

Active Matter Workshop 2020

VENUE:

Meiji University (Nakano Campus)

DATE:

10 - 11 January, 2020

Organiser

共同利用・共同研究拠点 明治大学

先端数理科学インスティテュート (MIMS) 現象数学拠点

MEXT Joint Usage/Research Center Meiji University
"Center for Mathematical Modeling and Applications" (CMMA)

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Program

2020/1/10 Fri.

- 9:30 - 10:00 **Registration**
- 10:00 - 10:10 **Opening** M. Tarama
“How adhesive cells crawl by regulating their active force”
- 10:10 - 10:50 **FL** M. Iwamoto
“Mechanism of Crawling Locomotion in Gastropods”
- 10:50 - 11:00 Break
- 11:00 - 11:20 **CT** S. Komura
“Non-equilibrium probability flux of a thermally driven micromachine”
- 11:20 - 11:40 **CT** K. Era
“Autonomous three-sphere microswimmers driven by coupled internal oscillations”
- 11:40 - 12:00 **CT** F. Fadda
“Hydrodynamics of sedimenting squirmers with rotlet dipole”
- 12:00 - 13:30 **Group photo**
Lunch
- 13:30 - 13:50 **CT** D. Nishiguchi
“Novel boundary conditions and topological dynamics of bacterial turbulence”
- 13:50 - 14:10 **CT** K. Sone
“Anomalous topological active matter”
- 14:10 - 14:30 **CT** H. Matsuyama
“Emergence of Hyperuniform state at Generalized Active Ornstein-Uhlenbeck Particle System”
- 14:30 - 14:40 Break
- 14:40 - 15:20 **PL** M. Turner
“Collective thinking in collective motion”
- 15:20 - 15:40 **CT** K. Nagai
“Collective motion of *C. elegans*”
- 15:40 - 16:00 Break
- 16:00 - 16:20 **CT** S. Yasuda
“Kinetic transport simulation of chemotactic bacteria”
- 16:20 - 16:40 **CT** F. Tsumori
“Locomotion of soft robot by applied magnetic field”
- 16:40 - 17:00 **CT** E. Gauquelin
“Emergence of large scale propagative signals during epithelial cell migration”
- 17:00 - 17:20 **CT** S. Schnyder
“Spontaneous spatiotemporal ordering of shape oscillations enhances cell migration”
- 17:20 - 17:30 Break

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- 17:30 - 17:50 **CT** T. Shibata
“Polar pattern formation induced by contact following locomotion in a multicellular system”
- 17:50 - 18:30 **FL** S. Sawai
“Crawling morphology and collective migration in amoeboid cells”
- 19:00 -
Banquet

2020/1/11 Sat.

- 10:00 - 10:20 **CT** H. Ebata
“Self-replicating pattern driven by granular segregation”
- 10:20 - 10:40 **CT** R. Kurita
“Active hole generation in an ionic liquid droplet into a binary solvent”
- 10:40 - 11:00 **CT** M. Okada
“Relationships between spontaneous deformation and fission of an oil droplet on a surfactant aqueous solution”
- 11:00 - 11:20 **CT** K. Yasuda
“State cycle model of biological nanomachines”
- 11:20 - 11:30 Break
- 11:30 - 12:10 **FL** Y. Iwadate
“*Rigidity sensing for directional migration in fast crawling cell*”
- 12:10 - 13:40 Lunch
- 13:40 - 14:20 **FL** J. J. Molina
“Modeling the mechanosensitive response of crawling cells”
- 14:20 - 15:00 **FL** P. Sens
“A scallop theorem for crawling cells”
- 15:00 - 15:10 Closing

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Presentation time

PL: Plenary lectures [40 min each, including discussions]

FL: Focused lectures [40 min each, including discussions]

CT: Contributed talks [15 min presentation + 5 min discussions for each]

Abstracts

Day 1

10 Jan., 2020

- 9:30 - 10:00 Registration
- 10:00 - 10:10 Opening (M. Tarama)
- 10:10 - 10:50 Focus lecture (M. Iwamoto)
- 11:00 - 12:00 Contributed talk (S. Komura)
Contributed talk (K. Era)
Contributed talk (F. Fadda)
- 12:00 - **Group photo**
- 13:30 - 14:30 Contributed talk (D. Nishiguchi)
Contributed talk (K. Sone)
Contributed talk (H. Matsuyama)
- 14:40 - 15:40 Plenary lecture (M. Turner)
Contributed talk (K. Nagai)
- 16:00 - 17:20 Contributed talk (S. Yasuda)
Contributed talk (F. Tsumori)
Contributed talk (E. Gauquelin)
Contributed talk (S. Schnyder)
- 17:30 - 18:30 Contributed talk (T. Shibata)
Focus lecture (S. Sawai)

How adhesive cells crawl by regulating their active force

Mitsusuke Tarama

RIKEN Center for Biosystems Dynamics Research, Laboratory for Physical Biology

Active matter is able to spontaneously exhibit various dynamics by autonomously generated forces. These active forces vanish in total due to the law of action and reaction. To achieve a net directional motion under this force-free condition, symmetry breaking plays a fundamental role. This is well-known as Purcell's scallop theorem in the case of microswimmers, such as bacteria and algae, that swim in an (almost) zero Reynolds number fluid.

In contrast to these swimming microorganisms, there are many cells that crawl by adhering to a substrate, the extracellular matrix, or other cells. A typical mechanism of cell crawling is thought of as a cycle of four processes: 1) protrusion of the leading edge, 2) adhesion of the leading edge to the substrate, 3) de-adhesion of the trailing edge from the substrate, and 4) contraction of the trailing edge. We demonstrated the importance of the temporal order of these four basic processes by introducing a simple model of a crawling cell composed of two elements connected by a viscoelastic spring [1]. The spring contains a linear actuator that elongates and shrinks in time, representing the protrusion and contraction. Since the force generated by the actuator acts on the two elements symmetrically, the force-free condition is satisfied. In addition, the substrate friction characteristics switches between an adhered stick state and a de-adhered slip state, modelling the adhesion and de-adhesion processes of the two elements. The phase shift between the stick-slip transitions in the substrate friction breaks the symmetry, which enables the cell to achieve a net migration.

The main components responsible for the active force generation are filamentous proteins and the associated molecular motors, such as actin filaments and myosin motors, which are typically much smaller in size than cells. Thus, it is not straightforward to understand how such microscale proteins can self-organise themselves to drive the cell and eventually lead to multicellular dynamics such as tissue formation and homeostasis. There have been many studies on the chemical signaling that regulates the polymerisation of actin monomers into actin filaments and the contraction of the actomyosin cortex both experimentally and theoretically. On the other hand, their study from a mechanical viewpoint is less developed. We recently developed a coarse-grained molecular dynamics simulation on the dynamics of the composite of actin filaments and myosin motors, in particular studying the formation of the actomyosin cortex [2].

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2. M. Tarama, T. Shibata, "In-silico experiment on the formation of actomyosin cortex", in preparation.

Mechanism of Crawling Locomotion in Gastropods

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Crawling locomotion is the one of the most fundamental locomotion strategies for various kinds of animals without legs, for example, slime, earthworm, slug, sea hare and snake. Many gastropods who are called generally “univalve shell” also realize crawling movement by propagations of muscular contraction waves along their pedal on the ground. The muscular contraction waves are classified into “direct wave” (Fig.1) and “retrograde wave” by the directions of body movement and muscular waves. It had already reported that friction control against the ground is important for realization of crawling motion for gastropods in addition to muscular waves, and the friction control would be realized by lifting up a part of their pedal or a viscoelasticity of the mucus covered their pedal.

