems-level functional and behavioral consequences of sensation of a tone that includes a cooperative population of neurons in electrocorticogram (ECoG) recordings. Available experimental data does not have the necessary flexibility and the rich variety of parameter adjustments in the single-electrode recordings needed in order to make the data amenable to conventional analysis. These constraints and potential imperfections in data pose new challenges in the mathematical, computational and statistical aspects of data analysis and modeling. We use the experimental setting called the *odd-ball paradigm*, to collect intracranial electrophysiological recordings using an  $8 \times 8$  grid. The evoked response potentials that are then analyzed using algorithms that utilize methods of information theory. The extracted patterns of auditory response are used to elucidate cortical substrates of "auditory attention and decision-making". While data analysis was performed for the cases of attention as well as inattention, the analysis used the data from inattention for statistical purposes to contrast with data for selective attention. This approach was useful to fine-tune optimization parameters, and to exploit a sharper computational rendering of the Principle of Economy of Resources. The main results presented here are: (1) a computational-mathematical methodology to study auditory cortical response to brief tones in the presence of attention; (2) an application of (1) to neurobiology that provides an algorithm to estimate the transmission time of an auditory stimulus from cochlea until the auditory cortex (approx. 50–60 msec).

**P133****Differential gene expression analysis in treatment of Parkinson's disease using the moduli space of triangles**

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The long-term utility of levodopa (l-dopa) treatment against PD is known to be limited by its subsequent induction of dyskinesia (l-dopa-induced dyskinesia or LID). Up to now, few treatment strategies have been identified to reverse LID and restore l-dopa efficacy in dyskinetic patients. Among various mechanisms, l-dopa sensitization ("priming") may play an important role in the development and maintenance of LID. Disregulation of dopamine (DA) synthesis, release and clearance of extracellular DA (due to DA neuronal death and consequent "ectopic" synthesis and release by 5-HT terminals) is thought to lead to exaggerated fluctuations in the synaptic DA concentrations and consequent neurobiological alterations during chronic intermittent l-dopa treatment. These fluctuations, in turn, induce long-term, synaptic alterations in the striatum and other brain areas comprising the basal ganglia. Previous studies have shown that long-term sensitization to cocaine can be reversed by injecting a dopamine receptor agonist, followed by a 5-HT<sub>2</sub> or 5-HT<sub>3</sub> antagonist approximately 3.5 hours later [1, 2]. To the extent that cocaine addiction may share similar neurobiological mechanisms with LID, it is reasonable to examine a regimen of the DA agonist pergolide followed by the 5-HT<sub>2</sub> antagonist ketanserin at the peak of acute withdrawal over a treatment period and reverse sensitization to l-dopa. Based on our previous finding that this specific drug combination regimen can reverse previously-established behavioral and molecular markers of cocaine or methamphetamine sensitization in rats [3], we determined the striatal mRNA expression profiles associated with l-dopa-induced dyskinesia in rats and its reversal by the pergolide-ketanserin regimen. 6-Hydroxydopamine (6-OHDA)-lesioned rats were treated with l-dopa twice a day for 21 days (days 1 – 21) to induce abnormal involuntary movements (AIM), a model of LID. Subsequently, they were treated subcutaneously once a day for 2 weeks with one of the following. Group A received pergolide followed by ketanserin; Group B received pergolide followed by saline; Group C, the control group, received saline on both occasions. The expression levels of mRNA were measured for 27,342 genes. The normalized values provide triplets of positive numbers  $D = \{ (A(n), B(n), C(n)) : n = 1, 2, \dots, 27342 \}$ . This paper reports progress in application of new mathematical methods for exploring this genome-scale gene expression data. The main geometric idea is to represent the data as a collection of points in a space that parameterizes congruence classes of triangles in the plane. The distinguishing advantage of this approach is in extracting significant (biological) features and patterns of triangle shapes that are not typically discernible by commonly used statistical analyses. This method is applied to the data set **D**, where a relatively small group of genes are identified and tabulated.

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## P134

### InfoMax gene networks constructed from intervention in the animal models of Parkinson's disease

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**Theoretical aspects:** This paper reports progress in construction of a new network structure, called the InfoMax Gene Network, for exploring genome-scale inter-relationships among families of genes in order to specify pathways activated during the experiments that perturb a control system. The basic mathematical theory, called Empirical Topology, provides the conceptual framework to estimate the affinity of families of genes according to their purported function in the course of perturbations. In the empirical topology approach to systems biology, the set of genes is endowed with a certain geometric structure, so that a genomic space is constructed according to representations of systems-level information carried by the gene expression data, as 'perturbed signals' carry information regarding the noise or other factors underlying the perturbation relative to the control group. Consideration of constrained symmetries in empirical topology of the genome space provides a representation that is 'essentially unique' relative to the entropy contents of each possible signal. Application of information theory to the above-mentioned signals provides a collection of gene families in the genomic space that indicate the nodes of the InfoMax Gene Network.

**Experimental and biological aspects:** In our previous research we have determined the striatal mRNA expression profiles associated with dyskinesia and its reversal by the pergolide-ketanserin regimen. In experiments designed to investigate the systems biology of pergolide-ketanserin drug action, dyskinetic rats are treated subcutaneously once a day: for group A, the rats receive pergolide followed by ketanserin; for group B, the rats receive pergolide followed by saline; for group C, the control group, the rats receive saline on both

occasions. 6-Hydroxydopamine (6-OHDA)-lesioned rats were treated with L-dopa twice a day for 21 days (days 1 – 21) to induce abnormal involuntary movements (AIM), a model of LID. The expression levels of mRNA are recorded for 27,342 genes. The normalized values provide triplets of positive numbers  $D = \{A(n), B(n), C(n)\} : n = 1, 2, \dots, 27342\}$ . In this application, empirical topology on the genomic space is constructed according to the representation of the gene expression data A and B as 'perturbation of the signal' carried by the control group C. The constrained symmetries in empirical topology of the rat genome are shown to be certain permutations of the values in the data, and suitable choices of such symmetries provide an organization of the three data sets that is 'unique' relative to the entropy contents of the signals. The InfoMax Gene Network is further constructed according to the above-mentioned theory. The biological advantage of this approach is in extracting significant functional/pathway features that are inherent in the data sets and do not require guesses or additional hypotheses that could be hard to verify under present circumstances of gene array technology. We present tables of gene families and their information-theoretic relationships, as well as the corresponding biological interpretation in the context of gene-protein networks and pathways.

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## P135

### Modeling selective attention using EEG data

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**Introduction:** Perceptual abilities in humans are shaped by attention. Assessing the underlying mechanisms is barely possible due to the distributed nature of cognitive processing. One of the gateways to selective attention is negative priming (NP), a slowdown of the reaction to previously ignored stimuli in a range of 10 to 40 milliseconds. Variants of NP reveal the active processing of irrelevant stimuli up to a semantic level. The occurrence of the effect is, however, sensitive to details of the experimental conditions, making it difficult to vary parameters experimentally. Due to the sparse insight, modeling remains to some stage arbitrary. To formulate a well-grounded model, we focus on (1) detailed computational modeling, (2) a psychophysical view in the brain with EEG-recordings, (3) elaborated data analysis.

**Computational model:** One of the aims of this study is the test of the imago-semantic-action model, a general model for decision making in action planning. It explains priming effects both positive in the case of stimulus repetition and negative in

the case of ignored repetition, with only one general mechanism accounting for selective attention. A global adaptive threshold defines the actual action alternatives and finally the decision between them. The model computes activation strengths in a semantic space.

**Psychological experiment:** We recorded about 40 minutes of 64-channel EEG-data from 9 female and 7 male persons between 22 and 42 years, average 25 years. Subjects were shown a total of 840 trials each consisting of a display of two superimposed pictograms out of eight different stimuli. The target stimulus appeared in green, whereas the distractor stimulus was shown in red. Subjects had to name the target and reaction time was determined via microphone. The reoccurrence of stimuli of the precedent display defined the priming condition. A repetition of the target led to a speedup, whereas the change of a stimulus from distractor to target resulted in a slowdown. All effects resulted in significant reaction time differences.

**Results:** Performing standard event-related-potential (ERP) analysis as well classification by machine learning algorithms and independent component decomposition, we could narrow neural correlates in time and in space. Frontal processes are believed to mediate other brain functions, but may not show any amplitude dependency on the priming condition. Left-hemispheric parietal electrodes showed visually strong evidences. This agrees with the fact that a multilayer perceptron taking tenfold cross validation was able to correctly classify more than 90% of the ERPs by time series of 25 parietal electrodes, whereas 25 frontal electrodes only produced a correct classification of 68%. Additionally independent component analysis revealed for several subjects a strongly localized dipole in the left hemispheric parietal region that is only present in negative priming trials. These results question inhibition based models in favor of retrieval based models in terms of classical explanations of priming effects. The imago-semantic-action model asserts its position as a comprehensive model as regards concrete brain activity.

## Acknowledgements

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## PI36

### Synchrony-based integration of EEG and fMRI-BOLD in cognitive state transitions

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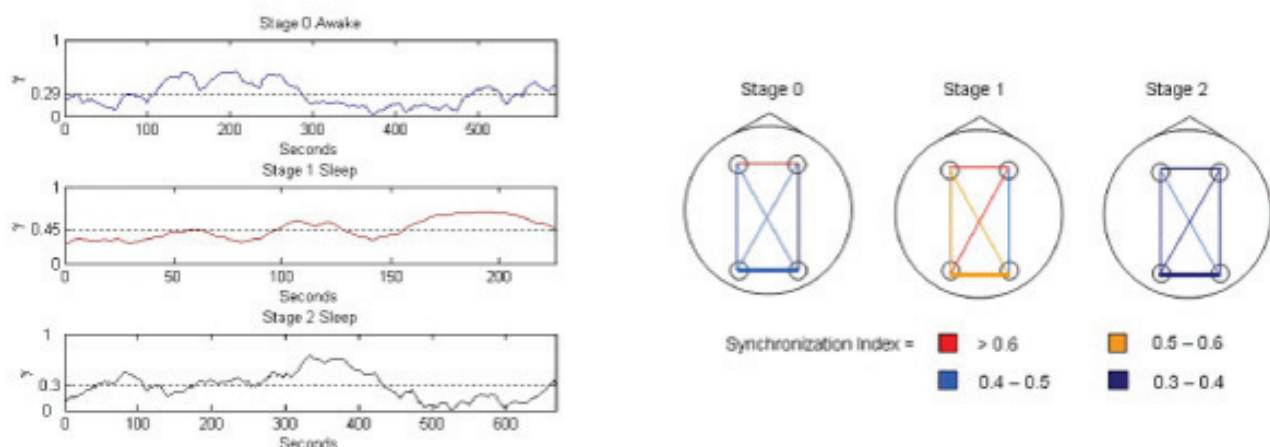
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**Background:** Both EEG and the blood-oxygen-dependent contrast (BOLD) signal used in fMRI are believed to reveal re-entrant signaling among complexly connected and dynamically reconfigured neural networks. As such, both signals show measurable responses to changes in global brain state. Simultaneous EEG and fMRI were collected during quiet waking rest after which subject's were asked to fall asleep. Using stochastic phase synchronization between low frequency amplitude envelopes (<0.2 Hz) created from alpha-band (8 – 12 Hz) filtered scalp EEG data and BOLD time series calculated from regions of interest in left and right visual cortex, we examined the feasibility of integrating information contained in both these signals.

Both the BOLD signal and the low frequency EEG envelope data from left and right visual cortices show increased synchronization in the descent into sleep (stage I; Figure 1).

Figure 1 (abstract PI36)



**BOLD signal and low frequency EEG envelope data.** (Left) BOLD synchronization index over time between left and right visual cortex. (Right) Regional synchronization using low frequency EEG.



**Conclusion:** It has been suggested that low frequency oscillations (<30 Hz) in scalp-recorded EEG organize spatially disparate regions [1] and data further suggests that slower rhythms can entrain such high frequency activity [2]. Recent data shows that low frequency oscillatory activity in the BOLD signal (<1 Hz) correlates activity in functional neural networks. Based upon these data, we suggest that very low frequency oscillation (0.1 Hz) common to both EEG and BOLD fMRI can be used to link the temporal resolution of neurophysiological activity seen in EEG to the excellent spatial resolution of the BOLD signal to create a fuller picture of neural functional activity.

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#### P137

##### **Respiratory rhythm and EEG oscillations in the olfactory system: a study using a biologically detailed model**

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EEG oscillations are found in several structures of the olfactory system, like the olfactory epithelium (OE), olfactory bulb (OB) and pyriform cortex (PC). From the theoretical side a possible way to study mechanisms responsible for the origin of these oscillations is the construction of biologically detailed computational models, which can exhibit oscillatory neural activity and allow simulations of EEG measurements which can be compared with real data. In this work we present a large-scale biologically detailed model of the olfactory system consisting of models of OE, OB and PC and use it to study relationships between EEG oscillations in these three areas and the respiratory rhythm. The OE model contains 2500 olfactory sensory neuron models (OSNMs) distributed in a  $50 \times 50$  square grid. The OB model has two cell layers, a  $8 \times 8$  grid of mitral cell models and a  $10 \times 10$  grid of granule cell models. The PC model has 96 pyramidal cell models distributed in a  $16 \times 6$  grid and 225 interneuron models arranged in three layers with 75 model cells in each one of them. These three layers are called, respectively, multipolar cell layer, horizontal cell layer and globular cell layer. We developed a function that generates a receptor current in the OSNM based on a respiratory frequency and odor concentration. This receptor current is injected directly at the

soma of an OSNM, simulating the effect of a stimulus. The responses of the OE, OB and PC were measured in terms of raster plots and simulated EEG records. In OE and OB, EEG records were made by single point electrodes placed at the centers of both the OE and OB models. In PC, the EEG was calculated as the average of the extracellular field potentials measured by a simulated grid of  $8 \times 5$  point electrodes placed at the surface of the PC model. The results show that the slow components of the electrical oscillations produced in OB and PC are directly associated with the respiratory frequencies and odor concentrations at the receptor layer while the fast components are related with the intrinsic synaptic activity at each neural layer.

#### Acknowledgements

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#### P138

##### **Exploring sparse connectivity in the motor system using multivariate autoregression analysis**

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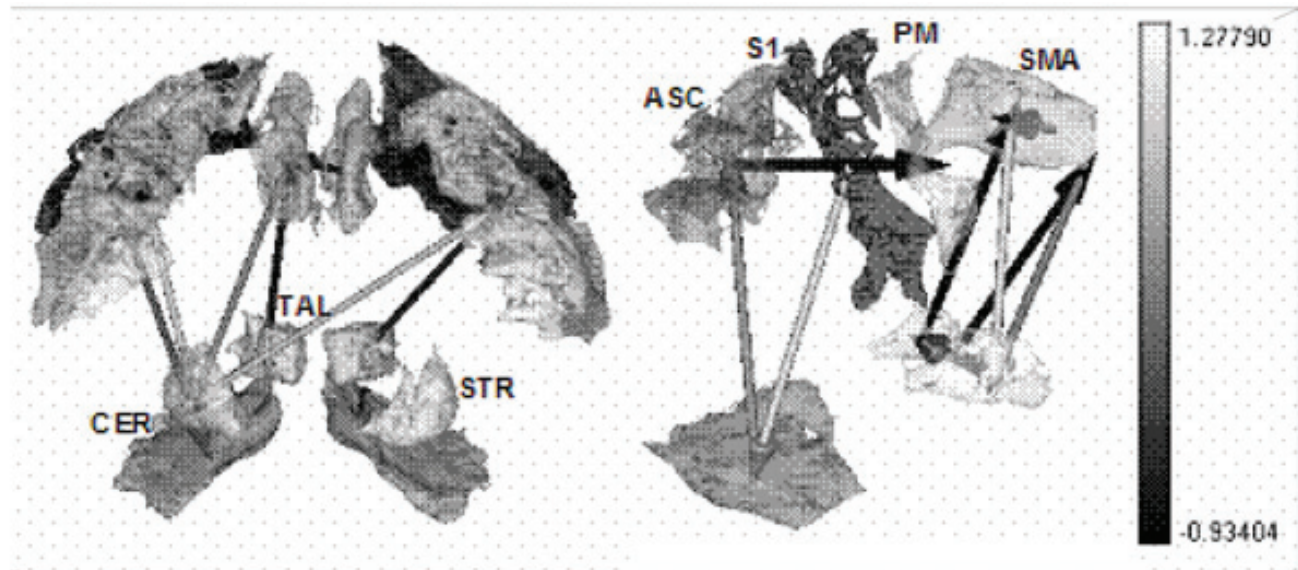
**Background:** Multivariate autoregressive (MAR) models can be used in the identification of causal relations from functional MRI time series. Connectivity information is extracted from large neural networks combining graphical modeling methods and Granger causality. The aim of this paper is to demonstrate the feasibility of working with the MAR models to identify functional circuits in the human motor system, and demonstrates their application to data of motor performance in patients with Parkinson's disease (PD).

**Methods:** In this work we incorporate a family of linear methods called penalized linear regression that were designed to deal with problems having a large set of variables (i.e. brain structures) and a relatively small set of observations (i.e. fMRI time points). One parkinsonian patient with early stage akinetic PD was studied by fMRI during the "drug-off" state and after reaches the "drug-on" state (table 1).

**Results:** The statistically most relevant connections from the connectivity matrix, in parkinsonian state, are summarized in the realistic rendering shown in Figure 1. These results indicate that the components of the basal ganglia-thalamus-cortical circuit were functionally connected to each other, but also functional connections in the cortico-cerebello-thalamo-cortical pathway are evidenced.

**Conclusion:** In opposition to widely spread methods for connectivity analysis, the proposed algorithm does not rely on preconditioned connections between regions from anatomical models. The penalized regression techniques expand the basic idea of ordinary least squares by means of the addition of new terms to the minimization equation. Our results support that MAR models form a valuable and feasible approach to study functional circuits in the human motor system, in normal and disease condition.

