Direct Dynamics with Nuclear-Electronic Orbital Density Functional Theory

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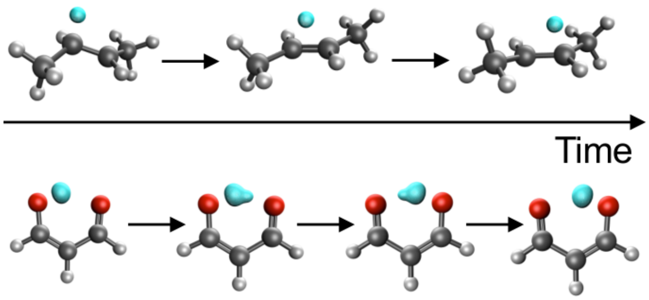
Conspectus

Direct dynamics simulations of chemical reactions typically require the selection of a method for generating the potential energy surfaces and a method for the dynamical propagation of the nuclei on these surfaces. The nuclear-electronic orbital (NEO) framework avoids this Born-Oppenheimer separation by treating specified nuclei on the same level as the electrons with wave function methods or density functional theory (DFT). The NEO approach is particularly applicable to proton, hydride, and proton-coupled electron transfer reactions, where the transferring proton(s) and all electrons are treated quantum mechanically. In this manner, the zero-point energy, density delocalization, and anharmonicity of the transferring protons are inherently and efficiently included in the energies, optimized geometries, and dynamics. This Account describes how various NEO methods can be used for direct dynamics simulations on electron-proton vibronic surfaces. The strengths and limitations of these approaches are discussed, and illustrative examples are presented. The NEO-DFT method can be used to simulate chemical reactions on the ground state vibronic surface, as illustrated by the application to hydride transfer in $C_4H_9^+$. The NEO multistate DFT (NEO-MSDFT) method is useful for simulating ground state reactions in which the proton density becomes bilobal during the dynamics, a characteristic of hydrogen tunneling, as illustrated by proton transfer in malonaldehyde. The NEO time-dependent DFT (NEO-TDDFT) method produces excited electronic, vibrational, and vibronic surfaces. The application of linear-response NEO-TDDFT to H_2 and H_3^+, as well as the partially and fully deuterated counterparts, shows that this approach produces accurate fundamental vibrational excitation energies when all nuclei and all electrons are treated quantum mechanically. Moreover, when only specified nuclei are treated quantum mechanically, this approach can be used to optimize geometries on excited state vibronic surfaces, as illustrated by photoinduced single and double proton transfer systems, and to conduct adiabatic dynamics on these surfaces. The real-time NEO-TDDFT method provides an alternative approach for simulating nonequilibrium nuclear-electronic dynamics of such systems. These various NEO methods can be combined with nonadiabatic dynamics methods such as Ehrenfest and surface hopping dynamics to include the nonadiabatic effects between the quantum and classical subsystems. The real-time NEO-TDDFT Ehrenfest dynamics simulation of excited state intramolecular proton transfer in o-hydroxybenzaldehyde illustrates the power of this type of combined approach. The field of multicomponent quantum chemistry is in the early stages, and the methods discussed herein provide the foundation for a wide range of promising future directions to be explored. An appealing future direction is the expansion of the real-time NEO-TDDFT method to describe the dynamics of all nuclei and electrons on the same level. Direct dynamics simulations using NEO wave function methods such as equation-of-motion coupled cluster or multiconfigurational approaches are also attractive but computationally expensive options. The further development of NEO direct dynamics methods will enable the simulation of the nuclear-electronic dynamics for a vast array of chemical and biological processes that extend beyond the Born-Oppenheimer approximation.



Key References

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Introduction

A vast array of chemical and biological processes relies on proton transfer, hydride transfer, or proton-coupled electron transfer.[4,5] In these types of reactions, nuclear quantum effects associated with the transferring hydrogen nuclei, such as delocalization, anharmonicity, zero-point energy, and tunneling, are often significant. The majority of direct dynamics simulations of chemical reactions propagate the nuclei with classical molecular dynamics and therefore neglect such effects, as well as non-Born-Oppenheimer effects between the electrons and nuclei. Various methods have been developed to include some of these quantum mechanical effects, such as path integral methods,[6,7] multiconfigurational time-dependent Hartree-Fock theory,[8,9] and multiple spawning,[10,11] as reviewed elsewhere.[12] This Account focuses on a specific method of this type, namely the nuclear-electronic orbital (NEO) approach,[13,14] for direct dynamics simulations.

Typically, direct dynamics simulations of chemical reactions require two choices: the level of electronic structure theory for generating the potential energy surfaces, and the method for propagation of the nuclear dynamics on these potential energy surfaces. The nuclear-electronic orbital (NEO) framework allows the same method to be used for both tasks without invoking the Born-Oppenheimer separation between the electrons and specified nuclei. In this case, the electrons and specified nuclei are treated on the same level with wave function methods or density functional theory (DFT). Within the realm of wave function theories, the NEO coupled-cluster,[15] orbital-optimized second-order perturbation theory,[16] complete active space self-consistent-field,[13,17] and equation-of-motion[18,19] methods may be used for either ground or excited state calculations. Within the realm of multicomponent DFT,[20-23] the NEO-DFT[24-27] and time-dependent DFT (NEO-TDDFT)[28,29] methods are options for ground and excited state calculations, respectively, and the multistate DFT (NEO-MSDFT) approach[1] may be used to describe hydrogen transfer and tunneling systems.