We have constructed a simple mathematical model of spring-mass system which captures essential factors of physical properties, i.e., the muscle and the mucus [1]. Our numerical calculations have indicated that the locomotion mechanism with mucus can achieve to move by crawling with both direct and retrograde waves, and the features of the mucus and muscle have an effect on the choice of locomotion styles. Furthermore, it has indicated that the regions where both locomotion styles are stable would exist in the region of a middle of contraction rate, and bifurcation phenomenon of locomotion styles as pitchfork appears with respect to the rate [2].

Now we are focusing a relationship between locomotion styles and surrounding environments. Loping (Fig. 2) is one of the specific locomotion styles separated from the ordinary crawling motions by muscular contraction waves [4]. In this presentation, we will introduce our observations on loping, and aim to build a mathematical model for understanding a mechanism of loping.

Acknowledgements

We would like to thank Prof. Akio Ishiguro and Prof. Takeshi Kano (Tohoku University), Prof. Hitoshi Aonuma (Hokkaido University) for the useful discussions. This study was supported by JSPS KAKENHI Grant Number JP17H04826.

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Fig. 1: Crawling locomotion of snail by direct wave.

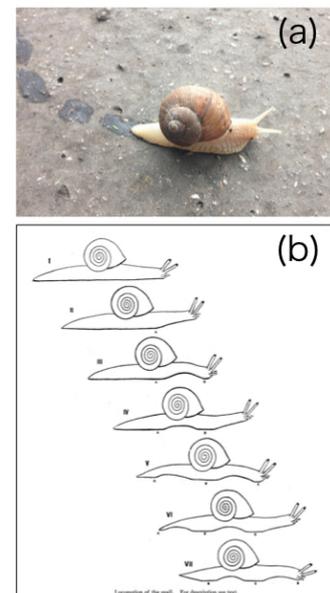


Fig. 2: Loping in snail. (a) loping on a road paved with asphalt, (b) sketch of loping [3].

Non-equilibrium probability flux of a thermally driven micromachine

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We discuss the non-equilibrium statistical mechanics of a thermally driven micromachine consisting of three spheres and two harmonic springs as shown in Fig.1 [1]. We obtain the non-equilibrium steady state probability distribution function of such a micromachine and calculate its probability flux in the corresponding configuration space [2]. The resulting probability flux can be expressed in terms of a frequency matrix that is used to distinguish between a non-equilibrium steady state and a thermal equilibrium state satisfying detailed balance. The frequency matrix is shown to be proportional to the temperature difference between the spheres. We obtain a linear relation between the eigenvalue of the frequency matrix and the average velocity of a thermally driven micromachine that can undergo a directed motion in a viscous fluid. This relation is consistent with the scallop theorem for a deterministic three-sphere microswimmer.

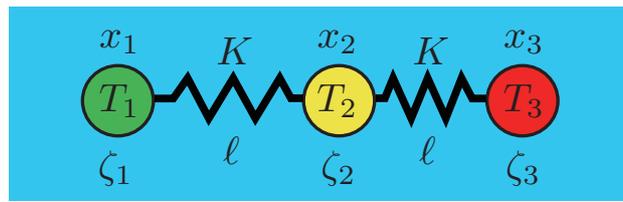


Fig.1: Thermally driven elastic three-sphere micromachine.

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Autonomous three-sphere microswimmers driven by coupled internal oscillations

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Microswimmers are small machines that swim in a fluid and they are expected to be used in microfluidics and microsystems. Over the length scale of microswimmers, the fluid forces acting on them are dominated by the frictional viscous forces. By transforming chemical energy into mechanical energy, however, microswimmers change their shape and move efficiently in viscous environments. According to Purcell's scallop theorem, reciprocal body motion cannot be used for locomotion in a Newtonian fluid with low Reynolds number. As one of the simplest models exhibiting nonreciprocal body motion, Najafi and Golestanian proposed a three-sphere swimmer (NG swimmer) [1], in which three in-line spheres are linked by two arms of varying length.

In recent years, such a swimmer has been experimentally realized by using colloidal beads manipulated by optical tweezers, or ferromagnetic particles at an air-water interface.

In this presentation, extending the mechanism of an elastic swimmer [2], we propose a new type of three-sphere swimmer which can autonomously determine its average velocity. In order to implement such a control mechanism, we introduce a coupling effect between the dynamics of the two natural lengths of an elastic microswimmer following the idea of the synchronization phenomena in coupled oscillator systems. Importantly, we find that the proposed microswimmer attains a finite steady state velocity in the long-time limit without any external control. The chosen steady state velocity can be tuned by changing the coupling parameter in the model. Moreover, we shall investigate the condition that a microswimmer can attain an autonomous locomotion and further perform the stability analysis of the synchronized states both numerically and analytically.

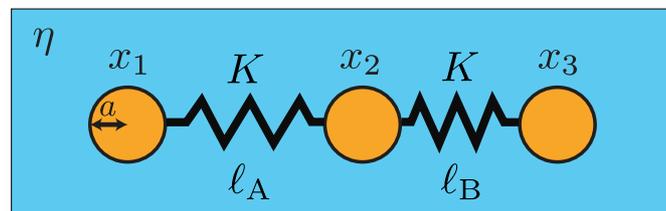


Fig. 1 An autonomous elastic three-sphere microswimmer in a viscous fluid characterized by the shear viscosity η .

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Hydrodynamics of sedimenting squirmers with rotlet dipole

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The squirmer model is a theoretical model introduced to study microorganisms like algae and bacteria. It consists in a spherical particle whose self-propulsion is ensured by a surface velocity field [1].

It is well established in literature that the presence of walls can strongly modify the motion of microorganisms. The bacterium *E. Coli*, indeed, is known to perform clockwise trajectories near a solid boundary [2]. On the other hand the gravity force, ubiquitous in nature, represents another factor that can affect the motion of microorganisms [3-4].

In this work, using the Smoothed Profile Method [5], we combine all of these features studying the dynamics of a sedimenting squirmer under the effect of the gravity force, near a solid boundary taking into account the rotlet dipole term [6].

Computing quantities like the stationary swimming velocity, the stable swimming height, the stationary orientation and curvature radius we are able to characterize the dynamics of the single squirmer.

In case of neutral squirmers and pullers, the gravity causes both of them to sediment to the bottom wall, arresting their motion and reorienting them in a direction perpendicular to the wall. Pushers, instead, exhibit continuous motion with tilted direction.

When the rotlet dipole term is neglected and the “classic” squirmer model is considered, all of types of squirmers swim in straight trajectory. When the rotlet dipole term is introduced, it causes a deviation from the straight path in circular trajectories whose radius of curvature strongly depends by the magnitude of the rotlet dipole term.

After studying the single squirmer, the collective dynamics of squirmers is considered.

Acknowledgements

F. Fadda warmly thanks Norihiro Oyama whereas R. Yamamoto thanks Holger Stark for enlightening and stimulating discussions.

