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Setting up the epigenome: a collective phenomenon

Thursday 24 September 2020 12:00 (30 minutes)

Recent breakthroughs in single-cell genomics allow probing molecular states of cells with unprecedented detail along the one-dimensional sequence of the DNA. Biological function relies, however, on emergent processes in the three-dimensional space of the nucleus, such as droplet formation through phase separation. Here, we combine single-cell multi-model sequencing with a theoretical approach to rigorously map measurements along the DNA sequence to a description of the emergent spatial dynamics in the nucleus. Drawing on scNMT-seq experiments in vitro and in vivo we demonstrate our approach in the context of early development. We show how epigenetic modifications of the DNA, DNA methylation, are established through the interplay between chemical and topological modifications of the DNA, leading to the formation of condensates of methylated DNA in the nucleus. Using this theoretical framework, we identify epigenetic processes that precede lineage decisions in the early embryo. Our work sheds new light on epigenetic mechanisms involved in cellular decision making. It also provides a general framework of how mechanistic insights into the spatio-temporal processes governing cell-fate decisions can be gained by the combination of methods from single-cell multi-omics and theoretical physics.

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