



Colloquium Series



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Multiscale Modeling to Understand Mechanisms of the Robustness of Stem Cell Maintenance

Abstract: The regulation and interpretation of transcription factor levels is critical in spatiotemporal regulation of gene expression in development biology. However, concentration-dependent transcriptional regulation, and the spatial regulation of transcription factor levels are poorly studied in plants. WUSCHEL, a stem cell-promoting homeodomain transcription factor was found to activate and repress transcription at lower and higher levels respectively. The differential accumulation of WUSCHEL in adjacent cells is critical for spatial regulation on the level of CLAVATA3, a negative regulator of WUSCHEL transcription, to establish the overall gradient. However, the roles of extrinsic spatial cues in maintaining differential accumulation of WUSCHEL are not well understood. We have developed a 3D cell-based computational model which integrates sub-cellular partition with cellular concentration across the spatial domain to analyze the regulation of WUS. By using this model, we investigate the machinery of the maintenance of WUS gradient within the tissue. We also developed a stochastic model to study the binding and unbinding of WUS to cis-elements regulating CLV3 expression to understand the concentration dependent manner mechanistically. The robustness mechanism and the concentration-dependent machinery discovered by the modeling analysis can be general principles for stem cell homeostasis in different biological systems.

Keywords: Multiscale modeling, stochastic simulations, developmental biology, stem cell homeostasis, robustness.

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