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A Simple Marcus-Theory Type Model for Hydrogen Atom Transfer/Proton-Coupled Electron Transfer

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Abstract

Hydrogen atom transfer reactions are the simplest class of proton-coupled electron transfer (PCET) processes. These reactions involve transfer of one electron and one proton from one reagent to another, in the same kinetic step: $XH + Y \rightarrow X + HY$. A predictive model for these reactions based on the Marcus cross relation is described. The model predicts rate constants within one or two orders of magnitude in most cases, over a very wide range of reactants and solvents. This remarkable result implies a surprising generality of the additivity postulate for the reaction intrinsic barriers, and a smaller role for the quantum mechanical details of the proton and electron transfers.

Keywords

PCET; CPET; H-atom transfer; proton transfer; electron transfer; EPT

The utilization of chemical energy and the production of chemical fuels typically involve proton-coupled electron transfer (PCET) reactions. One example is the key hydrogen atom transfer step in the combustion of hydrocarbons (eq 1). The cellular fixation of CO_2 to carbohydrates, or the reverse reaction in respiration, can also be described as PCET processes

(eq 2). PCET is particularly important in the interconversion of chemical and electrical energies, such as the splitting of water and the utilization of H₂ and O₂ in fuel cells (eq 3). PCET is also central to a wide range of other important chemical reactions, from the *in vivo* action of antioxidants such as vitamins C and E to the redox dissolution of metal oxides in the environment (eq 4). The importance and diversity of proton-coupled electron transfer (PCET) reactions have inspired studies by a remarkably broad range of chemists.^{123,4}

Most energy-important PCET reactions involve transfers of multiple electrons and protons, typically by complex multistep mechanisms. A very common step in these pathways is the concerted transfer of one electron and one proton. Concerted transfer has the advantage of bypassing intermediates that are often at high energy. Concerted 1e⁻/1H⁺ reactions have received the most experimental and theoretical attention because they are the simplest PCET processes. Despite this attention, there is still a gulf between the experiments and theories, in part because of the complexity of the theoretical descriptions. We are bridging this gulf by providing simplified yet quantitative tools for experimentalists that enrich and test the theoretical descriptions.

This *Perspective* is focused on reactions in which 1e⁻ and 1H⁺ transfer in a single kinetic step from one reagent to another, typically called hydrogen atom transfer (HAT) reactions (eq 5).¹⁻⁵ HAT reactions are one class of PCET processes, distinguished from reactions in which the e⁻ and H⁺ transfer to or from different reagents.¹ We

have found that rate constants for a wide variety of HAT reactions are well predicted by a simple model based on Marcus theory.^{6,7} This *Perspective* first describes the Marcus model for HAT, and then presents experimental data illustrating its value. The surprising success of this approach and its implications are then discussed, as well as some reactions that are not well predicted.

I. A predictive, Marcus-based model for hydrogen atom transfer reactions

A. The cross relation

Our goal has been to develop a model for HAT reactions that predicts rate constants and thereby indicates what parameters are most important to these reactions. Solution HAT reactions almost always follow bimolecular kinetics with rate constants that vary

$$k=Ae^{-\Delta G^*/RT} \quad (6)$$

$$\Delta G^*=(\lambda+\Delta G^{\circ'})^2/4\lambda \quad (7)$$

exponentially with temperature (eq 6). The Marcus equation gives the free energy barrier ΔG^* in terms of the adjusted reaction driving force $\Delta G^{\circ'}$ and the intrinsic barrier λ (eq 7).^{8,9} The components of $\Delta G^{\circ'}$, λ , and the pre-exponential term A are discussed below.

We have applied this approach, with additional assumptions, to HAT reactions (eq 5). The assumptions are those that were used in the early days of electron transfer (ET) studies, in applying Marcus theory to bimolecular reactions of the type $X^+ + Y \rightarrow X + Y^+$.⁸ First, we apply the ‘additivity postulate’ to HAT (eq 8), that the intrinsic barrier for a reaction $XH +$

