Nematically-guided morphogenesis

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Abstract

Tissue morphogenesis relies on the orchestration of subcellular contractility into supracellular force patterns by multicellular assemblies governed by an interplay of chemical and physical cues (1). Despite the numerous scientific opportunities associated with the creation of synthetic tissues in both fundamental and applied contexts, the precise control of tissue reshaping continues to pose a significant challenge (2). To address this, it is crucial to develop a theoretical and computational framework that leverages the inherent self-organization mechanisms of living tissues to promote force patterns leading to specific morphogenetic transformations. In this study, we have developed a mathematical model based on thin shell theory to model tissues comprising elongated cells. These tissues inherently exist in an out-of-equilibrium state, driven by active contractile forces exerted by the cell's cytoskeleton. These forces are regulated by the nematic orientation of cells and the presence of topological defects (3). Furthermore, a finite element-based computational model has been developed to solve the mathematical model over long-time scales in the nonlinear regime. In the computational experiments, by directly controlling cellular orientation and topological defects, we have obtained cellular monolayers that feature nematically guided tension patterns, producing three-dimensional tissue shapes. The results of the computational model are validated against in-vitro experiments, recapitulating the predictions of the model. By enabling the mapping of morphogenetic events within living tissues, this strategy has the potential to open doors to applications across diverse fields, ranging from tissue engineering to soft robotics.

References:
(1)Friedl, P., et al. Collective cell migration in morphogenesis and cancer. Int. J. Dev. Biol. (2004) doi:10.1387/ijdb.041821pf.

(2) Matejčić, M. & Trepat, X. Mechanobiological approaches to synthetic morphogenesis: learning by building. Trends Cell Biol. 33, 95–111 (2023).

(3) Doostmohammadi, A. & Ladoux, B. Physics of liquid crystals in cell biology. Trends Cell Biol. 32, 140–150 (2022).

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