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Understanding Dynamic Patterns of NF-κB Signaling: Derivation and Analysis of a Minimal Model through Sensitivity Analysis JAEWOOK JOO, STEVE PLIMPTON, SHAWN MARTIN, LAURA SWILER, Sandia National Laboratories, JEAN-LOUP FAULON, Sandia National Laboratoris — Understanding the pleiotropism of NF-κB signal transduction is a challenge of clear medical importance and systems biology. Current mathematical modeling frameworks for NF-κB signal transduction, though limited to a small signaling module located in a downstream of IKK, heavily rely on the parameterizations and the numerical studies of ODE models and doubtless lack intuitive explanations about underlying mechanisms of the dynamic patterns of the NF-κB signaling. Here we present a systematic way to derive a minimal model from an up-to-dated and detailed NF-κB signaling network by means of sensitivity analysis. Using analysis of the minimal model, we predict a dose-response curve shape, existence of Hopf-bifurcation, and underlying mechanisms of all possible dynamic patterns of NF-κB signaling. Simulating the detailed ODE model for NF-κB signaling network with large sets of the parameter values that are sampled from the biologically feasible parameter space, we present an ensemble of all possible dynamic patterns of NF-κB signaling and verify the predictions from the minimal model.

Jaewook Joo
Sandia National Laboratories

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