Nishinomiya-Yukawa International & Interdisciplinary Symposium 2007
"What is Life? The Next 100 Years of Yukawa's Dream"

Masatoshi Murase

Welcome to this international and interdisciplinary symposium on "What is Life?" Although the topic of "What is Life?" seems to be very popular and has attracted so many people including specialists and non-specialists, there are little chances to discuss such a topic with strong emphasis on making bridges among different disciplines such as physics, biology, psychology, mathematics, computer science, neuroscience, environmental science, economics, philosophy, religion, and even arts. In this sense, the present symposium should provide the most attractive and challenging program for all of us.

The late professor Hideki Yukawa was born in the year 1907. This year 2007, therefore, happens to be a centennial of Yukawa's birth. Indeed, Yukawa has been known as a theoretical physicist who got the first Nobel Prize as Japanese after the World War II. Yukawa, however, had been very interested in life and mind as he introduced the famous Schrodinger's book on "What is Life?" to Japan. He had studied not only the Western Science, but also Eastern Philosophy. Such a wide range of his background would be extremely important for developing his original theory of meson. Likewise, to attack the long-lasting problem of "What is Life?" we must have a synthetic view by integrating quite diverse disciplines as I introduced in this symposium. Although it is very difficult to get a final answer to this problem, I believe that we can contribute to successful advancement towards modern syntheses.

We are planning to publish the proceedings of this symposium in 2008 from the journal of ***Progress of Theoretical Physics: Supplement "What is Life? The Next 100 Years of Yukawa's Dream".*** Most of all the lectures will be incorporated in this volume. In addition, Kyoto University's Open

Course Ware will distribute visual data of some of the lectures over the world through the web-site: http://ocw.kyoto-u.ac.jp/en/index.htm.

We hope that such efforts about distributing the results of our present symposium will produce almost infinite effects in the future.

Fortunately, this symposium is sponsored by Kyoto University the 21st Century COE Program "Center of Diversity and Universality in Physics", The Kyoto University Foundation, and Grant-in-Aid for "Interdisciplinary and Advanced Study" from President, Professor Kazuo Oike, of Kyoto University. It is also co-sponsored by Nishinomiya City, Asia Pacific Center for Theoretical Physics, International Institute for Complex Adaptive Matter, and National Science Foundation. The symposium is further co-sponsored by the following Institutes and Centers of Kyoto University: San-sai Gakurin, Graduate School of Global Environmental Studies, Bioinformatics Center, Institute for Chemical Research, Center for Ecological Research, Primate Research Institute, Institute of Economic Research, Kokoro Research Center, and Kyoto-U Open Course Ware. We would be very grateful for these extraordinary supports.

湯川・朝永 生誕100年

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Masatoshi Murase
Chair
Organizing Committee of
Nishinomiya-Yukawa International & Interdisciplinary Symposium 2007 on
"What is Life? The Next 100 Years of Yukawa's Dream"

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Historical reasoning and abductive inference in phylogenetic reconstruction

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Phylogenetic reconstruction in general aims at estimating the most plausible tree (or network) based on character data. In evolutionary biology, comparative philology, and historical linguistics researchers have repetitively invented a set of rules for building phylogenetic trees from data on organisms, manuscripts, or languages. All these sciences have in common the basic features of historical sciences ("palaetiology" sensu William Whewell). Estimating evolutionary history searches for the best solution among possible alternative hypotheses. However, the best solution isn't necessarily historically true because we can't observe directly or experimentally the past evolutionary process and its products. All we can do is to find the best tree by comparing the universal set of possible trees on the basis of a given optimality criterion such as parsimony or likelihood. Thus historical reasoning is comparable in nature; it has been called "abductive" reasoning. Abduc

tion is a form of non-deductive inference to the best hypothesis for a given data. Abductive inference in phylogenetic reconstruction poses several mathematical problems which includes 1) how large-scale phylogenetic trees can be calculated in a reasonable computational time (an NP-complete problem); 2) what properties ancestral character states reconstructed on a given tree have (a lattice-theoretical problem); and 3) what relationships there are between phylogenetic trees and networks (a combinatorial problem).

Sorting of polar filaments by multiple motor action.

Assaf Zemel and Alex Mogilner.

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Interactions of multiple molecular motors with dynamic polymers, such as actin and microtubules, form the basis for many processes in the cell cytoskeleton. One of the examples is 'sorting' out bipolar microtubule bundles into aster-like arrays by dynein motors: initially disordered microtubules slide as a result of the action of the motors, one end of which is attached to a microtubule, while another 'walks' to the plus end of another, neighboring microtubule. A number of models were suggested to quantify similar phenomena; the main difficulty, still not been overcome, is that in the dense microtubule bundles each filament interacts with many neighbors, invalidating mean field and other approximations.

We use Monte Carlo type modeling to simulate dense microtubule bundles in which filaments slide as a result of the multiple motor action. The motors are characterized by linear additive force-velocity relations; force-balance equations in the low Reynolds number environment of the cell govern the bundle dynamics. We observed that the bundle behavior is determined by its average density. The bundle expands fast if there is, on the average, one to two neighbors with which each microtubule interacts. If the bundle is less dense than that, many microtubules move by diffusion, slowing down the dynamics. on the other hand, in denser bundles, motors start to interfere with each other behaving effectively as brakes and ultimately slowing the preading of filaments. Furthermore, the simulations demonstrate polarity sorting phenomenon observed and modeled before: depending on the motor polarity, either plus or minus ends of all microtubules eventually focus, while the opposite ends stick outward creating the aster-like structure. We discuss physical and biological implications of these results for understanding self-organization phenomena in cell biology.

Oct. 15 (Mon) 10:15-11:15

Alex Mogilner

Professor

My CV is here.

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Research Area

System/Computational Biology, Cell Biophysics.

Current Research Interests

Cell motility and cell division.

Single molecule study for elucidating the mechanism involved in utilizing fluctuations by biosystems

Toshio Yanagida

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Biomolecules assemble to form molecular machines such as molecular motors, cell signal processors, DNA transcription processors and protein synthesizers to fulfill their functions. The reactions and behaviors of molecular machines respond to their surroundings with great flexibility. This flexibility is essential for biological organisms and biological systems. The underlying mechanism of molecular machines is not as simple as that expected from an analogy with man-made machines. Since molecular machines are only nanometers in size and have a flexible structure, they are very prone to thermal agitation. Furthermore, the input energy level is not much different from that of average thermal energy, k_BT. Molecular machines can use this thermal noise with a high efficiency of energy conversion for their functions. This is in sharp contrast to man-made machines that operate at energies much higher than thermal noise. In recent years, single molecule detection (SMD) and nano-technologies have rapidly been expanding to include a wide range of life science applications. The dynamic properties of biomolecules and the unique operations of molecular machines, which were previously hidden in averaged ensemble measurements, are now being unveiled. The aim of our research is to approach the engineering principle of adaptive biological systems by uncovering the unique operation of biological molecular machines. Here, I review our SMD experiments designed to investigate molecular motors, enzyme reactions, protein dynamics and cell signaling, and discuss how thermal fluctuations (noise) play a positive role in the unique operation of biological molecular machines allowing for flexible and adaptive biological systems.

Reference: http://www.phys1.med.osaka-u.ac.jp/

A minimal cell model showing both amoebic movement and network formation

Gunji Pegio-Yukio

Kobe University

In the context of origin of life, self-sustained system boudanded by a membrane is adocatated, and then amoebic movement is focused in making a model cell.

By contrast, in the context of natural computing, computability of a cell is demonstrated by Physarum, and then its ability of forming adaptive transport network is described and analyzed.

However, there is little endeaver to connect them. Here we show that our minimal cell model called CELL that can show amoebic motion, can form an adaptive transport network, and can solve a maze, and some other graph theoretical problems like physarum.

Oct. 15 (Mon) 16:-00-17:00

Luciano Floridi
Oxford University & Università di Bari

What is bioinformation?

Abstract

In contemporary philosophy of biology and bioethics there is considerable discussion about the nature of biological information. In this paper, I argue that biological information is "information" in a procedural sense.

DNA contains the genetic code, precisely in the sense that it contains genes which code for the development of the phenotype. So DNA contains genetic information, roughly like a CD may contain some software. The genetic code, or better the genes, are the information itself. So genes do not *send* information, no more than a password sends any information to the system it interacts with. They work or they don't. Genes do not *contain* information (like envelops or emails), no more than a performative does: "I promise to come at 6" does not really *describe* (constative function) or *contain* a promise, it rather does something, i.e. it *effects* the promise itself through the uttered words. So genes are not information in a semantic-descriptive-constative sense, and they do not merely *contain* or *encode* instructions, as a string of lines and dots may encode a message in Morse alphabet. They are *instructions*, and instructions are a type of *effective information* (like recipes, software, commands).

The slogan that summarises this ontic interpretation is "in the genetic code, the medium is the message". Two implications of the ontic interpretation are:
1) a shift in the informational paradigm and
2) a unification between two ontological domains (physics and biology).
The ontic interpretation relies on the procedural programming one. Genes are dynamic procedural structures that control and guide organisms' development. Dynamic procedural structures are a special type of informational entities, those that are in themselves instructions, programs or imperatives (cf. imperative programming or procedural programming, where statements change a program state and programs are a sequence of commands for the computer to perform). Each step (each base) is an instruction, and the physical world holds the state that is modified by the instruction. The relation between instructions (genes, imperative programs, recipes) and the outcome is functional-causal and nomic.

The conclusion is that the difference between inanimate informational entities and living informational entities is the anti-entropic nature of the latter. A living system is any anti-entropic informational entity, i.e. any informational object capable of instantiating procedural interactions (it embodies information-processing operations) in order to maintain its existence and/or reproduce itself (metabolism). One of the great advantages of understanding the genetic code in terms of informational procedural structures is that this allows one to adopt a unified information perspective for the whole reality, both non-living (physis) and living (bios). This informational ontology is known as informational structural realism. Informational structural realism is a version of ontic structural realism supporting the ontological commitment to a view of reality as the totality of informational objects dynamically interacting with each other.

Luciano Floridi

Oxford University & Univerità di Bari

Current positions

Fellow of St Cross College and member of the Faculty of Philosophy and of the OUCL (Computer Science Department), University of Oxford

Coordinator of the IEG, the interdepartmental research group on the philosophy of information at the University of Oxford

Associate Professor of Logic and Epistemology, Dipartimento di Scienze Filosofiche, Università degli Studi di Bari

President, *International Association for Computing and Philosophy* (IACAP)

Director of SWIF- the Italian Web Site for Philosophy

Area editor (computing and information), editorial board of *Synthese*

Associate editor (philosophy of information), editorial board of *The Information Society*

Member of the editorial boards of *Ethics and Information Technology* | *Minds and Machines* | *International Journal of Technology and Human Interaction* | *Telematics & Informatics*

Research areas

Philosophy of Computing and Information **|** Information/Computer Ethics **|** Epistemology and Philosophy of Logic **|** History and Philosophy of Scepticism

NEURAL BASIS OF VOCAL COMMUNICATION IN SONGBIRDS

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The substrate of spoken language is a behavior known as *vocal learning* - the ability to learn vocalizations through imitation, or based on an auditory model, as opposed to instinct. This rare behavioral trait is just found in three groups of mammals (humans, cetaceans and some species of bats) and in three avian groups (songbirds, parrots and hummingbirds). All other animal groups, including non-human primates and rodents, do not exhibit vocal learning behavior and, therefore, only display innate species-specific vocalizations. Research conducted in songbirds has shown that, as is the case of humans, intact audition is required both for vocal learning and for the maintenance of the structure of learned vocalizations in adults. In addition, appropriate perception of auditory communication signals (songs) is required for other critical behaviors in songbirds such as territorial defense, mate selection and individual recognition. Thus, a significant effort in the field has been directed at understanding what brain structures and cellular mechanisms participate in the auditory processing of natural vocal communication signals during vocal learning and in adulthood. In my talk, I will present evidence that structures in the songbird auditory pallium, that are functionally equivalent to primary and association auditory areas in mammals, participate in auditory processing and sound discrimination and may be sites where auditory memories required for vocal learning are stored. I will show that auditory stimuli presented to freely-behaving birds drives vigorous electrophysiological responses and the expression of activity-dependent genes, including the immediate early genes *zenk*, *c-fos* and *arc*, in these regions, especially in the nucleus of the caudomedial nidopallium (NCM). NCM responses show preference for conspecific over heterospecific songs or artificial stimuli and are tuned to fine acoustic features of songs. Moreover, these responses are more robust when the species-specific songs are novel, and decrease as songs become familiar to the bird, suggesting that this area contributes to auditory discrimination of songs. Electrophysiological and gene expression experiments have also provided direct evidence indicating that NCM is a likely site where auditory memories required for vocal learning are formed and/or stored. The underlying neural substrates for these processes presumably involve large scale changes in protein networks, however, the regulation of only a few immediate early genes as a result of song

stimulation was known. To shed light onto the components of these regulatory networks, and how they dynamically change as a result of auditory experience and learning, we employed large scale quantitative proteomics to NCM (2D-DIGE-based proteomics coupled to tandem mass spectrometry). We found that a complex network of proteins is regulated by these processes; the identified proteins spanned a range of functional categories that included metabolic enzymes, cytoskeletal molecules, and proteins involved in neurotransmitter secretion and calcium binding. Overall, these findings suggest that auditory processing of vocal communication signals in freely-behaving songbirds triggers a cascade of protein regulatory events that are dynamically regulated through activity-dependent changes in calcium levels.

BOOKS

- Pinaud, R, Tremere, LA & De Weerd, P (Eds.) Plasticity in the Visual System: From Genes to Circuits. Springer-Verlag, New York (2005). ISBN: 0-387-28189-4.
- Pinaud, R & Tremere, LA (Eds.) Immediate Early Genes in Sensory Processing, Cognitive Performance and Neurological Disorders. Springer-Verlag, New York (2006). ISBN: 0-387-33603-6.

A Few Problems on Functional Self-organization in the Brain

Seunghwan Kim
APCTP & NCSL, Dept. Physics, POSTECH, Pohang, Korea 790-784

The brain is considered to be the most complex system, a fertile ground for understanding the complexity of its functions through dynamical modeling. In this talk, we present a few problems on the functional self-organization in the brain through biophysical and nonlinear analysis of the nervous system. In particular, we focus on how the complexity of the functional networks arises through synaptic interactions and the visual map forms through functional self-organization processes. We also present some recent results on how the changes in the functional connectivity in the brain can be reflected on some macroscopic brain dynamics of EEGs. The implications of our work to the brain function are discussed.

Oct. 16 (Tue) 9:00-10:00

Prof. Seunghwan (Swan) Kim

Research Interests

I am interested in diverse problems of complex systems:
nonlinear dynamics and chaos in coupled oscillator networks,
self-organization and pattern formation in complex systems, biophysics of the nervous system and neurodynamics, and applications of nonlinear time series analysis to biomedical and financial time series.

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A mathematical model for the hippocampus: towards the understanding of episodic memory and imagination

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ABSTRACT
How does the brain encode episode? Episodic memory has become interested in neuroscience community since the finding of malfunctions on the formation of episodic memory caused by the damage of hippocampus. On the other hand, simple memory has been explored in various contexts, in particular, since Marr's theory for archecortex (incl. the hippocampus), where Marr considered the hippocampal CA3 to be responsible for associative memory. However, a conventional mathematical model of associative memory guaranteed only a single association in case without any given rule for the order of successive association. Recently, the clinical studies for the patients who have the damage of hippocampus show that such patients cannot make a new story, caused by the lack of capability of imagining new things. Both episodic memory and imagining things include various common characteristics: imagery, the sense of now, retrieval of semantic information, and narrative structures. Taking into account these findings, we made a model of hippocampus CA3 and CA1. Our mathematical model shows striking characters such as representing episode, encoding input time series and decoding it, based on the emergence of affine rules in CA1 and chaotic rules in CA3. We also conducted experiments with rats' hippocampus slices. We obtained similar behaviors to those predicted by the model.

Ichiro Tsuda

Oct. 16 (Tue) 11:30-12:30

Creativity and Consciousness of the Human Brain

Tsutomu Murata

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One of the frontiers of the modern science is to understand how the human brain can work creatively. It seems natural to admit the human creativity when we invent new ways to solve the first facing problems being lacking for sufficient information or instructions. In contrast, artificial information processing systems such as today's computers are poor at answering problems whose solution algorithms are not programmed. A typical example that shows difference of creativity between the human brain and the computer is cognitive ability of degraded visual images. When a visual image is degraded by monochromatic binarization, only meaningless patterns are seen for the first time because of insufficient information of the image, which makes the computer system nearly impossible to recognize the hidden objects. However, we can perceive a meaningful object suddenly after some seconds or so, and this provides us a so-called 'Aha!' experience.

The recognition of such hidden figures requires appropriate object memory stored in the brain to interpret the degraded image in a top-down way. The unsolved question is how the brain can use the appropriate memory to identify the hidden object before it is identified. In psychophysical studies we found that the time taken to perceive a hidden object follows a rate equation that has a remarkable homology to the well-known Arrhenius equation for chemical reaction rates. This homology suggests that vast degrees of freedom held in random activity of neurons provide chance to find out the appropriate stored memory that meets the insufficient visual information, in a similar way to random molecular motions providing the chance for their chemical reactions. We propose that the vast of degrees of freedom held by the brain, which overwhelms the computer operations, is the key mechanism of the creativity in the memory search and flexible object recognition. Furthermore, it is noteworthy that the searching process before 'Aha!' cannot be conscious while after 'Aha!' the objects are consciously perceived. Therefore, cognitive consciousness seems to correspond to the brain state with reduced degrees of freedom, which is generated after the unconscious creative memory search with the vast degrees of freedom.