Figure 1 (abstract P138)



**Realistic rendering of effective connections in the motor system.** Note involvement of areas related to motor performance. **MI**: Primary motor cortex, **S1**: Primary somatosensory cortex, **PM**: Premotor cortex, **SMA**: Supplementary motor area, **ASC**: Associative parietal cortex, **STR**: Striatum, **TAL**: Thalamus, **CER**: Cerebellum.

**Table 1 (abstract P138) Effects of L-Dopa treatment on strength of inter-regional path coefficients**

Connection	OFF Medication	ON Medication
ASC – PRE	0.035	0.789
TAL – PM	0.062	0.154
TAL – SMA	0.093	0.256
STR – TAL	0.018	-0.386
TAL – SMA	0.093	0.256

### P139

#### Optimization of electrode channels in a visual discrimination task

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**Background:** Independent component analysis (ICA) is a well accepted blind source separation technique in electroencephalography (EEG) analysis to separate the independent sources of the electrical brain activity. Usually, the number of electrode channels in EEG analysis is selected arbitrarily in the cortical region of interest without any systematic study.

**Methods:** The number and location of scalp electrodes in a visual discrimination task were optimized by using ICA on a publicly available EEG database [1], a collection of 31-channel raw

data from 14 human subjects who performed a go-nogo categorization task and a go-nogo recognition task on natural photographs. The data were artifacts removed, average referenced, baseline removed, bandwidth (0.5 – 35 Hz) filtered, and epoched with 100 ms before and 1000 ms after the presentation of the cue. Three different sets of data consisting of 31, 16, and 8 channels with respect to the 10–20 international electrode placement criterion were generated for each of the categorization and recognition tasks. ICA was performed and event related potentials (ERPs) and 2-D maps of the independent components were compared for each of the data sets in the two tasks.

**Results:** Separate comparisons of ERPs and 2-D maps of the independent components in the target and non-target categorization task show that most of the components do not have a significant difference with increasing the number of channels from 8 to 31. However, for a number of the components, there exists some performance difference using 8 and 16 channels; but no significant difference between 16 and 31 channels. Similar results were observed in the recognition task and in different participant groups.

**Conclusion:** This study suggests that it was not helpful to include more than 16 channels in the visual discrimination task. Therefore, it is possible to reduce time, physical and computation efforts, and subject discomfort by using smaller number of electrodes when a systematic optimization is performed.

#### Acknowledgements

This work was supported by the “Keystone Innovation Zone Grant from the Economic Development Council of the Commonwealth of Pennsylvania”, USA.

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**P140****Biophysical cortical column model for optical signal analysis**

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We propose a biological cortical column model, at a mesoscopic scale, in order to explain and interpret biological sources of voltage-sensitive dye imaging signal. The mesoscopic scale, corresponding to a micro-column, is about 50  $\mu\text{m}$ . The proposed model takes into account biological and electrical neural parameters of the laminar cortical layers. Thus we choose a model based on a cortical microcircuit, whose synaptic connections are made only between six specific populations of neurons, excitatory and inhibitory neurons in three main layers, following [1] and [2]. For each neuron, we use a conductance-based single compartment Hodgkin-Huxley neuron model [3].

We claim that our model will reproduce qualitatively the same results as the optical imaging signal based on voltage-sensitive dyes, which represents the summed intracellular membrane potential changes of all the neuronal elements at a given cortical site [4]. Furthermore, this voltage-sensitive dye imaging has a submillisecond temporal resolution that allows us to explore the dynamics of cortical processing. An example of data of VI dye-signal in a cat, after a visual local stimulation, is shown in Figure 1. Therefore, the temporal dynamics of the measured signal will be carefully studied as being of primary interest for the proposed model identification.

**Methods:** We use the NEURON software to implement our cortical column model of about  $10^2$  neurons and run simulations. Larger-scale models are going to be developed with the event-based simulator MVASPIKE, or with a specific optimal software, thanks to PyNN.

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**P141****Intermittency in local field potentials recorded from the thalamus of patients with essential tremor**

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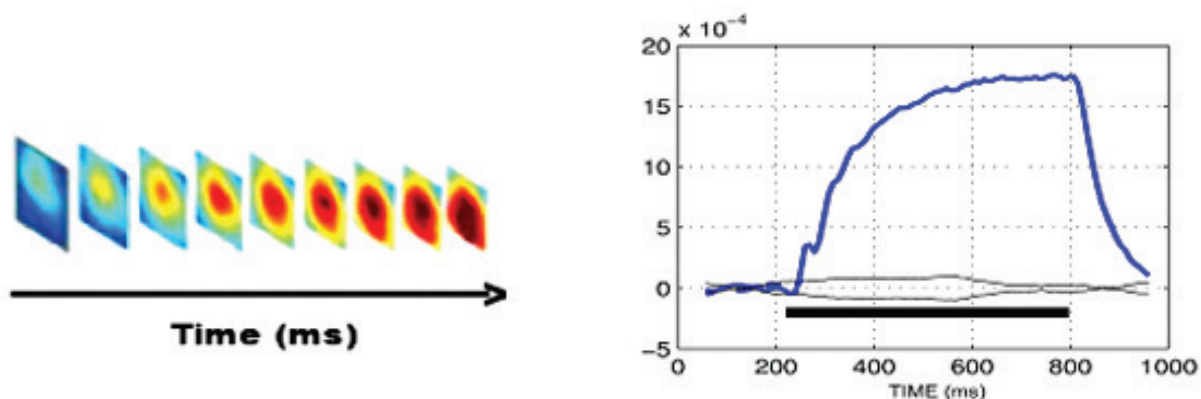
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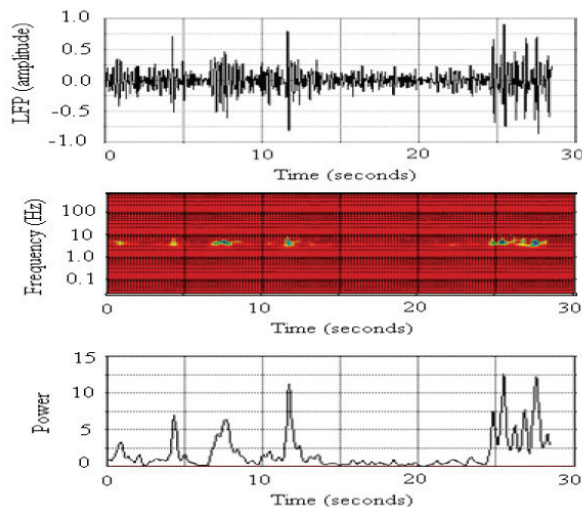
We have recorded the local field potentials (LFPs) from 12 sites in the motor thalamus of 4 patients with essential tremor who were undergoing surgery for implantation of deep brain stimulation (DBS) electrodes for the treatment of their tremor. By band-pass filtering the LFPs (20 – 40 seconds of recording at

**Figure 1 (abstract P140)**



**Voltage-sensitive dye optical imaging allows a real-time visualization of large neuron populations activity.** Left: Temporal evolution of the dye optical signal. Right: Response curve in one position of the map, same time scale.



**Figure 1 (abstract P141)**

**Wavelet analysis of the LFP signal from the thalamus of a patient with essential tremor.** Upper panel – Time series of the LFP signal; Middle panel – Wavelet power spectrum; Lower panel – Temporal variation of wavelet power; For this signal, the kurtosis is equal to 6.98.

each site) and applying a continuous wavelet transform on the filtered signals, we detected the presence of marked intermittency in the theta frequency band (4 – 8 Hz) at many of these sites (see Fig. 1). We have also computed the temporal variations of wavelet power to demonstrate that the intermittency is characterized by sudden bursts of power separated by intervals of very low power or almost quiescent periods. In addition, the kurtosis of the probability density functions of the LFP signals was used as a measure of the degree of intermittency at each site and revealed a wide variation ranging from 3.4 to 37.5. The larger the kurtosis, the greater is the intermittency in the signal. The origin and significance of the intermittency are presently unclear. It has been postulated that the cerebello-thalamo-cortical loop may be responsible for the generation of 6 – 9 Hz oscillatory electromyographic activity observed during voluntary movements, and possibly the bursts of theta oscillatory activity observed in the thalamus of these patients may be related to fluctuations of activity in this circuit.

#### P142

##### **The symptoms of schizophrenia related to the stability of attractor networks**

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We propose a hypothesis to account for the symptoms of schizophrenia in a statistical dynamical systems framework. We

propose that the symptoms of schizophrenia are related to alterations in the depth of the basins of attraction, and the statistical effects of spiking neurons, which together influence the stability of cortical attractor neural networks. The cognitive symptoms such as distractibility, working memory deficits and poor attention could be caused by instability of persistent attractor states in prefrontal cortical networks. The negative symptoms, which include a lack of affect and reduction of emotions, may be related to the concomitant decreased firing rates in cortical areas such as the orbitofrontal cortex and anterior cingulate cortex that occur when the depth of the basins of attraction are reduced. The positive symptoms including delusions, paranoia, and hallucinations could arise because the basins of attraction are shallow in temporal lobe semantic memory networks. This would lead thoughts to move too freely around the attractor energy landscape, loosely from thought to weakly associated thought. These hypotheses were investigated in a model of a cortical attractor network based on integrate-and-fire neurons and synaptic currents activated by AMPA, NMDA and GABA receptors [1]. It was found that a decrease in the NMDA receptor conductance leads to a decrease in the stability of working memory states, an increase in distractibility, and lower firing rates, and can potentially account for both the cognitive and negative symptoms. We observed a flat energy landscape associated with the positive symptoms of schizophrenia when, in addition to a reduction in the NMDA conductance, the GABA conductance was reduced. This caused the dynamical system not only to switch between the high firing rate attractor states, but also sometimes to jump from spontaneous activity into one of the attractor states. The findings are consistent with the neurophysiological effects of dopamine, which can influence NMDA and GABA currents. In this approach we thus start with a statistical dynamical systems framework, and use this to help understand how some of the different symptoms of schizophrenia might arise.

#### **Acknowledgements**

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#### P143

##### **Revealing the biophysical mechanism for configuring electrode contacts in deep brain stimulation**

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**Background:** Deep brain stimulation (DBS) is a widely used clinical treatment for various neurological disorders, and particularly movement disorders. The procedure involves implanting a four contact macro-electrode into disorder-specific targets within the brain, thereby creating a depth electrode



brain interface (EBI). In order to maximise the therapeutic effect, the current parameters and contact configurations need to be tuned for each patient, a process which is accomplished by systematic trial and error. The difficulty of this process is confounded by the fact that in vivo visualisation of the current spread is impossible.

**Methods:** We constructed a three-dimensional model of DBS using the finite element method, in order to compensate for the restrictions on the physiological study of the EBI in situ. We focused on the quantitative investigation of the changes in the electric field created during a number of both currently used and hypothetical configurations of the quadripolar electrode.

**Results:** Our results show that contact configuration has a significant effect on the shape and strength of the electric field created in the neural tissue. For example, monopolar stimulation creates a far-field dipole capable of stimulating relatively larger volumes of neural tissue, whilst bipolar stimulation creates a near-field dipole more suited to stimulating smaller volumes of tissue. Furthermore, by using the normally isolated "spare" electrode contacts, it is possible to further shape the field in order to better focus the electrical current.

**Conclusion:** In conclusion: (1) monopolar stimulation stimulates a larger volume of tissue than bipolar stimulation; (2) as the active contacts move further apart in bipolar stimulation, the field expands; (3) grounding the spare contacts shrinks the volume of tissue stimulated; (4) and using two contacts with the same polarity generates a stronger field than other settings, including monopolar setting. This provides a quantitative assessment on how to shape the electric field in DBS in order to optimise the therapeutic effects and minimise the undesirable side effects.

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#### PI44

##### An increased N-methyl-D-aspartate receptor conductance is associated with intrinsic bursting behavior

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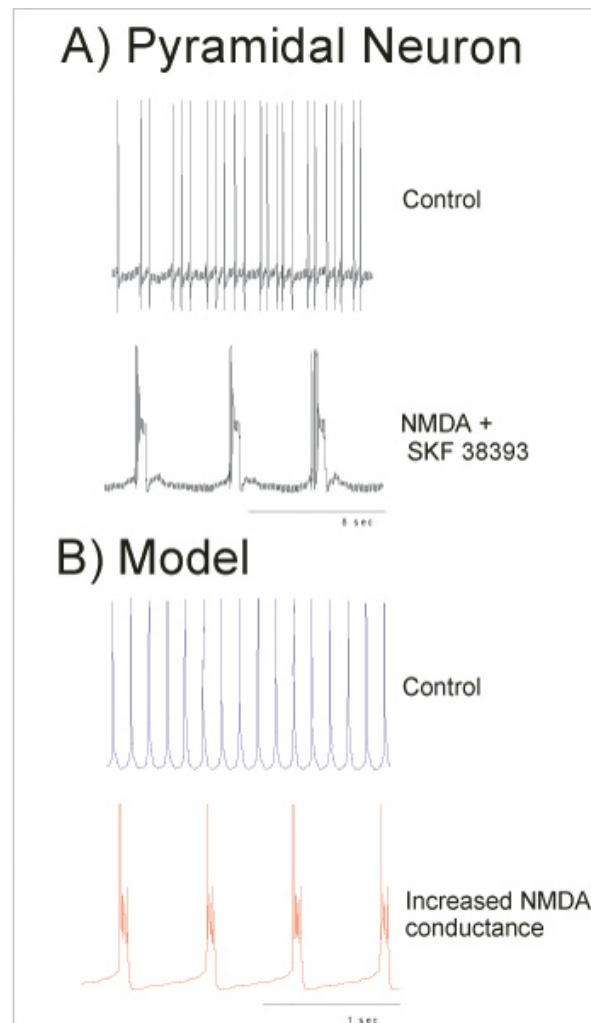
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**Background:** Seizure activity is often accompanied by an increase in the number of intrinsically bursting neurons [1]. The N-methyl-D-aspartate (NMDA) receptor, a channel known to be involved in many seizure models, represents one mechanism by which intrinsic bursting may arise, since 30–50% of these channels are bound at ambient concentrations of glutamate. In adult rat, intrinsic bursting has been induced in pyramidal neurons of the prefrontal cortex (PFC) through a combination of NMDA and dopamine type I (D1) receptor agonist [2]. Here we used the in vitro mouse neocortex and a computational model to further investigate the basis for bursting in the context of epileptiform activity.

**Results:** In mouse frontal cortex, application of 8–10  $\mu$ M NMDA and 2–5  $\mu$ M D1 agonist SKF 38393 elicited intrinsic bursting in ~50% of pyramidal neurons. A computational pyramidal neuron model consisting of five compartments with the sodium, potassium, calcium-activated potassium and NMDA channels was used to investigate the conditions necessary for bursting. In this model D1 agonist caused an amplification of the NMDA current. Our simulations indicate that increasing the NMDA receptor conductance transformed a regularly spiking neuron into a burster (see fig. 1). Interestingly, the bursting behavior appeared only when both NMDA receptor and calcium-activated potassium conductance were included.

**Conclusion:** The NMDA receptor is associated with production of intrinsic bursting behavior in mouse cortical pyramidal neurons, and, together with a calcium-activated K conductance, is sufficient to cause spontaneous bursting in a computational model of pyramidal neuron. These and previous results indicate that the NMDA receptor has the potential to drive the bursting behavior that characterizes seizures.

Figure 1 (abstract PI44)



Experimental and Model Neuron Firing Behaviour.

## Acknowledgements

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## P145

### High frequency oscillations in limbic rat model for temporal lobe epilepsy

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Recently a number of groups [1, 2] have reported on the existence of pathological High frequency oscillations (HFO's) (oscillations in the frequency range of 80–200 Hz, termed as Ripple band and oscillations in the frequency range of 200 Hz and above, termed as Fast Ripple band) in the epileptic brain both in in-vivo and in-vitro experiments. Our goal in this study is to study the statistical modulation of HFOs during epileptogenesis in order to characterize their function in progression to seizures in the epileptic brain.

In this study we define a HFO event as a subset of wave having significant high frequency component with low wave amplitude. HFO are detected from data recorded at a sampling rate of 12000 Hz for the entire duration of epileptogenesis which lasts anywhere from about 3–6 weeks.

Statistical analysis on the HFO suggest that occurrence of HFO's occur primarily during the 12 hour dark cycle whereas the HFO's primarily seem to occur during the 12 hour day cycle in the control rat. The video recording shows that the rat is primarily in active and exploratory state during the dark cycle. These observations suggest that HFO in epileptic rats are correlated with the state of arousal.

Spatial correlation of HFOs in different regions of the brain is also investigated with cross-correlogram. Comparison of cross-correlogram of the post-stimulus HFO in the epileptic rat to the pre stimulus HFO (control) suggests modification in the circuitry in the hippocampus, evidence for which in in-vitro experiments were provided by [3].

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## P146

### Neuronal desynchronization may act as a trigger for seizure generation

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**Background:** Experimental reports have appeared which challenge the dogma that epileptic seizures arise as a consequence of neuronal hypersynchronization. We sought to explore what mechanisms that desynchronize neuronal firing could induce epileptic seizures.

**Methods:** We constructed a computer model of the neuronal network in the CA3 region of hippocampus, a region in the brain frequently associated with seizure generation. The model incorporates two distinct inhibitory hippocampal feedback circuits that have recently been reported [1]. Selective changes in the distribution of interneurons in the hippocampus of patients with epilepsy have also been reported [2, 3]. Such changes could result in pathological alteration to synchronization of excitable cells with a potential causative role in epilepsy.

**Results:** When inhibition by interneurons that synapse on pyramidal dendrites was decreased, highly localized seizure-like bursting was observed in the CA3 region similar to that which occurs experimentally under GABAergic blockade. In contrast, when interneurons that synapse in the axosomatic region were similarly decreased, no such bursting was observed. However, when this transient inhibition was increased, normal coordinated spread of excitation was interrupted by high frequency localized seizure-like bursting. The increase of this inhibitory input resulted in decreased cell coupling of pyramidal neurons. A decrease in phase coherence was initially observed until seizure-like activity initiated causing a net increase in coherence as has been observed in epileptic patients.

