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Abstract

Mon. 9th

István Lagzi
Material design and engineering using reactions and mass transport processes

Jae Kyoung Kim
Mastering Noise in Rhythm Generation: Strategies for Utilization and Avoidance

Akiko Satake
Synchrony from genes to ecosystems

Hiroya Nakao
Dynamical reduction approach to the analysis and control of rhythmic systems

Takashi Miura
Self-organization of cell-cell boundary structures in kidney cells

Tue. 10th

Aneta Stefanovska
Imperfect clocks that govern mammalian physiological functions
– an overview from circadian to milliseconds scales

Haruna Fujioka
Individual activity-rest rhythms of ants under laboratory colony conditions

Daisuke Ono
Cytosolic circadian rhythms in the mammalian central circadian clock

Federico Rossi
Synthesis and Application of Giant Unilamellar Vesicles for Cellular Modeling and Advanced Materials

Wed. 11th

Hiroshi Ito
Cellular circadian rhythm can be more precise through output

Gisele Oda
Biological Clocks of Subterranean Rodents:
Field Work meets Mathematical Modeling in South America

Hiroyuki Kitahata
Relation between motion and shape in self-phoretic motions

Material design and engineering using reactions and mass transport processes

István Lagzi (Budapest University of Technology and Economics)

Wet synthesis is one of the most widely used techniques for generating crystalline materials. The reagents are mixed in this procedure, and crystals form due to the nucleation and growth processes. In crystal growth and engineering, the most crucial is the temporal control of the processes over time to obtain samples with a desired average size and dispersity. In the lecture, recently developed alternative methods will be presented and discussed for synthesizing various crystalline materials, such as inorganic precipitate particles, zeolitic imidazolate frameworks, and gold nanoparticles. We highlight the advantage of applying a gel reactor utilizing diffusion and ionic migration driven by a direct electric field. Additionally, we show that cell-sized microcompartments (giant unilamellar vesicles) can act as reactors for the synthesis of crystals. In these techniques, the mass transport affects the mass flux of chemical species in the system, influencing nucleation and crystal growth. Therefore, control of mass transport of the chemical species can be used to tune the morphology, average size, and size distribution of crystalline materials.

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Mastering Noise in Rhythm Generation: Strategies for Utilization and Avoidance

Jae Kyoung Kim (KAIST & IBS)

Circadian rhythms, despite being enveloped in inevitable biological noise, exhibit remarkable resilience, maintaining precise 24-hour cycles. This presentation delves into the sophisticated mechanisms by which circadian clocks navigate the challenges of noise, ensuring timely transcriptional regulation. We explore the orchestration of multiple repression strategies —encompassing sequestration, displacement, and blocking of PER proteins—employed by circadian systems to achieve robust transcriptional repression and activation amidst environmental and intrinsic fluctuations. A focal point is the utilization of photoswitches, a pivotal adaptation allowing PER proteins to accurately time their nuclear entry for transcriptional regulation, overcoming the heterogeneity in their perinuclear arrival times caused by spatiotemporal noise. Moreover, we shed light on the counterintuitive benefits of noise within this biological context. Specifically, we discuss how a controlled degree of noise can sharpen the circadian rhythm's waveform and enhance the signal-to-noise ratio, offering insights into the adaptive significance of noise in biological systems. This talk aims to underscore the intricate balance between noise utilization and avoidance, highlighting its role in the resilience and precision of circadian rhythms.

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Synchrony from genes to ecosystems

Akiko Satake (Kyushu University)

