RATE CONSTANTS ARE VARIABLES
IN ALMOST ALL CHEMICAL REACTIONS
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Abstract

Chemical reactions are almost always analyzed using rate constants assumed to be constants. Rate constants are constant if reactants do not interact and have zero excess free energy of interaction, and if spatial gradients are insignificant. Reactants in biology almost always interact strongly because charges attract or repel. Biology occurs in mixtures of ions and organic acids and bases with large permanent charge. Large partial charges are found in carbonyl, amine, and peptide bonds of biomolecules and in the solvent water itself. The energy of one charged reactant depends on all charge in the ionic atmosphere around that reactant. The atmosphere contains all species and so

The energy of reactants depends strongly on the concentrations of <u>all species</u>

with significant charge. Measuring excess free energy of interactions has been the life's work of generations of physical chemists. Rate constants in life's solutions should not be assumed constant when physical measurements show important excess interaction energ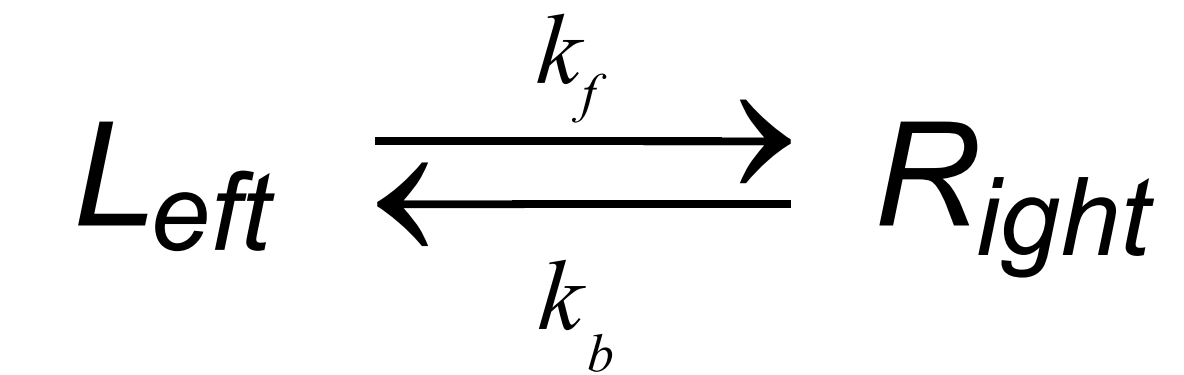y. **'Everything' interacts with everything** in those cases and rate constants are variables. If rate constants are assumed to be constant, **Interactions can be mistaken for conformational changes or complex reaction schemes.**

Physical models provide alternatives that reflect known properties of ionic solutions in confined spaces. Physical models of L-type Ca channels, DEKA Na channels, and most notably the Ryanodine Receptor, account for experiments, over five orders of concentration, in mixtures of many species. The Anomalous Mole Fraction Effect was predicted by Gillespie in the Ryanodine Receptor before it was found experimentally by Meissner and Xu. **The variational calculus provides an alternative description of interactions.** The Energy Variational Approach of Chun Liu [Journal Chemical Physics (2010) 133:104104] is mathematically well-defined, even unique (for a given physical model).It

Includes Interactions & Spatial Gradients that Allow Flow

Law of Mass Action

$$L_{eft} \xrightleftharpoons[k_b]{k_f} R_{ight}$$

$$J_k = \overbrace{l \cdot k_f \cdot C_k\left(L_{eft}\right)}^{\substack{\text{Unidirectional Efflux} \\ J_{out}}} - \overbrace{l \cdot k_b \cdot C_k\left(R_{ight}\right)}^{\substack{\text{Unidirectional Infflux} \\ J_{in}}}$$

$$J_{out} = \overbrace{\underbrace{C_k\left(L\right)}_{\substack{\text{Source} \\ \text{Concentration}}} \underbrace{\left(\frac{D_k}{l}\right)}_{\substack{\text{Diffusion} \\ \text{Velocity}}} \underbrace{\text{Prob}\{R|L\}}_{\substack{\text{Conditional} \\ \text{Probability}}}}^{\text{Unidirectional Efflux}}$$

$$k_f \equiv \frac{J_{out}}{C_k\left(L_{eft}\right)} = \frac{D_k}{l^2}\text{Prob}\{R_{ight}|L_{eft}\} = \frac{D_k}{l^2}\frac{\exp(z_k F V_{trans}/RT)}{\frac{1}{l}\int_0^l \exp(z_k F \phi(\zeta)/RT)d\zeta}$$

Probabilities and Electric Field are NOT CONSTANT. They vary with 'everything'

Biological Solutions are not Ideal Gases
Rate constants are constants for ideal gases