Non-Invasive Quick Diagnosis and Safe & Effective Treatment of Intractable Medical Problems: Anti-Aging and Anti-Cancer

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Abstract:

It is ideal to live many years with good health and continued activity in the field of interest. In the recent record, the French woman Jeanne Louise Calment lived 122 years and 164 days, and died in 1997 (born February 21, 1875 and died August 4, 1997). She lived the longest in recent years, and many people asked her what was her secret of longevity? She listed the following 3 items: 1) drink olive oil everyday, 2) drink port wine everyday, 3) she tried not to pay attention to or forget anything that would disturb her mind. When we examined a photograph of her face one year before she died, most striking abnormal appearance was a deep indentation of her upper eyelids, where we found organ representation areas for bone marrow, spleen, adrenal gland, thyroid gland, and thymus gland. It indicates these organ functions are markedly deteriorated. Unfortunately, many people cannot reach such a long life. The oldest woman living now is 114 years old, the oldest man now living is 111 years old, both from Kyushu, southern part of Japan, and their climate is relatively warm all year long and environment is better, in general more suitable for longevity. This 111 years old man reads newspaper everyday and drinks milk and writes diary. Unfortunately, many people die long before 100 years old due to a variety of diseases as well as accidents. Major causes of death are cardiovascular disease, cancer, and other malignant diseases, and unrecognized chronic mixed bacterial & viral infections, and many people die long before they reach 80 years of age. But if one managed to survive until 80 years old, about 20% of them develop Alzheimer's disease and eventually die from the consequence in less than 10 years. Therefore, target of our main research is to make early detection of these diseases rapidly and non-invasively with minimum expenses, and try to confirm by standard laboratory tests. However, when we make our diagnosis, often it takes a few months to a few years before laboratory tests can detect abnormalities. Within the past 10 years, we have developed a non-invasive, quick diagnostic method for cardiovascular disease and malignant tumors, Alzheimer's disease, and autism. Since our study indicated that in autism patients, the pathological findings are almost identical with Alzheimer's disease, the author considers autism as a juvenile Alzheimer's disease. Projecting ref soft laser beam to right and left palms, supra sternal notch, center between the nipples on the chest and equivalent position in a woman, umbilicus and right & left inguinal area, it becomes possible to detect all of these diseases by holding next to laser pointer known amounts of molecules which are increased in each of these diseases. And when the same substance exists in the laser beam projected area or its vicinity, due to electromagnetic wave resonance, which becomes maximum when information on molecular structure & amount carried by the laser beam is identical to the amount of the substance existing in the projected area, one can get a general idea where the disease characteristic substance is increased and located. This degree of resonance can be detected using Bi-Digital O-Ring Test without using costly and bulky instruments which can detect minute molecular electromagnetic

field. To localize the exact location, size, and boundary of the malignant tumor, we developed an X-axis and Y-axis laser line scanning method of the whole body surface. Among the crossing points of the X-axis positive line and Y-axis positive line drawn on the body surface, there is a center of true malignancy. The exact boundary will be mapped using identical microscope slide of malignancy. For the early screening of the malignant tumors the author uses Oncogene C-fos Ab2 or Integrin $\alpha 5\beta 1$ as reference control substances. For cardiovascular problems, L-homocystine and CRP or cardiac Troponin I & T are used. For Alzheimer's disease and Autism, β-Amyloid (1-42), Acetylcholine, Aluminum and asbestos are used, but we found mixed infection of Chlamydia Trachomatis, Mycobacterium Tuberculosis and CMV are often involved and can be treated. Our recent research also indicated that in most of the malignant tissue a large amount of asbestos is accumulated. Particularly, asbestos is very high in mesothelioma and brain tumor, compared with the amount of asbestos of other cancers and malignant tumors. Our study on mesothelioma indicated that an increase of the Oncogen C-fos Ab2 and Integrin $\alpha 5\beta 1$ are very mild and usually between 10ng-50ng (BDORT units). And unlike any known cancer tissue where glucose uptake is increased, in the mesothelioma, glucose uptake is markedly reduced, and therefore many radiologists often make a misdiagnosis believing that glucose uptake is also increased in mesothelioma. For screening of Mesothelioma, asbestos & microscope slides of 3 types of Mesothelioma are used.

For the treatment of all of these medical problems, once their causes were detected, and if any known beneficial medication is given to the patient, usually most of the effective medication goes to the normal part of the body. Only small portions of the effective medication reach the pathological area to be treated. To solve this problem, the author developed **Selective Drug Uptake Enhancement Method** in 1990 and was able to selectively deliver effective medication to the pathological area while reducing drug to reach normal parts of the body drastically, thus reducing drug side effect to normal parts of the body. This principle was discovered while measuring the drug distribution before, during, and after application of Selective Drug Uptake Enhancement Method by stimulating accurate organ representation area (which was mapped using Bi-Digital O-Ring Test resonance phenomena between two identical tissues). As a consequence, the author and his associates have been successfully using selective drug uptake enhancement method for every type of the treatment with effective medication, which shortened the time duration of the therapeutic period, and in some cases it becomes the only means of saving a life. When multiple medications are given simultaneously to a patient, often drug interaction takes place, which can cancel beneficial drug effects or sometimes create new toxic effects. This can easily be prevented before giving multiple drugs simultaneously by drug compatibility test using Bi-Digital O-Ring Test.

Using the Bi-Digital O-Ring Test in the 1980s, the author found that it was possible to localize the exact location of the meridians and acupuncture points. Up to now, no one knew what were the shape, diameter, and depth of the acupuncture points. But using the Bi-Digital O-Ring Test resonance phenomena, for example for stomach meridian one must use microscope slide of stomach tissue, not only can one image the outline of the stomach without using any imaging devices, but also can find all the meridian lines coming from the outline of the stomach and their acupuncture points accurately. At each acupuncture point the shape, diameters, and depths can be exactly localized. Using meridian and acupuncture localization method, based on Bi-Digital O-Ring Test resonance phenomena, the author evaluated many well-known acupuncture points.

The result of this study made it evident that many acupuncture point locations were surprisingly correct, although there was no reliable method available to identify exact location and shape of acupuncture point. It was found that most of them were round shaped and diameters changed depending upon location. But a few well known acupuncture points were found to be located in an incorrect location, as their true acupuncture point location was found to exist within 1-1.5cm of the traditional location. For example, one of the most famous traditional acupuncture points is ST 36 below the knee. In the location described in textbooks and taught, there is no acupuncture point. But about 1-1.5cm distance close to anterior tibial crest, there is true ST 36. When you insert acupuncture needle to traditional acupuncture point ST. 36 described in textbooks, very little effect is obtained. But at true ST 36, very significant, beneficial changes in circulatory system and blood chemistry take place but often by mistake true ST 36 is stimulated.

More than 10 years ago, with the help of a professor in biochemistry, we were able to synthesize a telomere (TTAGGG). Using known amount of artificially synthesized telomere, we have developed simple non-invasive method of detecting approximate amount of telomere, not from single cell but from a group of cells. Thus making known amount of synthesized telomere as reference control substance, it became possible to rapidly and non-invasively estimate amount of telomere of normal tissue and malignant tissue in BDORT units. Amount of telomere is highest at the time of birth, but many factors reduce the normal cell telomeres rapidly. Among many factors reducing normal cell telomere aging moderately reduced it but in the presence of malignant tumors, normal cell telomere often reduced to less than 1 yg. Therefore, when telomere is very low compared with the average normal value of the given age group; first, rule out possibility of presence of malignancy. If the Oncogen C-fos Ab2 or Integrin $\alpha 5\beta 1$ is more than 10ng (BDORT units), one have to suspect a presence of malignant tumor. In most of the cancers, these values are anywhere between 50ng-500ng (BDORT units). But in case of Mesothelioma it is often between 10-50ng (BDORT units). With a few exceptions, most of green tea and coffee lower normal cell telomere. In the case of green tea, it rapidly and markedly reduced telomere, toward 1yg (10^{-24} g), but amount of telomere came back to original state within one hour. In case of the coffee, one cup of coffee will often lower normal cell telomere toward 1yg and enhance cancer cell telomere. While the undesirable side effects will return to pre-consumption level again within 4 hours. But the author also found some coffee from Portugal and some green teas from Japan enhance normal cell telomere, and reduce cancer cell telomere. And the worst substance is the cigarette.

A number of the safe possibly effective treatments of malignant tumors has been studied by the author. Among them, one method is to reduce cancer cell telomere so low that cancer cell cannot divide any further, while increasing normal cell telomere to very high normal value of between 505ng-535ng. This was accomplished by periodically stimulating semi-permanently placed tiny press needles kept under a small round band-aid at the true acupuncture point, true St 36. We recommend 200 times of press and release procedure to this point, and repeat the procedure 4 times a day. Often cancer cell telomere reduces from few hundred ng to less than 1yg, while normal cell telomere increases to more than 500ng (BDORT units). Another important method is use of optimal dose of DHEA. For the past 10 years, often DHEA has been promoted as a miracle drug for rejuvenation. Most of the doctors recommend daily intake of anywhere between 10mg-100mg, but often 25mg daily. Some reported that it promotes prostate cancer and breast cancer, while some reported beneficial effects against these malignancies. To evaluate all these

claimed beneficial and adverse effects, the author evaluated optimal dose of DHEA for over 100 adults, ranging between 20 and 85 years old, using our new criteria, that optimal dose is defined as the amount of drug which increase telomere to maximum amount. According to this new criteria, for most of the adults, optimal dose of DHEA is anywhere between 5-12.5 mg, and effect of the 1 optimal dose often lasts more than several months to one year, in more than 50% of the subjects tested. And when optimal dose of DHEA is given to any individual, normal cell telomere goes up to anywhere between 505ng-535ng. When this happens, cancer cell telomere becomes practically zero (less than 1 yg). As a result, cancer cell can no longer divide. Also, circulation significantly improves with reduction of abnormally increased Thromboxin B2 and increased acetylcholine particularly in brain hippocampus and also in the rest of the body, often with marked decrease or elimination of pain with marked decrease in Substance P, and dry wrinkled skin becomes smoother, in addition to white hair often becomes darker, and muscle strength increases. Within 1st 3 hours after oral intake of optimal dose of DHEA, large amount of asbestos, and some of the preexisting viruses and bacteria are excreted in the urine. This often contributes to the additional improvement of the patient's general condition. Thus the proper use of one optimal does of DHEA is often highly beneficial to a variety of medical problems and has potential beneficial effects for treatment of malignant tumors and contributes to longevity, while current practice of giving every day of about 25mg DHEA reduces normal cell telomere to close to 1 yg, and increases cancer cell telomere and may contribute to genesis of malignant tumors.

Biological clock in the life and its clinical use

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1. Introduction: recent progress in chronobiology

"Chronobiology" as a science in its own right was proposed in 1950 by Franz Halberg, who found a genetic basis for a 24-hour variation in counts of circulating eosinophil cells in five different strains of inbred mice, and officially introduced this term and "circadian" to a nomenclature committee in Stockholm for the first time in 1955, but first published "circadian" in 1959. Chronobiology has developed worldwide since 1969, when the paper entitled "Chronobiology" was published in the Ann Rev Physiol and became a Current Contents "Citation Classic". In recent years, chronobiology has come into the limelight of brain research, showing associations even of human spirituality with solar cyclicity, as documented at the meeting reviewed herein.

Most organisms, from cyanobacteria to mammals, are known to use circadian mechanisms to coordinate their activities with the natural 24-hourly light/dark cycle and/or interacting socio-ecologic schedules. Fig. 1 shows for the human pulse that the extent of about-daily change has a genetic aspect, shown by the similarity of records from monozygotic but not from dizygotic twins reared apart. In this book, the built-in nature of the week is also documented by studies on twins complementing free-running. When the human clock gene was disclosed and mapped to chromosome 17p12-13.1 in 1997, it was surprising to see that the clock gene was very similar in all earthly life. In plants, several molecular components have been described in relation to the circadian system, including the blue light photoreceptor cryptochrome and the red light photoreceptor phytochrome. Cryptochrome also functions in mammalian circadian mechanisms. Recently disclosed facts suggest that organisms evolved on Earth acquired many of the visible and invisible cycles of their habitat and/or of their cosmos.

While circadian systems are well documented both time-macroscopically and time-microscopically, the temporal organization of physiological function is much more extensive. Long-term physiological quasi-ambulatory monitoring of blood pressure and

heart rate, among other variables, such as those of the ECG and other tools of the neuroendocrinologic armamentarium, have already yielded information on circaseptan (about 7-day) and circadecennian (about 10-year) cycles, which are found in bacteria and unicellular forms of life as well as built into human populations. In mammals, rhythms characterize mitoses and RNA and DNA synthesis in growth and during regeneration; hormones like melatonin are secreted time-dependently along several system scales; the nervous system certainly displays rhythms, chaos and trends, mapped as chronomes. Environmental and organismic interactions are also cyclic with a host of frequencies. These resolvable time structures, chronomes, in us have counterparts around us, also consisting of rhythms, trends and chaos, as is increasingly being recognized.

2. Chronomics and Chronoastrobiology

I would like to introduce here what is chronomics, and why we need it from a viewpoint of chronoastrobiology. Chronomes are time structures consisting of multifrequency rhythms covering frequencies over 10 orders of magnitude, elements of chaos, trends in chaotic and rhythmic endpoints, and other, as yet unresolved variability. The term “chronoastrobiology” is derived from “chronome” (time structure) and “astrobiology” (reciprocal implications of biology and space studies).

The magnetic activity of the sun has visible photic and invisible non-photic effects on life on earth. Effects of non-photic solar cycles upon plants were recognized by 1838 and championed by economists and transdisciplinary scientists like Alexander Leonidovich Chizhevsky. Reports of statistical documentation of a variety of effects upon organisms, including self-monitoring humans over decades, have been reviewed. Recent statistical studies have also revealed new non-daily, non-yearly, i.e. non-photic cycles in both magnetism and corresponding physiological cycles in humans and other organisms. But the physicists’ records of aurorae and sunspots are not long enough to look for cycles half a millennium in length. It seems of interest therefore to look again for a proxy marker of solar activity in tree ring widths that cover the past 2000 years or more. We had analyzed 11 sequoias and had found a period of 534 years as the most prominent feature. Thus it has become increasingly clear that invisible magnetic influences from the sun affect the cycles of life on earth today and apparently have even left genetic footprints in endogenous physiological chronomes (time structures).

Chronomics aims to increase life expectancy and life quality, as it strives for the stars by a timed and timely chronoastrobiology. Chronomic detection of elevated illness-risks aim at the prevention of diseases of individuals, such as myocardial

infarctions and strokes, and, equally important, chronomics resolves illness of societies, such as crime and war, all exhibiting mapped cycles, that are indispensable for the study of underlying mechanisms.

3. Chronomics of tree rings gauge climate change

As an aspect of chronomics, assessing broad time structures (of chaos, trends and cycles) in physiological and physical environmental variables and their interactions, the fractal nature of tree rings is here determined. The average measurements of 11 sequoia trees covering 2189 years were analyzed by the power spectrum obtained with the Maximum Entropy method (MEM). A robust line-fitting algorithm of log (power) on log (frequency) was used between 10^{-4} and 0.50 cycles/year, where the relationship appeared to be linear, to obtain an estimate of the slope (β). Analyses were repeated over an interval of 200 years progressively displaced by 5 years throughout the 2189 years, realizing that the interval's length may obscure or miss short-term effects. Overall, the slope (β) is -1.0017, similar to the slope of -1.0543 characterizing the MEM spectrum of sunspots between 1700 and 2000. A slope of about -1.00 is known to represent fractal nature. Whereas the slope usually assumes a value of about -1.00 in most intervals considered, in a few episodes the slope deviates from this value, reaching values closer to zero or slightly positive ones, suggesting a disruption of the fractal nature. Seven such episodes are found, the last two corresponding to the Spörer and Maunder minima. The other five episodes, occurring around 100 BC, 500, 700, 820 and 880 AD, may also correspond to climatic changes that happened during times when no record of sunspots is available. Whether changes in the 1/f structure of tree rings actually correspond to changes in solar activity or climate also should be scrutinized in auroral sightings or in other long records of reconstructed solar activity such as those based on the ^{10}Be concentration in polar ice. Our prior analyses of these data had found a periodicity of about 534 years as the most prominent feature with matching periods in and around us. By a combination of methods focusing on both specific spectral components like the Schwabe cycle and on 1/f behavior, as a feature of chaos, chronomics estimated an association of climate change, which occurred globally. The same combination of chronomic methods detects elevated illness-risks for the prevention of diseases of individuals, such as myocardial infarctions and strokes, and, equally important, aims at resolving illnesses of societies, such as crime and war, all exhibiting cycles mapped with their uncertainties, that are indispensable for the study of underlying mechanisms.

4. Community-based chronobiological study for Longevity

In 2000, we began a community-based study named "Longitudinal Investigation for Longevity and Aging in Hokkaido County (LILAC study)", and monitored 7-day/24-hour ambulatory BP of middle-aged subjects, aged 40 to 74 years, while also evaluating the cardiovascular and neurobehavioral functions of elderly people. Our goal was the prevention of stroke and myocardial infarction and of the decline in cognitive function of the elderly in a community.

