

## Marcus treatment of endergonic reactions

Antony Crofts and Stuart Rose, Dept. of Biochemistry, and Center for Biophysics and Computational Biology.

It has been suggested in (1) that an alternative form of the Marcus equation should be used for treatment of endergonic processes. In fact, application of the conventional treatment to the endergonic first electron transfer at the Q<sub>o</sub>-site (3), was criticized in review. However, the two are equivalent. The equation suggested in (1) is:

$$\log_{10} k_{et}^{end} = 13.0 - 0.6(R - 3.6) - 3.1(-\Delta G + \lambda)^2 / \lambda - \Delta G / 0.06$$

In addition to what appears to be a conventional Marcus term, this equation seems to contain an extra Boltzmann term contributing to the energy barrier (the right-most term). This is not an “additional term”, however, but simply arises when estimating the activation barrier and rate-constant in the endergonic direction (which cannot be measured easily) using the reaction properties measured in the exergonic direction. It can be derived in its simplest form as follows (using electrical units for  $\Delta G$ ):

$$A \xrightleftharpoons[k_b^{end}]{k_f^{end}} B ; \quad K_{end} = k_f^{end}/k_b^{end} = k_f^{end}/k_f^{ex}$$

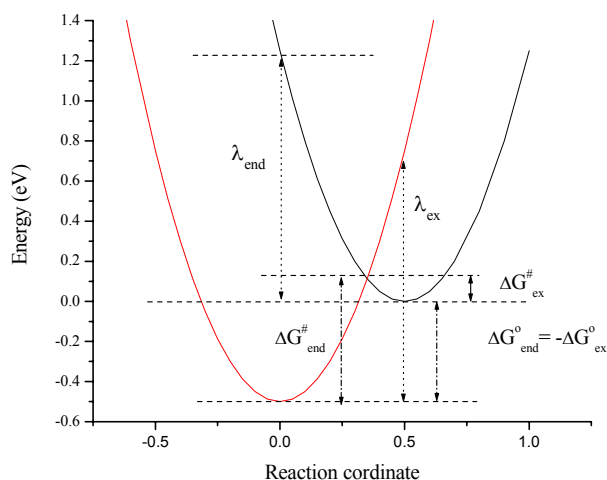
$$k_f^{end} = k_f^{ex} K_{end}$$

$$\log_{10} k_f^{end} = \log_{10} k_f^{ex} + \log_{10} K_{end} = \log_{10} k_f^{ex} - \Delta G_{end}^0 / F/2.303RT$$

This expression can be extended using classical Marcus treatment (4, 5), and substitution using the Arrhenius expression,  $k_f^{ex} = k_0 \exp(-\Delta G_{ex}^{\ddagger} \cdot F/RT)$ , the Marcus term,  $\Delta G_{ex}^{\ddagger} = (\Delta G_{ex}^0 + \lambda)^2 / 4\lambda$ , giving  $\gamma = 4.23$  at 298 K, and the Moser et al. (2) expression for  $k_0$  in terms of distance,  $R$ .

$$\log_{10} k_f^{end} = 13.0 - 0.6(R - 3.6) - \gamma(\Delta G_{ex}^0 + \lambda_{ex})^2 / \lambda_{ex} - \Delta G_{end}^0 / F/2.303RT$$

The Moser-Dutton (1, 2) formulation, in which quantum-mechanical corrections modify the pre-exponential factor, has  $\gamma = 3.1$  instead of 4.23. The Page et al. (1) version is then obtained by substituting  $-\Delta G_{end}^0$  for  $\Delta G_{ex}^0$ . The  $\lambda$  used here is actually that for the exergonic reaction; the value is the same in both directions if the parabolas have the same shape (the same “spring constant”), but not otherwise.



**Fig. 1.** Marcus parabolas for an endergonic process, labeled to show the terms discussed in the text.

An alternative treatment can be framed in terms of a set of Marcus parabolas (Fig. 1) (4, 5). The endergonic energy barrier,  $\Delta G_{end}^{\ddagger}$ , is calculated by adding  $\Delta G_{ex}^{\ddagger}$ , the energy barrier in the exergonic direction, to the energy difference in the endergonic direction (the Boltzmann term in question).  $\Delta G_{ex}^{\ddagger}$  is estimated using the

Marcus expression, with  $\Delta G_{ex}^0$  for the exergonic reaction direction, and a value for  $\lambda$ ,  $\lambda_{ex}$ , obtained in principle from measurement of the exergonic rate. The tricky factor is again the replacement of  $\Delta G_{ex}^0$  by  $-\Delta G_{end}^0$ , its numerical equivalent. The underlying rate equation in the endergonic direction has the same conventional Arrhenius form as that in the exergonic direction. Derivation of the Marcus term for  $\Delta G^\ddagger$  from Hooke's Law, using parabolas for either exergonic or endergonic reactions, gives the same result.

$$k_{cat} = k_0 \exp(-\Delta G_{end}^\ddagger / RT) = k_0 \exp(-(\Delta G_{ex}^\ddagger + \Delta G_{end}^0) / RT)$$

The "additional Boltzmann term" of the Page et al. (1) equation is not an extra term contributing to the barrier, and the treatment used in (3), in which the endergonic region is treated using the standard Marcus term, is perfectly appropriate.

$$\log_{10} k_f^{end} = 13 - \frac{\beta}{2.303} (R - 3.6) - \gamma \frac{(\Delta G_{end}^0 + \lambda_{end})^2}{\lambda_{end}}$$

This can most easily be demonstrated by numerical substitution, as in Fig. 2. Identical Marcus curves are generated using the exergonic or endergonic forms of the Page-Moser-Dutton equation, as long as a simple Marcus treatment (giving  $\gamma$  of 4.23 at 298 K) is used. However, it should be noted that with the Page et al. (1) equation, although  $\Delta G_{end}^\ddagger$  and  $(\Delta G_{ex}^\ddagger + \Delta G_{end}^0)$  have the same numerical value, the quantum mechanical correction implicit in  $\gamma = 3.1$  is applied only to the part of this value corresponding to  $\Delta G_{ex}^\ddagger$ . As a consequence, different values are generated for  $k_f^{end}$  when using the two equations, and the Marcus curve resulting from the treatment recommended in (1) (in which the "endergonic" equation is used only for the endergonic part) shows a discontinuity in slope at the exergonic to endergonic transition.

**Fig. 2.** Curves showing the dependence of rate constant on driving force using different versions of the Moser-Dutton equation.

#### References

1. Page, C.C., Moser, C.C., Chen, X. and Putton, P.L. (1999) *Nature* **402**, 47-52
2. Moser, C.C., Keske, J.M., Warncke, K., Farid, R.S., and Dutton, P.L. (1992) *Nature* **355**, 796-802
3. Crofts, A.R. (2004) *Biochim. Biophys. Acta* **1655**, 77-92
4. Marcus, R. (1965) *J. Chem. Phys.* **43**, 679-701
5. DeVault, D. (1980) *Q. Rev. Biophys.* **13**, 387-564