Y is equal to the mean of the intrinsic barriers for the self-exchange reactions (*e.g.*, $\lambda_{\text{XH/X}}$ for $\text{XH} + \text{X} \rightarrow \text{X} + \text{HX}$). Second, in the adiabatic limit the pre-exponential factor A is taken as the collision

$$\lambda_{\text{XH/Y}} = \frac{1}{2} (\lambda_{\text{XH/X}} + \lambda_{\text{YH/Y}}) \quad (8)$$

$$k_{\text{XH/Y}} = \sqrt{k_{\text{XH/X}} k_{\text{YH/Y}} K_{\text{XH/Y}} f} \quad (9)$$

$$\ln f = \frac{(\ln K_{\text{XH/Y}})^2}{4 \ln (k_{\text{XH/X}} k_{\text{YH/Y}} Z^{-2})} \quad (10)$$

frequency Z (taken as $10^{11} \text{ M}^{-1} \text{ s}^{-1}$).^{10,11} With these assumptions, equations 6 and 7 can be transformed into the ‘Marcus cross relation’ (eq 9). This equation predicts the rate constant $k_{\text{XH/Y}}$ (eq 5) using the intrinsic barrier derived from self-exchange rate constants, the K_{eq} as a surrogate for ΔG° . The factor f (eq 10) is close to 1 for most – but not all – of the reactions discussed here.

We have tested how well the cross relation holds for more than two dozen HAT reactions involving a transition metal coordination complex and an organic substrate.^{6,12-17} Two examples are shown in equations 11¹² and 12¹³ (eq 11 shows only the first, rate limiting step of a multistep reaction; in eq 12, only one of the three bidentate H_2bip ligands is drawn). In most cases, the cross and self-exchange rate constants are measured with good accuracy¹⁷ but the driving force (K_{eq}) has to be estimated from X–H bond strengths,¹⁸ which limits the precision of the calculated rate constants to *ca.* an order of magnitude. There is generally good agreement between the experimental (observed) bimolecular HAT rate constants and those calculated using eq 9, over more than a dozen orders of magnitude in $k_{\text{XH/Y}}$ (Figure 1A).¹⁷ The Figure 1A legend identifies the metal reactant; the multiple points for each metal complex are for HAT reactions with different organic substrates. Good agreement is taken as within 1-2 orders of magnitude, similar to the accuracy of the cross relation for ET.¹⁰ Some of the reactions that deviate significantly from the cross relation are discussed below.

Reaction 12 and its corresponding self-exchange reactions have been studied over a range of temperatures (Figure 1B).¹³ Surprisingly, the forward reaction becomes slower as the

temperature is raised, with an Eyring activation energy $\Delta H^\ddagger = -2.7 \pm 0.4 \text{ kcal mol}^{-1}$. Negative activation energies are rare but not unprecedented. This inverse temperature dependence is quantitatively predicted by the cross relation, as shown by the close agreement in Figure 1B between the cross rate constants (blue diamonds) and the predicted values (red line).¹⁹ The cross relation also shows that the origin of the negative $\Delta H^\ddagger$ is the large temperature dependence of K_{eq} . Marcus and Sutin showed some time ago that the cross relation predicts $\Delta H^\ddagger < 0$ for this situation, when $\Delta G^\circ \cong 0$, $\Delta H^\circ < 0$, and $\Delta S^\circ < 0$.²⁰ The ability of the cross relation to predict and explain the unusual temperature dependence indicates the power of this model for hydrogen atom transfer reactions.

B. Improvements to the model: Including precursor and successor complexes and hydrogen bonding

The Marcus treatment assumes a multi-step process in which the reactants assemble in a 'precursor complex' (PC) that undergoes H-atom transfer to make the successor complex (SC), which dissociates to products. For ET, the PC and SC are weakly associated species of undefined structure whose equilibrium constant for formation is determined mostly by the overall electrostatic attraction or repulsion between the reagents (the "work terms").^{8,21} In contrast, H-atom transfer requires fairly specific PC/SC structures, with close approach of the atoms that donate and receive the proton, because protons transfer over much shorter distances than electrons.²²