CHAT (short for circadian hyper-amplitude-tension), a condition defined by an excessive circadian amplitude of BP, above a threshold approximated by the upper 95% prediction limit of clinically healthy peers matched by gender, age and ethnicity, is associated with a large increase in vascular disease risk, cerebral ischemic events and nephropathy in particular. We have already monitored 7-day/24-hour ambulatory BP of 218 middle-aged citizens in Hokkaido county from April, 2001 to April, 2003. We observed circaseptan components for the average SBP value during the waking span, for the 24-hour average of HR, for the SD of HR and for the day-night (dipping) ratio of SBP. Specifically, SBP during waking was lowest on Sunday. The BP average during waking shows a circaseptan variation. Thus, we point out that ambulatory BP monitoring limited to 24 hours is not sufficient and propose a routine 7-day screen, which is continued when abnormality is found. Among the 218 records of 7-day/24-hour ambulatory BP, we also observed 32 (14.7 %) and 11 (5.0 %) cases of SBP and DBP CHAT, respectively. We have started several kinds of interventions, including life-style guidance, education from the viewpoint of clinical nutrition, and consultation of drugs for hypertension and hyperlipidemia, among other conditions.

We also determined in the longitudinal community-based study (LILAC) whether BP, HR and HRV are predictors of cognitive function in the elderly. We initially examined 115 people older than 75 years (average, 79.6 years). BP was measured at the beginning of the study in a sitting position, and pulse wave velocity (PWV) was measured between the right arm and ankle in a supine position, using an ABI/Form instrument (Nippon Colin Co., Ltd., Komaki, Japan). The first 1-hour of ambulatory ECG recording was obtained during routine medical examination conducted each year in July. The data were processed for HRV using a Fukuda-Denshi Holter analysis system (SCM-280-3). Time-domain measures (SDNN, pNN50, SDANN and Lorenz plot indices: Length (L), Width (W), and L/W ratio) and frequency-domain measures (spectral power in the "very low frequency" – "VLF": 0.003-0.04 Hz, "low frequency" – "LF": 0.04-0.15 Hz, and "high frequency" – "HF": 0.15-0.40 Hz regions, and the "LF/HF" ratio) were determined. Except for SDNN and HR, calculated over the whole

1-hour record, all indices were computed as averages over consecutive 5-min intervals. Spectral indices were obtained by the maximum entropy method (MEM) with the MemCalc/CHIRAM program (Suwa Trust Co., Ltd., Tokyo, Japan). Using as reference the data obtained in July 2000, the cardiovascular coordination function of each participant was scored as 3, 2 or 1 point for each of the following 3 indices (SBP, HR and "VLF" component of the HRV): SBP > 160, 140-159, or < 140 mmHg; HR > 80, 70-79, or < 70 beats/min; and "VLF" < 800, 800-1000, or > 1000 $msec^2$. Participants were classified into either the normal, mildly disordered, or disordered group when the sum of these indices was ≤ 4, 5 or 6, or ≥7, respectively.

The Japanese version of the Mini-Mental State Examination (MMSE) and the Hasegawa Dementia Scale Revised (HDSR) were used to measure the overall cognitive function, including verbal orientation, memory, and constructional ability. The Up & Go test measured, in seconds, the time it took the subject to stand up from a chair, walk a distance of 3 meters, turn, walk back to the chair, and sit down again. This test is a simple measure of physical mobility and demonstrates the subject's balance, gait speed, and functional ability (Up & Go). A lower time score indicates better physical mobility. Functional Reach, used to evaluate balance, represents the maximal distance a subject can reach forward beyond arm's length while maintaining a fixed base of support in the standing position. A higher score indicates better balance. Manual dexterity was assessed using a panel with combinations of 10 hooks, 10 big buttons, and 5 small buttons. There were three discrete measurements of time recorded for each participant (10 "hook-ons", 10 big "button-on-and-offs", and 5 small "button-on-and-offs"). Total manual dexterity time in seconds, defined as the button score (Button-S), was calculated by adding the average times for one hook-on and one big or small button-on-and-off. A lower button score indicates better manual dexterity.

We evaluated the effects of several kinds of health consultation, rehabilitation of disordered function, healthy lifestyle modification by promoting complete cessation of smoking, weight reduction, reduction of salt intake, moderation in the consumption of fruits and vegetables and alcohol intake, as well as advising medical prescription for the local general practitioner. The paired t-test was used to compare each neurobehavioral endpoint between 2000 and 2002. Results were considered to be statistically significant at $p<0.05$.

In 2000 (reference), the cardiovascular coordination score did not correlate with any index of neurobehavioral function, although it showed a negative correlation with SDNN, SDANN, pNN50, "LF" or "HF" components ($p<0.0001$), and a positive correlation with PWV ($p<0.01$). We were able to follow-up 72 of the 115 subjects. We

found that between 2000 and 2002 the cognitive function, estimated by MMSE and HDSR, was maintained or improved, as follows: In the cardiovascular coordination disordered group, MMSE and HDSR improved from 24.6 to 26.0 ($p=0.06$) and from 23.8 to 25.9 ($p=0.04$), respectively. In the mildly disordered group, these indices improved from 23.4 to 25.7 ($p=0.005$) and from 23.4 to 25.1 (N.S.), respectively. In the normal cardiovascular coordination group, MMSE and HDSR were maintained from 25.6 to 26.0 (N.S.) and from 24.9 to 26.4 (N.S.), respectively. There were no statistically significant alterations in activities of daily living (ADL), assessed by Up & Go, Functional Reach and Button score, in any of the groups.

Although a cross-sectional study did not show any apparent correlation between cardiovascular and neurobehavioral functions in subjects 75 years of age or older, an intervention aimed at preventing stroke and a decline in cognitive function in an elderly community population induced an improvement of the cognitive function, especially in people suffering from hypertension, tachycardia, or decreased HRV. This study demonstrates a positive impact of a simple social intervention, including advising on the implementation of a medical prescription, in improving a disordered cognitive function in elderly people. People with a disordered coordination of cardiovascular function are more sensitive to such an intervention, suggesting that the cardiovascular function is a major factor affecting cognitive function.

5. Conclusion: from rehabilitation to prehabilitation

We focused on another field of chrono-ecology in medicine. As mentioned above, most organisms on Earth, including humans, have developed "clock" genes of the circadian, and probably many other components in the spectral element of chronomes, beyond about-yearly (circannual) and about-weekly (circaseptan) features, as a product of adaptation to, or rather integration with, cycles in the cosmos. While life originally integrated itself into the cycles of an anthropogenically unpolluted environment, the environmental cycles are now being changed in keeping with the schedules of societal life, as in the case of global temperature, and perhaps the geomagnetic index, aa, that also shows an increase in the past century ($P<0.001$). Hence, a variety of cognitive, neurobehavioral and neuropsychological as well as cardiovascular functions will need to be investigated to more precisely map their chronomes in space and time, in order to understand chronoastrobiology, based on both the system times and time horizons yielded by chronomes assessed in communities worldwide. We have also just started a project on stroke prevention, based on 7-day/24-hour monitoring of blood pressure as a public service, in Urausu, a town in Hokkaido, Japan. In Urausu, Mayor Kaname

Yamamoto has extended to all residents of his city an offer of 7-day/24-hour blood pressure monitoring and has started a historic first chronome mapping for stroke prevention.

Being and Becoming Human: A dynamical systems perspective on development of brain and behavior

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Modern studies with human infants have revealed that newborns are not in the state of "tabula rasa" but have sophisticated abilities to perceive and act on the environment. This has led to the view that newborn infants are endowed with precursors for motion, perception, cognition and language. However, neural mechanisms for early behaviors and developmental changes in behaviors over the first year of life are not fully elucidated. Since human behaviors are generated through the nonlinear interaction among the brain, the body and the environment (taga et al. 1991), a dynamic systems theory is of great help to understand the developmental principle in humans. Here, I will focus on the U-shaped changes; infants demonstrate rather mature forms of behaviors near birth, do not exhibit similar ones later, and then acquire the mature ones (Taga et al. 2002). The U-shaped changes may reflect crucial aspects of the developmental construction for the hierarchical network composed of sub-cortex and the cortex as well as for the parallel network composed of functional modules within the cortex. Recent advancement in a neuroimaging technique using near infrared spectroscopy (NIRS) has opened the door for revealing the functional brain development in early infancy (Taga et al. 2003). Applying this technique, we have collected ample evidences to show that the cerebral cortex of infants as early as 3 months of age is highly organized to perceive the external world (Homae et al. 2006; Taga & Asakawa 2007). Our preliminary data further suggest that the specific activation of the local modules for visual perception may be differentiated from the general activation of the global regions of the cortex of younger age. Moreover, the prefrontal area of 3-month-olds is specifically involved in detecting invariance or changes in the world at greater temporal distances than other regions of the cortex, suggesting that differentiation of time scale of responses occurs at the cortex of 3-month-olds. General to specific changes are also observed in the development of memory in a task playing with a mobile between 2 to 4 months of age (Watanabe and Taga 2006). Over all, dynamic changes in brain activities and behaviors in early infancy should be a manifestation of the deeper problem that an infant who is already in being with innate constraints needs to solve to becoming a human embodied in the complex world.

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Gentaro Taga

Consnsitency Principe in Biological Dynamical System: Plastcity, Robustness, and Genotype-Phenotype Relationship

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Biological system generally consists of a hierarchy of different levels, each of which is under stochastic dynamics. We propose consistency between different levels, as a guiding principle to understand such system. We discuss four topics – reproduction, adaptation, development, and evolution – from the viewpoint of consistency dynamics in stochastic dynamics.

First, as a result of consistency between molecule replication and cell reproduction, universal statistical laws on chemical abundances over cells are derived as are also confirmed experimentally. They include power-law distribution (Zipf's law) of gene expressions and embedding of the power law into the network connectivity. Fluctuations of chemical abundances over (isogeinc) cells are shown to obey log-normal distribution, which are generally rather large in magnitude.

Second, a novel adaptation mechanism in a cell is proposed, that does not rely on specific signal transduction network but takes advantage of the stochasticity in gene expression, to show that the mechanism works as a universal property of a growing cell. An experimental demonstration of this mechanism is discussed by using bacteria with embedded gene network.

Third. robustness in developmental process is discussed in relationship with Waddington's canalization. Formation of attracting states is discussed as a result of consistency of cell reproduction and growth of cell ensemble, while relevance of chaotic Milnor attractor is suggested as a mechanism from stem cell differentiation with autonomous regulation.

Fourth, general relationship between phenotypic fluctuation and genetic variance is derived from evolutionary stability hypothesis. Proportionality between evolution speed and isogenic phenotypic fluctuation is derived as an extension of fluctuation-dissipation relationship in physics. The obtained relationships are confirmed in models of catalytic reaction network and gene expression dynamics, as well as in laboratory experiments in bacterial evolution. Link between robustness to mutation and to noise is discussed.

Reference: Life: An Introduction to Complex Systems Biology, Springer (2006);

Coupled oscillators in vertebrate segmentation

Takeda Hiroyuki

University of Tokyo

A unique feature of vertebrate segmentation is its strict periodicity, which is governed by the numerous cellular oscillators of the segmentation clock. These cellular oscillators are driven by a negative-feedback loop of the Hairy transcription factor, are linked through Notch-dependent intercellular coupling and display the synchronous expression of clock genes. Combining our transplantation experiments in zebrafish with mathematical simulations, we are analyzing how the cellular oscillators maintain synchrony and form a robust system that is resistant to the effects of developmental noise such as stochastic gene expression and active cell-proliferation. The accumulated evidence indicates that the segmentation clock behaves as 'coupled oscillators', which is a mechanism that also underlies the synchronous flashing seen in fireflies.

Oct. 17 (Wed) 11:30-12:30

How important is genetic relatedness for social behaviour?

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Groups of cells and groups of individuals often display cooperative behaviours that appear counter-intuitive from the point of view of classical Darwinian evolution. For example, in the social amoeba *Dictyostelium*, one finds that some cells die and sacrifice themselves in order to ensure the survival of the rest. In the social insects, the majority of the individuals work for the hive but do not reproduce – a task that is the exclusive prerogative of the queen (and, sometimes, 'king'). How can evolution favour individual behaviour of a sort that lowers the fitness of the individual? In such cases, simple-minded expectation is in conflict with the observed behaviour. The expectation is that the behaviour is mediated by the action of genes. On the other hand, the consequence of the behaviour is that any genes that facilitate it are *ipso facto* not transmitted to future generations. Therefore, it would seem that (a) the observed behaviour does not have a genetic basis, except in a trivial sense, or (b) there is some way in which genes that facilitate the behaviour can be selected for even though they reduce the fitness of individuals that exhibit the behaviour, or (c) the behaviour has positive consequences at the level of the group; and those positive consequences outweigh the negative consequences at the level of the individual. It should be stressed that neither (a) and (c) nor (b) and (c) are mutually exclusive. But they differ in degrees of emphasis. Possibility (c) is often referred to as 'group selection'. Modern evolutionary theory has tended to downplay its importance - except in situations where the group consists of individuals who are related by common descent (kinship). In that case the phenomenon is said to be an example of 'kin selection', which is one way of describing possibility (b). By combining hypotheses and experimental data, this talk will try to make a case for taking the third possibility, (a), seriously. Possibility (a) can be thought of as a 'sociological' explanation for cooperative behaviour in groups. I suggest that the underlying basis of the sociological explanation is a special form of phenotypic plasticity: namely, the ability, under certain circumstances, for individuals to exhibit distinct attributes that complement each other. This ability is known to be displayed by cells, and it is speculated that it may also be displayed by individual organisms.

Vidyanand Nanjundiah

Ph.D. students:
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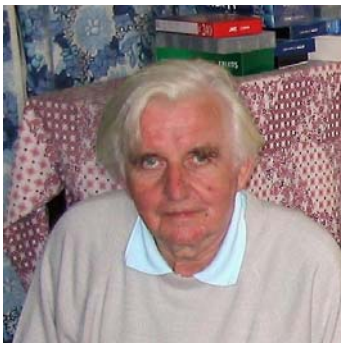
Project assistant:
Shankar Ganesh

Post-doctoral fellow: *Saby John*

Our aim is to understand multicellular development and pattern formation. The organism that we look at are the cellular slime mould or social amoebae, of which *Dictyostelium discoideum* is the best-studied species. We use two approaches, one of them that of developmental biology and the other based on evolution. Cells of *D. discoideum* start out as free-living amoebae that can be identical, both genetically and in terms of their overt phenotypes. Upon starvation they aggregate by chemotaxis and form a migratory structure known as the slug. Within the slug, differentiation takes place into presumptive stalk and presumptive spore cells. Eventually, the slug gives rise to an erect fruiting body that consists of a mass of spore cells supported by a column of dead stalk cells



John Evans graduated in mathematics at Cambridge University, and then spent several years as maths teacher and musician. In 1965 he changed to process control software, and developed one of the first real-time monitoring systems for an oil refinery. In 1975 he began serious study of physiology, with special interest in morphogenesis, and low-frequency electromagnetic effects. For the last twelve years he has been associated with the Department of Applied Mathematics and Theoretical Physics in Cambridge, and has developed a new Raphael Language for scientific computing. With this language, his earlier 2D model of vertebrate biofields has been extended into a full 3-dimensional system.

Vertebrate Growth and Form
A whole-body approach

The problems of growth and form in organic systems remain largely unsolved. Field methods applied to the whole body, for the later embryonic stages and beyond, provide a possible alternative to genetic and chemical analysis. Cells cohere according to the electrical forces between cell membranes; and an obvious place to begin applying field methods is to the major electrical pathways of the cerebrospinal system. The 2D and 3D models considered here assume the existence of a stable pattern of electrical sources throughout development, and that expresses itself in different ways according to the overall size. The *Morphos* computer program displays equipotential contour pictures for any cross-section in the principal planes, for different stages of growth, and for varied electrical conduction velocities.

1. Introduction
- Energy fields.
- Structural forces.

2. Basic embryology
- Gastrulation, gradients.
- Organizers, somites.
- Spemann, Child, Needham.

3. DC biofields
- Burr, Becker.
- Glial and Schwann cells.

4. AC biofields
- Tesla, Adey, Delgado.
- Spinal nerve geometry.
- Patterning effects of AC sources.

5. 2D models (1980s)
- Contouring experiments.
- Frequency sequences, conduction speed.
- Growth and time.

6. 3D models (2006-7)
- Symmetry and asymmetry,
- Spinal/autonomic nerve chains.
- Helical DC field.

7. Wider issues
- Biological resonance.
- Medical use of ELF oscillators.
- Geomagnetic field effects.

Nanoscopic Molecular Architectures in Supramolecular Science

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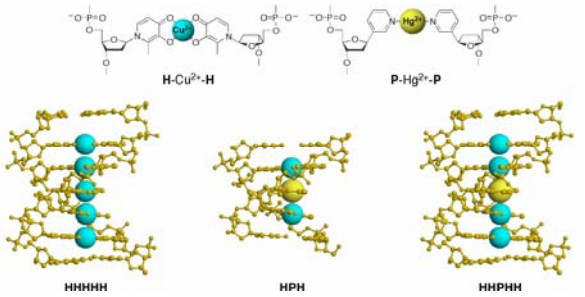
This paper describes our recent supramolecular approaches concerning nanoscopic molecular devices, especially focusing on metal-mediated nano-array, nano-space, and nano-motion. In the field of supramolecular science, a molecular-level device has been defined as a noncovalent assembly of a discrete number of molecular components designed to perform a specific function. Needless to say, the inspiration to construct such supermolecules comes from the sophisticated structures and functions of the natural molecular devices and machines. This paper will put stress on the availability of metal-assisted self-assembly using a discrete number of molecular components to construct nanometer-scale devices. Specifically, a few examples of self-assembled molecules, artificial metallo-DNA, dynamic molecular capsules, and a rotor-gear-rotor system using molecular ball bearings will be reported.

