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BOUNDS ON RATE CONSTANTS AND RELATIVE POTENTIALS IN ELECTRON TRANSPORT CHAINS

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Summary

Minimization of free-energy losses requires that the rate constants for reaction in both forward and reverse directions be several times the net rate of a reaction. In an electron transfer between bound molecules, the forward and reverse rate constants contribute separate factors to the free-energy drop across the reaction. If such a reaction has a reverse rate constant which is much greater than the net rate of reaction, then the midpoint potential of the acceptor may economically be more negative than the midpoint potential of the donor.

One often thinks of a sequence of biochemical reactions as having a number of highly irreversible reactions so that the loss of product through back reaction will be negligible. Unfortunately, irreversibility implies a large loss of free energy, and free energy is a valuable commodity. Reliable metabolic control appears to require that the price of irreversibility be paid at a few key points, but it is undesirable and avoidable elsewhere [1,2].

In this paper, we examine the free-energy losses that are implied by a particular choice of rate constants for the forward and reverse reactions between adjacent components of an electron transport chain, or, indirectly, by the relative electrode potentials of the two components. Much of what we say is applicable to other biochemical systems, but for simplicity and specificity the discussion is entirely in terms of electron transfer.

The importance of these losses was driven home to us by computer modeling studies of electron transport in photosynthesis, where we found [3] that keeping the ΔG of individual reactions small provides one of the principal limitations on the kinetic and thermodynamic parameters that are consistent with good free-energy efficiency in that system. Mitchell [4] has discussed the optimum poise of electron transfer intermediates in a similar context.

Consider adjacent members of an electron transport chain, I and J. The electron transfer reactions involving these two components may be represented as

$$\mathrm{e} + \mathrm{I} = \mathrm{I}^- \tag{1}$$

$$\mathrm{I}^-\mathrm{J} = \mathrm{IJ}^- \tag{2}$$

$$\mathrm{J}^- = \mathrm{J} + \mathrm{e} \tag{3}$$

Reaction 1 represents reduction of I by one or more molecules 'upstream' from I, and Reaction 3 represents oxidation of J by molecules 'downstream' from J. We focus our attention on Reaction 2.

Examining this reaction, we see that the net rate of electron transfer down the chain is

$$\text{net rate} = k_+[\mathrm{I}^-\mathrm{J}] - k_-[\mathrm{IJ}^-] \tag{4}$$

At equilibrium the net rate is zero, and

$$\frac{k_+}{k_-} = \frac{[\mathrm{IJ}^-]^{\mathrm{e}}}{[\mathrm{I}^-\mathrm{J}]^{\mathrm{e}}} \tag{5}$$

where the superscript e indicates that these are equilibrium concentrations.

Away from equilibrium, there is a free-energy drop across Reaction 2 which is given by the expression

$$\Delta G = RT \ln \left\{ \frac{[\mathrm{IJ}^-]}{[\mathrm{IJ}^-]^{\mathrm{e}}} \bigg/ \frac{[\mathrm{I}^-\mathrm{J}]}{[\mathrm{I}^-\mathrm{J}]^{\mathrm{e}}} \right\} \tag{7}$$

This free-energy drop may be rewritten as

$$\Delta G = -RT \ln \frac{k_+}{k_-} + RT \ln \frac{[\mathrm{P}]}{[\mathrm{S}]} \tag{8}$$

where we have used Eqn. 5, and identified $\mathrm{I}^-\mathrm{J}$ and IJ^-, the substrate and product of Reaction 2, as S and P.

There are two physical constraints which provide equations relating the variables found in Eqn. 8. The first of these is a stoichiometry restriction: the IJ pair must be in the substrate or product forms, $\mathrm{I}^-\mathrm{J}$ and IJ^-, or in the unreactive double oxidised or doubly reduced forms, IJ and $\mathrm{I}^-\mathrm{J}^-$. This implies that

$$[\mathrm{S}] + [\mathrm{P}] + \alpha = 1 \tag{9}$$

where [S] and [P] are the fraction of chains in the forms $\mathrm{I}^-\mathrm{J}$ and IJ^-, and α is the fraction of I-J pairs which are neither S nor P.

Secondly, the rate of electron transfer from I to J must equal the net rate of other reactions in the pathway.

$$k_+[\mathrm{S}] - k_-[\mathrm{P}] = N \tag{10}$$

where N is the net rate of electron transfer required per electron transport chain. This is presumably set and controlled by the metabolic needs of the organism.