For computational efficiency and to avoid challenges associated with translations and rotations, typically only select nuclei, often protons, are treated quantum mechanically within the NEO framework. In this case, the quantum subsystem is composed of the electrons and specified quantum protons, and the remaining nuclei are denoted "classical" for notational simplicity. Under such conditions, direct dynamics simulations require two choices: the NEO level of theory for generating the electron-proton vibronic potential energy surfaces, and the method for dynamical propagation of the classical nuclei on these vibronic potential energy surfaces. To describe adiabatic processes, these nuclei can be propagated according to Newton's equations of motion on an adiabatic vibronic surface that is generated on-the-fly with a NEO method. To describe nonadiabatic processes, a method such as Ehrenfest[30] or surface hopping[31] dynamics can be used to propagate these classical nuclei on multiple NEO vibronic surfaces.[3,32] Alternatively, all nuclei, as well as all electrons, can be treated quantum mechanically within the NEO framework. In this scenario, direct nuclear-electronic dynamics simulations may be performed using a real-time NEO method,[33,34] in which the time-dependent Schrödinger equation is propagated numerically for the coupled electrons and nuclei.

This Account will summarize the NEO-DFT, NEO-MSDFT, and NEO-TDDFT methods and their relationships to direct dynamics simulations. As each method is introduced, a chemical example will be provided to illustrate the basic concepts. The field of multicomponent DFT is still in the early stages, however, and some of the methods that will be discussed have not been fully developed yet. Thus, this Account should be viewed as an initial foray into the exciting world of NEO direct dynamics.

NEO-DFT

In NEO-DFT,[24,25] the energy is a functional of the electronic and nuclear densities. Within the multicomponent DFT Kohn-Sham formalism,[20-22] the densities are expressed in terms of electronic and nuclear Kohn-Sham orbitals, which are expanded in electronic and nuclear basis sets. The reference system is defined as the product of the electronic and nuclear Slater determinants $\Phi^{e}\Phi^{p}$ (or Hartree product for some nuclei) built from the electronic and nuclear orbitals, respectively. Optimizing the energy with respect to the orbital coefficients leads to two sets of strongly coupled electronic and nuclear Kohn-Sham equations:

$$\begin{aligned}\mathbf{F}^{e}\mathbf{C}^{e} &= \mathbf{S}^{e}\mathbf{C}^{e}\boldsymbol{\varepsilon}^{e}\\ \mathbf{F}^{p}\mathbf{C}^{p} &= \mathbf{S}^{p}\mathbf{C}^{p}\boldsymbol{\varepsilon}^{p}\end{aligned} \tag{1}$$

where $\mathbf{F}^{e}$, $\mathbf{C}^{e}$, $\mathbf{S}^{e}$, and $\boldsymbol{\varepsilon}^{e}$ are the electronic Kohn-Sham matrix, orbital coefficient matrix, overlap matrix, and orbital energy matrix, respectively, and the protonic matrices are defined analogously. Because $\mathbf{F}^{e}$ and $\mathbf{F}^{p}$ each depend on both $\mathbf{C}^{e}$ and $\mathbf{C}^{p}$, these equations must be solved self-consistently to obtain the energy and densities.

Most current implementations utilize Gaussian-type nuclear basis functions of varying angular momenta, although other options are possible. Some NEO calculations use even-tempered nuclear basis sets, such as 8s8p8d8f,[26] and others use recently developed optimized nuclear basis sets,[35] such as PB4-D (4s3p2d). For systems with both quantum and classical nuclei, the user has the freedom to select the quantum nuclei (e.g., all hydrogen nuclei or only the hydrogen nuclei actively involved in chemical bond breaking and forming). In this case, the electronic and nuclear basis function centers associated with the quantum nuclei can be optimized variationally for each configuration of the classical nuclei.

Accurate calculations require functionals associated with electron-electron exchange and correlation, nucleus-nucleus exchange and correlation, and electron-nucleus correlation. Standard electronic exchange-correlation functionals can be used for NEO calculations on the basis of the multicomponent DFT formalism,[36] as well as the transferability of results across a range of electronic functionals.[37] For molecular systems with specified protons treated quantum mechanically, proton-proton exchange and correlation energies have been shown to be negligible because of the localized nature of the protons.[14] Several electron-proton correlation functionals, such as epc17 and epc19,[26,27,38] have been developed at the local density approximation and generalized gradient approximation levels, respectively. NEO-DFT, combined with these electron-proton correlation functionals and standard electronic functionals, has been shown to provide accurate energies, proton densities, and optimized geometries.[26,27,37,38] Analytical gradients of NEO-DFT energies with respect to the classical nuclear coordinates[2] enable geometry optimizations and provide the forces required for molecular dynamics simulations.

NEO-DFT direct dynamics simulations can be performed by propagating the classical nuclei according to Newton's equations of motion on the NEO-DFT ground vibronic state. In particular,

$$M_I \ddot{\mathbf{r}}_I^{\mathrm{c}} = -\nabla_I \left\langle \Phi^{\mathrm{e}} \Phi^{\mathrm{p}} \middle| H_{\mathrm{NEO}} \middle| \Phi^{\mathrm{e}} \Phi^{\mathrm{p}} \right\rangle \tag{2}$$

where M_I and $\mathbf{r}_I^{\mathrm{c}}$ are the masses and coordinates, respectively, of the classical nuclei. Moreover, H_{NEO} is the NEO Hamiltonian, which includes the kinetic energies of the electrons and quantum nuclei, as well as all Coulombic interactions, and $\Phi^{\mathrm{e}}\Phi^{\mathrm{p}}$ is the electronic-protonic Kohn-Sham wave function associated with the NEO-DFT ground vibronic state.

The intramolecular hydride shift in $C_4H_9^+$ has been studied at the NEO Hartree-Fock level,[39] treating only the transferring hydrogen nucleus quantum mechanically. The minimum energy path from the transition state on the NEO vibronic surface to the reactant and product minima on this surface has been generated. Analysis of the imaginary mode at the transition state and the contributions to the intrinsic reaction coordinate indicate that the dominant mode driving hydride transfer is the tetrahedral-to-planar (i.e., sp^3 to sp^2) rearrangement of the two central carbon atoms.

