Letter

Multicomponent Density Functional Theory: Impact of Nuclear Quantum Effects on Proton Affinities and Geometries

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ABSTRACT: Nuclear quantum effects such as zero point energy play a critical role in computational chemistry and often are included as energetic corrections following geometry optimizations. The nuclear—electronic orbital (NEO) multicomponent density functional theory (DFT) method treats select nuclei, typically protons, quantum mechanically on the same level as the electrons. Electron—proton correlation is highly significant, and inadequate treatments lead to highly overlocalized nuclear densities. A recently developed electron—proton correlation functional, epc17, has been shown to provide accurate nuclear densities for molecular systems. Herein, the NEO-DFT/epc17 method is used to compute the proton affinities for a set of molecules and to examine the role of nuclear quantum effects on the equilibrium geometry of FHF^-. The agreement of the computed results with experimental and benchmark values demonstrates the promise of this approach for including nuclear quantum effects in calculations of proton affinities, pK_a's, optimized geometries, and reaction paths.
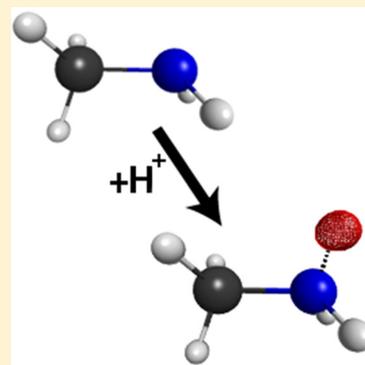
Nuclear quantum effects such as nuclear delocalization, tunneling, and zero point energy (ZPE) are important in a variety of computational chemistry applications.[1−6] The inclusion of ZPE is necessary for the accurate calculation of reaction energies, proton affinities, and other thermochemical properties.[7,8] In most mechanistic reaction studies, the ZPE of a system is calculated using a harmonic approximation for the vibrational modes, which are computed from the Hessian at a geometry corresponding to a stationary point on the potential energy surface within the Born—Oppenheimer approximation. This standard normal mode approach does not include anharmonic effects, although such effects can be included with approaches such as the vibrational self-consistent-field (SCF) methods.[9−11] In addition, because the normal mode analysis is only physically meaningful at a stationary point on the potential energy surface, this approach does not provide information about the ZPE along the entire reaction pathway. Moreover, adding the ZPE as a correction after the geometry optimization does not include the impact of the nuclear delocalization and ZPE on the equilibrium or transition state geometries, as well as on the reaction pathway itself.

The nuclear—electron orbital (NEO) approach[12] and related methods[13,14] address these issues by treating select nuclei, typically protons, quantum mechanically on the same level as the electrons in quantum chemistry calculations. The NEO approach incorporates the effects of vibrational anharmonicity, nuclear density delocalization, and ZPE associated with the quantum nuclei directly into the SCF procedure to generate a mixed nuclear—electronic wave function. Due to the inadequate treatment of electron—proton correlation, typically these types of multicomponent SCF calculations produce highly over-localized proton densities, resulting in qualitative inaccuracies in computed properties that depend on the proton density,

including vibrationally averaged geometries, frequencies, and ZPEs. The inclusion of explicit electron—proton correlation in the wave function ansatz via geminal functions, as in the NEO explicitly correlated Hartree—Fock methods,[15−17] provides proton densities that are more accurate for hydrogen vibrational stretching modes but are still qualitatively inaccurate for associated bending modes. Additionally, these explicitly correlated NEO methods are computationally expensive because integrals with up to five particles must be computed.[18]