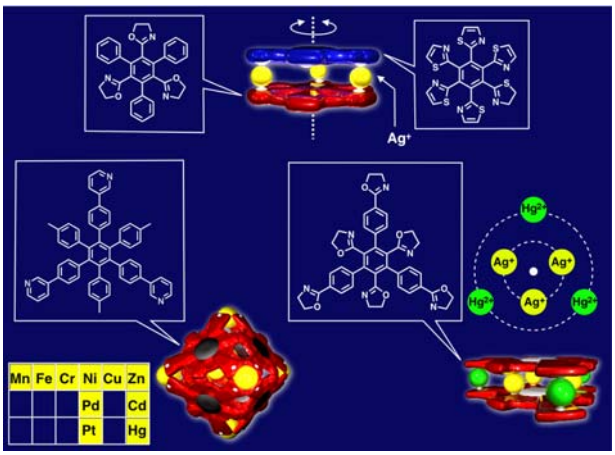
Programmable Homogeneous and Heterogeneous Metal Arrays in Artificial DNA



Replacing DNA natural bases by alternative ones makes it possible to chemically modify DNA in a highly specific and site-selective manner, because DNA has a structural basis to array functionalized building blocks. This strategy allows the formation of up to five Cu^{2+} inside the DNA as well as metal-triggered stabilization of the duplex and triplex structures. Furthermore, using two different nucleobases (**H** and **P**, which represent a hydroxypyridone and a pyridine nucleobase, respectively), Cu^{2+} and Hg^{2+} can be heterogeneously assembled exactly as programmed. By varying the number and the sequence of ligand-type nucleobases, it becomes possible to precisely control the number and the sequence of metal ions inside the duplex.

Functionalized Nanoscopic Metal-assembled Architectures using Disk-shaped Ligands

Disk-shaped tris- or hexa-monodentate ligands are useful as building blocks in constructing meal-assembled architectures with metal ions. For example, a combination of tris- and hexa-monodentate ligands and Ag^{+} ions allows the quantitative formation of a molecular ball bearing in which the two rotors can rotate relative to each other. Moreover, a tris-monodentate ligand forms ten kinds of structurally equivalent 3 nm-sized coordination capsules from ten kinds of divalent d^5 to d^{10} metal ions. Disk-shaped ligands also act as templates for hierarchical metal arrays and as parts of rotor-gear-rotor systems.



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Educational and Professional Experience

1982-1986 The University of Tokyo (Pharmaceutical Sciences)
1986-1988 Assistant Professor, Hiroshima University
1988-1990 Associate Professor, Institute for Molecular Science
1990-1991 Assistant Professor, Hiroshima University
1991 Visiting Researcher, University of Texas at Austin, USA
1991-1994 Lecturer, Hiroshima University
1994-1995 Associate Professor, Hiroshima University
1995-1999 Professor, Institute for Molecular Science
1995-1999 Professor, The Graduate University for Advanced Studies
1999- Professor, Department of Chemistry, The University of Tokyo
2003 Guest Professor, Louis Pasteur University
2007 Guest Professor, Ludwig-Maximilians-Universität Munich

Awards

2007 Inoue Prize for Science
2007 The Chemical Society of Japan Award for Creative Work

Research Interests and Subjects

Bio-inorganic/organic Chemistry, Supramolecular Chemistry
(1) Programming Array of Metals and Molecules
(2) Nanoscopic Molecular Machines
(3) Nano-Space Molecular Recognition and Reactions

Recent Publications

1. 3 nm-Scale Molecular Switching between Fluorescent Coordination Capsule and Nonfluorescent Cage, K. Harano, S. Hiraoka, and M. Shionoya, *J. Am. Chem. Soc.*, **2007**, *129*, 5300.
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“Life is a Gnarly Computation”

Rudy Rucker

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We’re in the midst of a new intellectual revolution: we’re coming to realize that physics, biology, minds and societies all emerge from interacting laws that can be regarded as computations. Everything is a computation, and everything interesting is a *gnarly* computation.

I use “gnarly” to refer to richly complex phenomena which operate at the interface between periodicity and chaos. It is likely that most naturally occurring gnarly computations are also “universal” computations in the sense that they can emulate any other computation.

A tree’s growth, an embryo’s development, the changes in the weather, the flow of daily news, a person’s ever-changing moods --- all of these are naturally occurring gnarly computations. Although law-like and deterministic, gnarly computations are --- and this is a key point --- inherently unpredictable. When we think of living biological systems as gnarly computations, the goal is not to deny the complexity of the natural world, but rather to savor it. The world’s mystery is preserved.

One formal result from computer science is of some significance here: the “Principle of Unpredictability,” which states that the behaviors of naturally occurring complex processes are formally impossible to predict by any conceivable means. This principle opens up new ways of thinking about biological evolution, about artistic creation, and about human history.

One practical consideration is that actual living systems seem to be something more than *just* gnarly universal computations: they have memory of state, such as is found in DNA, in the biochemistry of an organism’s immune system, and in a brain. I’ll discuss a recent fictional thought experiment of mine: a novel called *Hylozoic*, in which every object gets memory, and every object becomes alive and conscious.

Biographical Note on Rudy Rucker

Rudy Rucker is a novelist, a mathematician and a computer scientist. Rucker moved to Silicon Valley when he turned 40, and is now an emeritus professor of Computer Science at San Jose State University, where he developed a course on game programming and design. He has published twenty-nine books, primarily science-fiction and popular science and is known for his novels *Software* and *Wetware* (both won Philip K. Dick Awards), as well as for his classic nonfiction book, *Infinity and the Mind*. Nearly all of his earlier books appeared in Japanese editions from Hayakawa Publishing in the 1980s and 1990s.

His most recent books are: a science fiction novel, *Postsingular* (Tor, 2007), and a non-fiction book on the meaning of computation, *The Lifebox, the Seashell and the Soul* (Thunder's Mouth, 2005).

Links:

- Rudy Rucker's Home Page
- Rudy's Blog at RudyRucker.com

Co-creation of Presence and its Application to Human Interface

An example: Cooperative walking system using interpersonal mutual entrainment

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Everybody would have an experience that your footsteps are unconsciously synchronized with your partner's when you walk together. Since such an interpersonal synchronization of body motion has been widely observed and is deeply related with co-creation process of subjective presence, these phenomena are interested in the context of social psychology and developmental psychology. For example, synchronization phenomena in a temporal pattern of dialogue and imitation phenomena in a mother-infant interaction have already been reported. However, the mechanism of such an embodied cooperation still remains obscure, and its engineering application is not substantially progressed. In this study, therefore, assuming a mutual entrainment as an interpersonal synchronization mechanism, we established a cooperative walking system between a human walking and a walking model (virtual walking robot) using a nonlinear oscillator. This system was constructed as a system in which rhythm sounds corresponding to the timings of heel contact are exchanged between the human walking and the walking model in the basis of our previous studies. As a result, it was demonstrated that their walking rhythms adapt mutually after the start of interaction and a stable synchronization is self-organized and sustained. And this global entrained state including the human and the model showed dynamic stability of walking. Applying this system to walking support for gate disturbance, effectiveness for the stabilization and rehabilitation as an emergence process was also clarified. These results indicate the importance of interpersonal mutual-entrainment of rhythmic motion with co-creation of presence, and establishment of a new interactive human interface technology is expected as an extension of this embodiment mechanism.

Network perspective in bioinformatics

Susumu Goto
Kyoto University

Bioinformatics is a research area for understanding life from the bulk of molecular biology data such as genome sequences, protein structures, protein interactions, and gene expressions. After elucidating the human genome sequence as well as those from various model organisms including bacteria, we are now facing the problem on how these data can be utilized for understanding life. One of the recent approaches to this problem is the analysis of protein interaction network based on the concept that we cannot understand biological systems only by the genome sequence but it is also necessary to see how genes and their products work together. In fact, we see many types of networks in biological systems, e.g. protein interaction network, metabolic network, cellular interaction network, neural network, host-parasite interaction network, food web, and social network. From the bioinformatics point of view, we are mainly interested in networks at the molecular biology level including metabolic network, protein interaction network and protein domain network. Those are important for elucidating functions of proteins with unknown function as well. I will talk about our approach to analyze those networks in terms of the evolutionary history and functional prediction and the importance of a database maintaining the various types of network data. I would also like to discuss how we should further proceed to understand life.

Radiation and anti-cancer drug: How to cope with DNA damage?

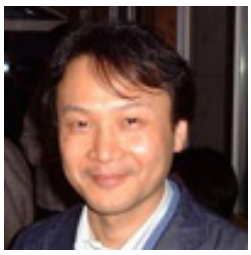
Miyagawa Kiyoshi

University of Tokyo

DNA double-strand breaks are assumed to be the most deleterious DNA damages. There are two major pathways to repair these DNA lesions. Non-homologous end-joining was thought to the primary mechanism for repairing double-strand breaks in mammals. However, it is established that both non-homologous end-joining and homologous recombination are required for repairing these DNA lesions in mammals. Homologous recombination is a high fidelity repair pathway that mediates transfer of genetic information between homologous DNA sequences. Impaired homologous recombination is the underlying cause of breast, ovary and other cancers. How these pathways influence human health will be discussed.

Importance of periodicity in the genetic information and a new hypothesis of the tRNA evolution

Akio Kanai



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Approximately 50 years have passed since the establishment of the central dogma of genetic code - the concept of information flow of DNA→ RNA→ protein. During this period, the partial modification of the flow has been requested such as due to the discovery of reverse transcriptase. RNA is mostly regarded as the information transmitter and it is considered that the rough scheme of the concept has remained unchanged. However, subsequent to the genome project, especially the elucidation of non-coding RNA (untranslated RNA) during these 5 years has seemingly entrenched the concept of RNA as more active and functional molecules.

On the other hand, it has been proposed that the last universal common ancestor (LUCA) was a thermophile or a hyperthermophile. Thus, genome-wide analysis of gene function in very ancient organisms such as the hyperthermophilic archaeon *Pyrococcus* species that thrive at temperatures above 95 ℃ could lead to new insights into the fundamental knowledge of life. We, therefore, are developing efficient methods for identifying new "RNA-related" genes present in the hyperthermophilic archaeon *Pyrococcus furiosus.* We are investigating this aspect both theoretically (1, 2) and experimentally (3, 4).

My presentation is focused on two major topics. First, I will represent our

recent studies of proteome-wide prediction of novel DNA/RNA-binding proteins using amino acid composition and periodicity (1). The purpose of the study was to demonstrate that a bioinformatics approach focusing on the periodicity in a protein's primary structure could be a suitable method for elucidating DNA/RNA-binding proteins. We used the Support Vector Machine (SVM) method to discriminate DNA/RNA-binding proteins from proteins with other functions. SVM is one of the most powerful supervised learning algorithms that recently have been widely used in the field of bioinformatics. Second, I will explain about the novel RNA-binding proteins found in *P. furiosus* using the proteome-wide expression cloning method (3, 4). Here, we found novel RNA ligase from the organism. Further, detailed analysis has suggested that this protein may play an important role in the tRNA ligation. This has led to a development of genome-wide analyzing method to detect novel tRNAs in Archaea (2). We are planning to propose a new hypothesis about the origin and the evolution of tRNAs and how universal genetic code was constructed (Please also see the Kosuke Fujishima's abstract).

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Oct. 18 (Thu) 11:45-12:45

THE FOUNDATIONS OF MATHEMATICS AS A STUDY OF LIFE

Mark van Atten

The Dutch mathematician and philosopher L.E.J. Brouwer (1881-1966) developed a foundation for mathematics called `intuitionism'. Intuitionism sees mathematics as acts of mental construction based on internal time awareness. According to Brouwer, that awareness provides the fundamental structure to the various phenomena in conscious life. In this talk, some consequences of this view for arithmetic, analysis and the notion of mathematical truth will be sketched, culminating in the example of an intuitionistic function that is effectively computable yet not recursive.

Life's waves in space-time in and around us

Franz Halberg

(with Othild Schwartzkopff, Germaine Cornélissen and Kuniaki Otsuka)

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Dedicated to the memory of Arthur MARCH (1891-1957), Professor and Head of Physics at the University of Innsbruck (1), who with Erwin Schrödinger (2) asked "What is life?" in 1946, and prompted the studies summarized herein, reflecting what biomedicine learned between presentations in Alpbach, Tyrol, Austria in 1946 (3), 2000 (4) and 2007.
In 1946 (3), life was defined as a statistical entity subject to measurement when possible and with the need to render measurable what as yet is not measurable. Here, the interim findings of this endeavor are summarized.

Life and its environment share many periods, τ, found in more or less stationary periodicities, some long-known and common to the biology of a bacterium, to a human and to their environments, others novel, intermittent, but congruent in that the 95% confidence intervals of their τs overlie or overlap. A transdisciplinary spectrum includes photic τs in the visible range, such as a day or a year in us and around us, coexisting and competing with unseen nonphotic, mostly magnetoperiodisms, associated with the difference between survival or death (suicide or other). The outcome of the competion is decided by geographic and temporal location sometimes for the same variable, such as the incidence pattern of sudden cardiac death (5).
By a combination of gliding and global spectra with population mean cosinor summaries of single cosinor parameters, derived from consecutive sections of long time series, the ensemble of periods with their uncertainties can be assessed in decades-long time series and further investigated by a remove and replace approach, applied by the sun or the earth to the intermittent waxing and waning magnetoperiodisms, that drift in frequency, bifurcate and then disappear or join again outside us, while we monitor their signatures in us. When congruent τs are found in the magnetisms of the sun, in the solar wind's speed, in the North-South component of the interplanetary magnetic field, in the metabolism of a unicell, in human blood pressure, in endocrinology, pathology and epidemiology, the transdiciplinarity of the findings supports both their reality and their broad importance as a novel, unseen but resolvable feature of life. When changes in the time structure outside us are associated with predictable changes in our psychophysiology, we find that the fields around us pull or drive, when they do not synchronize life. The same fields or rather their unsteady as well as steady cycles may be indispensable for life, as is oxygen and if so we have to broaden the definition of life beyond localized structures in space and time, that, albeit transient, are self-sustaining for a sufficient duration to reproduce as individuals while also evolving as populations. Life is more than a bacterium, a cell or an assembly of them in space and its structure in time; it is a field awaiting further mapping with a temporal microscopy for which the methodology has become available. Histology has been criticized as the study of consistent artifact in denatured tissue, yet it serves to diagnose the cancer of an individual and in some cases prompts successful removal of the tumor before it metastasizes. Structures resolved by combined global and gliding spectra and population mean cosinors may be consistent artifact in time series amenable to collection and analyses by modern technology with the application of methods that qualify the inferences from violated regression diagnostic tests (by population mean cosinor). If we split the normal

range of values in whatever we measure in life we may come closer to defining life by the cycles upon which it depends, as statistical transdisciplinary entities that abide by rules embracing and transcending those of any single field such as biology, chemistry or physics and in so doing, in any event in splitting the normal range, we may implement prehabilitation to avoid the need for rehabilitation by costly cardiac bypass grafting and after-stroke care, in the example of detecting and treating a set of heretofore unrecognized vascular variability disorders.

Toward such goals, we resolve chronomes, structures in space-time in and around us, e.g., at the boundaries of the solid or liquid earth and terrestrial (6) and solar (7) atmospheres as a statistical entity consisting of (deterministically and otherwise) chaotic changes undergoing trends, organized by rhythms, covering in the frequency domain 18 orders of magnitude, the rhythmic elements of which are approached by subtractions (and additions) made by the sun and the earth. Humans may attempt to persist and to withstand a possible, also present cycle in the extinction of some genera (8, 9) so that intellectual acquisitions of information in the sense of Chizhevsky (6) and Vernadsky (10, 11) also persist in an ever wider range of intermodulations (5).

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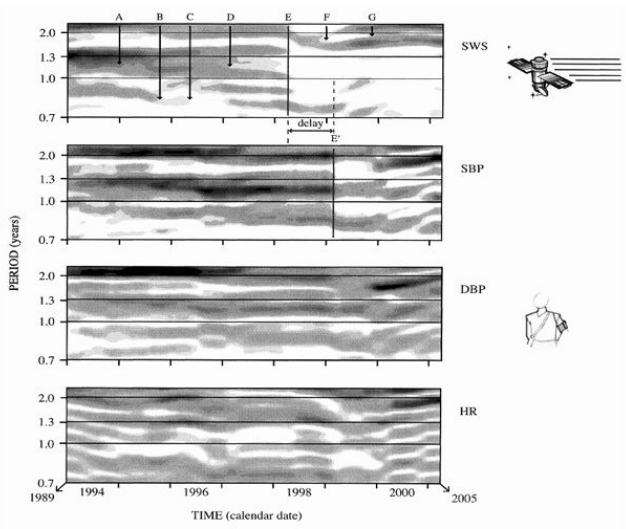

Figure 1. Time courses of the frequency structures of the speed of the solar wind (SWS) (top) and of an elderly man's (FH) systolic and diastolic blood pressure and heart rate, SBP, DBP and HR (rows 2-4, respectively), examined by gliding spectral windows. Human systolic (S) blood pressure (BP) selectively resonates with solar wind speed (SWS) (top 2 sections). Aeolian rhythms in gliding spectra of SWS and SBP change in frequency (smoothly [A] or abruptly [B,C,D], bifurcating [D,F] and rejoining [G], they also change in amplitude (B) (up to disappearing

[C,E] and reappearing) (N=2418 daily averages, total ~ 55000). Gliding spectra computed with interval = 8 y, resolution low in time but high in frequency, increment = 1 month, trial periods from 2.5 to 0.4 y, with harmonic increment = 0.05. Darker shading corresponds to larger amplitude. When several of these broad bands disappear in the SWS, at E, parts of the bands in SBP also disappear, with a lag (delay) at E', while other parts persist. These components are presumably built into organisms over billions of years, as persistence without corresponding components in SWS shows, but can be driven in part by the solar wind, as their disappearence after loss of corresponding components in SWS suggests.