Direct dynamics simulations of this hydride transfer reaction have been performed at the NEO-DFT level. A representative trajectory is depicted in Figure 1. This trajectory was initiated at the reactant geometry and assigned initial velocities in the direction toward the transition state corresponding to a temperature of 500 K. The classical nuclei (i.e., all nuclei except the transferring hydrogen) were propagated on the NEO ground state electron-proton vibronic surface. The electronic and nuclear basis functions associated with the transferring hydrogen were assumed to be positioned at the same center, which was optimized variationally at each time step of the molecular dynamics trajectory. All NEO calculations were performed in a development version of Q-Chem,[40] propagating the classical molecular dynamics trajectories with an in-house code, unless otherwise specified. Figures 1b and 1c depict the planarity angles associated with the two central carbon atoms and the distances between each of these carbon atoms and the expectation value of the transferring hydrogen coordinate as a function of time along this trajectory. The donor carbon becomes more planar and the acceptor carbon becomes less planar as the hydrogen transfers from the donor to the acceptor. Note that this trajectory should be viewed only as an illustration of adiabatic NEO-DFT direct dynamics, and the timescale is not experimentally relevant. The calculation of an experimentally meaningful timescale for this chemical reaction would require propagation of an ensemble of trajectories sampling the initial coordinates and velocities pertaining to the experimental conditions.

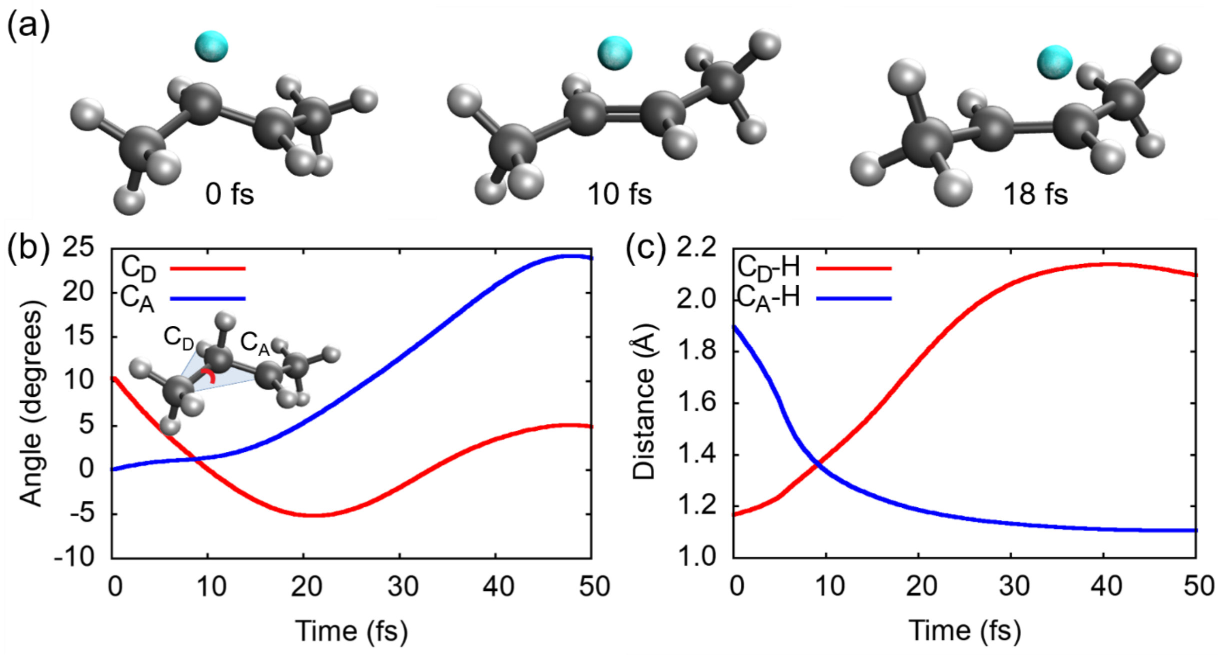

Figure 1. NEO-DFT direct dynamics trajectory illustrating hydride transfer in $C_4H_9^+$. (a) Snapshots along this trajectory, where the quantum proton density is plotted in cyan with an isosurface value of 0.07. (b) Out-of-plane angles and (c) distance from the expectation value of the quantum proton coordinate to the donor carbon (C_D, red) and acceptor carbon (C_A, blue) as a function of time. This trajectory was propagated with the B3LYP electronic functional[41] and the epc17-2 electron-proton correlation functional[27] using the 6-31G(d,p) electronic[42] and PB4-D' protonic[35] basis sets.

Within the conventional Born-Oppenheimer approach, the transferring hydrogen can be viewed as moving in a single or double-well potential on the electronic potential energy surface for a fixed configuration of the other nuclei. For hydride transfer in $C_4H_9^+$, the transferring hydrogen is always moving in a single-well potential. In this case, the hydrogen can be represented by a single basis function center within the NEO approach (Figure 1). In many hydrogen transfer reactions, however, the transferring hydrogen moves in a double-well potential for relevant regions of the conventional electronic potential energy surface. In this case, the transferring hydrogen should be represented by at least two sets of basis functions, where one set is centered near each minimum, within the NEO approach. Moreover, these types of systems often exhibit two different NEO self-consistent-field (SCF) solutions (i.e., orbital coefficients satisfying the Kohn-Sham equations), corresponding to the hydrogen localized in each well. For example, 2-cyanomalonaldehyde has been shown to have two NEO SCF solutions corresponding to the proton localized near each oxygen atom (Figure 2).[43] In molecular dynamics simulations, the proton could become stuck in the higher-energy SCF solution (i.e., a local minimum in the orbital coefficient space). In such cases, a multireference approach may be warranted to ensure that the system remains on the ground state electron-proton vibronic surface.

