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A genuinely stochastic modeling approach for understanding cell fate specification during early mouse development

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The delicate balance necessary for ensuring reliable segregation of cell lineages is an intriguing problem in developmental biology. For mammals, and specifically for the early mouse embryo, cell fate decisions have been extensively researched, but the underlying mechanisms remain poorly understood. Current theoretical approaches to this problem still primarily rely on deterministic modeling, although stochasticity is an essential feature of this biological process. As such, we are developing a multi-scale event-driven spatial-stochastic simulator for emerging-tissue development. In this particular study, we focus on the mouse blastocyst stage embryo. We construct an archetypical multicellular model system in order to understand how positional information is robustly achieved and preserved. To this end, we adapt well-known event-driven simulation schemes for incorporating suitable tissue-scale phenomena, and determine biophysically-feasible parameter regimes via a recent simulation-based inference framework: a novel machine-learning based approach for Bayesian inference exploiting artificial neural networks. We uncover a signaling mechanism for reliable patterning emergence and maintenance which is independent of system size. Importantly, our approach allows us to properly quantify the robustness of this patterning process under realistic noise constraints. Moreover, we elucidate the importance of auto- and paracrine signaling for proper cell fate specification. Perspectively, our efforts will lead to a versatile framework capable of performing realistic-yet-efficient simulations of intracellular biochemical dynamics and intercellular communication for a wide range of biological systems.

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