The University of Tokyo – Korea University

The 2nd Joint Workshop on Bio-Soft Matter

Date: 28 February – 3 March 2013

Venue: Hana Square (Feb. 28th) & Frontier Hall (March 1st and 2nd),

Korea University, Anam, Seongbuk, Seoul, Korea

Organizers:

Kyoung J. Lee (KU)

Seok-Cheol Hong (KU)

Kwang-Il Goh (KU)

Wonshik Choi (KU)

Funding:

National Research Foundation of Korea

Program Overview

	28 Feb.	1 Mar.	2 Mar.	3 Mar.
9:00		A. Nose	H. Higuchi	
		J. H. Choi	W. Choi	
10:00		M. Tomishige	M. Kim	Lab Tour
		BREAK	BREAK & PHOTO	
11:00		S.-C. Hong	K.-I. Goh	
		I.-B. Lee	K.-M. Lee	
12:00		LUNCH	Closing remark	
			LUNCH	
1:00			EXCURSION	
2:00		S. Chung		
		H. Noguchi		
3:00		H. Shiba		
		BREAK		
4:00		K. Takeuchi		
		K. Nagai		
5:00	Welcome address	POSTER SESSION		
	K. J. Lee			
6:00	M. Sano			
7:00	Welcome dinner	Banquet		

Speakers:

Kyoung Jin Lee (KU)

Masaki Sano (TU)

Akinao Nose (TU)

Joon Ho Choi (KU)

Michio Tomishige (TU)

Seok-Cheol Hong (KU)

Il-Buem Lee (KU)

Seok Chung (KU)

Hiroshi Noguchi (TU)

Hayato Shiba (TU)

Kazumasa Takeuchi (TU)

Ken Nagai (TU)

Hideo Higuchi (TU)

Wonshik Choi (KU)

Moonseok Kim (KU)

Kwang-Il Goh (KU)

Kyu-Min Lee (KU)

Program:

28 February (Thu)

5:00 – 5:10
Opening Remark: Kyoung Jin Lee

5:10 – 5:50
Kyoung Jin Lee
"Collective Patterns and Waves in Populations of Biological Cells."

5:50 – 6:30
Masaki Sano
"How Do Cells Crawl: A Simple Force-Velocity Relationship Revealed by Multipole Analysis of Traction Force Dynamics."

1 March (Fri)

9:00 – 9:40
Akinao Nose
"Optogenetic dissection of the neural circuits that regulate rhythmic movement in *Drosophila* larvae."

9:40 – 10:00
Joon Ho Choi
"Modulating the Precision of Recurrent Bursts in Cultured Neural Networks."

10:00 – 10:40
Michio Tomishige
"Structural basis for the coordinated processive movement of kinesin motor protein."

10:40 – 11:00 BREAK

11:00 – 11:40
Seok-Cheol Hong
"Nanoscopic conformational diversity and dynamics of DNA: physics, biology, and beyond."

11:40 – 12:00
Il-Buem Lee
"Rupturing of the Hoogsteen base pairing in triplex DNA by magnetic tweezers"

12:00 – 14:00 LUNCH

14:00 – 14:40
Seok Chung
"Microfluidic assay for three-dimensional and heterotypic cell culture"

14:40 – 15:20
Hiroshi Noguchi
"Structure formation in surfactant mixtures: membrane self-assembly, bicelle formation, and detergent-adsorption-induced vesicle division"

15:20 – 15:40
Hayato Shiba
“Structure formation of surfactant membrane under shear flow”

15:40 – 16:00 BREAK

16:00 – 16:20
Kazumasa Takeuchi
“Exploring universal scaling laws out of equilibrium with turbulent liquid crystal”

16:20 – 16:40
Ken Nagai
“Vortex lattice formation of self-propelled particles through steric interaction”

16:40 – 18:00
POSTER SESSION (23 posters)

2 March (Sat)

9:00 – 9:20
Hideo Higuchi
“Single molecule biophysics toward *in vivo*”

9:20 – 10:00
Wonshik Choi
“Beyond the turbidity”

10:00 – 10:20
Moonseok Kim
“Maximal energy transport through disordered media”

10:20 – 11:00 BREAK & PHOTO

11:00 – 11:40
Kwang-Il Goh
“Multiplexity in networks”

11:40 – 12:00
Kyu-Min Lee
“Cascade Dynamics on Multiplex Networks”

12:00 – Closing Remark & LUNCH & EXCURSION

3 March (Sun)

10:00 – 12:00 Lab Tour: 3 groups visit 3 labs for 40 minutes each.

Oral Session Abstracts

Collective Patterns and Waves in Populations of Biological Cells

Kyoung Jin Lee*

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My laboratory has been interested in biophysical problems in which nonlinear, nonequilibrium, many-body systems approach plays an important role. Most “living creatures” are composed of interacting cells that are inherently nonlinear. And, the interactions among them often lead to fascinating macroscopic structures and patterns, which play a significant role in biology. We have been investigating several different issues along this line of viewpoint, ranging from “phase waves in mammalian circadian clocks,” “trail formation by crawling microglia” to “density waves in populations of tumor cells." This lecture will review some of the latest developments in our laboratory.

Acknowledgments
This work was supported by the National Research Foundation of Korea grant funded by the K orean government (2012R1A2A1A01008021).

How Do Cells Crawl:
A Simple Force-Velocity Relationship Revealed by Multipole Analysis of Traction Force Dynamics

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In the efforts to understand cell motility, locomotion of Eukaryotic cell on the substrate is much less understood compared with Prokaryotic cells such as swiming bacteria. How do cells crawl on the substrate and what determine the direction of migration are key questions in cell biophysics. We recently performed traction force spectroscopy for migrating Dictyostelium discoidium ameoboid cells and analysed how single cells exerts forces to the substrate during migration. Improving tracton force spectroscopy technique now enabled us to monitor highly localized nature of force spots created between cell membrane and the substrate. We suceeded to measure force distribution of dividing cells by this method. Furthermre, by employing multipole exapnsion of the stress field distribution we found a simple force-velocity relationship for migrating ameoboid cells. It turns out that force dipole determines the axis of moving direction, and force quadrupole determines the direction of migration. Detailed analysis of multipole and deformation dynamics elucidated three different modes in crawling motion. Among them two modes had a truely 2D nature. We also found phase delay between force dipole and quadrupole in crawling motion which may shed light on modeling of cell migration mechanism.

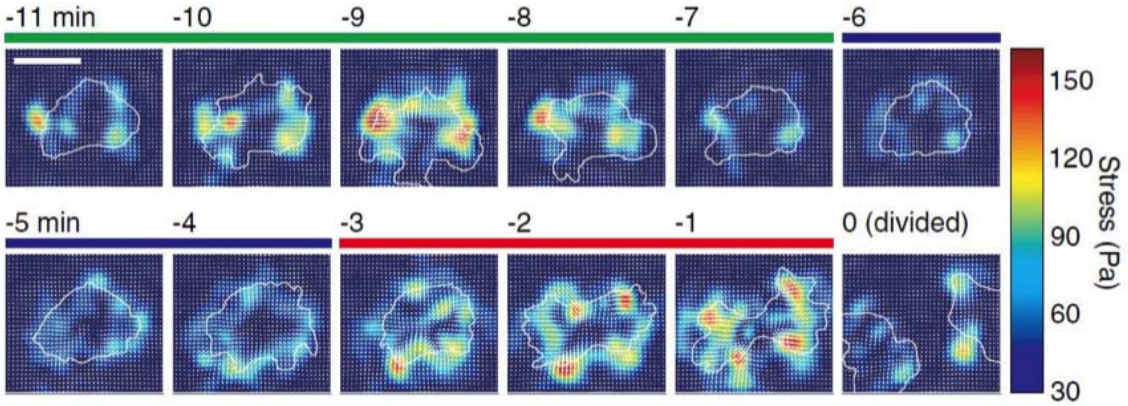

Fig.1 Force distribution of dividing cell. Bar corresponds to 10 μ m.

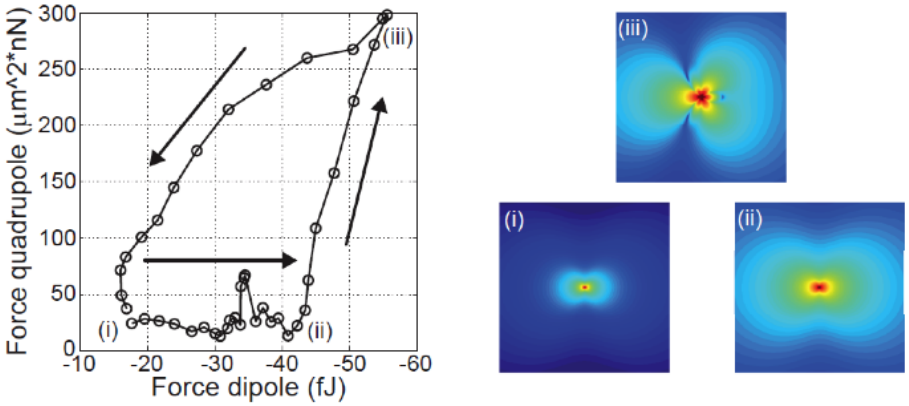

Fig.2. Dynamics of force dipole and quadrupole in inchworm motion (left). Corresponding deformation fileds (right).

[1] H. Tanimoto and M. Sano, Phys. Rev. Lett. 109, 248110 (2012).
[2] H. Tanimoto and M. Sano, preprint (2013).

Optogenetic dissection of the neural circuits that regulate rhythmic movement in *Drosophila* larvae

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[2]*Department of Physics, Graduate School of Science,*
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Understanding how motor pattern is regulated by the central circuits remains a major goal in neuroscience. While previous studies in several species have implicated specific classes of interneurons in the regulation of locomotion, their roles and activity pattern during ongoing behavior remain poorly understood. The *Drosophila* larval peristalsis is generated by a traveling wave of motor activity from the posterior to anterior segments. The pattern of peristalsis, including rhythm and speed, is remarkably stereotypic, providing an excellent system in which to investigate motor control.

We used calcium imaging to search for interneurons that show wave-like or oscillating activity and thus may be involved in the locomotion. One class of interneurons identified, period-positive median segmental interneurons, or PMSIs, displayed a wave-like activity, concomitant with the propagation of muscular contraction. PMSIs are a group of ~15 local interneurons in each segment. They seem to be pre-motor inhibitory interneurons since they form potential synaptic contacts with motor neurons (visualized with GFP Reconstitution Across Synaptic Partners) and secrete glutamate, a neurotransmitter known to inhibit motor neurons. Consistent with this, photo-activation of these neurons with ChR2 induced local relaxation of the musculature in a segment-specific manner. When the activity of PMSIs was inhibited optogenetically with NpHR or thermogenetically with the temperature sensitive Shibire, the speed of locomotion was greatly reduced. These results and our electrophysiological analyses suggest that local and sequential inhibition of motor neurons by PMSIs controls the speed of larval locomotion. PMSIs share a number of functional and morphological characteristics with vertebrate V1 neurons, including the expression of the transcription factor Engrailed, implying that the role of this class of interneurons in locomotion may be phylogenetically conserved.

Modulating the Precision of Recurrent Bursts in Cultured Neural Networks

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Synchronized bursts are a very common feature in biological neural networks, and they play an important role in various brain functions and neurological diseases. This study investigates "recurrent synchronized bursts" induced by a single pulse stimulation in cultured networks of rat cortical neurons. We look at how the precision in their arrival times can be modified by a noble time-delayed stimulation protocol, which we term as "Δt training." The emergence of recurrent bursts and the change of the precision in their arrival times can be explained by the stochastic resonance of a damped, subthreshold, neural oscillation.

