Simulating Organogenesis with COMSOL Multiphysics® Software: Phase-Field Based Simulations of Embryonic Lung Branching Morphogenesis

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Abstract

Organogenesis has been studied intensively. While many biological details have been uncovered, fundamental questions regarding the control of growth and shape during lung and kidney morphogenesis remain unsolved. We have recently shown that of all proposed mathematical models, only ligand-receptor based Turing models successfully reproduce the experimentally determined growth fields of the embryonic lung and thus provide a mechanism for growth control during embryonic lung development [1].

Turing models are based on at least two coupled nonlinear reaction-diffusion equations. In case of the lung model, the two components (ligands and receptors) are produced in two different tissue layers [1]. Thus the ligand is produced in the outer mesenchymal layer and the receptor is produced in the inner, branching epithelial layer; the diffusion of receptors is restricted to this epithelial layer. COMSOL Multiphysics® offers two different methods, Arbitrary Lagrangian-Eulerian (ALE) and phase fields, to efficiently solve such a Turing system on growing and deforming (branching) domains [1-3]. Here, we compare the performance of these two numerical techniques with a Turing model for the control of lung branching morphogenesis.

We use COMSOL Multiphysics to perform the simulations [2-4]. The Phase-Field method is used to track and advect the phase field; the phase transition represents the epithelial-mesenchymal border (Figure 1). The reaction-diffusion process on this surface is modelled with the Coefficient Form PDE interface. The ALE simulations make use of the Coefficient Form PDE interface, the Surface Reactions interface for the surface restricted reaction-diffusion process, and the Moving Mesh interface for the displacement.

The ALE method yields good results, but its performance and stability is limited by mesh displacement. The phase-field method overcomes such limitations. Figure 2 shows the concentration-patterning on the initial geometry (Figure 2A) and at a later time point after outgrowth (Figure 2B). Here, the growth field is normal to the surface and the growth speed is proportional to the local concentration of the ligand-receptor complex that arises from the Turing system. The ALE based simulations show a similar behavior. However, we note that several properties of the phase-field framework, including interface thickness, mobility parameter etc., have to be adjusted to approach the ALE based simulation results.

We successfully demonstrate the feasibility to model morphogenesis using the phase-field approach. We will present extended results and conclusions in the talk.

Reference

[1] D. Menshykau et al., "An interplay of geometry and signaling enables robust lung branching morphogenesis.", Development 141(23): 4526-4536 (2014)

[2] D. Menshykau and D. Iber, “Simulation Organogenesis in COMSOL: Deforming and Interacting Domains,” Proceedings of the 2012 COMSOL Conference in Milan (2012)

[3] Z. Karimaddini et al., “Simulating Organogenesis in COMSOL: Image-based Modeling.”, Proceedings of the 2014 COMSOL Conference in Cambridge (2014)

[4] P. Germann et al., “Simulating Organogenesis in COMSOL,” Proceedings of the 2011 COMSOL Conference in Stuttgart (2011)

Figures used in the abstract

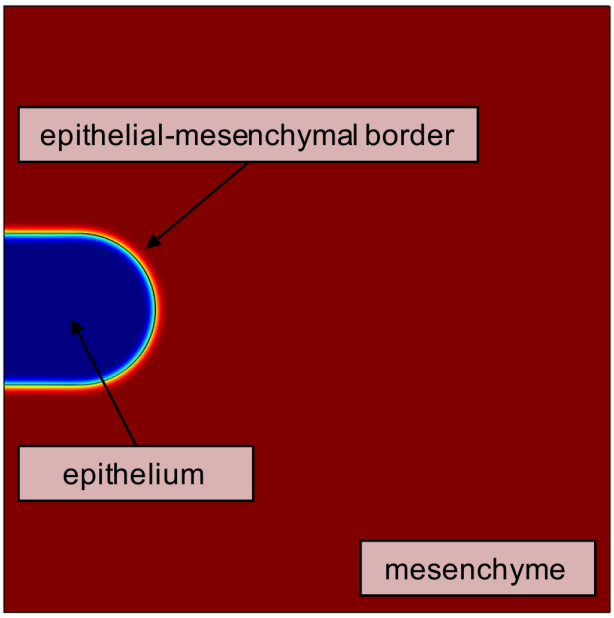

Figure 1: The two phases representing the epithelium (blue) and the mesenchyme (red). The continuous transition between the two phases acts as the epithelial-mesenchymal border. The two components, the receptor and the ligand, react on this border only.

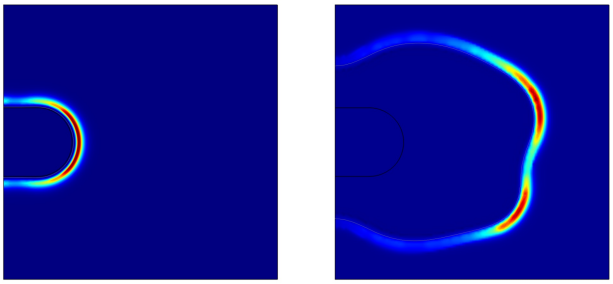

Figure 2: The concentrations of the ligand-receptor complex is shown (A) at the stationary distribution on the initial geometry and (B) at a later time point after outgrowth. The thin grey layer represents epithelial-mesenchymal border. The black line in (B) indicates the initial geometry.