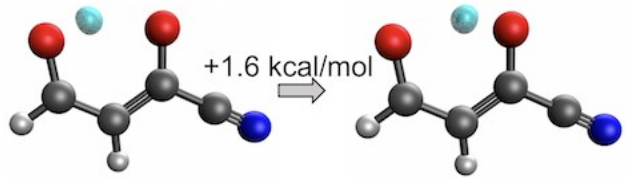

Figure 2. The two NEO-DFT/epc17-2 SCF solutions for fixed classical nuclear coordinates of 2-cyanomalonaldehyde. The quantum proton density is shown in cyan with an isosurface value of 0.02. The NEO-DFT solution on the right is 1.6 kcal/mol higher than the NEO-DFT solution on the left. Additional computational details are provided in Ref. [43]

NEO-MSDFT

The NEO-MSDFT method is designed to describe hydrogen transfer systems in which the hydrogen moves in a double-well potential.[1] For an individual hydrogen transfer reaction, the ground and first excited state vibronic surfaces are obtained by diagonalizing a 2×2 Hamiltonian matrix in the basis of two localized NEO-DFT states. The transferring hydrogen is represented by a set of electronic and nuclear basis functions centered near each of the two minima of the double-well potential. Even with two basis function centers, the NEO-DFT method leads to SCF solutions localized in one of these wells for symmetric systems such as malonaldehyde (Figure 3, left side). The inability of the NEO-DFT method to generate delocalized, bilobal vibrational wave functions for these types of symmetric systems is presumably due to the limitations of the underlying single-reference wave function or the electron-proton correlation functional.

The NEO-MSDFT method mixes these two localized NEO-DFT solutions through a nonorthogonal configuration interaction approach to produce delocalized, bilobal ground and excited vibronic states (Figure 3, right side).[1] The diagonal elements of the NEO-MSDFT Hamiltonian matrix are simply the NEO-DFT energies of the localized states. The off-diagonal elements have a physically motivated form inspired by the conventional electronic MSDFT method.[44] To account for limitations of the electron-proton correlation functional and the approximate form of the off-diagonal matrix element, a correction function is applied to the overlap between the localized Kohn-Sham wave functions. This correction function was parameterized for simple model systems and fixed for all subsequent applications. The NEO-MSDFT method has been shown to produce accurate hydrogen tunneling splittings for fixed classical nuclear configurations,[1] as determined by comparison to numerically exact adiabatic grid-based methods. Analytical gradients of the NEO-MSDFT energy with respect to the classical nuclear coordinates enable geometry optimizations and molecular dynamics simulations.

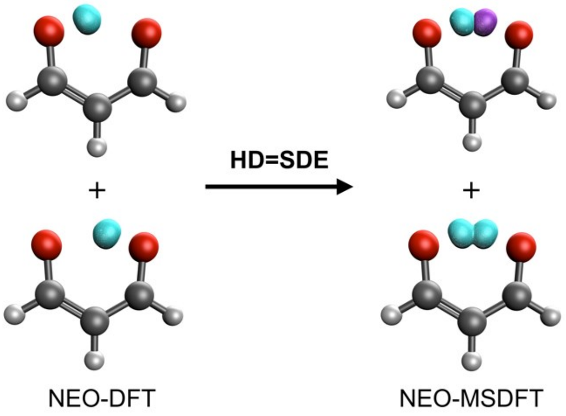

Figure 3. Illustration of NEO-MSDFT method for describing hydrogen tunneling in malonaldehyde. Two localized electronic-protonic wave functions (left) are generated from the NEO-DFT method, and these wave functions are mixed to produce bilobal, delocalized wave functions (right). **H**, **D**, **S**, and **E** correspond to the Hamiltonian, coefficient, overlap, and energy matrices in the basis of the two localized NEO-DFT states. Figure adapted with permission from Ref. [1]. Copyright 2020 American Chemical Society.

An advantage of the NEO-MSDFT method for direct dynamics simulations of hydrogen transfer reactions is that it will remain on the lowest electron-proton vibronic surface as the system moves between asymmetric and symmetric double-well potentials. Figure 4 depicts a NEO-MSDFT direct dynamics trajectory on the ground state electron-proton vibronic surface for malonaldehyde, where the proton density evolves from being localized near the donor oxygen to being delocalized between the two oxygen atoms and finally to being localized near the acceptor oxygen. Both basis function centers associated with the quantum proton were optimized variationally at each time step. This continuous trajectory was generated by combining two separate trajectories initiated at the transition state geometry with equal and opposite velocities chosen to slightly perturb the system. Figure 4a clearly illustrates the evolution of the proton density from the donor oxygen to the acceptor oxygen, exhibiting both asymmetric and symmetric delocalized, bilobal proton densities along the trajectory. As discussed above, this trajectory should be viewed only as an illustration of adiabatic NEO-MSDFT direct dynamics, and the timescale is not experimentally relevant.