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Novel boundary conditions and topological dynamics of bacterial turbulence

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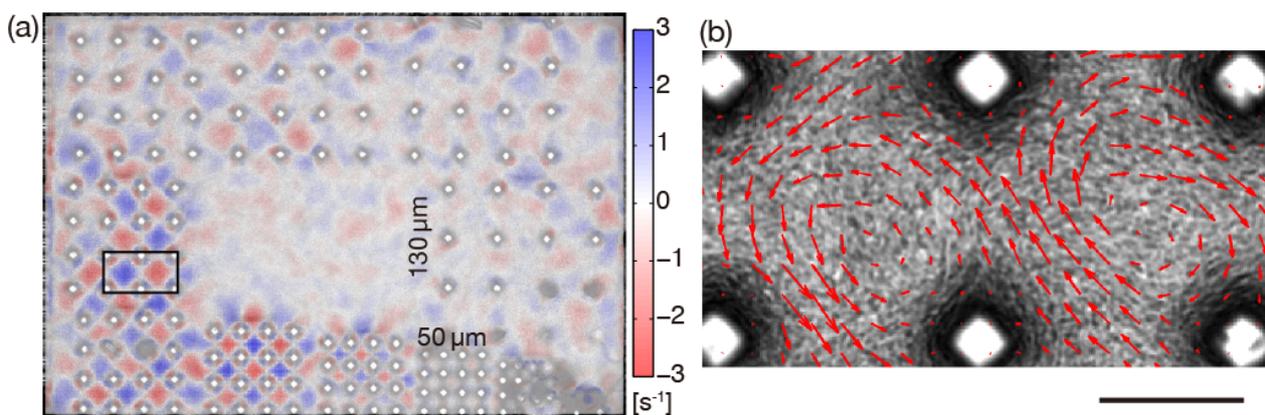
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Collective motion of swimming rod-shaped flagellated bacteria, such as *Escherichia coli* and *Bacillus subtilis*, emerges as a result of competition between excluded volume interaction and hydrodynamic instability [1]. In usual situations, hydrodynamic instability leads to spatio-temporally chaotic collective behavior only with local short-range orientational order, which is termed active turbulence. Such turbulent behavior has been observed in many systems including bacteria, mammalian cell culture, active colloids [2], and reconstituted biofilament systems. Although such turbulent phases seem rather universal, many realistic situations require ordered and/or robust motion of the moving elements as seen in collective cell migrations during developmental processes of multicellular organisms. How can such orders arise from intrinsically chaotic fluctuating phases?

To address this question, we have previously conducted systematic experiments of bacterial turbulence under periodic constraints and reported that bacterial turbulence self-organizes in antiferromagnetic vortex lattices between microscopic pillar arrays with periodicity comparable to its intrinsic correlation length [3]. Recently we have found that the pillars generate characteristic topological flow profiles around them depending on their diameters. To explain the macroscopic emergent order and the topological properties of bacterial turbulence, we have experimentally extracted new boundary conditions for continuum equations of bacterial turbulence. By using these boundary conditions, we have succeeded in numerically reproducing all of our experimental findings both qualitatively and quantitatively [4]. By making use of our understanding on the topology of bacterial flow field, we can predict that bacterial turbulence can also self-organize in both hexagonal-lattice and Kagome-lattice antiferromagnetic vortex order. This gives a new methodology to topologically control microbial systems.



(a) Vorticity of bacterial turbulence in square lattices. (b) Instantaneous flow. Scale bar: 50 μm

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Anomalous topological active matter

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Topological materials including topological insulators have attracted much interest in condensed matter physics. The topologically nontrivial systems exhibit unidirectional modes propagating along the edge of the sample. Such edge modes accompany a nonzero topological index calculated from the bulk mechanics, which is known as the bulk-edge correspondence. The topological index is invariant under the continuous deformation of the Hamiltonian, and thus guarantees that the edge modes exist robustly against disorder. The most prototypical example is the quantum Hall effect observed under a strong magnetic field, where the quantized Hall conductance can be linked with the bulk topological invariant. Nowadays, similar phenomena are observed without external magnetic fields (i.e., the quantum anomalous Hall effect) and in time-reversal symmetric systems (i.e., the quantum spin Hall effect), which are considered as typical topological systems.

While conventional topological materials are studied in the electronic systems described by quantum mechanics, recent researches have shown that classical systems can also exhibit topologically nontrivial features. In classical systems, one can make the analogy between linearized dynamics and the Schrödinger equation and thus can obtain the mathematically equivalent problems. The classical counterpart of eigenstates in quantum mechanics is the natural oscillation modes of physical observables, such as density and velocity. Therefore, a topological classical system exhibits robust unidirectional wave modes localized at the edge of the system.

Here, we construct an active-matter counterpart of the quantum anomalous Hall effect [1]. While previous studies must introduce intricate structures to realize the counterparts of the quantum Hall effect, our model removes them and expands the possibility of experimental realizations and applications. In this presentation, I will show some numerical results demonstrating the existence of a topological edge mode in our active-matter model.

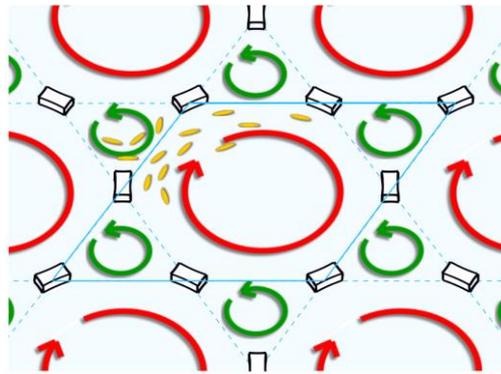


Fig. 1 : Topological active matter with a kagome-lattice structure [1].

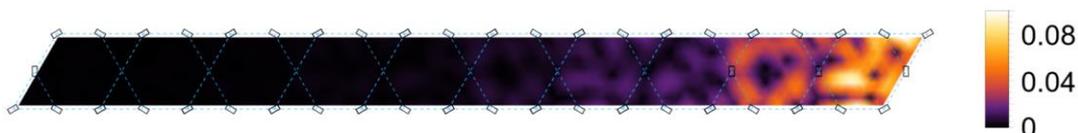


Fig. 2 : Edge-localized topological sound mode in our model [1]. Its density-oscillation profile is presented.

References

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Emergence of Hyperuniform state at Generalized Active Ornstein-Uhlenbeck Particle System

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Active Matter system features the emergence of the various collective behavior due to their self-propelling force [1]. One of the most famous examples of collective behavior is Motility induced phase separation (MIPS). MIPS is resemble to liquid-vapor phase separation even when there is no attractive interaction force and no alignment force. The long ranged density fluctuation is observed when MIPS takes place [2].

Active Ornstein-Uhlenbeck Particle (AOUP) is one of the theoretical models for active matter [3]. Self-propelled force of AOUP obeys Ornstein-Uhlenbeck process. Therefore, self-propelled force is basically same as the Non-Markov noise with a finite memory time τ_p . AOUP model also exhibits MIPS.

We have generalized AOUP model to add the finite memory time τ_m for particle interaction [4]. Our new model which is called Generalized AOUP (GAOUP) has two memory time scales. This model enables us to connect seamlessly the non-equilibrium AOUP model with non-Markov equilibrium Brownian motion. Previous works pay attention only the two limited cases: $\tau_m \rightarrow 0$ (AOUP system) and $\tau_p = \tau_m$ (equilibrium underdamped Langevin system).

We have performed Brownian dynamics simulation of GAOUP system and found the MIPS emerges in the $\tau_p > \tau_m$ regime. In this regime, the static structure factor $S(k)$ develops a pronounced peak at small k 's. On the other hand, we have found Hyperuniform state emerges in the $\tau_p < \tau_m$ regime. Hyperuniformity is the phenomena which the long-range density fluctuations of the system is suppressed [5]. This is opposite behavior of MIPS. In previous work, it is known that hyperuniformity emerges near the critical point of absorbing transition and Jamming transition. The chiral active particle which undergoes absorbing transition also shows hyperuniform state [6]. However, our GAOUP system does not undergo any phase transition behavior. The Hyperuniform state is characterized by the behavior of $S(k)$ near the original point. Our GAOUP model shows $S(k) \sim k^{1.5}$ at small k 's. This exponent is not same as any of those previous work. In this talk, I discuss about the feature of Hyperuniformity in GAOUP system.

