

International workshop: Complex motile matter from single agents to collective behaviors

Date/Time: July 21st (Fri.) and 22nd (Sat.)
Venue: Nakano campus, Meiji University
Organizers: Carsten Beta (Univ. Potsdam, Kanazawa Univ.) Satoshi Nakata (Hiroshima Univ.),
Nobuhiko J. Suematsu (Meiji Univ.), Masaki Itatani (Budapest Univ. Technol. Econ.)
Hiroyuki Kitahata (Chiba Univ.)

July 21st (Fri.)

12:50 - 13:00 Opening

[Chair: Hiroyuki Kitahata (Chiba University)]

13:00 - 13:45 Kei Fujiwara (Keio University)
"Behaviors and characteristics of intracellular Reaction-diffusion wave revealed by a reconstitution system in artificial cells"

13:45 - 14:30 Natsuhiko Yoshinaga (Tohoku University)
"Reaction-diffusion models for Min oscillations: wave instability in a confined space"

14:30 - 14:45 break

[Chair: TBA]

14:45 - 15:30 Satoshi Sawai (The University of Tokyo)
"Cell-cell contact mediated regulation of cell polarity and collective movement"

15:30 - 16:15 Masatoshi Ichikawa (Kyoto University)
"Self-propelled droplets: from model system to living cell"

16:15 - 16:30 break

[Chair: Carsten Beta (University of Potsdam, Kanazawa University)]

16:30 - 17:05 Muneyuki Matsuo (The University of Tokyo)
"Supramolecular recursion due to complex motility"

17:05 - 17:40 Masaki Itatani (Budapest University of Technology and Economics)
"Design of transient pH oscillations utilizing a combination of two antagonistic enzymatic reactions and implementing it to synthetic cells"

17:40 - 17:50 Announcement

18:30 - Party

July 22nd (Sat.)

[Chair: Nobuhiko J. Suematsu (Meiji University)]

10:00 - 10:45 Akihiro Isomura (Kyoto University)
"Illuminating oscillatory gene expression in cell-cell communications"

10:45 - 11:30 Shuji Ishihara (The University of Tokyo)
"Onset of pattern propagation on curved surfaces"

11:30 - 13:00 Lunch

[Chair: Satoshi Nakata (Hiroshima University)]

13:00 - 13:45 Carsten Beta (University of Potsdam, Kanazawa University)
"Hybrid active matter – how motile cells actuate passive micro-cargo"

13:45 - 14:30 Akira Kakugo (Kyoto University)
"Implementation of transport tasks by Active Matter"

14:30 - 14:40 Closing

This workshop is supported by MEXT Joint Usage/Research Center Meiji University "Center for Mathematical Modeling and Applications" (CMMA).

Behaviors and characteristics of intracellular Reaction-diffusion wave revealed by a reconstitution system in artificial cells

Kei Fujiwara

Keio University, Japan

Coupling of chemical reaction and molecular diffusion emerges nonlinear wave such as propagation wave and stationary periodic patterns. These reaction-diffusion waves are known as the underlying mechanism of animal skins and their behavior has been analyzed by model systems such BZ waves. Recently, biological studies found that these reaction-diffusion waves are associated with molecular placements in living cells. However, the wavelength of these waves is comparable to the size of the space size, and their behaviors should be extensively distinct from those in the bulk. To elucidate this point, we focused on a reaction-diffusion waves for cell division plane determination (Min wave) and analyzed their physics by reconstituting them in artificial cells. In this presentation, we will discuss the characteristics of Min waves, including the relationship between spatial size and structure, methods of controlling their periodicity, its conversion to Turing patterns, and the principles governing the selection mechanism to select traveling and standing waves.

References

- [1] S. Takada, et al., *Sci. Adv*, 2022, 8, eabm8460.
- [2] S. Takada, et al., *ACS Nano*, 2022, 16, 10, 16853–16861.