**Conclusion:** In addition to producing electrical behavior consistent with other models of epileptogenesis, our results indicate how preservation or relative augmentation of a particular inhibitory circuit could produce initial desynchronization ultimately initiating neuronal activity characteristic of partial seizures in which the aberrant electrical activity originates from and remains restricted to a limited region of the brain. Our analysis of these results also resolved conflicts in previously reported experimental results between brain slice and in vivo recordings of epileptiform activity. These results provide a possible pathway in which a decrease in synchronization could provide the trigger for inducing epileptiform activity.

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## P147

### A model of spatiotemporal desynchronization for seizure control

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Contemporary approaches to controlling bursting behavior in brain slice models of epilepsy have typically emphasized spatially simplified strategies such as uniform DC fields or chaos control techniques using a single stimulating electrode. While such approaches have produced some promising results in these models, the recent development of multielectrode stimulating array systems for neuroprosthesis applications suggests that spatiotemporal approaches to controlling seizures *in vitro* may present opportunities for more flexible and robust control of ictal activity in slice models (as well as in potential clinical applications). We investigate several such control strategies in a spatially distributed model network of integrate-and-fire neurons based on Izhikevich's Simple Model [1]. This model was designed to mimic neocortical networks consisting of interconnected excitatory and inhibitory neurons. We show that waves of synchronous activity within the model can be blocked by regions of spatiotemporally asynchronous firing mimicking activity that could reasonably be generated by a microstimulation array. This desynchronization of seizure-like activity can be produced over a range of stimulation parameters and in networks with mixed or purely excitatory connections, suggesting that these effects may also be reproducible in neocortical slices *in vitro*.

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## P148

### Task and timing in visual processing

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The study of visual perception abounds with examples of surprising results, and perhaps none of these has generated more controversy than the speed of object recognition. Some complex objects can be recognized with amazing speed even while attention is engaged on a different task. Some simple objects need lengthy attentional scrutiny, and performance breaks down in dual-task experiments [1]. These results are fundamental to our understanding of the visual cortex, as they clearly show the interplay of the representation of information in the brain, attentional mechanisms, binding and consciousness.

We argue that the lack of a common terminology is a significant contributor to this controversy, and define several different levels of tasks as: Detection – is a particular item present in the stimulus, yes or no?; Localization – detection plus accurate location; Recognition – localization plus detailed description of stimulus; Understanding – recognition plus role of stimulus in the context of the scene.

It is clear from performance results that detection is not possible for all stimuli, and the difference must be in the internal representation of the different stimuli. For detection to be possible, the fast, feed-forward activation of a neuron (or pool of neurons) must represent the detected stimulus, which is consistent with the experimental finding that only highly over-learned and biologically relevant stimuli or broad stimulus categories can be detected. In detection tasks localization is poor or absent [2], so location needs to be recovered based on this initial representation. Given that detailed location and extent information is only available in the early processing areas, this must be accomplished by the ubiquitous feedback connections in the visual cortex. Once the location of a stimulus has been recovered and distracters inhibited, one or more subsequent feed-forward passes through the system can create a detailed representation of the selected stimulus.

Here we present a computational demonstration of how attention forms the glue between the sparse, fast, and parallel initial representation that supports object detection and the slow, serial, and detailed representations needed for full recognition. The Selective Tuning (ST) model of (object based) visual attention [3] can be used to recover the spatial location and extent of the visual information that has contributed to a categorical decision. This allows for the selective detailed processing of this information at the expense of other stimuli present in the image. The feedback and selective processing create the detailed population code corresponding to the attended stimulus. We suggest and demonstrate a possible binding mechanism by which this is accomplished in the context of ST, and show how this solution can account for existing experimental results.

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## P149

### Spike timing – an incomplete description of neural code

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Starting with Hebb's investigations the time domain was an important apparatus to study neuronal activity. Increases or decreases in firing rate, precise spike timing sequences or

particular spike time patterns were perceived as the only reliable measures of neural code. Despite considerable efforts and some success, the time approach does not seem to offer responses to several questions. What is the meaning of the time code in terms of behavior? Is the time domain consistent enough to measure complex neuronal activity?

One can answer these questions by measuring spike directivity in neurons as rats learned a T-maze procedural task. Based on in vivo recordings we recently demonstrated that spike time alone does not reflect the richness of neuronal activity [1, 2, 3]. Additionally, we showed that the electrical flow has directionality which becomes organized with behavioral learning. We performed neuron simulations with plausible models of biophysically realistic neurons and demonstrated that mutual information between input signal and sodium flux is about two times that between input signal and output spikes during each spike within a millisecond-level time domain [2]. Consistent with this model and previous analyses we reveal that complex coding occurs in expert neurons and spike directivity analyses are able to reliably predict future animal actions [4]. This important feature in the spatio-temporal domain characterized by subtle changes in spike directivity at certain moments in time represents basic steps towards reading the neural code and marks a final requiem for spike timing era.

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#### P150

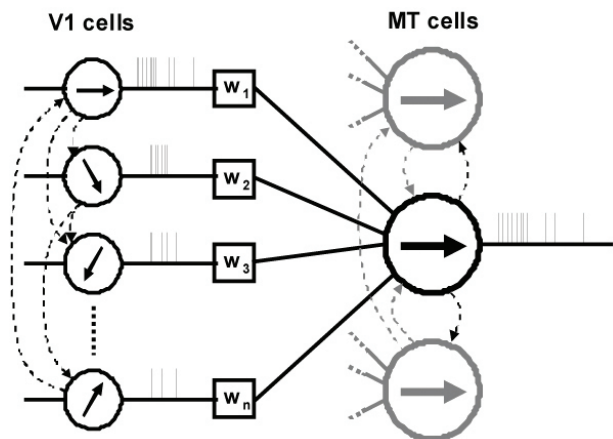
##### Spike to spike MT model and applications

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**Our contribution:** We propose a bio-inspired MT model working in a fully spiking mode: our MT layer receives spiking inputs coming from a previous spiking V1 layer. The MT layer integrates this information to produce spikes as output. Interestingly, this spike to spike model allows us to study and model some of the dynamics existing in V1 and MT, and due to the causality of our cell representations it is also possible to integrate some top-down feedback. This model differs from existing ones such as e.g. [1] and [2], that generally have analogue entry and consider motion stimuli in a continuous regime (as plaids or gratings) discarding dynamic behaviours. In this model we also propose an implementation for the inhibition done between cells in V1 and MT. The interaction between V1 cells is done both for neighbouring cells with the same velocity and for cells with the same receptive field but different velocity orientations. On the other hand, the inhibition between MT cells is done to help the model in the detection of the pattern

Figure 1 (abstract P150)



**Architecture of model here presented.** The first layer is formed as an array of direction-selective V1 complex cells tuned for different speeds and directions of motion. Each V1 complex cell is modelled with a motion energy detector following [5]. The second layer of the model corresponds to a spiking MT cell array. Each MT cell has as input the spike trains of the V1 complex cells inside its receptive field; all the V1 cells considered inside the MT receptive field have the same orientation, the model data being based on biological findings [2]. The dashed lines represent the interactions between V1 and MT cells. The values of the weights  $w_i$  are adjusted (they could also be found through learning as STDP) to tune the MT neuron for a certain motion pattern direction.

motion direction. The architecture and details of our model are shown in Figure 1.

**Interest of a spike to spike model:** We are interested in validating the behaviour of our model with:

Grating and plaids. We will compare our results with e.g. [1] and [2].  
Dynamic. The activation of MT cells is not constant in time, it suddenly increases when the motion direction is changed. We study the dynamical effects as described in [3].  
Motion recognition. We will show how the spiking output of MT can be successfully used to recognize biological motion starting from real video sequences [4].

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**P151****Bayesian binning for maximising information rate of rapid serial presentation for sensory neurons**

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Understanding the response properties of single neurons is seriously limited by the available experimental time and the rate [bit/s] at which information can be gained from the neurons. A substantial improvement in the latter can be achieved by speeding up the presentation of stimuli.

We show how the novel technique of Bayesian Binning [1] can be used to find the optimal stimulus presentation rate of a continuous sequence of stimuli.

This method applied to neurons in high-level visual cortical area STSa gives optimal presentation rates of approximately 56 ms/stimulus (18 stimuli/s) which is significantly faster than conventional presentation rates, allowing a better sampling of stimulus space. We relate these results to findings obtained with the Bayesian Bin Classification method [2, 3], which can be used to select the optimal time window for the analysis of the continuous response stream. Both methods will soon be freely available as standalone command-line applications or Matlab/Octave plugins.

The optimal window duration is equal to the stimulus duration near the best presentation rate. Interestingly, this duration also corresponds to the peak of spike efficiency [bit/spike] of a rate code whose firing rates match those found in visual neurons (area STSa).

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**P152****Opponent motion tuning of neurons in area FST of the macaque**Ari Rosenberg<sup>1</sup>, Pascal Wallisch<sup>2</sup> and David C Bradley<sup>1,2</sup><sup>1</sup>Committee on Computational Neuroscience, University of Chicago, Chicago, IL 60615, USA<sup>2</sup>Department of Psychology, University of Chicago, Chicago, IL 60615, USAE-mail: [arirose@uchicago.edu](mailto:arirose@uchicago.edu)

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The superior temporal sulcus (STS) of the macaque monkey contains several distinct motion sensitive visual areas. Neurons in these areas are typically responsive to specific kinds of motion patterns such as a direction, optic flow, or biological motion. Recent fMRI data from the monkey suggests that the fundal surface of the STS (FST) contains neurons tuned for opponent

motion. However, this has not yet been confirmed electrophysiologically. Here, we present single-unit recordings confirming that a large subpopulation of neurons within area FST are tuned for opposite directions of motion and are equivalently tuned for opponent motion.

The tuning properties of this population of FST neurons are markedly different from those typically observed in MT, one of the principal input areas to FST. When tested with translating random-dot patterns, the FST neurons responded strongly to motion in two opposite directions but were weakly driven or inhibited (relative to static response) by motion in the orthogonal directions. In contrast, MT neurons are highly direction selective, responding strongly to one direction and weakly to motion in the opposite direction. Hand-mapping revealed that FST neurons have spatially homogeneous receptive fields with respect to direction selectivity. Specifically, each neuron was selective for two opposite directions of motion at all locations within the receptive field.

Further, when tested with a type of opponent motion stimulus called transparent motion, in which two random-dot patterns translate in opposite directions in the same depth plane, the FST opponent motion tuning curves were matched to the direction tuning curves in response pattern and amplitude. In MT, the response pattern is matched but the response amplitude is significantly weaker for transparent motion stimuli.

We propose that the tuning properties of the opponent motion responsive FST neurons reported here can be reproduced by performing a linear transformation followed by a static nonlinearity on the output of a population of MT neurons. In this model, an FST neuron sums the output of MT neurons that prefer two opposite directions of motion and subtracts the output of MT neurons preferring the two orthogonal directions.

**P153****Optimal spatio-temporal pooling of neural responses in area MT**Hualou Liang<sup>1</sup>, Zhisong Wang<sup>1</sup>, David A Leopold<sup>2</sup> and Alexander Maier<sup>2</sup><sup>1</sup>School of Health Information Sciences, Univ Texas Houston, Houston, TX, USA<sup>2</sup>Unit on Cognitive Neurophysiology and Imaging, National Institute of Health, Bethesda, MD, USAE-mail: [hualou.liang@uth.tmc.edu](mailto:hualou.liang@uth.tmc.edu)

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Bistable visual stimuli such as Rubin's vase/face or the Necker cube refer to the phenomena of spontaneously alternating percepts while viewing the same visual image. The uncoupling between the stimulus and percept offers a means for understanding neural basis of visual perception. Here we asked whether pooling the responses of a large population of MT neurons over time and space could improve the predictability of perceptual decisions during ambiguous visual stimulation. Two well trained rhesus monkeys indicated the perceived direction of rotation of bistable structure-from-motion (SFM) stimuli by pushing one of two levers. During this task, multi-channel intracortical recordings including single-unit activity (SUA), multi-unit activity (MUA), and local field potentials (LFP) were collected from area MT. We sorted the neural data according to the monkeys' behavioral choices and employed statistical algorithms to classify brain states (i.e., the subjective

interpretation of a bistable stimulus). Classification was performed with linear discriminant analysis with leave-one-out cross-validation. We found that SUA, MUA and LFP all had a rather modest capability of predicting the monkeys' perceptual report when considered in isolation. We developed dynamic models for spatio-temporal integration of distributed neural signals. We found that the discriminative information of neuronal population activity accumulates over time and the combination of simultaneously collected data greatly improved the prediction accuracy of each of the signals. The accuracy and statistical power of determining the monkeys' perception increased with the number of channels as well as with the types of neural signals used for analysis. Our results demonstrate that simultaneous collection of multiple neural responses in area MT can improve the determination of perceptual states.

#### P154

##### **Detection of gabor patch arrangements is explained by natural image statistics**

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In human vision, the perception of localized stimuli is strongly influenced by the presence and nature of surrounding elements. It has been suspected that these contextual effects are linked to the processes of image segmentation and recognition, by enhancing the representation of specific configurations of elementary features which are typical for certain objects or other important aspects of a visual scene. In this contribution, we show that psychophysical detection thresholds for stimulus configurations comprising four Gabor patches of different orientations and spatial frequencies are strongly related to the probabilities that these configurations occur in 'natural' images. This almost perfect match holds for patch distances of 2.8 degrees of visual angle, whereas for 1.4 degrees of visual angle we find strong inhibitory effects, actually leading to increased thresholds for all configurations. Our results suggest that natural image statistics capture specific patterns of local interactions in early, feature-specific layers in visual cortex. This finding indicates that the zoo of contextual interactions actually observed both in psychophysics and electrophysiology may be interpreted in a more systematic way by a careful analysis of the statistical properties of our environment.

#### P155

##### **Do high order cross-correlations among neurons convey useful information?**

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Populations of neurons in the brain encode information about the external environment as time-cell series of spikes.

A fundamental question in systems neuroscience is how this information can be decoded by a downstream neural system. Since the responses of different neurons are statistically correlated [1], it is possible that such correlations convey important information and thus need to be taken into account by any decoding algorithm. Although coding by correlations may increase the capacity of a neural population to encode information, it may greatly complicate its decoding. In fact, it is possible that all neurons within the population interact with each other, and that their interaction cannot be described only in terms of "pair-wise" or low order interactions between neurons, but it reflects a genuine higher order interaction among a larger population. In such case, the number of parameters describing such correlations would increase exponentially with the population size drastically increasing the complexity of the codes we want to investigate. On the other hand, it is also possible that a downstream system can access all the information available in the population activity even when taking into account only low-order correlations among neurons. In this way, the brain could exploit some of the representational capacity offered by correlation codes, but at the same time limit the complexity needed to decode it.

Conceptualizing neurons as communications channels, we can quantify how much Shannon's mutual information,  $I$ , is available to a decoder that is observing the neural responses and who knows the true stimulus-response probabilities. We can also compare it with a lower bound,  $I_k$ , of how much information could be decoded by a decoder that assumes some simpler structure of correlation taking into account only statistical correlations between neurons up to the  $k$ -th order [2, 3]. A principled way to construct such models from experimental data is to build the maximum-entropy response probability among those with the same marginal probabilities (and thus correlations) up to order  $k$  as the real population responses. We quantify the importance of higher order correlations as the decoding cost ( $I - I_k$ ) of neglecting higher order correlation. We demonstrate that, by using appropriate bias correction statistical techniques [4], this lower bound can be made data-robust and computed with the limited number of trials typically recorded in neurophysiology experiments. With 200 trials per stimulus, we could compute the contribution of information conveyed by all higher order correlations for a group of up to 10 neurons. Taken together, these results suggest that the application of the method proposed here will unravel the role of high order correlations among neurons in sensory coding, thus giving an insight into the complexity of the coding.

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## P156

### Modelling the population of olfactory receptor neurons

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**Introduction:** Biological experiments have shown that olfactory receptor neuron responses to an odour stimulus vary substantially, even between two ORNs expressing the same receptor type [1]. This variation is likely the result of heterogeneity in geometrical as well as electrical and odour/receptor-dependent properties. The total response relayed to the olfactory bulb, which is a sum of many convergent ORN responses, will depend on the distribution of variation in single ORN responses. This distribution is not known, but may be estimated through modelling.

**Methods:** For modelling the ORNs we used biophysical equations based on experimental data [2], whose parameters belong to three different sets describing the odorant-receptor interaction (**R**; especially the dose at half-maximum conductance  $C_{g/2}$  expressed in log molar), the geometrical shape and size (**G**) and the electrical characteristics (**E**) of ORNs. We let the parameters of these equations vary stochastically according to probability distributions which were chosen to correspond to experimental data, as established by Rospars et al [2]. The firing frequency distributions of a population of ORNs stimulated by a given odorant at various concentrations were investigated in two cases: (i) ORNs expressing a single olfactory receptor type (stochastic variation of only **G** and **E**), and (ii) a population of ORNs expressing many receptor types (stochastic variation of **G**, **E** and **R**). The current model only gives the steady-state frequency distributions as a function of the strength of the odour stimulus, and the stimulus is a single odorant.

**Results:** We find that the frequency distributions become rather different for the two cases. (i) The firing frequencies of a simulated population of ORNs expressing the same receptor – for instance, receptor neurons projecting to the same glomerulus in the olfactory bulb – are normally distributed. The mean value and standard deviation of the frequency distribution increase with odour stimulus strength, up to a limit. (ii) Frequency responses of a simulated population of neurons expressing different receptors are approximately lognormally distributed for weak odour stimuli and near normally distributed for strong odour stimuli. Both families of distributions can be described mathematically, with equations detailing the distribution of frequencies in the response depending on odour stimulus strength.

**Conclusion:** The current model is, to our knowledge, the first computational model of the population of ORNs – i.e. of what the olfactory bulb "sees". As the bulb is specialized for the type of input provided by the ORNs, we believe our model could be valuable both for generating input to computational models of the olfactory bulb, as well as for improving understanding of the olfactory system as a whole. Our mathematical descriptions are much simpler to implement than the original biophysical model, and can be used for both modelling and theoretical work.

