Spatial-Stochastic Model of Cell Fate Decisions in Early Mouse Development

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The delicate balance necessary for sustaining cell plasticity and ensuring reliable specification of cell lineages is an intriguing problem in developmental biology. In the mouse embryo, the Nanog/Gata-6 (N/G) gene regulatory network plays a crucial role in the delicate balance of the early cell fate decision process. Although stochasticity is an inherent feature of any gene expression process, the current approaches to this problem still primarily rely on deterministic modelling techniques, while generally treating noise as an ad hoc property. Therefore, we are developing a multi-scale event-driven spatial-stochastic simulator for emerging-tissue development. This allows us to perform realistic-yet-efficient simulations of intracellular biochemical dynamics, tissue-scale biomechanical interactions, and intercellular communication. We use well-established event-driven simulation schemes and adapt them for incorporating suitable tissue-scale phenomena, such as cell division and growth. Whenever possible, important biophysical and morphological parameters are fixed by values provided by experimental collaborators or found in recent literature. Otherwise, numerical optimization techniques are implemented to infer biologically-feasible regimes for relevant parameters. We begin by studying the biochemical characteristics of the N/G network in a single-cell setting. We simulate and analyze the dynamics of its core network motif components and their interplay. We subsequently extend the study to a multi-cellular setting, in order to understand the importance of cell-to-cell communication, and how positional information is robustly achieved and preserved. These efforts converge toward a versatile framework capable of efficiently simulating emerging-tissue dynamics coupled with intracellular biochemical processes, in a biophysically faithful fashion.