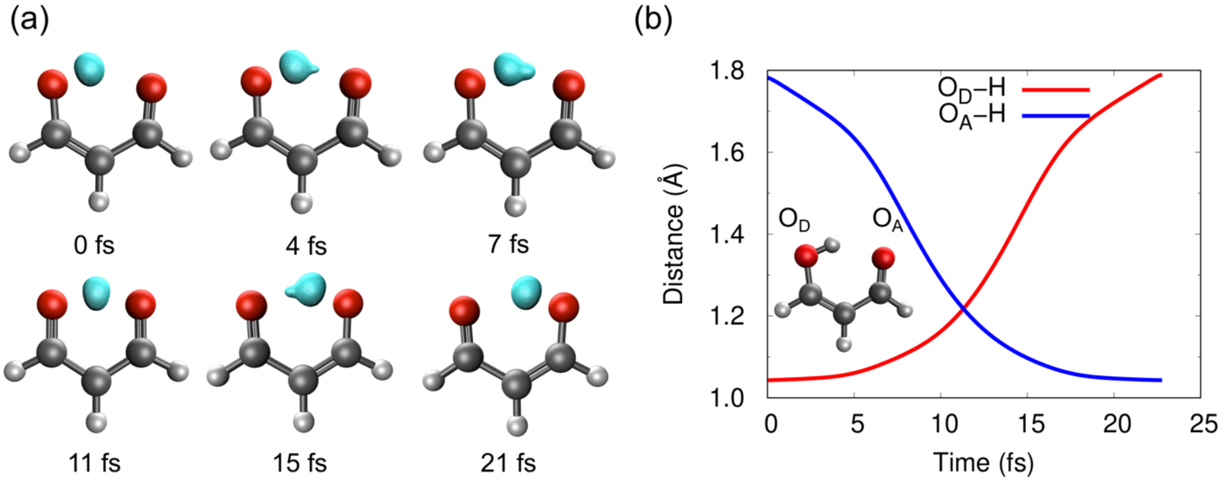

Figure 4. NEO-MSDFT direct dynamics trajectory illustrating proton transfer on the ground vibronic state in malonaldehyde. (a) Snapshots along this trajectory, where the quantum proton density is plotted in cyan with an isosurface value of 0.02. (b) Distance from the expectation value of the quantum proton coordinate to the donor oxygen (O_D, red) and acceptor oxygen (O_A, blue) as a function of time. This trajectory was propagated with the B3LYP and epc17-2 functionals using the cc-pVDZ electronic basis set[45] and a minimal $1s1p$ protonic basis set with exponents of 4.0.

For malonaldehyde, the tunneling splitting between the symmetric ground vibronic state and antisymmetric excited vibronic state (Figure 3, right side) is relatively small.[1,46] Thus, adiabatic dynamics on the ground vibronic state does not provide a complete picture for this system. Instead, the NEO-MSDFT method can be combined with Ehrenfest dynamics,[30] where the classical nuclei move on a mean-field vibronic surface. This surface is computed on-the-fly by integration of the time-dependent Schrödinger equation for a vibronic wave function expanded as a linear combination of the two NEO-MSDFT vibronic states. It is straightforward to extend the NEO-MSDFT method to describe systems with multiple proton transfer reactions by including more localized NEO-DFT states in the nonorthogonal CI expansion. In general, for N transferring hydrogen nuclei, 2^N states are required, although some of these states may be omitted due to their very high energies. The description of dynamics in excited electronic states requires significant extensions of NEO-MSDFT or an alternative approach such as NEO-TDDFT.

NEO-TDDFT

The NEO-TDDFT method,[28] which is a form of multicomponent TDDFT,[23] allows the investigation of dynamics in excited electronic, vibrational, and vibronic states. The linear-response NEO-TDDFT method is predicated on the linear response of the NEO Kohn-Sham system to perturbative external fields. The solution of the resulting matrix equation provides the excitation energies and the transition amplitudes for characterizing these excitations.[29] The implementation based on the adiabatic approximation is able to describe single excitations associated with linear combinations of products of electronic and nuclear determinants with only one single excitation per term. Double excitations can be described by combining NEO-TDDFT with ΔSCF methods,[14] utilizing a different reference state, or with spin-flip methods,[47] although such approaches require further development within the NEO framework.

As an illustration of the NEO-TDDFT method for systems in which all nuclei are treated quantum mechanically, consider the simple molecular systems of H_2, H_3^+, and their partially and fully deuterated counterparts. In this example, the geometries are optimized at the conventional DFT level, and NEO-TDDFT calculations are performed at these optimized geometries with the same electronic functional and no electron-proton correlation functional. As mentioned above, typically nuclear exchange and correlation energies are negligible in molecular systems due to the localized nuclear densities.[14] Thus, all of the nuclei were treated with the Hartree product approximation for these calculations.[48] (For all other calculations described herein, the protons were treated as fermions using Slater determinants.) Moreover, the lowest-energy solutions for these molecular systems correspond to the single occupation of each spatial nuclear orbital, avoiding some complications that could be associated with bosonic systems.

These relatively localized nuclear basis sets with fixed basis function centers provide accurate vibrational excitations without rigorously removing the translations and rotations. In this framework, the lowest five or six NEO-TDDFT excitations for H_2 and H_3^+, respectively, or their deuterated counterparts correspond to translations and rotations. For these fixed basis functions, the corresponding excitation energies approach zero as the sizes of the electronic and nuclear basis sets are increased and are not relevant for studies that focus on the vibrational molecular motions. The fundamental vibrational excitation energies can be computed with NEO-TDDFT, and these vibrational excitations can be characterized by the NEO-TDDFT transition densities and dipole moments, as shown in Figure 5. An advantage of the NEO-TDDFT method for computing vibrational spectra is that the anharmonicities are inherently included in a computationally tractable manner.

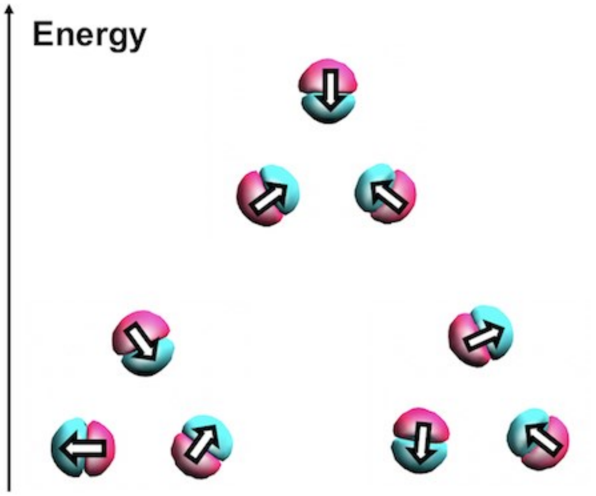

Figure 5. NEO-TDDFT transition densities and schematic transition dipole moments of H_3^+, where the lowest two excited vibrational states are degenerate. The transition densities were plotted with an isosurface value of 0.02. Positive and negative values of the transition densities are represented by cyan and magenta, respectively. These transition densities, along with the transition dipole moments, were used to characterize the three fundamental vibrations of H_3^+.

