

Current Theoretical Challenges in Proton-Coupled Electron Transfer: Electron—Proton Nonadiabaticity, Proton Relays, and Ultrafast Dynamics

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ABSTRACT: Proton-coupled electron transfer (PCET) reactions play an important role in a wide range of biological and chemical processes. The motions of the electrons, transferring protons, solute nuclei, and solvent nuclei occur on a wide range of time scales and are often strongly coupled. As a result, the theoretical description of these processes requires a combination of quantum and classical methods. This Perspective discusses three of the current theoretical challenges in the field of PCET. The first challenge is the calculation of electron—proton nonadiabatic effects, which are significant for these reactions because the hydrogen tunneling is often faster than the electronic transition. The second challenge is the modeling of electron transfer coupled to proton transport along hydrogen-bonded networks. The third challenge is the simulation of the ultrafast dynamics of nonequilibrium photoinduced PCET reactions in solution. Insights provided by theoretical studies may assist in the design of more effective catalysts for energy conversion processes.



Proton-coupled electron transfer (PCET) reactions are essential for a broad range of biological processes, such as photosynthesis and respiration, and are at the heart of many energy conversion devices, such as solar cells. These reactions have been studied extensively with both experimental and theoretical methods.¹⁻¹² The motions of the electrons, transferring protons, solute nuclei, and solvent nuclei occur on a wide range of time scales and are often strongly coupled. Over the past decade, a general theoretical formulation of PCET that includes the quantum mechanical effects of the electrons and transferring proton(s), as well as the solvent and proton donor-acceptor motions, has been developed.8 The fundamental theoretical concepts of PCET reactions have been reviewed recently^{8,10} and will not be covered here. Instead, this Perspective will be forward-looking and focus on three current theoretical challenges in this field. The first challenge is the accurate description of electron-proton nonadiabatic effects, which are significant for PCET reactions because the hydrogen tunneling time scale is typically shorter than the electronic transition time scale. The second challenge is the development of strategies for investigating electron transfer coupled to proton transport along hydrogen-bonded networks, rather than to a single proton transfer. The coupling of electron transfer to proton transport over multiple sites plays an important role in biological systems such as photosystem II, cytochrome c oxidase, and ribonucleotide reductase, as well as in biomimetic systems for artificial photosynthesis and other energy conversion processes. The third challenge is the study of the nonequilibrium dynamics of ultrafast photoinduced PCET reactions, which are particularly relevant to solar energy conversion.

The motions of the electrons, transferring protons, solute nuclei, and solvent nuclei occur on a wide range of time scales and are often strongly coupled.

In concerted PCET reactions, the electron and proton transfer in a single step without a stable intermediate. Typically, these reactions are vibronically nonadiabatic because the quantum subsystem comprised of the electrons and transferring proton does not respond instantaneously to the solvent motions. In this regime, PCET reactions are described in terms of nonadiabatic transitions between charge-localized diabatic electron – proton vibronic states.⁸ The reactant diabatic vibronic states correspond to the electron and proton localized on their donors, and the product diabatic vibronic states correspond to the electron and proton localized on their acceptors. Within this regime, the proton transfer may be electronically adiabatic, where the electrons respond instantaneously to the proton motion, or electronically nonadiabatic, where the response of the electrons is slower than the proton motion.

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Figure 1. Electrostatic potential maps for the ground adiabatic electronic states for the reactant (top), transition state (middle), and product (bottom) positions of the transferring hydrogen for the phenoxylphenol self-exchange reaction. Negatively and positively charged regions are indicated by red and blue coloring, respectively. Figure reproduced with permission from ref 14.

Although both types of proton transfer fall under the umbrella of general PCET, the electronically adiabatic and nonadiabatic proton transfer limits have been associated with hydrogen atom transfer (HAT) and PCET mechanisms, respectively. 13,14 The criteria for distinguishing between HAT and PCET mechanisms have been debated in the literature.^{13–16} The PCET mechanism has been attributed to reactions with different donors and acceptors for the electron and proton, and the HAT mechanism has been attributed to reactions with the electron and proton coming from and going to the same bond or the same molecular orbital.¹⁶⁷These criteria are not rigorous because of the quantum mechanical behavior and associated delocalization of both the electron and the proton, as well as the dependence of molecular orbital analyses on the level of theory and representation. Qualitatively, significant molecular charge redistribution is associated with the PCET but not the HAT mechanism. The quantitative distinction between these two mechanisms via the degree of electron-proton nonadiabaticity is important because the expressions for the vibronic coupling and the rate constant are different in these two limits.

