fluctuate around the long-time average, is needed.

In this study, we develop a statistical mechanical theory of the single cell reaction network using a large deviation theory of temporal fluctuations proposed by Fujisaka et al. [e.g., Prog.Theor.Phys.Suppl.99, 82 (1989)], which can describe the static and dynamic statistical features in the finite-length time domains within which the average deviates from the ensemble or the long-time average. We apply the theory to small networks of gene regulation and signal transduction. Noise effects and sensitivity in reactions will be discussed in terms of characteristic functions and power spectra.

1P318 質量顕微鏡法による一細胞示量変数計測に向けて Toward Single Cell Extensive Variable Analysis by Mass Microscopy

mitsutoshi setou, (Hamamatsu Univ.Sch.Med)

Recently, our high resolution imaging mass spectrometry -mass microscopy -technique made it possible to measure the amount of over 20,000 kinds of molecular species in over 10,000 individual cells. The individual molecular species is assumed to be one dimension in a state space. 10,000 cells are examined as the 10,000 vectors in this state space of 20,000 dimensions. Their distribution dynamics are examined by the function of ageing time. These points are not distributed randomly in state space because there is a condition on binding to keep the basic and common property of the cell. The same kind of cell is sure to come to be near. These points are not necessarily come to the completely same point because of the fluctuation and the individuality of the cell. Chaos theory predicts that these points migrate to the attractor neighborhood. The number of such attractors corresponds to the number of the types of cell biologically. When the cell chemically copy oneself, it keeps acquiring individuality by the stochastic error and the input from the environment. There is little chance to be made uniformly except the death of the cell. Therefore, I advocate that, after the development, the vectors around the attractor are likely to decentralize slowly but monotonously during the ageing. In this presentation, I will discuss this hypothesis and the preliminary real data in this measurement.

1P319 近接場光学プローブを備えた蛍光顕微鏡によるミトコンドリア周囲のpHの計測の試み An attempt to measure pH around mitochondria by using fluorescence microscopy with near field optical probe

Keisuke Haseda, Yongbo Li, Ryosuke Shinohara, Yasuaki Kanezashi, Takumi Onojima, Kentaro Iwami, Norihiro Umeda, Yoshihiro Ohta, (Tokyo Univ. of Agri. & Tech.,)

Mitochondria are organelles which produce most of intracellular ATP. For ATP production, they utilize proton motive force consisting of membrane potential and proton gradient. Although imaging of membrane potential in single mitochondria has revealed important characteristics of mitochondrial function, it has been impossible to observe proton gradient generated in single mitochondrion. Since proton gradient but not membrane potential is utilized for transfer of negatively charged molecules, it is important for us to observe proton gradient generated by single mitochondrion when we understand precise mechanism underlying the transfer of negatively charged molecules across the membrane.

To observe proton gradients around mitochondria, we used fluorescence microscopy with near field optical probe. Proton concentrations are measured with pH-sensitive fluorescent probe, SNARF. Mitochondria were prepared from porcine hearts and adsorbed on a glass-based dish. The decrease in pH around mitochondria was detected upon addition of respiration substrate to mitochondria, although it was not observed when mitochondria were absent. The detailed results will be reported and discussed.

1P320 ラマン分光による生体システムおよび生細胞の非侵襲的計測および分析 1YA1100 Raman spectroscopy for non-invasive microscopic analysis of biological systems and single live cells

Shinichi Morita¹, Sota Takanezawa^{1,2}, Michio Hiroshima¹, Toshiyuki Mitsui³, Yasushi Sato¹, (¹RIKEN; ²Toin University of Yokohama; ³Aoyama Gakuin University)