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## P157

### Visualization and classification of neural ensemble encoding patterns by subspace analysis methods

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Recent advances in multi-electrode recording techniques in freely-behaving animals allow the simultaneous monitoring of large-scale neural activity patterns. Analysis of such complex high-dimensional datasets presents challenges as the efficiency of traditional statistical is greatly decreased when the numbers of dimensions becomes very large. To address this issue, we employed a series of projection methods, such as Multiple Discriminant Analysis (MDA), Principal Components Analysis (PCA) and Artificial Neural Networks (ANN), and compared them with non-projection multivariate statistical methods such as Multivariate Gaussian Distributions (MGD). We use two simulated data sets of monkey cortical activity during face perception or arm movements, and recorded data sets from mouse hippocampus during exposure to startling episodic events to illustrate how different network-level ensemble patterns can be projected and classified in low-dimensional encoding subspaces. We investigate how over-fitting of training data sets, which can occur when due to experimental constraints the number of training data points is much smaller than the number of recorded units, can be prevented by using regularization methods. Evaluation of discrimination accuracy of these methods indicates that the projection methods outperform the multivariate methods that operate in the original large-dimensional parameter space (MDA > PCA > ANN > MGD). We also show that the computations implemented by the projection methods reflect the hierarchical features implemen-

ted in the simulated neural data sets. We conclude that subspace projection methods, in particular MDA and PCA, are effective not only in extracting essential features from complex data sets, but also in allowing the visualization of the neural network-level encoding patterns and their temporal dynamics.

## P158

### From spikes to space: reconstructing features of the environment from spikes alone

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A common stimulus reconstruction paradigm involves first computing the receptive fields of recorded neurons (using both spike trains and the presented stimuli), and then using the receptive field information together with neuronal activity in order to "predict" the pattern of stimuli based on local stimulus features. Some brain regions (such as hippocampus) undergo remapping of receptive fields, depending on context. How do downstream neurons integrate the mosaic of individual neuronal responses, with potentially varying receptive fields, to extract global characteristics of presented stimuli?

In rodent dorsal hippocampus spatial information is encoded by place cells, i.e. pyramidal cells that fire in a restricted convex area of the spatial environment, and are mostly silent outside. The receptive fields of individual place cells (place fields) can be thus thought of as small convex domains in a two-dimensional environment. The place fields for the same neurons re-map from one spatial environment to another.

In this work we show how certain global features of a spatial environment can be computed from hippocampal spiking activity alone. In particular, we consider a variety of two-dimensional environments which differ in the number of obstacles (or holes) constraining the region accessible to a freely-foraging rat. Assuming only basic properties of hippocampal place fields, we construct an algorithm that distinguishes between these different environments by computing standard topological invariants (homology groups) from population spiking activity. These invariants precisely determine the numbers of obstacles/holes in the environment – and can be computed without ever using any position-tracking information, or any other feature of the rat's trajectory through space. In particular, we never compute place fields or any other correlations between cell firing and external stimuli.

We tested the algorithm using simulated data, staying as close as possible to physiological parameters seen in real data. For each of five distinct environments, open field and N-obstacle environments for  $N = 1, \dots, 4$ , we simulated place cell spike trains corresponding to a random walk. (Place fields in different environments were completely unrelated.) The algorithm correctly identified each environment from the population

spiking data. Furthermore, on shuffled data sets, the computed homology groups reflected high-dimensional, non-physical environments. We have thus shown that global features of the spatial environment can be reconstructed from hippocampal place cell spiking activity alone.

### Acknowledgements

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## P159

### Pairwise correlations in cricket cercal interneurons are significant for decoding

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**Background:** To what extent do pairwise correlations exist in sensory systems? Neurons communicate independently, pairwise, or as large populations through features including spike rates and interspike intervals. Previous nonlinear decoders of the *acheta domestica* cercal system estimated stimuli using responses of single primary afferent neurons and interneurons (Z. Aldworth, T. Ganje: private communication). Here, we develop new decoders based on multi-unit data to quantify the interdependence of the interneuron responses. Our first decoder estimates stimuli from a joint probability distribution. Our second decoder assumes interneurons can be decoded independently. Through the correlation measure  $\Delta I$  developed by Latham et al. [1], we demonstrate that the joint decoder reveals more information about the stimulus than the independent decoder.

**Methods:** We present repetitions of white noise sensory stimuli to the preparation and record spike trains extracellularly. After spike sorting, we quantize the times of spikes to create short patterns based on interspike intervals. We approximate marginal, conditional, and joint probabilities of stimuli and responses to measure correlations between pairs of neurons. For the independent interneuron decoder, we calculate the individual stimulus-conditioned response distribution. For the decoder which assumes the interneurons are dependent, we calculate the joint stimulus-conditioned response distribution. With Bayes' theorem, we create an estimate of the joint response and stimulus distributions for each of the two decoders.

**Conclusion:** Substantial  $\Delta I$  values indicate significant pairwise correlations in cricket cercal interneurons. Our results imply that decoders which incorporate correlation are needed to understand the processing of sensory stimuli in the cricket cercal sensory system.

### Acknowledgements

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**P160****Analysis of the factors influencing information transmission at the calyx of Held**

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The calyx of Held is a giant glutamatergic synapse located in the medial nucleus of the trapezoid body (MNTB) of the mammalian auditory brainstem. It is an important model system for studying short-term plasticity because each postsynaptic MNTB neuron receives only one giant synapse, and it is possible to record both pre- and postsynaptic events simultaneously. Physiological experiments show that the evoked excitatory postsynaptic current (EPSC) from the calyx displays a significant depression in response amplitude during a sustained stimulus train [1]. This observation is the result of interactions between various pre- and postsynaptic components occurring across multiple time-scales. Hundreds of readily releasable vesicles (RRVP) aggregate at the different active zones on the presynaptic terminal. The stochastic release of neurotransmitter from the RRVPs (triggered by influx of calcium ions during action potentials, APs), can exhaust the supply of vesicles. Simultaneously, the depleted RRVPs are constantly replenished by a large vesicle reserve pool, and this replenishment is also enhanced by a calcium-dependent process (mediated by the presynaptic APs). The amplitude of the presynaptic AP-evoked calcium ion concentration is affected by inactivation and facilitation of voltage-gated calcium channels as well as activation of presynaptic metabotropic glutamate receptors (mGluRs). In this study we extend our deterministic, multiple time-scale model of the calyx of Held [2, 3] to a stochastic version. We use information theory to measure the amount of information transmitted between pre- and postsynaptic compartments [4]. A series of long, homogeneous Poisson spike trains with mean frequencies up to several hundred Hertz are used to stimulate the calyx model. This spike train is repeated many times, allowing the calculation of the conditional and unconditional entropy of the postsynaptic EPSC amplitude in response to presynaptic interspike intervals (ISI). The mutual information, a measure of the information content of the postsynaptic response (EPSC) about the afferent spike train (ISI), is then computed in terms of conditional and unconditional entropies. The results show that the information content in the postsynaptic response is influenced by the degree of variation of presynaptic calcium ion concentration. Rapid onset and recovery from facilitation maintains high information transfer rates across the frequency range. Suppression of calcium transients by slowly recovering inactivation and mGluR activation results in less information transmission, but prevents depletion of the RRVPs. Fast-acting postsynaptic receptor desensitisation also contributes to information transmission, but in a competitive way to facilitation.

**Acknowledgements**

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**P161****Adaptive rescaling extends the dynamic ranges of central vestibular signals in the alert cat**

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**Background:** Adaptive rescaling adjusts the sensitivities of sensory responses for efficient signal transmission under varying stimulus conditions. The possibility that rescaling could improve the performance of the vestibulo-ocular reflex (VOR) after sensory loss has not been investigated.

**Materials and methods:** We recorded from isolated vestibular neurons in alert cats that had recovered from peripheral vestibular damage. Stimuli consisted of rotation at 1 Hz with peak velocities of 10–120 deg/s. The sensitivities and dynamic ranges of vestibular neurons were measured.

**Results:** Significant rescaling was seen both ipsilateral and contralateral to the damaged side. When the peak velocity increased by a factor of 8, the average sensitivity to rotation of the sample of neurons decreased by roughly a factor of 2. The dynamic ranges of central neurons and of the VOR appeared to increase at higher peak velocities.

**Conclusion:** Our results suggest that after vestibular damage, adaptive rescaling improves signal transmission by central vestibular neurons and may act to restore the dynamic range in the response of the VOR to rotation at high speeds.

**P162****Granule cell activity in the cerebellum during delay eyelid conditioning**

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Although granule cell activity is crucial in defining the information processing performed by the cerebellum, in vivo single unit

recordings of granule cells are scarce. Granule cells, which make more than half of all neurons in the brain, are not currently amenable to in vivo recordings due to their small size. To compensate for this lack of experimental data we performed an optimization analysis that predicts the dynamics of granule cell activity during delay eyelid conditioning. We used a simplified version of a model developed by Mauk and Donegan to optimize granule cell activity given that we have available eyelid conditioned responses for interstimulus intervals ranging from 100 to 750 ms. The solutions found by the optimization algorithm converge on three important aspects of stimulus evoked activity of the granule cells: (a) during stimulus presentation different granule cells become active at different times, (b) for the majority of granule cells the duration of the stimulus evoked responses is not dependent on the duration of the stimulus and (c) peaks of granule cell activity are preceded and/or followed by inhibition. While the first feature has been suggested to be the byproduct of interactions between granule and Golgi cells, the latter two predictions are novel. The utility of these predictions is supported by tests in a detailed simulation of the cerebellum.

### P163

#### The costs of axonal communication

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Previously we evaluated the metabolic cost inherent in action potential velocity and found squid sodium channel density to be at an energy-efficient, optimal level [1]. However, in addition to velocity it is sensible to conjecture that metabolic energy must also pay for information transmission. Indeed Levy and Baxter [2] used an optimization perspective that demonstrated the average firing rate of forebrain cortical neurons corresponds to an optimized value of bits per unit of metabolic energy.

These two distinct optimizations force us to ask: (1) Are these two optimizations distinct, and (2) how – in the biophysical sense – has Nature (natural selection) addressed these two optimizations.

The key insight, which can be seen in [3], is that a substantial fraction of metabolic energy must be devoted to ion fluxes that seem to do nothing. Specifically, the overlapping sodium and potassium currents are neutralizing but the ion fluxes themselves must, eventually, be reversed by the Na-K ATPase pump. We will present biophysical simulations showing that velocity and the energy devoted to velocity can be separated from the energy devoted to information. At the heart of this answer is the presumed ability of Nature to evolve voltage-dependent potassium channels with a range of possible onset delays and the possibility of action potentials that need little if any voltage-dependent potassium channels.

When we create a variable artificial delay of potassium channel activation, we affect both the information rate and the metabolic costs with little or no effect on velocity or its cost. In particular, by altering the delay of the voltage-dependent potassium conductance, we alter the neutralized currents without altering the sodium current of the wave front. Thus nature can

independently evolve signalling systems that pay for velocity and independently pay for information.

The cost of higher information rates is an increasing function of neutralized currents. Thus we conclude the two optimizations are separately evolvable and it is easy to identify distinct examples in nature.

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### P164

#### Systematic computational exploration of the parameter space of the multi-compartment model of the lobster pyloric pacemaker kernel suggests that the kernel can achieve functional activity under various parameter configurations

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The pyloric network in the lobster stomatogastric ganglion (STG) produces rhythmic activity generated by a pacemaker group of electrically coupled neurons AB (anterior burster) and PD (pyloric dilator). The AB neuron is an intrinsic burster and is smaller than the two PD neurons, which can either spike tonically or burst if isolated from AB. We explored the 23-dimensional parameter space of a 4-compartment model of this pacemaker kernel to examine why it includes two types of neurons with different properties, and how its behavior depends on their cellular and synaptic properties. The model consisted of one AB coupled to one PD model neuron, each with a somato-neuritic and an axonal compartment. Our computational exploration started with a hand-tuned pacemaker model [1] and systematically varied maximal conductances of membrane currents, axial conductances, and the electrical coupling strengths. To reduce computation time, the parameter space of each individual neuron was first explored separately. Every parameter set for an individual model neuron was simulated and classified as functional if it produced biologically feasible spiking or bursting (for PD) or bursting (for AB) activity. Specifically, we were looking at the period, amplitude, burst duration, number of spikes per burst, and spike frequency, which all had to be within limits determined in our physiological experiments. Furthermore, in order to be classified as "good," the models had to exhibit proper responses to STG deafferentation (i.e., neuromodulator deprivation) as well as current injections (also determined in our experiments). Functional single neuron

parameter combinations were then joined with a range of coupling strengths and again tested with current injections and model deafferentation. Many different parameter sets performed successfully under all tested conditions. This suggests that the properties of a pacemaker kernel with multiple neurons do not have to be narrowly tuned to achieve functional and robust pacemaker output. Furthermore, our step-by-step approach to selection of "good" models, allowed us to determine criteria that are crucial for classification (e.g., proper activity with and without neuromodulation) and others that seem redundant (e.g., response to current injections).

#### Acknowledgements

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#### PI65

##### Variations of neuronal parameters that do not change network output

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Neuronal network modeling and experiments indicate that the same physiologically relevant patterns of the network activity can be observed for quite different sets of neuronal parameters. These findings imply that parameters, each of which affects network functionality, co-vary in real networks; i.e. the variations of these parameters must be concordant. Finding such concordant variations can advance our understanding on how the properties of individual neurons determine network functionality. In particular, they may explain variability of neuronal parameters observed in living systems, and show possible paths for homeostatic regulation.

In this study, we sought local interrelations between neuronal parameters that did not change network output by using the implicit function theorem. This theorem, under certain conditions, establishes the existence and uniqueness of such interrelations, and specifies them in linear approximation. By assessing such interrelations at different points in the parameter space of a model of the leech heartbeat central pattern generator (CPG) [1], we found a linear correlation between neuronal parameters that preserve a primary output characteristic of this CPG, the cycle period. The correlated parameters were the maximal conductance of the spike-mediated synaptic current, and of the hyper-polarization activated inward current,  $I_h$ . We also found that this linear correlation was different for model neurons with different endogenous activity: silence, bursting or tonic spiking. For neurons of one type, however, the correlation was similar.

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#### PI66

##### Modeling the output of a central pattern generator

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Experimental analysis in our lab has provided a quantitative description of the spatiotemporal pattern of inhibitory synaptic input from the heartbeat central pattern generator (CPG) to segmental motor neurons that drive heartbeat in the medicinal leech. To begin the process of elucidating the relative roles of this pattern of input and motor neuron intrinsic properties and electrical coupling in the elaboration of the heartbeat fictive motor pattern, we constructed a conductance-based ensemble model of all the segmental heart motor neurons and their known synaptic inputs. Our focus was intersegmental and side-to-side coordination of the asymmetric motor pattern: motor neurons on one side fire nearly in synchrony (synchronous coordination), while on the other they fire in a rear-to-front progression (peristaltic coordination). The model reproduces the general trends of the two intersegmental phase relations among motor neurons, but the match with the living system is quantitatively poor, particularly for the peristaltic coordination mode where the phase progression among the segmental motor neurons in the model is only half that observed in the living system. Thus the realistic inputs (experimentally determined) do not produce similarly realistic output in our model.

Modeling experiments, indicate that the most important determinant of the intersegmental and side-to-side phase relations among the heart motor neurons in the model was the spatiotemporal pattern of synaptic inputs, yet phasing was influenced by electrical coupling between the motor neurons in each segment, intersegmental conduction delays in the pre-motor interneurons, intra-burst synaptic plasticity, and intrinsic membrane currents of the motor neurons.

Understanding the shortcomings of the model required that we establish experimentally the precise timing of motor neuron activity in each segment with respect to CPG activity. This analysis show quantitatively how motor neurons in the model fail to fire at the appropriate time with respect to their synaptic inputs and suggest that the intrinsic properties of the model motor neuron are simplistic.

#### PI67

##### Irregular persistent activity induced by synaptic excitatory feedback

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Neuro-physiological experiments on monkeys [1] have reported highly irregular persistent activity during the performance of an

oculomotor delayed-response task. These experiments show that during the delay period the ISI's coefficient of variation (CV) of prefrontal neurons is above 1, on average, and larger than during the fixation period, regardless of whether the cue is preferred or nonpreferred.

Previous models [2, 3] of spontaneous and selective persistent activity in the cortex based on excitatory synaptic feedback do not reproduce this feature because the excitatory feedback during persistent activity brings neurons in a region of the f-I curve in which the firing is relatively independent from fluctuations and hence the CV is small. To overcome this problem, we introduced two ingredients: (1) a high post-spike reset potential (close to threshold), (2) a non-linear relationship between synaptic efficacy and pre-synaptic firing rate via a short-term depression (STD) mechanism.

We show that when the reset potential is close enough to the threshold, the CV-I curve has a maximum above 1 for a sub-threshold mean current. The range of the mean synaptic input values for which the CV is greater than 1 is always in the sub-threshold regime in which firing is dominated by fluctuations of the mean synaptic input. With short-term depression, synaptic efficacies saturate at a certain limiting value of the presynaptic frequency; this in turn provokes a saturation of the mean synaptic current to a neuron at the same limiting presynaptic frequency. This allows the persistent state solution to reach the region of the f-I curve which corresponds to high values of the CV.

We tested this idea both with numerical simulations and analytical techniques. For the analytical studies we used mean-field techniques, recently extended in presence of STD [4], that involves the use of the distribution of the interspike intervals of an integrate-and-fire neuron receiving a Gaussian current in input; this permits to obtain an accurate estimate of the statistic of the postsynaptic current in presence of STD and hence to find the stationary states in a self-consistent way. We also simulated both a fully connected excitatory network of leaky integrate-and-fire neurons endowed with STD, and a cortical network model composed of an inhibitory population and several stimulus selective excitatory populations.

In both cases we find a large range of values of the synaptic efficacies for which the persistent activity is irregular, with values of the CV in agreement with the physiological findings.

