

Mathematical modeling of biological events and cell-cell communication

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The modeling of cellular migration and intracellular communication at the scale of small to medium sized collections of cells is challenging due to the complexity of the systems involved and the diversity of their behavior (Tomita, 2001). Several attempts at constructing models have been made (e.g., Cickovski et al., 2005; Takahashi et al., 2004), and fall into two categories. Top-down models begin with phenomenology and attempt to model behavior using either deterministic or stochastic methods, while bottom-up models begin with molecular dynamics or measurable physical properties of cell components and attempt to derive larger-scale behavior. To date, the top-down models have failed to reproduce observed cell behaviors during migration and tissue formation, and bottom-up models cannot simulate a large enough collection of cells for sufficient time to produce testable predictions. A new class of model is needed that can predict cell behavior at a scale between the limits of current top-down and bottom-up models.

The analyses begin with examples of cell motion measured in live tissue (Tobet et al., 2003; McClellan et al., 2008), and pursue a phenomenological analysis to demonstrate the challenges of constructing a model of this system. Cell trajectories are extracted, mean squared displacements of cells over time are measured, and cells are classified according to the exponent in a best-fit diffusive model of this data (subdiffusive, diffusive, or superdiffusive) as well as speed and direction of motion, then these measures are correlated with tissue domains in the sample. Results show distinctly different cell behavior over the visualized tissue region.

Finally, we present highlights of our models of cell components that attempt to fill this modeling middle ground, including a cell membrane model based on discs that exhibit Lennard-Jones interactions in the transverse plane and elastic membrane forces in the axial direction, a cytoskeleton model consisting of Lennard-Jones spheres that change size or divide based on a regional polymerization/depolymerization bias created by diffusion of signaling chemical, and an extension of the membrane model to organelles with cells. These models, in combination, demonstrate chemotactic behavior with both attractive and repulsive signals, and take on expected membrane deformations and cell shapes in aggregations.

References:|

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