1P-288 真性粘菌変形体の細胞運動における履歴依存性

Cell motility of *Physarum* plasmodium depends on its locomotive history

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Physarum plasmodium is a very large, unicellular and multinuclear organism, and its computational ability is attracting a lot of attention in the field of nature-inspired computing. Using the organism, various kinds of computation such as maze-solving, calculation for graph theoretical problems, construction of logical gate, robot control and neuron-computing, have been implemented. To further investigate the potential usage of the organism in computation, we have also tried to implement the computation for graph theoretical problems using the plasmodium. In other words, we let the plasmodium form a tubular network as a solution for the problems. In these experiments, we found that the morphology of a local part of the plasmodium network tends to be homologous with the other parts of the network. Namely, the property of the local network was spatially transferred to the other part of the network. Then we tested whether such an effect is also present temporally. In the experiment, we provided narrow paths with various shapes, which are several centimeters in length, on agar plates. The plasmodium traveled along with the path, and then the organism entered a plane without any obstacle. We observed the motility of the plasmodium on the plane, and found that the motility depends on the shape of the path. This data indicates that the motility of the plasmodium is dependent on its locomotive history, and implies the presence of "memory" in the organism.

1P-289 たんぱく質間相互作用ネットワークの進化における非同類結合性の生成について

The emergence of a disassortative structure in the evolution of protein-protein interaction networks

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Protein-protein interaction networks (PIN) exhibit several interesting properties, especially a disassortative structure. In a network with disassortative structure, links between hubs and low-degree nodes are favored. To uncover the evolutionary mechanism shaping the structure of PINs, several network growth models have been proposed. Recently, we proposed the non-uniform heterodimerization (NHD) model, in which a link is preferentially attached between duplicated nodes when they share many common neighbors [1]. Although the NHD model could reproduce various properties in PINs, this model could not reproduce a disassortative structure. To overcome this difficulty, we modified the NHD model by adding the process of preferential duplication of low-degree nodes. In this presentation, we showed that the modified model could successfully reproduce several properties, especially a disassortative structure in PINs. Moreover, by investigating the orthologous relationship among genes of 19 Ascomycota fungi, we showed that many genes are orthologous to a gene encoding a low-degree protein. These results suggest that the probability that a gene is duplicated could not be uniform and that the non-uniform duplication could shape a disassortative structure in the evolution of PINs.

References:

[1] Hase T, Niimura Y, Kaminuma T, and Tanaka H (2008) Non-uniform survival rate of heterodimerization links in the evolution of the yeast protein-protein interaction network. PLoS ONE e1667

1P-290 信号伝播履歴に依存して伸長・縮退する樹状場上の信号伝播特性
Signal propagation on deforming branching paths correlated with a history of signal propagation.

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In living systems, the formation of branching structures in open systems is often observed. For example, branching patterns can be observed in neurons, protoplasmic streaming tubes of slime molds, trees, bacterial colonies, and so on. In these branching structures, propagation of physical states (e.g., action potentials in neurons) or transportation of substances (e.g., plasma in slime mold tubes) is observed, particularly in the structures of living organisms. These propagation or transportation can be considered as "signal propagation". In these phenomena branching paths often deform depends on a history of signal propagation.

In this study I adopt the system that path formation dynamics correlates with signal propagation for the first step to know signal processing function with characteristic geometrical paths. I studied the geometrical property of path deformation and the dynamics of signal propagation with discretized reaction-diffusion model. I found the shape of branching path become distorted by autonomous generation of spiral of the signal. I will present the correlation between path deformation and signal propagation.