Oct. 18 (Thu) 17:30-18:30

Environmental stress and atopic dermatitis: Cure with steroid-free treatment and mutual trust.

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Explanation of technical words: Atopic dermatitis is an eczematous skin disease with severe itching. IgE is one of the immunoglobulins, and it induces various responses upon interaction with allergic substances. Steroid is glucocorticoid hormone in a body, and it has an anti-inflammatory effect, but it has also immunosuppressive effect, and thus long- term use of steroid disrupts immunity.

The prevalence of atopic dermatitis is increasing all over the world. Steroid ointment has been used for long years. However, it became clear that treatment with steroid ointment only temporally improved inflammation of skin and it did not cure atopic dermatitis. Moreover, there were safety concerns associated with long-term use of steroid ointment. In fact, use of steroid ointment for several years in adults or even for several months in children induced skin infection, skin atrophy and skin addiction to steroid, and rebound phenomenon occurred upon discontinuation of steroid ointment. Consequently, patients suffered from intractable atopic dermatitis, and they finally stopped trusting treatment with steroid ointment. Atopic dermatitis is a mutlifactorial disease, and its pathophysiology has been linked to allergy and bacterial colonization/infection in skin. Allergy is equivalent to enhancement of IgE antibody production to various environmental substances. IgE antibody induced numerous immune responses including 1) immediate allergic responses by mast cells and 2) cytokine-mediated inflammation by various cells. On the other hand, bacterial colonization/infection not only directly damaged skin but also induced IgE antibodies against soluble and membrane-bound antigens of bacteria, which in turn aggravated IgE-mediated immune responses. Although steroid had potent anti-inflammatory activity, it had also immunosuppressive activity. Moreover, steroid enhanced IgE production. Thus, topical application of steroid ointment aggravated bacterial colonization/infection on one hand, while it enhanced IgE production on the other hand, which resulted in exacerbation of atopic dermatitis.

I have been treating atopic dermatitis with combination of oral antiallergic medication and steroid-free ointment. Patients with atopic dermatitis were vulnerable to various environmental stress, which aggravated allergic responses and clinical symptoms. Moreover, patients suffered from lack of improvement after long-term treatment with steroid ointments, and thus they were dubious about medical treatment. Therefore, treatment should include 1) reduction of stress in a good lifestyle, and 2) mutual trust between patients and doctor.

In information technology age, technological apparatus and environmental pollution became environmental stress. I previously reported that 1) microwave radiation from cellular phone, 2) exhaust gas from car, and 3) volatile organic compounds from paint in a room, enhanced allergic responses in patients with atopic dermatitis. It was important for patients to understand these truths and avoid environmental stress as possible. Patients with atopic dermatitis were also deficient in laughter or emotion with happiness in daily life. I previous reported that laughter induced by viewing a humorous film or kissing to partner reduced allergic responses. Thus, patients should be advised to change of lifestyle in everyday life, which in turn accelerated to improve atopic dermatitis.

I will present cases of patients including children and adults, who suffered from intractable atopic dermatitis with rebound phenomenon. Atopic dermatitis was improved or cured in them with steroid-free treatment, mutual trust and good lifestyle,

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Understanding of others: From the view point of mentalizing

Shoji Itakura

Kyoto University

For the human infants, agents-other humans are the fundamental units of their social world. Agents are very special stimuli to the infants. Quite many researchers who study object-person differentiation have derived a set of rules that they postulate infants use when they react to objects as opposed to people in the world. Premack & Premack (1995) proposed that infants perceive people as perceptual events that are self-propelled and goal-directed objects. In such case, we adults also perceive the agent has intention. Spelke, Phillips, and Woodward (1995) described the concept of human in infants as follows: “Three aspects of human interactions that are accessible in principle to young infants are contingency (humans react to one another), reciprocity (humans respond in kind to one to another’s actions), and communication (humans supply one another with information).” Spelke et al. showed the evidence that infants object movement using three principles, including the “Principle of Contact”. To explain the contact principle, they used habituation procedure to show that infants expect an object that moves to have been set in motion by another object (or person) pushing it. On the other hand people did not need an external force to be applied for them to begin moving. They demonstrated that this kind of perception of agency is appeared by 7-month-old. Agents are not simply physical objects with new properties added to them. They are entities of

an animate that move on their own, breath, eat, drink, look, and engage in actions with objects or interact with other agents (Gomez, 2004).

From the view point of social cognitive development, there are two questions as follows pointed at by Johnson (Johnson, 2003): 1) when do children first attribute mental state to others, and 2) when they do so, whom do they attribute mental state to?

In our presentation, we will review a line of research conducted to investigate how children understand and detect agents not only humans but also nonhuman agents. We start with the first cue for agents as a social partner for infants. That is an ability to detect whether caretakers and social partners are attentive and responsive to their own behavior in social exchanges. We call this social contingency. In second part, we introduce our study concerns to the relationship between understanding of other's mental state and inhibitory control in infants by using card sorting tasks. In third part, we review the several studies investigated the infant's interpretations of nonhuman agents from the action. Especially, we will review the studies of Csibra and his colleagues. Recently, they claimed that there are two fundamentally different ways to attribute intentional mental states to others upon observing their actions, those are teleological understanding and referential understanding. We will focus on teleological stance in this section. Finally, we will propose the new idea of research domain called "*Developmental Cybernetics*" and introduce some of our studies. Developmental cybernetics is a study of interaction and integration between children and robots (Kojima, 2005). Futurists and technologists have long predicted that the 21st century will see a wide application of robotics technology in common households where robots will be as ubiquitous as refrigerators and dishwashers (Asada & Kuniyoshi, 2006; Ishiguro, 2005).

Oct. 19 (Fri) 9:00~9:20

The Premodern Japanese Approach to Life: Sharing the World with Non-Humans

Toshio YOKOYAMA

Toshio Yokoyama, B.LL. and M.LL. (Kyoto); D.Phil. (Oxford) Vice-President (International Relations) of Kyoto University, with a double professorship at the Graduate School of Global Environmental Studies, and the Institute for Research in Humanities.

Born in Kyoto, he entered Kyoto University to study law, which did not satisfy him. While staying in Eastern Java in 1970, he became interested in things Japanese for the first time. In 1972, he joined the Institute for Research in Humanities at Kyoto University, to pursue his interest in a Japanese nativist poet. In 1983, he received a doctorate from the University of Oxford where he studied modern British history during the latter half of the 1970s. In 1993, he was Erwin von Bälz Guest Professor at Tübingen, and in 1999 Visiting Lecturer at Pembroke College, Oxford. In 2001, he joined the founding of the above-mentioned graduate school, and opened within the school a common space named ‘Sansai Gakurin’ dedicated to the promotion of universal learning. He has been in the chair of the Advisory Committee of Lake Biwa Museum since 2004.

He is the author of *Japan in the Victorian Mind* (London: Macmillan, 1987). His other works and edited volumes include *Kaibara Ekiken* (Tokyo: Heibonsha, 1995): an introduction to the neo-Confucian thinker of a classical civilization. Currently, he is a co-editor of an English journal, *SANSAI, An Environmental Journal for the Global Community*. To its inaugural issue of 2006, he contributed an article entitled ‘Even a sardine’s head becomes holy: the role of household encyclopedias in sustaining civilisation in pre-industrial Japan’.

Oct. 19 (Fri) 9:20-10:20

"Plasticity of the brain: For Good and Bad"

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The brain's ability to change its organization and function according to circumstances (neural plasticity) is a property of the nervous system. It is only evident when induced, very much like genes. Plastic changes can be programmed such as for childhood development and probably also for the changes that occur during aging.

Neural plasticity makes it possible to adapt to changing demands. For example, the portion of the somatosensory cortex that is activated by movements of a finger expands when the finger is used extensively such as in string players; the vestibular ocular reflex that normally ensure a stable image on the retina during head movements can adapt to situations where people wear different spectacle {Elbert, 1995 #1566}, it is even possible to adapt to wearing reversing prisms. Many other internal and external factors can activate neural plasticity. In sensory systems, deprivation of input is perhaps the strongest promoter of neural plasticity. Understanding speech through the use of prostheses such as cochlear and brainstem implants is possible because the brain can be can reorganize to properly interpret the neural code provided by these prostheses despite the code is different from that of the messages the ear normally sends to the brain.

Strokes or trauma can destroy parts of the brain and while the function of destroyed parts cannot be restored neural plasticity often makes it possible to redirect functions to parts of the brain that are not destroyed and thereby gain some of the lost functions back.

These are examples where expression of neural plasticity provides a benefit to an individual person. Activation of neural plasticity can also cause changes in the function of the brain that are not beneficial and instead cause symptoms and signs of disease. Pain and ringing in the ears (tinnitus) are the best known examples of "bad" neural plasticity. Phantom sensations after leg amputations are other examples of misdirected activation of neural plasticity. Some forms of muscle spasm are also caused by such incorrect activation of neural plasticity. The programs that control childhood development of the brain may be faulty and that has been hypothesized as a cause of developmental disorders such as autism. Addiction is another kind of disorders that most likely is caused by an (unfortunate) activation of neural plasticity.

The cause of such flawed activation of neural plasticity is complex; many disorders or insults of various kinds can induce neural plasticity causing symptoms of disorders but often no cause can be identified. Re-organization and change in the function of the brain cannot be examined by objective tests such as common imaging tests. This makes it difficult to properly diagnose the disorders that have neural plasticity as a cause. Newer so called functional imaging may provide some clues regarding the nature and the extension of plastic changes of the brain.

Oct. 19 (Fri) 9:20-10:20

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About Aage Møller

My previous research has mainly concerned the function of the auditory system but I have also studied the somatosensory and visual systems and I have done research on pain and hyperactive motor disorders. More recently, I have studied neural plasticity in the auditory system and its role in disorders that have tinnitus, hyperacusis and chronic pain as symptoms. I also have studied autism and the involvement of non-classical auditory pathways. I am the author of nine (single author) books in hearing science, intraoperative neurophysiologic monitoring and neuroscience. Recent books are "Intraoperative Neurophysiological Monitoring, 2nd Edition" and "Neural Plasticity and Disorders of the Nervous System" (2006). I am editor or co-editor of seven published books, author or co-author of 181 articles in refereed journals, 206 book chapters, review articles etc. I was Editor-in-Chief (and founder) of the international journal, Hearing Research (1978-2005), and member of the Editorial Board of other international journals. I am interested in teaching and I have developed new courses and have been writing

books that are used in teaching. I am interested in the role of neural plasticity in disorders of the nervous system and I teach a course on that topic that I developed. I also teach courses in the physiological basis for intraoperative neurophysiologic monitoring. This course, which I developed at BBS in our neuroscience program, is the only university-based course in the topic.

Research Interests

My research concerns the function of the normal and the pathologic ear and the auditory nervous system. I am particularly interested in neural plasticity and its role in tinnitus, hyperacusis and phonophobia. A specific aim of my research is to explore the possibilities of affecting these disorders by pharmacologic manipulation of GABAergic neurons in the inferior colliculus. Closely associated with these studies is research that focuses on the role of the non-classical auditory system in disorders of the auditory system.

Recent Publications

Møller, A.R., Kern, J. K., Grannemann B. Are the non-classical pathways involved in autism and PDD? Neurol Res. 2005, 625-629.

Møller, A.R. Neural Plasticity and Disorders of the Nervous System, Cambridge University Press, 394 pages, 2006.

Møller, A.R. Intraoperative Neurophysiologic Monitoring, 2nd Edition, Humana Press, Inc. 356 pages, 2006.

Oct. 19 (Fri) 10:35-11:35

Self-assembly processes in the prebiotic environment.

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Our laboratory is exploring self-assembly processes and polymerization reactions of organic compounds in natural geothermal environments and related laboratory simulations. Although the physical environment that fostered primitive cellular life is still largely unconstrained, we can be reasonably confident that liquid water was required, together with a source of organic compounds and energy to drive polymerization reactions. There must also have been a process by which the compounds were sufficiently concentrated to undergo physical and chemical interactions. We have found that macromolecules such as nucleic acids and proteins are readily encapsulated in membranous boundaries during wet-dry cycles such as those that would occur at the edges of geothermal springs or tide pools. The resulting structures are referred to as protocells, in that they exhibit certain properties of living cells and are models of the kinds of encapsulated macromolecular systems that would have led toward the first forms of cellular life. We have also determined that RNA-like polymers can be synthesized non-enzymatically from ordered arrays of mononucleotides in lipid microenvironments. Chemical activation of the mononucleotides is not required. Instead, synthesis of phosphodiester bonds is driven by the chemical potential of fluctuating anhydrous and hydrated conditions, with heat providing activation energy during dehydration. In the final hydration step, the RNA is encapsulated within lipid vesicles. We are now extending this approach to template-directed synthesis of RNA, in which lipid-assisted polymerization serves as a model of an early stage of evolution toward an RNA World.

In my talk, I will discuss recent results in which we attempted to relate such laboratory simulations to natural geochemical conditions that were likely to prevail on the early Earth. The variables to be considered include temperature, pH, salinity, self-assembly of amphihilic compounds and adsorption of solutes to mineral surfaces. Our general observation is that the organic compounds required for the origin of life in the natural setting would have had a variety of possible fates other than those observed in a laboratory, where pure compounds react in glass containers. Our results show that self-assembly of boundary structures cannot occur under hot acidic conditions, at least with a simple amphiphile such as myristic acid. Furthermore, if di- and trivalent cations are present, amphiphiles are likely to precipitate as insoluble soaps, which inhibits potential membrane formation. Interactions of organic solutes with mineral surfaces would tend to concentrate organic solutes, and it is possible that such processes would enhance condensation reactions leading to polymers. However, adsorption of organic solutes and

phosphate to clay mineral surfaces also has the potential to isolate reactant molecules and thereby inhibit polymerization.

These considerations suggest that, from a biophysical perspective, the most plausible planetary environment for the origin of life would be an aqueous phase at moderate temperature ranges (<60 ^{o}C) and low ionic strength, having a pH value near neutrality and divalent cations at submillimolar concentrations. This suggestion is in marked contrast to the view that life most likely began in a geothermal or marine environment, perhaps even the extreme environment of a hydrothermal vent. A more plausible site for the origin of cellular life would be fresh water pools maintained by rain falling on volcanic land masses resembling present-day Hawaii and Iceland. After the first cellular life was able to establish itself in a relatively benign environment, it would rapidly begin to adapt through Darwinian selection to more rigorous environments, including the extreme temperatures, salt concentrations and pH ranges that we now associate with the limits of life on the Earth.

Oct. 19 (Fri) 11:45-12:45

WHY AND HOW WE AGE…..AND IS THAT PROCESS MODIFIABLE?

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It is a paradox as to why an organism that is capable of using a intricate process of development to transform itself from a single cell into a large and complex adult cannot merely maintain itself once mature. The eventual failure of our self-maintenance ability leads to the loss of function characteristic of aging and death. Humans have long been intrigued by this paradox and have come up with religious, medical, and biological answers to this puzzle. A review of these alternative explanations shows that aging is best understood when viewed through the lens of evolutionary biology: we age not because we are programmed to age but rather because there is normally no biological reason not to age. This existentialist view depresses some but it intrigues biologists who recognize that the absence of a biological imperative to age means that pro-longevity interventions are possible.

None of society's earlier efforts to increase life span had anything to do with altering the aging process. This may seem contradictory in view of the fact that one of the great achievements of the 20th century was the ~60% increase in mean life span that took place in developed countries. But that result of public and individual health interventions had everything to do with improving the human environment, thereby decreasing the premature mortality inherent in a harsh environment and increasing the mean life span, than it did with slowing down the aging process and thus increasing the maximum life span. Our ability to manipulate the aging process in the laboratory and significantly increase the maximum life span of our model systems has been laboriously developed only over the past 25 years or so, and their elucidation was made possible only when investigators used evolutionary principles to uncover them.

All organisms must allocate their available energy between reproduction or somatic maintenance and repair. They face a tough problem: what is the best allocation of a finite energy resource to maximize reproduction and repair? Both functions cannot be simultaneously maximized; and there is in fact an inverse relationship between the two alternatives. A choice must be made. Reproduction costs less than somatic maintenance. In addition, the organism's Darwinian fitness is determined solely by how many copies of its genes it successfully transmits to the next generation. How long it lives is of no consequence in this calculation. Accordingly maximizing the organism's Darwinian fitness will result in somatic repair and maintenance activities taking place at a level lower than that required for indefinite somatic repair, and so the organism eventually dies. It has, however, been evolutionarily successful at the only game that counts.

The lives of animals can be lengthened in three ways: increasing their early survival rate; increasing their late survival rate or delaying the onset of senescence. The first two approaches decrease the mortality rate at the beginning or end of life but do not affect the basic aging process. The third approach causes the organism to enhance its existing repair and maintenance capabilities so as to slow the aging rate and delay the onset of senescence. This results in an extended “health span” while having no effect on the length of the “senescent span”. How does the body do this? It turns out that the body has its own genetic systems for regulating its maintenance and reproductive activities. For example, it has long been known that reducing the number of calories in the diet by ~40%, while keeping normal nutrient levels, results in healthy and long-lived worms, flies, mice, rats, monkeys, and probably humans. The body interprets the low caloric level as indicating an environment hostile to successful reproduction. In such conditions, the best strategy is to defer reproducing until the environment changes for the better. But in the meantime, the animal needs to survive until it can reproduce, and so it shifts from maximizing reproductive activities to maximizing maintenance activities. In context, this shift away from reproduction will indirectly enhance its Darwinian fitness. Investigations by many laboratories have uncovered the genetic and physiological pathways involved in this type of shift, and an overview of these will be given in the talk. It seems reasonable that the body’s existing repair and maintenance capabilities for extended survival should be the prime candidates for a pharmecutical intervention which would activate them without the necessity of reducing one’s caloric intake. The development of effective pro-longevity pharmaceutical interventions is now underway in both the private and public sectors. [I emphasize that these scientifically based pro-longevity advances should not be confused with the present day anti-aging industry, which has engendered much justified scientific criticism.]

