Coupling a Continuum Model and Live Imaging to Infer Tissue Spreading Mechanics: A Bayesian Approach

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ABSTRACT:
Collective cell migration is a major contributor to embryonic development, wound healing, and the progression of many diseases, and it has been successfully simulated using a range of modeling formalisms. If different types of collective cell migration are driven by a set of shared behaviors, a mathematical model of collective migration should successfully model different tissues with only a change in parameters. Here, we extend a two-dimensional Eulerian continuum mechanical model of a spreading tissue that was previously developed for cultured epithelial cell sheet migration in combination with quantitative image analysis to describe collective migration of embryonic tissue explants excised from the animal cap region of gastrulating Xenopus laevis embryos. This model assumes that the main parameters that influence collective migration are the forces on the free edge, tissue stiffness, and the strength of cell-ECM adhesions. We apply an automated methodology using approximate Bayesian computation to integrate kinematic data with an appropriately constrained computational model to predict physical properties of collectively spreading cell sheets. Our results suggest both the force of lamellipodia and cell-ECM adhesion vary with the initial area of the tissue explants; in particular, high lamellipodial force together with weaker cell adhesion enable fast spreading in explants with a larger initial area. Such predictions can be used to guide further experiments to better understand how collective migration is regulated during development and dysregulated during the metastasis of cancer.

Host: Mary Sehl, M.D., Ph.D. and Tom Chou, Ph.D.
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