Abstract

Self-organization involves the coordination of cell behavior to generate structures many orders of magnitude greater than the individual cells. Self-organization is a hallmark of embryonic development, is central to the immune response, and is involved in tumor metastases. The multitude of possible behavioral cues, the presence of redundant systems, and high levels of noise obscure coordination mechanisms in self-organizing processes. This dissertation proposes a framework to overcome the challenges of studying self-organizing systems by utilizing *in vivo* time-lapse fluorescent imaging of moving cells and their environment to constrain computer simulations to experimental results. A simple nearest-neighbor sampling technique is described to parameterize simulations with experimental data, eliminating the need for broad assumptions or detailed knowledge about the underlying mechanisms generating cell behavior and behavioral cues. The resulting simulations provide a framework for testing hypotheses that are challenging, costly, or impossible to test via traditional biological experiments. Using this framework, a unified understanding of the cell behavior and behavioral cues required for development in the bacterium *Myxococcus xanthus* was identified, and previously unknown cell behaviors required for development were discovered. These results revealed that decreased cell motility inside the aggregates, a biased walk toward aggregate centroids, and alignment among neighboring cells and in a radial direction to the nearest aggregate are behaviors that enhance *M. xanthus* development. The simulations also indicated that aggregation is generally robust to perturbations in these behaviors and identified possible compensatory mechanisms. The framework can be applied to answer new questions about *M. xanthus* self-organization using the same fluorescent tracking and simulation framework to compare mutant cell behavior to that of the wild type.