Although folding reactions and fluctuations of small and single domain proteins have been relatively well understood by now, much less is clear for folding and functional dynamics of larger and multi-domain proteins. Here, we present our recent computational work on three case studies of large and/or multi-domain proteins. First, we discuss both folding and conformational dynamics of adenylate kinase, a model allometric protein, which shows rather rich behaviors. Second, we discuss folding-coupled docking in a split GFP. Finally, importance of co-translational folding is addressed for a three-domain protein sur1 by computer simulations.

1SF-01
細胞の変形と動力：理論と実験の挑戦
Deformation and motion of cell: theoretical and experimental challenges
Masaki Sano
Grad. Sch. Sci. U. Tokyo

Deformation and motion are indispensable features for the understanding of living systems. Recent development in theoretical approaches on deformation and motion of living systems will be discussed in this session. After taking a bird’s eye view of these concepts, I will discuss on deformation and motion of single amoeba cell with regard to a mathematical modeling based on recent experimental findings.

Cell migration is a highly complex process that integrates many spatial and temporal cellular events. Motile bacteria and most eukaryotic cells can move in a directed manner or spontaneous fashion depending on the presence or absence of external cues. In general, motile cells are able to migrate spontaneously in a seemingly random manner even in the absence of external stimuli. It is this characteristic that allows the cells to forage and explore their surroundings by balancing random and directed migrations. To understand how amoeboid cell crawls on the substrate by deforming its shape, we performed a multipole expansion analysis of traction force distribution exerted by individually migrating amoeboid Dictostelium cells and looked at correlations to their motion. Interestingly enough, some new modes in traction force dynamics are found in this analysis. In addition to a familiar inowel-like mode, we found other modes, i.e., squeezing-stretching mode and crawling mode. These modes are found to be fundamental modes in deformable objects that migrate on the substrate. Possible relations to a recent theoretical approach will be discussed.

1SF-02
マウスの左右決定の過程に見るノード線維の回転運動の同調
Synchronization of rotational movement in mouse node cilium during left-right determination
Atsuko Takamatu, Kyoosuke Shinohara, Takui Ishikawa, Hiroshi Hamada

Animals have slight left-right (LR) asymmetry. The LR body axis in a mouse is considered to be established by unidirectional flow in a node cavity of mouse embryo. The unidirectional flow is generated by rotation of tilting monocilia. It has long been believed that rotation of the numerous cilia is necessary to trigger the LR determination. However, recently we found rotation of only two cilia is sufficient [1].

To investigate what only the two cilia can achieve, we focus on the relation of rotational movement between a pair of isolated two cilia in a mutant mouse. The cilia intervals are much larger than those for systems with densely arranged cilia such as epithelium or swimming protozoan showing metachronal waves. Thus the establishment of the cooperative movement is considered to be difficult. However, we found the phase locking is easily observed in the mouse system.

To verify the existence of phase locking state theoretically, we applied the phase reduction theory combined with computational fluid dynamics under a hypothesis there is hydrodynamic interaction among cilia. Analysis results using the same parameter as those of the experimental condition such as cilia length, intervals, tilting angle, and etc. was compared. The results suggest the phase locking can be established via only hydrodynamic interaction even though the cilia arrangements are sparse. Finally the biological advantage of the phase locking will be discussed.


Unicellular organisms such as E. Coli and Paramecium swim in viscous environment using flagella or cilia. Coordinated motion of these active filaments, known as flagellar bundling and ciliary metachronal waves, are important for achieving efficient propulsion. The roles of long-range hydrodynamic interaction in their synchronized motion were addressed as early as in 1951 by G. I. Taylor, and are recently attracting increasing attention. While large-scale numerical simulations of the filament dynamics have been developed, the key mechanism of synchronization is still far from well understood. In this talk, we consider a couple of minimal models of hydrodynamic synchronization, in which the center-of-mass motion of cilia or flagella is represented by a rigid bead making a fixed trajectory. In the first model, the driving force acting on the bead is a periodic function of its phase, which generalizes the effective and recovery strokes of ciliary beating. For arbitrary trajectory shape, we derive sufficient and necessary conditions for two parallel rotors to synchronize. In the second model, each bead exerts a radial pumping force on the surrounding fluid, and at the same time is driven by a constant torque. The model exhibits various collective behavior such as defect coarsening, turbulent spiral waves, traveling waves, and order-disorder transition. We discuss the results from the perspective of coupled oscillators with long-range interactions.