Reaction-diffusion models for Min oscillations: wave instability in a confined space

Natsuhiko Yoshinaga

WPI Advanced Institute for Materials Research (WPI-AIMR), Tohoku University, Japan

The emergence of patterns in biological cells has attracted much attention to understanding the generic mechanism of biological functions associated with these patterns. The Min system may be the best example of such pattern formation due to its robust realisation both for in vivo and in vitro systems[1]. The Min system exhibits a standing wave of higher concentrations of Min proteins on a cell membrane. FtsZ proteins accumulate at the wave node and, as a result, the cell is divided into two daughter cells. Therefore, the wave plays a role in finding the centre of the cell. Motivated by these experiments, several reaction-diffusion models have been proposed. Nevertheless, the mechanism underlying the wave generation remains controversial.

In this presentation, I shall summarise the models for the Min system and discuss the potential mechanism of wave generation. Particular focus is on the effect of confinement; the proteins are distributed on the closed membrane and its inside. I shall discuss how the confinement results in wave instability by suppressing uniform oscillation on the membrane[1]. I shall also discuss how the cell chooses standing and travelling waves[2].

[1] S. Kohyama, Shunshi, N. Yoshinaga, M. Yanagisawa, K. Fujiwara, and N. Doi, *eLife*, 8, e44591 (2019).

[2] S. Takada, N. Yoshinaga, N. Doi, and K. Fujiwara, *Science Advances*, 8, eabm8460 (2022).

Cell-cell contact mediated regulation of cell polarity and collective movement.

Satoshi Sawai

Univ of Tokyo, Japan

The social amoeba *Dictyostelium* is well-known for chemotaxis-mediated aggregation, however it has noticed that these cells switch to another mode of movement mediated by cell-cell contact. I will go over our recent findings and discuss their relevance to the collective dynamics and pattern formation.

Self-propelled droplets: from model system to living cell

Masatoshi Ichikawa

Graduate School of Science, Kyoto University, Japan

A swimming microdroplet is one of simplest systems of self-propulsion modeling microorganisms and living cells. Various mode of motions, straight, curvilinear, spiral, reciprocal, figure-8s and zigzag motions have been demonstrated by controlling an anisotropic nature of the internal liquid [1]. Interestingly, even for droplets composed with isotropic liquids, diversification of motion occurred. In this study, we measured the motion and internal flow of a swimming micro-droplet of water, and quantitatively identified the mechanism of a straight-to-curvilinear motion transition [2,3].

References

- [1] M. Suga, S. Suda, M. Ichikawa, Y. Kimura, *Phys. Rev. E* 97, 062703 (2018).
- [2] S. Suda, T. Suda, T. Ohmura, M. Ichikawa, *Phys. Rev. Lett.* 127, 088005 (2021).
- [3] S. Suda, T. Suda, T. Ohmura, M. Ichikawa, *Phys. Rev. E* 106, 034610 (2022).

Supramolecular recursion due to complex motility

Muneyuki Matsuo

Graduate School of Arts and Sciences, The University of Tokyo, Japan

There is no room to differ that part of the organism's characteristic feature lies in the supramolecular recursion due to the complex motility. Such recursion could appear at any scale, i.e., molecules, reactions, supramolecules, and supramolecular populations. It is well known that the recursion itself is realized by coupling a system with periodic perturbations or an oscillatory reaction. Self-oscillating systems have also been constructed by introducing structural anisotropy, in which an oscillation emerges from non-oscillatory perturbations. Here, however, we report complex recursive systems in which the system itself spontaneously forms structural anisotropy based on non-recursive perturbations, and then recurses using the spontaneous symmetry breaking as the mechanism of oscillation. In these systems, autocatalytic processes are incorporated, which dynamically couple the apparent rates of chemical reactions and the physical properties of supramolecules far from equilibrium, and the structural anisotropy required for recursion emerges autonomously. Such systems may provide an insight into the process by which life spontaneously acquired recursivity in the ancient terrestrial environment, which was likely to have been random and homogeneous.