The degree of electron—proton nonadiabaticity can be evaluated quantitatively with a semiclassical formalism, where an adiabaticity parameter is defined as the ratio of the proton tunneling time $\tau_{\rm p}$ and the electronic transition time $\tau_{\rm e}$.¹⁷ In the electronically nonadiabatic regime, the proton tunneling time is less than the electronic transition time, whereas in the electronically adiabatic regime, the proton tunneling time is greater than the electronic transition time. These two limits are illustrated by a comparison of the phenoxyl-phenol self-exchange reaction, which is identified as a PCET mechanism, to the benzyl-toluene self-exchange reaction, which is identified as a HAT mechanism.^{13,14} For the phenoxyl-phenol self-exchange reaction, $\tau_{\rm e} \approx 80 \tau_{\rm p}$, whereas for the benzyl-toluene self-exchange reaction, $\tau_{\rm p} \approx 4 \tau_{\rm e}$.¹³ The former reaction is electronically nonadiabatic and is associated with substantial molecular charge redistribution, while the latter reaction is electronically adiabatic without significant molecular charge distribution.¹⁴

The degree of electron—proton nonadiabaticity in a PCET reaction can also be evaluated quantitatively using other diagnostic tools.¹⁴ For example, it can be evaluated through the magnitudes of the first-order nonadiabatic coupling terms between the adiabatic electronic states with respect to the proton coordinate. In addition, the electron—proton nonadiabaticity can be evaluated through analysis of the charge transfer properties of the adiabatic electronic wave functions along the proton transfer coordinate. Significant transfer of electronic charge distribution from the donor molecule to the acceptor molecule and substantial changes in the molecular dipole moment during proton transfer are hallmarks of electronically nonadiabatic proton transfer. Figure 1 illustrates the qualitative change in the electrosstatic potential of the molecular system along the proton transfer coordinate for the phenoxyl-phenol self-exchange reaction, which has been identified as a PCET mechanism.¹³⁻¹⁶

PCET reactions are described in terms of nonadiabatic transitions between diabatic electron-proton vibronic states.

As mentioned above, PCET reactions are described in terms of nonadiabatic transitions between diabatic electron-proton vibronic states. Recently, a method has been developed for generating these charge-localized diabatic states directly from standard quantum chemistry calculations.¹⁴ In this scheme, the adiabatic electronic states are transformed into charge-localized diabatic electronic states using an adiabatic-to-diabatic transformation matrix^{18,19} defined to ensure that the first-order nonadiabatic coupling with respect to the one-dimensional transferring hydrogen coordinate vanishes exactly. Application of this scheme to the phenoxylphenol self-exchange reaction depicted in Figure 1 illustrated that the resulting diabatic electronic states possess physically meaningful, localized electronic charge distributions that are relatively invariant along the hydrogen coordinate.¹⁴ The proton vibrational states can be calculated for each charge-localized diabatic electronic state using grid-based methods. The diabatic electron-proton vibronic states that form the basis of nonadiabatic PCET theories can be represented as products of the diabatic electronic states and associated proton vibrational states.

The nuclear-electronic orbital (NEO) approach provides an alternative strategy for incorporating electron-proton nonadiabatic effects into quantum chemistry calculations and generating diabatic electron-proton vibronic states.²⁰ In the application of the NEO approach to PCET reactions, the transferring hydrogen nuclei are treated quantum mechanically on the same level as the



Figure 2. (a) Electrochemical PCET system involving a proton relay. (b) Two-dimensional proton potential energy surfaces (left panels) and associated hydrogen vibrational wave functions (right panels) for the reduced (top panels) and oxidized (lower panels) states of this system. The coordinate $r_p^{(OO)}$ represents the position of the hydrogen transferring between the two oxygens, and the coordinate $r_p^{(ON)}$ represents the position of the hydrogen and nitrogen, where each hydrogen moves along a one-dimensional axis. Each two-dimensional hydrogen vibrational wave function is labeled with a single quantum number. The results are shown for the main contributing pair of reduced/oxidized vibronic states (i.e., the 0/3 pair) at the dominant proton donor-acceptor distances (i.e., $R_{OO} = 2.45$ Å and $R_{ON} = 2.53$ Å) for the anodic process. The progression of colors from the maximum to the minimum value is as follows: magenta, blue, green, yellow, orange, and red. Figure reproduced with permission from ref 28.