Self-organized synchrony among diverse biological components has been identified in many biological systems. The synchronized flowering and fruiting observed in temperate and tropical rainforests represent one of the most mysterious and large-scale events in ecosystems. Occurring at irregular intervals spanning several years, a remarkable phenomenon unfolds where nearly all tree individuals within a population, sometimes alongside species from other families, simultaneously burst into flower. The proposed explanation posits that an internal nutrient cycle, coupled with an external water-stress signal, orchestrates this synchrony, drawing parallels to the intricate mechanisms of molecular circadian clocks (1). However, in contrast with the extensive theoretical and ecological analysis of phenotypic observation, little is known about the molecular mechanisms underlying the synchrony, since dominant tree species in forest ecosystems are non-model species in terms of molecular and genome biology. Leveraging the progress in genome sequencing and information technologies, we can generate genome-wide transcriptomic data at the ecosystem level under naturally fluctuating conditions (2). Our spatiotemporal gene expression data revealed a hierarchical synchrony that manifests within the genome, tissues, individual trees, and populations. We found distinctive gene expression profiles in leaf tissues as opposed to buds and flowers, and parallel expression profiles between different species during both summer and winter. When coherence in gene expression at the individual level aligns at the forest level, it induces feedback effects on the atmosphere and climate. This feedback loop, in turn, influences the reproductive success and survival of plants, a topic we'll delve into further. (3)

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Dynamical reduction approach to the analysis and control of rhythmic systems

Hiroya Nakao (Tokyo Institute of Technology)

Dynamical reduction provides a powerful approach to the analysis and control of nonlinear oscillators. In this talk, three recent topics illustrating the use of such dynamical reduction will be briefly presented.

(i) Koopman operator and phase-amplitude reduction. The relationship between Koopman operator theory and phase reduction theory for limit-cycle oscillators has recently become clear. This has led to a generalization of classical phase reduction to phase-amplitude reduction, which incorporates deviations from the limit cycle as amplitudes. The theoretical framework and a simple application to optimal entrainment with amplitude suppression are briefly explained.

(ii) Phase-reduction approach to noise-induced coherent oscillations. Noise can induce stochastic oscillations in excitable systems without limit cycles. It is shown that, for some fast-slow systems, we can construct hybrid (piecewise-continuous) dynamical systems approximating their stochastic oscillations. As an example, entrainment and synchronization of a noisy fast-slow excitable system is discussed.

(iii) Design of nonlinear oscillators based on phase reduction. Using the reduced phase equation, we can develop a method to design a dynamical system with a prescribed trajectory and phase response characteristics. As an example, an artificial star-shaped oscillator that exhibits multi-stable entrainment to high-frequency periodic input is designed.

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Self-organization of cell-cell boundary structures in kidney cells

Takashi Miura (Kyushu University)

Recently, the multicellular structure in biological systems has been extensively studied by combining experimental and theoretical approaches. On the other hand, shapes within cells have not received much attention. Individual cells show very complex structures, and understanding the mechanism of subcellular pattern formation should facilitate cell biology.

The kidney is a highly specialized organ for generating urine. Cells in the kidney have various unique shapes to implement their function. For example, Podocytes have numerous intricate secondary processes that act as filters to generate urine from blood. The cell-cell junction of renal tubules sometimes shows an intricate shape to facilitate paracellular transport. We formulated mathematical models of self-organization of these two cell-cell junctions and tried to verify the models experimentally.

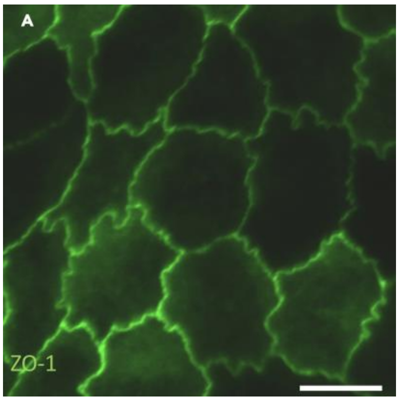

Figure 1. Interdigitation of cell-cell junction in MDCK cell sheet.

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Imperfect clocks that govern mammalian physiological functions – an overview from circadian to milliseconds scales

Aneta Stefanovska

Physics Department, Lancaster University, Lancaster, UK

Oscillatory dynamics pervades the universe, appearing in systems on all scales. It can be studied within the frameworks of either autonomous or nonautonomous dynamics. Autonomous dynamical systems serve as mathematical models for the time-evolution of the states of isolated physical systems, whereas non-autonomous dynamics describes open systems subjected to external driving with time-varying parameters. While autonomous dynamics can be studied within the long-time asymptotic framework, including asymptotic stability, we will argue that this framework can be inadequate or unsuitable when investigating open systems and studying the parameter-dependence of their stability. We will provide a new framework for non-autonomous oscillatory dynamics, within which we can define intermittent phenomena such as intermittent phase synchronisation, evaluated as the stability of phase interactions.

