

## **Time Delay in Structural Shifts: Modeling Multiple States**

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The reaction rates of most biological processes are linked to the concentrations of reactants. Models of the simplest systems (many with biological importance) consider two states: “on” and “off” or “open” and “closed”. However, state mediation takes place via any number of intermediary states that correspond to structural shifts, allosteric interactions, induced fitting, etc. Although intermediate observation is difficult experimentally, our introduction of time-delay and intermediate states can more accurately model entire systems where only equilibria were before considered. Specifically, intermediate steps prevent the subtle assumption of simpler models that structural conformations shift immediately, and provide instead predictions correlating with the experimentally observed and intuitive. By carefully choosing intermediate rate coefficients, we can describe an “on/off” system with equilibria identical to the simpler model, but with different mediating landscapes and time scales. Because structural shifts always involve an intermediate state or states, we see this approach as providing needed variability.