PHYSICAL MATH SEMINAR

A generative model of the first cell fate decision in mammalian development

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ABSTRACT:

The first cell fate bifurcation in mammalian development—the segregation of the trophectoderm (TE) and inner cell mass (ICM)—unfolds across asynchronous cell divisions, making its dynamics extremely challenging to reconstruct from fixed embryos. To overcome this, we developed a framework combining quantitative live imaging of key regulatory proteins with a generative probabilistic model, an approach broadly applicable to non-deterministic systems where live imaging is feasible.

Our model fuses partial, pairwise observations of the transcriptional co-activator YAP with its targets, CDX2 (TE) and SOX2 (ICM), to reveal the joint dynamics of the complete regulatory network. This approach uncovered the time-dependent statistics of the cell fate allocation and allowed us to identify specific features of YAP's dynamic behavior necessary or sufficient for downstream gene induction. Notably, we uncovered significant temporal heterogeneity in SOX2 induction among ICM cells. Heterogeneities within the ICM have been linked to the initiation of the second cell fate decision in the embryo. Our work therefore sets the stage for dissecting subsequent lineage decisions and understanding how stochasticity in cell fate allocation leads to robust developmental outcomes, such as precise cell fate proportions and spatial patterning.

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2:30 PM – 3:30 PM

Building 2, Room 449

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