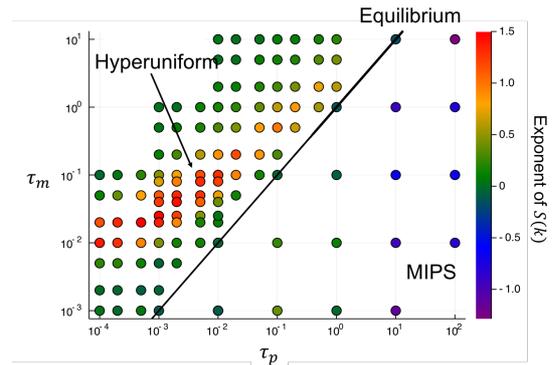


Figure 1: The $\tau_p - \tau_m$ phase diagram in GAOUP system. Red dots represent Hyperuniformity state. Blue and Purple dots represent MIPS state. Black line represents the equilibrium state. The value corresponds of color bar correspond to the exponent of $S(k)$ near the original point.

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Collective thinking in collective motion

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Life requires movement. This is seen in individual cells, organisms and collections of organisms. The purpose of motion is to enhance an organism's *fitness* in an uncertain world. For example, the fitness associated with a wound-healing skin cell is not directly related to its speed but rather to what its motion contributes to the fitness of the organism that it repairs, given a risk of infection or mis-function.

I ask whether those of us interested in understanding the movement of animal swarms may have been too ready to use “off-the-shelf” theoretical physics. For example, the prevailing assumption that all animal swarms are controlled by *local* interactions, like the spin models familiar in physics, has never been properly tested. More physiologically plausible models, based directly on vision, are now becoming available [1,2].

Our recent work involves a “bottom-up” approach. Here, a fitness principle is used to *derive* the dynamics, rather than these being coded into the structure of a model at the outset. We study such a fitness principle in which agents take actions that give them access to the greatest number of different (visual) states of the world in the future [2]. They do this by first explicitly computing each state on a decision tree of their future actions and then selecting the best branch/action in the present. Such “Future State Maximisation” (FSM) algorithms may provide fitness in an uncertain world for rather general reasons, giving more options to choose between in the future. They are also naturally consistent with a propensity for energy accumulation, providing more options; and risk avoidance, mitigating against option-poor outcomes. Finally, we construct *heuristics* mimicking FSM could operate under animal cognition in real time. Such an inheritable heuristic trait may represent the first candidate for a “bottom-up” explanation of the emergence of swarm behaviour in higher animals.

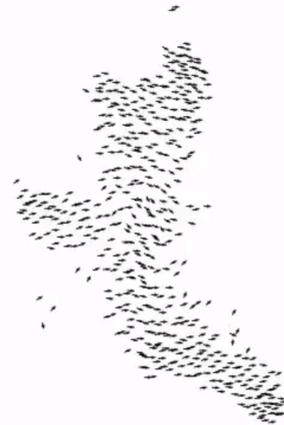


Fig. 1 : Agents, moving together in a swarm, decide how to move by using sensory input to inform a (heuristic) model of the *future*. They employ such a model to choose actions in the present that give them access to *the maximum number of different states in the future*. This generates remarkably realistic collective dynamics (snapshot shown). We propose heuristics based on this principle that could operate under animal cognition. Counter-intuitively, the collective motion of higher animals may be the most promising system in which to test these ideas, although they may also apply much more generally, even to single-celled organisms.

Acknowledgements

My talk incorporates the work of several dedicated PhD students, including D. Pearce, A. Miller, A. King and, in particular here, H. Charlesworth.

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Collective motion of *C. elegans*

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Ordered structures ubiquitously emerge in collective motions of self-propelled objects including birds and fish. Using bacteria and motile cells on a substrate, it has been found that various animate collective motions are governed by simple rules [1, 2]. In contrast to unicellular living organisms, unclear is what kinds of collective motion of animals can be described by simple descriptions like the Vicsek model, since animals generically have little experimentally controllable parameters.

It is known that some kinds of nematode collectively form ordered structures in natural environments. To reproduce the structures in a laboratory, we developed a new cultivation method of *Caenorhabditis elegans* (*C. elegans*) with which the density of worms become much higher than conventional methods. The highly concentrated worms formed dynamical networks on various substrates as seen in Figure 1. The structure was kept dynamically agitated and transformed into a different network in around 100 s.

C. elegans is one of model animals used in various fields of study; therefore, various methods to affect the motility and various motility mutants are known. Utilizing the knowledges about *C. elegans*, we investigated the dependence of the dynamical network on various parameters such as the ambient humidity, the density of the worms, and the motility characteristics which can genetically be modified.

Next, we formulated a minimal self-propelled multi-agent model which have two characteristics which were found in isolated worm's motility: long-time memory of rotation rate, and nematic alignment of two worms after collision. The model reproduced the formation of the dynamical network of the worms. Not only the formation but the dependences on various parameters were well reproduced by the simple model, which indicates that the two characteristics mainly govern the collective motion of *C. elegans* [3].

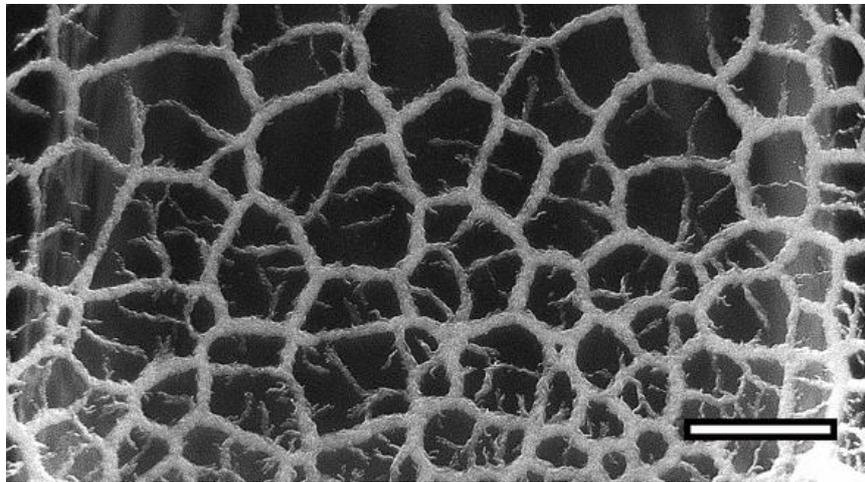


Figure 1: Dynamical network formed by a large number of *C. elegans* on a glass plate. The scale bar corresponds to 2 mm.

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Kinetic transport simulation of chemotactic bacteria

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Collective dynamics of autonomous agents such as bacteria swarm and fish school have long been an active research area in natural sciences. Nowadays, it also draws great attention from engineering researchers due to the emergence of autonomous technologies such as swarm robotics and intelligent materials.

Simulation technology for the collective dynamics of autonomous agents may play an important role in elucidation of the complex natural phenomena and innovative development of the cutting-edge technologies.

This talk concerns a novel computational approach to the collective dynamics of chemotactic bacteria based on a Boltzmann type transport equation, say a kinetic chemotaxis equation. The kinetic chemotaxis equation¹⁻³ and its novel stochastic numerical method⁴ are introduced. Traveling band and colony pattern formation of chemotactic bacteria are investigated focusing on the multiscale mechanics behind the collective dynamics^{5,6}. Simulation results are also compared to some experimental and theoretical results.