The future of aging research will depend on whether public debate on the induced extension of the human health span will encourage or inhibit the use of our knowledge. My “guesstimate” is that an effective intervention might add perhaps 15 to 25 years to a person’s lifespan, such that humans might be healthy adults from the age of 20 to 80 years instead of the current 20 to 55 or so. Some critics see only increased despair and financial costs in such an extension of human life, and wish to ban the intervention. I disagree, and will make the case that such interventions are not only ethical but desirable. The critics overlook the likely fact that the senescent span will stay the same in absolute temporal terms, and its associated costs will not change. In fact, an increased health span will not cost more. Instead, it would give us longer, healthier, and more productive lives, which is certainly a goal worth the striving.

The Multiple Implications and Functions in Mandalas

Motohiro YORITOMI
Shuchiin University, Kyoto

In ancient India “mandalas” were discovered as tools or systems that present the symbols of the cosmology and ontology of the Indian religions. The original Sanskrit language “maṇḍala” is a compound word composed by the two elements; “maṇḍa” implies “essence” or “core”, and ‘ ̊ la’ , suffix which means “possession”. As a result “mandala” was considered as a sacred sphere in which various holy Buddhas and Indian Gods have their own functions, positions, energies and meanings. Philosophically cosmos, nature and human being are always included in ordinal mandalas.

In China and Japan new implications and understanding of a set of two mandalas became popular, especially by Kukai (774-835), founder of the Shingon Buddhism.

The Garbha-dhātu (Mother type) mandala and the Vajra-dhātu (Father type) mandala symbolized the union of the dualism in Chinese Taoism. This kind of idea has a little dogmatic and theoretical function, however, it is also necessary to recognize the difference of the structures of the two mandalas.

Recently the third type of mandalas was highly estimated by philosophers, psychologists and naturalists.

In this case, the main characteristics of the mandalas, that is to say, “sacredness” or “holiness” are not indispensable. These types of mandalas make stresses on their “structure” and their “symbolism” as ideal models of human ideas and theories. For example, Kumagusu Minakata (1867-1941), naturalist and philosopher presented his own mandala under the suggestion by Venerable Horyu Toki, abbot of Koyasan Temple. His idea of the mixture of causality and accidentalism through the image of some mandalas seem to me more attractive for the further inspections of the mandala idea in the future.

Oct. 19 (Fri) 14:15-15:15

Professor Motohiro Yoritomi
President of Shuchiin University

Oct. 19 (Fri) 15:40-16:30

Leaf Volatile Ecology: Multitrophic Interaction Networks Mediated by Leaf Volatiles

Junji Takabayashi
Center for Ecological Research, Kyoto University

In response to feeding by phytophagous arthropods, plants emit volatile chemicals. This is shown to be an active physiological response of the plant and the released chemicals are therefore called herbivore-induced plant volatiles (HIPV). One of the supposed functions of HIPV for the plant is to attract carnivorous natural enemies of herbivores. Depending on which plant and herbivore species interact, blends of HIPV show qualitative and/or quantitative variation. An intriguing question is whether this allows the natural enemies to discriminate between volatiles from plants infested by herbivore species that are either suitable or unsuitable as a food source for the natural enemy. Another question is, whether natural enemies can also recognize HIPV when two or more herbivore species that differ in suitability as a food source simultaneously attack the same plant species. Here, I will show that arthropod parasitoids can tell different HIPV blends apart in single-plant-single-herbivore systems and even in single-plant-multiple-herbivore systems. Yet, there are also cases where they do not discriminate or discriminate only after having learned the association between HIPV and herbivores that are either suitable or non-suitable as a source of food. HIPV further mediate interactions between two plant individuals of the same/different species, and between plants and phytophagous arthropods. The resulting interaction networks mediated by HIPV would have important consequences in ecological community.

Oct. 19 (Fri) 16:45-17:45

The Necessity of Consciousness: Why Human Zombies Would be an Evolutionary Dead-End

Nicholas Humphrey

The hard problem of consciousness is to explain where the *phenomenal feel* comes from – why it's "like something" to experience sensations, and what biological purpose this *being-like-something* serves. I will propose an entirely new solution, by arguing as follows: 1. Sensations don't *have to have* a phenomenal feel to them in order to serve their basic role; indeed, in the early stages of evolution, sensations were surely *non-phenomenal.* 2. Phenomenality must have been added by natural selection as a quite peculiar *design feature,* probably relatively late in evolution (and possibly only in mammals). 3. It will have been selected because the *psychological changes* that the experience of phenomenality brings about in the conscious subject are highly adaptive. 4 . Arguably these changes were – and are – nothing less than an enhanced sense of self and a new enchantment with the world outside. 5. Even if phenomenal consciousness is present in other species, human beings have built on it in ways none others have. 6. It has allowed humans to occupy what I call the "soul niche", that's to say , the cultural and biological territory, rich with almost unlimited opportunities, that must have opened up for our ancestors once they first began to think of themselves as *spiritual beings* .

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Oct. 20 (Sat) 9:00-9:40

Faith Ethics for Sustainable Development

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10-45 Uchihata-cho Hanazono Ukyo-ku,Kyoto City, Japan

Abstract

Major faith systems were compared in terms of monotheism, polytheism, and interpretation of after life. Reincarnation was interpreted in terms of a material dimension with the concept of DNA vehicles. Faith ethics on nature conservation among major religions were compared. The Rio declaration was interpreted in terms of faith ethics. There is no fundamental conflict in principles between the Rio declaration and major faith ethics of environment. It will be necessary to develop the Rio declaration into a new form of the global environmental ethics in future, when environmental scientific society must provide more clear pictures to faith societies that can help sustainable development of Earth.

Key words: Global Environment, Faith Ethics, Rio declaration, DNA vehicles

" The central neural foundations of awareness and self-awareness"

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In the past, neuroscientists have done very well to concentrate on explaining the mechanisms for very specific, simple behaviors. For example, my laboratory's work with molecular and neural mechanisms of a simple sex behavior proved for the first time that specific biochemical reactions in specific parts of the brain govern a specific behavior(Pfaff, "Drive", The MIT Press, 1999). Now, advances in our field coupled with new techniques permit us to attack the problems of explaining global changes of state in the central nervous system. Of surpassing interest is the explanation of the primary causes of brain arousal (Pfaff, "Brain Arousal and Information Theory" , Harvard University Press, 2006). I have hypothesized that the earliest and most elementary event in waking up the brain is the activation of certain primitive nerve cells in the hindbrain reticular formation. Hypothesizing a 'generalized arousal' force emanating from these cells puts forth an idea roughly analogous to the hypothesis of a 'big bang' in astrophysics or to our ideas about the magma of the earth in geophysics. Following the activation of this primitive arousal force we are able to be alert and aware. The neuroanatomical pathways serving brain arousal are fairly well known: they are Bilateral, Bidirectional, Universal among vertebrate animals including humans, and they are always involved in Response Potentiation, approach or avoidance responses (BBURP theory). More than 120 genes are involved in the regulation of brain arousal.

In theoretical terms, the discussion so far has dealt with 'bottoms up' approaches to awareness -- from mechanisms in the hindbrain working through several phylogenetically ancient pathways, to higher levels of awareness. However, we must also consider 'top down' approaches. Based on our thinking and our fantasies, arousal of the central nervous system may be modulated up or down. And then, if through memory of our behavioral activity we can reflect on our own mental state, self-awareness eventuates.

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Laboratory history.

Some of the laboratory work can be summarized in four steps. First we worked on the localization of hormone target neurons in the brain and discovered estrogen-binding neurons in a limbic/hypothalamic system. The discovery initially was made in rat brain, but our work on fish CNS through monkey CNS showed it to be a general vertebrate system . We followed up the histochemical findings to demonstrate consequences of hormone binding for electrophysiological activity and neuronal growth. Secondly, we then worked out the first neural circuit for a vertebrate behavior, the estrogen-dependent lordosis behavior. The lordosis behavior circuit proved that it is possible to explain how mechanisms for a vertebrate behavior work. Third, we found hormone-dependent genes in the brain . Their induction by estrogenic hormones has temporal, spatial and gender specificities appropriate to reproductive behavior. Fourth, in turn, the products of some of these hormone-dependent genes are required for hormone-dependent lordosis behavior. Taken together, these four findings showed that specific neurochemical reactions in specific parts of the brain determine a specific mammalian behavior.

Naoko Tosa,

Kyoto University

The way cultural computing models human conduct and grammar in every culture and expresses them using cutting-edge IT. This method will rock memory and awareness to the deeply-rooted ethnic foundations for American and Japanese people as we know them. As a means of cultural translation using scientific methods to represent essential aspects of Japanese culture. To develop new theories, models, and methods, that may shed new light on how a given culture may be translated into a format that would enable users from different cultural origins to access the deeper significance and construction of culture.

ZENetic Compuer. `http://www.tosa.media.kyoto-u.ac.jp/`

Including images that heretofore have not been the focus of computing, such as images of Eastern thought and Buddhism, and the Sansui paintings, poetry and kimono that evoke these images, we projected the style of communication developed by Zen schools over hundreds of years into a world for the user to explore - a somewhat exotic Eastern Sansui world. Through encounters with Zen Koans and haiku poetry, the user is constantly and sharply forced to confirm the whereabouts of his or her self-consciousness. However, there is no "right answer" to be found anywhere.

ZENetic applies some aspects of Buddhist philosophy as a model in computational science. Our motivation derives from the more than 2,000 years of innovative Buddhist tradition. Methods of interaction between Zen master and pupil, developed to sharpen the understanding of human consciousness, provide a rich base for interactive modeling -- a field still unexplored in the Western scientific tradition.

Hitch-Haiku System

“HITCH-HAIKU” is a haiku creation support system that allows you to experience Japanese haiku by “hitching” together phrases from book contexts. The man behind its conception, Seigow Matsuoka, is also responsible for the Navigation of City of Books, full of meanings and contexts from books spanning all eras and origins. A user can select a key word / phrase and be connected to the text of an arbitrary book including the selected word/phrase through the reading methods of the seven volumes of 1,000 Books and 1,000 Nights. When the user arbitrarily selects words/phrases from the haiku, the computer “hitches” them together using association capabilities which surpass human imagination, and generates a haiku.

Oct. 20 (Sat) 11:00-12:00

Haiku, Japan's ancient poetry, made up of five, seven, and five-character lines, are the world's shortest and include "kigo" which are used to describe any season, New Year's, spring, summer, autumn, or winter. Despite having the least words, haiku are deep with multiple meanings which can portray a broad scene in the reader's mind. The poetry with these features originates in the Muromachi Period, the top and bottom verses were then linked, and Basho Matsuo fathered "hokku" in the 17th Century. Basho created a masterpiece known as The Narrow Road to the Deep North. Basho's style reflects "artistic elegance", which, in other words, stays away from vulgarities. There is a sense of "feeling" in the "subtlety" which leads to a "phrase".

The modification of biocellular chemical reactions by physicochemical stimulants in the environment

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Our health has been affected by many environmental factors, which are dramatically increasing in a parallel to the development of our society. To assess environmental risk of these factors, it is important to estimate the human exposure levels. Since it is extremely hard to achieve, extrapolation from experimental animals to humans has been performed under the environmental exposure scenarios of daily life. The current methodology for risk assessment is focused on its source, route, and the amount of those factors exposed. For detection of any effects of environmental factors, a biomonitoring system with high sensitivity has been required to be established. To this end, we have to know how environmental factors would affect our health at molecular levels.

Discovery of apoptogenic nature of environmental factors has been expected to develop new means of health risk assessment. One of advantages is that apoptosis induced by environmental factors occurs before they induce necrosis, indicating that it will make the detection of health effects of the factors earlier than the methods based on necrosis. Another advantage is that apoptotic phenomena are seen by a variety of environmental factors such as cadmium, methylmercury, diesel exhaust particles, uv, dioxin, bisphenol A, and several kinds of phthalates, suggesting that unidentified factors in the environment would be detectable by apoptotic signaling if an apoptosis signal is in general for toxic actions of environmental factors. Ultimately, apoptotic signals leads to cell death, probably due to shut down cellular metabolism in cells affected by the environmental factor before killing all healthy cells left.

Recent efforts have been made to detect the subtle influences of environmental factors in human biological system without a catastrophe of cell death. Since environmental factors evoke both death signaling and cellular protective reactions against toxicity, cell fate is committed by the resultant which reaction exceeds the others. This escapes the detection of trace effects of toxicants. It has applied to seek the biological effects of electromagnetic fields exposure, leading to a finding of the modification of hormonal melatonin signaling and gene expression of several

oncogenes. It will be further examined if the long-term effects of these biological modifications would be linked to the disease such as carcinogenesis.

The etiology of multifactorial disorders such as neurodevelopmental disorders of attention-deficit hyperactivity disorder (ADHD) or autism has been considered to be the interaction between a range of intrinsic (gene) and extrinsic (environment) factors. The symptoms of ADHD and autism are inattention, excess impulsivity, uncontrolled hyperactivity, and the deficit in social communication. Recent evidence in animal models has shown that environmental chemicals *per se*, including endocrine-disrupting chemicals and a pesticide rotenone, cause hyperactivity, seen in patients with ADHD or autism. Impairment of immunoreactivity for tyrosine hydroxylase, a rate-limiting enzyme for catecholamine synthesis, was associated with these hyperkinesias, indicating that the developmental deficit of dopaminergic tone may underlie motor hyperactivity. Although this is a case of ruin of neuronal cell death, it is unknown whether the environmental chemicals might interact with epigenetic programme.

Sporadic neurodegenerative diseases and mental disorders have well-documented environmental causes. The expanded Barker's hypothesis proposed that the environmental origins of these disorders in later life might be early in life during windows of developmental vulnerability. The vulnerability to environmental factors is dependent on the period of their exposure: *in utero* and in early postnatal life may be most sensitive. Furthermore, early exposure to environmental toxicants could lead to persistent changes in later life. Thus, children are victim of environmental violence and predictors of disease in later life. Parkinson's disease represents clinically as a disorder of motor function characterized by tremor, bradykineasia, muscular rigidity, poor balance, and problems in gait. The environmental origins of human sporadic Parkinson's disease might be also early in life. Possible explanation for this mechanism is that early exposures to neurotoxic chemicals reduce the number of dopaminergic neurons in critical areas of the brain such as the substantia nigra to levels below those needed to sustain function in the face of the neuronal attrition associated with advancing age.

An animal model of Parkinson's disease has been developed by selective dopaminergic degeneration with neurotoxicants, pesticides, or endocrine-disrupting chemicals in adult animals. Although one of etiologies of animal models of both Parkinson's disease and hyperkinetic disorders is apparently dopaminergic dysfunction, behavioral features of both diseases are opposite, e.g. hypokinesia versus hyperkinesia. This fact suggests that the same action of an environmental

toxin would develop very different disorders, dependently of periods of exposure.

Human biological system consists of not only physicochemical but also psychiatric networks. As seen above, environmental factors affect both dimensions to different extent from modifications of biochemical reaction to cellular catastrophe. Future studies in understanding the affection of environmental risk factors on the body and mind, and our adaptation are possible approach to look for an answer to '*what is life*?'.

The mammalian brain in the electromagnetic fields designed by man.

Leif G. Salford, Henrietta Nittby, Arne Brun, Jacob Eberhardt, Gustav Grafström, Lars Malmgren, Marianne Sommarin, Bengt Widegren and Bertil R.R. Persson. Lund University, Lund Sweden

Life on Earth was formed during billions of years, exposed to, and shaped by the original physical forces such as gravitation, cosmic irradiation, atmospheric electric fields and the terrestrial magnetism. The Schuman resonances at 7,4 Hz are an example of oscillations possibly important for life (Cherry, 2002).
The existing organisms are created to function in harmony with these forces. However, in the late 19th century mankind introduced the use of electricity, in the early 20th century long-wave radio and in the 1940-ies short-wave radio. High frequency RF was introduced in the 50-ies as FM and television and during the very last decades, microwaves of the modern communication society spread around the world. Until then microwaves had principally never been experienced on the Earth. Today, however, one third of the world's population is owner of the microwave-producing mobile phones and an even larger number is exposed to the cordless RF emitting systems. To what extent are all living organisms affected by these new, almost everywhere present radio frequency fields? And what will be the effects of many years of continuing exposure?
Since 1988 our group has studied the effects upon the mammalian blood-brain barrier (BBB) in rats by non-thermal radio frequency electromagnetic fields (RF-EMF). These have been shown to cause significantly increased leakage of the rats' own blood albumin through the BBB of exposed rats as compared to non-exposed animals—in a total series of about two thousand animals (Salford et al. 1992, 1994, 1997, 2001, Persson et al. 1997). One remarkable observation is the fact that the lowest energy levels give rise to the most pronounced albumin leakage. If mobile communication, even at extremely low energy levels, causes the users' own albumin to leak out through the BBB, also other unwanted and toxic molecules in the blood, may leak into the brain tissue and concentrate in and damage the neurons and glial cells of the brain. In later studies we have shown that a 2-h exposure to GSM 915 MHz at non- thermal levels, gives rise to significant neuronal damage, seen 28 and 50 days after the exposure (Salford et al 2003, Eberhardt et al. 2007). In our continued research, the non-thermal effects (histology, memory functions) of long-term exposure for 13 months are studied. We have also performed micro-array analysis of brains from rats to short term GSM both at 1,800 MHz and at 900MHz and have found significant effects upon gene expression of membrane associated genes as compared to control animals (Belyaev et al. 2006, Salford et al. 2007).
Most of our findings support that living organisms are affected by the non-thermal radio frequency fields. Studies from other laboratories in some cases find effects, while in other cases effects are not seen.