A promising alternative to wave function-based NEO approaches is multicomponent density functional theory (DFT),[19−23] which includes electron—proton correlation using an electron—proton correlation functional while also consistently including electron—electron correlation using a standard electronic exchange—correlation functional. Previous NEO-DFT electron—proton correlation functionals derived from a wave function ansatz similar to NEO explicitly correlated Hartree—Fock[22,24−26] suffer from the same problems as the explicitly correlated wave function-based NEO methods. Recently, a new type of electron—proton correlation functional, denoted epc17,[27] was derived analogously to the Colle—Salvetti formulation of the electron correlation energy[28] and was shown to provide accurate proton densities for two molecular systems, HCN and FHF^-. Herein we utilize the NEO-DFT method in conjunction with an epc17-type functional to calculate proton affinities for a series of molecules, as well as to optimize the geometry of the FHF^- molecule. Our results illustrate that the NEO-DFT/epc17 approach describes the impact of nuclear quantum effects such as proton delocalization and ZPE on the

energies and geometries of molecular systems in an accurate and computationally practical manner.

In multicomponent DFT, the system is divided into electrons, quantum protons, and classical nuclei, and the total energy is the sum of the kinetic energies, the classical Coulomb interaction energies between all types of particles, the electron exchange–correlation energy, the proton exchange–correlation energy, and the electron–proton correlation energy. For molecular systems, where the proton orbitals are relatively localized, the proton exchange–correlation energy is negligible and can be approximated by the diagonal Hartree–Fock exchange terms to eliminate self-interaction errors. The development of electron–proton correlation functionals is challenging, but the recently developed epc17 class of functionals[27] is promising. The original derivation of the epc17 functional is analogous to the Colle–Salvetti formulation for electron correlation[28] but invokes different approximations suitable for electron–proton correlation. The electron–proton correlation functional based on the local density approximation has the form

$$E^{epc} = -\int d\mathbf{R} \frac{\rho_e(\mathbf{R})\rho_p(\mathbf{R})}{a - b\rho_e^{1/2}(\mathbf{R})\rho_p^{1/2}(\mathbf{R}) + c\rho_e(\mathbf{R})\rho_p(\mathbf{R})}$$

(1)

where ρ_e and ρ_p are the electron and proton densities, respectively. The parameters a, b, and c were determined by targeting the proton density for the FHF^- molecule, as obtained from a grid-based calculation that is considered to be the benchmark for electronically adiabatic systems. This electron–proton functional, denoted epc17-1 herein, was also found to yield a more accurate proton density for the HCN molecule than any previously published functional. For these calculations, all electrons, as well as the hydrogen nucleus, were treated quantum mechanically on the same level. Because the present Letter focuses on energies, rather than proton densities, a slightly modified parameter set was utilized. Specifically, the parameters were determined by targeting the absolute ZPEs for FHF^- and HCN as obtained from grid-based calculations, resulting in $a = 2.35$, $b = 2.4$, and $c = 6.6$, where only the parameter c differs from the epc17-1 parameters. This parameter set, denoted epc17-2, improves absolute energies, and although it leads to slightly less accurate proton densities than the epc17-1 functional, the epc17-2 densities are still much more accurate than calculations that neglect electron–proton correlation entirely. The ultimate goal is to derive an electron–proton correlation functional that provides accurate densities and energies simultaneously, but such a functional probably requires the inclusion of gradient terms beyond this local density approximation form.

Note that previous attempts to develop an electron–proton correlation functional based on the Colle–Salvetti formulation[29,30] made several questionable assumptions in the derivation. Moreover, these previous attempts computed the electron–proton correlation functional only as a post-SCF correction to the total energy and therefore did not improve the proton densities relative to the highly overlocalized proton densities generated in the absence of electron–proton correlation.[29,30] In contrast, the epc17 functionals are included in the multicomponent Kohn–Sham equations, which are solved self-consistently, thereby allowing the calculation of accurate electron and proton densities as well as total energies.