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## P168

### Emergent functional neural networks organized by spike timing dependent synaptic plasticity

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The synchronization of neural activities plays very important roles in the information processing in the brain. Recent studies on complex systems have shown that the synchronization of oscillators, including neuronal ones, is faster, stronger, and more efficient in small-world networks than in regular or random networks, and many studies are based on the assumption that the brain may utilize the small-world and scale-free network structure. The collective dynamical response and the functional neural network structure depend on each other due to synaptic plasticities, and this feedback process is believed to be closely linked to the mechanisms for learning and memory in the brain. Recent experimental studies have shown that in various brain regions, such as the hippocampus and the neocortex, both the sign and the magnitude of synaptic modification depend on the precise temporal relation of spike timing of two neurons, which is called the *spike timing dependent synaptic plasticity* (STDP). Here, we study the emergent functional neural networks organized by STDP. We show that STDP can lead a neural oscillator network into a functional structure which has both the small-world behaviors and the scale-free properties with hierarchical modularity. The STDP network has small average shortest path length between the neurons and high clustering coefficient. The degree distributions and the clustering coefficient depending on the degree follow power-law decays. We also show that the balance between the maximal excitatory and the inhibitory synaptic inputs is critical in the formation of the nontrivial functional structure, which is found to lie in a self-organized critical state.

## P169

### Age-related neuromorphological distortion affects stability and robustness in a simulated test of spatial working memory

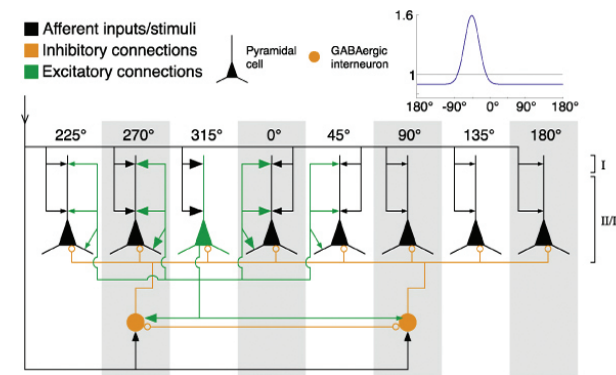
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Normal aging in humans and nonhuman primates is associated with cognitive decline, particularly in tasks involving working memory function that relies on the prefrontal cortex [1]. Because normal aging is not correlated with widespread neuron death or gross morphological degeneration, the biological substrate of these deficits remains unclear [2]. We have constructed a simulated network of model neurons with sufficient detail to model age-related perturbations to morphology and network connectivity, in order to investigate the extent



**Figure 1 (abstract P169)**

**"Bump" attractor network model receiving input encoding the direction '315°' (green neuron), with fully interconnected populations of layer 2/3 pyramidal neurons and GABAergic interneurons.** Neurons are arranged in direction-selective columns. Directionally-tuned input arrives along afferent collaterals (black arrows). Excitatory connections project preferentially to cells in similarly tuned columns (weighting in inset, upper right).

to which these morphological changes in single neurons could explain the functional degradation.

Spatial working memory can be modeled with a "bump"-style network of recurrently connected model neurons, characterized by a continuum of dynamical attractor states that provide an analogue of working memory of spatial orientation [3]. A bump-attractor network (Figure 1) was constructed using branching compartmental models of layer 2/3 neocortical pyramidal neurons [4]. Spine number and density are reduced with age in this neuron type [5], a morphological perturbation that was modeled as a reduction in both recurrent network connectivity and equivalent dendritic surface area. Network function was quantified in terms of the dynamical stability of network attractor states during the delay period of a simulated memory task, as well as the robustness of task performance against perturbation of network parameters. Stability and robustness were compared between "young" and "aged" model neuron populations with the multi-dimensional stability manifold method, which has been used in a previous study to examine the dependence of network simulations on modeling methodology [6].

By defining a stability manifold, we demonstrate how stability and robustness can be quantified as a function of biologically relevant perturbations to single cell morphology and network parameters. This provides a novel technique for evaluating the functional significance of local morphological changes, caused by age, disease or injury, upon cognition at the organism scale.

#### Acknowledgements

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#### P170

##### Integration as sequence detection in a feedforward neural integrator

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In neural integrator networks, transient inputs are accumulated into sustained output signals that reflect the mathematical integral, over time, of their inputs. This computation has been identified as an important component of a wide variety of brain functions ranging from accumulation of sensory evidence for decision making to the motor control of eye movements. All current network models of neural integration assume that the conversion of transient inputs to sustained responses is accomplished by feedback among recurrently connected neuronal elements. Here we show that neural integration can occur even in feedforward networks and describe the properties of this novel class of integrators.

We consider a feedforward network consisting of multiple stages that each have a time constant  $\tau$  with which they linearly filter their inputs. We show that the effective dynamics of this network can be reduced to that of a simple network consisting of a linear chain of neurons with input entering one end and getting successively filtered by each successive stage of the network. As a result of this filtering, later stages of the network have prolonged responses that peak at successively later times. Thus, the network effectively forms a delay-line set of basis functions that are localized in time and that can be flexibly summed to generate a variety of temporal responses. We show analytically that with appropriate choices of synaptic weights, the network can perform a nearly perfect integral of its inputs over a duration of time of order  $N\tau$ , where  $N$  is the number of stages in the network. We further show that although the performance of the network is best understood in terms of basis functions corresponding to a delay-line, the responses of the actual neurons in the network will generally be linear combinations of these basis functions that may not be easily recognized as originating from dynamics governed by a delay line.

The robustness of the network to uniform changes in all synaptic weights can be shown analytically to be similar to that of linear recurrent networks, exhibiting exponential decay of the integrated activity if the weights are too small and exponential growth until signals begin to exit the network if the weights are too large. We show that proper tuning of the weights can be accomplished by a homeostatic learning rule in which neurons scale their intrinsic gain and/or synaptic weights until their activity reaches an average target level over time.

In conclusion, this work suggests a novel mechanism for neural integration. Although we focus on its role as an integrator, the network bears strong similarities to previous networks proposed for temporal sequence recognition and production. This suggests that common underlying principles may be relevant to a host of temporal processing computations.

### P171

#### **Can a temporal code be transferred from one brain region to another? Lessons from phase precession**

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Hippocampal CA1 pyramidal cells in both rodents and humans fire in a spatially selective manner, and are called place cells. These place cells also display a prominent temporal code known as phase precession. As a rat enters the place field of a cell, the cell fires its first spike very late in the first theta cycle, but the phase of the spikes with respect to theta steadily precesses to lower values, all the way to 0 degrees as the rat reaches the end of the place field. CA1 is not alone in showing such phase precession: cells in CA3 and the dentate gyrus have long been known to show phase precession. CA3 cells are the main source of input to CA1. More recently, cells in layer II of the entorhinal cortex (grid cells) have also been shown to phase precess as a rat runs across a single grid field. These cells provide input to both the CA3 and dentate gyrus. However, cells in layer III of the entorhinal cortex do not show phase precession. These layer III cells provide direct input to CA1. Here, we use integrate and fire as well as Hodgkin-Huxley style conductance models to explore the conditions necessary for a CA1 place cell to 'inherit' phase precession from its inputs. We show how CA1 phase precession depends on the standard deviation of the phase of its excitatory inputs, as well as on the precise timing and strength of theta-modulated inhibitory inputs.

### P172

#### **A conductance-based network model of the basal ganglia for probabilistic action selection**

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The basal ganglia (BG) have been implicated in the learning of a sequence of action selections through trial-and-error.

A reinforcement learning-based approach has proposed that the cortico-BG circuit is involved in three basic stages of learning: evaluation of actions, probabilistic selection of an action, and learning from experience. The striatum and mid-brain dopaminergic neurons have been suggested as neural substrates for the first and third stages. Theoretical studies have pointed out the importance of a probabilistic action selection mechanism for learning and on-line adaptation of the behavior. However, the neural substrate of the action selection is still an open question. Our hypothesis for the issue is that the indirect pathway of the BG selects an action to be executed and the direct pathway determines the timing of its execution. Using a conductance-based network model of spiking neurons, we show that the dynamics in the network of the globus pallidus external and the subthalamic nucleus in the indirect pathway provides binary modulation on the substantia nigra pars reticulata, that signals a selected action. Furthermore, binary modulation occurs stochastically, and the selection probability is sensitive to inhibitory input on the globus pallidus. These results suggest that the subthalamopallidal network is capable of probabilistic action selection and the selection probability can be biased by the activities of the striatopallidal projection neurons in the indirect pathway, hence can be optimally tuned by the strength of the cortico-striatal synapses through dopamine-dependent plasticity. We conclude that the indirect pathway of the BG is a neural substrate of the probabilistic action selection.

### P173

#### **Stimulus specific activity patterns in the granule cell networks of mice**

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*BMC Neuroscience 2007, 8(Suppl 2):P173*

It has been speculated that the olfactory bulb encodes information in the form of stimulus specific activity patterns. One of the key features of this population activity is the emergence of odor-specific spatial patterns of mitral cell spiking over a time course of 200–800 ms following stimulus (-odor) onset. We are interested in understanding the mechanisms involved in establishing and maintaining these spatial patterns. Here, we investigated the temporal response characteristics of granule cell activity by imaging activity in populations of olfactory bulb cells following bulk loading of calcium dye in olfactory bulb slices. We found that granule cells show varied (ranging from 0–900 ms) but reliable activation latencies (std. dev. = 50 ms). Moreover, we found that these activity patterns played a significant role in the generation and the maintenance of reliable spike patterns in mitral cells. Experiments in which multiple glomeruli were stimulated showed that the latency of granule cell activity is input specific and that individual granule cells respond most reliably to specific temporal patterns of stimulation. These data suggest that glomerular (~stimulus) identity is encoded in the form of latencies of granule cells activity, which in turn results in distinct stimulus specific changes in the pattern of mitral cell activity.

**P174****Physics of psychophysics: optimal dynamic range of critical excitable networks**Mauro Copelli<sup>1</sup> and Osame Kinouchi<sup>2</sup><sup>1</sup>Laboratório de Física Teórica e Computacional, Departamento de Física, Universidade Federal de Pernambuco, 50670-901, Recife, PE, Brazil<sup>2</sup>Departamento de Física e Matemática, Faculdade de Filosofia, Ciências e Letras de Ribeirão Preto, Universidade de São Paulo, 14040-901, Ribeirão Preto, SP, Brazil  
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BMC Neuroscience 2007, 8(Suppl 2):P174

A recurrent idea in the study of complex systems is that optimal information processing is to be found near phase transitions [1, 2, 3]. However, this heuristic hypothesis has few (if any) concrete realizations where a standard and biologically relevant quantity is optimized at criticality. Here we give a clear example of such phenomenon: a network of excitable elements has its sensitivity and dynamic range maximized at the critical point of a nonequilibrium phase transition. Our results are compatible with the essential role of gap junctions in olfactory glomeruli and retinal ganglion cell output. Synchronization and global oscillations also emerge from the network dynamics. We propose that the main functional role of electrical coupling is to provide an enhancement of dynamic range, therefore allowing the coding of information spanning several orders of magnitude. The mechanism provides a microscopic neural basis for psychophysical laws.

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**P175****Temporal coding of continuously-varying inputs**

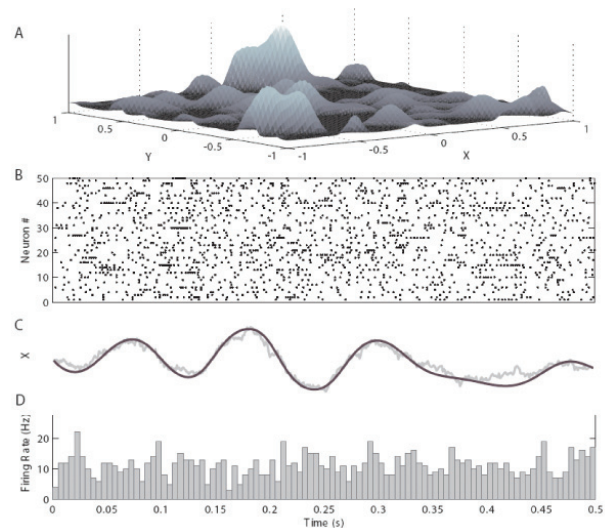
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In many neural circuits, precise patterns of spike timing contain information beyond that contained in mean firing rates. Here we illustrate a simple mechanism by which an ensemble of leaky-integrate-and-fire (LIF) neurons can represent continuously-varying input signals in a timing code. Neurons that are post-synaptic to this ensemble can reliably extract these signals (or functions thereof) in the absence of both spike time coincidence and firing rate variations. Irregular firing is often modelled phenomenologically, for example as a Poisson process with a rate that depends on synaptic input. In contrast, the irregular firing of our LIF neurons is a deterministic consequence of wide variations in applied current over the space of inputs (e.g. Figure 1A). Applied current functions of this kind can arise from weighted output from a previous layer, and we discuss their establishment via Hebbian plasticity. By inclining these functions along a preferred direction, and scaling the peaks, we obtain a continuum between timing and rate codes.

**Figure 1 (abstract P175)**

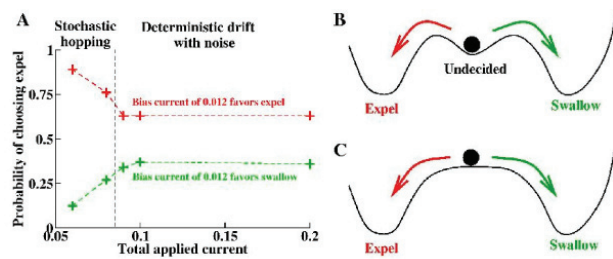
**Temporal coding and decoding with LIF neurons.** **A**, Net synaptic current (arbitrary units) experienced by an example LIF neuron, as a function of two inputs (X and Y). **B**, Irregular firing in 50 different neurons (each with different current functions) as inputs X and Y vary at low frequency. **C**, Estimate of X decoded from activity of an ensemble of 1000 LIF neurons firing as in B. Black line indicates ideal decoding (post-synaptic current dynamics applied to input X). Gray line indicates the estimate of X by a neuron post-synaptic to the ensemble. This estimate is a weighted sum of post-synaptic currents generated by the firing of the ensemble. **D**, Firing rate histogram showing a lack of mean firing rate dependence of an example neuron on input X, over 30 trials. In each trial the input X is identical, but Y varies randomly.

**P176****Stochastic transitions between discrete attractor states in a model taste-processing network**Paul Miller<sup>1,3</sup> and Don Katz<sup>2</sup><sup>1</sup>Department of Biology, Brandeis University, Waltham MA 02454, USA<sup>2</sup>Department of Psychology, Brandeis University, Waltham MA 02454, USA<sup>3</sup>Volen Center for Complex Systems, Brandeis University, Waltham MA 02454, USAE-mail: [pmiller@brandeis.edu](mailto:pmiller@brandeis.edu)

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Trial-to-trial variability in neuronal systems can arise from the timing of stochastically induced, rapid changes between discrete, metastable network states. Such transitions between states produce correlated, rapid changes in firing rates of the neurons. The sharp changes occur at a discrete but unpredictable time in an individual trial, but can be rendered into slow variations of activity when standard trial-averaging is used. Hidden Markov modeling has been used to verify such discontinuous network activity during taste processing in gustatory cortex [1]. Here we model a network of discrete attractor states, where taste-specific inputs bias the stochastic transitions between states to produce a sequence that is taste-specific, as seen in the experimental data. As in the experimental data, hidden Markov



**Figure 1 (abstract P176)**

**Stochastic hopping between metastable states improves accuracy of choice.** (A) Results of 100 simulations with two mutually inhibiting populations, each of 100 neurons and fixed noise. Current is applied to each group, with a bias to favor one outcome. With low applied current, both populations would remain inactive (undecided state) in the absence of noise, so a change in state corresponds to stochastic hopping (B). With greater applied current the inactive (undecided) state is unstable so a deterministic drive (C) causes one population to become active.

analysis reveals the discrete transitions between attractor states that are obscured by trial averaging. Furthermore, we find for a given noise level, that when external inputs provide a bias to one attractor state rather than another, that bias more strongly influences the trajectory of the system if the initial state remains stable, so that the noise itself produces the transition (see Figure 1). We consider the decision-making aspect of taste processing, "to swallow" or "to expel", as corresponding to a transition to one of two final attractor states. We suggest that a noise-induced transition to one of these decisive states leads to fewer mistakes and matches the activity of recorded neurons better than the alternative of a slowly ramping accumulation of evidence.

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#### P177

#### Modeling large-scale neural network culture interface on very-high density multi-electrode arrays

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The use of multi-electrode arrays (MEA) technology is developing in neuroscience fields like neuro-pharmacology [1, 2], network plasticity investigation [3, 4, 5] or neurological diseases [6] and disorders [7]. Dissociated cultures or slices are now often employed on 60–100 multi-site arrays. Recently, matrixes of several thousands of microelectrodes have been

developed in order to gain higher spatial resolution from the cell scale up to large network scale. With the framework of a European Consortium (IDEA Project) we developed a 4096 electrode MEA using the Active Pixel Sensor APS technology as well as a computer model of cortical dissociated cultures grown on this device including the neuron-to-electrode interface. Our goal is to better understand the network mechanisms responsible for recorded activity, and to provide integrated software for Computer Aided Design (CAD) of neural engineering devices. Since it was computationally too heavy to work with thousands of interconnected Hodgkin-Huxley cell models, we chose to implement the Izhikevich model which is known as a good compromise between realistic cellular properties and computation time [8]. Indeed, the classical standard leaky integrate-and-fire cellular model can hardly mimic the rich repertoire of intrinsic cellular properties that can be found in biological substrates. We present here the first recordings of high-density MEAs together with dedicated software which can simulate the complete system composed of the electrode matrix and the biological network grown on top. The first results of these large-scale interconnected networks simulations (size and number of cells similar to those recorded *in vitro*) are consistent with the first recorded data using our prototype of high-density MEAs: (i) the bursts initiation location varies randomly from one place to another, (ii) their propagation varies with the connectivity and the level of presynaptic firing, (iii) the average bursting frequency with no inhibitory connections is close to 1 Hz and similar activity is obtained with bicucullin treated dissociated culture activity. Finally, (iv) the model burst propagation speed is about 100 mm/s and this value has also been computed on real cultures in our lab. This tool is currently used to optimize the design and to investigate the properties of large-scale MEA devices under development and constitutes an innovative neuro-engineering CAD environment.