Acknowledgments
This study was supported by the Acceleration Project (R17-2007-017-01000-0) of the Korea Ministry of Science and Technology

Structural basis for the coordinated processive movement of kinesin motor protein

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Kinesin is a dimeric motor protein that hydrolyzes ATP and moves along microtubules to transport cargoes inside the cells. Recent studies showed that kinesin walks along microtubules in a hand-over-hand manner by alternately moving two motor domains ("heads"), although it is still unclear how two motor domains coordinate to move processively. To understand the structural basis for the walking mechanism, atomic-detailed information of kinesin at various nucleotide states are essential, however the nucleotide-free crystal structure had been unavailable. Here we report the first crystal structure of kinesin-1 motor domain without bound nucleotide solved at a 2.8A resolution. The nucleotide-free structure showed marked differences from the previously solved ATP- and ADP-like crystal structures. The structure when compared with ADP-like structure explains how microtubule-binding stimulates ADP release from the motor domain. Furthermore, we modeled dimeric kinesin on microtubule based on these crystal structures and found that kinesin cannot adapt two-head-bound state when both heads are nucleotide-free due to a constraint posed on the neck linker, and that the tethered head can bind preferentially to the forward binding site after the trailing head binds ATP. We obtained functional supports for this structural model by directly observing the conformational changes of kinesin dimer while moving along microtubules using single molecule fluorescence resonance energy transfer (FRET) technique. These findings provide structural basis for the coordinated processive movement of kinesin.

Nanoscopic conformational diversity and dynamics of DNA: physics, biology, and beyond.

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A variety of non-canonical DNA structures are known to exist and some of them exist even *in vivo*. Examples of such structures are left-handed Z-DNA, triple helical H-DNA, and intercalated i-motif to name a few. Over recent years, biological roles of such DNA structures have been suggested and mainly implicated in gene expression. Moreover, various disease-related genetic regions are found to have the potential to form such non-canonical structures. Although there is ample evidence for the significance of those structures in numerous biological processes, fundamental understandings of the structures are far from complete. The kinetics of the structures has not been measured straightforwardly and the effects of physical factors such as tension and torsion on the conformational transitions have been rarely addressed. Here, we used single-molecule biophysical methods to observe conformational dynamics of the aforementioned non-canonical structures occurring at the nanometer-scale and to study the effects of physical and chemical factors on their formation. From the studies, we found that those structures are highly dynamic and the mechanical factors are critical in the transition. Biological significance of the results will be discussed as well.

This work is supported by mid-career research program (NRF 2010 00 10594).

Rupturing of the Hoogsteen base pairing in triplex DNA by magnetic tweezers

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Watson and Crick found that DNA exists as a double helix of two strands and the two strands are connected by “Watson-Crick” base pairs (A-T and G-C). Years later, Karst Hoogsteen reported new binding modes between A and T and between G and C, which were now known as "Hoogsteen base pairing". The geometries of Hoogsteen base pairing and Watson-Crick base pairing are markedly different. Soon it was known that Hoogsteen base pairing plays important roles in forming non-conventional nucleic acid structures such as hairpin motifs of tRNA, triplex DNA, and quadruplex DNA to name a few. Despite intensive chemical and biochemical studies on the Hoogsteen pairing, the physical nature of the pairing remains largely unknown. Thus, triplex DNA being a model system for the Hoogsteen pairing, we investigated the mechanical and dynamical behaviors of the Hoogsteen pairing. More specifically, force-induced rupturing of the Hoogsteen pairs has not been reported. In order to monitor the nano-scale conformational transition upon unzipping of the Hoogsteen pairs in the presence of tension, we utilized the hybrid technique of single-molecule FRET and magnetic tweezers. We found that a few picoNewton’s tension is sufficient to rupture the Hoogsteen pairs in triplex DNA at pH = 6.5 and observed frequent interconversions between zipped and unzipped states implying a small energy barrier between them under given conditions.
Our biophysical results shed new light on the nature of the Hoogsteen base pairing and underpin relevant biological phenomena from more quantitative viewpoints.

This work is supported by mid-career research program (NRF 2010 00 10594).

Microfluidic assay for three-dimensional and heterotypic cell culture

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A simple but robust microfluidic assay for three-dimensional and heterotypic cell culture has been developed by incorporating hydrogel between microchannels. Using this assay, well-defined biochemical and biophysical stimuli can be applied to multiple cell types interacting each other, thereby replicating many aspects of the in vivo microenvironment. Capabilities exist for time-dependent manipulation of flows and chemical gradients as well as high-resolution real-time imaging for observing spatial-temporal single cell behavior, cell-cell communication, cell-matrix interactions and cell population dynamics. These assays can be used to study cell survival, proliferation, migration, morphogenesis and differentiation under controlled conditions. Applications include the study of previously unexplored cellular interactions, and have already provided new insights into how biochemical and biophysical factors regulate interactions between populations of different cell types.

Structure formation in surfactant mixtures: membrane self-assembly, bicelle formation, and detergent-adsorption-induced vesicle division

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Topological changes of surfactant mixtures are studied using coarse-grained molecular simulations. It is found that a wide variety of structures are formed in binary mixtures of lipid and other surfactants depending on critical micelle concentration, spontaneous curvature of monolayer, and initial conditions.

Amphiphilic molecules, such as lipids and detergents, self-assemble various structures in aqueous solutions such as spherical and worm-like micelles, and bilayer membranes. When different types of surfactants are mixed, many different self-assembled structures can be observed. The edges of bilayer membranes can be stabilized by cone-shaped surfactants. Thus, discoidal bilayer membranes called bicelles are formed. Recently, an undulating cylinder and a bilayer disk connected with several worm-like micelles, which shape looks like an octopus, have been observed in binary mixtures of diblock copolymers by cryo-TEM [1]. Mixtures of lipids and detergents are used for solubilization, reconstruction, and crystallization of membrane proteins. Compared to single-component surfactant systems, structure formation of surfactant mixtures is not well understood.

We have studied structure formation dynamics in mixtures of lipids and detergents using coarse-grained molecular simulations [2,3]. Bicelles are formed by selfassembly from a binary mixture of isolated molecules. The size of self-assembled bicelles increases with the increasing number fraction of lipids and repulsion between different molecules [3]. When a vesicle is used as an initial simulation state, a large bicelle can be formed, and the excess amount of the detergent molecules forms worm-like micelles [2]. In contrast, in self-assembly, most of detergent molecules are contributed to surround the rims of bicelles. Thus, the size of the bicelles is determined by the initial states and assembly kinetics.

When a vesicle is placed in detergent solution, the detergent adsorption induces vesicle division or vesicle rupture into worm-like micelles [3]. The vesicle transforms into a pear shape and the contact of the inner monolayers (leaflets) on the inside of the pear neck induces vesicle division via the stalk intermediate in the modified stalk model. At large values of spontaneous curvature of the detergent monolayers, a pore is often opened in the pear neck, and this leads to vesicle division or worm-like micelle formation. A similar vesicle division has been experimentally observed in multi-component surfactant systems.

When both surfactants have very low critical micelle concentration (CMC) (e.g. lipids), it is found that octopus-like micelles are formed (see Fig. 1) [2]. Excess cone-shaped surfactants to surround a bilayer disk form connected worm-like micelles. The obtained octopus shape of micelles agrees with those observed in the cryo-TEM images [1]. Two types of connection structures between the worm-like micelles and the bicelles are revealed.

Fig.1. Snapshot of octopus-like micelle. Light and dark grey particles represent cylindrical and corn shaped surfactant molecules, respectively.

[1] S. Jain and F. S. Bates, Macromol. 37, 1511 (2004).
[2] H. Noguchi, Soft Matter 8, 8926 (2012).
[3] H. Noguchi, J. Chem. Phys. 138, 024907 (2013).

Structure formation of surfactant membrane under shear flow

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We investigate structure formation in aqueous surfactant solution under simple shear flow, using a meshless membrane model, in combination with a mesoscale explicit solvent technique. At appropriately large membrane volume fractions, lamellar states exhibit undulation instability in vertical directions to the shear velocity at high shear rates, leading to a buckled or cylindrical shape. Dependence of the structure factor on the shear rate exhibits a qualitative agreement with the experiments. Structure evolution in time exhibits moderate dependence on the initial conditions.

Background

Structure formation in surfactant membrane system under shear flow has been one of the leading themes in the last two decades. In the experiments, formation of closely-packed multi-lamellar vesicles are observed in non-ionic surfactant systems, mainly in aqueous environments under shear flow. Thus, hydrodynamics are supposed to play important roles in these phenomena. Until now, the reasons why such structures arise have not been understood from the physical principles.

Very few simulations have been addressing this problem, due to huge spatial scales involved in this phenomenon. Coarse-grained simulations recently exhibit a large extent of applicability on complex phenomena induced by surfactant membranes. Among them, the meshless membrane model [1,2] is a particle-based method where self-assembly and ruptures of the membranes are allowed. This model can be extended straightforwardly into an explicit solvent simulation by adding solvent particles with simple repulsive interactions [3].

Model and Method

To simulate the structure formation of surfactant membranes, we employ an explicit-solvent meshless membrane model. The membrane particles interact via curvature potentials, in addition to the repulsive and attractive interactions, while solvent particles have the repulsive potentials only. The curvature model is defined as penalty energy for a degree of deviation from the planar shape, and thus it works as a bending curvature potential. Each membrane particle is considered to be a coarse-grained representation of a bilayer patch of surfactant molecules. Dissipative particle dynamics thermostat is used. The system is calculated a code parallelized by the special division method, to perform massive simulations including millions of particles.

Results

We investigate the morphological states as functions of the shear rate and the volume fraction of the membrane component [3]. Various structures including vesicles, lamellae, and multi-lamellar states with nearly cylindrical symmetry are obtained, some of which are in qualitative consistency with the experiments of nonionic surfactant membranes. Especially, cylindrical instability of multilamellar membrane occurs perpendicularly to the shear flow velocity when the volume fraction of the membrane is high enough, and their scattering pattern is qualitatively similar to the results of small angle neutron (or X-ray) scattering patterns obtained in time evolution under shear flow. It might be a candidate for the intermediate structure on the way to the onion state observed in the experiments.

[1] H. Noguchi and G. Gompper, Phys. Rev. E.. **73**, 021903/1-12 (2006).
[2] H. Shiba and H. Noguchi, Phys. Rev. E.. **84**, 031926/1-13 (2010).
[3] H. Shiba, H. Noguchi, and G. Gompper, to be submitted (2013).

Acknowledgments

This work was supported by Grant-in-Aid for Young Scientists 24740285 from JSPS In Japan, Computational Materials Science Initiative (CMSI) from MEXT in Japan, and the European Soft Matter Infrastructure project (ESMI) in the EU. The numerical calculations were carried out on SGI Altix ICE 8400EX and NEC SX-9 at ISSP in University of Tokyo (Japan), Fujitsu FX10 at Information Technology Center in University of Tokyo, (Japan), Hitachi SR16000 at YITP in Kyoto University (Japan), and JUROPA at Jülich Supercomputing Centre in Forschungszentrum Jülich (Germany).

Exploring universal scaling laws out of equilibrium with turbulent liquid crystal

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Recent theoretical progress has revealed a variety of universal scaling laws describing various scale-invariant phenomena out of equilibrium, but even the most basic and important of these developments had largely remained without complete experimental verification [1,2]. Here, I show that chaotic convection of electrically driven nematic liquid crystal is an ideal system to overcome past difficulties, which allows thorough experimental tests of theoretical predictions and beyond.

