Mechanical Feedback during Ventral Furrow Formation in the *Drosophila* embryo: Intercellular Coordination and Robustness

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ABSTRACT

Morphogenesis involves complex genetically regulated pattern-formation processes leading to spontaneous emergence of a well-organized three-dimensional shape. The importance of biochemical signaling systems has been extensively investigated in morphogenesis, while the role of mechanical feedback in generating tissue structure has largely been neglected.

To demonstrate a subtle but profoundly important role of mechanical feedback in guiding form generation, I will describe our recent investigations of ventral furrow formation (VFF) in the *Drosophila* embryo. It has long been known that the key process giving rise to VFF is apical (outer side) constriction of cells in the ventral region; the constrictions produce negative spontaneous curvature of the cell layer, which buckles inwards. To elucidate the effects of mechanical feedback, we have developed two complementary particle-based models that represent active cells involved in VFF as mechanically excitable objects.

Our active granular fluid (AGF) model focuses on the apical (outer) surface of the embryo, and represents the apical cell ends as mechanically active particles capable of constrictions. We show that stochastic constrictions correlated via tensile stress result in formation of cellular constriction chains (CCCs), similar to those observed in vivo. A statistical comparison of the simulation results and time lapse images of live embryos provides strong evidence that mechanical feedback is involved in coordinating apical constrictions. We also demonstrate that CCCs can penetrate regions of reduced constriction capability, and we argue that CCC formation increases the robustness of VFF to spatial variation of cell contractility.

The AGF modeling is paired with a complementary approach that focuses on the transverse cross-section of the embryo and describes non-spherical cell shapes using multiple force centers (MFC). The AGF and MFC models show how cells in different regions work in concert to ensure completion of the invagination process. We have found that mechanical feedback can allow for successful furrow closure in systems with perturbed or weakened constrictions.