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## P178

### Synchronizing a 2D continuum of two populations of neural masses

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**Background:** Neural field models of firing rate activity have played a major role in developing an understanding of the dynamics of neural tissues [1]. In this paper we study the possibility of synchronizing a two-dimensional neural field of excitatory and inhibitory layers of neural masses. This is the first step toward an investigation of the properties of visual areas in man and monkey. Each population is described by its post-synaptic potential (PSP), hence the state space is a two-dimensional function defined on the 2D continuum. The field is modeled by an integro-differential equation. At a given point in the continuum this equation models the synaptic integration of the neural mass through a linear term and the contributions of its neighbors to the variation of its PSP through a spatial integration of their firing rates weighted by a connectivity function. The firing rates are classically related to the PSPs through sigmoidal functions.

**Methods:** We use techniques from functional analysis to establish a sufficient condition for the neural masses in the continuum to globally synchronize. The Frechet derivative of the right-hand side of the integro-differential equation is shown to define a compact operator on the set of square integrable functions. The sufficient condition described below is obtained by imposing that the spectrum of the symmetric part of this operator be negative.

**Results:** We provide sufficient conditions on the connectivity matrix of the neural field for the existence of an homogeneous solution. We perform a classical linear stability analysis of this solution in this multidimensional framework [2]. We then use an extension of the contraction analysis for nonlinear systems [3] and of the analysis of concurrent synchronization in dynamic system networks [4] to obtain sufficient conditions for the neural masses in the continuum to globally synchronize when they receive the same input. In the case where the connectivity matrix of the network is translation invariant the condition can be elegantly expressed in terms of its Fourier transform. We also show that this condition implies the linear stability of the homogeneous solution.

**Conclusion:** The sufficient condition described above raises interesting biological questions that may be partially answered through such measurement techniques as Optical Imaging (OI). Conversely, OI measurements can provide clues for the spatial shape of the connectivity matrix. Finally these results open the door to a principled investigation of the properties of the visual areas in man and monkey where spatial synchronization would

be the support of spatial similarity in terms of such visual features as color, texture, edges, optical flow.

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## P179

### Experimenting the variational definition of neural map computation

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### Variational formulation to spiking neural networks:

**A top-down approach:** We bring new insights to better understand the link between spiking neural networks and variational approaches. To do so, we consider two simple visual tasks formulated as variational approaches, related to linear/non-linear filtering [1] and input selection: Image denoising via edge-preserving smoothing, and focus of attention via a winner-take-all mechanism. Variational approaches, which refer to an energy minimization formulation, are defined in a continuous setting. Our goal is to show how spiking neural networks can be used to minimize those energies. Based on some recent advances [2, 3], including spiking neurons [4], the key point is to understand the relation between smoothness constraints and cortical activity diffusion (as observed with extrinsic optical imaging). In particular, we will focus on the two following issues:

**Diffusion:** Depending on the task, and given the underlying neural circuitry and computational power, how far, and how fast should local information be transmitted (e.g., intensity, local gradient, local movement)?

**Feedback:** How can different information pathways, associated with different processing tasks, interact?

**Results and discussion:** Input images, encoded by means of a simple latency code, are processed by a network of spiking neurons generated from the variational description of the task. A simple temporal coding scheme is used in this initial study, the underlying

Figure 1 (abstract P179)

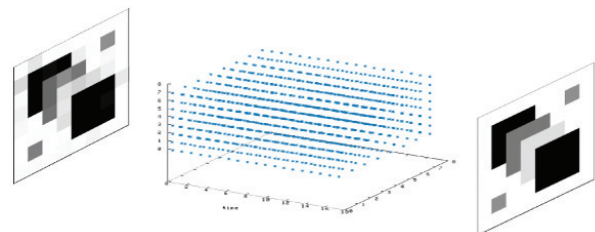


Image denoising by a spiking neural network with local interactions (nearest neighbors).

idea being to analyze the possible role of synchrony as a support for diffusing information [5]. A step further, this relates to more general forms of computation in the brain, in terms of propagation of information, neural coding. It has also been linked [3] to modulation of a feed-forward processing track by various feedback mechanisms.

#### Acknowledgements

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#### P180

##### Synchrony in thalamic inputs enhances propagation of activity through cortical layers

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Sensory input enters the cortex via the thalamocortical (TC) projection, where it elicits large postsynaptic potentials in layer 4 neurons [1]. Interestingly, the TC connections account for only ~15% of synapses onto these neurons. It has been therefore controversially discussed how thalamic input can drive the cortex. Strong TC synapses have been one suggestion to ensure the strength of the TC projection ("strong-synapse model"). Another possibility is that the excitation from single thalamic fibers are weak but get amplified by recurrent excitatory feedback in layer 4 ("amplifier model"). Bruno and Sakmann [2] recently provided new evidence that individual TC synapses *in vivo* are weak and only produce small excitatory postsynaptic potentials. However, they suggested that thalamic input can activate the cortex due to the synchronous firing and that cortical amplification is not required. This would support the "synchrony model" proposed by correlation analysis [3].

Here, we studied the effect of correlation in the TC input, with weak synapses, to the responses of a layered cortical network model. The connectivity of the layered network was taken from Binzegger et al. 2004 [4]. The network was simulated using NEST [5] with the Python interface PyNN [6] to enable interoperability with different simulators. The sensory input to

layer 4 was modelled by a simple retino-geniculate model of the transformation of light into spike trains [7], which was implemented by leaky integrate-and-fire model neurons.

We found that introducing correlation into TC inputs enhanced the likelihood to produce responses in layer 4 and improved the activity propagation across layers. In addition, we compared the response of the cortical network to different noise conditions and obtained contrast response functions which were in accordance with neurophysiological observations.

#### Acknowledgements

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#### P181

##### The effect of gap junctions on the dynamic range in a model of the rod photoreceptors layer

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Recent studies suggest the existence of electrical synapses (gap junctions) in the vertebrate retina, which would be present in at least three different circuits responsible for transmission of rod signals to ganglion cells. In this work we present a computer model of the receptor layer made of 900 biologically realistic rods coupled by gap junctions. The rod model has six types of ionic currents and the connectivity patterns within the receptor layer are based on experimental data available from the literature. We study the role of the gap junction coupling on the enhancement of the dynamic range of the photoreceptor layer beyond the dynamic range of a layer made of uncoupled rods. Simulation results show that the presence of gap junctions in early stages of signal processing could increase the dynamic range of the photoreceptor layer by preventing early saturation.

**P182****Spontaneous pattern generation by a network with dynamic synapses**Dmitri Bibitchkov<sup>1,2,3</sup>, Barak Blumenfeld<sup>1</sup> and Misha Tsodyks<sup>1</sup><sup>1</sup>Department of Neurobiology, Weizmann Institute of Science, Rehovot, Israel<sup>2</sup>Department of Membrane Biophysics, Max-Planck Institute for Biophysical Chemistry, Göttingen, Germany<sup>3</sup>Bernstein Center for Computational Neuroscience, Göttingen, Germany

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Experimental evidence demonstrates that the ongoing spontaneous activity in the visual cortex in the absence of visual stimulation can exhibit complex spatiotemporal patterns. Voltage-sensitive dye imaging studies reveal that activity patterns similar to orientation maps can emerge and dynamically switch in V1 of anesthetized cats [1]. It has been shown that these patterns can be generated by an intracortical network which has intrinsic preferred states correlated with functional maps [2]. The suggested connectivity in such a network depends on the preferred orientation and on the degree of orientation selectivity of the interconnected neurons. In this network, single condition orientation maps are steady states of the neural dynamics and form a ring attractor. To account for dynamical switching between these intrinsic states, we introduced short-term depression into the synaptic connections in the network. We study the effects of synaptic dynamics on the stability of attractor states. We found that synaptic depression, first, stabilizes the overall network activity excluding the possibility of amplitude instability. On the other hand, synaptic depression provides a mechanism of smooth transition between states corresponding to neighboring orientations, observed experimentally. Together with a fluctuating afferent input synaptic dynamics induce dynamic switches between the ring attractor and linear phases. As a result, a complex behaviour emerges with statistical properties similar to the experimentally observed phenomena.

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**P183****A generic model for selective adaptation in networks of heterogeneous populations**Avner Wallach<sup>1</sup>, Danny Eytan<sup>1</sup>, Shimon Marom<sup>2</sup> and Ron Meir<sup>1</sup><sup>1</sup>Department of Electrical Engineering, Technion, Haifa 32000, Israel<sup>2</sup>Faculty of Medicine, Technion, Haifa 31096, Israel  
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Adaptation is a biologically ubiquitous process whereby features of the system's responsiveness change as a result of persistent input. Most often, the kinetics of the change are monotonic and depend

upon the input frequency. Adaptation in neural systems is inherently selective to the input characteristics; not only between sensory modalities, but even within a given modality, the system is capable of reducing its sensitivity to frequent input while preserving (or even enhancing) its sensitivity to the rare (e.g. [1, 2, 3, 4]). *In-vivo* analyses suggest that a within-modality selective adaptation does not require concrete, precise point-to-point wiring (which would be a trivial yet non-physiological realization) [5]. Indeed, theoretical considerations indicate that, for the case of a single neuron, selective adaptation can be explained in terms of synaptic population dynamics (e.g. [6]). *In-vitro* analyses in networks of cortical neurons show that, beyond temporal dynamics, differences between topologies of excitatory and inhibitory sub-networks account for the full range of selective adaptation phenomena, including increased sensitivity to the rare [7]. Formal descriptions of selective adaptation are hindered by the problem of representing these different topologies in an analytically useful manner. In this study we offer a formalism that expresses topologies of connectivity in terms of temporal input gain modulation. Using this technique, we are able to formulate a generic analytic model for selective adaptation, which reconstructs all the major experimentally observed phenomena, offers predictions for further experimental analyses, and caters for a rigorous characterization of adaptation in general, and selective adaptation in particular.

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**P184****How intrinsic dynamics and coupling architecture interact to generate bursting dynamics in a model network of respiratory conditional pacemakers**Christopher Gaiteri<sup>1</sup> and Jonathan Rubin<sup>2</sup><sup>1</sup>Center for Neuroscience, University of Pittsburgh, Pittsburgh, PA, USA<sup>2</sup>Department of Mathematics, University of Pittsburgh, Pittsburgh, PA, USA

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Experiments suggest that the generation of robust, synchronized bursting within the pre-Bötzinger complex (pre-BötC) of the



mammalian brainstem may be critical for respiration, particularly in low oxygen states. The intrinsic dynamics of individual respiratory cells within the pre-BötC, in the absence of coupling, varies widely, with some cells exhibiting tonic spiking, others generating rhythmic bursting, and still others remaining predominantly quiescent. How such a heterogeneous population can produce highly adaptable synchronized bursting remains an open question.

We explored how the distribution of cell types, together with the details of the coupling architecture, shape dynamics in a model pre-BötC network. Dynamics of individual cells were represented using a model developed previously, based on experimental data from pre-BötC recordings [1]. Heterogeneity was introduced by selecting parameter values from distributions; however, we controlled the proportions of each cell type present in each simulation. We focused on three different coupling architectures, namely nearest-neighbor, random, and small-world, representing extremes of order and disorder as well as a neuronally relevant intermediate case. In small-world simulations, we manipulated the intrinsic dynamics of the cells at nodes involved in long-range interactions. To detect bursting in these networks, given the complicated time course of the overall synaptic input to each cell, we developed a novel algorithm based on our knowledge of the dynamical mechanisms underlying the bursting behavior in the pre-BötC model [2]. Our algorithm was able to distinguish between epochs of bursting driven by inactivation of inward currents and epochs of tonic spiking that were abruptly interrupted by withdrawal of inputs. Although networks consisting solely of intrinsic bursters can generate synchronized bursting, the presence of intrinsically quiescent and intrinsically tonic cells was found to enhance the coherence of bursting across the network and the adaptability of bursting. Under appropriate conditions, tonic cells can promote network activity, which can be sculpted into bursting through the dynamics of other cells in the network. Quiescent cells can lead the termination of activity, ensuring that pauses occur between bursts (see also [3]), and can relatively cleanly transmit activity produced by other cells, promoting synchronization. Intriguingly, the most effective burst generation within small-world networks occurred in those with a mixture of quiescent and tonic cells, rather than bursters, at the long-range nodes.

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## P185

### Predicting spike activity in neuronal cultures

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Discovering the functional connectivity and modeling the dynamics of neuronal networks is essential to understand neural information processing. Here we focus on neuronal cultures of neocortical tissue, which are closed system in vitro neural networks. Recordings of spontaneous activity from neuronal cultures using multi-electrode array (MEA) technology have revealed that the activity is composed of irregular network-wide bursts of spikes, even in the absence of any external stimulation [1]. Although it is reasonable to think of 'spontaneous' fluctuations which start a burst in these cultures, the spatio-temporal spread of activity is nevertheless generated and shaped by the underlying network. It is then an interesting problem to characterize the underlying synaptic connectivity based on activity measurements. This knowledge will help us understanding how a given anatomical structure generates different activity patterns, and hence would be a significant step towards understanding structure-function relations in the neural networks of the brain.

Activity dynamics in neuronal cultures display both non-linear and non-stationary characteristics. Noise is another innate property of those networks causing high variability of the activity. The combination of these properties suggests the use of automated adaptive methods, (i.e. machine learning algorithms) to infer appropriate models of the activity dynamics. Specifically, we propose an algorithm to learn a predictive computational model of spontaneous activity in neuronal cultures. The learned model may also be regarded as an abstraction of the underlying effective network connectivity, i.e. its functional connectivity. Although similar functional connectivity models have been described previously [2, 3], we take a steepest descent approach to learn functional connectivity, which naturally allows for online learning and, hence, is able to capture network plasticity, i.e. changes in the structure. We use the log-likelihood of point processes as a criterion for optimization. This approach has previously been suggested to analyse neural receptive field plasticity [4]. Here we apply it to multi-channel recordings from neuronal cultures, and demonstrate its use for learning functional connectivity and predicting upcoming spike activity. A ROC curve analysis of our experiments shows that this online approach predicts upcoming spike activity very well.

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## P186

### Intrinsic hippocampal network activity is altered in MeCP2-deficient mice

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The mammalian medial temporal lobe is capable of generating synchronous rhythmic activities in isolation. For example, brain slices prepared from patients with temporal lobe epilepsy, as well as slices prepared from normal monkey hippocampus, exhibit spontaneous, IPSP-based rhythmic field potentials that have frequencies of between 0.5–3 Hz. These inhibitory rhythmic activities are mediated by GABA-A receptors, and culminate from the network activity of local GABAergic inhibitory interneurons. Analogous spontaneous population rhythmic activities of 0.5–4 Hz are also evident in the isolated rodent hippocampus. These IPSP-based population activities are referred to as spontaneous rhythmic field potentials (SRFPs), as they are readily detected with conventional extracellular recordings. Several lines of evidence suggest that the SRFPs are of physiological significance. The SRFPs spread from the hippocampus to subicular and entorhinal cortical areas, and their frequencies and regional spread are similar to hippocampal electroencephalographic irregular activities that occur in behaving animals during slow wave sleep and wake immobility. In addition, the SRFPs appear during the 2<sup>nd</sup> postnatal week and then persist in adulthood. Such development profile is in keeping with activity-dependent modifications of hippocampal networks. Moreover, field rhythms similar to SRFPs have been shown to regulate memory-related synaptic plasticity such as long-term potentiation. It remains to be explored whether SRFPs can be used as a neurophysiological marker for detecting disease-related alterations in hippocampal networks.

Rett syndrome is a neurodevelopmental condition caused by loss of function mutations within the gene encoding methyl-CpG-binding protein 2 (MeCP2). While a subtle decrease in synaptic activity has been found in *Mecp2*-deficient mouse cortical and hippocampal neurons, it remains to be determined whether or how these changes affect the network activity of the *Mecp2*-deficient brain. To address this issue, we examined the SRFPs in conventional hippocampal slices via extracellular and whole-cell patch recordings. We found that although SRFPs were present in *Mecp2*-deficient slices, their frequency was significantly reduced. This reduction was not associated with significant alterations in the intracellular correlates of SRFPs, but was associated with diminished glutamate receptor-mediated

excitatory activities in individual hippocampal CA3 neurons. The diminished excitatory drive appears to contribute to the slow SRFPs in the *Mecp2*-deficient hippocampus, as pharmacological attenuation of glutamate receptor activity was sufficient to induce similar slow SRFP activity in wild type slices. However, high frequency electrical stimulation of CA3 circuit in *Mecp2*-deficient slices did not reverse the slow SRFP phenotype, but rather induced excitatory, sharp wave like population events that were not observed in wild type slices. Taken together, our data indicate that the *Mecp2*-deficient hippocampus displays a reduction in basal glutamatergic activity in the CA3 recurrent network, that this reduced activity provides insufficient drive to the GABAergic inhibitory interneuronal network that establishes the normal SRFP frequency, but that there is a narrow window of tolerance for the *Mecp2*-deficient hippocampal network to excitatory stimulation.

## P187

### Scaling, stability and synchronization in mouse-sized (and larger) cortical simulations

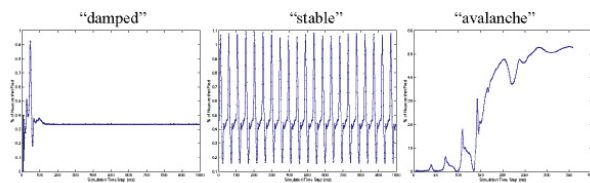
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Together, the two hemispheres of the mouse cortex contain,  $16 \times 10^6$  neurons and 8,000 synapses per neuron. We have recently developed a massively parallel cortical simulator [1] that incorporates relatively simpler single compartment spiking neurons [2], spike-timing dependent plasticity (STDP) [3], and axonal delays.

