# 6.8: Marcus Theory

In classical transition-state theory, the expression for the rate constant of a bimolecular reaction in solution is

$$k = \left( \kappa \nu_n \right)^{\frac{-\Delta G^*}{RT}}, \tag{6.16}$$

where $\nu_n$, the nuclear frequency factor, is approximately $10^{11}$ M$^{-1}$s$^{-1}$ for small molecules, and $\Delta G^*$ is the Gibbs-free-energy difference between the activated complex and the precursor complex. This theoretical framework provides the starting point for classical electron-transfer theory. Usually the transmission coefficient $\kappa$ is initially assumed to be unity. Thus, the problem of calculating the rate constant involves the calculation of $\Delta G^*$, which Marcus partitioned into several parameters:

$$\Delta G^* = w^r + \left( \frac{\lambda}{4} \right) \left( 1 + \frac{\Delta G^{o\,\prime}}{\lambda} \right)^2, \tag{6.17}$$

$$\Delta G^{o\,\prime} = \Delta G^o + w^p - w^r. \tag{6.18}$$

Here $w^r$ is the electrostatic work involved in bringing the reactants to the mean reactant separation distance in the activated complex, and $w^p$ is the analogous work term for dissociation of the products. These terms vanish in situations where one of the reactants (or products) is uncharged. $\Delta G^o$ is the Gibbs-free-energy change when the two reactants and products are an infinite distance apart, and $\Delta G^{o\prime}$ is the free energy of the reaction when the reactants are a distance r apart in the medium; $\Delta G^o$ is the standard free energy of the reaction, obtainable from electrochemical measurements (the quantity - $\Delta G^o$ is called the *driving force* of the reaction).

The reorganization energy $\lambda$ is a parameter that contains both inner-sphere ($\lambda_i$) and outer-sphere ($\lambda_o$) components; $\lambda = \lambda_i + \lambda_o$. The inner-sphere reorganization energy is the free-energy change associated with changes in the bond lengths and angles of the reactants. The $\lambda_i$ term can be evaluated within the simple harmonic-oscillator approximation:

$$\lambda_i = \left( \frac{1}{2} \right) \sum_j k_j (\Delta x_j)^2, \tag{6.19}$$

where $k_j$ values are normal-mode force constants, and the $\Delta x_j$ values are differences in equilibrium bond lengths between the reduced and oxidized forms of a redox center.

The outer-sphere reorganization energy reflects changes in the polarization of solvent molecules during electron transfer:

$$\lambda_o = e^2 \left[ \left( \frac{1}{2r_A} \right) + \left( \frac{1}{2r_B} \right) - \left( \frac{1}{d} \right) \right] \left[ \left( \frac{1}{D_{op}} \right) - \left( \frac{1}{D_s} \right) \right]; \tag{6.20}$$

d is the distance between centers in the activated complex, generally taken to be the sum of the reactant radii $r_A$ and $r_B$; $D_{op}$ is the optical dielectric constant of the medium (or, equivalently, the square of the refractive index); and $D_s$ is the static dielectric constant. This simple model for the effect of solvent reorganization assumes that the reactants are spherical, and that the solvent behaves as a dielectric continuum. (Sometimes the latter approximation is so rough that there is no correspondence between theory and experiment.)

Variations in $\lambda$ can have enormous effects on electron-transfer rates, Some of the possible variations are apparent from inspection of Equation (6.20). First, $\lambda_o$ decreases with increasing reactant size. Second, the dependence of the reaction rate on separation distance attributable to $\lambda_o$ occurs via the $\frac{1}{d}$ term. Third, $\lambda\_o$ decreases markedly as the solvent polarity decreases. For nonpolar solvents, $D_s \simeq D_{op} \simeq 1.5$ to $4.0$. It is significant to note that protein interiors are estimated to have $D_s \simeq 4$, whereas, $D_s \simeq 78$ for water. An important conclusion is that metalloproteins that contain buried redox cofactors need not experience large outer-sphere reorganization energies.

The key result of Marcus theory is that the free energy of activation displays a quadratic dependence on $\Delta G^o$ and $\lambda$ (ignoring work terms). Hence, the reaction rate may be written as

$$k_{et} = \left( \nu_n \kappa \right)^{\frac{-(\lambda + \Delta G^o)^2}{4\lambda RT}}. \tag{6.21}$$