1P-291 拡散係数の異なる2状態を遷移する分子の拡散過程の解析

A method for analyzing diffusion process of single molecules switching between two states with different mobility

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Signaling molecules on cell membranes can operate their functions under influence of environmental changes arisen from heterogeneities in membranes. According to recent technological progresses in single-molecule imaging and single-particle tracking, it is now possible to follow whole trajectories of the molecules moved during association with membrane in living cells. We have noticed the possibility that the diffusion mobility and membrane association are variable temporally for the individual molecules. However, there are no theoretical descriptions of the diffusion process of such molecules and no methodology to analyze experimental data from that viewpoint. We propose a method to deduce kinetics of both diffusion and dissociation from trajectories of single molecules. In the method, we assumed the simplest 6 schemes: a molecule with unique diffusion coefficient (D), a mixture of molecules in two states with different D , a molecule switching between two states with different D , and more 3 cases made by further classification of above 3 cases regarding whether the molecule exhibits dissociation from membrane or not. Using trajectories made by numerical simulation, these schemes were shown to be distinguishable by referring the lifetime on membrane, and the probability density function and autocorrelation function of displacements. At last, an application to experimental data, including a limit of this method, will be discussed. By this method, the heterogeneities in membranes and signaling events might become visible.

1P-292 アメーバ状細胞の運動戦略の数理的解析

A theoretical study of strategies for amoeboid locomotion

Shin I. Nishimura and Masaki Sasai

Eukaryotic cells such as cellular slime molds and other animal cells are thought to share unified mechanisms for locomotion. In this work, emergence of "intelligent" behaviors of cells is discussed by developing a simple computational model of locomotion. The model describes changes in cell shape on the two-dimensional plane by considering a cell membrane, actin filaments embedded in the membrane, and an intracellular control factor that suppresses actin polymerization. We assume that the reception of external chemical signal suppresses the activity of control factor, leading to chemotaxis of a cell toward the source of the chemical signal. We consider that there exist obstacles intercepting a cell on its way to the source of signal. When signal permeates through some obstacles to attract the cell (i.e. traps), the simulated cell falls into a trap at first but it suddenly escapes from the trap to find a way to get it around. The cell finds this detour because the distribution pattern of control factor is flushed while the cell is trapped and the occasional fluctuation in cortical factor amplifies locomotion against the gradient of the external signal. In this way, the feedback loop between cell movement and control factor is a key mechanism of the emergent behavior to find a detour. Cognitive locomotion of the model eukaryotic cells is the result of the fluctuating dynamics in which the interaction with the environment and the internal chemical reactions are coupled through the feedback between cell movement and control factor.

1P-293 揺らぐ環境下でのロバストネスの進化の統計力学的研究

A statistical mechanical study of evolution of robustness under noisy environment
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In biological systems, expression dynamics to shape a fitted phenotype for function has evolved through mutations to genes, as observed in the evolution of funnel landscape in protein. We study this evolutionary process with a statistical-mechanical model of interacting spins, where the fitted phenotype is represented by a configuration of a given set of "target spins" and interaction matrix J among spins is genotype evolving over generations. The expression dynamics is given by stochastic process with temperature T_s to decrease energy for a given set of J . The evolution of J is also stochastic with temperature T_j , following mutation in J and selection based on a fitness given by configurations of the target spins. Below a certain temperature T_s^{c2} , the highly adapted J evolves, whereas another phase transition characterized by frustration occurs at $T_s^{c1} < T_s^{c2}$. At temperature lower than T_s^{c1} , the Hamiltonian exhibits a spin-glass like phase, where the dynamics requires long time steps to produce the fitted phenotype, and the fitness often decreases drastically by single mutation. In contrast, in the intermediate temperature phase between T_s^{c1} and T_s^{c2} , the evolved genotypes, that have no frustration around the target spins (we call "local Mattis state"), give a funnel-like rapid expression dynamics and are robust to mutation. These results imply that evolution under thermal noise beyond a certain level leads to funnel dynamics and mutational robustness. We will explain its mechanism with the statistical-mechanical method.

1P-294 2次元弾性バネネットワークのパターン形成とダイナミクス

Pattern formation and dynamics in the two-dimensional elastic spring network model

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We present a new two-dimensional elastic network model that shows various patterns and dynamics. We set up a certain threshold for the length of each spring, beyond which the interaction between elements is switched off, so that the elastic spring connecting the elements is broken. As a result, many kinds of dynamical patterns are realized, and finally the system approaches the stationary states,

which depend on the values of several parameters such as the elastic constant of the spring and the size of the system. In the stationary states, only a part of the springs remain unbroken. As an application of this model, we consider the dynamics of the cross-section of striated muscle by arranging the elements in a hexagonal lattice. In the muscle fiber, it is well known that the thick (myosin) and thin (actin) filaments are arranged in a hexagonal lattice. In this study we report the dynamic behavior of this model including the avalanche-like behavior in the spring fracture pattern. We apply this model to the changes in the Z-line structure in the striated muscle.