We created a mouse-scale network by using 32,768 "groups" (80% excitatory) each with 500 neurons such that each group connects to 100 randomly selected groups and each neuron from the projecting group makes a total of  $c = 80$  synapses with the neurons of the receptive group. Excitatory groups had axonal delays uniformly ranging from 1–20 ms, and inhibitory groups had a fixed delay of 1 ms. All simulations used a 1 ms time step. Using a BlueGene/L with 8,192 processors, with 4 TB of memory, using a super-threshold stimulus delivered to every neuron at 4 Hz, we were able to simulate 5 s of model time in 168 s of real-time at a mean firing rate of 4.95 Hz (in stable mode). To further push the boundaries of scaling, by using  $c = 160$  above, we created a network with 16,384,000 neurons and 16,000 synapses per neuron. Using 16,384 processors and 8 TB of memory, using a 5 Hz stimulation, we were able to achieve 5 s of model time in 265 s of real-time at a mean firing rate of 5 Hz (in stable mode).

While it is very easy to drive a network into a damped state or into an avalanche mode, stabilizing cortical simulations is enormously difficult (p. 167, [4]), [5]. We found that the allowed *maximum synaptic efficacy* (which upper bounds the growth of excitatory synaptic efficacies under STDP) and the *probability of the super-threshold stimulus* together greatly affected the behavior of networks. We explored several models with varying numbers of synapses from 1 to 16,000 synapses per neuron. We observed that finding a range of maximum synaptic efficacies corresponding to stable models is harder to achieve for higher number of synapses per neuron if the stimulus probability is kept low. Further, there appears to be a threshold

**Figure 1 (abstract P187)**

Damped, stable and avalanche modes in network simulations.

stimulus probability below which – when maximum synaptic efficacy is varied – models make a sharp transition from damped to avalanche mode. For both the networks with 16,000 and 8,000 synapses per neuron, we observed three distinct modes, namely, damped, stable, and avalanche (shown in figure 1 for the larger network).

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#### P188

##### **Novel application of principal component analysis to understanding visual cortical development**

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Visual experience has a profound effect on cortical development and function. Monocular deprivation early in life leads to anatomical and physiological changes in visual cortex that result in poor visual acuity in the deprived eye. Multiple mechanisms mediate this synaptic plasticity in developing visual cortex, including excitatory (NMDA, AMPA) and inhibitory (GABA<sub>A</sub>) receptors and their subunit composition. However, as the number of mechanisms under consideration increases beyond 2 or 3, it becomes difficult to understand the multidimensional nature of the data and to identify the significant combinations and interactions. We overcame this complexity by applying Principal Components Analysis.

We conducted a comprehensive study of changes in excitatory and inhibitory receptors in visual cortex of cats reared with either normal vision, monocular deprivation, or monocular deprivation followed by a short period of binocular vision. Using Western blot analysis of samples from different regions of visual cortex, we examined changes in excitatory (NR1, NR2A, NR2B, GluR2) and inhibitory (GABA<sub>A</sub>α1, GABA<sub>A</sub>α3) receptor subunit

expression. Monocular deprivation promoted a complex pattern of changes that were most severe in regions of visual cortex where the central visual field is represented.

To understand the complex nature of these changes, we applied a neuroinformatics approach using Principal Component Analysis (PCA) to address the global pattern of change in these plasticity mechanisms. The biological significance of the principal components was determined by correlating them with the ratios of various synaptic proteins. Principal components reflected the overall receptor expression, the balance between excitation and inhibition, and the maturational shift in receptor subunit composition. PCA showed that monocular deprivation causes a significant shift of the developmental trajectory, bypassing a large proportion of the normal developmental path, and accelerating maturation of the receptor subunit expression. This analysis suggests that monocularly deprived animals have less developmental plasticity and lack the molecular machinery needed for functional maturation of cortical circuits. A brief 4 day period of binocular vision was sufficient to restore these important plasticity mechanisms towards that of normal animals.

The application of Principal Components Analysis allows us to understand the overall changes in this multidimensional data and the correlation analysis enables us to understand their biological significance. These results provide insights into molecular mechanisms underlying amblyopia, why binocular vision is crucial for optimal recovery, and why recovery of vision is so poor when deprivation extends beyond 6 weeks of age.

#### P189

##### **Dynamic topography and receptive fields in a model of auditory cortical plasticity**

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Self-organizing maps provide a useful framework for exploring the mechanisms of experience-dependent changes in auditory representations, including those induced by learning. Such models do a good job of explaining many of the changes in tonotopic structure and neural sensitivities produced by classical and operant conditioning involving pure tones [1], but are not able to account for several effects seen after cortical microstimulation, or after basal forebrain stimulation is repeatedly paired with presentations of sounds containing multiple frequencies. In particular, electrical stimulation of rat auditory cortex produces more changes in the responses properties of adjacent sites than they do at the site of stimulation [2], and these receptive field changes are not consistent with a process that makes the neighboring neurons more similar to the most strongly activated neurons. We developed a simple mapping network with a "center-surround" neighborhood function, and a cumulating training function, to assess whether such non-Hebbian learning could account for the kinds changes in cortical response properties seen after neurostimulation. The model exhibits many of the properties of self-organizing maps, but with more dynamic interactions between adjacent nodes that may better account for the variability in auditory cortical plasticity observed experimentally. Ongoing simulations with this model are providing new insights

into how complex perceptual experiences restructure existing cortical representations.

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## P190

### The learning dynamics of spike-timing-dependent plasticity in recurrently connected networks

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**Background:** Functional organization in neural networks is believed to arise from synaptic plasticity. Spike-Timing-Dependent Plasticity (STDP) is a candidate for such plasticity which has received considerable experimental support and been the subject of considerable theoretical investigation. Our work extends the framework developed in [1] for analyzing the learning dynamics of STDP in feed-forward network architecture to the case of recurrently connected networks.

**Methods:** We investigate the dynamics of a network consisting of Poisson neurons recurrently connected with alpha-synapses, where the synaptic weights are modified by a version of STDP incorporating both rate-based and pairwise-correlation-based changes [1]. The network activity is evaluated in terms of the steady-state fixed points of its dynamic variables (firing rates, correlations and weights, all averaged over time). The framework has general applicability and can be applied to any network architecture. The focus of this paper is on a fully connected network with no external synaptic input, in which the neurons are driven only by their spontaneous spiking-rates. This case is not only the most accessible, but it also illustrates the impact of recurrent connectivity upon the learning dynamics.

**Results:** A dynamical system involving the neuronal variables is derived to describe the network spiking dynamics, which involves only fairly general and well-founded assumptions on the parameter values. For a fully recurrently connected network with no external input, the conditions for the existence of a stable homeostatic equilibrium of the weight dynamics are found. The respective fixed points for both the firing rates and the correlations are uniquely determined. A continuous manifold of fixed points for the weights exists. Numerical simulations confirm the stability of the predicted homeostatic equilibrium and the equilibrium values of the spiking-rates and

the average weight. While individual spiking-rates and correlations remain stable (i.e., the time evolution of their variance is stable and relatively small), individual weights diverge on the manifold of the fixed points due to stochastic noise in the network. The evolution of the variance is approximately linear for identical initial weights at the homogeneous fixed point, similar to the case with feed-forward network structure [1].

**Conclusion:** The results obtained here for a recurrently connected network with no external input are qualitatively similar to the results obtained for feed-forward networks with correlated inputs [1], although in the case investigated here the correlations are intrinsic to the recurrent network. The equilibrium values of the parameters are obtained and, although the mechanisms are similar to the feed-forward case [1], the quantitative values differ. The analysis of the stability of the whole manifold of fixed points (using matrix notation) is currently in progress. Future work involves the cases of fully connected networks with (i) uncorrelated and (ii) correlated external synaptic inputs, which are more relevant from a biological point of view.

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## P191

### Learning through activity-dependent plasticity modulation

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Hebbian learning has been implicated as a possible mechanism in a wide range of learning and memory functions in the brain. A large body of theoretical studies and simulations has investigated its implications in the dynamics of single neuron as well as network models. For example, neural network models have been found to produce meaningful internal states when driven by structured external stimulation. These studies, however, typically lack a notion of a "desired output" in the form of a well specified pattern of network activity, corresponding to a relevant functional output. To impose a desired input-output relation, various forms of supervised learning (or at least reinforcement in the form of an external cue) are often invoked. Recently there has been increasing interest in computational models that involve a separation of time scales between relatively fast plasticity rules and considerably slower reinforcement mechanisms. A large majority of these studies focuses on the role of neuromodulators, such as dopamine. Here, we study a training protocol within such a closed loop setup, with the separation of time scales appearing between a fast learning rule and slower synaptic fatigue.

Our model is motivated in part by a series of experiments on ex-vivo cultures of neuronal networks [1, 2]. Such self-assembled networks are perhaps closest in their topology to the random, recurrent networks underlying typical neural network simulation models and lack the complexity of a whole brain, or even a slice. It is an open question whether ex-vivo cultures of neurons and glia can support learning, and if so, what is their capacity and

what mechanisms underlie such phenomena [2]. Here, we study a recurrent network of integrate-and-fire neurons with competitive Hebbian learning (STDP), subject to a learning protocol, in which stimulation is suppressed in response to the onset of a desired output. A local activity-dependent second messenger is used to modulate the level of plasticity. The activity of the network (mediated by external stimulation and reinforcement) directly regulates the second messenger, thus effectively closing the loop. We show how successful learning in these networks depends on the interplay between the network's ability, first, to explore its space of configurations to obtain a desired output, and second, to converge reliably to that configuration in response to the external cues. These results extend the traditional competitive view of Hebbian learning by refining the dependency of the rule to slow (or long-term) input patterns. By explicitly subjecting the network to (i) competitive learning, (ii) explicit reinforcement and (iii) activity-dependent plasticity modulation, meaningful patterns of input-output relations can be learned by the network.

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#### P192

##### A model for correlation detection based on $\text{Ca}^{2+}$ concentration in spines

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Understanding the mechanisms of correlation detection between pre- and postsynaptic activity at a synapse is crucial for the theory of Hebbian learning and development [1, 2] of cortical networks. The calcium concentration in spines was experimentally shown to be a correlation sensitive signal confined to the spine: A supralinear influx of calcium into spines occurs when presynaptic stimulation precedes a backpropagating action potential within a short time window. The magnitude of the influx depends on the relative timing  $t_{\text{post}} - t_{\text{pre}}$  [3]. There is strong evidence that NMDA (N-methyl d-aspartate) receptors are responsible for the supralinear effect [3]. Previous simulation studies relate the occurrence of spike time dependent plasticity to this calcium signal [4, 5]. However, these simulations mainly focus on pairs and triplets of pre- and postsynaptic spikes, rather than on irregular activity. Here, we investigate the properties of a biologically motivated model for

correlation detection based on the calcium influx through NMDA receptors under realistic conditions of irregular pre- and postsynaptic spike trains with weak correlation. We demonstrate that a simple thresholding mechanism acts as a sensitive correlation detector robustly operating at physiological firing rates. We identify the regime (rate, correlation coefficient, detection time) in which this mechanism can assess the correlation between pre- and postsynaptic activity. Furthermore, we show that correlation controlled synaptic pruning acts as a mechanism of homeostasis, and that cooperation between synapses leads to a connectivity structure reflecting the spatial correlations in the input. The detector model allows for a computationally effective implementation usable in large-scale network simulations. On the single synapse level most of the results are confirmed by an analytical model.

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#### P193

##### Identifying spike-timing dependent plasticity in spike train models of synaptically-coupled neuronal ensembles

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Identifying plasticity in cortical neural ensembles is important in studying systems neuroscience to permit tracking the dynamics of biological cortical networks during learning and behavior. Recently, we proposed an algorithm to identify clusters of neurons that exhibit functional interdependency in local and global contexts across multiple time scales. In this paper, we examine the applicability of the algorithm to identify and track functional plasticity in a probabilistic point process model of integrate and fire neural network with time varying synaptic coupling. Three types of coupling between the neurons are considered: auto-inhibition, cross-inhibition, and excitation.



A stimulus-dependent synaptic plasticity is induced randomly to mimic artificial sensory inputs. The results demonstrate that when the stimulus input duration increases such that new synaptic coupling occurs between otherwise uncoupled neurons, the algorithm correctly identifies the change in the circuit topology indicated by the number of clusters of functionally interdependent neurons and their labels. We report the clustering performance of the approach applied to simulated data with spontaneous activity as well as a stimulus driven activity across multiple trials.

## P194

### Modelling structural plasticity

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**Introduction:** Structural changes in neuronal networks occur not only during development but also in adulthood. Modern imaging techniques have shown pronounced structural plasticity in the living animal, e.g., spontaneous spine dynamics and axonal turnover. Furthermore, network rewiring is a precondition for integrating new neurons into mature neural networks, as occurs in the hippocampal dentate gyrus. In contrast to the importance of structural plasticity in biological neural networks, most models of neural networks only include synaptic plasticity. To our knowledge, only two models exist that study structural neural network formation [1, 2]. However, these models lack a precise representation of individual synapses and do not allow for the modelling of neurogenesis. Here, we present a new model for activity-dependent structural plasticity that implements separate axonal and dendritic elements in order to model synaptic turnover and neurogenesis. We have applied the model to two situations. First, we used the model to explain the different response with respect to prefronto-cortical connectivity to enriched and impoverished rearing in an animal (gerbil) model of psychosis [3]. In this animal model, the PFC is disinhibited by applying methamphetamine (MA). Second, we used the model to account for the observed inverse relation between cell proliferation and synaptogenesis in the hippocampal dentate gyrus.

**The model:** The model consists of simple integrate-and-fire neurons, which can be either excitatory or inhibitory. When the activity of a neuron deviates from a desired value, structural changes in connectivity occur to restore the desired level (homeostatic plasticity). The activity-dependent homeostatic outgrowth rules in Van Ooyen et al. [2] were transferred to discrete excitatory and inhibitory axonal ( $A_i$ ) and dendritic elements ( $B_i$ ):

$$\Delta A_i := v \cdot \Delta S_i \cdot A_i, \Delta B_i^{exc} := -v \cdot \Delta S_i \cdot B_i^{exc},$$

$$\text{and } \Delta B_i^{inh} := v \cdot \Delta S_i \cdot B_i^{inh}$$

where  $v$  gives the velocity of synaptic changes and  $\Delta S_i$  is the deviation of the neuronal average activity from a desired mean value. In addition, new cells can be added, which then integrate into the network following the above rules. Cells are deleted

(apoptosis) if their average activity is very much higher or lower than the desired value [4].

**Results: Prefronto-cortical connectivity:** The simulation revealed that the course of structural reorganisation shaping excitatory and inhibitory connections depend on the previous network connectivity. Under enriched-rearing, early well-matured prefronto-cortical networks compensate a MA induced disinhibition by reducing excitatory contacts. Under impoverished rearing, in contrast, weakly connected networks profit from the activation (caused by disinhibition) and increase connectivity and rather compensate the disinhibition by increasing GABA inhibition. *Cell proliferation versus synaptogenesis in the hippocampus.* The inverse relation between cell proliferation (CP) and synaptogenesis occurs because high CP rates rapidly exhaust available synaptic elements, whereas moderate CP rates leave enough synaptic elements for subsequent synaptogenesis. In general, the model suggests that activity-dependent homeostatic plasticity underlies structural changes observed in adult cortical and hippocampal networks.

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## P195

### Does reliable neuromodulation require that neuronal network parameters are tightly regulated?

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Previous experimental results and simulation studies show that similar spontaneous electrical activity can arise from different cellular and synaptic properties, both at the level of single neurons and at the level of neuronal circuits [1, 2]. Neuronal circuits thus appear to have large "solution spaces" at their disposal, rather than having to fine-tune their cellular and synaptic parameters to specific values in order to function properly. On the other hand, neuromodulators often have reliable and reproducible effects on the same circuit in different animals [3]. If different animals generate the same circuit output on the basis of different circuit properties, how can they react in the same way to application of a neuromodulator?

To address this question we separately simulated the cellular and synaptic effects of the  $I_A$  channel blocker 4-aminopyridine (4-AP) and of dopamine in 452,516 models of the pyloric

pattern-generating network of crustaceans. These three-cell circuit models differed substantially in their cellular membrane conductance composition and in the strengths of the seven synapses in the circuit, but all 452,516 circuit models had previously been shown to generate spontaneous network activity that closely mimics the biologically observed pyloric rhythm [2]. We then identified those pyloric network models among the 452,516 original models that responded to application of 4-AP or dopamine in the same way that the biological circuit responds [3, 4] with respect to rhythm criteria such as period, burst frequencies, and duty cycles.

For both 4-AP application and dopamine application, we found that only a subset of the original 452,516 network models showed a response similar to that of the biological circuit. This implies that although similar spontaneous circuit activity can arise from different circuit properties, the requirement that a circuit respond correctly to neuromodulation can impose additional constraints on circuit parameters and thus decrease the size of the solution space available to a neuronal circuit. However, the subset of network models that performed correctly during simulated application of 4-AP or dopamine contained models that differed widely in some of their cellular and synaptic parameters. This suggests that even neuronal networks that need to be able to generate a variety of biologically functional behaviors in the presence of different neuromodulators can do so without having to narrowly tune their circuit parameters.

#### Acknowledgements

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#### P196

##### **A simple spontaneously active Hebbian learning model: homeostasis of activity and connectivity, and consequences for learning and epileptogenesis**

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As suggested by recent experimental evidence, a spontaneously active neural system that is capable of continual learning should

also be capable of homeostasis of both activity and connectivity. The connectivity appears to be maintained at a level that is optimal for information transmission and storage. We present a simple stochastic computational Hebbian learning model that incorporates homeostasis of both activity and connectivity, and we explore its stability and connectivity properties. We find that homeostasis of activity and connectivity imposes structural and dynamic constraints on the behavior of the system. For instance, the connectivity pattern is sparse and activation patterns are scale-free. Additionally, homeostasis of connectivity must occur on a timescale faster than homeostasis of activity. We demonstrate the clinical relevance of these constraints by simulating a prolonged seizure and acute deafferentation. Based on our simulations, we predict that in both the post-seizure and post-deafferentation states, the system is over-connected and, hence, epileptogenic. We further predict that interventions that boost spontaneous activity should be protective against epileptogenesis, while interventions that boost stimulated or connectivity-related activity are pro-epileptogenic.

