Abstract Submitted
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Coarse-Grained Molecular Simulations of Allosteric Cooperativity[1] PRITHVIRAJ NANDIGRAMI, JOHN PORTMAN, Kent State University — We develop a mixed Monte Carlo-Molecular Dynamics scheme to simulate the classic Monod-Wyman-Changeux (MWC) model of allostery at the molecular level. Ligand binding in this model is cooperative due to the coupling between the binding sites provided by the conformational transition of the protein. We present results for calcium binding to the two binding loops within each domain of Calmodulin (CaM). We find that relative binding free energies of an individual loop is determined by the conformational compatibility of the binding site in the bound conformation, as well as the conformational flexibility of the binding site in the unbound conformation. This simple coarse-grained model captures the qualitative differences for calcium binding to the isolated domains of CaM such as overall affinity and the relative binding cooperativity. A simple two state MWC model provides an accurate description of the simulated population for the ligation states of each domain as a function of concentration.

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