ABSTRACT

Theoretical study on ordering of polarity and oscillation in cell populations
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Polarity and phase ordering are greatly important in biology. The former is essential, e.g., for alignment of hair follicles and oriented cell division. The latter is known as synchronization, which is required, e.g., for normal operation of the heart and circadian rhythms. In this thesis, the ordering dynamics of cellular polarity and oscillation phase is elucidated.

In Chapter 1, polarity and phase ordering and some mathematical models of ordering are introduced.

The first and second parts of this thesis deal with the polarity alignment process (Chapters 2 – 4) and the phase ordering process (Chapters 5 – 7), respectively.

In Chapter 2, first, the planar cell polarity (PCP) is explained. PCP refers to the coordinated alignment of cell polarity across a planar tissue, and many biological experiments have been performed on PCP in the wing epithelium of *Drosophila*. The present study is based on those experimental results. The previous mathematical models of PCP and general models describing ordering of spins and oscillators are introduced.

In Chapter 3, a reaction–diffusion model of cellular polarity alignment is constructed. Nonetheless, this model is costly for numerical analysis when many cells are considered. Therefore, in the second half of Chapter 3, a reduced model using the phase reduction theory for systems with a spatially translational mode is derived. The derived phase model is drastically simpler and easier to analyze than the reaction–diffusion model, yet it is a reasonable approximation. It contains the terms representing geometric information, such as cell shape and relative position of adjacent cells in addition to the terms similar to ferromagnetic spin models. In contrast to previously proposed phenomenological models, these terms are derived directly from the reaction–diffusion model.

In Chapter 4, the newly derived phase model is analyzed. As a result, it becomes clear that shapes of cells and anisotropy of a coupling strength distribution affect the global orientation of polarity. In fact, when the distribution of coupling strengths is uniform, the polarity is oriented perpendicular to the direction of cell elongation, and in the case where the distribution of coupling strengths is heterogeneous, the polarity is ordered toward a strongly coupled adhesive side. These dynamical properties are elucidated numerically and theoretically. Moreover, other properties including the effects of the form of the system boundary, an external signal and noise, and defects of polarity are presented.

In Chapter 5 and the following chapters, the ordering dynamics of cellular phases are focused upon, by considering spiral chaos in which spirals repeat to generate and annihilate. This study is motivated by atrial fibrillation whose dynamics resemble spiral chaos. The atrium is supposed to show spiral chaos of electrical waves when the heart undergoes atrial fibrillation. Catheter ablation, by which the atrium is subdivided into several parts, is known to be effective at terminating chaotic dynamics. Hence, it is theoretically expected that there is a relation between the stability of a chaotic state and its system size. Indeed, it is known that the lifetime of transient spiral chaos grows exponentially as the system size increases.

In Chapter 6, a theoretical formula for predicting the lifetime of spiral chaos in excitable media is derived. The distribution of the number of defects approaches the Gaussian distribution according to central limit theorem as the system size increases. Using this fact, a general expression for the dependence of lifetime on system size is provided; this relation is valid for large system sizes, and the dependence is indeed exponential. It is confirmed that the expression of lifetime is in good agreement with numerically obtained lifetime values with parameter sets near the onset of transient chaos.

In Chapter 7, to verify generality of the argument in Chapter 6, a model of oscillatory media manifesting transient spiral chaos is numerically analyzed and consistency of the claims is confirmed.

In Chapter 8, after summarizing this research, possible applications are discussed.