#### P197

##### **Direct reinforcement learning, spike time dependent plasticity and the BCM rule**

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Learning agents, whether natural or artificial, must update their internal parameters in order to improve their behavior over time. In reinforcement learning, this plasticity is influenced by an environmental signal, termed a reward, which directs the changes in appropriate directions. We model a network of spiking neurons as a Partially Observed Markov Decision Process (POMDP) and apply a recently introduced policy learning algorithm from Machine Learning to the network [1]. Based on computing a stochastic gradient approximation of the average reward, we derive a plasticity rule falling in the class of Spike Time Dependent Plasticity (STDP) rules, which ensures convergence to a local maximum of the average reward. The approach is applicable to a broad class of neuronal models, including the Hodgkin-Huxley model. The obtained update rule is based on the correlation between the reward signal and local data available at the synaptic site. This data depends on local activity (e.g., pre and post synaptic spikes) and requires mechanisms that are available at the cellular level. Simulations on several toy problems demonstrate the utility of the approach. Like most stochastic gradient based methods, the convergence rate is slow, even though the percentage of convergence to global maxima is high. Additionally, through statistical analysis we show that the synaptic plasticity rule established is closely related to the widely used BCM rule [2], for which good biological evidence exists. The relation to the BCM rule captures the nature of the relation between pre and post synaptic spiking rates, and in particular the self-regularizing nature of the BCM rule. Compared to previous work in this field, our model is more realistic than the one used in [3], and the derivation of the update rule applies to a broad class of voltage based neuronal models, eliminating some of the

additional statistical assumptions required in [4]. Finally, the connection between Reinforcement Learning and the BCM rule is, to the best of our knowledge, new.

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## P198

### Stimulus reconstruction reveals extended 'replay' in the rat hippocampus during exploration

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Spatially-modulated firing of hippocampal 'place cells' is thought to subserve spatial learning in the rat. Ensemble recordings have shown that these cells re-express behavioral firing sequences during sleep. Recently, replay of the reverse of behavioral sequences has been reported in the awake rat at reward sites. These phenomena are hypothesized to play a role in memory formation and consolidation.

Here we report findings from simultaneous recordings of ensembles of place cells in area CA1 of the hippocampus during exploration of a 10 m linear track. In contrast to existing replay detection methods which look for patterns in the spiking records of cells, we employ a Bayesian algorithm to reconstruct the position stimulus, and detect replay as trajectories in the stimulus space. Notably, due to the directionality of the recorded place cells, we can reconstruct both the animal's position and direction of movement, which allows us to differentiate between forward and reverse replay.

We apply our method to periods of immobility, and find that both forward and reverse replay are prevalent. Either the start or end point of the replayed trajectories are often anchored to the rat's current location. We detect significant replay events several times per minute. Replay episodes have a mean duration of ~300 ms (max. 700 ms); replayed trajectories span on average ~3 m of the track (max. 8 m) with a corresponding 'virtual' velocity of 8 m/s (0.3 m/s s.e.m.). Replay is correlated with increased power in the ripple-band (150–250 Hz) in the local field potential.

These findings show that place cells in the hippocampus of the behaving rat can express patterns of activity corresponding to traversal of remote locations. The observed 'virtual' trajectories proceed in both the forward and reverse order and extend across a longer timescale than has previously been appreciated.

## P199

### Biological plausibility of kernel-based learning

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We argue that kernel-based learning algorithms and, more generally, linear-in-the-parameters learning are more biologically plausible than has been supposed, and that they can be combined with neural-network ideas to gain advantages of both approaches. **1.** While linear-in-the-parameters learning is fast, it seems to waste neurons because it does not permit as high a ratio of adjustable synapses to cells as does nonlinear learning. But we show that the ratios become comparable as the number of output variables increases – i.e. linear learning becomes plausible when one considers that a brain has to learn many different, high-dimensional tasks. **2.** Fast linear algorithms like RLS involve computations with large matrices, but we show that the matrices needn't be represented in transmissible form, in cell firing, but can be stored in synapses, which are much more plentiful than cells in the brain – i.e. there is, plausibly, enough storage space for these matrices. **3.** Linear algorithms train just one layer of synapses, but with appropriate internal models we show how the process can be repeated at different stations in series, to get supervised learning at many different layers. **4.** We show that it is possible to back-propagate through kernels, without needing the weight transport that is the implausible aspect of backprop, and so get more-effective feature-shaping than is normally possible with kernel methods. **5.** We show that linear learning does not imply that most, or even necessarily any, neurons stay inside their linear ranges. **6.** More speculatively, we point out that aspects of kernel-network learning agree with certain of our intuitions about learning and memory, e.g. that at least some kinds of memory consist largely of specific experiences, not blends, and that when an experience is repeated over and over, we remember later instances less well.

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## P200

### Learning in spatially extended dendrites

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Dendrites are not static structures, new synaptic connections are established and old ones disappear. Moreover, it is now

known that plasticity can vary with distance from the soma [1]. Consequently it is of great interest to combine learning algorithms with spatially extended neuron models. In particular this may shed further light on the computational advantages of plastic dendrites, say for direction selectivity or coincidence detection. Direction selective neurons fire for one spatio-temporal input sequence on their dendritic tree but stay silent if the temporal order is reversed [2], whilst "coincidence-detectors" such as those in the auditory brainstem are known to make use of dendrites to detect temporal differences in sound arrival times between ears to an astounding accuracy [3]. Here we develop one such combination of learning and dendritic dynamics by extending the "Spike-Diffuse-Spike" [4] framework of an active dendritic tree to incorporate both artificial (tempotron style [5]) and biological learning rules (STDP style [2]).

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#### P201

##### Learning sensitivity derivative by implicit supervision

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In control theory, variables called sensitivity derivatives quantify how a system's performance depends on the commands from its controller. Knowledge of these derivatives is a prerequisite for adaptive control, including sensorimotor learning in the brain, but no one has explained how the derivatives themselves could be learned by real neural networks, and some say they aren't learned at all but are known innately. Here we show that this knowledge can't be

solely innate, given the adaptive flexibility of neural systems. And we show how it could be learned using forms of information transport available in the brain. The mechanism, which we call implicit supervision, explains how sensorimotor systems cope with high-dimensional workspaces, tools, and other task complexities. It accelerates learning and explains a wide range of findings on the limits of adaptability, which are inexplicable by any theory that relies solely on innate knowledge of the sensitivity derivatives.

#### P202

##### Anticipative adaptive muscle control: forward modeling with self-induced disturbances and recruitment

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A motor system must be able to adapt to perturbations in a fast and robust way. Additionally, in the long run learning leads to motor skills which, for example, allow humans to move the forearm with varying speeds. A generally expected view on motor learning includes forward models that are generated on top of an existing control loop provided by reflexes. Through closed-loop feedback control a much improved motion sequence "without thinking" can be executed and later be adapted to changes in the environment. In this study we show that it is possible to combine temporal sequence learning with compliant joints and antagonistic muscle control to learn a forward model of a reflex.

We also show that the model is executed with the required strength, which depends on self-induced perturbations or external forces. Here self-induced perturbation means, for example, the change of torque by accelerating the forearm. For this purpose we apply a learning rule paired with recruitment which we have recently introduced. The rule correlates the mono-synaptic reflex loop provided by each muscle with an anticipative control signal which is used to move the upper arm segment of a two-joint arm. Without learning the deviation is compensated after some delay. After learning the antagonistic muscle pair stiffens and immediately reacts to the self-induced disturbance with the required muscle force. With this simple recruitment mechanism it is also possible to compensate different forces, caused by varying upper arm accelerations, without delay and re-learning. This kind of learning creates a forward model of the already existing mono-synaptic feedback loop and we are able to show that applying learning with recruitment to a compliant motor control structure quickly compensates self-induced disturbance.

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**P203****Functional mechanisms of motor skill acquisition**Ashvin Shah<sup>1</sup> and Andrew G Barto<sup>2</sup><sup>1</sup>Neuroscience and Behavior Program, University of Massachusetts Amherst, Amherst, MA 01003, USA<sup>2</sup>Department of Computer Science, University of Massachusetts Amherst, Amherst, MA 01003, USA  
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As a motor skill is learned, behavior progresses from execution of movements that appear to be separately generated to recruitment of a single entity. Movements come to be executed more quickly, require less attention, and behavior loses flexibility. Neural activity also changes. Task-related neuron activity during a movement executed as part of a motor skill differs from that during the same movement executed alone. Also, cortical planning areas (e.g., frontal and prefrontal cortices) dominate control early in learning, while less cognitive areas (e.g., striatum) dominate later. The change in behavior and neural activity suggests that different control strategies and systems are employed as the motor skill develops.

We propose that the behavioral and neural progression is due to a transfer of control to different types of controllers: *explicit planner*, which selects movements by considering the goal; *value-based*, which selects movements based on estimated values of each choice; and *static-policy*, in which a sensory cue directly elicits a movement – no decision is made. Explicit planners require much computation (and thus time and attention) and pre-existing knowledge, but are able to make reasonable decisions with little experience and are flexible to changes in task and environment. Static-policy controllers require little computation and knowledge, but must be trained with experience and are inflexible. Value-based controllers have intermediate characteristics. Neural systems can implement these mechanisms: frontal cortices conduct planning, striatum and prefrontal cortex estimate values, and the static policy controller can be implemented by a direct mapping, such as thalamus (sensory) to striatum (motor). The progression of the behavior and neural systems associated with the progression of the controllers is similar to that seen in motor skill development.

We test the validity of this scheme with computational models – based on biologically plausible mechanisms and architecture – in which an agent must execute a series of actions (analogous to movements), elicited by the controllers, to solve tasks. As the succeeding controller is trained, it selects a movement faster than the preceding controller, which relinquishes control. By comparing model behavior to human and animal behavior in analogous tasks, we show that it exhibits qualities indicative of motor skill acquisition. We also investigate how task specification and environmental conditions affect motor skill development and strategy, how the presence of existing motor skills affect the agent's strategy in solving other tasks, and the parallels between resulting model behavior and human and animal behavior.

Previous models have investigated how different controllers participate in biological decision making [1] and motor control [2, 3, 4]. While each model has unique properties, they all show that the availability of different controllers improves learning and behavior.

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**P204****A computational approach for modeling the infant vision system in object and face recognition**

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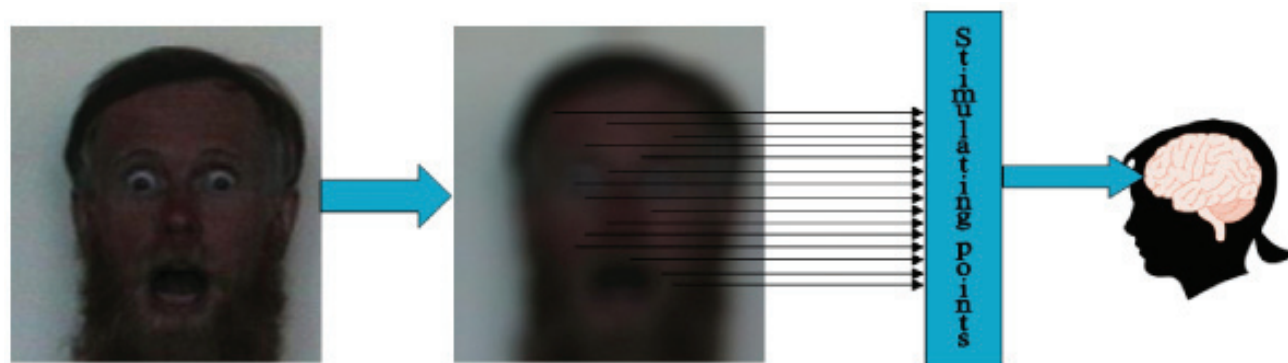
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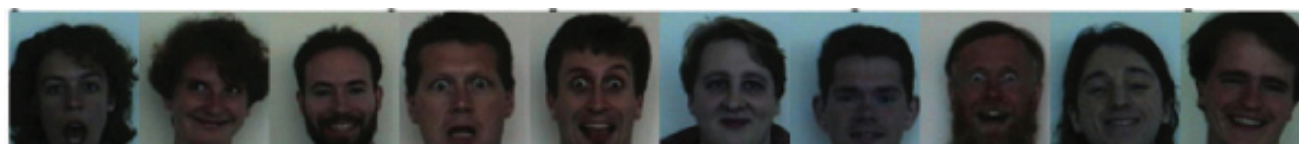
**Background:** Most research in vision systems has been focused on the fully developed visual system of adult humans. During early developmental stages, there are communication pathways between the visual and other sensory areas of the cortex, showing how the biological network is self-organizing. Within a few months of birth, the brain can differentiate faces from other faces or objects from other objects.

**Proposal:** In this research, we investigate the learning process of face and object recognition of the infant's brain. The biological hypotheses of this model are based on the role of responses to low frequencies in early stages [1], and some conjectures concerning to how an infant detects subtle features (stimulating points) in a face or object [2]. We simulate the infant's brain using the dynamic associative model (DAM) deeply described in [3]. This model changes their synapse connection strengths according to an input stimulus based on the Hebbian learning rule. The model for infant vision consists of a DAM used to recognize different images of faces and objects. As the infant vision responds to low frequencies of the signal, a low-filter is first used to remove high frequency components from the image. Then we detect subtle features in the image by means of a random selection of stimulating points. At last, the DAM is fed with this information for training and recognition (Fig. 1).

**Results:** To test the accuracy of the model, we performed two experiments. In experiment 1, we used a benchmark of faces of 15 different people (Fig. 2). In experiment 2, we use a benchmark of 5 objects (Fig. 3). During the training process in both experiments, the DAM performed with 100% accuracy using only one image of each person and object. During testing, the DAM performed in average with 99% accuracy for the remaining 285 images of faces (experiment 1) and 99% accuracy for the remaining 90 images of objects (experiment 2) by using different sized-filter and stimulating points.

**Figure 1 (abstract P204)**

Schematic representation of the model.

**Figure 2 (abstract P204)**

Some of the 20 images of each person with different gesticulations used in experiment 1.

**Figure 3 (abstract P204)**

Some of the 20 images of each object at different orientations (from 0 to 95 degrees) used in experiment 2.

**Conclusion:** The model learned to distinguish faces and objects accurately in a similar manner that an infant's brain builds the neural connections after birth. Preprocessing images used to remove high frequencies and random selection of stimulating points contribute to eliminating unnecessary information and help the DAM to learn efficiently the faces and the objects. Successful results suggest the proposal could serve as a biological model to explain the learning process in infant's brain for face and object recognition.

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#### P205

##### Unsupervised learning is crucial to learning the names of objects

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Children learn to name the objects they see by forming general associations between the words they hear and the images

arriving at their retina. Discriminative neural network models can also be taught to classify objects, but to do so they require more information about how images pair with words (i.e. supervised data) than the brain seems to receive. We propose that the brain exploits unsupervised learning on raw sensory input to compensate for the scarcity of supervised data in its environment. Here we show that artificial neural networks which first develop a statistical model of the world in an unsupervised fashion are capable of learning good image-word pairings using dramatically less supervised data. This idea may help to explain how the brain learns sensorimotor problems for which there is little feedback available about the success of selected actions.

## P206

### On efficient sparse spike coding schemes for learning natural scenes in the primary visual cortex

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We describe the theoretical formulation of a learning algorithm in a model of the primary visual cortex (V1) and present results of the efficiency of this algorithm by comparing it to the SparseNet algorithm [1]. As the SparseNet algorithm, it is based on a model of signal synthesis as a Linear Generative Model but differs in the efficiency criteria for the representation. This learning algorithm is in fact based on an efficiency criteria based on the Occam razor: for a similar quality, the shortest representation should be privileged. This inverse problem is NP-complete and we propose here a greedy solution which is based on the architecture and nature of neural computations [2]. It proposes that the supra-threshold neural activity progressively removes redundancies in the representation based on a correlation-based inhibition and provides a dynamical implementation close to the concept of neural assemblies from Hebb [3]. We present here results of simulation of this network with small natural images (available at <http://incm.cnrs-mrs.fr/LaurentPerrinet/SparseHebbianLearning>) and compare it to the Sparsenet solution. Extending it to realistic images and to the NEST simulator <http://www.nest-initiative.org/>, we show that this learning algorithm based on the properties of neural computations produces adaptive and efficient representations in V1.

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### A neurologically plausible implementation of statistical inference applied to random dot motion

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We propose a model of basic motion perception consisting of a hierarchical non-linear state space model (NSSM) developed within a variational Bayesian (VB) framework. Each level of the hierarchy is a 'cause' that generates a prior distribution on the level below via a generative function.

The temporal dynamics and generative functions between layers of the hierarchy are implemented as neural networks with non-linear activation functions. Optimization of model parameters and causes proceed concurrently as a combination of fixed-point rules and gradient decent schemes. To make the optimization problem tractable, the standard mean-field and Laplace approximations are employed. The precise factoring used in the mean-field approximation is designed to meet a balance between tractability, neurological plausibility and modeling power. In this approach inference and learning proceed concurrently, in an online and unsupervised fashion.

Other work has produced similar implementations of NSSMs that have been successful in predicting low-dimensional temporal signals, but with highly restrictive assumptions on the form of the posterior distributions and with learning done in batches instead of online [1].

Competing work has relaxed many of these implementation assumptions and achieved prediction of high dimensional input but at the cost of discarding VB techniques in favor of inefficient discrete state-space methods [2]. Moreover, such techniques have been demonstrated only with pre-learned weights and simplistic statistical models.

Our model is primarily tested on realistic high-dimensional input generated by randomly moving dots over a detection grid. The results from a spiking neuron implementation of the model based on the Neural Engineering Framework (NEF) are compared directly to single cell recordings in random dot motion perception and decision-making tasks.

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