

21.2: Statistical Thermodynamics of Biomolecular Reactions

Statistical mechanics can be used to calculate K_a on the basis of the partition function. The canonical partition function Q is related to the Helmholtz free energy through

$$F = -k_B T \ln Q \quad (21.2.1)$$

$$Q = \sum_{\alpha} e^{-E_{\alpha}/k_B T} \quad (21.2.2)$$

where the sum is over all microstates (a particular configuration of the molecular constituents to a macroscopic system), Boltzmann weighted by the energy of that microstate E_{α} . The chemical potential of molecular species i is given by

$$\mu_i = -k_B T \left(\frac{\partial \ln Q}{\partial N_i} \right)_{V, T, \{N_{j \neq i}\}} \quad (21.2.3)$$

We will assume that we can partition Q into contributions from different molecular components of a reacting system such that

$$Q = \prod_i Q_i \quad (21.2.4)$$

The ability to separate the partition function stems from the assumption that certain degrees of freedom are separable from each other. When two sub-systems are independent of one another, their free energies should add ($F_{\text{TOT}} = F_1 + F_2$) and therefore their partition functions are separable into products: $Q_{\text{TOT}} = Q_1 Q_2$. Generally this separability is a result of being able to write the Hamiltonian as $H_{\text{TOT}} = H_1 + H_2$, which results in the microstate energy being expressed as a sum of two independent parts: $E_{\alpha} = E_{\alpha,1} + E_{\alpha,2}$. In addition to separating the different molecular species, it is also very helpful to separate the translational and internal degrees of freedom for each species, $Q_i = Q_{i,\text{trans}} Q_{i,\text{int}}$. The entropy of mixing originates from the translational partition function, and therefore will be used to describe concentration dependence.

For N_i non-interacting, indistinguishable molecules, we can relate the canonical and molecular partition function q_i for component i as

$$Q_i = \frac{q_i^{N_i}}{N_i!} \quad (21.2.5)$$

and using Sterling's approximation we obtain the chemical potential,

$$\mu_i = -RT \ln \frac{q_i}{N_i} \quad (21.2.6)$$

Following the reasoning in eqs. (2)–(5), we can write the equilibrium constant as

$$K_a = \frac{N_C}{N_A N_B} = \frac{q_C}{q_A q_B} V \quad (21.2.7)$$

This expression reflects that the equilibrium constant is related to the stoichiometrically scaled ratio of molecular partition functions per unit volume $K_a = \prod_i (q_i/V)^{v_i}$. Then the standard binding free energy is determined by eq. (4).

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