Seventeenth International Conference Zaragoza-Pau on Mathematics and its Applications
Jaca, September 4–6th 2024

Porous-media characteristics of embryo tissue regulate morphogen gradient formation

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SUMMARY

We combine image-based modeling with geometry-adaptive numerical simulation methods [1] to study the role of complex embryo geometry in the formation of long-range morphogen gradients [2]. Morphogens are signaling molecules, mostly proteins, that control cell differentiation during embryonic development by forming graded concentration fields in the extracellular space (ECS). These gradients have been proposed to form by morphogen diffusion from a localized source through the ECS to distributed sinks in the target tissue [3]. The role of the porous ECS geometry in this process is less well understood and has not been resolved in existing models. We address this by reconstructing pore-scale 3D geometries of a gastrulating zebrafish embryo from a light-sheet microscopy video. In this reconstructed geometry, we simulate Fgf8a gradient formation using GPU-accelerated sparse grids with fully resolved interstitial space and surface biochemistry. Our simulations show that when realistic embryo geometries are considered, a source-diffusion-degradation mechanism with binding to extracellular matrix polymers (HSPGs) is sufficient for spontaneous formation and maintenance of Fgf8a gradients [2]. The normalized gradient is robust against changes in source and sink rates but sensitive to changes in transient HSPG binding and the ECS pore connectivity, suggesting that binding reactions and geometry play an important role in gradient shaping and robustness.

Keywords: biological tissue, extracellular space, complex geometry, image-based model, reaction-diffusion, morphogen gradient, zebrafish embryo

AMS Classification: 92-04, 92-08, 92-10

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