Design of Transient pH Oscillations Utilizing a Combination of Two Antagonistic Enzymatic Reactions and Implementing it to Synthetic Cells

oMasaki Itatani,¹ Gábor Holló,² Paola Albanese,³ Nadia Valletti,³ Sándor Kurunczi,⁴
Róbert Horváth,⁴ Federico Rossi,³ István Lagzi¹

[1] Department of Physics, Institute of Physics, Budapest University of Technology and Economics, Budapest, Hungary.

[2] Department of Fundamental Microbiology, University of Lausanne, Lausanne, Switzerland.

[3] Department of Earth, Environmental and Physical Sciences, University of Siena, Siena, Italy.

[4] Nanobiosensorics Group, Institute of Technical Physics and Materials Science, Centre for Energy Research, Budapest, Hungary.

Implementing internal chemical oscillations to synthetic cells and inducing dynamic behaviors such as self-propelled motion and self-replication of vesicles by the internal oscillators are still challenging although internal reaction-induced self-organization is originally adopted by living cells. pH oscillations are one of the eligible candidates for internal oscillators because they can combine with many bio-related molecular self-assembly. However, an autonomous pH oscillator having a mild pH range has not been reported, that can straightforwardly apply to synthetic cells. In this study, we show a novel concept to design pH oscillations satisfying the above biological requirements utilizing a combination of two antagonistic enzymatic reactions which produce basic and acidic compounds, namely urea–urease and ester–esterase reactions. The basic properties of the designed pH oscillations have been investigated in a batch system and pH oscillated transiently ranging from ~6.8 to ~8.5, which could be controlled depending on the concentration ratio between two enzymes and substrates. Furthermore, we have tried to construct a skeleton model to explain the mechanism of the obtained oscillation. At the end of the presentation, we would like to show some possible applications of the designed oscillators to liposomes, to extend our developed system to synthetic cell studies.

Illuminating oscillatory gene expression in cell-cell communications

Akihiro Isomura

Institute for Life and Medical Sciences, Kyoto University, Japan

Dynamic cell-to-cell communication is prevalent and plays pivotal roles in embryonic development and tissue formation of multicellular organisms. One of the most striking example is somitogenesis; in developing embryos of vertebrates, regular sizes of metameric structures called somites are formed in a synchronized and periodic manner [1]. Top-down approaches based on genetic or pharmacological perturbations have revealed dynamic signaling molecules involved in somitogenesis, such as periodic activity of Delta-Notch signaling. However, it has been challenging to identify minimally sufficient condition for synchronized generation of somites. Here, we introduce a bottom-up approach that combines optogenetics, synthetic biology and live-cell imaging to dissect functional capabilities of signaling molecules in collective behaviors of coupled genetic oscillators [2-5].

References

- [1] A. Hubaud, O. Pourquie, *Nat. Rev. Mol. Cell Biol.* 15, 709 (2014).
- [2] A. Isomura, F. Ogushi, H. Kori, R. Kageyama, *Genes & Dev.* 31, 524 (2017).
- [3] M. Matsumiya, T. Tomita, K. Yoshioka-Kobayashi, A. Isomura, R. Kageyama, *Development* 145, dev156836 (2018).
- [4] K. Yoshioka-Kobayashi, M. Matsumiya, Y. Niino, A. Isomura, H. Kori, A. Miyawaki, R. Kageyama, *Nature* 580, 119 (2020).
- [5] A. Isomura, R. Kageyama, unpublished.