electrons, and a mixed nuclear–electronic time-independent Schrödinger equation is solved with molecular orbital techniques. Electron–proton dynamical correlation is particularly significant for these types of systems due to the attractive electron–proton Coulomb interaction. To include sufficient electron–proton correlation, explicitly correlated wave function methods using Gaussian-type geminal functions have been developed.^{21,22} In addition, multicomponent density functional theory methods with electron–proton density functionals based on the explicitly correlated electron–proton pair density have been developed.²³ These approaches include electron–proton nonadiabatic effects implicitly and can be used to generate charge-localized electron– proton vibronic states when combined with existing diabatization schemes, such as block diagonalization^{24–26} or generalized Mulliken–Hush.^{23,24}

In addition to the accurate description of electron—proton nonadiabatic effects, another current challenge is the development of methods for studying proton relays in PCET processes. The majority of theoretical studies of PCET reactions, particularly those treating the transferring proton(s) quantum mechanically, have focused on single proton transfer reactions. Understanding the fundamental principles underlying the coupling of electron transfer to proton transport over multiple sites is important for the design of catalysts in electrochemical fuel cells and artificial photosynthetic systems. Recently, the proton transfer system depicted in Figure 2a and a related single proton transfer system were synthesized and studied electrochemically.²⁷ The cyclic voltammetry experiments indicated that the electron and two proton transfer reactions occur by a concerted mechanism without any stable intermediates in this proton relay model system. The standard rate constant was found to be a factor of 16 less for the double proton transfer than for the single proton transfer system.

Understanding the fundamental principles underlying the coupling of electron transfer to proton transport over multiple sites is important for the design of catalysts in electrochemical fuel cells and artificial photosynthetic systems.

These types of electrochemical proton relay experiments may be interpreted within the framework of vibronically nonadiabatic PCET.⁸ In this theoretical framework, the standard rate constant is a linear combination of nonadiabatic rate constants for each pair of reduced/oxidized electron-proton vibronic states. Each term is proportional to the square of the vibronic coupling, which is expressed as the product of an electronic coupling and the overlap integral between the reduced and oxidized proton vibrational wave functions. The application of this theory to PCET reactions involving proton relays requires the calculation of multidimensional proton vibrational wave functions representing the transferring protons, incorporation of the proton donor-acceptor motions for all proton transfer reactions, and inclusion of excited electron–proton vibronic states.²⁸ Typically, the overlap integral between the ground state reduced and oxidized proton vibrational wave functions is smaller for a multidimensional wave function than for the corresponding onedimensional wave function. If only the ground vibronic states were included at the equilibrium proton donor-acceptor distances, the rate constant would be expected to be significantly smaller for double proton transfer systems than for single proton transfer systems. The decrease in the proton donoracceptor distances due to thermal fluctuations and the contributions from excited electron-proton vibronic states, however, may enhance the rate constants of PCET processes, particularly for proton relay systems.

Recently, this theoretical approach was applied to the experimentally studied proton relay system depicted in Figure 2a.²⁸ The two-dimensional proton potential energy surfaces for the reduced and oxidized states and the dominant pair of reduced/ oxidized proton vibrational wave functions for the anodic process are depicted in Figure 2b. Note that the two-dimensional

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potential energy surfaces corresponding to the two transferring protons are generated by assuming that each proton moves along a one-dimensional axis. Moreover, each two-dimensional proton vibrational wave function, which is determined by solving a twodimensional Schrödinger equation neglecting kinetic coupling between the two proton coordinates, is labeled with a single quantum number. For this system, the dominant contribution to the standard rate constant arises from the ground reduced vibronic state and the third-excited oxidized vibronic state (i.e., the 0/3 pair of vibronic states) at a proton donor-acceptor distance significantly smaller than the equilibrium distance. This behavior is due to the greater overlap between the reduced and oxidized proton vibrational wave functions for shorter proton donor-acceptor distances and excited vibronic states. The standard rate constant is a factor of 16 lower for the double proton transfer system than for the related single proton transfer system because the dominant excited vibronic states are associated with higher free energy barriers in the double proton transfer system. This application illustrates the importance of including the proton donor-acceptor motions and excited electron-proton vibronic states in theoretical studies of PCET processes, particularly for proton relay systems. It also predicts that the rate constant may be increased by decreasing the equilibrium proton donor-acceptor distances or altering the molecular thermal motions to facilitate the concurrent decrease of these distances. These theoretical studies of relatively simple model systems provide insight into the fundamental physical principles underlying the more complex processes in biological systems and energy conversion devices.

