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Data Driven Modelling of Limb Bud Growth and Morphogenesis

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Limb development is regulated by feedback between the tissue-scale mechanics and cellular decisions—migration, contraction, division, and death—implemented through gene-regulatory networks. The dynamically changing states of these cellular networks reflect the decisions being made. To integrate these interactions across 3 scales: genes, cells, and tissues, we develop a 3D cell-based model in which cellular decisions are spatially regulated by morphogen gradients. By constraining parameters with empirical data and optimizing against wild-type limb-bud shape, we obtain a model that links signal distributions to emergent mechanical behaviors. Multiple mechanisms have been proposed for limb-bud morphogenesis, including ectodermal mechanical constraints, proliferation gradients, oriented divisions, distally biased migration, motility gradients, and convergent extension. Yet which spatio-temporal combinations of these activities generate correct morphology remains unresolved. We use the model to test whether convergent extension alone is sufficient to reproduce limb-bud outgrowth and shaping. We compare 2 distinct modes of convergence: (1) orthogonal to an AER/FGF8-associated proximo-distal cue, and (2) parallel to a surface-to-core (radial) cue consistent with Wnt5a. For each mode, we quantify how the strength and timing of convergent extension affects predicted shape trajectories and whether either mode—or a combination of both—can match wild-type morphology.

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Session Classification: Short Talk