For reactions in which H^+ transfers between electronegative atoms, the PC and SC often involve hydrogen bonds. This is illustrated, for instance, by our study of HAT reactions of the cobalt-biimidazole complexes $[\text{Co}(\text{Hbim})(\text{H}_2\text{bim})_2]^{2+}$ ($\text{Co}^{\text{III}}\text{Hbim}$) and $[\text{Co}(\text{H}_2\text{bim})_3]^{2+}$ ($\text{Co}^{\text{II}}\text{H}_2\text{bim}$). HAT from TEMPOH to $\text{Co}^{\text{III}}\text{Hbim}$ to give TEMPO + $\text{Co}^{\text{II}}\text{H}_2\text{bim}$ shows kinetic saturation at high [TEMPOH] due to the formation of the PC.²³ The results indicate that the PC is more strongly bound than the SC, by $2.7 \pm 0.9 \text{ kcal mol}^{-1}$. Therefore the free energy for the actual H-atom (PCET) step $\text{PC} \rightarrow \text{SC}$, termed $\Delta G^{\circ'}_{\text{Co}}$, is less favorable than the ΔG° for the overall reaction by this amount (Figure 2). The Marcus analysis should use $\Delta G^{\circ'}$ rather than the overall ΔG° .⁸ However, for most HAT and PCET reactions the $\Delta G^{\circ'}$ is not known, only the ΔG° . Ignoring the difference between these may be the cause of some of the deviations from the cross relation in Figure 1A. In the cobalt reaction, using $\Delta G^{\circ'}_{\text{Co}}$ instead of $\Delta G^\circ_{\text{Co}}$ would introduce an error of an order of magnitude in the predicted rate constant.

Organic hydrogen atom transfer reactions can have very large solvent effects because, as shown by Ingold and co-workers,²⁴ H-atom donors are unreactive when hydrogen bonded to solvent. Thus a more complete description of HAT reactions involves de-solvation of XH, followed by precursor complex formation *etc.* (Scheme 2). Ingold *et al.* have developed a quantitative model of this kinetic solvent effect (KSE), using Abraham's empirical hydrogen bonding parameters.²⁴ We have combined the KSE with the cross relation to give a composite model that can predict organic HAT rate constants in one solvent even when the self-exchange and equilibrium constants are known only in other solvent(s).⁷ Figure 3 shows that this model gives excellent agreement with experimental rate constants, over a set of 36 organic reactions. Thirty of the 36 predicted $k_{\text{XH/Y}}$ are within a factor of 5 of the measured value, and there is an overall correlation coefficient (R^2) of 0.97. These reactions involve oxyl radicals abstracting $\text{H}^\bullet$ from substrates with reactive O–H or C–H bonds, in solvents that range from water to alkanes. The reactions have equilibrium constants spanning more than 10^{20} , the cross rate constants range from 10^{-3} to $10^9 \text{ M}^{-1} \text{ s}^{-1}$, and the values of f (eq 10) are as small as 6×10^{-5} . The data come from many different laboratories and were measured with many different techniques,⁷ indicating that the model is robust and general.

C. The success of the cross relation

The accuracy of the cross relation in describing HAT reactions is remarkable. The agreement is as good as is found for application of the cross relation to ET.¹⁰ Because Marcus theory was derived for electron transfer and weakly interacting reactants, its success for HAT/PCET is surprising. Current PCET theories do not appear to reduce to the simple classical Marcus expression, and there is little theoretical justification for applying Marcus theory to HAT (although Marcus has briefly discussed this²⁵⁻²⁸). Still, the Marcus equation has been successfully applied to many types of chemical reactions, and the cross relation has been shown to hold for hydride transfers between NADH analogs and for proton transfers between metal-tricarbonyl complexes.^{29 - 32}

From one perspective, the Marcus analysis is a correlation of rate constants with driving force, related to the linear free energy relationships (LFERs) $\Delta G^\ddagger = \alpha \Delta G^\circ + \beta$ that are so common in Chemistry. At low driving forces ($\Delta G^\circ \ll 2\lambda$), the Marcus equation reduces to an LFER, $\Delta G^\ddagger = \lambda/4 + \Delta G^\circ/2$, and the majority of experimental test shown above fall in this limit. However, there are a number of cases in which the quadratic dependence of barrier on ΔG° is important, as indicated by the values of f that deviate substantially from unity.

The most remarkable feature of the success of the cross relation for HAT is the breadth of reactions that are covered. LFERs and the previous non-ET applications of the cross relation are all restricted to sets of very similar reactants, and to reactions in a single solvent. This is evident in the well-known correlation of HAT rate constants with bond strengths, the Evans-Polanyi relation: different correlations are observed for different classes of reactions, for instance reactions of alkyl radicals vs. those of oxyl radicals.^{5,33} But the reactions analyzed in Figures 1 and 3 are *not* similar: they include transition metal complexes and oxyl radicals as the H-atom abstractors, they involve H-atom donors with O–H, N–H, and C–H bonds, and they occur in a wide range of solvents. This much wider scope of reactions shows that the Marcus analysis is much more powerful than a simple LFER. In a LFER, the parameters α and β are defined only by the $\Delta G^\ddagger = \alpha \Delta G^\circ + \beta$ relationship. In contrast, the values that enter into the cross relation, $K_{XH/Y}$, $k_{XH/X}$ and $k_{YH/Y}$ together with the parameters for the KSE model, are all independently measured and have independent meaning. Using the additivity postulate, there are no fitted parameters in the application of the cross relation/KSE model.