A third current theoretical challenge in this field is the development of methods to investigate the ultrafast dynamics of photoinduced PCET processes. In this context, ultrafast dynamics refers to the nonequilibrium dynamics prior to solvent equilibration. The ultrafast dynamics of photoinduced PCET in the hydrogen-bonded adduct of *p*-nitrophenylphenol and *tert*butylamine, as depicted in Figure 3, has been studied experimentally with femtosecond transient absorption methods.^{29,30} In this system, photoexcitation induces intramolecular electron transfer within the *p*-nitrophenylphenol, accompanied by intermolecular proton transfer from the phenol to the amine. One possible mechanism is that the vertical photoexcitation leads to occupation of an excited electronic state corresponding to the intramolecular electron transfer with the proton still bound to the phenol oxygen, followed by standard excited-state proton transfer from the oxygen to the nitrogen. Another possible mechanism is that the vertical photoexcitation leads to occupation of an excited electronic state corresponding to concerted electron-proton transfer (i.e., the electronic configuration corresponds to the intramolecular electron transfer, as well as a highly stretched bond between the transferring hydrogen and the amine nitrogen), followed by proton vibrational relaxation within this electronic state. The calculation of these two types of excited electronic state surfaces and the simulation of the nonadiabatic dynamics, including the complex coupling among the electrons, transferring proton, solute nuclei, and solvent nuclei, represent significant challenges for theory.

The ultrafast dynamics of photoinduced PCET has also been studied in even more complex systems. For example, this process has been studied in double-stranded DNA with time-resolved femtosecond transient absorption methods.³¹ The experimental data exhibit a pronounced deuterium isotope effect after an initial fast decay. One possible interpretation of these data is that



Figure 3. Photoexcited PCET in the hydrogen-bonded adduct of *p*-nitrophenylphenol and *tert*-butylamine, as studied experimentally in ref 30.

photoexcitation induces intrastrand electron transfer between two stacked bases and interstrand proton transfer between two hydrogen-bonded bases. Interfacial photoinduced PCET has been studied with time-resolved two-photon photoemission experiments for a system comprised of methanol adsorbed on a titanium dioxide surface.³² In these experiments, an electron is photoexcited from the defect band in the semiconductor to the methanol adsorbate layer, and proton transfer is hypothesized to occur between a methanol molecule and a bridging oxygen on the titanium dioxide surface as the electron transfers back to the semiconductor. The population dynamics of the resulting solvated electron state in the methanol adsorbate layer exhibited both a fast and a slow decay process, with a distinct deuterium isotope effect for the slower component.

These types of experimentally studied processes can be investigated theoretically using nonadiabatic molecular dynamics methods. Recently, a theoretical formulation was developed for modeling photoinduced nonequilibrium concerted PCET reactions in solution.³³ In this formulation, the solvent is represented as a dielectric continuum, and the solvent polarization is mapped onto a single collective solvent coordinate that evolves according to a Langevin equation. An ensemble of nonadiabatic surface hopping trajectories is propagated with Langevin dynamics on electronproton vibronic free energy surfaces that depend on the collective solvent coordinate. Application of this approach to a series of model photoinduced PCET systems illustrated the potential impact of nonequilibrium solvent dynamics on the overall charge transfer process.³³ These calculations also provided an explanation for the experimental observation of the onset of a deuterium isotope effect only after an initial fast decay in double-stranded DNA and methanol adsorbed on titanium dioxide surfaces.³⁴