Eqns. 9 and 10 may be solved to determine [S] and [P] in terms of the other variables

$$\frac{[S]}{N} = \frac{k_-(1-\alpha)+1}{k_+ + k_-} \tag{11}$$

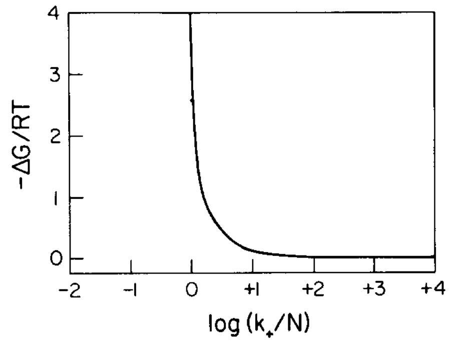
and

$$\frac{[P]}{N} = \frac{k_+(1-\alpha)-1}{k_+ + k_-} \tag{12}$$

Inserting Eqns. 11 and 12 into Eqn. 8, and grouping terms containing k_+ and k_- separately, we find that the free-energy loss for I-to-J electron transfer is

$$\frac{\Delta G}{RT} = \ln\left[1 - \frac{N}{k_+(1-\alpha)}\right] + \ln\left[1 + \frac{N}{k_-(1-\alpha)}\right]^{-1} \tag{13}$$

We see that the forward and reverse rate constants can be written as contributing separate factors to the free-energy drop across the electron transfer reaction. These contributions, the first and second terms of Eqn. 13, are graphed in Figs. 1 and 2. As one would expect, the presence of inactive I-J pairs increases the free-energy loss, with this effect declining to zero when both k_+ and k_- are large. More significantly, we see that it is important that both k_+ and k_- be several times the net rate of reaction.



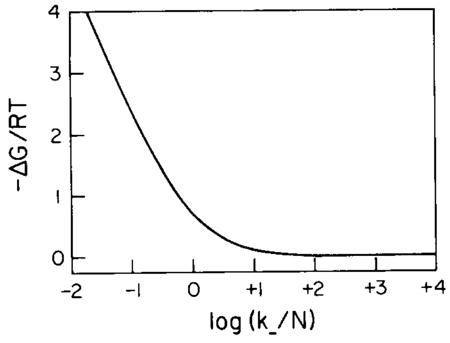


Fig. 1. Minimum free-energy drop across an electron transfer reaction as a function of the ratio (forward rate constant/net rate of reaction).

Fig. 2. Minimum free energy drop across an electron transfer reaction as a function of the ratio (reverse rate constant/net rate of reaction).

If upper bounds are known for the rate constants, then one may use these in conjunction with the lower limits just discussed to establish limits on the ΔG^0 of a reaction. Since this ΔG^0 is related to the standard electrode potentials of the participating molecules by the relationship

$$\Delta G^0 = F(E^0{}_{I/I^-} - E^0{}_{J/J^-}) \tag{14}$$

one also has limits on the relative standard potentials of I and J.

The effect of knowing an upper bound on a rate constant is shown in

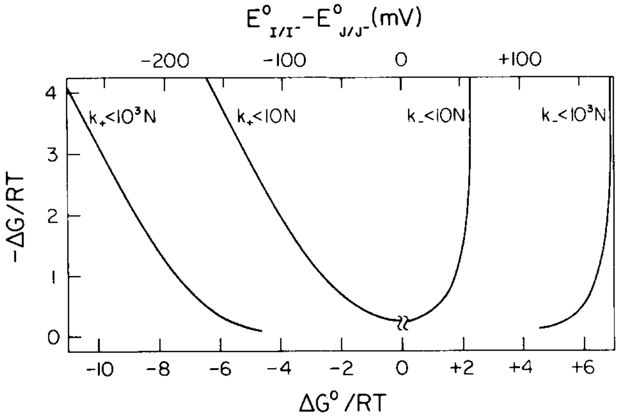


Fig. 3. Minimum free energy drop across an electron transfer reaction as a function of the ΔG^0 of the reaction, equivalent to the relative standard potentials of the donor I and acceptor J.

Fig. 3. As an example, if it is known that both the forward and reverse rate constants are no more than 10 times the net rate of reaction, then ΔG^0 can range only between $-3\ RT$ and $+2\ RT$ without causing a loss of more than RT (600 cal) per mol of reaction. In terms of half-cell potentials, the acceptor J can have a midpoint potential (standard electrode potential) which lies between −40 and +60 mV relative to the midpoint potential of the donor I for this same amount of loss.

It is often assumed that the midpoint potential of an electron acceptor must always be more positive than the midpoint potential of the donor. This is not true, any more than it is true that standard free energies must constantly decrease in any other metabolic sequence. However, as this example points up, a substantial decrease in midpoint potentials requires that the reverse rate constant be much greater than the net rate of reaction. This seems to happen infrequently, so that the midpoint potential of an acceptor is seldom below that of its donor, but we can see no bar to occasional reversals in the usual trend. If the reverse rate constants are large enough, these reversals can be quite large.

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