情報統計力学の最前線−情報と揺らぎの制御の物理学を目指して−

Mechanical control of hexagonal cell packing in *Drosophila* wing

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In the course of animal development, tissues undergo deformation, which is driven by the mechanical forces regulated by the activity of constituent cells. Thus, to understand variety of morphologies of multi-cellular organisms one must elucidate physical process as well as molecular processes to determine the eventual forms of their bodies ~~from embryos~~. Recent studies have clarified how geometrical changes of cells are coordinated via the activity and/or localization of force-generating molecular machineries within a cell. On the other hand, it remains unclear how the mechanical interaction among cells and the resulting stress field of a tissue are organized to control cellular pattern formation. One of the difficulties to characterize mechanical processes of morphogenesis is the lack of proper experimental methods to directly measure and quantify the forces in the cell population inside the animal body.

Here we propose a novel method to estimate the forces from observed cell shapes. Consider that the geometry of epithelial cell population is represented by an assemblage of 2D polygons ('vertex model': Fig. 1a). Forces in the cell population are described by the isotropic pressures of respective cells and tensions applied in the adherent surface between cells. By considering the geometrical forms of the cells, we obtained balance equations of the aforementioned forces. We can estimate the unknown values of forces by solving the balance equations, however, the number of conditions is less than that of unknowns. To overcome the difficulty, we incorporated the experimental fact that the tensions of cell-cell surfaces are positive as the expected feature of the system, which is indicated from the responses to laser ablation of acto-myosin cable in the cell. Then by adopting the expectation as a prior, inverse problem is formulated in the scheme of Bayesian statistics (Fig. 1b-d). Present method has several advantages. At first, it is applicable to variety of systems. Second, the method is noninvasive and it can capture the dynamics of force field. Thirdly, it can distinguish pressures and tensions among respective cells, thus we can compare estimated forces with molecular activities responsible for

generating forces in each cell. Forth, several hundreds of cells are simultaneously estimated, thus we can approach for their relationship between cell level and tissue level kinetics.

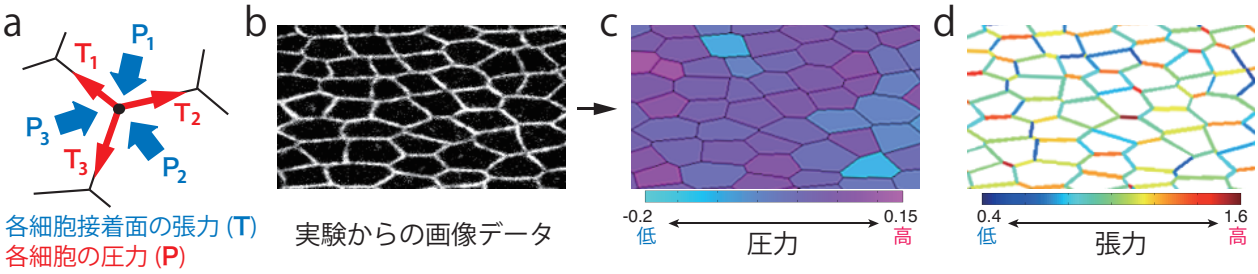

図1. 力の推定手法 (a)細胞集団中の細胞配置は、各細胞の圧力(P)、細胞接着面の張力(T)のバランスから決まる。この逆問題を理論的に定式化することで、細胞の形態画像(b)から個々の細胞の圧力(c)や接着面での張力(d)を推定する。画像は蛹期のショウジョウバエの翅上皮。

Using our method, we studied mechanical basis of hexagonal packing (the increase of hexagonal cells in the *Drosophila* wing during the pupal stage). Our quantification of developmental changes of the stress distribution within a tissue and of corresponding rearrangements of cells provides a physical mechanism for cell packing: biased external forces acting on the tissue provide the directional information for local orientation of hexagonal cells which underlies the global hexagonalization. Our force estimation method will become a powerful tool in analyzing how information for orchestrating cellular behaviors during morphogenesis is encoded in distributions of forces within a tissue.