First we study the route to turbulence in the electroconvection, focusing in particular on the transition between two regimes of spatiotemporal chaos, called the dynamic scattering modes (DSM) 1 and 2. Spatiotemporal intermittency is found near the transition, where DSM2 patches move around, coalesce, and sometimes disappear, somewhat resembling a percolation process along the time axis (Fig.1 inset). We characterize this transition by measuring both static and dynamic critical behavior (Fig.1), providing clear evidence, indeed, for the directed percolation universality class [3], which is theoretically known as the most fundamental class for absorbing-state phase transitions [1]. By controlling alignment of liquid crystal molecules, we can also investigate how different symmetries lead to different universality classes, which constitutes a crucial advantage of the electroconvection for studying critical phenomena.

We then study the DSM2 regime under higher applied voltage, where DSM2 domains grow with fluctuating interfaces (Fig.2 photos). Measuring how the interfaces roughen in course of time, we find evidence for the scaling laws of the Kardar-Parisi-Zhang class [4], the prototypical class for stochastic growing interfaces [2]. Remarkably, fluctuations in the interface positions obey the largest-eigenvalue distribution of certain random matrices (Fig.2) [4], indicating that recent rigorous results for solvable models [5] are universal and robust enough to emerge in a real phenomenon.

In the talk, I will also illustrate mutual relations among these universality classes and explain how they arise in the single experimental system.

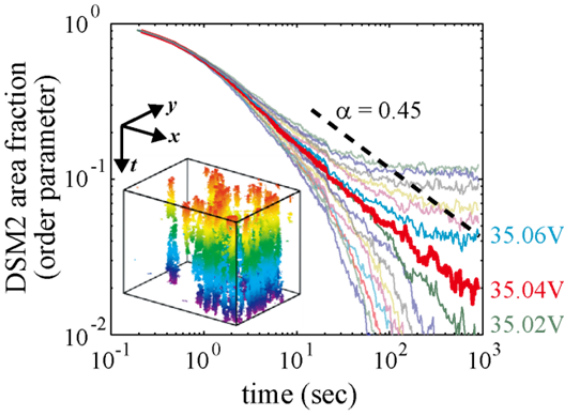

Fig.1. Critical behavior at the DSM1-DSM2 transition [3]. The area fraction of the DSM2 domains ρ exhibits power-law decay at the critical voltage (red curve), $\rho \sim t^{-\alpha}$, with the critical exponent of the directed percolation class $\alpha \approx 0.45$ [1].

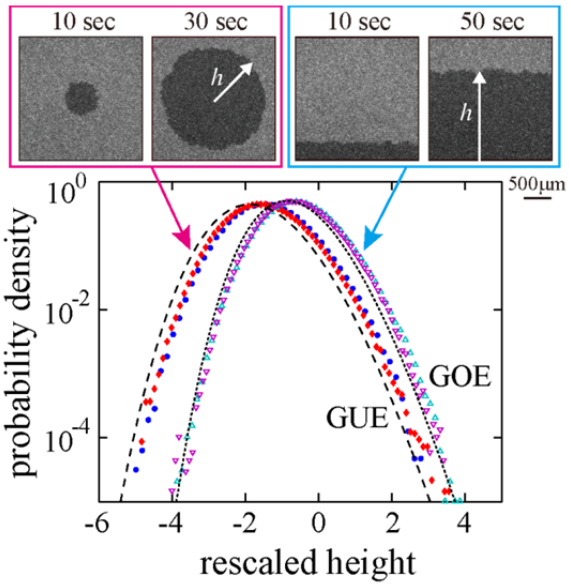

Fig.2. Growing DSM2 domains (black) [4]. Fluctuations of the height h (as defined in the top figures) for the circular and flat interfaces obey the largest-eigenvalue distributions of the GUE and GOE random matrices, respectively, in the appropriately rescaled units.

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[4] K. A. Takeuchi and M. Sano, Phys. Rev. Lett. **104**, 230601 (2010); K. A. Takeuchi et al., Sci. Rep. **1**, 34 (2011); K. A. Takeuchi and M. Sano, J. Stat. Phys. **147**, 853-890 (2012).

[5] For recent reviews, see, e.g., T. Kriecherbauer and J. Krug, J. Phys. A **43**, 403001 (2010); T. Sasamoto and H. Spohn, J. Stat. Mech. (**2010**), P11013; I. Corwin, Random Matrices: Theory and Applications **1**, 1130001 (2012).

Acknowledgments

I wish to thank my collaborators, M. Sano, H. Chaté, and M. Kuroda for the work on the DSM1-DSM2 transition [3], and M. Sano, H. Spohn, and T. Sasamoto for that on the DSM2 growing interfaces [4].

Vortex lattice formation of self-propelled particles through steric interaction

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Recently, collective behaviours of self-propelled particles are extensively studied [1]. For example, swarming behaviour of birds or fish are analyzed using simple mathematical models [2] and collective migration of an epithelial cells during wound healing has been reported [3]. As one of such phenomena, we reported the formation of the vortex lattice of self-propelled particles using microtubules driven by dyneins fixed on a glass plate [4]. Using the model described in Eq. (1), the vortex lattice formation was reproduced as shown in Fig. 1 and it was found that the long-time memory related to motion is one of the important factors for the vortex lattice formation. Here, $\boldsymbol{x}_i$ and θ_i are the position and the direction of motion of particle i, respectively, ω_i is a noise with finite correlation time such as an Ornstein-Uhlenbeck process and a telegraphic noise, and A is the strength of interaction between two particles. To clarify the mechanism of the formation of the vortex lattice, we made the continuum description for the collective behaviour of microtubules based on this multi-agent model.

Now, we consider only the situation where ω_i is a telegraphic noise and the correlation time of ω_i is very long compared to the time for one rotation of a particle. In this situation, an isolated particle moves on a circle trajectory for a long time; therefore, we focused only the motion of the center of the circle. We evaluated the interaction of two centers and concluded that there are a short-range attraction and a long-range repulsion. Using the evaluated interaction, we obtained the continuum description, which forms a hexagonal lattice with a large density of the particles. This result corresponds to the original multi-agent model. Based on the comparison with the original model, we concluded that the effective interaction of the centers is the key factor for the formation of the vortex lattice.

Figures, Photos, Tables, and Equations

$$\frac{\mathrm{d}\boldsymbol{x}_i}{\mathrm{d}t} = (\cos\theta_i, \sin\theta_i),$$
$$\frac{\mathrm{d}\theta_i}{\mathrm{d}t} = \omega_i + A\frac{\sum_{|\boldsymbol{x}_i-\boldsymbol{x}_j|<1}\sin 2(\theta_j-\theta_i)}{\sum_{|\boldsymbol{x}_i-\boldsymbol{x}_j|<1}}, \quad (1)$$

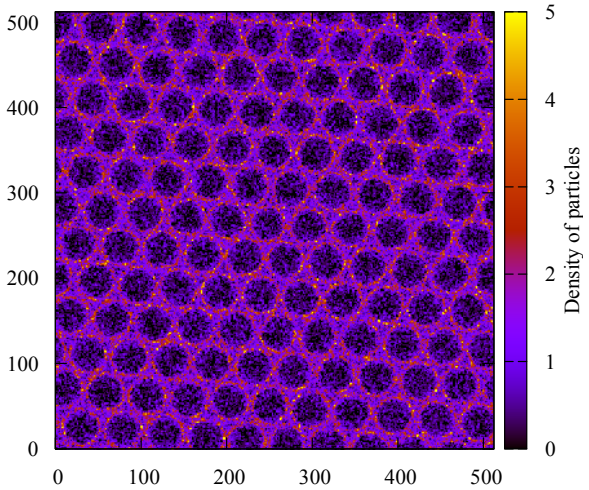

Fig.1. Hexagonal lattice of self-propelled particles. The average of density was 1 and the switching rate of ω during unit time was 0.02. A telegraphic noise was used.

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[4] Y. Sumino, et al., , *Nature*, **483**, 448-452 (2012).

Acknowledgments
This study is supported by JSPS Research fellowships for young scientists (No. 23-1819) to K. H. N.

Single molecule biophysics toward *in vivo*

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We had investigated deeply single molecular functions of purified motor proteins. However, physiological conditions in the cell environment are very different from those in *in vitro* assays of purified proteins; for example, the ion composition is different in the cells and the assays cells have adaptor proteins and cytoskeletal networks that are not present in the assays. Therefore, it is crucial to measure the molecular functions of motor proteins in cells and *in vivo* to understand the molecular mechanisms of vesicle transport by motor proteins. Here we measured the stepwise movements generated by myosin, dynein, and kinesin were observed in cultured cells. The sequential process of the transport of vesicles, including human epidermal factor 2 receptor, was observed for long periods in three dimensions using quantum dots (QDs). QD vesicles, after being endocytosed into the cells, moved along the membrane by transferring actin filaments and were then rapidly transported toward the nucleus along microtubules. The position of vesicles was detected with a precision up to 1.9 nm and 330 ms using a new two-dimensional tracking method. The stepwise movements of these motor proteins in cells were observed using new imaging methods.

We also image the vesicle transport in mice under a noninvasive condition. We developed a non-invasive technique for the in vivo imaging of neutrophils labeled with quantum dots, up to 100 μm below the skin surface of mice. The quantum dots were endocytosed into vesicles in the neutrophils, allowing us to track the vesicles with high spatiotemporal precision at ~10 msec per frame with 15 nm accuracy. When the neutrophils were moving within the interstitium, the speed of the vesicles was very fast. The speed is about four times faster than the in vitro velocity of a molecular motor, such as kinesin or dynein. This is the first report in which non-invasive techniques have been used to visualize the internal dynamics of neutrophils. The observed high-speed vesicle transport is likely important for the bactericidal function of neutrophils.

Beyond the turbidity

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"Turbidity" caused by multiple light scattering interrupts the propagation of waves, and thus undermines optical imaging. For example, translucent biological tissues exhibiting optical turbidity have posed limitations on the imaging depth and energy transmission. In this talk, I will describe the counterintuitive finding that optical turbidity, rather than being a hindrance to imaging, can in fact dramatically improve both the spatial resolution and the field of view of the target images. As an immediate biomedical application of the developed technique, we demonstrated that an endoscopic imaging is made possible by using a single multimode fiber, a kind of a turbid medium. I will close my talk by introducing our recent experimental work that demonstrated the significant enhancement of light energy delivery through a highly turbid medium. This seemingly implausible task was made possible by coupling light into the resonance modes, called transmission eigenchannels, of the medium. These studies will lead to great important applications in deep-tissue optical bio-imaging and disease treatment.

[1] Youngwoon Choi, Taeseok Daniel Yang, Christopher Fang-Yen, Pilsung Kang, Kyoung Jin Lee, Ramachandra R. Dasari, Michael S. Feld, and Wonshik Choi, Physical Review Letters **107,** 023902 (2011)

[2] Youngwoon Choi, Changhyeong Yoon, Moonseok Kim, Taeseok Daniel Yang, Christopher Fang-Yen, Ramachandra R. Dasari, Kyoung Jin Lee, and Wonshik Choi, Physical Review Letters **109,** 203901 (2012)

[3] Moonseok Kim, Youngwoon Choi, Changhyeong Yoon, Wonjun Choi, Jaisoon Kim, Q-Han Park and Wonshik Choi, Nature Photonics **6,** 581 (2012)

Maximal energy transport through disordered media

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Even for a highly disordered medium, it is possible in principle to enhance the delivery of energy to the far side of the medium. Specific modes called eigenchannels exist for a disordered medium which have extraordinarily high transmission. We report the first realization of the transmission eigenchannels in a disordered medium and show that an eigenchannel transport 3.99 times more energy than uncontrolled waves, which is the best experimental record reported so far. Our study will open up new avenues for enhancing light energy delivery to biological tissues for medical purposes and controlling the lasing threshold in random lasers.

