Middle-out Modeling of Multiscale Morphodynamics

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Extended Abstract

How a fertilized egg develops into a multicellular organism remains one of the most challenging questions in biology. Novel techniques provides unprecedented high-resolution data on the spatiotemporal dynamics of the developing embryo. However, interpretation of these data requires both wet lab experiments and computational modeling (Oates et al., 2009). Here, we present a new modeling environment that is based on the following principles: Developmental systems (i) are multiscale systems, (ii) are morphodynamic, and (iii) require a middle-out modeling approach.

(i) Embryogenesis unfolds as a dynamic interplay of gene regulation, cellular signaling, differentiation, proliferation, and tissue mechanics. Developmental processes are coupled over multiple spatial and temporal scales and across structural levels. Understanding developmental processes implies unraveling how these scales are coupled.

(ii) Two main components of development can be distinguished: (a) induction, change of cell state and (b) morphogenesis, change in spatial distribution of cells. Although typically modeled as distinct processes, these mechanisms in fact occur concurrently and are causally interdependent (Salazar-Ciudad et al., 2003). Such 'morphodynamic' mechanisms enable a rich variety of tissues and provide correction mechanisms and robustness.

(iii) Restraining complexity in models of multiscale morphodynamics is essential to gain explanatory potential. Bottom-up approaches (from molecular kinetics pathways up) and top-down approaches (from tissue biophysics down), run into difficulties when attempting to encompass all relevant scales. The alternative is a middle-out strategy in which the cell is taken as a basic unit of modeling and only those molecular and tissue-level processes are included that are relevant to the phenomenon under investigation (Noble, 2002).

Similar to the popular CompuCell3D package (Cickovski et al., 2007), our modeling environment uses the well-known cellular Potts model (Glazier and Graner, 1993), reaction-diffusion solvers, a flexible plug-in architecture and an easy-to-use model description language. Several subtle yet crucial differences render our software pre-eminently suitable to model multiscale morphodynamics. Most prominently, the symbolic nature of description language enables the modeler to symbolically link all processes over spatiotemporal scales and structural levels without programming. This makes systematic exploration possible of the effects of multiscale and morphodynamic coupling. We demonstrate the conceptual and computational framework in the context of pattern formation models on neurogenic differentiation.

References

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