MODELING CELL POLARIZATION AND INTERCALATION DURING *DROSOPHILA* GERMBAND EXTENSION

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INTRODUCTION

During development of the fruit fly (*Drosophila melanogaster*) embryo, a morphogenetic process known as axis elongation establishes its head-to-tail or anterior-posterior (AP) axis through the extension of the germband, a monolayer of cells that eventually develops into segmented trunks. In this convergent-extension process, the germband approximately doubles in length by elongating along the AP axis and narrowing along the back-to-front or dorsal-ventral (DV) axis [1]. Cell intercalation is one of the primary means of realizing convergent-extension. It is regulated by signaling proteins on the one hand, and mechanical forces and deformation on the other. Both components have been examined separately in prior experiments. However, the connection between those components is still elusive. We propose a biomechanical model for cell intercalation and tissue elongation that couples molecular signaling with cell deformation and rearrangement. Planar cell polarity arises naturally from kinetic and spatial interaction among Shroom, Rho-kinase, Bazooka and myosin motors. Upregulation of myosin on edges oriented along the DV axis produces anisotropic contraction of the tissue and neighbor exchange through a T1 process. The model predictions show quantitative agreement with experimental observations.

METHODS

We propose a 2D vertex-based mechanical model where each cell is initialized as a perfect hexagon with 6 vertices and 6 edges as described in [2]. The elastic cell edges carry cortical myosin that is dictated by Rho-kinase and Bazooka. Within each cell, six spokes connect the vertices to a centroid, representing cyclic medial myosin pulses that causes cell area oscillations. On the outer boundary, the peripheral vertices are connected to external cables that exert a constant force that represents the tension of the surrounding tissue [3]. The mechanical model is integrated with a kinetic model that describes the polarization of Shroom, Rho-kinase, Bazooka and myosin. Vertex motion and cell deformation are determined by driving forces due to myosin overcoming elastic resistance of cell edges. The polarization of those protein species gives rise to anisotropic contraction forces that modify the detachment rate of myosin in a dynamic feedback loop. The model consists of 733 coupled ordinary differential equations (ODEs) describing the motion of the vertices and the dynamics of four protein signals. The temporal evolution of our system is investigated by solving the ODE with a second-order Runge-Kutta method.

RESULTS AND DISCUSSION

Figure 1 shows a representative model simulation of the germband extension process. A total of 52 hexagonal cells are used to represent the germband. Through the protein signaling dynamics and mechanical driving forces, the tissue undergoes multiple T1 transitions that elongate it along the AP axis and contracts it in the transverse direction. The degree of protein polarity, anisotropy in the contractile forces, timing of the morphological changes, and final amount of convergent-extension are all in reasonable agreement with experimental data.

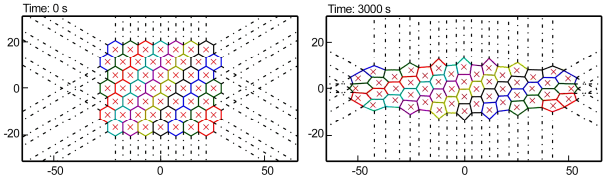

Figure 1: Comparison of tissue shape for a total simulation time of t=3000s with 52 hexagonal cells. The external cables are represented by dashed lines connecting the peripheral vertices to an outer boundary. The final tissue shape is the result of multiple T1 transitions that intercalate the cells through neighbor exchange, thus extending the tissue along the AP axis and narrowing it along the DV axis.

CONCLUSIONS

Our model differs fundamentally from prior vertex models for tissue deformation and morphogenesis in that we do not postulate mechanical rules governing cell-cell interaction. Rather we account for the underlying biochemistry, and predict the mechanical outcomes, e.g. cell deformation and rearrangement, naturally from the polarization of signaling proteins and anisotropic contraction forces. This opens a new route through which physics and mechanics can shed light on complex biological processes.

REFERENCES

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