The mechanisms by which the EMFs may alter BBB permeability are not well understood. At low field strengths, the effects on body temperature are negligible and thus heating effects are not involved. It has been suggested that physicochemical characteristics of membranes are changed (Shivers at al.1987)
We have performed experiments based upon a quantum mechanical model for interaction with protein-bound ions which show that controlled frequency and amplitude of ELF EM fields upon spinach plasma vesicles can steer transport over the membrane (Bauréus-Koch et al. 2003) and this may be a first proof of a resonance phenomenon where appropriate levels of frequency and amplitude in the right combination have the potency to communicate with the biology of membranes and transport systems. Some other concepts to consider in the continued search for the answer should be: Microwaves have effect directly on the protein conformation (vibration energy levels) (de Pomerai et al. 2003); Autooxidative processes which lead to oxidation in the cells (Ilhan et al. 2004, Friedman et al. 2007); Or possibly interaction microwaves –> water molecules, bound in biologically active molecules (Pang and Zhang, 2003, 2004, Persson et al. 2001).

This symposium raises the question: What is Life? An obvious and simple answer could be: It is DNA! The DNA strand can be looked upon as an antenna resonating in the microwave band 6GHz with its harmonics and subharmonics (Chitanvis, 2006, Edwards et al., 1984, Golo, 2005, Prohofsky, 2004, Zhang, 1987, 1989). If this holds true, the dramatic situation might exist, that all living organisms have a receptor for the newly constructed and world-wide man-made microwaves, leading to a direct effect upon the function of DNA - in concordance with our experimental findings!

Our generation has an imperative obligation to further investigate the links between EMF and biology in order to prevent possible detrimental effects of its invention of the microwave emitters.

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Life from the Outside/Life from the Inside*

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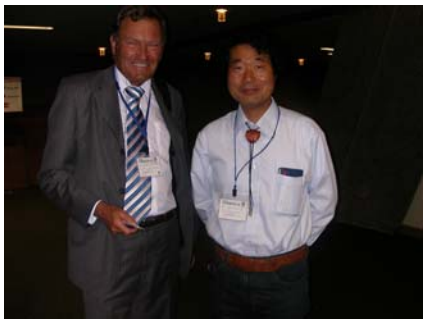
Many non-living materials can grow in apparently coordinated ways, as in fractal or crystalline structures dictated by molecular combinations. And many living organisms that have no neural apparatus and show no evidence of consciousness also behave in complex ways that further their survival, as in the cases of viruses and bacteria, plants and corals. For humans, however, an indispensable aspect of life is consciousness. Consciousness is so central that most countries consider the irreversible loss of consciousness equivalent to the death of a person. The human body may still be kept alive by mechanical respiration and circulation. But if the body has no potential for consciousness, it has neither human behavior, nor arguably legal status. In other words, the physical prolongation of cellular life is not generally considered equivalent to human life; what makes a PERSON alive or dead is the presence of or potential for consciousness.
(This is not to argue that we should not respect and care for the dead, just as we should respect and care for unconscious rivers and forests; it is rather an argument about what we mean by PERSONhood and HUMAN life.)

Almost every culture in the world has accounts of people's consciousnesses leaving their bodies, of consciousness surviving after death, and of messages received from dead consciousnesses. The past century of the scientific study of the phenomena of consciousness gives many evidences that consciousness is not necessarily limited to the human brain. Nobel Prize-winning neuroscientist Sir John Eccles (who often visited Osaka University when I was there) has published technical proofs that human intention precedes brain activity. Robert Crookall, Robert Monroe, Robert Jahn, Robert Morris, and many other scientists have carefully studied the evidentiality of out-of-body-experiences, in which people's consciousnesses correctly see and hear things in locations distant from their bodies. More recently, the veridicality of near-death experiences in which revived patients correctly report events that occurred while they were considered dead or brain dead has been reported in the
Lancet, the BMJ, JNMD, and studied in major universities around the US., UK., and Europe. While we do not yet understand the mechanisms of these phenomena, modern

Oct. 20 (Sat) 14:20-15:20



medical science has come to recognize that the ability of consciousness to separate from body in extreme situations is not only a phenomenon reported by pre-literate tribespeople, but also occurs to highly educated modern people in clinical hospital settings. In short, human consciousness can sometimes operate independent from the brain and body.

This leads to more questions than it answers. How does consciousness emerge, evolve, develop, and continue? Must we not only distinguish animate and inanimate states, but also refrain from concluding that death extinguishes consciousness or personhood? For laboratory purposes, we can use criteria like metabolism or cellular function to determine whether an organism is living or dead. But for human purposes, further research seems required on the relation between human bodies, minds, energies, and consciousness. This report will introduce some evidence of the above phenomena, and propose that further study of consciousness may have major implications for law, medicine, and ethics, as well as philosophy and possibly biology.

Oct. 20 (Sat) 16:45-17:45

Chimpanzee mind:
The evolutionary basis of human mind

Tetsuro Matsuzawa

For Nishinomiya-Yukawa Memorial International Syposium:
What is Life? The Next 100 Years of Yukawa's Dream

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Recent advances in the study of the human and the chimpanzee genome have revealed just how close the two species are. Differences at the level of the DNA are as low as 1.23%. In other words, we are 98.77% chimpanzee. The genomic difference between the two species is comparable to that between horses and zebras, who differ by about 1.5%. The human mind is the product of millions of years of evolution, just as the human body, human society, and the human genome are. *Homo sapiens* is one of roughly 220 extant primate species. A community of 14 chimpanzees of 3 generations inhabits an enriched, semi-natural environment at the Primate Research Institute of Kyoto University (KUPRI). My research partner here is named "Ai", a 30-year-old female chimpanzee. I have been working with Ai since 1977, when she was just 1 year old. A community of 12 chimpanzees of 3 generations inhabits the forests at Bossou, Guinea, West Africa. KUPRI researchers have been studying these chimpanzees for 30 years. Bossou chimpanzees are well known to use a pair of stones as hammer and anvil to crack open nuts. Since 1986, I have been visiting Bossou once a year to explore developmental changes in tool use technology. The combination of laboratory and field studies has revealed a unique mode of social learning in chimpanzees. Referred to as "Education by master-apprenticeship", this mechanism is characterized by three main behavioral attributes: 1) Infants' prolonged exposure to adult behavior based on the strong mother-infant bond, 2) Lack of active teaching (no formal instruction, and no positive/negative feedback from the mother), and 3) The infants' intrinsic motivation to copy the mother's behavior. Each chimpanzee community in the wild has its own unique set of cultural traditions. Through education by master-apprenticeship, chimpanzees seem able to pass knowledge, skills, and values from one generation to the next, thereby maintaining their community's cultural repertoire.

Dynamic polymorphism of signal transduction protein Ras studied by single molecule FRET

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Abstract:Ras plays an important role in cellular signal transduction pathways. Upon binding to GTP, Ras-GTP complex binds to various effectors such as Raf, RalGDS and PI3K. This new complex activates signaling pathways corresponding to the cellular events. However, it has not been well understood how Ras can interact with many effectors despite having only one effector binding site. To understand the mechanism of Ras function, its conformational dynamics were measured in the absence and presence of effectors using single molecule fluorescence resonance energy transfer (FRET) between probes located on the Switch II region and GTP. The time trajectories of FRET efficiency from GTP-bound Ras showed that this conformation spontaneously varies among multiple states. The fluctuation lasted ~30 ms but converged to a specific conformational state upon binding to an effector. Thus, Ras conformation spontaneously fluctuates to readily interact with various effectors.

A New Hypothesis that tRNAs May Have Emerged Through the Combination of Ancestral 5’ and 3’ tRNA Fragments

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Transfer-RNA (tRNA) is a small RNA chain that transfers specific amino acid to a growing polypeptide during translation. All living organism use tRNA as a universal dictionary to decode nucleic acid language (genetic information) into protein language. Therefore, tRNA is recognized as one of the most important molecules for constructing the system of life. Recent discovery of the completely separated 5' and 3' tRNA genes; so-called split tRNA in Nanoarchaeota *Nanoarchaeum equitans* [1] and many intronic tRNAs in archaea has brought us question whether ancient form of tRNA was codified on single or separated genes. To answer this question, we have predicted total 1953 tRNA sequences from 45 archaea genomes using tRNA prediction program SPLITS and performed phylogenetic analysis to observe the relationship of split, intronic and non-intronic tRNAs. All split tRNAs located adjacent to other tRNAs with same anticodon except split $tRNA^{Glu}$, suggesting that all three types of tRNA should have emerged from a common ancestral tRNA gene(s).

Next, we divided 304 tRNAs in the 7 representative archaeal genus into two tRNA fragments to mimic the split tRNA and examined the phylogeny of 5’ and 3’ tRNA halves respectively. Network analysis revealed specific characteristics and topological differences between 5’ and 3’ tRNA halves; the 5’ half sequences categorized into 9 distinct groups at sequence similarity >80%, while 3’ half sequences categorized into 8 groups at relatively higher sequence similarity of >88% suggesting different evolutionary background of the two tRNA regions. Furthermore, combination of 5’ and 3’ halves corresponded well with the variation of amino acids in the codon table. We have found universally conserved combination of 5’ – 3’ tRNA halves in $tRNA^{iMet}$, $tRNA^{Thr}$, $tRNA^{Gly}$, $tRNA^{Gln}$, $tRNA^{Glu}$, $tRNA^{Asp}$ and $tRNA^{Leu}$ but also phyla specific combinations in $tRNA^{Pro}$, $tRNA^{Ala}$ and $tRNA^{Trp}$. Thus, our results support the hypothesis that tRNAs may have emerged though the combination of ancestral 5’ and 3’ tRNA fragments and explains the sequence diversity during the archaeal tRNA evolution.

Understanding Cooperation in a Captive Chimpanzee (*Pan troglodytes*)

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Many primate species including humans live in groups with specific social structures. Much attention has been given to the social intelligence hypothesis, which claims that higher cognitive ability is required to survive in a complex than in a simple social world. Researchers have argued that group-living primates are constantly competing against conspecifics for access to food and mates, and it thus follows that selection has favored individuals capable of out-competing conspecifics. However, primates are not always competing with other group members in their natural group lives. They also engage in cooperative acts such as cooperative parenting by some species of New World monkeys, reciprocal grooming in many species of monkeys, and cooperative hunting in chimpanzees. Yet, few experimental studies have investigated cooperative abilities in non-human primates.

I carried out two experiments to test the ability of chimpanzees to cooperate with another individual. In the first experiment, two chimpanzees were required to pull each end of a rope simultaneously to drag blocks supporting food into reach. The chimpanzees did not succeed in initial tests. However, the frequency of success gradually increased as the number of sessions increased and the task was varied. They began to look at the partner frequently, wait if the partner was not holding the rope, and pull the rope in synchrony with the partner. One chimpanzee was then paired with a human partner in the same situation. After initial failures, the chimpanzee began to solicit the human partner for cooperation: looking up at his face, vocalizing, and taking the partner's hand. When this chimpanzee was again paired with the chimpanzee partner, no soliciting behavior was observed. In the second experiment, I dug a hole in the ground of the chimpanzee enclosure, put a piece of food into the hole and placed a cover over it. The chimpanzee first learned to pull the cover by herself in order to obtain the food. Then, the weight of the cover was gradually increased until the chimpanzee could no longer pull it. When the maximum load was introduced, a human experimenter stayed in the enclosure to work as a cooperative partner. In the beginning, the chimpanzee showed no signs of understanding the possibility of cooperation. However, the subject gradually learned to pull the cover together with the partner. After a repetition of trials, the chimpanzee began to solicit cooperation also in this experiment. In sum, the present study confirms the ability of chimpanzees to coordinate the behavior and communicate with the partner in cooperative tasks. Communicative behavior emerged during the task, but the communication differed according to the identity of the partner.

Title & Abstract : ¥title{Reciprocal Relations in Evolutionary Processes}

¥abstract{
I wish to propose reciprocal relations in evolutionary processes,
considering a qualitative and phenomenological
approach for evolutionary processes.

Recently, Aita and Husimi¥cite{AitaHusimi03,AitaHusimi04,AitaHusimi06} have proposed a thermodynamic
interpretation of evolutionary processes such as
evolutions of proteins and biopolymers.
They have found the appropriate definitions of
free fitness,
evolutionary temperature,
evolutionary entropy,
evolutionary force,
and
evolutionary flux, etc.
And using such quantities, they have found
the relationship between the evolutionary entropy generation
as a Lyapunov function L and the evolutionary flux J and force X,
${¥cal L} = JX$.
This theory suggests us that there may exist a theory
of irreducible processes in evolution of a "single species".
It is thought of as a generalization of Onsager's theory¥cite{Onsager}
of irreducible processes to that of evolutionary processes.

In this work, I would like to generalize the above to
the evolutionary processes of multi-species.

In nature, our biological world consists of many species
of biological contents such as DNA, RNA, and proteins, etc.
As frequently phrased as "Which is first between egg or chicken?",
in the evolution of life, we always encounter
a question of "Which is first between RNA, DNA or protein?"
Or "how do they co-evolute?"

In such real biological systems,
a theory of co-evolution of biopolymers is necessary.
However, we have not yet been able to tame
such a tough issue in the problem.

So, as a first step towards such a direction,
I would like to postulate a generalization of
Onsager's theory of irreducible processes-like approach
to the theory of evolution/co-evolution.
When we consider co-evolutionary processes of
two species such as protein(denoted 1) and DNA(denoted 2),
we may represent the evolutionary process as
$T¥frac{dS(t)}{dt} = {¥cal L} = J_{1}X_{1} + J_{2}X_{2}$,
where T is the evolutionary temperature,
J_{k} the evolutionary fluxes and X_{k} the evolutionary forces.
We now have
$J_{1} = L_{11}X_{1} + L_{12}X_{2}$,
$J_{2} = L_{21}X_{1} + L_{22}X_{2}$,
respectively.
Here, L_{11} means the self-evolution of species 1
and L_{22} the self-evolution of species 2,
while
L_{12} means the co-evolution(mutual evolution) of species 1 induces by
the evolution of species 2, and
L_{21} means the co-evolution(mutual evolution) of species 2 induces by
the evolution of species 1, respectively.
The Onsager's reciprocal relation $L_{12} = L_{21} $ensures that
the reciprocity in the co-evolutionary processes.
This may suggest us a way to solve the "egg or chicken" problem.
This type of theory can be generalized to the co-evolutionary processes of
multi-species as well.

Finally, I would like to give some comments on the relationship between
the Aita-Husimi's interpretation, the Kauffman's point of view
of generalized thermodynamics¥cite{Kauffman} and the R. Backminster Fuller's

synergetics philosophy¥cite{Fuller,Iguchi}.
They are essentially all the same.
¥end{abstract}

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Role of membrane fluctuation in lamellipodial protrusion

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Cell locomotion is a complex process where protrusion and adhesion at the cell front is coordinated with contraction of cell body and de-adhesion at the cell rear. Protrusion of cell edge (lamellipodium) is an important step in the forward motion of the cell. The mechanism of lamellipodial protrusion is a theme of many experimental and theoretical studies. Since lamellipodium contains a network composed of branched and cross-linked actin filaments, the plus ends (sites of addition of actin monomers) of which are directed toward the cell front, it has been anticipated that elongating actin filaments push out the cell membrane. Fluctuation of the cell membrane and/or the branched portion of actin filament have been proposed (Peshkin et al., 1993; Mogliner et al., 1996) to allow insertion of actin monomer between the plus end and the cell membrane, but the evidence of fluctuation during the protrusion has not been presented.

We have measured the motion of cell edge by pushing a 1 mm bead against the cell edge with optical tweezers (spring constant ranging 0.008-0.087 pN/nm) and analyzed the bead position with 33 ms time resolution and 10 nm position accuracy. The velocity of forward motion of the probe bead tended to decrease with trap force, but the relation was not clear. However, the velocity decreased from 180 to 20 nm/s with increase in the spring constant of the trap suggesting that cell edge is highly compliant. Power spectra of the fluctuation of the bead during the forward motion showed that in the frequency range 0.96-7.6 Hz the spectra deviated upward from that of the bead not contacted with the cell edge. The upward deviation was most prominent at the trap spring constant of 0.007 pN/nm. We suggest that the bead reported the fluctuation of the membrane, which is characterized with the few Hz motion.

Attrctor states of Boolean dynamics in complex networks

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We study the intrinsic properties of attractors in Boolean dynamics in complex networks, comparing with that of random Kauffman networks. We have numerically investigated frozen and relevant nodes for each attractor, in the relatively small network ($N ¥sim 200$). Furthermore, we investigate the probability to be remained in the original attractor by the inversion of single node state. We have found that in complex networks with fluctuation of in-degree number the attractors are more robust to state flip than that of random Kauffman networks. Furthermore, it is found that increasing of the average in-degree $<k>$ enhances the robustness to the flip.

A model for intermittent animal foraging behavior.

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Waseda University 21COE research student

Abstract.
Scale-invariant temporal and spatial patterns have been observed in a wide variety of animal behaviors, for example, the movement activity of Drosophila, the flight-time of wandering albatross, behavioral patterns of nesting gilts, and so on. They have been argued in terms of Levy flights which is an optimal strategy for random foragers in some cases. However, the origins of such scale-invariant behaviors are elusive. We consider that animal behaviors are the result from the interaction between the individual and their environment. In the present session, we propose a model for an animal foraging behavior, where the movement is assumed to be affected by two factors with different spatial periods. One of factors corresponds to a food distribution, the other correspond to another factor. Although the equation of motion is 1-D quasi-periodic gradient system, the model exhibits intermittent dynamics near feeding points. The main result is that probability density for the residenc
e time near feeding points becomes an asymptotic power-law distribution. Moreover, their scaling exponent is exactly -2, which characterizes the behavioral patterns of a wide variety of animals.