Acknowledgements

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Locomotion of soft robot by applied magnetic field

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In this work, authors propose a simple system to realize bio-mimic motion using a soft material dispersed with magnetic particles. The developed elastic body with magnetic elements could be actuated by an applied magnetic field.

Schematic image of the proposed actuator is shown in Fig. 1. A rubber magnet sheet, which is a mixture of rubber and magnetic particles, is magnetized by an applied magnetic field (Figs. 1a, b). The sheet is cut into block elements (Fig. 1c), and these magnetic elements are embedded in a silicone structure (Fig. 1d). Figure 2 shows an example of a fabricated worm-type soft robot actuated under a rotating magnetic field. The structure had 8 magnetic elements, which were arranged with their magnetized orientation changed by 90 degrees to the neighbors. As a result, the structure generated wavy motion, and propagation of this wave caused simple crawling locomotion in a gap between 2 parallel walls.

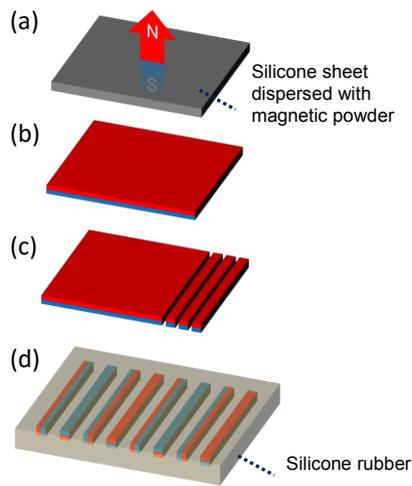


Fig. 1: Flow of the fabrication process.

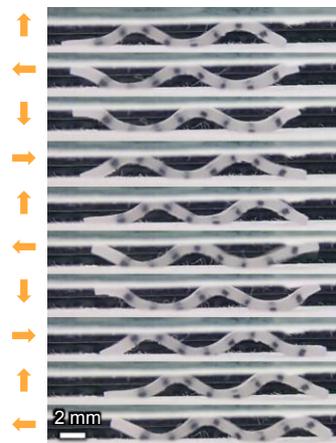


Fig. 2: Snapshots of actuated sample between a gap under a rotating magnetic field.

In the previous example, worm-like motion was realized with a simple arrangement of magnetic elements. Next, we show one design method of this arrangement using genetic algorithm (GA). We prepared a mass-spring-damper model to express the elastic structure as shown in Fig. 3. We could set magnetic elements inside, to which rotation moments were exerted by an applied magnetic field. This virtual structure can deform periodically under a rotating magnetic field. We prepared 32 virtual crawlers in a computer for GA. Figure 4 shows an example of a crawler. After evolution of 100 generation, the crawler obtained wavy motion for locomotion.

Detailed explanation of the experiment and GA calculation will be given in the workshop.

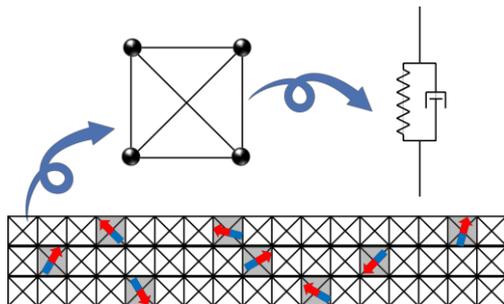


Fig. 3: Schematic of mass-spring-damper model of a crawler.

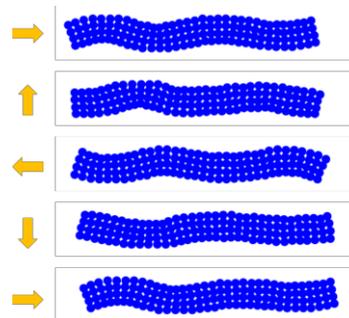


Fig. 4: Crawler after evolution of 100 generation. The structure obtained wavy motion for locomotion.

Emergence of large-scale propagative signals during epithelial cell migration

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Collective cell migration is a fundamental phenomenon in biology involved in processes such as morphogenesis and tissue repair. Various mechanisms play a role in the regulation of tissue expansion during collective cell migration, including cell proliferation, as it can indeed disturb the dynamic organization of cell monolayer. This work was thus focusing on the study of collective cell behaviors and their link with cell proliferation.

We developed an *in vitro* assay using micro-fabrication techniques (Figure 1.a), including micro-contact printing, to compare the migrating behavior of cell monolayers with and without cell proliferation, and to measure the local effects of cell division on their environment in migrating tissues.

We first measured velocities within the monolayer on a global scale. In the case of migration without proliferation, patterns of high velocities appear in the monolayer, propagating from the front of migration toward the bulk (Figure 1.d) [1], [2]. Those velocity waves can propagate on distances as long as few millimeters within the tissue. When there is proliferation, the waves are unable to propagate on long distances and are rapidly damped within the monolayer (Figure 1.c) [1]. Our study of local velocity fields surrounding division events during migration shows that there is a competition between velocities induced by division events and the global velocity of migration, suggesting that divisions create defects that prevent the propagation of the velocity waves towards the back of the migrating monolayer.

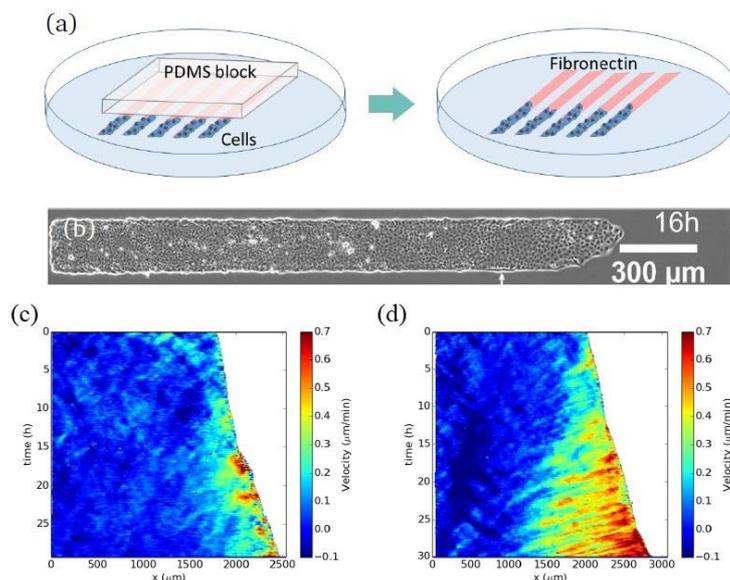


Figure 1. (a) Schematic representation of the protocol. Cells are first cultured overnight on a segment of micropatterned lines restricted by a block of PDMS (left), then the block is removed and the cells are free to invade the fibronectin substrate (right). (b) Snapshot of a monolayer 16 hours after the start of the experiment. The white arrow indicates the location of the front at $t = 0$, that is when recording starts. (c) Spatiotemporal diagrams of the velocity with divisions. (d) Spatiotemporal diagrams of the velocity without divisions.

Acknowledgements

We acknowledge Sham Tlili and Francois Graner for the discussions.

