リーダー細胞に誘導される集団細胞回転

松下勝義, 薮中俊介 [A], 橋村秀典 [B], 桑山秀一 [C], 藤本仰一

阪大院理 生物, [A] 九大院理 物理, [B] 東大総合文化 相関基礎, [C] 筑波大 生命環境

概要

生物系においては細胞の集団での回転運動がしばしば現れる. 我々はこれらの回転運動の誘導要因がリーダー細胞である可能性について調べた. この目的の下, 我々はリーダー細胞が異種分子細胞間接着に持続的な極性を持つことを仮定し, 細胞 Potts 模型を基に集団細胞回転運動の模型を構成した. そして, リーダー細胞がこの回転運動を誘導する可能性を示した.

Leader-guiding collective cell rotation

Katsuyoshi Matsushita, Sunsuke Yabunaka[A], Hidenori Hashimura[B], Hidekazu Kuwayama[C], and Koichi Fujimoto

Department of Biological Science, Graduate School of Science, Osaka University.
[A]Department of Physics, Graduate School of Science, Kyushu University.
[B]Department of Basic science, Graduate School of Arts and Sciences, The University of Tokyo.
[C]Faculty of Life and Environmental Sciences, University of Tsukuba.

Abstract

In biological systems, collective rotations frequently appear in cell aggregations. We examine leader cells as a possible guide for these collective rotations. For this purpose, we model the multicellular system based on the cellular Potts model for these rotations by assuming the persistently-polarized heterophilic cell-cell adhesion of leader cells. We show a possibility that the leaders guide these rotations.

1 Introduction

In developmental processes in biological systems, eukaryotic cells collectively and spontaneously move to their suitable positions for their fates [1]. One of the spontaneous collective movements is a persistent collective rotation of cell aggregations [2–4]. For example, this rotation sorts out *Dictyostelium discoideum* cells by their fates [3, 5]. This rotation has been investigated by biologists and its guiding mechanisms were speculated to be chemotaxis [6, 7] and molecular chirality [8]. In addition to these mechanisms, the persistence of the rotation lets us deduce the persistent motility in individual cells [9, 10]. This rotation, however, is naively contradictory to the persistent motility, because the persistent motility seems to stabilize only the unidirectional order of movements instead of the rotation [11–15]. Therefore, improvements for matching these mechanisms to the persistence is necessary for the understanding of the collective cell rotations.

As such an improvement, the contact following was theoretically considered and successfully reproduced the rotation [6,7,16,17]. Because the contact following is implemented by the Vicsek-like interaction based on visual recognition [18], it is not simply supposed for natural cells in contrast to birds or fishes. As an alternative improvement independent of such recognition, we focus on the effects of the leader cells which drag the surrounding cells [19]. Namely, we hypothesize that the leader cells guide the rotation. In this case, only the leader cells have the persistent motility, while the surrounding cells do not. Hereinafter, we call the surrounding cells follower cells for convenience in explanation. This hypothesis is based on the fact that leader cells cannot stabilize the unidirectional order in their low concentrations below a certain threshold value necessary for the order.

In the present work, to examine this hypothesis, we model these leading and follower cells based on the cellular Potts model [19, 20]. As a test case of this hypothesis, we consider a persistent motility due to the persistently-polarized heterophilic cell-cell adhesion between leader and follower cells [21] for tractability in this model. By this model, we confirm that the leaders successfully guide these rotations by avoiding the unidirectional order in the case of a few leaders.

2 Model

For our purpose, this work utilizes the two-dimensional cellular Potts model. In this model, cell configurations are represented as Potts states

4 Summary and Remarks

In conclusion, we confirm the collective cell rotation guided by leader cells. From our simulation, the number of leader cells is necessary to be small for stabilizing the rotation. This is because the dense leader cells stabilize the polar order and thereby inhibit the rotation [19].

This collective cell rotation has two prominent properties. One prominent property is the persistence of the collective cell rotation. Namely, the direction of the rotation does not change in a long time. The mechanism of this persistence may originate from the persistence of leaders' polarities. However, as shown in Fig. 1(b), the direction of leaders' polarities are not always aligned in the same direction consistent with the rotation. Namely, the persistence of polarities apparently does not contribute to the persistence of the rotation. Therefore, another origin of the persistence of rotation is expected. One possibility of this alignment is the long-range coupling of leaders' polarities through the motion of follower cells as shown by Kabla for the collective migration [19]. This coupling may statistically stabilize a slight net polarity consistent with the rotation.

The other prominent property is the fact that the velocities of leader cells are two times faster than those of follower cells as shown in the number of trajectory circles in Fig. 2(b). This property may be useful as a sufficient marker of the leader-guiding. Namely, the leader mechanism can be explored by the experimental observation of the cell trajectories in the collective cell rotation in the future. When our setting is realized, the distribution of cell velocity or displacement is predicted to become bimodal because of the difference between the leader and follower cells in their velocities. Such a bimodal distribution has never been reported in experiments of *Dictyostelium discoidem* at least. Therefore, this absence of the report at least in *Dictyostelium discoidem* implies another still-uncovered solution where the leader and follower have the same velocity.

For the universality of these properties on the propulsion, we additionally give a remark. In the present work, we assume the heterophilic cell-cell adhesion as a propulsion source of leader cells. We expect that these properties do not depend on the origin of the motility and depend only on the persistence of motility's polarity. This is necessary for rotations of leaders to avoid simple random walks. If the polarity has persistence, this leader mechanism is applicable to the cases of propulsion by either chemotaxis or molecular chirality.

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E-mail: kmatsu@bio.sci.osaka-u.ac.jp