EMBRIO
Emergent Mechanisms in Biology of Robustness, Integration & Organization

EMBRIO ALL-HANDS SEMINAR: DECEMBER 9, 3PM ET VIA ZOOM

Combined multiscale modeling and experimental study of mechanisms of shape formation during tissue development and growth

Mark Alber
Department of Mathematics, Center for Quantitative Modeling in Biology
University of California Riverside, USA

The regulation and maintenance of a tissue's shape and structure is a major outstanding question in developmental biology and plant biology. In this talk, through iterations between experiments and multiscale model simulations that include a mechanistic description of interkinetic nuclear migration, we will show that the local curvature, height, and nuclear positioning of cells in the *Drosophila* wing imaginal disc are defined by the concurrent patterning of actomyosin contractility, cell-ECM adhesion, ECM stiffness, and interfacial membrane tension [1]. The biologically calibrated model describing both tissue growth and morphogenesis incorporates the spatial patterning of fundamental subcellular properties. Additionally, the model implements for the first time the dynamics of interkinetic nuclear migration within the simulated pseudostratified epithelium. This includes the basal to apical motion of the nucleus, mitotic rounding, and cell division dynamics. Key characteristics of global tissue architecture, such as the local curvature of the basal wing disc epithelium, cell height, and nuclear positioning, serve as metrics for model calibration. The experiments have shown how these physical features are jointly regulated through spatiotemporal dynamics in the localization of pMyoII, β-Integrin, and ECM stiffness. As the disc grows, there are progressive changes in the patterning of key subcellular features such as actomyosin contractility. The predictions made by the model simulations agree with the observed changes in contractility and cell-ECM adhesion during wing disc morphogenesis. Multiscale modeling approach combined with experiments was also applied to studying stem cell maintenance in multilayered shoot apical meristems (SAMs) of plants which requires strict regulation of cell growth and division. In this talk, the combined approach will be demonstrated through testing three hypothesized mechanisms for the regulation of cell division plane orientation and the direction of anisotropic cell expansion in the corpus [2].

1. Nilay Kumar, Jennifer Rangel Ambriz, Kevin Tsai, Mayesha Sahir Mim, Marycruz Flores-Flores, Weitao Chen, Jeremiah J. Zartman and Mark Alber [2024], Balancing competing effects of tissue growth and cytoskeletal regulation during Drosophila wing disc development, *Nature Communications*, volume 15, 2477.
2. Mikahl Banwarth-Kuhn, Kevin Rodriguez, Christian Michael, Calvin-Khang Ta, Alexander Plong, Eric Bourgain-Chang, Ali Nematbakhsh,Weitao Chen, Amit Roy-Chowdhury, G. Venugopala Reddy and Mark Alber [2022], Combined computational modeling and experimental analysis integrating chemical and mechanical signals suggests possible mechanism of shoot meristem maintenance, *PLOS Computational Biology* 18(6): e1010199.

About the speaker: Professor Mark Alber earned his Ph.D. in mathematics at the University of Pennsylvania. He held several positions at the University of Notre Dame including most recently Vincent J. Duncan Family Chair in Applied Mathematics. He is currently Distinguished Professor in the Department of Mathematics and Director of the Center for Quantitative Modeling in Biology, University of California, Riverside. Dr. Alber was elected in 2011 Fellow of the American Association for the Advancement of Science (AAAS) and received 2024 US Fulbright Scholar Award, The Netherlands. He is currently a section editor in systems biology of PLoS Computational Biology and member of editorial board of Bulletin of Mathematical Biology.