1. Introduction

A disordered medium, however high its degree of disorder becomes, is a linear system. Therefore the input-output response of a disordered medium can be described by a so-called transmission matrix which relates free modes at the input to those at the output. According to random matrix theory (RMT)[1], the transmittance of the eigenchannels can reach to unity in an ideal condition where entire solid angles for the illumination and detection are covered. In spite of recent technical advances on the recording of transmission matrix[2-4] and the application of wavefront shaping for the disordered media[5-8], the coupling of light into individual transmission eigenchannels has remained unrealized.

In this study, we report the first experimental implementation of individual transmission eigenchannels for a highly disordered medium. To this end, we experimentally record a transmission matrix of the disordered medium for a limited numerical aperture (0.32 NA) and acquire its transmission eigenchannels. Using a wavefront shaping method, we generate an optical wave corresponding to each eigenchannel and record its transmission. In doing so, we have demonstrated that the eigenchannel with the maximum transmittance transports 3.99 times more energy than the uncontrolled waves.

2. Experimental Procedure

The experimental setup is shown in Fig. 1. We construct an off-axis interference microscope[3] for the recording of the amplitude and phase of the light wave. For the purpose of recording a transmission matrix, scanning mirrors (GM) are installed in the sample beam path to scan the angle of a plane wave incident on a disordered medium. A spatial light modulator (SLM) that can generate an arbitrary wavefront is installed in the sample beam path to generate an optical wave of an eigenchannel. A disordered medium is placed between the IP and OP. For clarity, we define the spatial coordinates at the IP and OP as (ξ, η) and (x,y), respectively. As a disordered medium, a 27 μm-thick ZnO nanoparticle layer is used. The transport mean free path of the medium is measured to be 0.6 ± 0.2 μm such that the transmitted light is scattered thousands of times on average. The average transmittance of this medium is measured to be 0.79 % at the collection angle corresponding to 0.32 NA. In other words, the fraction of the total incident power detected at the given collection angle after being diffusely transmitted to the sample is 0.79 %.

For the measurement of a transmission matrix, a flat pattern is written on the SLM to make it work as a simple mirror. We then scan the angle of the GM to control the angle, (θ_ξ, θ_η), of the plane wave incident to the medium at the IP, and record transmission image at each incident angle. Typically, 3,000 images are recorded at a frequency of 500 frames/s in such a way to uniformly cover the angular passband of 0.32 NA.

In order to acquire the transmission eigenchannels and their corresponding transmission eigenvalues, singular value decomposition is performed for the constructed transmission matrix in accordance with RMT. Specifically, the transmission matrix is factorized into $T = U\Sigma V^*$, where Σ is a rectangular diagonal matrix with nonnegative real numbers on the diagonal called singular values and V^* denotes the conjugate transpose of the matrix V. The V and U are the unitary matrices whose columns are the transmission eigenchannels at IP and OP, respectively.

3. Results and Discussion

The complex field map of the first eigenchannel that has the maximum transmittance is acquired at the IP from the first column vector of V after converting the column into discrete 2D map (Fig. 3a). The output intensity map (Fig. 3c) of the first eigenchannel is obtained by multiplying the transmission matrix by the input eigenchannel. Although the eigenchannels are acquired from the measured transmission matrix, it is important to implement each eigenchannel in the experiment to verify whether it truly exhibit either enhanced or reduced transmission in accordance with its eigenvalue. By using SLM, we experimentally generate an optical wave corresponding to the eigenchannel and send it to the medium.

The optical wave of the first eigenchannel shown in Fig. 3a is generated by the SLM (Fig. 3b). When it is compared with Fig. 3a, the patterns are in excellent agreement, confirming the accuracy of our wavefront shaping method. The cross correlation of complex field maps between Fig.3a and Fig.3b is measured to be 0.75. After sending the first eigenchannel, we capture complex field map at the OP (Fig. 3d). It can be clearly seen that the output of the eigenchannel is almost identical to the prediction (Fig. 3c) made by the transmission matrix. The cross correlation of complex field maps between Fig.3c and Fig. 3d is measured to be 0.80. This suggests that the eigenchannel is successfully implemented in the experiment. Regarding the transmittance of the eigenchannel, the total energy of the output (Fig. 3d) is about 2.24 % of the input (Fig. 3b). Therefore the enhancement factor, which is defined as the ratio of the transmittance of the first eigenchannel (2.24 %) to that of the uncontrolled wave (0.79 %), is 2.84 for this particular sample. We repeated the same experiment for more than 20 different samples and observed that the transmission enhancement was highly reproducible. The enhancement factor varies somewhat from sample to sample, typically in the range of 2 to 4. The maximum enhancement factor that we have achieved is 3.99.

4. Summary

In summary, we demonstrated that we can control the wave interference, either constructively or destructively for a highly disordered medium by means of coupling light into individual transmission eigenchannels. In particular, we could selectively generate an eigenchannel of maximum transmittance and achieve significant transmission enhancement. Our method could potentially be useful in facilitating laser radiation therapy and biomedical imaging by enhancing light energy delivery deep into biological tissues.

5. Figures and Captions

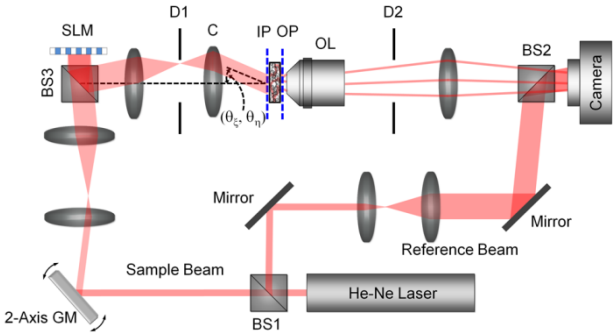

Fig. 1. Experimental setup for recording a transmission matrix and generating each transmission eigenchannel.

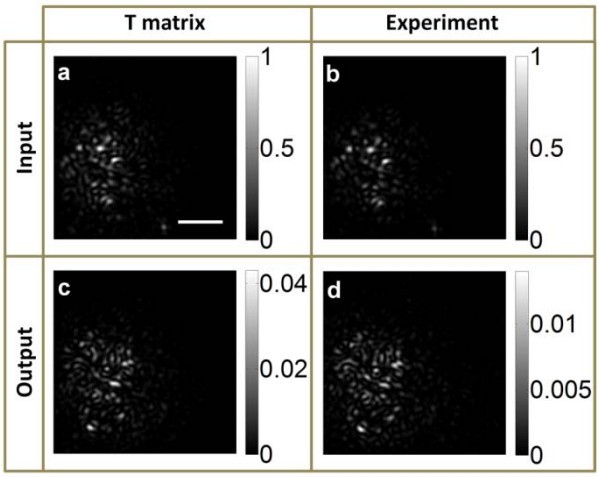

Fig.2. Experimental implementation of the maximum transmission eigenchannel.

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Multiplexity in networks

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Most complex network studies thus far have been focused on single-layer framework. It becomes increasingly clear, however, that many real-world complex systems are multiplex---nodes interact with multiple types of interactions (links) which coexist, co-depend, co-operate, and co-evolve. The interplay of such multiplex interactions may confer nontrivial consequences on network dynamics. We present some recent results regarding the network multiplexity. We first show how such multiplexity affects dynamic processes on multiplex networks. We then discuss the correlated multiplexity and its structural impact and evolution model. This talk is based on the works done in collaboration with Kyu-Min Lee, Jung Yeol Kim, Byungjoon Min, Jeehye Choi, Charlie Brummitt, and In-mook Kim.

Cascade Dynamics on Multiplex Networks

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Most of real world complex system such as the modern infrastructure, human society, cellular network, human brain network, and global economic system contain various types of interactions between individual agents. How these multiple types of relations affect the vulnerability to the system remains poorly understood yet vitally important. Here we investigate the extended Watts threshold cascade model in multiplex networks with a mixture of two response functions: OR and AND model. In OR model, each node's activates if enough neighbors in any layer are active. This model shows the facilitation of global cascades. In contrast, the AND model gives each node's activation only if enough neighbors in all layers are active, so that cascades are significantly inhibited. Interpolating between these two extremes shows a cusp catastrophe. These results suggest fundamental limitations to predict cascades without full knowledge of a system's multiplexity.

Poster Session Abstracts

Pos-1	Fushiki et al	Identification and functional analysis of a class of local GABAergic interneurons in the *Drosophila* larval motor circuits
Pos-2	J. Y. Kim et al	Correlated multiplexity in coevolving multiplex networks
Pos-3	Kinoshita et al	Power Stroke Measurement of Human Cytoplasmic Dynein
Pos-4	B. Jeong et al	The coexistence of “heterogeneity” and “coherence” in the phase distribution of clock cell populations in SCN
Pos-5	kawaguchi et al	Integral fluctuation theorem in the presence of hidden entropy production
Pos-6	J. Choi et al	Majority-Vote Model on Multiplex Networks
Pos-7	Nishiguchi et al	Self-Propelling Motions of Asymmetrical Colloidal Particles induced by AC electric field
Pos-8	J. H. Kim et al	Transitions among multiple burst-oscillators in cultured neural networks
Pos-9	Yamamoto et al	The Observation of Lehmann Rotation of Cholesteric Droplets under Temperature Gradient as an Effect of Thermo-mechanical Coupling
Pos-10	H.-J. Lee et al	The evolution of synaptic weight distribution of a model neuronal network subject to a “Dt stimulation”
Pos-11	Itakura et al	Identification and functional analyses of interneurons in the neural network that regulates the peristaltic locomotion of *Drosophila* larvae
Pos-12	S. E. Kim et al	A single-molecule investigation of the i-motif structure
Pos-13	Hirayama et al	Extracting Work from an Isothermal Cycle: Experimental Verification of the Generallized Jarzynski Equality
Pos-14	B. Min et al	Epidemic Spreading on Multiplex Networks
Pos-15	Wu et al	Polymer-induced entropic effects on mechanical properties and domain separation of biomembranes
Pos-16	T. G. Kwon et al	Trail Networks Formed by Populations of Immune Cells
Pos-17	Matsui et al	Heat Transfer Characteristics on Nucleate Boiling in Two-Phase Rayleigh Benard Convection
Pos-18	T. D. Yang	Waves of ratcheting cancer cells in proliferating tumor layer
Pos-19	Otomura et al	The Shear Stress increase by Interaction-Induced Forces in a Non-Brownian Suspension
Pos-20	S. H. Kim et al	The B-Z transition of the sequence with TG repeats: a mechanical study
Pos-21	Y. Yoon et al	4D calcium imaging of central neurons in *Drosophila* larvae
Pos-22	D. Kim et al	Fluorescence Endomicroscopy using a Single Multimode Fiber
Pos-23	S. Lee et al	The Pattern of Vesicle Movement in Cytoplasm
Pos-24	J.-I. Sohn	The Fluctuation Theorems in Three Different Time Scales

Identification and functional analysis of a class of local GABAergic interneurons in the *Drosophila* larval motor circuits

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The balance between excitatory and inhibitory neurons is believed to be critical for rhythmic animal movements. Yet, little is known about the mechanisms of how excitatory and inhibitory neurons interact to generate appropriate motor outputs in the developing and mature nervous system. We are trying to address this question using the motor circuits of *Drosophila* larvae as a model. By using GAL4/UAS system and GCaMP-based calcium imaging, we identified a class of GABAergic interneurons that show propagating activity patterns corresponding to the wave of muscle contractions during larval locomotion. These neurons are segmentally repeated (one neuron per hemisegment) and are located in the dorsolateral areas of the ventral nerve cord. Channelrhodopsin-2 (ChR2)-mediated activation of these neurons in the 3rd instar larvae induced acute paralysis of muscles in the abdominal segments and ceased locomotion, suggesting that these neurons act to inhibit motor outputs. When we blocked their neurotransmitter release throughout embryonic and larval periods by expression of tetanus toxin light chain (TeTxLc), the larval locomotion was severely defected: there was a dramatic decrease in the frequency and speed of peristalsis. In contrast, acute inhibition with halorhodopsin (NpHR) or archaerhodopsin (Arch) in the 3rd instar larvae did not alter the mobility of larvae. These results may suggest that the activity of these neurons is essential during the development and/or maintenance of the neural circuits that generate appropriate larval locomotion. To further pursue this possibility, we are currently studying the effects of temporal inhibition of these neurons in specific stages of embryonic and larval life. We are also trying to identify upstream and downstream neurons by reconstruction from electron microscope (EM) image data (in collaboration with Dr. Albert Cardona in Janelia Farm Research Campus).