1P-295 立体構造特異性の情報を得る：数値モデルの提案

Theoretical model to deduce specificity on the higher-order structure of genomic DNA from the experimental pattern of enzymic cleavage

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It is known that ladder pattern often appears in images of gel electrophoresis when DNA is depicted from apoptotic cells[1]. The DNA cleavage is caused by enzymes such as DNase γ , and the cleavage side is linker portion between neighboring nucleosomes. Thus, the pattern of the enzymic cleavage from giant genomic DNA is expected to reflect specificity on its original higher order structure. In the present presentation, we propose a simple model to interpret the cleavage pattern of DNA. We assume DNA to be a chain composed of unit length of number of segments, which corresponds to the DNA-length wrapped around a mono-nucleosome. Firstly, by adapting random stochastic assumption, we derived the expected pattern, showing Poisson distribution. From this mode, time-course on the cleavage pattern development is derived under the condition purely stochastic mechanism. Thus, the deviation of the experimental ladder pattern from such simple model implies the incorporation of certain non-stochastic scenario. Such deviation is discussed in relation to the steric hindrance owe to specific higher order structure in giant genomic DNA molecules existing in living cells.[1] R. Mizuta et. al., BBRC, 345 (2006) 560.

1P-296 複雑な生態系理解へ向けた細胞集団の動的適応モデル

A dynamic adaptive model of cell population for the emergence of complex ecosystem

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Many species coexist in ecosystem, in which mutual symbiotic relationships among species are generally observed. However, the mechanism for the emergence of such complex ecosystem with many species and symbiotic relationships still remains unclear. In this study, we sought development a model of cell population to investigate the emergence of such complex ecosystem. Recently, a model of cellular adaptation driven by fluctuation was proposed, in which cells whose gene expressions fluctuate stochastically can select an adaptive cellular state with high growth rate by the fluctuation [1,2]. We expanded this model to describe a dynamics of cell population to demonstrate an adaptive dynamics at cell population level. In this model, each cell has chemical reaction network consisting of plural chemical components and the cells interact with each other through the environment. We simulated this cell population model under a condition that each cell's internal state fluctuates. Based on the simulations, we found that each cell changes their internal state adaptively by the fluctuation and as the result of the adaptation at each cell level, a mutual beneficial relationship among cells with different internal states generally emerges. These results provide a new viewpoint to understand the emergence of complex ecosystem with many species and symbiotic relationship. Evolutionary dynamics in the cell population model will also be discussed.

[1] Kashiwagi et al., PLoS One 1(1), e49, 2006

[2] Furusawa and Kaneko, PLoS Comp. Biol. 4(1), e3, 2008

1P-297 多段階適応反応系が導く多様な応答過程と環境依存性応答

Relation between multi adaptive reaction system and environment-dependent response

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Microorganisms change behaviors or functions according to their environment. In the case of thermotaxis of *Paramecium*, they change the tumbling frequency immediately after the change of temperature, and then relax to and stay at a certain level in a few minutes and return to the original level after hours. In the case of yeast, expressions of some genes increase rapidly at first and then reduce to a certain level when the temperature is increased, while it only relaxes monotonically and more quickly to the original level when the temperature is decreased. Another example is seen in thermotaxis by *C. elegans*; if they were cultured with nutrition under a growth temperature, they move toward the direction of the temperature. On the other hand, if they were cultured without nutrition, they avoid the original temperature. In general, microorganisms regulate the intracellular reactions to show "homeostasis" when the external condition is changed, whereas they also show history dependent response following some environmental change. This implies that in the intracellular reaction system, some set of state variables show environmental independence and some show environmental dependence. These variables are not separated but mutually interacting, which allows for flexible behaviors of microorganisms from homeostasis to history-dependence. We study a variety of adaptation process by

using a dynamical system model and show how these two behaviors, adaptation and environment-dependent response, emerge and mutually influence with each other.