It should be emphasized that we are claiming good agreement when the calculated rate constant is within one or two orders of magnitude of the experimental value. For organic reactions, for which we can apply Ingold's kinetic solvent effect (KSE) correction, the agreement is better, in most cases within a factor of five. The deviations are larger for the transition metal reactions. This is likely because the hydrogen-bonding parameters are not available to apply the KSE correction, and because in general the data are not available to correct for the energetics of the precursor and successor complexes. While this 'broad-brush' model cannot give highly accurate relative rate constants or kinetic isotope effects, the prediction of rate constants for most HAT reactions to within one or two orders of magnitude is a remarkable result.

II. Implications of the success of the cross relation, and exceptions

A. Intrinsic Barriers

The cross relation, equation 9, is derived from the adiabatic form of the Marcus equation (eqs 6 and 7), taking the pre-exponential term to be simply the collision frequency Z .¹⁰ This is how the cross relation is usually applied for electron transfer reactions.^{8,10} Conceptually, some of these reactions may well be better described by a non-adiabatic model, as discussed below, but in most cases the adiabatic model provides good agreement with experiment.

The cross relation is successful because it captures the most important effects: the driving force ($\Delta G^\circ_{\text{HAT}}$) and the intrinsic barrier λ_{HAT} . The concept of an intrinsic barrier was developed for ET theory, and λ_{ET} can be defined as the free energy to distort the reactants to the nuclear configuration of the products without the electron transferring. The results presented here empirically show that the ET formalism works just as well for reactions in which $\text{H}^\bullet$ is transferred. In this semiclassical model, λ_{HAT} is the free energy to take the reactants to the configuration of the products without the $\text{H}^\bullet$ (e^- and H^+) transferring. In application of the adiabatic cross reaction, equation 9, λ_{HAT} is taken as one quarter of the free energy barrier for a reaction with $\Delta G^\circ_{\text{HAT}} = 0$. Using the additivity postulate in the adiabatic limit, $\lambda_{\text{XH/Y}}$ is taken as the mean of the λ 's for the self exchange reaction (eq 8), or $1/8(\Delta G^*_{\text{XH/X}} + \Delta G^*_{\text{YH/Y}})$, where $\Delta G^*_{\text{XH/X}}$ is derived from the self-exchange rate constant via $k = Ze^{-\Delta G^*/RT}$ (eq 6). As noted above, this is how the cross relation has typically been applied to ET reactions.^{8,10}

A very surprising aspect of the success of the cross relation for HAT is the accuracy of the additivity postulate, over a wide range of reactions and solvents. For electron transfer, the additivity postulate is intuitively reasonable because the reactants are only weakly interacting. However, HAT and PCET reactions appear to involve strongly coupled systems because the cleavage of a strong X–H bond is coupled to the formation of a strong Y–H bond.

The additivity postulate would seem to require that the transition structures for the cross and self reactions are similar, but this is not always the case for HAT. In reactions of an oxyl radical $\text{RO}^\bullet$ with a C–H bond, for example, the $\text{RO}^\bullet \cdots \text{HOR}$ self-exchange reaction can have a transition structure stabilized by a hydrogen bond,^{34,35} while there is no hydrogen bond in the other self-exchange reaction ($\text{>C}^\bullet\text{--H--C}\leq$) or in the cross reaction ($\text{RO}^\bullet\text{--H--C}\leq$). In this light, the accuracy of the cross relation for oxyl radicals reacting with both O–H and C–H bonds (Figure 3) is remarkable.

According to the additivity postulate, the intrinsic barrier depends only on the properties of the individual reagents. This predicts that if reagent AH has a lower λ_{HAT} than another reagent BH, AH will always react faster with any $\text{H}^\bullet$ abstracting agent. This is unusual: for many types of chemical reactions, rate constants depend not only on the properties of the individual reagents but also on the specific combination of reactants (*e.g.*, for hard and soft acids and bases). As one example of this, some HAT reactions have well-documented ‘polar effects,’ in which an electrophilic radical reacts faster with an electron-rich A–H bond than with an electron poor B–H bond, while a nucleophilic radical exhibits opposite selectivity.^{33,36} This dependence of reactivity on the reaction partner is a clear violation of the additivity postulate.

