REINHART HEINRICH AWARD

QUANTITATIVE APPROACHES TO INVESTIGATING EPITHELIAL MORPHOGENESIS

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ABSTRACT

Morphogenesis - the generation of biological shape and form - is fascinating, and its study promises to shed light on a wide range of developmental defects and inform strategies for the artificial growth of organs. Recently, the experimental study of morphogenesis has thrived due to a rise in quantitative methods. The resulting avalanche of quantitative data requires us to rethink the scientific method. We need to design quantitative hypotheses through mathematical models, make quantitative experimental predictions, devise methods for quantitative data analysis, and design methods for quantitative inference using models and data. Our work aims to enable this transition for the integrative analysis of morphogenesis in epithelia, one of the major tissue types in animals. We conduct the first systematic numerical analysis of a widely used cell-based model of epithelia, the vertex model, and estimate to what extent quantitative model predictions may be influenced by parameter values and implementation details. We then apply this model to a key question in developmental biology by constructing a quantitative theory for tissue size control in the embryonic epidermis of the fruit fly *Drosophila*, using the model to predict the outcomes of future experiments. We further devise a method for estimating mechanical parameters of vertex models from imaging data and quantify the uncertainty associated with such estimates. Finally, we propose a novel algorithm for robust cell tracking in live-imaging microscopy videos of epithelial tissues that illustrates how graph theoretic concepts may be used to overcome challenges in quantitative data analysis. Together, these contributions will enable the quantitative study of epithelia for a wide range of applications.

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References

[1] J. Kursawe, R. E. Baker, A. G. Fletcher. (2017). *Impact of implementation choices on quantitative predictions of cell-based computational models* J. Comp. Phys. 345, 752-767

[2] J. Kursawe, P. A. Brodskiy, J. J. Zartman, R. E. Baker, A. G. Fletcher (2015). *Capabilities and Limitations of Tissue Size Control through Passive Mechanical Forces.* PLoS Comput. Biol. 11, e1004679

[3] J. Kursawe, R. E. Baker, A. G. Fletcher. (2018). *Approximate Bayesian computation reveals the importance of repeated measurements for parameterising cell-based models of growing tissues* J. Theor. Biol. 443, 66-81

[4] J. Kursawe, R. Bardenet, J. J. Zartman, R. E. Baker, A. G. Fletcher. (2016). *Robust cell tracking in epithelial tissues through identification of maximum common subgraphs* J. R. Soc. Interface 13, 20160725