For intramolecular reactions, the nuclear frequency factor ($\nu_n$) is ~$10^{13}$ s$^{-1}$. One of the most striking predictions of Marcus theory follows from this equation: as the driving force of the reaction increases, the reaction rate increases, reaching a maximum at - $\Delta G^o$ = $\lambda$; when - $\Delta G^o$ is greater than $\lambda$, the rate decreases as the driving force increases (Figure 6.23).
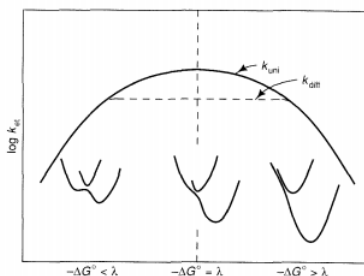
Figure 6.23 - Plot of log $k_{et}$ as a function of increasing driving force (- $\Delta G°$). Three $\Delta G°$ regions are indicated: normal ( - $\Delta G° < \lambda$); activationless ( - $\Delta G° = \lambda$); and inverted (- $\Delta G° > \lambda$). The corresponding two-well ($E_R$, $E_P$), diagrams also are shown. The dashed curve ($k_{diff}$) is for a bimolecular reaction. The predicted behavior of a unimolecular reaction ($k_{uni}$) is given by the solid curve; here the rate could be as high as $10^{13}$ s$^{-1}$, because it is not masked by diffusional processes.

Two free-energy regions, depending on the relative magnitudes of - $\Delta G°$ and $\lambda$, are thus distinguished. The normal free-energy region is defined by - $\Delta G° < \lambda$A. In this region, $\Delta G^*$ decreases if - $\Delta G°$ increases or if $\lambda$ decreases. If - $\Delta G° = \lambda$, there is no free-energy barrier to the reaction. In the inverted region, defined by - $\Delta G° > \lambda$, $\Delta G^*$ increases if $\lambda$ decreases or if - $\Delta G°$ increases. Another widely used result of Marcus theory deals with the extraction of useful kinetic relationships for cross reactions from parameters for self-exchange reactions. Consider the cross reaction, Equation (6.22), for which the rate

$$A_1(ox) + A_2(red) \rightarrow A_1(red) + A_2(ox) \tag{6.22}$$
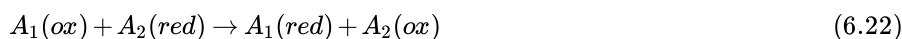
and equilibrium constants are $k_{12}$ and $K_{12}$, respectively. Two self-exchange reactions are pertinent here:

$$A_1(ox) + A_1(red) \rightarrow A_1(red) + A_1(ox) \tag{6.23a}$$

$$A_2(ox) + A_2(red) \rightarrow A_2(red) + A_2(ox) \tag{6.23b}$$
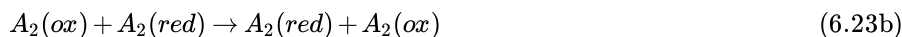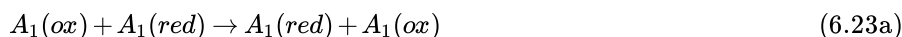
These reactions are characterized by rate constants $k_{11}$ and $k_{22}$, respectively. The reorganization energy ($\lambda_{12}$ for the cross reaction can be approximated as the mean of the reorganization energies for the relevant self-exchange reactions:

$$\lambda_{12} = \frac{1}{2}(\lambda_{11} + \lambda_{22}) \tag{6.24}$$

Substitution of Equation (6.24) into Equation (6.17) leads to the relation

$$\Delta G_{12}^* = \frac{1}{2}(\Delta G_{11}^* + \Delta G_{22}^*) + \frac{1}{2}\Delta G_{12}^*(1+\alpha), \tag{6.25a}$$

where

$$\alpha = \frac{\Delta G_{12}^*}{4(\Delta G_{11}^* + \Delta G_{22}^*)}. \tag{6.25b}$$

When the self-exchange rates $k_{11}$ are corrected for work terms or when the latter nearly cancel, the cross-reaction rate $k_{12}$ is given by the **Marcus cross relation**,

$$k_{12} = (k_{11}k_{22}K_{12}f_{12})^{\frac{1}{2}}, \tag{6.26a}$$

where

$$ln f_{12} = \frac{(ln K_{12})^2}{4\, ln\left(\dfrac{k_{11}k_{22}}{\nu_n^2}\right)}. \tag{6.26b}$$

This relation has been used to predict and interpret both self-exchange and cross-reaction rates (or even $K_{12}$, depending on which of the quantities have been measured experimentally. Alternatively, one could study a series of closely related electron-transfer reactions (to maintain a nearly constant $\lambda_{12}$) as a function of $\Delta G_{12}$; a plot of In $k_{12}$ vs. In $K_{12}$ is predicted to be linear, with slope 0.5 and intercept 0.5 In ($k_{11}k_{22}$). The Marcus prediction (for the normal free-energy region) amounts to a linear free-energy relation (LFER) for outer-sphere electron transfer.
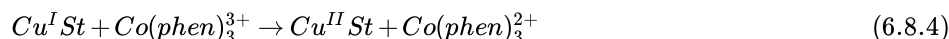
## Cross Reactions of Blue Copper Proteins

