Multi-Tier Models of Protein Action

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The role of protein relaxation in protein action has been modeled as a bounded diffusion process, involving a single Smoluchowski equation with a sink term [1,2]. This is insufficient when the ligand within the protein, or the active site, can have multiple states. Examples are the states of the active site of an enzyme, such as cholesterol oxidase (unbound, bound, reduced) or the ligand location within myoglobin. To treat such situations, we consider multi-tier bounded-diffusion models, which involve coupled Smoluchowski equations for harmonic potentials with appropriate sink terms. Results are compared with experimental data for two systems:

(a) The conformation cycle of a single cholesterol oxidase enzyme is described by a three-tier model [3]. From the model, the non-exponential on-time distribution and autocorrelation function are obtained, in agreement with data by Xie and coworkers. The agreement suggests that protein conformational states function like the internal states of a cyclic microscopic engine.

(b) The Agmon-Hopfield model for ligand binding to myoglobin is extended to include two states for the photolized CO: within the heme pocket and in the xenon cavities. The time-dependence of the unbound heme survival probability is compared with MbCO absorption measurements in glycerol-water and in sol-gel solutions. The model gives a quantitative fit to complex kinetic data and allows to separate out the effects of inhomogeneous kinetics, protein relaxation and ligand migration.