We will briefly address the question of how to effectively analyse time series measured from open oscillatory systems operating on multiple timescales and with time-variable characteristic frequencies that enable explicit tracking of time-localised dynamical behaviour, as opposed to the traditional framework for dynamics analysis focused on time-independent dynamical systems and based on long-term statistics. Methods to extract modes, their coherences and couplings from measured data will be also presented.

We will then discuss imperfect biological clocks manifesting on scales of days, known as circadian or bi-circadian rhythms, metabolic oscillations acting on minutes' scales related to glucose and oxygen metabolism, to seconds' scales related to vascular motion, respiration, and heartbeat, to millisecond scales related to brain waves. Recent works on behavioural rhythms and rhythms related to cardiovascular and brain interactions in ageing will be reviewed.

Individual activity-rest rhythms of ants under laboratory colony conditions

Haruna Fujioka (Okayama university)

Most organisms exhibit a periodic activity of about 24 hours. This circadian rhythm is considered to be an adaptation to the fluctuations of the environment. In ants, individual behaviors, including activity-rest rhythms, is influenced by social interactions within their colony [1]. However, monitoring individual activity-rest rhythms in an ant colony is challenging due to their large group size and small body size. To address this, we developed an image-based tracking system using 2D barcodes in a monomorphic ant (Fig 1a) and measured the locomotor activity of all colony members under laboratory conditions [2]. Activity-rest rhythms appeared only in isolated ants, not under colony conditions (Figure 1b). This suggests that a mixture of social interactions, not light and temperature, induces the loss of activity-rest rhythms. These findings contribute to our understanding of the diverse patterns of circadian activity rhythms in social insects.

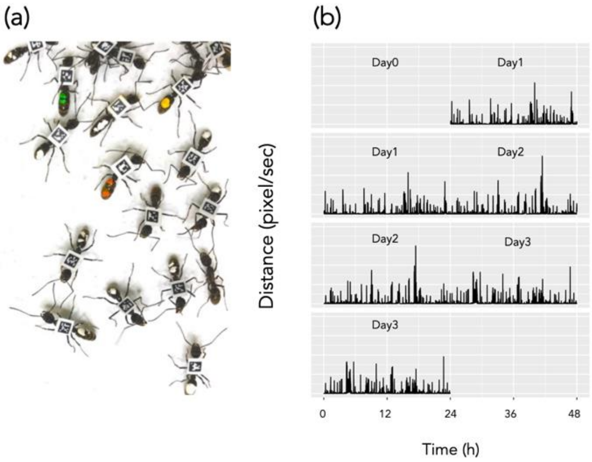

Figure 1. Tagged and untagged ants (a). The species is *Diacamma* cf. *indicum*. Different color on their gaster indicates different age. Actogram of worker for 3 days activity-rest rhythms (b).

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Cytosolic circadian rhythms in the mammalian central circadian clock

Daisuke Ono (Nagoya University, Japan)

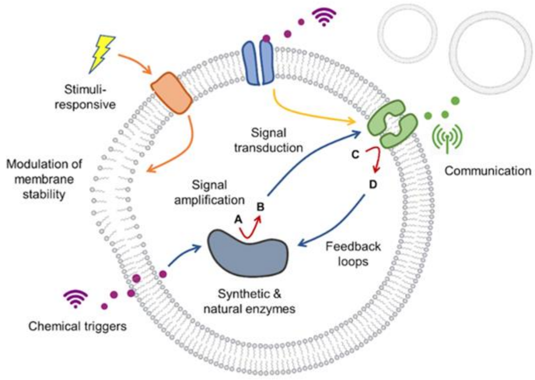
In mammals, the suprachiasmatic nucleus (SCN) plays a crucial role in the timing of physiology and behavior, such as sleep/wakefulness. In the SCN, several neurotransmitters are involved in the neuronal network. The receptors for these neurotransmitters are coupled with G-proteins and second messenger signaling pathways, including cAMP and Ca^{2+}. Pharmacological studies suggest that in the SCN, intracellular cAMP and Ca^{2+} are involved in the input and/or output of the molecular circadian clock and/or in the circadian oscillations within the SCN. However, the functional roles and dynamics of cAMP and Ca^{2+} within the SCN neuronal network remain largely unclear.