As shown in Table 1, the NEO-TDDFT fundamental vibrational excitation energies are in good agreement with second-order perturbation theory (VPT2)[49] results for these systems. This agreement provides a degree of validation for the NEO-TDDFT method. Both the NEO-TDDFT and VPT2 results agree much better with the experimental data than do the frequencies obtained from a conventional harmonic treatment. The remaining deviations from the experimental data are presumably due to limitations of the B3LYP functional and other approximations underlying linear-response TDDFT. Although these systems are composed of only hydrogen or deuterium nuclei, the extension to heavier nuclei is reasonably straightforward.

Table 1. Fundamental Vibrational Frequencies (cm^{-1}) for H and D only systems[a]

	Harmonic	VPT2	NEO-TDDFT	Experiment[b]
H_2	4416	4071	4047	4161
D_2	3124	2959	2942	2994
HD	3825	3577	3561	3632
H_3^+	2695	2400	2424	2521
	3380	3093	3068	3178
D_3^+	1906	1759	1774	1835
	2391	2247	2235	2301
HD_2^+	2043	1888	1920	1968
	2201	1983	1996	2078
	2879	2660	2644	2737
H_2D^+	2342	2112	2127	2206
	2460	2239	2262	2355
	3177	2897	2884	2993

[a] All calculations were performed with the B3LYP functional and the Cartesian version of the cc-pV6Z electronic basis set.[50] The NEO calculations were performed with no electron-proton correlation functional and the PB4-F2a′ protonic basis set[35] for the hydrogen nuclei and an even-tempered Cartesian 8s8p8d8f basis set with exponents ranging from $4\sqrt{2}$ to 64 and a spacing of $\sqrt{2}$ for the deuterium nuclei.

[b] The experimental frequencies were obtained from the National Institute of Standards and Technology (NIST) website.

Although the quantum mechanical treatment of all nuclei with NEO-TDDFT is a viable option, such an approach may become computationally intractable for large molecules. In these cases, the quantum mechanical treatment of only specified hydrogen nuclei provides a practical alternative. The NEO-TDDFT method has been shown to produce accurate fundamental proton vibrational excitation energies for molecular systems with one or two quantum mechanical protons,[29,51] as determined by comparison to numerically exact adiabatic grid-based calculations. The analytical gradients for NEO-TDDFT[2] enable geometry optimizations and molecular dynamics simulations in excited vibronic states. The NEO-TDDFT method was found to provide reasonably accurate 0-0 adiabatic excitation energies for a set of small molecules when comparing to experimental data.[2] The NEO-TDDFT calculations inherently include the anharmonic zero-point energies of the quantum nuclei, and the zero-point energies associated with the classical nuclei are computed from the NEO Hessian.

An illustrative example is provided by the geometry optimizations of two intramolecular proton transfer systems: [2,2′-bipyridyl]-3-ol, denoted BPOH, and [2,2′-bipyridyl]-3,3′-diol, denoted $BP(OH)_2$. The geometries of the BPOH and $BP(OH)_2$ systems were optimized with NEO-TDDFT treating one or two protons, respectively, quantum mechanically (Figure 6).[2] These optimizations were performed on the ground state and the excited state corresponding to the highest occupied molecular orbital to the lowest unoccupied molecular orbital transition with ππ* character. For both systems, the ground state corresponds to the enol form, with the proton(s) bonded to the oxygen(s), and photoexcitation to the excited electronic state induces proton transfer to the nitrogen(s), generating the keto form. The BPOH system exhibits a second excited state minimum associated with twisted intramolecular charge transfer (TICT) after proton transfer. The $BP(OH)_2$ system exhibits two excited state minima, corresponding to single and double proton transfer. Moreover, a third slightly twisted single proton transfer stationary point was obtained with NEO-TDDFT and higher levels of theory but not conventional TDDFT with the same basis set. The quantization of the transferring proton(s) with NEO-TDDFT resulted in stronger intramolecular hydrogen bonds for all of the planar and near-planar optimized geometries.

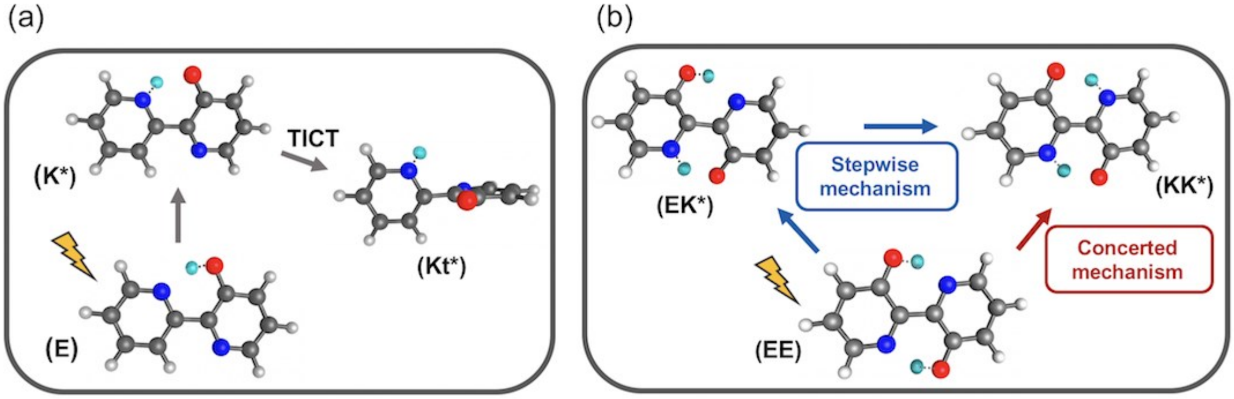

Figure 6. NEO-DFT and NEO-TDDFT optimized geometries of (a) BPOH and (b) $BP(OH)_2$. Both systems undergo an excited state intramolecular proton transfer process to the keto form (K*) after photoexcitation of the ground state in the enol form (E). In BPOH, an additional twisted keto (Kt*) geometry has been located. In $BP(OH)_2$, the two protons can transfer through either a stepwise mechanism, passing through an EK* intermediate, or a concerted mechanism, forming KK* directly. The quantum proton densities are depicted in cyan. Adapted with permission from Ref. [2]. Copyright 2021 American Chemical Society.