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Spontaneous spatiotemporal ordering of shape oscillations enhances cell migration

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The migration of cells is relevant for processes such as morphogenesis, wound healing, and invasion of cancer cells. In order to move, single cells deform cyclically. However, it is not understood how these shape oscillations influence collective properties. Here we demonstrate, using numerical simulations, that the interplay of directed motion, shape oscillations, and excluded volume enables cells to locally “synchronize” their motion and thus enhance collective migration. Our model captures elongation and contraction of crawling ameboid cells controlled by an internal clock with a fixed period, mimicking the internal cycle of biological cells. We show that shape oscillations are crucial for local rearrangements that induce ordering of neighboring cells according to their internal clocks even in the absence of signaling and regularization. Our findings reveal a novel, purely physical mechanism through which the internal dynamics of cells influences their collective behavior, which is distinct from well known mechanisms like chemotaxis, cell division, and cell–cell adhesion.

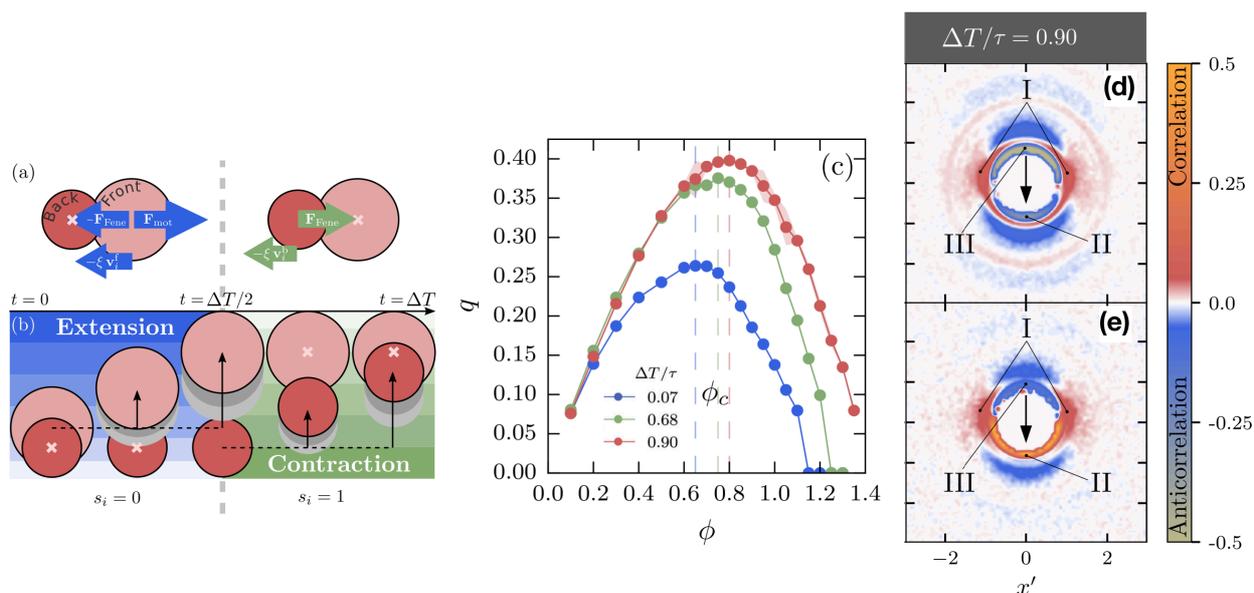


Figure: a) Sketch of cell shape and forces in the extension and contraction states. b) Illustration of the cyclic crawling. c) The flux of cells is significantly enhanced when increasing the duration of the cell cycle, and the critical packing fraction shifts from 0.65 to 0.8. (d,e) Local correlation function of the internal time $C(r)$ and stage $S(r)$ for long cycle duration, showing the emergence of the correlation/anti-correlation pattern in space, responsible for the enhancement of the flux.

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Polar pattern formation induced by contact following locomotion in a multicellular system

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Biophysical mechanisms underlying collective cell migration of eukaryotic cells have been studied extensively in recent years. One paradigm that induces cells to correlate their motions is contact inhibition of locomotion, by which cells migrating away from the contact site. Here, we report that tail-following behavior at the contact site, termed contact following locomotion (CFL), can induce a non-trivial collective behavior in migrating cells. We show the emergence of a traveling band showing polar order in a mutant *Dictyostelium* cell that lacks chemotactic activity. We find that CFL is the cell–cell interaction underlying this phenomenon, enabling a theoretical description of how this traveling band forms. We further show that the polar order phase consists of subpopulations that exhibit characteristic transversal motions with respect to the direction of band propagation. These findings describe a novel mechanism of collective cell migration involving cell–cell interactions capable of inducing traveling band with polar order.

Comparative Mapping of Migrating Cell Morphology and Phase-Field Modeling

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Cell shape itself is one of the key factors in deciphering how the direction of cell migration is determined. Studies over the years have described the shape dynamics of migrating cells mathematically. Due to the complexity and the dynamic nature, however, how well mathematical models describe the real cell morphologies has remained almost completely untested. This is challenging especially for highly dynamic and varying morphologies in various cell-types of amoeboid and mesenchymal natures that are largely context-dependent and plastic. In this talk, I will introduce a conceptual model that describes the core regulatory logics of cytoskeletal regulation combined with interface dynamics using the phase-field approach. We demonstrate that similarities between the simulated data and real cell data can be assessed by feature extraction by deep learning and that by doing so allows one to understand some key parameter important for shape determination both between species and within differentiating cells.

Day 2

11 Jan., 2020

- 10:00 - 10:20 Contributed talk (H. Ebata)
- 10:20 - 10:40 Contributed talk (R. Kurita)
- 10:40 - 11:00 Contributed talk (M. Okada)
- 11:00 - 11:20 Contributed talk (K. Yasuda)

- 11:30 - 12:10 Focus lecture (Y. Iwadate)

- 13:40 - 14:20 Focus lecture (J. J. Molina)
- 14:20 - 15:00 Focus lecture (P. Sens)
- 15:00 - 15:10 Closing

Self-replicating pattern driven by granular segregation

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Self-replicating patterns reminiscent of biological cell replication have been discovered in chemical reaction-diffusion systems [1] and vertically vibrated wet granular systems [2]. However, it is still unclear whether universal laws underlay the dynamics of self-replicating patterns in the different systems. Does self-replication in different systems merely resemble each other in appearance? To answer the question, we investigate the statistical features of different types of self-replication especially around the bifurcation point. Here, we report a new experimental system of self-replicating pattern, which is horizontally shaken dry granular bed. The granular bed that consists of two different particles is placed in quasi-2D container (Fig. 1 (a)). We horizontally shake the container parallel to short axis of the container. As a result, granular segregation occurs, and band pattern appears parallel to the short axis. Segregation bands are widely reported for the granular mixture in the rotating drum. In the case of rotating drum, segregation is driven by the avalanche. Similar to the rotating drum, in our experiment, segregation is driven by surface flow. As we increase the size ratio of two particles, the dynamics of bands bifurcate from coarsening through replication to oscillation (Fig. 1 (b)). Above certain vibration frequency, the bands continuously replicate and annihilate as they spread out upon the surface of the granular bed. Spatiotemporal plot of the replicating band resembles the Sierpinski Gasket which was found in the replicating spot of a 1D reaction-diffusion system [3]. Statistical properties of birth and death rates of patterns are similar to those in the Gray-Scott model [4] and vibrated wet granular systems [2] (Figs. 1 (c) and (d)).

