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Molecular stripping in the $NF\kappa B/I\kappa B/DNA$ genetic regulatory network DAVIT POTOYAN, PETER WOLYNES, Rice University — Genetic switches based on the $NF\kappa B/I\kappa B/DNA$ system are master regulators of an array of cellular responses. Recent kinetic experiments have shown that $I\kappa B$ can actively remove NFκB bound to its genetic sites via a process called "molecular stripping". This allows the $NF\kappa B/I\kappa B/DNA$ switch to function under kinetic control rather than the thermodynamic control contemplated in the traditional models of gene switches. Using molecular dynamics simulations of coarse grained predictive energy landscape models for the constituent proteins by themselves and interacting with the DNA we explore the functional motions of the transcription factor $NF\kappa B$ and its various binary and ternary complexes with DNA and the inhibitor IκB. These studies show that the function of the $NF\kappa B/I\kappa B/DNA$ genetic switch is realized via an allosteric mechanism. Molecular stripping occurs through the activation of a domain twist mode by the binding of $I\kappa B$ which occurs through conformational selection. Free energy calculations for DNA binding show that the binding of $I\kappa B$ not only results in a significant decrease of the affinity of the transcription factor for the DNA but also kinetically speeds DNA release. Projections of the

Davit Potoyan
Rice University

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