The linear-response NEO-TDDFT method can be used to perform adiabatic direct dynamics in an excited vibronic state. This approach was used to propagate a trajectory corresponding to excited state proton transfer dynamics in the electronic singlet excited $\pi\pi^*$ state of o-hydroxybenzaldehyde (oHBA) with the transferring proton treated quantum mechanically (Figure 7). The initial geometry was generated from a conventional ground state geometry optimization at the DFT/B3LYP level of theory with the TZVP basis set,[52] as obtained from Ref. [53]. Photoexcitation to the lowest singlet electronic state was modeled by initiating the trajectory in the lowest vibronic state dominated by an electronic transition. Setting all initial velocities to zero, the trajectory was propagated on this adiabatic vibronic surface. The transferring proton was represented by a single basis function center that was optimized variationally in the excited state at each time step of the molecular dynamics trajectory.

As discussed above, single-reference methods such as NEO-DFT and linear-response NEO-TDDFT may encounter difficulties in describing hydrogen transfer reactions due to local

SCF solutions (Figure 2). Such local solutions tend to be pervasive when the proton moves in a double-well potential on the conventional electronic potential energy surface. To address this issue, two different NEO-TDDFT excited state energies, corresponding to the proton density localized near the donor or acceptor oxygen, were computed at each time step. The classical nuclei were propagated on the vibronic surface corresponding to the lower energy of these two excited state surfaces. Initially, the quantum proton remained localized near the donor oxygen. At around 3.3 fs, however, the proton transferred instantaneously to the acceptor oxygen because the associated excited state energy became lower. Note that the smooth transition between these two localized solutions may be more accurately described by a multireference excited state method for reasons discussed above (Figure 4).

This type of adiabatic excited state dynamics within the NEO framework assumes that the electrons and the transferring proton respond instantaneously to the classical nuclear motion. However, the fast time scale obtained for excited state proton transfer in oHBA is not physically meaningful. Instead of responding instantaneously, the proton would be expected to remain localized near the donor oxygen until the associated wavepacket gained sufficient momentum to transfer to the acceptor oxygen in conjunction with the motion of the other nuclei. The description of this type of process requires a nonadiabatic dynamics method that is capable of simulating the nonequilibrium dynamics of the electrons and quantum protons, incorporating the nonadiabatic effects associated with other excited vibronic states. The real-time NEO-TDDFT Ehrenfest dynamics method is well-suited for this purpose.

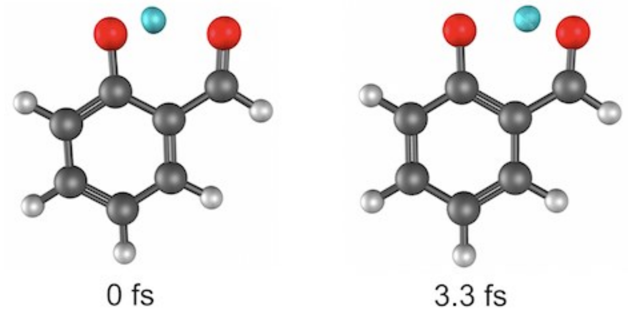

Figure 7. Linear-response NEO-TDDFT adiabatic dynamics trajectory illustrating excited state proton transfer in oHBA. This trajectory was propagated with the B3LYP and epc17-2 functionals using the cc-pVDZ electronic and PB4-F2 protonic[35] basis sets. The extremely fast time scale for proton transfer arises from the assumption that the proton responds instantaneously to the classical nuclear motion in NEO-TDDFT adiabatic dynamics. This process is described more accurately with nonadiabatic NEO dynamics methods.

Real-time NEO-TDDFT

The real-time NEO-TDDFT method[33] allows the simulation of nonequilibrium nuclear-electronic dynamics without the Born-Oppenheimer separation between the electrons and quantum nuclei. Substitution of the product of the electronic and nuclear Slater determinants into the time-dependent Schrödinger equations leads to two sets of strongly coupled electronic and nuclear time-dependent equations that are propagated numerically in time:

$$\begin{aligned} i\hbar \frac{\partial}{\partial t} \mathbf{C}^{\mathrm{e}}(t) &= \mathbf{F}^{\mathrm{e}}(t)\mathbf{C}^{\mathrm{e}}(t) \\ i\hbar \frac{\partial}{\partial t} \mathbf{C}^{\mathrm{p}}(t) &= \mathbf{F}^{\mathrm{p}}(t)\mathbf{C}^{\mathrm{p}}(t) \end{aligned} \tag{3}$$

Because the nonequilibrium electronic and nuclear densities are propagated in real time, the issues related to the local SCF solutions in NEO-DFT and NEO-TDDFT are no longer relevant. Thus, this method is well-suited for simulating photoinduced proton transfer reactions.

Moreover, this approach can be combined with Ehrenfest dynamics for the classical nuclei to incorporate nonadiabatic effects between the classical nuclei and the quantum subsystem composed of the electrons and quantum nuclei.[3,32] In this case, the classical nuclei are propagated according to Eq. (2), but the electronic-protonic Kohn-Sham wave function represents the nonequilibrium, time-dependent vibronic state obtained from Eq. (3), and therefore the classical nuclei are moving on a mean-field nonequilibrium vibronic surface. To account for the limitations of a finite basis set, a semiclassical traveling proton basis function method[32] has been developed, where the proton basis function centers are also propagated according to Eq. (2). Further computational details are provided elsewhere.[3,32]

The real-time NEO-TDDFT Ehrenfest dynamics method has been used to study the excited state intramolecular proton transfer in oHBA using Chronus Quantum.[3,54] The initial geometry and velocities were the same as described above, and only the transferring proton was treated quantum mechanically. In this case, photoexcitation was modeled by the electronic transition from the highest occupied molecular orbital to the lowest unoccupied molecular orbital. The classical nuclei moved on a mean-field vibronic surface according to Ehrenfest dynamics, and the semiclassical traveling proton basis function method was used. As shown in Figure 8, the NEO Ehrenfest dynamics timescale for proton transfer was slower than the timescale obtained with the linear-response NEO-TDDFT adiabatic dynamics approach (Figure 7). Including the nonadiabatic effects between the classical nuclei and the quantum proton provides a more physically meaningful description of photoinduced proton transfer.