Given the measured self-exchange rate constant for stellacyanin ($k_{11}$ 1.2 x $10^5$ M$^{-1}$s$^{-1}$), the Marcus cross relation (Equation 6.26a) can be used to calculate the reaction rates for the reduction of $Cu^{II}$-stellacyanin by Fe(EDTA)$^{2-}$ and the oxidation of $Cu^{I}$-stellacyanin by Co(phen)$_3^{3+}$. E°(Cu$^{2+/+}$) for stellacyanin is 0.18 V vs. NHE, and the reduction potentials and self-exchange rate constants for the inorganic reagents are given in Table 6.3.[66,67] For relatively small $\Delta$E° values, $f_{12}$ is ~1; here a convenient form of the Marcus cross relation is log $k_{12}$ = 0.5[log $k_{11}$ + log $k_{22}$ + 16.9$\Delta E_{12}$°]' Calculations with $k_{11}$, $k_{22}$, and $\Delta E_{12}$° from experiments give $k_{12}$ values that accord quite closely with the measured rate constants.

$$Cu^{II}St + Fe(EDTA)^{2-} \rightarrow Cu^{I}St + Fe(EDTA)^{-} \tag{6.8.1}$$

$$k_{12}(calc.) = 2.9 \times 10^5 M^{-1}s^{-1} \qquad (\Delta E_{12}^o = 0.06V) \tag{6.8.2}$$

$$k_{12}(obs.) = 4.3 \times 10^5 M^{-1}s^{-1} \tag{6.8.3}$$

$$Cu^{I}St + Co(phen)_3^{3+} \rightarrow Cu^{II}St + Co(phen)_3^{2+} \tag{6.8.4}$$

$$k_{12}(calc.) = 1.4 \times 10^5 M^{-1}s^{-1} \qquad (\Delta E_{12}^o = 0.19V) \tag{6.8.5}$$

$$k_{12}(obs.) = 1.8 \times 10^5 M^{-1}s^{-1} \tag{6.8.6}$$

**Table 6.3 - Reduction potentials and self-exchange rate constants for inorganic reagents.**

| Reagent | E°(V vs. NHE) | $k_{22}$ (M$^{-1}$s$^{-1}$) |
|---|---|---|
| Fe(EDTA)$^{-/2-}$ | 0.12 | 6.9 x $10^4$ |
| Co(phen)$_3^{3+/2+}$ | 0.37 | 9.8 x $10^1$ |

The success of the Marcus cross relation with stellacyanin indicates that the copper site in the protein is accessible to inorganic reagents. The rate constants for the reactions of other blue copper proteins with inorganic redox agents show deviations from cross-relation predictions (Table 6.4).[68] These deviations suggest the following order of surface accessibilities of blue copper sites: stellacyanin > plastocyanin > azurin. Rate constants for protein-protein electron transfers also have been subjected to cross-relation analysis.[69]

**Table 6.4 - Reactions of blue copper proteins with inorganic reagents.**
a) M$^{-1}$s$^{-1}$

| Protein | Reagent | $k_{12}$ (obs.)[a] | $\Delta E_{12}$° | $k_{11}$ (obs.)[a] | $k_{11}$ (calc.)[a] |
|---|---|---|---|---|---|
| Stellacyanin | Fe(EDTA)$^{2-}$ | 4.3 x $10^5$ | 0.064 | 1.2 x $10^5$ | 2.3 x $10^5$ |
| | Co(phen)$_3^{3+}$ | 1.8 x $10^5$ | 0.186 | 1.2 x $10^5$ | 1.6 x $10^5$ |
| | Ru(NH$_3$)$_5$py$^{3+}$ | 1.94 x $10^5$ | 0.069 | 1.2 x $10^5$ | 3.3 x $10^5$ |
| Plastocyanin | Fe(EDTA)$^{2-}$ | 1.72 x $10^5$ | 0.235 | ~$10^3$ - $10^4$ | 7.3 x $10^1$ |
| | Co(phen)$_3^{3+}$ | 1.2 x $10^3$ | 0.009 | ~$10^3$ - $10^4$ | 1.1 x $10^4$ |
| | Ru(NH$_3$)$_5$py$^{3+}$ | 3.88 x $10^3$ | -0.100 | ~$10^3$ - $10^4$ | 4.9 x $10^4$ |
| Azurin | Fe(EDTA)$^{2-}$ | 1.39 x $10^3$ | 0.184 | 2.4 x $10^6$ | 2.8 x $10^{-2}$ |
| | Co(phen)$_3^{3+}$ | 2.82 x $10^3$ | 0.064 | 2.4 x $10^6$ | 7.0 x $10^3$ |
| | Ru(NH$_3$)$_5$py$^{3+}$ | 1.36 x $10^3$ | -0.058 | 2.4 x $10^6$ | 1.1 x $10^3$ |