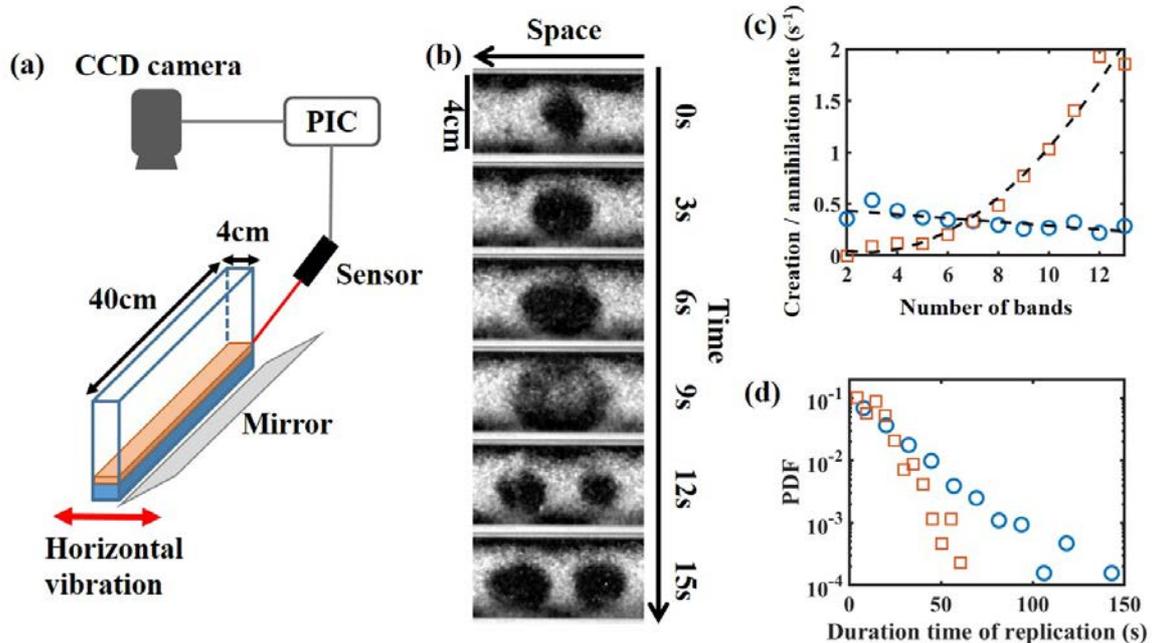


Fig. 1 (a) Experimental set up. Orange and blue colors indicate different types of granules. (b) Snap shot of a self-replicating band. Black and white color indicate small and large particles. (c) Birth (blue) and death (red) rates of bands as a function of total number of bands. (d) Probability distribution function of duration time of replication.

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Active hole generation in an ionic liquid droplet into a binary solvent

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Liquid–liquid dissolution, which is a dissolution of a liquid solute into a liquid solvent, is one of the basic and typical processes in non-equilibrium systems. In the liquid–liquid dissolution, in which substances are transported and exchanged in the solvent, the local free energy should be taken into account, as well as the total free energy of the whole system. The dynamics of the dissolution is separated by a critical point of the phase separation. Above the critical temperature, the dissolution follows the diffusion equation, on the other hand, the droplet shrinks with sharp interface below the critical temperature. In liquid–liquid dissolution, the critical point of phase separation is determined by the temperature. When the solvent consists of multi-components, in contrast, the mole fractions in the solvent also take on the role of control parameter.

In this study, an ionic liquid dissolves into a binary solvent composed of ethanol and water. It is found in this system that, near the critical point, a hole is spontaneously created in the droplet of the ionic liquid [1]. The creation of the hole is initiated by a mutual interaction between the concentrations of the ionic liquid and the binary solvent via their affinity. A spatial inhomogeneity of the interfacial tension is induced through an amplification of fluctuation in the concentration due to an instability mechanism, and causes the Marangoni effect to create the hole. The hole moves inside the droplet and consequently leads to the motion of the droplet. The present system provides not only a new type of dissolution process but also a peculiar example of active matter realized in a liquid droplet.

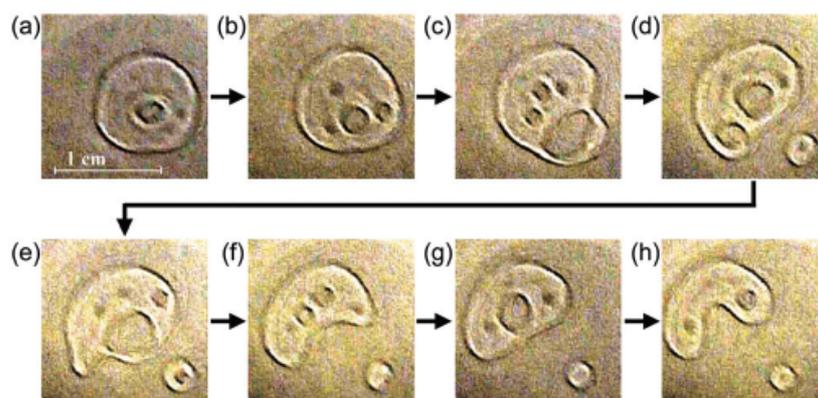


Fig. 1 : Dynamics of the active holes [1]. The time interval between the images is 10 s. The images are trimmed at the same position and the contrast was added. The bar in (a) indicates 1 cm.

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Relationships between spontaneous deformation and fission of an oil droplet on a surfactant aqueous solution.

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Oil droplets of tetradecane with palmitic acid (PA) on an aqueous solution of stearyltrimethylammonium chloride (STAC) exhibit spontaneous deformation and fission[1-2]. The droplet behavior depending on the concentration of STAC and PA was reported[1]. The droplet that exhibits deformation without fission has been well studied. Boundaries of the droplets expand in a circular shape and then shrink (blebbing). The blebbing of the droplet is driven by the generation and rupture of a gel layer composed of STAC and PA and leads the droplet deformation and fission[2]. The fission mechanism of the droplet is different from that of typical droplet systems, in which droplet fission is driven by Marangoni effect[3].

Figure 1 shows typical droplet behaviors for the STAC concentration $C = 2$ mM. The oil droplet spontaneously splits into small fragments. To investigate the characteristics of the fission, we measured the time series of the number of the droplets for various C . From the time series, we confirmed that the final number of the droplets N_{fin} has a peak at a certain C as shown in Fig. 2. Since the droplet fission should be induced by the deformation, we analyzed the droplet deformation for various C and obtained the time evolution of the boundary velocities of the droplet deformation. From the analysis, we estimated the four parameters that may have positive correlation with the droplet fission: typical angle of blebbing, typical timescale of expansion, growth rate of blebbing, and blebbing size. From our experimental results, we will discuss the relationship between the droplet fission and the four parameters.

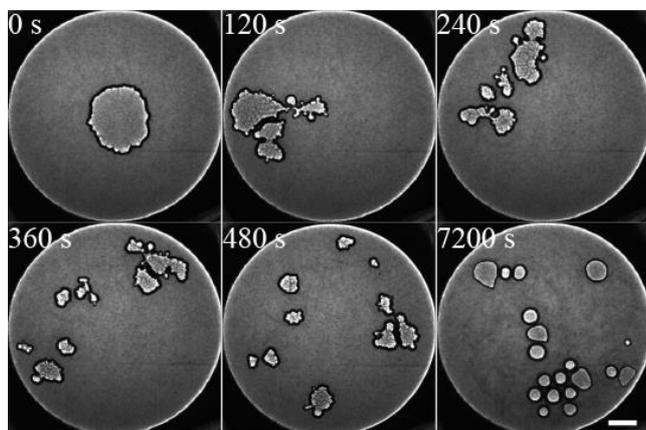


Fig. 1: Typical snapshots of the droplet fission for the STAC concentration $C = 2$ mM. Scale bar: 10 μm .