Onset of pattern propagation on curved surfaces

Shuji Ishihara

Graduate School of Arts and Sciences, The University of Tokyo, Japan

Pattern formation often occurs on curved surfaces, and the influence of surface geometry on pattern dynamics has attracted much attentions in recent years. For Turing pattern, previous studies have reported that the stability conditions and positions of the pattern change depending on the surface geometry, while it has been considered that the pattern remains static regardless of the surface geometry. We find that a static Turing pattern on a flat surface can become a moving pattern on a curved surface [2]. This propagation is not allowed in 1D systems where there is no intrinsic curvature, but can occur on curved 2D surfaces. By investigating patterns on axisymmetric surface, some generic conditions on the symmetry of the surface and pattern for pattern propagation were identified. Our results provide new mechanism of pattern propagation and insights into the general role of surface geometry.

References

- [1] A. L. Krause et al., Modern perspectives on near-equilibrium analysis of Turing systems, *Phil. Trans. R. Soc. A.* 379, 20200268 (2021).
- [2] R. Nsishide and S. Ishihara, Pattern Propagation Driven by Surface Curvature, *Phys. Rev. Lett.* 128, 22410 (2022).

Hybrid active matter – how motile cells actuate passive micro-cargo

Carsten Beta

Institute of Physics and Astronomy, University of Potsdam, Potsdam, Germany

WPI Nano Life Science Institute, Kanazawa University, Kanazawa, Japan

Biohybrid micro-transport – the movement of micron-sized cargo particles by motile cells – is one of the most prominent applications in the emerging field of biohybrid systems. Here, we demonstrate that motile amoeboid cells can act as efficient and versatile transport agents [1]. Their transport properties result from the mechanical interactions with the passive cargo particle and reveal an optimal cargo size that enhances the locomotion of the load-carrying cells, even exceeding their motility in the absence of cargo. The experimental findings are rationalized in terms of an active particle model that describes the observed cell-cargo dynamics and enables us to derive the long-time diffusive transport of amoeboid microcarriers [2]. We have estimated the peak transport forces under different environmental conditions [3] and also extended our studies to more complex situations, where cargo particles are collectively actuated many cells at the same time, aiming at an overall understanding of this novel type of composite active matter.

[1] Nagel, Frey, Gerhardt, Beta (2019), *Advanced Science* 6 (3), 1801242.

[2] Lepro, Großmann, Panah, Nagel, Klumpp, Lipowsky, Beta (2022), *Physical Review Applied* 18 (3), 034014.

[3] Panah, Großmann, Lepro, Beta (2023), arXiv e-prints, arXiv: 2305.15298.

Implementation of transport tasks by Active Matter

Akira Kakugo

Division of Physics and Astronomy, Graduate School of Science, Kyoto University, Japan

Email: kakugo.akira.8n@kyoto-u.ac.jp

Cooperation is a strategy that has been adopted by groups of organisms to execute complex tasks more efficiently than single entities. Cooperation increases the robustness and flexibility of the working groups and permits sharing of the workload among individuals. Here, we demonstrate molecular transportation through the cooperative action of a large number of artificial molecular machines, photoresponsive DNA-conjugated microtubules driven by kinesin motor proteins. Mechanical communication via conjugated photoresponsive DNA enables these microtubules to organize into groups upon photoirradiation. The groups of transporters load and transport cargo, and cargo unloading is achieved by dissociating the groups into single microtubules. The group formation permits the loading and transport of cargoes with larger sizes and in larger numbers over long distances compared with single transporters. We also demonstrate that cargo can be collected at user-determined locations defined by ultraviolet light exposure.

References

1. C.W. Reynolds et al. *Computer Graphics*, 21, 25 (1987)
2. Jakia Jannat Keya et al. *Nature Communications*, Vol. 9 (453) (2018)
3. Daisuke Inoue et al. *Nature Communications*, Vol. 7:12557 (2016)
4. Kento Matsuda et al. *Nano Letters*, Vol 19 (6), pp. 3933-3938 (2019)
5. Daisuke Inoue et al. *ACS Nano*, Vol. 13 (11), pp. 12452-12460, (2019)
6. Mousumi Akter et al. *Sci. Robot.*, Vol. 7 (65), eabm0677 (2021).