One of the ways that HAT differs from ET is the requirement of well-defined precursor and successor complexes. This means that HAT reactions can be susceptible to steric effects. Sterics may also influence λ_{HAT} , for instance if bulky groups limit the close association of the proton donor and acceptor. If one of the reagents (XH/X) is very crowded, the effect on the cross reaction $\text{XH} + \text{Y}$ may not be the mean of effects on the self-reactions $\text{XH} + \text{X}$ and $\text{YH} + \text{Y}$, in violation of the additivity postulate. Steric effects have been observed in some HAT reactions (*cf.*,^{37–39}) and may be the cause of some of the deviations in Figure 1A, such as the points for the reactions of osmium-aniline/anilide complexes $\text{TpOs}(\text{NH}_x\text{Ar})\text{Cl}_2$ (Tp = hydrotris(pyrazolyl)borate).¹⁶ Introducing an *ortho-tert*-butyl group into the aniline/anilide ligand increases steric hindrance about the transferring hydrogen, as can be seen from the structure in Figure 4, and slows the apparent HAT self-exchange rate constant by two orders of magnitude.¹⁶

This discussion indicates the need for a better understanding of the magnitudes of λ_{HAT} . In electron transfer, λ_{ET} is taken as the sum of inner-sphere reorganization (within the reagents) and the solvent reorganization energies that result from the transfer of charge. HAT reactions, in contrast, do not involve a net transfer of charge, rather transfer of a neutral atom. Therefore the intrinsic barriers (and free energies) of HAT reactions are much less dependent on solvent than are electron or proton transfers. The extensive experimental database of organic HAT rate constants shows that there is little if any solvent influence on the actual HAT step (as opposed to the de-solvation and precursor complex formation steps discussed above). In one study, HAT from cyclohexane to the cumyloxyl radical $\text{PhCMe}_2\text{O}^\bullet$ was found to have the same rate constant *within 10%* in six solvents with dielectric constants that range from 2 to 36 (CCl_4 , C_6H_6 , $\text{C}_6\text{H}_5\text{Cl}$, $t\text{BuOH}$, MeCN , MeCO_2H).⁴⁰ HAT reactions of C–H bonds are often similar in solution and in the gas phase, which is in part the origin of the common intuition that gas-phase C–H bond dissociation energies can be used to understand solution reactions. Much less is known about solvent effects on transition metal HAT reactions, but computationally there can be significant outer-sphere (solvent) reorganization when the proton and electron move significantly different distances.⁴¹

The same factors that affect intrinsic barriers for electron transfer (ET) also appear to affect λ_{HAT} . Large changes in bond lengths of high-frequency modes result in large inner-sphere reorganization energies for both ET and HAT. This was illustrated by a study of vanadium–oxo vs. ruthenium–oxo compounds, in which the higher force constants and larger bond-length changes in the vanadium case give a much larger λ_{HAT} .¹⁵ HAT reactions of the high-spin Co^{II} /low-spin Co^{III} redox couple are much slower than analogous all high-spin $\text{Fe}^{\text{II/III}}$ reactions, just as is found for ET reactions.⁶

For proton transfer (PT), it is well known that C–H bonds are intrinsically much slower than reactions of O–H bonds. The same kinetic pattern is found in HAT reactions, where $\text{R}^\bullet \cdots \text{HR}$ self-exchange reactions are *ca.* 10^8 slower than $\text{RO}^\bullet \cdots \text{HOR}$ self-exchange reactions.⁴² It is tempting to ascribe this similarity to trends in intrinsic barriers, although the differences in proton transfer rate constants could be due to non-adiabatic effects⁴³ (see below). Whatever the origin, the experimental data show that factors that slow electron or proton transfer reactions, such as using C–H bonds or large reorganization energies, also slow HAT processes.