Acknowledgements

Global COE Program "the Physical Sciences Frontier", MEXT, Japan

Correlated multiplexity in coevolving multiplex networks

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Nodes in a complex networked system often engage in multiple types of interactions among them; they form a multiplex network with multiple layers that can be interdependent and co-evolve. In many real-world complex systems, such multiple network layers are not randomly coupled but correlated. Such a correlated multiplexity can imprint nontrivial structural correlations in the multiplex network, which in turn can impact the dynamical processes on it. Here, we introduce an evolution model of co-evolving multiplex networks by generalizing the well-known Barabási-Albert- type model, to show how the co-evolution of network layers can induce and modulate the degree of correlated multiplexity.

Power Stroke Measurement of Human Cytoplasmic Dynein

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Cytoplasmic dynein is a motor protein moving along microtubules toward the minus-end, and plays an important role in many cellular processes such as intracellular transport and cell division in eukaryotic cells. It was reported that dynein moves continuously along microtubule and takes 8-32 nm steps. Cytoplasmic dynein might move along microtubule by dynein's head which was imaged under electron microscope without microtubules. However, nobody detected the conformational change bound microtubule under physiological condition. Therefore, we are interested in the detection of the conformational change of dynein head in the condition. We choose recombinant motor domain of mammalian (human) dynein to investigate the conformational change because information of motor functions in cells was accumulated by mammalian cell works. Taken together, my object is to find out the motion mechanism by which human recombinant dynein changes its conformation with generating force after hydrolyzing ATP.

In this study, we are developing optical tweezers to measure the power stroke distance of single molecule of dynein. Fig.1 is our experimental design: the beads coated with inactive kinesin are trapped by laser and then bound to both ends of microtubule via the kinesin. The microtubule interacts with dynein fixed on a cover slip. Finally, we measure the change of trapped bead position by a quadrant photodiode, which is equal to dynein's power stroke distance.

We expressed human cytoplasmic dynein using baculovirus expression system. In motility assay, the velocity of microtubule with multiple dynein is around 600nm/s and Michaelis-Menten constant is ~140μM at 26℃. This result means that purified dynein remains its motor activity. I also purified inactive mutant recombinant kinesin. The mutant kinesin tightly bound to microtubule independent of states in ATPase and doesn't move microtubules in motility assay. However, biotin-rate of kinesin is so low that I'm now purifying higher biotin-rate kinesin. After confirming the binding of beads, kinesin and microtubule, I measure the power stroke distance.

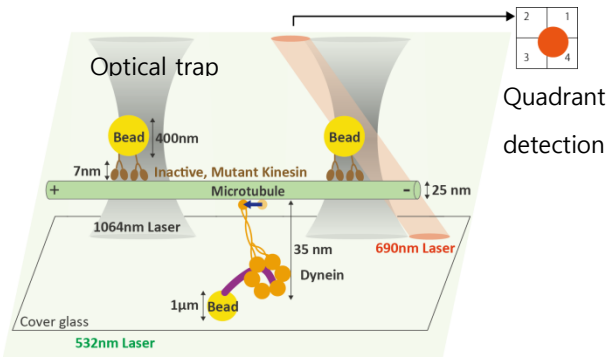

Fig.1. The schematic drawing of measuring the power stroke distance

The coexistence of “heterogeneity” and “coherence” in the phase distribution of clock cell populations in SCN

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Suprachiasmatic nucleus (SCN) is the master clock keeping an endogenous circadian rhythm for mammals. As a SCN nucleus is composed of multiple oscillators, clock cells, that are quite heterogeneous in their intrinsic periods (20 ~ 28 hr), a natural question to ask is how well they are ‘frequency-locked’ to each other and what is their phase distribution like in space. Are they phase-synchronized? Earlier investigations, based on luciferase imaging of clock-genes (eg. per-1, per-2, Bmal) as well as in situ hybridization images of peptides such as VIP, unanimously suggest that the clock cells in an intact SCN support macroscopic phase waves, although their features vary significantly from one case to the others. On the other hand, our recent experimental investigation [1], which monitored the concentration of cytosolic free calcium, showed that the phases of individual clock cells were distributed very randomly. Subsequently, we hypothesized that the difference in the imaging techniques, in particular, different spatial resolutions and the way a SCN nucleus is anatomically structured could attribute to the seemingly conflicting results -- namely, ‘coherent macroscopic phase wave’ vs. ‘random phase distribution.’ In this work, with a dual imaging of Per-2 luminescence and Ca2+ sensing cameleon FRET signal of organotypic SCN slice cultures of mice, we explicitly demonstrate that SCN nucleus is structured such that the phases of individual cells vary widely at the resolution of a single cell, while their mean (over a distance of 10 ~ 100 cell length) phase field supports a coherent progression. In addition, we show that upon an extrinsic stimulation of temperature shock the degree of phase shift varies widely from one cell to the others, even in a coupled intact network.

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Integral fluctuation theorem in the presence of hidden entropy production

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In the general process of eliminating dynamic variables in Markovian models, there exists a difference in the value of irreversible entropy production between the original and reduced dynamics. We call this difference the hidden entropy production [1,2], since it is an invisible quantity when only the reduced system's view is provided. Understanding the behavior of such hidden entropy is important for example in discussing the efficiency of Brownian heat engines [3,4], and more generally the origin of the arrow of time. We show that this hidden entropy production obeys a new integral fluctuation theorem under a certain condition, therefore supporting the intuition that entropy production should decrease by coarse-graining. It is found, however, that in cases where the condition for our theorem does not hold, entropy production may also increase due to the reduction. Explicit examples for both scenarios will be discussed.

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Majority-Vote Model on Multiplex Networks

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The majority-vote model is a simple rule to describe social networks with two opposite opinions. To expand our understanding for social communities we study this model on multiplex networks which is distingushing several type of connections and their communities. On the multiplex networks we will consider two dynamics which is called AND- and OR- rule. The difference between two models is that a agent takes into account two different local networks with entirety or probability. More specifically the AND-model has the flip probability when majorities of all communities are the same while the OR-model has 1/n flipping chance every time where n is the given networks. How global consensus reaches on the multiplex networks and what different microscopic origins is working with the normal, AND- , and OR- rules. We also discuss the critical ph
enomena and numerical solutions using the pair approximations.

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[2] James P. Gleeson, arXiv:1209.2983, (2012).

Self-Propelling Motions of Asymmetrical Colloidal Particles induced by AC electric field

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Asymmetrical colloidal particles (called 'Janus particles') made by polystyrene with half side coated with gold exhibit self-propelling motion under AC electric field. Under high frequency AC field (~400kHz), the difference of the permittivity of the both hemispheres causes the attractive force between particles due to the induced quadrupole. This makes some interesting colloidal complexes such as doublets, triplets and snake-like structures shown in photos below.

In the previous study [1], the power of the self-propelling force and its dependence on the intensity of the electric field were evaluated by using Janus doublets. Some Janus doublets whose particles of one side was attached to the surface of the glass substrate show rotational motion and this enabled measuring the motion for a long time without going out of view. These experiments have verified the theory that the self-propelling force is proportional to the amplitude of the electric field squared. However, this kind of Janus doublet is hard to deal with because one side is attached on the glass and the effect of wall must be taken into consideration.

Here we analyzed the motions and the fluctuations of these complexes besides doublets. The Janus triplets have a favorable feature that they do not attached to the surface in spite of showing rotational motion. The snake-like structures exhibit propagating wave on their body. To understand these behaviors, the correlations of the motions of particles in the same complex were analyzed and we evaluated how these correlations depend on the intensity of the electric field.

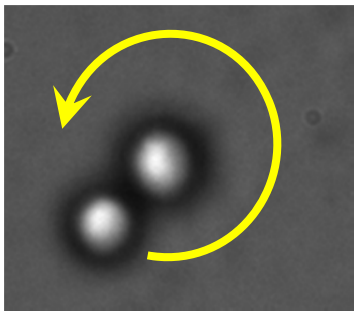

Fig.1. rotating Janus doublet.

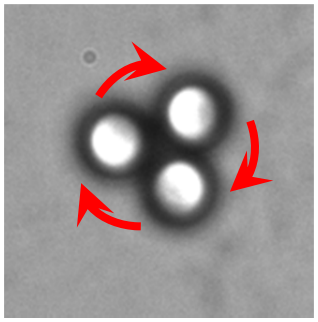

Fig.2. rotating Janus triplet.

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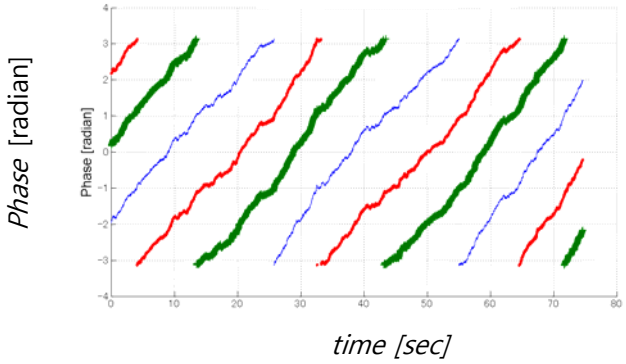

Fig.3. rotation of each particle in a triplet.

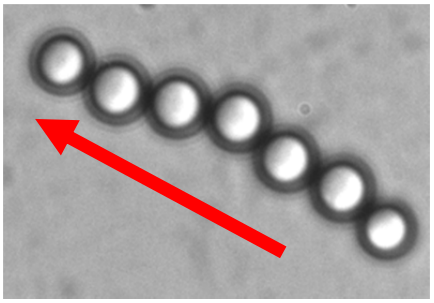

Fig.3. snake-like structure.

[1] R. Suzuki, H. R. Jiang, M. Sano arXiv:1104.5607 (2011)

Transitions among multiple burst-oscillators in cultured neural networks

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Synchronized neural bursts are a salient dynamic feature of biological neural networks, having important roles in brain functions. This study investigates the deterministic nature behind seemingly random temporal sequences of inter-burst-intervals generated by cultured networks of cortical cells. We found that the complex sequences were an intricate patch work of several noisy 'burst oscillators,' whose periods covered a wide dynamic range, from few tens of milliseconds to tens of seconds. The transition from one type of oscillator to the other favored a particular passage, while the dwelling time between two neighboring transitions followed a Poisson statistics. With different amounts of bicuculline application, we can tune the periods of the oscillations, terminate some of them, or generate new ones.