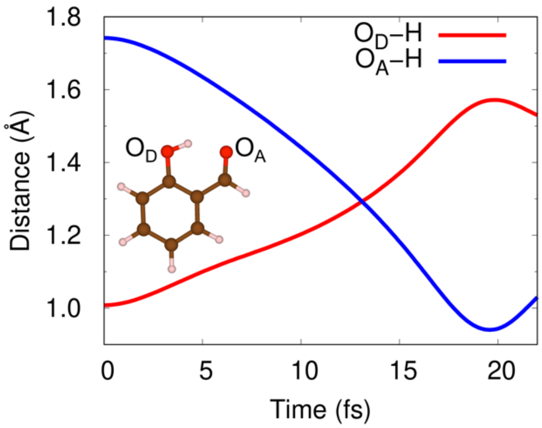

Figure 8. Real-time NEO-TDDFT Ehrenfest dynamics trajectory illustrating excited state proton transfer in oHBA. The distance from the expectation value of the quantum proton coordinate to the donor oxygen (O_D, red) and acceptor oxygen (O_A, blue) is shown as a function of time. Figure adapted with permission from Ref. [3]. Copyright 2021 American Chemical Society.

Another important finding is that proton transfer occurs on a faster timescale with the real-time NEO-TDDFT Ehrenfest method than with a classical treatment of the transferring hydrogen nucleus,[3] mainly because the delocalization of the quantized proton allows proton transfer to occur at longer proton donor-acceptor distances. Thus, a quantum mechanical treatment of the transferring hydrogen nucleus is essential for describing these types of processes. A known limitation of Ehrenfest dynamics is the inability to describe branching processes. In principle, surface hopping dynamics[31,55] can be performed on the adiabatic linear-response NEO-TDDFT or NEO-MSDFT vibronic surfaces to describe such branching processes.

Summary and Outlook

This Account has discussed the strengths and limitations of various NEO direct dynamics approaches. The NEO-DFT and NEO-TDDFT methods have been benchmarked by comparison to other levels of theory, as in Table 1 and elsewhere,[29,32,51,56] and by comparison to experimental proton affinities[27,38] and 0-0 adiabatic excitation energies.[2] The NEO-MSDFT method has been benchmarked by comparison of hydrogen tunneling splittings to numerically exact grid-based methods for fixed geometries.[1] The scaling of NEO methods is the same as the scaling of the analogous electronic structure methods with respect to the number of electronic and nuclear basis functions. Analogous to the conventional electronic counterparts, Ehrenfest and surface hopping dynamics with NEO-MSDFT or linear-response NEO-TDDFT require the calculation of nonadiabatic coupling elements, whereas Ehrenfest dynamics with real-time NEO-TDDFT does not require these elements. The NEO approaches provide a computationally efficient and user-friendly alternative to approaches that separate the electronic structure and nuclear dynamics parts of the calculations. Moreover, the real-time NEO-TDDFT method can simulate nonequilibrium electronic as well as nuclear dynamics. In terms of accessibility, certain NEO methods are available to the community in the GAMESS[57] and Q-Chem[40] packages, and various NEO methods are in the process of being implemented in these and other quantum chemistry packages.

The NEO-DFT direct dynamics method is suitable for a relatively small subset of ground state proton transfer reactions and for general chemical reactions that do not involve proton transfer. The NEO-MSDFT direct dynamics method is suitable for a broader range of ground state proton transfer reactions. When excited vibrational states contribute significantly to the reaction, the NEO-MSDFT approach can be combined with a nonadiabatic dynamics method such as Ehrenfest or surface hopping. The linear-response NEO-TDDFT adiabatic dynamics method is suitable for a relatively small subset of electronically or vibrationally excited proton transfer reactions and for general chemical reactions that do not involve proton transfer. This method can be combined with a nonadiabatic dynamics method to describe a wider array of proton transfer reactions. The real-time NEO-TDDFT Ehrenfest dynamics method is a more general, computationally practical approach for simulating excited state proton transfer processes but may not provide accurate descriptions of branching processes. None of the NEO-TDDFT approaches based on the adiabatic approximation can describe double excitations, such as excited proton vibrational states within an excited electronic state.

The real-time NEO-TDDFT method is powerful in that it can simulate nonequilibrium nuclear-electronic dynamics. The quantum mechanical treatment of all nuclei, rather than only the key transferring hydrogen nuclei, would remove the Born-Oppenheimer approximation entirely.

This approach would avoid the need for Ehrenfest or surface hopping dynamics. Although it may be necessary to develop nuclear-electronic correlation functionals for each type of nucleus, the results in Table 1, which were generated in the absence of an electron-proton correlation functional, suggest that such functionals may not be essential. An encouraging development for fully quantum mechanical treatments is the constrained NEO-DFT approach,[58] in which the basis function centers are constrained to the expectation values of the corresponding nuclear coordinates.

Another promising strategy is to perform direct dynamics with NEO wave function methods. The time-domain NEO equation-of-motion coupled cluster approach has already been implemented and has been shown to describe double excitations,[19] but it is computationally expensive compared to the NEO-DFT and NEO-TDDFT methods. The NEO multiconfigurational wave function approaches[13] are capable of accurately describing double excitations and hydrogen tunneling with the use of sufficiently large active spaces, but they have not yet been implemented for direct dynamics. Embedding and other hybrid approaches for combining different levels of theory could render these types of approaches computationally tractable. Thus, many promising avenues remain open for exploration within the realm of NEO direct dynamics.

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