While these relative arguments are useful, we know of no experimental or theoretical study that shows any clear relationship among the rate constants or intrinsic barriers for HAT, ET, and PT. In the osmium-anilide system mentioned above, we found that ET and PT self-exchange reactions occur rapidly ($k = 10^3 - 10^5 \text{ M}^{-1} \text{ s}^{-1}$) while HAT self exchange is a million times slower ($3 \times 10^{-3} \text{ M}^{-1} \text{ s}^{-1}$).¹⁶ In contrast, Bullock, Norton, and co-workers found for $\text{CpW}(\text{CO})_3\text{H}$ compounds that ET and HAT self-exchange rate constants were both faster than that for PT.^{44,45} Protasiewicz and Theopold reported yet another pattern of self-exchange rate constants: $k_{\text{ET}} (9 \times 10^7 \text{ M}^{-1} \text{ s}^{-1} \text{ at } 30^\circ\text{C}) \gg k_{\text{PT}} (3.5 \text{ M}^{-1} \text{ s}^{-1} \text{ at } 30^\circ\text{C}) > k_{\text{HAT}} (9 \times 10^{-3} \text{ M}^{-1} \text{ s}^{-1} \text{ at } -34^\circ\text{C})$.⁴⁶ No simple relationship among λ_{HAT} , λ_{ET} and λ_{PT} is expected, since λ_{HAT} contains much less solvent reorganization than λ_{ET} or λ_{PT} .

B. A deeper look: The reaction coordinate, non-adiabatic effects, and proton tunneling

The use of the Marcus cross relation suggests a particular reaction coordinate. For ET, the Marcus-Hush model includes a Born-Oppenheimer separation of electronic and nuclear motions.⁸ The reaction coordinate describes only nuclear motion, without the “position” of the transferring electron. Using the cross relation for HAT implies an additional pseudo-Born-Oppenheimer separation between motions of the proton vs. the heavier nuclei, and the reaction coordinate does not include the positions of either the proton or the electron. The e^- and H^+ transfer from the reactant and product diabatic vibronic surfaces (the iconic Marcus

parabolas adapted for this purpose) when the heavy nuclei reach the intersection of the two surfaces. It is a little odd that the reaction coordinate for hydrogen atom transfer, at least at this simple level, does not involve the hydrogen.

In electron transfer and in some PCET theories, the reaction coordinate is often described as a collective solvent coordinate, indicating the typical dominance of solvent effects over inner-sphere reorganization.^{8,47-49} The sum of many low-frequency solvent modes gives the parabolic Marcus potential energy surface. However, as noted above, HAT reactions are often insensitive to solvent, indicating that the reaction coordinate and the intrinsic barriers predominantly derive from motions within the reagents. The sum of such higher frequency inner-sphere vibrations is less likely to be well approximated by a parabola. In this light, it is remarkable that the cross relation works well even at high driving forces, when the quadratic nature of the Marcus equation is important.

The one-dimensional PCET reaction coordinate outlined above is related to the two-dimensional coordinate used by Hammes-Schiffer and co-workers in their influential theory of PCET.^{47,50} Because the model is two-dimensional and includes vibrational excited states, this theory has nested two-dimensional vibronic paraboloids. Typically, reactions are treated as non-adiabatic, with a probability for the proton and electron hopping together from a reactant to a product vibronic surface. From one perspective, this theory derives conceptually from the non-adiabatic Marcus equation for ET, where the pre-exponential includes a probability of electron hopping in the form of the square of the electronic matrix element H_{AB} (eq 13). In PCET theory,

$$k_{et} = \frac{2\pi}{\hbar} H_{AB}^2 \frac{1}{\sqrt{4\pi\lambda RT}} \exp\left(-\frac{(\Delta G^\circ + \lambda)^2}{4\lambda RT}\right) \quad (13)$$

the proton is treated as a quantum particle, and the double hopping probability is (to a first approximation) a combination of the electronic matrix element H_{AB} and Frank-Condon overlaps of proton vibrational wavefunctions.⁴⁷⁻⁴⁹ This probability is one of the most interesting features of the theory, for instance being in large part responsible for the magnitude of the H/D kinetic isotope effect. For simplicity in the following discussion, we will assume that the non-adiabatic character (the hopping probability) is primarily evident in the pre-exponential term A in the rate expression (eq 6 above), as it is for ET (eq 13), although PCET theory unfortunately does not have such a simple separation between exponential and pre-exponential terms.