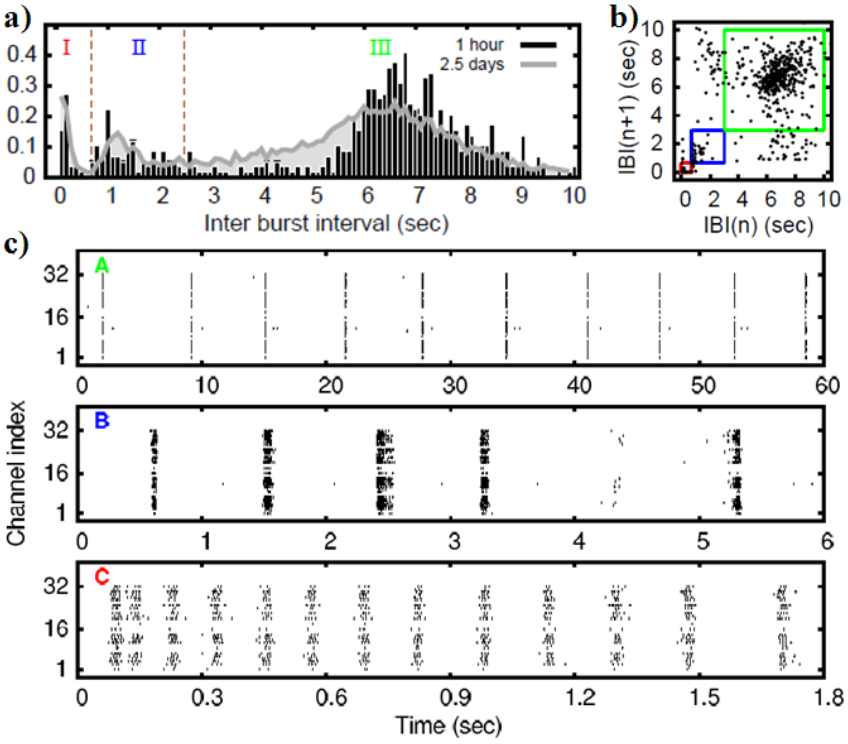

Fig.1. Three different SB oscillators (a) The IBI histogram of 1-hr SB time series (black) and that of 2.5 days SB time series (grey, based on 11 sets of 1-hr time series recorded every 6-hr). The labels I, II and III mark the different ranges of periods for the three different noisy oscillators, C, B, and A, respectively in (c). (b) An IBI return map of 1-hr time series; same time series with black bars in (a)

Acknowledgments
This work was supported by the National Research Foundation of Korea (NRF) grant funded by the Korea government (MEST) (No. 2012R1A2A1A01008021).

The Observation of Lehmann Rotation of Cholesteric Droplets under Temperature Gradient as an Effect of Thermo-mechanical Coupling

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The cholesteric liquid crystal is one of the liquid crystal phases which consists of chiral molecules and has helical structure. Due to its structural chirality, it is reported that cholesteric liquid crystal has some significant characteristics such as selective reflection and circular polarization of light in equilibrium state. In contrast to these characteristics in equilibrium state, behaviors of cholesteric liquid crystal in non-equilibrium state have been less understood.

As for behavior under non-equilibrium condition, in 1900, O. Lehmann observed the rotation of the texture of cholesteric liquid crystal when heated from below [1]. After his first observation, F. M. Leslie explained the rotation of the texture, which is now called "Lehmann rotation", by considering the thermo-mechanical coupling due to the chiral nature of cholesteric liquid crystal phase [2]. However, it is still under discussion whether the phenomenological transfer coefficient of thermo-mechanical coupling, which is called "Lehmann coefficient", is determined by molecular chirality ('microscopic') or helical structure ("macroscopic"). To answer this unsolved problem, we subjected the cholesteric liquid crystal to temperature gradient (Fig. 1) and observed the rotation of the texture of cholesteric liquid crystal. Although the rotation of cholesteric droplets with banded texture in coexisting region (isotropic phase and liquid crystal phase) has been already reported in the liquid crystal cell with sliding and planar anchoring (Fig. 2) [3], we observed the rotation of the cholesteric droplets with the texture shown in Fig. 3 under homeotropic anchoring condition. In the poster session, we will discuss this rotation of cholesteric droplets in homeotropic anchoring condition.

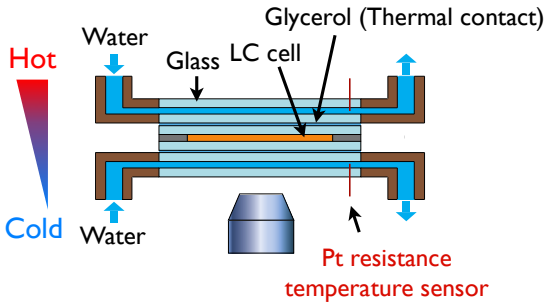

Fig. 1 Experimental setup for the observation of Lehmann rotation.

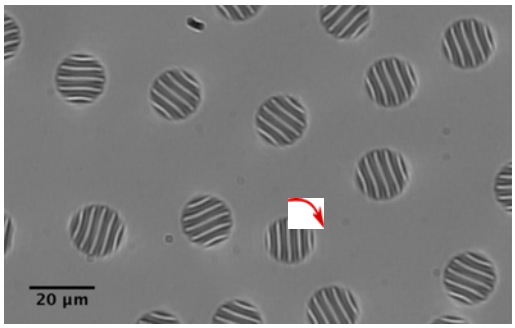

Fig. 2 Rotation of the cholesteric droplets under temperature gradient with sliding and planar anchoring.

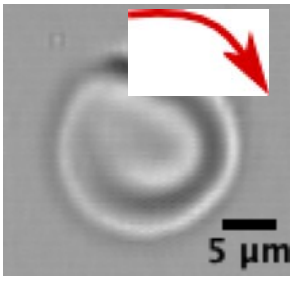

Fig. 3 Rotation of the cholesteric droplet under temperature gradient with homeotropic anchoring.

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The evolution of synaptic weight distribution of a model neuronal network subject to a "Δt stimulation"

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"Spike-timing dependent plasticity (STDP)" is perhaps the most noble concept as for the learning mechanism of biological neural systems[1]. Its inception was originally based on a system of only two neurons. Generalizing the original STDP concept, one can imagine various repeated spatiotemporal patterns of spikes and their impacts on the distribution of synaptic weights in large populations of neurons. Earlier, with in vitro neuronal cell cultures we demonstrated that "Δt stimulation," a repeated sequence of paired electrical pulses delivered to two different groups of neurons with a Δt time delay, could bring some significant changes to the fidelity of the timing of "synchronized burst oscillations[2]. Interestingly, the changes (or responses) were significant only for some particular values of Δt, and we believed that they were caused by the transformation of synaptic weight landscape. In this report, we discuss why the responses are significant only for some particular values of Δt. Namely, we discuss how the effective values of Δt depend on the shape of STDP curve as well as the choice of two stimulated groups of cells.

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Acknowledgments
This work was supported by the National Research Foundation of Korea grant funded by the Korean government (2012R1A2A1A01008021).

Identification and functional analyses of interneurons in the neural network that regulates the peristaltic locomotion of *Drosophila* larvae

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Muscles, motoneurons, central neurons, and peripheral sensory neurons all have distinct important functions in coordinating locomotion. Whereas muscles, motoneurons and sensory neurons are well investigated, far less is known about interneurons that generate motor patterns. We use the *Drosophila* motor circuit underlying larval crawling as a model to identify such interneurons and try to elucidate the operational principle of the motor circuits.

Here we identified small subsets of interneurons and found that forced inhibition of these neurons with temperature sensitive Shibire slowed the propagation of muscle contraction during crawling. In contrast, artificial activation of these interneurons, by the use of *Drosophila* TRPA1 or channel rhodopsin-2, temperature or light-sensitive cation channel, impaired the locomotion. These observations suggest that the interneurons are involved in crawling locomotion. They include two characteristic types of glutamatergic interneurons, both of which might synapse on motoneurons. According to previous reports, the neurotransmitter glutamate has inhibitory effects on motoneurons. In order to clarify their involvements and furthermore to predict the functions in crawling behavior, we next performed calcium imaging and observed their notable activity patterns. One class showed a wave-like activity at timing slightly subsequent to motoneurons, and the other class became active at once along the neuromeres, at timing close to the initiation of a motor wave. The activities of the two interneurons and motoneurons showed time-correlations.

Taken together, we identified two types of interneurons involved in peristaltic locomotor circuit, which might control motoneuronal activity by providing inhibitory inputs. A unique feature of the identified interneurons is that they exhibit activities at a different phase during the motor cycle from motoneurons.

A single-molecule investigation of the i-motif structure

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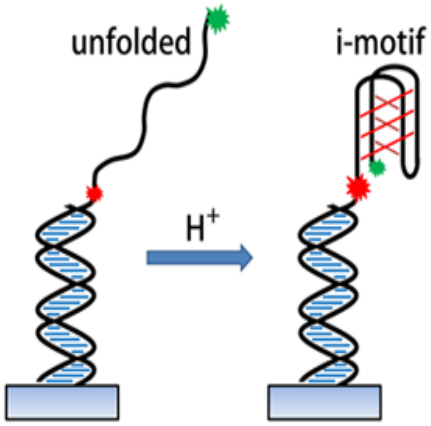
In the end of human chromosome, a special DNA sequence (5'-TAACCC-3') is frequently found and thought to play important roles in protecting its terminal from nucleases. The cytosine-rich sequence was known to form a folded quadruplex structure named i-motif. It has been shown that the i-motif structure can be formed in acidic condtions and further stabilized by the presence of monovalent cation.
In order to examine the nano-scale conformational transition of the cytosine-rich sequence and the effect of the aforementioned chemical factors on the transition at the molecular level, we utilized the single-molecule FRET technique. Based on the well-resolved FRET efficiency values, we clearly distinguished the folded i-motif structure from unfolded extended forms and were able to construct the population of the two states under various chemical conditions such as pH from 6.0 to 6.4 and concentrations of three different cations (Li^+, Na^+, and K^+) ranging from ~ 30 mM to 500 mM. We found that the i-motif structure is more easily formed in lower pH conditions while the sequence remains unfolded at a weak acidic condition (pH = 6.4). Surprisingly, Li+ appears to be inhibitory to the formation of i-motif, which is in sharp contrast with other physiological monovalent cations. We discuss a possible physico-chemical principle behind the phenomena. In summary, we gain insight into the formation of the i-motif structure and demonstrate that single-molecule FRET technique is a versatile tool to investigate nano-scale conformational transition occurring to non-canonical DNA structures.



This work is supported by mid-career research program (NRF 2010 00 10594).

Extracting Work from an Isothermal Cycle: Experimental Verification of the Generalized Jarzynski Equality

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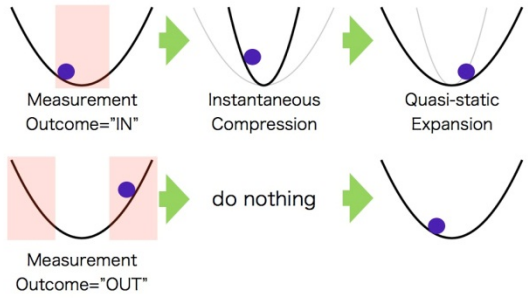
The second law of thermodynamics prohibits cyclic extraction of work from a single heat bath. In an isothermal process between two equilibirm states, the work which can be extracted from (must be exerted on) the system is at most (at least) the free energy difference. However, it is known that one can extract work beyond the limit of the conventional second law by performing measurement and feedback control[1-4]. The source of the extracted work is considered to be the information obtained by the measurement. In this study, we experimentally realized such an ”information-to-heat” engine in a microscopic classical system: A colloidal particle trapped by optical tweezers plays the roll of gas contained in a cylinder in the macroscopic counterpart. By modulating the potential landscape depending on its position (Figure 1), we have succeeded in extracting positive work from an isothermal cycle. Also we tested a recently discovered non-equilibrium relation[2-4], which is a generalized version of the Jarzynski equality[5] to a situation where feedback control is adopted.

Figure 1



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Epidemic Spreading on Multiplex Networks

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We study a model of disease spreading or information diffusion on multiplex social networks, in which the transmissibility over a contact is dynamically determined dependent on incoming and outgoing infection channels (layers). We formulate a generalized theory with a novel mapping to deal with such a path-dependent transmissibility, and demonstrate that network multiplexity can bring about non-additive and non-monotonic effects in spreading dynamics. Our results suggest that explicit consideration of multiplexity can be crucial in realistic modeling of spreading processes on social networks in an era of ever-diversifying social interaction layers.