The results from a specific model system are summarized in Figure 4. In this model system, the excited-state donor and acceptor proton potentials were represented by shifted harmonic potentials, and the initial proton wavepacket corresponded to the ground vibrational state of a proton potential centered midway between the donor and acceptor proton potentials. The initial photoinduced nonequilibrium state of the solvent coordinate distribution and the proton wavepacket was prepared by instantaneous vertical photoexcitation from the ground electronic state to the donor electronic state. Thus, the system was photoexcited into a coherent mixture of electron-proton donor vibronic states with the initial populations determined by the Franck-Condon factors. As depicted in Figure 4, immediately following photoexcitation, the population is distributed among higher vibronic states, where the vibronic couplings are similar for hydrogen and deuterium, resulting in the absence of an isotope effect. After the initial vibrational relaxation, the population is distributed among the lower vibronic states, where the vibronic couplings are significantly larger for hydrogen than for deuterium, leading to faster population decay for hydrogen. The final populations of the acceptor vibronic states



Figure 4. (a) Snapshots of the ensemble of trajectories during the nonadiabatic dynamics on the adiabatic electron—proton vibronic free energy surfaces, which depend on the collective solvent coordinate *x*, for a model photoinduced PCET system. (b) Population of the donor state as a function of time for hydrogen (red) and deuterium (blue) transfer for this model system. (c) Square of the vibronic coupling between the ground donor vibronic state and the *v*th acceptor vibronic state as a function of the quantum number *v* of the acceptor vibronic state for hydrogen (red) and deuterium (blue) transfer. The vibronic couplings that impact the nonadiabatic dynamics at early times are indicated with filled triangles, and the vibronic couplings that impact the nonadiabatic dynamics at early times are indicated with filled squares. Figures reproduced with permission from ref 34.

do not reflect an equilibrium distribution because the model does not include direct coupling between the proton and the solvent to enable direct proton vibrational relaxation within the donor or acceptor diabatic state. On the basis of the qualitative behavior of the nonequilibrium dynamics, these calculations predict that the isotope effect will be very small or absent when highly excited vibronic states dictate the nonadiabatic dynamics but will increase with greater participation of the lower vibronic states.

A variety of other types of nonadiabatic dynamics methods may be used to study photoinduced PCET processes. A disadvantage of the dielectric continuum theory approach described above is that proton vibrational relaxation cannot occur by a direct mechanism (i.e., within the donor or acceptor diabatic state) but rather can occur only by an indirect mechanism via nonadiabatic transitions between the donor and acceptor states. A worthy challenge for the future is the inclusion of direct proton vibrational relaxation within this framework. Direct proton vibrational relaxation may be included by propagating Langevin equations for two collective solvent coordinates corresponding to electron and proton transfer. This extension also enables the description of both sequential and concerted electron-proton transfer reactions. This approach may also be extended to describe solvents characterized by two different relaxation time scales, as well as to include the proton donor-acceptor motion and other solute modes. In addition, the ultrafast dynamics of photoinduced PCET can be investigated with all-atom nonadiabatic molecular dynamics methods that include explicit solvent molecules. In this case, the surface hopping trajectories are propagated on electron-proton vibronic potential energy surfaces generated onthe-fly using, for example, an empirical valence bond potential. The further development of these nonadiabatic dynamics methods and applications to experimentally studied photoinduced PCET processes may assist in the design of more efficient solar energy cells.

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This Perspective has discussed three of the current theoretical challenges in the field of PCET. Although progress has been made in addressing each of these challenges, additional theoretical developments are essential for further advances. Both the grid-based and NEO methods for generating diabatic electron-proton vibronic states require further developments for more general applications. The approaches described above for studying proton relays may also be extended to include additional potentially significant effects, such as other solute modes. In addition, methods such as centroid molecular dynamics³⁵ and ring polymer molecular dynamics³⁶ could be used to study certain aspects of electron transfer coupled to proton transport in the presence of explicit solvent or protein. The promising directions discussed above for simulating the ultrafast dynamics of photoinduced PCET including direct proton vibrational relaxation and explicit solvent molecules are also expected to play an important role in this field.

In the future, these types of methods may be applied to a wide range of experimentally studied systems, including biological systems such as photosystem II, cytochrome *c* oxidase, and ribonucleotide reductase,^{3,11,12} as well as cobalt and nickel catalysts for hydrogen production^{37,38} and interfacial systems such as methanol adsorbed on titanium dioxide surfaces.³² The continuous feedback between theoretical and experimental studies is critical for testing and improving the theoretical methods. Future theoretical investigations may play a role in biomedical and technological advances that rely on a deep understanding of the coupling between electrons and protons.

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