Data-driven multiscale mathematical models of signaling in the maintenance of transcription factor distribution in stem cell homeostasis

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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. Experiments show that subcellular partitioning and protein destabilization control the WUSCHEL protein level and spatial distribution. Meanwhile the destabilization of WUSCHEL also depends on the protein concentration which in turn is influenced by intracellular processes. However, the roles of extrinsic spatial cues in maintaining differential accumulation of WUSCHEL are not well understood. Moreover, the utilization of transcriptional regulatory domains for sensing hormones in regulating protein concentration forms a feedback which is difficult to understand in experiments alone. We develop a 3D cell-based mathematical model which integrates sub-cellular partition with cellular concentration across the spatial domain to analyze the regulation of WUS and stem cell homeostasis in quantitative level. By using this model, we investigate the machinery of the maintenance of WUS gradient within the tissue. We also incorporate cell division in this model to study the shoot apical meristem growth under chemical signaling network.

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