Polymer-induced entropic effects on mechanical properties and domain separation of biomembranes

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A coarse-grained biomembrane model is proposed to study the entropic effect on lipid domain separation on cell membrane. In our ternary membrane system, three states during domain transition are classified according to different grafting polymer density. It is found that a dendritic pattern is formed at critical polymer density. This structure is a basic unit for the intermediate state observed in experiments (M. Yanagisawa *et. al.*, Soft Matter, 2012, **8**, 488).

Microdomains, called lipid rafts, on the surface of cell membrane have been one of the hot topics in the biophysics since it was found [1,2]. To understand the formation of lipid rafts, some micrometer circular domains have been created and observed in artificial multicomponent membrane system [3-5]. But recently M. Yanagisawa *et. al.* [6] confirmed that non-circular domains can merge experimentally and segregation can be triggered by increasing the fraction of PEG lipids.

We applied a coarse-grained MD simulation by using meshless membrane model [7] and measured the interfacial tension (shown in Fig. 1) between two domains.

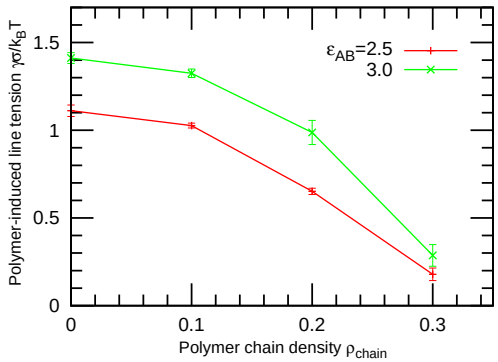

Fig.1. Interfacial tension can be reduced by increasing anchored polymer chain density.

We found that microdomain separation can be driven by grafting a high polymer chain density (shown in Fig. 2). These phenomena were also verified by a recent experiment [6]. A dendritic intermediate state was found in membranes consisting of DOPC, DPPC, cholesterol and PEG-cholesterol.

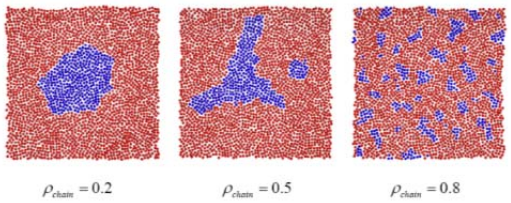

Fig.2. Microdomain separation is driven by increasing anchored polymer chain density.

Our results show that the entropic effect caused by anchored polymers plays a crucial role in the scenery of microdomain separation. This effect also likely has important contributions on cell membranes and artificial multicomponent fluid membranes. The anchored polymer density changes the interfacial tension between two domains so that the pattern shape of domain and the boundary length can change accordingly.

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Acknowledgments

H.W. acknowledges the support by a MEXT scholarship (Japan).

Trail Networks Formed by Populations of Immune Cells

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Populations of biological cells that communicate with each other, can self-organize to generatelarge-scale patterns. Examples can be found in diverse systems, ranging from developing embryos, cardiac tissues, chemotaxing amoeba and swirling bacteria. The similarity, often shared by the patterns, suggests the existence of some general governing principle. On the other hand, rich diversity and system-specific properties are exhibited, depending on the type of the involved cells and the nature of their interactions. The study on the similarity and diversity constitutes a rapidly growing field of research. Here, a new class of self-organized patterns of cell populations that we term as “cellular trail networks” is reported. The exquisite patterns, very similar to highway networks of automobiles, were observed with populations of rat microglia, the immune cells of the brain. The essential features of the observed patterns were well captured by mathematical model cells that actively crawl and interact with each other through a chemical attractant released by themselves. Our finding suggests a mechanism of socially cooperative and efficient traffic for the crawling immune cells.

Acknowledgments
This work was supported by the National research Foundation of Korea grant funded by the Korean government (2012R1A2A1A01008021).
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Heat Transfer Characteristics on Nucleate Boiling in Two-Phase Rayleigh Benard Convection

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Rayleigh Benard Convection (RBC) system is a typical research subject focused on out of equilibrium or nonlinear physics. One of the recurrent topics in RBC is to reveal the heat transfer mechanism [1], however, the interest of most previous studies on RBC is limited to single phase systems without distinction of theoritical or experimental works.

In this experimental study, we investigated the boiling heat transfer characteristics in gas-liquid two-pahse RBC with pure water as the working fluid. When the applied temperature difference ΔT is sufficiently large, boiling and condensation occured. At the nucleate boiling regime [2], the heat flux transported by bubble nucleation and growth through cavities on the heating surface sensitively depends on the surface condition of the heating surface. Therefore the temperature fluctuation due to the latent heat is strongly localized and causes temperature heterogeneity on the heating surface. We introduced eight thermistors into the heating unit of the experimental setup to measure the local temperature of the heating surface Tb_i with sampling frequency 0.2 Hz. Thus the heterogeneity Wb was defined by Eq. 1. We consider that the boiling state is characterized by Wb, which leads to intermittency and enhances the heat transfer efficiency.

In Fig. 1, we plotted the probability distribution of Wb which clearly showed bimodal. We binarized Wb time series with threshold $Wb_c=2.35*10^{-4}$ and defined the boiling state as follows: enhanced boiling state for $Wb >= Wb_c$ and week boiling state for $Wb< Wb_c$ respectively. We found that the cumulative probability distribution of the persistent time of enhanced boiling state decayed with exponent -5/4 as in Fig. 2. The persistent time is relevant to the magnitude of the enhanced boiling. We consider that this power low decay in Fig. 2 is analogously interpreted as models discussed in terms of self-organized criticality.

$$Wb = \frac{(\sum_i^8 Tb_i^{\,2} - \langle Tb \rangle_i^{\,2})^{1/2}}{\langle Tb \rangle_i} \qquad (1)$$

Here,

$$\langle Tb \rangle_i = \frac{1}{8}\sum_i^8 Tb_i \qquad (2)$$

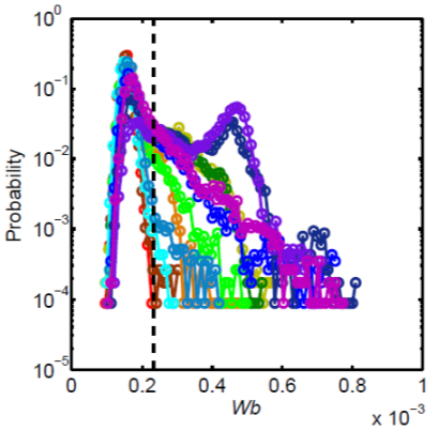

FIG. 1. The probability distribution of Wb. Time elapse is represented as color (red to purple). Dashed line indicates Wb_c.

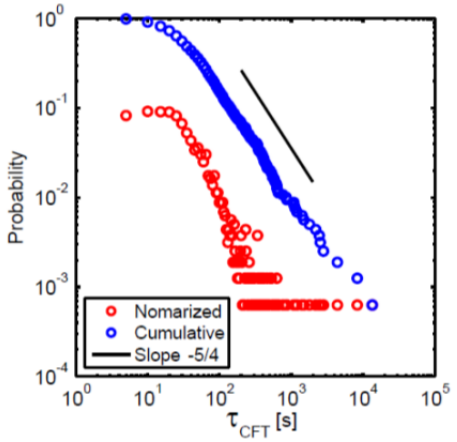

FIG. 2. The probability distribution of the persistent time of enhanced boiling state (τ_{CFT}). The cumulative probability decayed with exponent -5/4 at τ_{CFT}>100 sec.

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Waves of ratcheting cancer cells in proliferating tumor layer

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Over many years researchers have shown that the mechanical forces generated by, and acting on, tissues influence the way they grow, develop and migrate. As for cancer research goes, understanding the role of these forces may even be as influential as deciphering the relevant genetic and molecular basis. Often the key issues in the field of cancer mechanics are to understand the interplay of mechanics and chemistry. In this poster, we discuss very intriguing population density waves observed in slowly proliferating of tumor cell layers. The temporal periods are around 4 hr and their wavelength (or spatial correlation length) is in the order of 1 mm. Tumor cell layer, which is initially plated in a small (diameter ~2 mm) disk area, expands as a band of tumor cells is "ratcheting" in concert in radially outward direction. By adding different doses of Cytochalasin D, an inhibitor of actin polymerization, or Mytomycin, a chemotherapeutic agent, we could halt and modulate the wave activities reversibly. The observed waves are visually quite similar to those of chemotaxing dictyostelium discodium amoeba population, which are driven by nonlinear chemical reaction-diffusion waves of cAMP. So far, we have not been able to show any relevant chemo-attractants inducing the collective behavior of these tumor cells. On the other hand, we could reproduce some essential features of the observed tumor waves with a purely mechanical model of coupled nonlinear cells. The key elements were nonlinear elasticity of model cells, their self-propulsion and the friction with substrate. Researchers have been investigating how forces from both within and outside developing cancer cells interact in intricate feedback loops. This work reports the first example of periodic density waves of tumor cells with an explanation purely based on nonlinear mechanics.

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Acknowledgments
This work was supported by the National Research Foundation of Korea grant funded by the Korean government (2012R1A2A1A01008021).

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The Shear Stress increase by Interaction-Induced Forces in a Non-Brownian Suspension

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Non-Brownian particles in a low Reynolds number fluid show a non-equilibrium phase transition, which called Absorbing Phase Transition, when the periodically shear stress is applied. And the viscoelastic property of this suspension behaves as the order parameter of this transition. Here, we suggest that the model for the viscoelasticity of suspension and discuss the relation between this transition and viscoelasticity of non-Brownian suspension.

The flow of a Newtonian fluid at low Reynolds number (Re) shows a reversible behavior when periodic shear is applied. However, when we add the non-Brownian particles i.e., the particles with enough large size not to be affected by thermal fluctuation, the orbits of the particles are not necessarily reversible. One of steady states is the all particles shows the reversible orbits, another is the particles with irreversible orbits remain at some proportion. The suspension with a fixed volume fraction ϕ goes into the irreversible steady state when we apply the shear with its shear amplitude γ_0 above threshold amplitude γ_c. On the other hand, if the shear amplitude γ_0 is below γ_c, the suspension finally goes into totally reversible state. And this steady state transition is considered as a kind of phase transition, absorbing phase transition (APT)[1,2].

The order parameter of this APT should reflect on the particles orbits. One of the well-defined order parameter is the stroboscopic-measured mean square displacement (MSD) of particles per cycle. However, there are some reports that the elastic (imaginary) component η'' of complex viscosity $\eta^* = \eta' + i\eta''$ of suspension shows the same dynamics as MSD per cycle [2,3]. Notice that fluid itself is the Newtonian fluid, so fluid never shows elastic property without particle. Therefore, particles should be the source of this elastic property of suspension, but the mechanism of this elastic behavior is not clear.

In this presentation, we suggests that a model for considering the suspension rheology. In the shear flow, particles may collide with each other, and this collision is the source of the irreversible orbits. Fig.1 shows the configuration of the typical collision in the Couette cell, looks from top of the cylinder gap. The basic idea of the model is that 1) the angles of collision-derive forces are always the direction such that they disturb the wall motion, and 2) these angles tend to have a correlation each other. If that is true, the shear stress should be increased, so the suspension shows a greater value of viscosity when there are many irreversible particles. To check this idea, we had a numerical simulation in 2-dimensional plane. In this simulation, the particles are governed by overdumped equation, and interactions between particles are Lennard-Jones potential with cut-off. Fig.2 is the histogram of the distribution of the collision angle. This histogram shows there are 4 peaks of angle and the directions is the direction preventing motion of the shear flow, which we expected. Such a correlation in angle of force direction can be the source of the viscoelasticity [4]. In the poster presentation, we discuss about how these correlated force yields the elastic force.