Recent developments in Raman microscopy now permit the non-invasive sensing of major components of biological systems and single live cells. Raman spectroscopy provides information about composition, structure, and interaction of molecules. In our research group, for instance, a miniaturized fiber probe was developed as an optical path which enabled to measure Raman spectra of a tissue in living organs. Also, we examined whether the Raman technique was applicable to the early stage sensing of the human skin pigmentation. The main interest of this presentation is to confirm whether the Raman technique is effective and versatile for distinguishing cellular conditions and

properties, especially when the conventional observations using biochemistry and fluorescence imaging provide us ambiguous pictures. Here, MCF-7, a breast cancer cell line, was used. In population, MCF-7 is differentiated by heregulin into mammalian gland-like cells which produce lipid droplets in the cytoplasm, but the response is diverse in each single cell. Raman spectra of the single live cells were examined in the time course of the differentiation. A 'phase' diagram of the cells was successfully developed, utilizing the classical least squares (CLS) and principal component analysis (PCA). The diagram allowed us to estimate the relative concentrations of such major components as lipid, protein, and water in order to identify and characterize each single cell.

1P321 原子間力顕微鏡によるβラクトグロブリン-抗βラクトグロブリン抗体相互作用に対するイオン強度の影響の計測 Evaluation of ionic strength effect on interaction between beta-lactoglobulin and anti-beta-lactoglobulin antibody by AFM

Jun'ichi Wakayama, Shigeru Sugiyama, (INano-Biotechnology Laboratory, National Food Research Institute)

Intermolecular recognition such as interaction between receptor and ligand, as well as antigen and antibody plays an important role in biological system. The biological interactions consist of the formation of non-covalent bonds by such as electrostatic forces, hydrogen binding, hydrophobic interactions and van der Waals bonds. To understand the entire mechanism of the interaction between antibody and antigen, one should clarify the origin of the binding force between antibody and antigen. Atomic force microscope (AFM) has been a useful tool for measuring the intermolecular force between a molecule of interest immobilized on the AFM probe and a complementary molecule immobilized on a substrate at a single molecule level. In the present study, we investigated the binding forces between beta-lactoglobulin, which is one of the major allergen in bovine milk, and anti-beta-lactoglobulin antibody under different ionic strength conditions using AFM; the ionic strength variation is a useful method for distinguishing between the ionic and nonionic forces. The resulting force data obtained by AFM can also be transformed into the parameters of the energy landscape for dissociation process of complex of antigen and antibody using several models. Based on the results, we will report the ionic strength effect on the binding forces between beta-lactoglobulin and the antibody and the parameters of energy landscape for the dissociation process of the complex. This work is supported by Food Nanotechnology Project, MAFF.

1P322 原子間力顕微鏡を用いた形質転換過程における線維芽細胞のレオロジー特性評価 Rheology of transformed fibroblast cells investigated by atomic force microscopy

Yusuke Mizutani, PingGen Cai, Masahiro Tsuchiya, Koichi Kawahara, Takaharu Okajima, (Graduate School of Information Science and Technology, Hokkaido University)

The measurements of single cell mechanics are crucial for understanding various cell behaviors. To understand the mechanics of rat fibroblast cells in the process of transformations such as growth (Phase II), senescence (Phase III) and immortalization (IM), we measured the viscoelastic properties of a large number of cells transformed from Phase II to IM by atomic force microscopy (AFM) combining with a microarray technique [1]. The force modulation mode was used to measure the complex shear modulus, G^* , of single cells placed in microarray wells in a frequency range of 2-180 Hz [2]. In order to describe our data, we used the power-law structural damping model [3]. The data was well fitted to this model as similar to previous study [3], and the averaged power-law exponent, α , of cells in phase III and IM was significantly larger than that in phase II. In addition, we obtained the number distribution of the model parameters (α , Newtonian viscous term, μ and scale factor, G_0) and the relationships among them. These results suggest that the rheological properties of cells are one of indicators to identify the phase of transformed cells.

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1P323 蛍光相関分光法とマイクロウェルを用いた単一細胞内タンパク質発現量の定量解析 Quantitative analysis of protein expression in single-cell using fluorescence correlation spectroscopy and microwell system

Akira Sasaki, Sho Oasa, Masataka Kinjo, (Laboratory of Molecular Cell Dynamics, Faculty of Advanced Life Science, Hokkaido University)