J. B. S. HALDANE'S INDIAN PERIOD*

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J. B. S. Haldane was among the most erudite and prescient biologists of the 20th century. Together with R. A. Fisher, S. Wright, and S. S. Chetverikov, he is acknowledged as one of the founders of the modern evolutionary synthesis, especially that part of it called "Population Genetics"- the unification of Darwinian ideas with the principles of genetics. The credit for developing human genetics as a seperate discipline goes largely to him. It would be no exaggeration to call him the father of biochemical genetics.

Born in an aristocratic family, Haldane preferred to spend his last years in India along with his wife, Helen Spurway (a distinguished student of genetics and behaviour in her own right). Ultimately they took up Indian citizenship. Haldane was attracted towards India since his childhood. This was reinforced during World War I, when Haldane had to spend many months in India as part of his war service. Even before he moved to India, Haldane possessed scholarly knowledge about Indian epics, Indian religions and the ancient Hindu scriptures. This is evident in a paper published by him (much later) in *Sankhya*, the Indian journal of statistics, entitled "The Syadvada system of Predication", which dealt with the many-valued system of logic of the Jainas. His letters were often punctuated with quotes from Vedas and Upanishads. A great admirer of Mahatma Gandhi, Haldane took to wearing Indian dress and having vegetarian diet and practicing non-violence in his life and research work.

Haldane exerted a great influence on the development of science, especially genetics, in India. He took a keen interest in establishing research work in genetics and sent the then prime minister, Jawaharlal Nehru, a list of suggestions and offering his help. This was due to the fact that Haldane had not only been impressed by the rich natural resources but also by the young, enthusiastic and brilliant scholars that he got to know after coming to India. An exclusive research laboratory was built in Calcutta due to efforts put in by Haldane and his closeness to Pandit Nehru. After he moved to India, Haldane contributed his expertise and intellectual versatility for the improvement of the quality of science education at different levels by travelling all over India as a part of a University Grants Commission team. The very presence of Haldane in India generated curiosity and attracted many well known scientists from abroad to visit him. Haldane too made huge efforts to bring scientists from abroad to visit and interact with the young scientists and scholars in India. Thanks to the unique atmosphere so created, he motivated and inspired many young scholars to pursue research work in India. Haldane was known to be a superb popularizer of science. His many books, scientific papers, lectures,

broadcasts and regular articles in the daily news papers made him one of the best known scientists in India.

Haldane was a great ambassador for India at international conferences. Resplendent in Indian dress, he projected India as a country with great potential for research work in population genetics. He insisted that his junior colleagues, who had a paper to present, should attend a conference even if he had to personally finance them. Many research programmes too were partially or fully financed by Haldane. Important among them was the project, in the coastal malarial areas of Andhra Pradesh in India, which was based on his landmark work in the area of Disease and Evolution. This work was carried out by by Marcello Siniscalco and assisted by Meera Khan and Ajit Ray (junior colleagues of Haldane).

Haldane's Indian period is also memorable because of the famous dispute between Haldane and Ernst Mayr, a major contributor to the way we understand evolution today. This resulted in what was perhaps the last scientific paper by Haldane, *A Defense of Bean Bag Genetics*(1964). This was in response to Ernst Mayr's comments at the 1959 Cold Spring Harbor Symposium on the work of Haldane, R. A. Fisher and S. Wright. Mayr had wondered whether population genetics (as it then was) was useful at all for understanding evolution. Haldane's response came just before his death in 1964. It contained a vigorous defence, not just of population genetics, but also of the usefulness of mathematical modelling in biology. Mayr and Haldane agreed over the broad explanatory framework for understanding evolution but differed over the basic entities necessary to underpin that framework. While the difference of opinion persisted - and was not glossed over -, the two protagonists continued to remain good friends. In a touching tribute, Ernst Mayr wrote to me just before he passed away saying "Haldane was a most brilliant scientist with original ideas. Did pioneering work in genetics. Indian scientists can learn a lot from him".

*** Abstract of poster to be presented at the Nishinomiya-Yukawa symposium, Kyoto, 15-20 October 2007. Work supported by the award of a research grant by the Indian National Science Academy, New Delhi, India.**

Self-organization of small-world scale-free functional neural networks 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 properties. The collective dynamical response and the functional neural network structure depend on each other due to synaptic plasticity, 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 oscillators 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-low decays. The STDP network shows as fast and strong as or faster and stronger synchronization than random networks depending on the external stimulus. 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.

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An Optimization Principle for Determining Movement Duration

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Movement duration is an integral component of motor control, but nearly all extant optimization models of motor planning prefix duration instead of explaining it (e.g., Flash and Hogan, 1985; Uno, Kawato and Suzuki, 1989; Harris and Wolpert, 1998). Here I propose a new optimization principle that predicts movement duration. The model assumes that the brain attempts to minimize movement duration under the constraint of meeting an accuracy criterion. The criterion is task and context dependent but is fixed for a given task and context. The model determines a unique duration as a trade-off between speed (time optimality) and accuracy (acceptable endpoint scatter). I analyzed the model for a linear motor plant and obtained a closed-form equation for determining movement duration. By solving the equation numerically with specific plant parameters for the eye and arm, I found that the model can reproduce saccade duration as a function of amplitude (the main sequence, Figure 1), and arm-movement duration as a function of the ratio of target distance to size (Fitts' law, Figure 2). In addition, it explains the dependency of peak saccadic speed on amplitude (Figure 3) and the dependency of saccadic duration on initial eye position (Figure 4). Furthermore, for arm movements, the model predicts a scaling relationship between peak velocity and distance and a reduction in movement duration with a moderate increase in viscosity. Finally, for a linear plant, the model predicts a neural control signal identical to that of the minimum-variance model set to the same movement duration. This control signal is a smooth function of time (except at the endpoint), in contrast to the discontinuous bang-bang control found in the time-optimal control literature. I suggest that one aspect of movement planning, as revealed by movement duration, may be to assign an endpoint accuracy criterion for a given task and context.

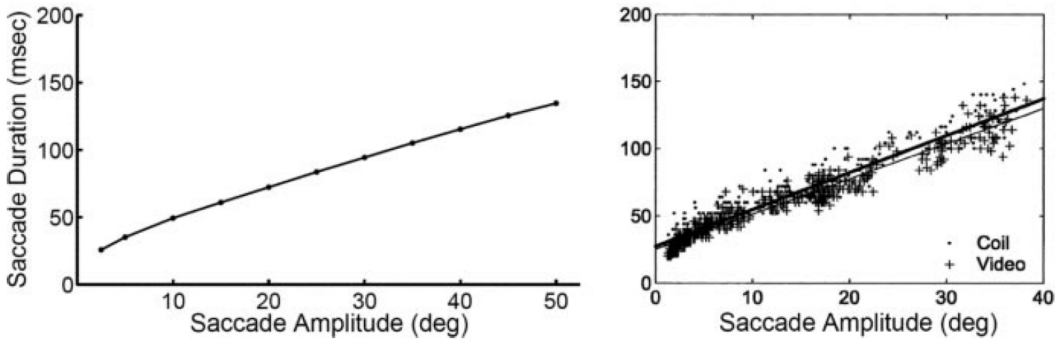

Figure 1: Saccadic duration that is predicted by the model (Left) and that was measured in experiment (Right).

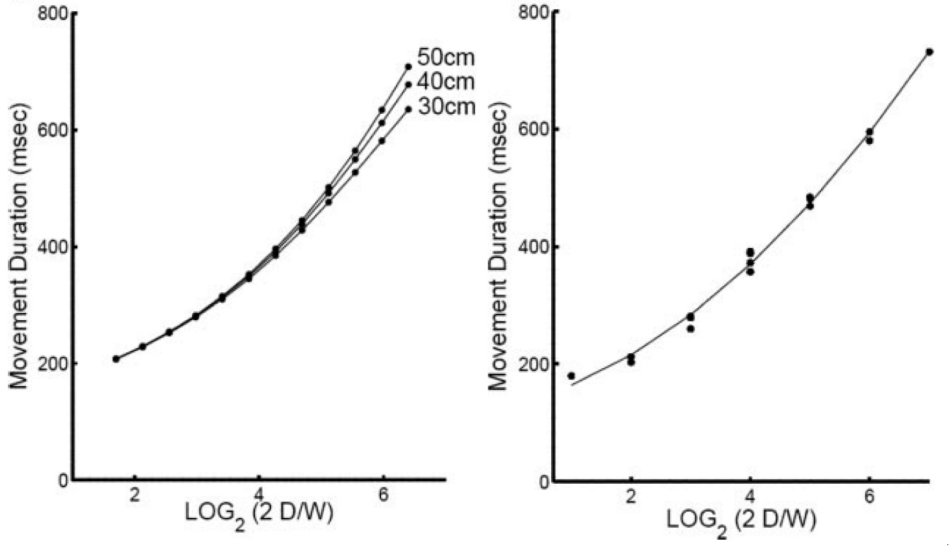

Figure 2: Hand reaching duration as a function of D (movement distance) and W (target width) predicted by the model (Left) and observed in experiment (Right).

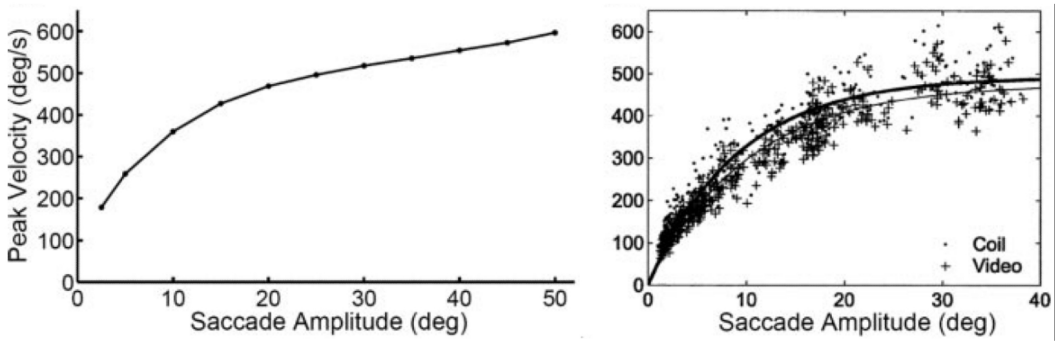

Figure 3: Peak velocity in saccadic eye movement as a function of amplitude, predicted by the model (Left) and measured in experiment (Right).

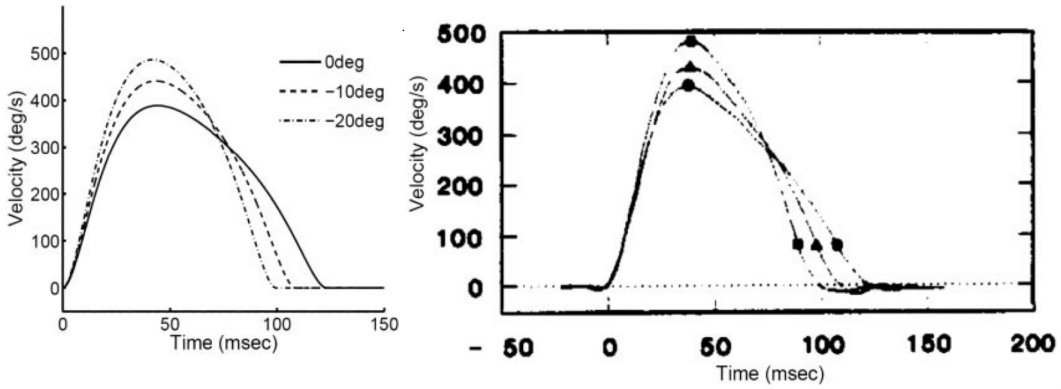

Figure 4: Initial position dependence of eye movement duration predicted by the model (Left) and observed in experiment (Right).

Detection of Thinking Activities in Frontal Lobe by MEG

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We measured neuromagnetic brain activities while normal subjects were presented with a series of thinking tasks intended to induce (a) the natural thought like image thinking or (b) the language thinking. Changes in the spontaneous brain activities were assessed by using a while-cortex-type SQUID neuromagnetometer. Our findings revealed transition of the active portions of the brain during a special task: non-thinking. We analyzed brain magnetic fields spread over head generated from frontal lobe at various frequency range:α(8-12Hz),β(12-24Hz),γ(24-60Hz),θ(4-8Hz) with an equivalent dipole current estimation method. According to the data we obtained, αwave from the left hemisphere observes more prominent than β,θ and γwaves, which is distinctive feature of brain activity with non-thinking task. In addition, α wave was prominently detected on every task in the left hemisphere. It was also the most promin ent under the non-thinking task.

Constructing an Interdisciplinary Context for Definition of Life.

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One of the main problems in understanding life is that that life cannot be defined as a self-evident phenomenon. Instead, definitions of life inevitably depend on the context: social, ethical, theological, and scientific. Even in a purely scientific context, different scientific disciplines and approaches provide a variety of criteria related to life. My intention is to define life in an interdisciplinary context, where the class of living systems can be presented as a particular case in series of systems: physical, chemical, prebiotic, biotic, ecological, social, cognitive, etc. related by a universal principle. To this end, the first step in establishing general criteria for life is to define the essential features of life processes. The very functional principle of living beings is feedback circularity embedded on different levels of organization: molecular, genetic, cellular, neural, behavioural, mental, and social. Understanding that the degree of system's wholene

ss, i.e. degree of feedback net integration can serve as a primary parameter, we can in principle construct an interdisciplinary context in which different systems including living beings can be analyzed, defined and compared.

Insights into microRNA guided endogenous and exogenous gene regulations

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The completion of genomic sequencing within various species had provided an overview of genes and messenger RNAs (mRNAs) encoding various types of proteins. Meanwhile, existence of non-coding RNA (ncRNA) genes, diverse non-messenger RNA molecules with specific structures and different functions, was proposed. Increasing knowledge about enzymatic and regulatory functions of these ncRNAs revolutionized our understanding of RNAs as an intermediate in central dogma. microRNAs (miRNAs) are small (approximately 22 nt long) ncRNAs, which have been identified as translational regulator of complementary mRNAs. Despite several hundreds of miRNAs are contained in a broad range of metazoans and their importance as control of development and physiology are indicated, abundance of their target mRNAs still remain to be revealed.

Here, we performed combined computational and experimental approach aiming to understand the regulatory function of miRNAs. We developed computational methods to predict the interactions between miRNAs and their target mRNAs. These methods were based on particular hybridization pattern of miRNA and mRNA, phylogenetic conservation of miRNA target sites and specificity of the interaction between miRNA and mRNA. Using these methods, we performed genome-wide prediction of miRNA target genes using Caenorhabditis elegans and Drosophila melanogaster. Moreover, the predicted candidates were verified experimentally using reporter gene assay method. The result of these analyses suggested that many developmental genes are likely to be regulated by combination of several miRNA target sites. Also, the existence of feedback control within miRNA translational regulation pathway was revealed. While most of the miRNAs are known to regulate endogenous mRNAs as the cases mentioned above, we su

ggest that number of human miRNAs target not only endogenous but exogenous genes, in means of the viral infection. We computationally extracted human miRNA target sites within hundreds of human and

infecting virus genomes, and proposed that the miRNAs may mediate antiviral defense extensively in human. From these different analyses using various species, we would like to discuss the biological significance of gene regulation by miRNAs from the comprehensive point of view.

Concept of metabolic networks as atom networks

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Viewing the entire metabolism as a network gave us a theoretical framework to investigate the organization of the entire metabolism, stimulating studies on global topological nature of metabolic networks. In most of such studies, metabolites are assumed as nodes, where topological analysis of metabolic networks has been conducted based on binary relationships of metabolites via enzymatic reactions without care of stoichiometry of reactions except for approaches using stoichiometric matrices. On the other hand, instead of metabolites, atoms can be assumed as nodes, where metabolic networks are defined by inter-metabolite atom-level connectivity through enzymatic reactions and by intra-metabolite atom-level connectivity through chemical bonds. Inter-metabolite atom-level connectivity is the basis of stoichiometry. Thus, in principle, stoichiometry of reactions is expressed through inter-metabolite atom-level connectivity in atom network structure. Concept of metabolic networks as networks of atoms provides an idea, co-evolution of inter- and intra-metabolite atom-level connectivities corresponding to co-emergences of new reactions and compounds as their products. Further, assuming that each atom is a person leads us to notice analogy of metabolic networks to social networks. This poster introduces the concept of metabolic networks as atom networks and discusses potential of the concept.

Synchronization of a Neuronal Oscillator Network with Multiple Connections

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Abstract:
The human brain is a dynamical system containing an extraordinarily large number of units of neurons with even larger number of interconnections among them. Synchronized rhythms in various frequency ranges over cortical areas is one of the intriguing issues in neuroscience. Especially, several EEG analyses have revealed that rhythms in the gamma range and the beta range are associated with information processings such as perception and memory and that the rhythms occur in a hierachical way along the direction of the information flow over the involved cortical areas. That is, it is seen that the frequency range of the synchronized rhythms is correlated with the spatial range of synchrony over the cortical areas. In this work we perform dynamical systems analysis on a model for the hippocampal CA1 area. The model is analyzed to reveal the distinctive dynamical structure of different rhythms and their stability regimes. Roles of the synapses of different nature in multiply connected neuronal oscillators are identified in a systematic way. It is also shown that multiple connections with distributed conduction time delays can be a mechanism for an efficient synchronization of an ensemble of spatially distributed neuronal oscillators.