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From Genes to Morphogenetic Movements: How Cell-level Modeling Makes such Connections Possible
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New understanding provided by computational modeling makes it possible to identify, in detail, the sequence of events by which gene expression gives rise to specific morphogenetic movements. Convergent extension (CE), an important developmental process in which embryonic tissues undergo self-driven narrowing in one in-plane direction and expansion in the other, is one such example. CE is triggered by gene expression and, in amphibian gastrulae, involves cephalocaudal (CC) gradients of the morphogens Xbra and Chordin and signalling molecules that include planar cell polarity (PCP) and Wnt/Ca²⁺ (Nature 2004, 430: 305-306). When these pathways have established suitable biochemical conditions, cellular protrusions called lamellipodia, which previously arose with random orientations, form preferentially in the mediolateral (ML) direction. To investigate whether lamellipodium action has the mechanical capacity to drive cell intercalation and its attendant cell reshaping, the cell-level finite element model of Chen and Brodland (ASME J. Biomech. Eng., 2000, 122: 394-401) was modified so that lamellipodia could originate from randomly selected cells, connect to next-neighboring cells in the ML direction and then contract. The simulations show that lamellipodia with these characteristics can, indeed, drive CE and that adjacent tissue must resist ML narrowing in order for characteristically elongated cells to result, predictions that have been confirmed experimentally. When these meso-scale findings are integrated with tissue- and whole-embryo mechanics, multi-scale “mechanical pathways” become evident. These pathways, in turn, interface directly with known biochemical pathways to produce an unbroken causal sequence from gene expression to specific morphogenetic movements.