homogeneous due to smaller obstruction effects from the molecular crowding. Accordingly there is a difference in the diffusivity, one with normal diffusivity and the other with anomalous diffusivity. We would like to discuss the physiological implications of this effect using Lattice Monte Carlo simulation and theoretical analysis based on the Fractal reaction theory.

2PT212 Counting statistics for genetic switches

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The number of switching between activate and inactivate states in a genetic switch is investigated. Counting statistics is a scheme to study the number of specific transitions in a stochastic system. While the counting statistics has been studied a lot for a stochastic system with a finite number of states, the genetic switches are formulated as a system with an infinite number of states. Hence, it is needed to check the applicability of the counting statistics for the genetic switches. Actually, it immediately becomes clear that a straightforward application of the scheme derives intractable non-closed equations. We here use an effective interaction approximation, and it is shown that the switching problem can be treated as a simple two-state model approximately, which indicates that the switching obeys non-Poisson statistics.

2PT213 分化多能性を持つ細胞の分化初期段階における状態遷移

Transitions of the cell state in the early stage of differentiation from the pluripotent cell

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Embryonic stem (ES) cells have the ability to differentiate into all three germ layers, mesoderm, endoderm and ectoderm. This capability of ES cells is called pluripotency, and it has been shown that Sox2, Oct4, and Nanog (SON) are the important genes for maintaining pluripotency. We built a model of the network of core genes including SON, and performed the stochastic simulation of the early stage of differentiation starting from the pluripotent ES cells. We take into account three types of processes to regulate the gene expression in the model; binding/unbinding of transcription factors (TF), formation of the transcription apparatus (TA), and the modification of epigenetic histone code. The simulated population of pluripotent cells becomes phenotypically heterogeneous showing the different patterns of gene activity in individual cells when the rate of forming TA is slower than the rate of change in the copy number of TF. We will discuss the diversity of patterns of gene activity arising from the difference in the time scale among the processes to regulate the gene expression.

2PT214 シロイヌナズナにおける植物ホルモンの制御ネットワーク解析

Regulation network analysis of plant hormones in *Arabidopsis thaliana*

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The plant hormone is low-molecular-weight chemical that is produced in the plant body and affects the plant activity in minute amounts. The plant produces several kinds of plant hormones and hormone-like substances which play the roles of the signaling molecules for gene expressions related to the growth, stress response, etc... In general, each of these hormones and hormone-like substances does not work independently but works cooperatively or competitively with each other, and the production of them are mutually regulated.

In this study, we extrapolate the regulation network among several plant hormones and hormone-like substances by the statistical analysis of the database of gene expression levels of microarray. We analyze the data set released in the Internet produced by "At Gen Express" project through the statistical methods such as Gaussian graphical modeling. Based on this analysis, we also construct the dynamical system model of the plant hormone regulation network of *Arabidopsis thaliana* to unveil physiological mechanism of the stress response and adaptation against the environmental fluctuation.

2PT215 Toward simulation of epidermal growth factor (EGF) pathway at the molecular resolution for K computer

Kazunari Iwamoto, Kazunari Kaizu, Koichi Takahashi (*Laboratory for Biochemical Simulation, QBiC, RIKEN*)

Cellular environment consists of the localization of various proteins, clustering of membrane molecules and cytoskeleton. Recently, the simulation at the

molecular resolution indicated that characteristic of molecular network such as bistable and ultrasensitivity under such environment was different from prediction by conventional non-space simulation, which was supported by in vitro experiments. Therefore, the simulation at the molecular resolution is useful to understand the characteristic of cellular signaling pathways. In this study, we will implement the simulation at the molecular resolution of epidermal growth factor (EGF) signaling pathway which regulated cell proliferation and differentiation, and elucidate the characteristic.

The simulation software at the molecular resolution, Spatiocyte, was developed by Arjunan et al. (2010). However, it was difficult to execute the cellular-scale simulation at the molecular resolution using Spatiocyte. Thus, we are developing new software for supercomputer, especially K computer, based on the algorithm of Spatiocyte. On the other hand, prototype model of EGF pathway was constructed and preliminary simulation at one hundredth scale of actual cell was implemented. The simulated results showed heterogeneity of ERK activation, which qualitatively agreed with observed data. Further analysis suggested that this heterogeneity resulted from the minority of specific species in EGF pathway.

2PT216 Emergence of a spatial structure with a minority molecule in a catalytic reaction network

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It is crucial to explain the emergence of primitive cellular structure from a set of chemical reactions to unveil the origin of life and to experimentally synthesize protocells. Recently, we considered a hypercycle with two mutually-catalyzing chemicals to demonstrate that the reproduction of a protocell with a growth-division process occurs when the replication and degradation speeds of one chemical are, respectively, slower than those of the other chemical, and molecules are crowded as a result of replication. In this presentation, we discuss the effects of the crowding molecule in details on the formation of primitive structure and also show results when we consider more complex reaction networks.

2PT217 Complex biological networks from the standpoint of the category theoretical duality

Taichi Haruna (*Kobe University*)

In general, there are two pictures on directed biological networks. The first picture is structural one: a network is a collection of passages on which something flows. In the second picture, networks are seen as more functional entities: a network is a collection of local workings of the biological system which the network represents glued together. In our previous work, we showed that these two pictures can be described as a category theoretical duality and two path notions corresponding to each picture emerge as a result of a category theoretical universality. Conventional directed path and a path notion called lateral path correspond to the first and second pictures, respectively. Here, to examine how this duality is embedded in real directed biological networks, we introduce lateral betweenness centrality and directed betweenness centrality of arcs based on the corresponding path notions. Both centralities measure importance of a given arc by counting the number of shortest paths in each path notion that pass through the arc. We found that there exists a significant trade-off relationship between them in real biological networks. We show that the trade-off relationship can emerge mainly from an optimization process maximizing efficiency with respect to lateral path by numerical simulations. We also found that the optimized networks have similar qualitative features with real biological networks in the view of standard network analysis.

2PT218 分子混み合いが小胞内反応系に与える影響の理論的考察

Theoretical study of influence of molecular crowding to enzyme reaction system in vesicle

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Several living systems contain a variety of macromolecules, and the large number of such molecules is confined in small internal spaces of cells or intracellular organs. Some recent studies pointed out that the reactions and diffusions of these molecules are extremely restricted by their excluded volume. In this study, we investigate the effects of the excluded volume of densely confined molecules, commonly called 'molecular crowding' effects, to the biochemical reaction. In order to consider this issue, we propose a coarse-