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Conformational-Modulated Enzyme Catalysis: Generalized Michaelis-Menten Equation and Single Molecule Measurements

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The Michaelis-Menten (MM) equation is a basic rate equation to describe the substrate-dependence of enzymatic reactions; therefore, it is important to establish the validity of the MM-equation for complex enzymatic reactions and derive the correction terms when the MM equation fails. Indeed, single molecule experiments reveal complex catalytic behaviors induced by conformational dynamics and possible deviations from the MM rate equation. To model such complex catalytic reactions, we construct a generic kinetic network model characterized by multiple intermediates and multiple conformational sub-states and, by solving for the turnover rate of this network, we extend the MM equation into a general form. The generalized MM equation predicts that (i) the MM equation holds under detailed balance and (ii) the correction to the MM expression depends on the unbalanced conformational currents. Using these predictions, we can establish a relationship between the substrate-dependence of the turnover rate and the connectivity of the enzymatic network. To confirm these predictions, we propose several single molecule indicators to test the violations of detailed balance. However, these single molecule indicators may be difficult to resolve from noisy single molecule data. To address these issues, we propose information theory based data analysis methods to process single molecule time series, and apply the Bayesian technique to analyze a single protein fluctuation experiment.

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