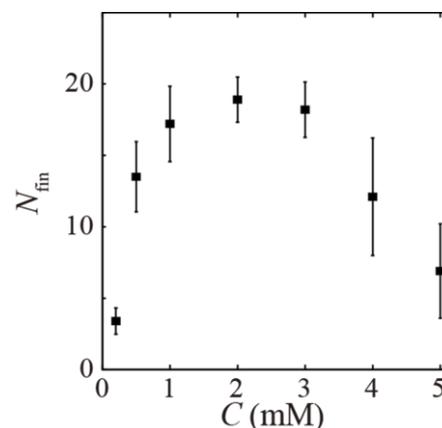


Fig. 2: Final number of the droplet N_{fin} for various C . Error bars represent standard deviations.

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State cycle of biological nanomachines

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Recently, biological nanomachines, such as enzymes and motor proteins, are studied from a physical point of view [1]. These machines are defined as micromachines performing mechanical works through catalyzed reactions of chemical spices such as ATP. It is important to understand the physical chemistry of chemical reactions and dynamics of these micro objects. In the over dumped systems, it was pointed out that a cycle in the state space is important for the net functions [2]. In this research, we focus on the state cycle and propose a simple model of nanomachines. Especially, we investigate the relationships between the state cycle and the parameters of chemical reactions.

To describe the system including the nanomachines and the chemical spices, we introduce the reaction coordinate θ describing the level of chemical reactions, and the state variables s_i which characterizing the state of a nanomachine. The free energy is given by

$$G = -A\cos\theta - F\theta + \sum_i \frac{k_i}{2} (s_i - d_i \sin(\theta - \phi_i))^2,$$

where A is the activation energy of the chemical spices, F is the tilting force of this system. The third term describes the coupling between chemical reaction and state of a nanomachine. In the above, the reaction coordinate and the state variables interact periodically, and k_i is the connectivity, d_i is the amplitude, ϕ_i is the phase shift. We assume that the dynamics of the variables obey Onsager's phenomenological equations with thermal fluctuations determined by the fluctuation dissipation theorem. Furthermore, we focus on the state cycle quantified by "state cyclone", which is defined by

$$C = \lim_{t \rightarrow \infty} \frac{2}{t} \int_0^t dt' s_1 s_2.$$

First, we perform the Langevin simulation of the model and calculate the state cyclone. The state cyclone shows nontrivial dependences on A and F (see Fig 1). To understand this nontrivial results, we solve the Fokker-Planck equation analytically.

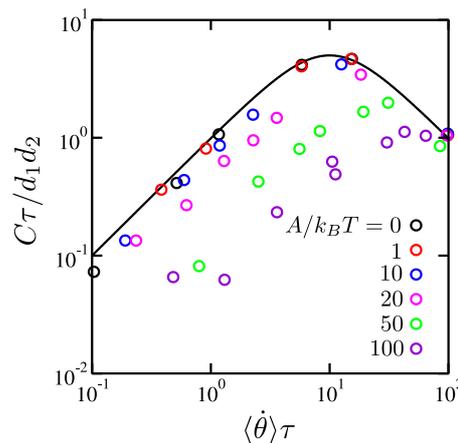


Fig. 1 State cyclone as the function of the reaction rate, extracted from the Langevin simulations.

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Rigidity sensing for directional migration in fast crawling cells

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Living cells sense the mechanical properties of their surrounding environment and respond accordingly. Crawling cells detect the rigidity of their substratum and migrate in certain directions. They can be classified into two categories: slow-moving and fast-moving cell types. Slow-moving cell types, such as fibroblasts, smooth muscle cells, mesenchymal stem cells, etc., move toward rigid areas on the substratum in response to a rigidity gradient. This directional migration is called "durotaxis". However, there is not much information on rigidity sensing in fast-moving cell types, such as neutrophils and *Dictyostelium* cells, whose size is $\sim 10 \mu\text{m}$ and migration velocity is $\sim 10 \mu\text{m}/\text{min}$ (Fig. 1A).

We recently demonstrated that both *Dictyostelium* cells and neutrophil-like differentiated HL-60 cells show directional migration in response to repeated stretching of the substratum in myosin II-dependent manner¹. Cells that moved parallel to the direction of stretch changed their direction perpendicular to it² (Fig. 1B). This observation suggests that not only slow-moving cell types but also fast types may sense the rigidity of the substratum and use this rigidity information to generate migration polarity.

To test this hypothesis, we used an anisotropic substratum that is rigid on the x axis but soft on the y axis to demonstrate rigidity sensing by fast-moving *Dictyostelium* cells and HL-60 cells³. They migrated in the "soft" direction on the anisotropic substratum (Fig. 1C), although myosin II-null *Dictyostelium* cells migrated in random directions, indicating that rigidity sensing of fast-moving cell types differs from that of slow types and is induced by a myosin II-related process. This directional migration appears to be a strategy adopted by fast-moving cells in which they do not migrate faster in the direction they want to go, but migrate to avoid a direction they do not want to go.

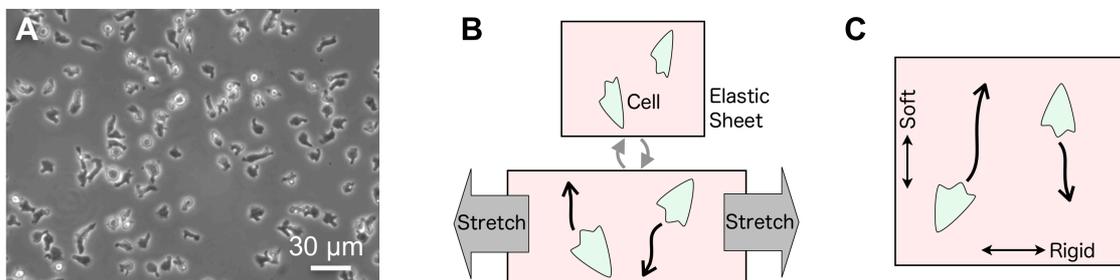


Fig. 1: Rigidity sensing in fast-moving cells. A typical fast-moving cell type, neutrophil-like differentiated HL-60 cells (A). Migration of cells in response to repeated stretching of the substratum (B) and on an anisotropic substratum (C).

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Modeling the Mechanosensitive Response of Crawling Cells

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In this work, we study the ability of cells to probe and dynamically adapt to the mechanical properties of their surroundings, i.e., their mechanosensitivity. Experimentally, this can be studied by observing the reorientation of crawling cells over cyclically stretched substrates[1] or their motion across inhomogeneous or patterned substrates. To understand the observed cell-specific response, a model that couples the substrate to the sub-cellular elements responsible for the cell shape and motility is needed: cell membrane, actin cytoskeleton, and focal adhesions, among others. For such situations, continuum phase-field models have quickly become one of the most powerful and popular computational techniques. We will present a brief overview of these modeling efforts, before showing how we have extended them in order to describe the reorientation of crawling cells over cyclically stretched substrates, among others.

Our results show that, depending on which of the sub-cellular processes is being probed, and the type of coupling with the stretching substrate, the cells can exhibit no reorientation, a bi-stability in the parallel or perpendicular orientations, or a systematic reorientation in either direction[2]. In particular, we show that an asymmetry in the adhesions dynamics during the loading and unloading phases of the stretching can be used to selectively align the cells. The phase-field model we have proposed can be generalized to study the mechanosensitive response of distinct cell types moving in complex environments, as well as incorporate detailed bio-chemical/mechanical couplings, and will hopefully lead to a deeper understanding of experimental observations.

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