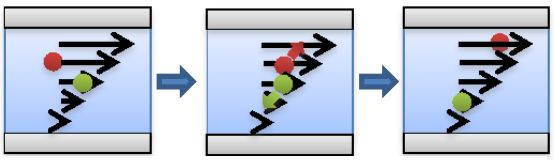

Fig.1. the configuration of a typical collision

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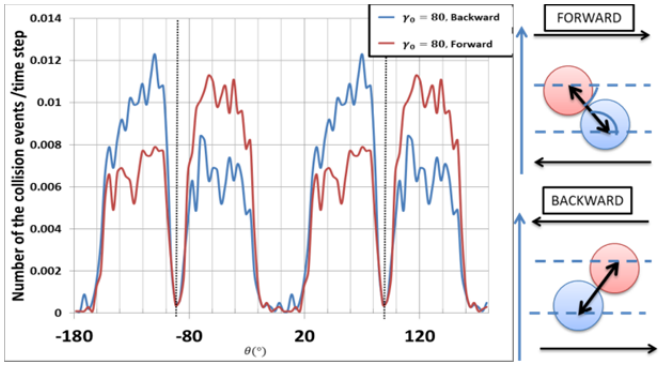

Fig.2 [left] Histogram of the collision angle per time step. [right] Schematic image of collision versus shear direction.

The B-Z transition of the sequence with TG repeats: a mechanical study

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Although Z-DNA, the left-handed DNA, is an unstable state in comparison with B-DNA, Z-DNA exists stably under certain conditions such as high salt concentrations or negative supercoiling. In biological systems, potential Z-DNA-forming sequences are located near the promoter region of many genes and are thought to play a role in transcription initiation. Recently we studied the B-Z transition in a short d(GC/GC)n repeats in the presence of controlled tension and superhelicity via a hybrid technique of single-molecule FRET and magnetic tweezers[1]. In fact, another Z-DNA-forming sequence, d(CA/TG)n, is more frequently and widely found in eukaryotic genome and believed to have more important biological functions although the B-Z transition in that sequence is much less studied.

Here, we examined the B-Z transition of the TG repeat sequence using the hybrid method from the mechanistic viewpoints. We found that negative supercoiling is more effective in inducing the Z-conformation than high salt concentrations. Even at room temperature, the sequence undergoes dynamic inter-conversion between the two states permitting direct determination of kinetic constants and implying smaller energy barrier between the states. Compared to the GC repeat, TG repeats required more torsional energy to trigger the transition and the repeat length dependence of the critical superhelicity provides quantitative information about the transition. In summary, this study provides the biophysical details of the transition and also demonstrates that physical factors such as tension and torsion play critical roles in biological phenomena.

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This work is supported by mid-career research program (NRF 2010 00 10594).

4D calcium imaging of central neurons in *Drosophila* larvae

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To fully understand how the neurons interact with each other, it is necessary to obtain the information about the activities of the entire population of neurons in the system. With conventional microscopy, one can only obtain the spatio-temporal pattern of neural activity in one plane. The neural circuitry, however, is distributed in a 3-dimensional space. In this study, we used a high-speed Piezo Z stage to monitor in real time the activity of neurons in a 3-dimension space. In this presentation, we introduce the experimental system and an application to study the activity of multiple motor neurons (MNs) in the central nervous system (CNS) of *Drosophila* (fruit fly) larvae.

We used the 4D calcium imaging method to probe neural activities in *Drosophila* larval CNS. When a neuron bursts, the concentration of the calcium ion increases in the neuron. One can therefore measure the activities of a neuron indirectly with the fluorescence changes of a calcium indicator. In this study, we used the genetically encoded calcium indicator GCaMP5, which emits fluorescence when a calcium ion binds to the protein. Because *Drosophila* is a genetically tractable organism, one can target the expression of GCaMP5 to specific neurons, including MNs.

After dissecting the larvae, we recorded MN activities that occur when the larvae undergo peristalsis. We successfully obtained 4D images that included the information on the fluorescent change in a population of MNs. To test the validity of the experimental system, we compared the timings of the activity of MNs innervating dorsal muscles (dorsal MNs) and of those innervating lateral muscles (lateral MNs). A previous study showed that lateral muscles contract after dorsal muscles in the same segment with a delay corresponding to the motor wave propagation along one segment. We confirmed this tendency in the activity of MNs (Figure 1).

In this experiment, we only compared two subpopulations of motor neuron. We plan to apply this method to record activities of a larger population of neurons, including interneurons.

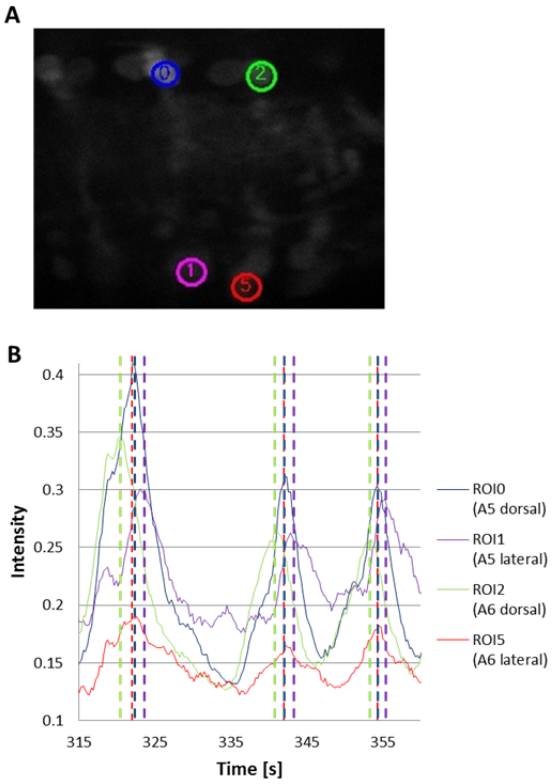

Figure 1 The delay of burst-timing between dorsal motor neurons and lateral motor neurons

(A) A image of the 4D calcium imaging method. To compare the burst-timing, we measured fluorescent change in the ROI (region of interest) corresponding to dorsal MNs and lateral MNs (colored circles). (B) There was a significant delay (almost equal to the time for the locomotion wave to propagate along one segment) between activity of the dorsal and lateral MNs.

Fluorescence Endomicroscopy using a Single Multimode Fiber

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A multimode optical fiber has drawn interest because numerous independent spatial modes can be used for parallel information transport. Recently, we have shown that a single multimode optical fiber can be used as an endoscopic imaging tool by the use of the input-output response of the fiber [1]. However, the transported parallel information is distinguishable only when the reflected light waves are spatially coherent. Since the fluorescence image information is spatially incoherent, a different approach is required for the fluorescence endoscopy. In this paper, the methods for the fluorescence endomicroscopy using a single multimode fiber will be presented.

Endoscopy has become a widely used tool for industrial, military, and medical purposes because of its ability to visualize otherwise inaccessible structures. In recent years, the demand has been grown for the endoscopy with high spatial resolution due to the necessity of visualizing subcellular structures. This is important in particular for the accurate identification of the disease states in the suspicious regions. To meet this need, two different approaches – use of a fiber bundle or a single-mode fiber with a mechanical scanner attached to the tip of the fiber have been used. However, the size of the imaging units in these approaches is rather large because the fiber bundle is composed of a large number of single fibers for the one case and the dimension of the mechanical scanner is much large than the fiber core diameter itself for the other case. To be the least invasive, it will be desirable to have the probe size to its fundamental limit, which can be the core diameter of a single fiber.

In a recent study, we have demonstrated that the endoscopic imaging can be made possible by using a single multimode optical fiber. The image information is delivered through multiple propagating modes supported by the fiber. Since the mode density of the single multimode fiber is higher than the pixel density of the fiber bundle by two or three orders of magnitude, the diameter of the imaging unit can be reduced at least more than tenfold. But this method has been applicable only to the reflectance imaging of the specimen, and its use for the fluorescence imaging has been limited due to the necessity of the spatial coherence of the signal wave.

In this talk, we present a new single-fiber endomicroscopy technique that can acquire a fluorescence image, as well as a reflectance image, of a specimen. I have used a digital micromirror device (DMD) as a high-speed spatial light modulator, and recorded transmission properties of a multimode fiber. From this measurement, a proper shape of incident wave that would generate a focused spot at the opposite side of the fiber was found and then subsequently generated by the same DMD. By scanning the focused spot with the use of different shapes of the incident wave, fluorescence signal at each spot in the specimen was excited and then collected by the same fiber. In this way, we could obtain high-resolution fluorescence images of live biological cells with the highest frame rates reported to date. The developed method will find its good use for many biomedical and biological studies where minimally invasive in-vivo fluorescence imaging is essential.

[1] Y. Choi, C. Yoon, M. Kim, T.D. Yang, C. Fang-Yen, R.R. Dasari, K.J. Lee, W. Choi, Scanner-Free and Wide-Field Endoscopic Imaging by Using a Single Multimode Optical Fiber, Phys Rev Lett, 109 (2012)

Acknowledgments
The authors may acknowledge the funding and contributions.

The Pattern of Vesicle Movement in Cytoplasm

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Vesicles are very small and membrane-enclosed sacs which carry molecules in a cell. These vesicles in cytoplasm play an essential role in intracellular transportation. When they are budding from the plasma membrane and move into the cell, it is called endocytosis, while the opposite process is called exocytosis. Basically vesicles are carried by motor proteins along the microtubule : kinesin and dynein carry them from microtubule's plus-end to minus-end, and minus-end to plus-end, respectively. Although many researches regarding the intracellular transportation have been performed, what kind of movement pattern a single vesicle follows along the microtubule is not yet clearly understood, which can be a crucial key to elucidate the mechanism of drug delivery inside a cell. The purpose of this research is, with the human breast cancer cell, KPL-4-PAR-1-GFP, to find out the pattern of the vesicle's movement. The vesicles carrying PAR-1 in the KPL-4 cancer cell bud from Golgi Apparatus and fuse to the cell membrane then come back to the centrosome. The movements of vesicles including GFP-attached PAR-1, a thrombin receptor, have been detected and analyzed. As a result, vesicles show distinctive stop-and-go pattern when they move, and the run length during the fast-speed interval tends to be longer when the speed of the vesicle is faster. Additionally, the angles between the vesicle's trajectories during they move in fast-speed intervals show higher probability to be smaller than $\pi/2$.

The Fluctuation Theorems in Three Different Time Scales

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We study the integral fluctuation theorems in three different time scales, which are the adiabatic, the mesoscopic and the isothermal time scales.

To perform this work, we introduce the adapted state and the intermediate state by which a given process is divided into the changing process and the adapting process sequentially, and the slow process approximations are applied in the adapting process.

In the changing process, the control parameter changes immediately thereby performing work to the system and the system goes to the intermediate state instantly by storing the work as the excessive energy.

Then, during the adapting process, the system goes from the intermediate state to the adapted state, and the excessive energy makes the temperature of the system changing in the adiabatic time scale.

If the relaxation time of the process is longer than the adiabatic time scale, i.e. in the mesoscopic or the isothermal time scale, the excessive energy is dissipated.

By the approximations, the general form the integral fluctuation theorem is derived in the mesoscopic time scale.

If the relaxation time is getting short, the process goes to adiabatic, so the integral fluctuation theorem of the house-keeping heat is derived.

If the relaxation time is in the isothermal time scale, it goes to the generalized Jarzynski equality.

Interestingly, the integral fluctuation theorem of the house-keeping heat is also derived in the isothermal time scale because the time scale of steady state limit is in the isothermal time scale.