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Protein scaffolds can enhance the bistability of multisite phosphorylation systems

The phosphorylation of a substrate at multiple sites is a common protein modification that can give rise to important structural and electrostatic changes. Scaffold proteins can enhance protein phosphorylation by facilitating interaction between a protein kinase enzyme and its target substrate. In this work, we consider a simple mathematical model of a scaffold protein and show that under certain conditions, the presence of the scaffold can substantially raise the likelihood that the resulting system will exhibit bistable behavior. This phenomenon is especially pronounced when the enzymatic reactions have a Km larger than 10 micromolar. We also find that bistable systems tend to have a specific kinetic conformation, and we provide through mathematical analysis a number of necessary conditions for bistability, such as the presence of multiple phosphorylation sites and the dependence of the scaffold binding/unbinding rates on number of phosphorylated sites.