To investigate the functional roles of cAMP, we first visualized the spatiotemporal pattern of circadian rhythms of cAMP in the SCN using bioluminescent cAMP probes (Okiluc-aCT) that we recently developed (Ono et al., 2023, Science Advances). For comparison, we also visualized the rhythm patterns of Ca^{2+} using the fluorescent Ca^{2+} probe (GCaMP6s). Blocking the function of the neural network in the SCN slice resulted in the loss of circadian rhythms of cAMP, whereas circadian rhythms of Ca^{2+} persisted but decreased in amplitude. These results suggest that in the SCN, circadian rhythms of cAMP are regulated by the neural network, while circadian rhythms of Ca^{2+} are regulated by both intracellular mechanisms and neural networks.

To further understand these cytosolic events and their relation to the circadian clock, we used *Bmal1*-deficient mice that show arrhythmic behavior under constant conditions. We confirmed the presence of circadian rhythms of PER2::LUC in the SCN of *Bmal1*-deficient mice, as previously reported (Ko et al., 2010, PLoS Biology). These rhythms exhibited the three key aspects of the circadian clock: autonomous oscillation, temperature compensation, and entrainment. Additionally, we observed cAMP and Ca^{2+} rhythms in the SCN of these animals. These results suggest that *Bmal1* is not essential for circadian rhythms in the SCN.

Synthesis and Application of Giant Unilamellar Vesicles for Cellular Modeling and Advanced Materials

Federico Rossi
(Department of Physical Sciences, Earth and Environment,
University of Siena, Italy)



We present the synthesis and multifaceted applications of Giant Unilamellar Vesicles (GUVs) in cellular modeling and the development of advanced materials. GUVs, known for their capacity to mimic cell membranes, are synthesized through a phase transfer method using self-assembling amphiphilic molecules that form bilayers, creating isolated environments ideal for both biological and material science experiments. In the realm of cellular modeling, GUVs are utilized to replicate complex cellular behaviors, such as enzymatic reaction networks, signal transduction, and self-division, offering a simplified yet dynamic model to explore fundamental biological processes and the mechanisms underlying cellular communication. The reconstitution of photoswitchable amphiphilic molecules within GUV membranes, also enable the modulation of membrane properties in response to external stimuli like light. This development is pivotal for creating stimulus-responsive biomimetic systems that have potential applications in smart drug delivery and biocompatible devices. Concurrently, these vesicles can serve as microreactors for the controlled synthesis of novel materials, including Metal-Organic Frameworks (MOFs) like Zeolitic Imidazolate Frameworks 8 (ZIF-8). The unique environment provided by GUVs may allow for precise control over the nucleation and growth of these crystalline structures, leading to materials with potential applications in catalysis, drug delivery, and gas storage.

Cellular circadian rhythm can be more precise through output

Hiroshi Ito (Faculty of Design, Kyushu University)

Circadian rhythms are biological phenomena that repeat with a 24-hour cycle. Even individual cells can exhibit a self-sustained rhythmicity. In this talk, I will focus on the accuracy of cellular circadian rhythms. Circadian rhythms exhibit smaller fluctuations when cells are coupled as a group, e.g. organs. However, at the single-cell level, circadian rhythms are less robust. For instance, mammalian cultured cells have a period variation of about 1 hour. In contrast, prokaryotic cyanobacteria show a fluctuation of 0.1 hours, indicating a more accurate circadian clock. Why do these differences arise? One possibility we theoretically proposed is the control of fluctuations in the output system. We considered a simple circadian clock model coupled with its output system. We found that the output system's fluctuations could be smaller than those of the circadian clock itself. Furthermore, this is not dependent on the expression level of the promoter but rather on the degradation rate of the output protein or the functional system that determines its transmission. We also discovered that the sinusoidal regulation effectively reduces fluctuations. Compared to the rhythms of neuronal firing or cell cycles, the rhythm of the circadian clock tends to be sinusoidal. This might be the result of optimization aimed at reducing circadian rhythm fluctuations. Furthermore, our recent analysis revealed that feedback loops output waveforms very close to sine function. The fact that the circadian clock is generated by feedback might be linked to these fluctuations. So far, chronobiologists have devoted huge effort to examine the central circadian oscillator. Yet, there would be unresolved issues on the clock's output.