The experimental applications of the cross-relation above have for simplicity assumed the adiabatic limit, that the pre-exponential terms A in eq 6 are simply the collision frequency Z . In many cases, however, A is found to be smaller than Z , perhaps due to the reactions being non-adiabatic or to entropic effects in forming the precursor complexes. When A is less than Z , the experimental adiabatic intrinsic barrier is an upper limit to $\lambda_{XH/Y}$. For the adiabatic cross relation to hold when $A \neq Z$, the pre-exponential terms must also roughly follow an ‘additivity postulate’ of sorts, that $A_{XH/Y}$ for a cross reaction is close to the geometric mean of $A_{XH/X}$ and $A_{YH/Y}$ for the

$$A_{XH/Y} \cong (A_{XH/X} A_{YH/Y})^{1/2} \quad (14)$$

self-exchange reactions (eq 14). To my knowledge, PCET theory does not predict that this postulate should hold.

One experimental system we have examined, the reaction of a ruthenium imidazole complex with the nitroxyl radical TEMPO (eq 15), shows a wide range of experimental A values: $\log(A_{\text{RuH/TEMPO}}) = 5.6 \pm 0.3$, $\log(A_{\text{RuH/Ru}}) = 9.4 \pm 0.2$, and $\log(A_{\text{TEMPOH/TEMPO}}) = 3.8 \pm 0.3$.¹⁴ The

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low A values may indicate that the reactions are non-adiabatic, or (as a referee emphasized) could be simply be due to steric factors. Calculations suggest that the TEMPOH/TEMPO self-exchange reaction proceeds by protons transferring below the classical barrier, by tunneling.⁵¹ This is also suggested by the large H/D kinetic isotope effects (KIEs): $k_{\text{H}}/k_{\text{D}} = 23$ for both the cross reaction and for the TEMPOH/TEMPO self-exchange reactions, and $k_{\text{H}}/k_{\text{D}} = 1.5$ for $\text{Ru}^{\text{II}}\text{H}/\text{Ru}^{\text{III}}$ self-exchange.¹⁴ The cross relation treatment described above is a semiclassical model that does not include quantum effects such non-adiabaticity or proton tunneling, so it is not surprising that k_{15} is not very well predicted: the calculated values for $k_{15\text{H}}$ and $k_{15\text{D}}$ are 31 ± 4 and 140 ± 20 times larger than the experimental ones. Some of this deviation comes from the A values, as the geometric mean of the self-exchange values ($\log A_{\text{calc}} = 6.6 \pm 0.4$) is an order of magnitude larger than that observed. The $k_{15\text{H}}/k_{15\text{D}}$ of 23 is significantly larger than the 5.9 predicted from simplistic application of the cross

relation ($\text{KIE}_{\text{XH/Y}} = \sqrt{\text{KIE}_{\text{XH/X}} \text{KIE}_{\text{HY/Y}}}$ assuming negligible isotopic effects on K_{eq} and f).

Still, it should be emphasized that the influence of non-adiabaticity, precursor complexes, and other effects that are not included in the cross relation are typically less than the estimated accuracy of this approach, ± 1 -2 orders of magnitude. Even in this unusual ruthenium reaction, the deviation implied by the KIEs is only a factor of 10 in A and a factor of 4 in KIE. In the cobalt reaction shown in Scheme 1 above, the error introduced by ignoring the energetics of precursor and successor complex formation is again only a factor of ten in the calculated rate constant. As Sutin has pointed out, Marcus theory and the cross relation in particular have a lot of inherent averaging, which partially alleviates the simplifications of the treatment.⁸

III. Conclusions and future challenges

A model based on the Marcus cross relation in most cases predicts rate constants for hydrogen atom transfer (HAT) reactions to within 1-2 orders of magnitude. The inputs to the model are the free energy of the reaction and the HAT self-exchange rate constants for the reactants. There are no adjustable parameters. This model has been successfully applied to a wide range of reactions, including transition metal complexes and organic reagents, reactive C–H, N–H, and O–H bonds, and in a variety of solvents. For organic reactions, including the kinetic solvent effect model of Ingold and coworkers allows predictions from one solvent to another, and improves the overall accuracy. The success of the model for such a wide range of reactions is unprecedented for any rate/driving force analysis of a chemical reaction other than outer-sphere electron transfer.

