Biomechanical modeling frameworks for morphogenesis: from cells to tissues and back

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Abstract

A common challenge in the numerical modeling of tissue morphogenesis is the fact that mechanical effects are at play at different length scales and time scales. Cells obtain their mechanical properties from molecular forces, and their collective behavior gives rise to tissue shape and function at scales that can be orders of magnitude greater. A modeler is thus faced with the question of which modeling approach, and which level of detail, to use to study morphogenetic processes in silico: Continuum models may be appropriate at the tissue scale but can work also to represent individual cells. Discrete or particle-based approaches are needed for molecular simulations but have also proven to be successful in bridging the scales to model collective cellular behavior. Which method to use for which problem? In this talk, I will present several recently developed modeling frameworks and their applications to morphogenetic problems. With a continuum model of the elasto-plastic behavior of different tissue layers, we have been able to explain the emergence of bending sites in the folding neural tube in the developing vertebrate, and the emergence of folds and protrusions at the onset of bladder cancer formation. These two morphogenetic processes were previously viewed primarily through the lense of discrete cell shape changes, in particular cell wedging through apical constriction. Taking the opposite route, we have also developed cell-based simulations tools in 2D ("PolyHoop") and 3D ("SimuCell3D" and "OptiCell3D") to address the question how cellular organization can give rise to morphogenetic events at the tissue scale. With such tools at hand, it is becoming possible to infer mechanical cell properties at subcellular resolution. Eventually, improved macroscopic continuum models of tissue mechanics might result from a deeper understanding of cellular processes within them.

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