

Coupled Reaction Theory

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Short Abstract — A statistical mechanical formulation of the law of mass action has been developed, coupled reaction theory, that is on equal theoretical footing with kinetic rate laws and describes chemical kinetics exactly. The formulation is based on a fluctuation theorem for coupled reactions and uses chemical potentials instead of rate constants. Furthermore, using this approach, it can be demonstrated that for many systems, the highest rate of flux at steady state corresponds to the optimal thermodynamic conditions as well. We discuss the significance of coupled reaction theory for applications in systems biology.

Keywords — kinetics, thermodynamics, law of mass action, transition state theory, stochastic.

I. MOTIVATION

ONE hundred and fifty years ago Peter Waage and Cato Maximillian Gulberg published their first article describing the law of mass action, that the rate of a chemical reaction is proportional to the concentration of the reacting species [1].

Forty years after Waage and Gulberg's initial publication, efforts were made to merge the law of mass action with Gibbs ensemble formulation of statistical thermodynamics, which culminated in 1935 with the Absolute Rate Theory of Eyring [2], and Polanyi and Evans [3]. While transition state theory, as it is now known, has been enormously successful as a framework for understanding chemical reactions, it has not had success in being a convenient formulation of statistical mechanics that can be used for large-scale modeling of coupled reactions [4].

II. A FLUCTUATION THEOREM FOR COUPLED REACTIONS

Fluctuation theorems are used to describe stochastic models of dynamics [5]. In stochastic models of reactive systems (Markov models) the usual differential equation relating rate to concentrations is replaced by the change in probability of a state as a function of time. Fluctuation theorems relate conjugate processes from the same original state via the dissipation,

$$\frac{\Pr(J)\pi_1(t|J)}{\Pr(J)\pi_{-1}(t|J)} = e^{a_1(t)}$$

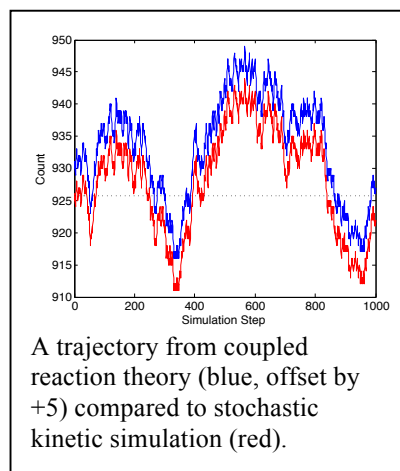
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where $\Omega_1(J)$ is a dissipation function for reaction 1 from state J . This is a significant aspect of fluctuation theorems – they relate the ratio of the probabilities of conjugate processes to a value that is potentially measurable or calculable. If one could determine $\Omega_1(J)$ then the relative reaction probabilities could be determined and the system could be modeled without the use of the rate constants first described by Waage and Gulberg over 150 years ago.

Using a fluctuation theory, we have been able to model the dynamics of coupled chemical reactions with the same precision as kinetic rate laws using differential equations or stochastic kinetic models.

The dynamical trajectory of a reaction intermediate B from a stochastic simulation using coupled reaction theory is shown below along with a trajectory from a stochastic kinetic simulation and the steady state solution to the deterministic ordinary differential equation for comparison. When using the same set of random numbers, the trajectories



are exactly the same, which indicates that the reaction probabilities are also exactly the same. In this case the ratio of the forward rate constants for the two coupled reactions was 10^{-4} . However, we have also been able to demonstrate that the exact results are obtained regardless of the

difference in rate constants between sequential reactions. That is, coupled reaction theory represents one solution to multiscale modeling challenges.

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