The success of this model provides significant insights into the hydrogen atom transfer or proton-coupled electron transfer process. The applicability of the additivity postulate for HAT intrinsic barriers is surprising and is not predicted by current theory. The quantum

mechanical aspects of PCET such as proton tunneling, which are among the most conceptually interesting theoretical aspects, are not included in this treatment and do not usually play a major role in determining the size of the HAT rate constant. The cross relation model omits a number of the essential aspects of these reactions, and is not appropriate for calculation of parameters such as the kinetic isotope effect. The cross relation/kinetic solvent effect treatment is successful because it captures the largest effects on these reactions: the driving force ΔG° , the intrinsic barrier λ , and the hydrogen bond formed by the H-atom donor. An ongoing challenge for both experimentalists and theorists is to provide better understanding of HAT intrinsic barriers.

The success of the Marcus treatment for hydrogen atom transfer is an important first step in designing and understanding pathways for the multi-electron, multi-proton PCET reactions that are so important in energy conversions. These reactions may involve HAT, or they may involve other kinds of concerted proton-electron transfers. Energy applications such as water oxidation likely involve reactions in which an electron and a proton transfer to *different* reagents, as illustrated schematically in eq 16 (termed ‘multiple site’ EPT by Meyer *et al.*).¹ Such

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reactions are being studied in many laboratories, (*cf.*,^{1,52-56}) especially phenol oxidations as models for steps in biochemical processes that involve tyrosyl radicals.⁵⁷ It will be valuable to have experimentally accessible and predictive models of these reactions, similar to the cross relation model presented here in philosophy and Marcus-theory origin but different in form. Finally, it would be particularly valuable to be able to design reactions in which multiple electrons and protons were transferred in a single kinetic step, as this would likely enable pathways with fewer intermediates and higher efficiencies.

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Biography

Biography. James Mayer did undergraduate research with Edwin Abbott at Hunter College, and with William Klemperer while earning his A.B. at Harvard. He completed his PhD with John Bercaw at Caltech in 1982, and after two years as a Visiting Scientist at DuPont moved to the University of Washington.
<http://depts.washington.edu/chem/people/faculty/mayer.html>

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Quotes to Highlight

The cross relation/kinetic solvent effect treatment is successful because it captures the largest effects on hydrogen atom transfer reactions: the driving force ΔG° , the intrinsic barrier $\Delta^\ddagger$, and the hydrogen bond formed by the H-atom donor.

The success of the model for such a wide range of reactions is unprecedented for any rate/driving force analysis of a chemical reaction other than outer-sphere electron transfer.

A very surprising aspect of the success of the cross relation for HAT is the accuracy of the additivity postulate, over a wide range of reactions and solvents.

The success of this model provides significant insights into the hydrogen atom transfer or proton-coupled electron transfer process.

Figure 1.

Tests of the Marcus cross relation for HAT. **A:** log/log plot of experimental vs. calculated bimolecular HAT rate constant for a number of metal complexes reacting with various organic substrates. The diagonal line illustrates $k_{\text{obs}} = k_{\text{calc}}$; the estimated errors on k_{calc} are typically ± 1 log unit. **B:** Combined Eyring and van't Hoff plot for reaction 12: $K_{\text{XH/Y}}$ (right axis); self-exchange rate constants for $[\text{Fe}^{\text{II}}(\text{H}_2\text{bip})_3]^{2+} + [\text{Fe}^{\text{III}}(\text{Hbip})(\text{H}_2\text{bip})_2]$ ($k_{\text{XH/X}}$) and for $\text{TEMPOH} + \text{TEMPO}$ ($k_{\text{YH/Y}}$); and the cross rate constants measured ($k_{\text{XH/Y}}$, blue circles) and calculated from the cross relation ($k_{\text{XH/Y}}$, red line) (left axis). Reprinted from references 17 (**A**) and 13 (**B**).

Figure 2.
Schematic free energy surface, with precursor complex (PC) and successor complex (SC)
for the reaction in Scheme 1.

Scheme 1.
Precursor and successor complexes

Scheme 2.

Mechanism of HAT reactions for H-atom donors that form a hydrogen bond to solvent.

Figure 3.

Comparison between organic HAT rate constants measured experimentally (k_{obs}) versus those determined from the composite KSE/cross relation model (eq 9, k_{calc}). The line indicates perfect agreement. The reactions involve oxyl radicals + O-H bonds (red ●) or + C-H bonds (blue □). Reprinted from reference 7.

Figure 4.

One of the independent molecules in the unit cell of $\text{TpOs}(\text{NH}_2\text{C}_6\text{H}_4^t\text{Bu})\text{Cl}_2$, from reference 16.