they provide a deeper understanding of the intrinsic properties of cardiac cells.

2C1510 CA モデルによる多細胞性シアノバクテリアの形態形成ダイナミクスの解析

Analysis of the internal dynamics for pattern formation in multi cellular cyanobacteria by CA model

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The multicellular cyanobacteria, *Anabaena* sp. PCC 7120, differentiates cells named heterocysts for nitrogen fixation at every ~10 cells under nitrogen-depleted culture. This is known as one of the simplest pattern formation, but a detailed mechanism has not yet been validated theoretically.

To address this question, we made a 1-dimensional cellular automaton (CA) model for the pattern formation, including stochastic cell cycle processing, cell division and differentiation. And a differentiated cell suppresses differentiation of neighboring cells. In the CA model, we considered that the division and/or differentiation probability may depend on time after cell birth, "cell age". Some parameters were quantitatively determined from cell-lineage analysis made by our group.

To evaluate our models, we compared the distribution of heterocyst interval between experimental data under microscope and computer simulation data by CA models. As a result, respective features in steady-state of simulation data agreed with that of the experimental data if cell division and differentiation depended on cell age in CA model. These result suggested that the probability of cell differentiation and division connected to cell age was very important condition. Moreover, pattern formation in transitional state of experimental data agreed with that of simulation data if cell differentiated independently of cell age in CA model.

We also succeeded in solving the distribution of heterocyst interval of CA model by Markov process including cell age transition.

2C1522 Modeling the mammalian circadian clock

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Life generally runs on a schedule. The earth's rotation creates daily changes in light, temperature, and other environmental conditions, and many organisms respond to this by synchronizing their behavior and physiology with the day/night rhythm. We have developed a simplified model of the circadian clock system in mammals that captures many of its key features and can be parameterized by fitting to cellular-level measurements of biological rhythms. By using Monte Carlo sampling of the parameter-fitting landscape, we have been able to create an ensemble of data-fitted models and use tools from statistical mechanics to assess the system's robustness to parameter variations. We are currently using this model to explore the effects of external perturbations on the cellular clock, which can be important for tissue-level synchronization and entrainment to environmental signals.

2C1534 Determining the ratio of longitudinal to transverse conductivity in a cardiac tissue culture through application of FFP

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Tachycardia and fibrillation are potentially fatal arrhythmias associated with the formation of rotating spiral waves in the heart. Low-energy far-field pacing (FFP) has recently been proposed as a superior therapy, and it has been found that the formation of such sites can lead to the termination of undesired states in the heart and the restoration of normal beating. In this study, we investigate a particular aspect of this method. Here, we seek to determine how the activation site density depends on the applied electric field through in vitro experiments carried out on neonatal rat cardiac tissue cultures. The results indicate that the activation site density increases exponentially as a function of the intracellular conductivity and the level of cell isotropy. Additionally, we report numerical results obtained from bidomain simulations that are quantitatively consistent with our experimental results. Also, we derive an intuitive analytical framework that describes the activation site density and provides useful information for determining the ratio of longitudinal to transverse conductivity in a cardiac tissue culture. The obtained results should be useful in the development of an actual therapeutic method based on low-energy far-field pacing. In addition,

2C1546 気道上皮細胞における Cl⁻分泌の数理モデル

Mathematical model of Cl⁻ secretion in airway epithelial cells

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Transcellular Cl⁻ secretion in airway epithelial cells followed by paracellular Na⁺ secretion from the basolateral space to the apical one increases osmotic pressure in the apical space, which induces water secretion. Therefore, transcellular Cl⁻ secretion plays a crucial role in prevention from infection of bacteria and virus etc, by producing water secretion into the apical space covering airway epithelial cells.

Even using various techniques, we could not exactly get ideas how transcellular Cl⁻ secretion varies in its magnitude and time course due to modification of activity of Cl⁻ channels and transporters located at the apical and basolateral membranes. In the present study, we try to clarify how transcellular Cl⁻ secretion varies in its magnitude and time course when activity of Cl⁻ channels and transporters located at the apical and basolateral membranes changes using mathematical simulation with three parameters.

(1) the entry step; Cl⁻ into the intracellular space across the basolateral membrane

(2) the secretion step; Cl⁻ from the intracellular space across the apical membrane

(3) the recycle step; Cl⁻ across the basolateral membrane

This novel method reported in the present study provides us how activity of Cl⁻ channels and transporters located at the apical and basolateral membranes changes and understandings on roles of intracellular signaling in transcellular Cl⁻ secretion.

2C1558 エラーカスτροφイーによる HIV-1 擬種集団の自壊過程に関する研究

A Study on a Self-Destruction Process of a HIV-1 Quasispecies Population through the Error Catastrophe

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The present study examines possibility of a new AIDS treatment without using anti-HIV-1 drugs to avoid drug resistance. It is well-known that HIV-1 is frequently-mutated. Our idea for the new treatment is by inducing excess mutations to HIV-1 genome, to drive HIV-1 population to self-destruction. Namely, we will use the HIV-1's remarkable character of its mutating at high rate as an underhanded way. Our study proposes a novel HIV-1 mathematical model considered viral kinetic processes such as mutation, replication, infection and an action of a mutagen to control HIV-1 mutation rate. In terms of HIV-1 population, our model considers a quasi species formed by four different traits. Fast and slow replicators and either type can take viable and defective form. Through some numerical simulations of the model we will present that increasing HIV-1 mutation rate causes HIV-1 population to the error catastrophe.

2C1610 Characterization of Death and Division Process in Synthetic Bacterial Population with Antibiotic Treatment

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We previously succeeded in observing non-genetic adaptation in antibiotic exposure by using a synthetic *E. coli* strain, expressing antibiotic resistant gene as fusion with fluorescent protein. Generally, phenotypic adaptation requires cell-to-cell variation of fitness, which is defined as difference between division rate and death rate. So, there are three possibilities on how phenotypic adaptation occurs in lethal environment; (i) growth rate varies among cells while death rate not, (ii) death rate varies while division rate not, and (iii) both rates vary. To test which scenario would be probable, we estimated, as a first step, temporal transitions in division frequency and death frequency, which were defined against a whole population. Time-lapse observation on a microfluidics device enabled us to directly observe growth, division and death in antibiotic exposure at single-cell level, followed by acquisition of time-series of division and death events. Consequently, it was clarified that death frequency decreased in antibiotic exposure while division frequency was almost constant