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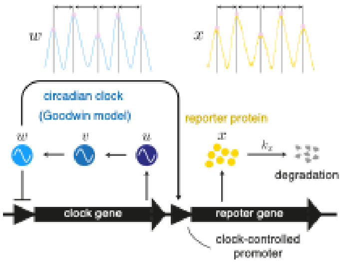

Figure 1. Fluctuation in period of circadian clock and its output.

Biological Clocks of Subterranean Rodents: Field Work meets Mathematical Modeling in South America

Gisele A. Oda, Veronica S. Valentinuzzi

(Laboratório Binacional Argentina-Brasil de Cronobiologia, CRILAR Argentina, University of São Paulo, Brazil)

Photic synchronization mechanisms of biological clocks have long been investigated in model species, under manipulation of light/dark cycle parameters in the laboratory. In particular, it has been shown that even daily minute light pulses are able to synchronize circadian oscillators, being this a link between biological clock studies and periodically pulsed oscillator theories. Parallel lines of investigation, have considered how wild organisms are daily exposed to the light/dark cycle in nature, questioning the artificially imposed light/dark conditions in the lab and associated models. Wild organisms that inhabit the extreme photic environment of the subterranean provide an opportunity to verify persistence and minimal photic input for daily and seasonal synchronization. Here we present our joint field, laboratory and modeling work investigating the chronobiology of subterranean rodents known as "tuco-tucos" (*Ctenomys coludo*), which are widespread in South America. Using miniature bio-loggers, we obtained automated, continuous and individual recordings of daily light exposure and activity rhythms of these desert subterranean animals (La Rioja, Argentina, 12oS Latitude), which revealed how they expose to light throughout the 24h and the drastic changes of these patterns throughout the seasons. The joint analysis of seasonal variation of daily light exposure and the associated changes in daily activity rhythms enabled testing the two-oscillator model of the biological clock, whose seasonal changes in phase relationship accounts for decoding of daylength in mammals. By using minimal light inputs in computer simulations, we developed a mathematical model of a clock that works for all seasons, even in the subterranean. Support: (FAPESP, CONICET, CAPES, CNPq).

Relation between motion and shape in self-phoretic motions

Hiroyuki Kitahata (Department of Physics, Chiba University)

When a particle or droplet of surface-active chemicals like camphor is floated on the water surface, surface-active molecules are released from it to the water surface. Due to the spatial difference in concentration, a surface tension gradient is generated and can drive the particle or droplet. When its shape is circular, the concentration field should be isotropic with respect to the center, and the forces originating from the surface tension acting on it should be balanced. However, such an isotropic balanced state can become unstable due to fluctuations. Consequently, the particle or droplet starts to move in a direction determined by the fluctuations. This can be called "self-phoretic motion" since the concentration field is generated by itself. This self-phoretic motion can be adopted in some other cases. For example, if a living cell emits a harmful chemical for itself and it escapes from the region with a higher concentration, then the cell motion should exhibit qualitatively the same characteristics.

If the shape of a particle or droplet has anisotropy, its shape should affect motion. We constructed the mathematical model describing such motions of a particle or droplet, including the effect of its shape, and performed the numerical simulation and theoretical analyses. For example, the mathematical analysis suggests that an elliptic particle moves in its minor-axis direction, and we confirmed it by experiments [1]. Using an alcohol droplet floating at the surface of an almost saturated solution of the alcohol, we can realize a spontaneous motion with deformation [2]. We experimentally observed the relationship between motion and deformation and analyzed the generic features of the coupling between motion and deformation. We also discussed the large deformation of an oil droplet with camphor moving and deforming on a water surface [3].

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