1SF-03
鞭毛や触毛の交互力の相互作用を用いた同期：ミマルアブローチ
Synchronization of flagella and cilia by hydrodynamic interactions: minimal approach

Unicellular organisms such as E. Coli and Paramecium swim in viscous environment using flagella or cilia. Coordinated motion of these active filaments, known as flagellar bundling and ciliary metachronal waves, are important for achieving efficient propulsion. The roles of long-range hydrodynamic interaction in their synchronized motion were addressed as early as in 1951 by G. I. Taylor, and are recently attracting increasing attention. While large-scale numerical simulations of the filament dynamics have been developed, the key mechanism of synchronization is still far from well understood. In this talk, we consider a couple of minimal models of hydrodynamic synchronization, in which the center-of-mass motion of cilia or flagella is represented by a rigid bead making a fixed trajectory. In the first model, the driving force acting on the bead is a periodic function of its phase, which generalizes the effective and recovery strokes of ciliary beating. For arbitrary trajectory shape, we derive sufficient and necessary conditions for two parallel rotors to synchronize. In the second model, each bead exerts a radial pumping force on the surrounding fluid, and at the same time is driven by a constant torque. The model exhibits various collective behavior such as defect coarsening, turbulent spiral waves, traveling waves, and order-disorder transition. We discuss the results from the perspective of coupled oscillators with long-range interactions.

1SF-04
重質性化学系流に駆動される遊泳細胞の形態ダイナミクスの数値モデル
Modeling morphological dynamics of migrating cells governed by self-organized excitable waves
Shuji Ishihara1, DaiSa TeKunjichi1, Satoshi Sawal1,2 (1Grad. Sch. Arts & Sciences, Univ. Tokyo, 2JST PRESTO)

Cell migration is one of the fundamental processes that support various biological functions such as immune response and development. In rapidly moving cells, phosphatidylinositol (3, 4, 5)-trisphtosphatide (PIP3) and F-actin propagate as waves at the basal membrane that act to push out the cell border, and such chemical waves are responsible for the observed cyclic yet complex dynamics of cell migration. Although many of the molecular mechanisms underlying the process are known, how they give rise to these patterns is not well understood. Here, by using Dictostelium discoideum as a model system, we address how the complex morphological change arises from the underlying molecular interactions. We present a theoretical description that integrates molecular processes inside cell and dynamics of cellular morphological change. In the model, excitability of the system is governed by positive feedback from PIP3 to PI1K activation that is mediated by actin polymerization. By incorporating membrane deformation into the model, we demonstrated how geometries of competing waves explain most of the observed dynamics of amoeboid morphology. The parameter dependence of the model, especially actin-mediated feedback strength, is compared with experimental observations for cells in which actin is perturbed.

1SF-05
細胞の力学と、人工システムにおける自己発動
Mechanics of gels and spontaneous motion of droplets as biologically-motivated systems
Natsuhiko Yoshinaga (WPI-AIMR, Tohoku Univ.)

In this talk, I will present two topics which would be hopefully merged in future: one is about mechanics of biological gels and the other is spontaneous motion of droplets. (i) Cross-linked actomyosin bundles retract when severed in vivo by laser ablation, or when isolated from the cell and micromanipulated in vitro in the presence of ATP. We identify the time scale for contraction as a viscoelastic time, where the viscosity is due to (internal) protein friction. The results are supported by an hydrodynamic model of a retracting bundle as a cylinder of isotropic, active matter, from which the order of magnitude of the active stress is estimated. (ii) I shall also show that spontaneous motion (also called as self-propulsion) of droplets driven by a surface tension gradient (Marangoni effect) coupled with internal and/or external patterns of chemicals. Such systems have been attracting attention in last decades for its potential application to biological problems such as cell motility. Recently several model experiments showing spontaneous motion have been proposed. The systems in these works consist of relatively simple ingredients, for instance, oil drops in water nevertheless the motion is as if the drops are alive. I will address why the particle moves without external force and why it breaks symmetry and chooses one direction.