1P-298 二重リン酸化 ERK の細胞サイズ依存的な平衡状態の安定性評価

Cell size dependency of the bistability in the dual-phosphorylation state of ERK

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ERK, the mitogen-activated protein kinase (MAPK) in Raf-MEK-ERK cascade, has two phosphorylate sites which are phosphorylated by MEK (MAPKK) and dephosphorylated by MKP. Bistability and hysteresis between the dual-phosphorylation state and the dephosphorylation state of ERK has been predicted assuming infinite volume of cells (Markevich et al., JCB: 353, 2004). We evaluated the cell size dependency of the bistability in ERK phosphorylation in stochastic simulations using the Gillespie method. Bistability was observed at the same region of reaction parameters predicted in the analytical calculations with certain stochastic transitions between two stable (dual-phosphorylation and dephosphorylation) states. The transition rate depended on the cell size: When cell size was reduced to $0.17 \mu\text{m}^3$, which is smaller than general mammalian cells by a factor of more than 100, life time of the stable states were about 3 hours. When cell size was $1.7 \mu\text{m}^3$, the duration increased to over 300 hours. Since ERK activation sustained for 12 hours are known to be sufficient for stimulate cell proliferation, our result suggests that bistability of ERK double phosphorylation is effective for stabilize cell response in real size of cells. We are planning to confirm the stability of two steady states experimentally by reconstituting the reactions in *E. coli* cells.

1P-299 多重分子修飾による記憶、ヒステリシス、振動とそのシアノバクテリアの概日リズムへの応用

Memory, hysteresis and oscillation induced by multiple covalent modifications and its application to circadian rhythm of Cyanobacteria

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No transcription-translation feedback system of circadian clock by KaiC protein's phosphorylation is very interesting and also significant as a kind of core cycle of the circadian rhythm in Cyanobacteria. In order to understand the oscillation phenomena, we pay attention to a function of memory in a cell level. A standard structure of such binary digit of memory is presented by use of multiple covalent modifications in this presentation. A key idea is bistability of covalent modification states which creates hysteresis and digitally switching mechanism between them. By use of this kind of memory, we see the circadian oscillation be realized. In fact, by deterministic simulations as well as by stochastic simulation, it is shown that the system obtains stable circadian oscillations, and shown that multiplicity of modification sites reinforces the stability of memory in several senses. Moreover, it is reported that this model explains well several molecular biologically experimental facts about period's change by use of mutants of Kai proteins in the circadian rhythm of Cyanobacteria.

1P-300 真正粘菌変形体が形成するパターンの時系列解析

Quantitative analysis on growing pattern in *Physarum plasmodium*

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Living organisms can adapt to environment. This results from, e.g., information processing by brains and complicated interaction among cells. Surprisingly, plasmodia of true slime mold *Physarum polycephalum*, which have neither any nervous system nor any differentiation structure, can adapt to the environments as well as higher animals.

The plasmodium is an amoeboid multinucleated unicellular organism and forms a network of tubular structures which transport intracellular substances by protoplasmic streaming. It was reported that the growth patterns of plasmodia show rich ones depending on environments, in which one of characteristic patterns is a round shaped thin sheet in attractant environments and another is a dendritic one in repellent environments [1].

In this study, we observed time course of growth patterns under various environmental conditions by changing concentration of agar or chemicals in culture medium.

To analyze the characteristics of the patterns quantitatively, we measured area size (S), perimeter (L), complexity ($E=L^2/S$), and fractal dimension. The result shows that these quantities depend on the concentration of agar or chemicals in culture medium.

[1] A. Takamatsu (2007) Morphology and Biological Function -Spatio-temporal Structure in an Oscillating Amoeboid Unicellular Organism of True Slime Mold-Hyomen Kagaku, 28, 653-658 (in Japanese).

1P-301 1次元形状に制御した真正粘菌変形体におけるアロメトリックスケール則

Allometric scaling law in *Physarum plasmodium* controlled into one dimensional shape.

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It is known that the relation between organism's body mass M and metabolic rates B shows allometric scaling law, $B=aM^a$, where a is a constant that is characteristic