


复旦大学数学科学学院
数学综合报告会

报告题目：**A synthetic biology approach to Waddington landscape and cell fate determination**

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摘要：The process of cell fate determination has been depicted intuitively as cells travelling and resting on a rugged landscape, which has been probed by various theoretical studies. However, few studies have experimentally demonstrated how underlying gene regulatory networks shape the landscape and hence orchestrate cellular decision-making in the presence of both signal and noise. Here we tested different topologies and verified a synthetic gene circuit with mutual inhibition and auto-activations to be quadrastable, which enables direct study of quadruple cell fate determination on an engineered landscape. We show that cells indeed gravitate towards local minima and signal inductions dictate cell fates through modulating the shape of the multistable landscape. Experiments, guided by model predictions, reveal that sequential inductions generate distinct cell fates by changing landscape in sequence and hence navigating cells to different final states. This work provides a synthetic biology framework to approach cell fate determination and suggests a landscape-based explanation of fixed induction sequences for targeted differentiation.

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