To assess the ability of the NEO-DFT/epc17-2 method to predict proton affinities, it was used to calculate the proton affinities for a test set of 24 molecules. For comparison, NEO-DFT/no-epc calculations, which do not include any electron–proton correlation functional in the Kohn–Sham equations (i.e., the electron–proton correlation functional for NEO-DFT/no-epc is uniformly zero for all electron and proton densities), were also performed on these molecules. The test set of molecules is the same as that used for a previous study[31] of proton affinities and contains a wide variety of chemical systems. All of the calculations presented herein were performed with the B3LYP electronic exchange–correlation functional[32−34] and the def2-QZVPP[35] electronic basis set. The geometry optimizations for the unprotonated and protonated molecules were performed with conventional electronic DFT, where the most basic site in each molecule was protonated. The NEO calculations treated the single additional proton quantum mechanically using a $10s10p10d$ even-tempered proton basis set,[36] $\zeta_i = \alpha\beta^i$, where ζ_i is the ith proton basis function exponent with $\alpha = 2.0$ and $\beta = \sqrt{2}$ for each shell type. The proton basis functions were centered at the corresponding hydrogen position in the optimized geometry. To facilitate convergence of the NEO calculations, the eigenvectors of the proton basis set overlap matrix with eigenvalues less than 10^{-5} were discarded, and the remaining eigenvectors were used as the vector space for the proton basis set. All calculations were performed using a locally modified version of the GAMESS program.[37] Figure 1a depicts the delocalized proton density for the $CH_3CH_2NH_3$ molecule produced from the NEO-DFT/epc17-2 calculation.
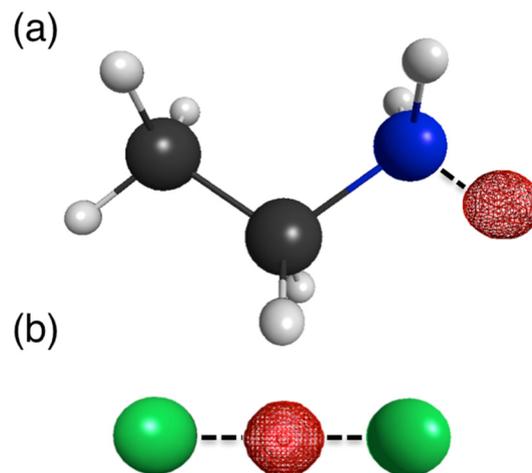

Figure 1. Depiction of the delocalized nuclear density of the quantum mechanically treated proton for (a) $CH_3CH_2NH_3$ and (b) FHF^- at the equilibrium geometry obtained with conventional electronic DFT. The quantum proton is in red and is represented by a contour plot with a contour value of $\rho_p = 0.001$. Note that even though the other nuclei appear to have finite volume, these nuclei are point charges during the NEO calculations.

The proton affinity, PA, of a species A is defined as the negative of the enthalpy change for the reaction

$$A + H^+ \rightarrow AH^+$$

(2)
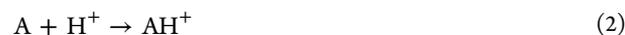
where the negative of the reaction enthalpy ΔH is defined in terms of the reaction energy ΔE as

$$PA(A) = -\Delta H = -\Delta E + RT \tag{3}$$

For a nonlinear polyatomic molecule, the energy can be approximated as a sum of electronic, translational, rotational, and vibrational energy contributions:

$$E(T) = E_{\text{elec}} + E_{\text{trans}}(T) + E_{\text{rot}}(T) + E_{\text{vib}}(T) \tag{4}$$

Assuming the ideal gas approximation, the change in translational energy upon protonation is $-\frac{3}{2}RT$. The change in rotational energy is expected to be negligible because the bare proton has no rotational kinetic energy and the rotational energies of the species A and AH$^+$ are approximately the same. Thus, the PA can be expressed as

$$PA(A) = -\Delta E_{\text{elec}} - \Delta E_{\text{vib}} + \frac{5}{2}RT \tag{5}$$

NEO calculations inherently include the vibrational energy associated with the quantum proton. Assuming that the vibrational energy associated with the classical nuclei remains constant upon addition of the quantum proton, the PA of a species A is

$$PA(A) = E_A - E_{AH^+} + \frac{5}{2}RT \tag{6}$$

where E_{AH^+} is calculated with the NEO-DFT/epc17-2 or NEO-DFT/no-epc method and E_A is calculated with conventional electronic DFT.

The proton affinities computed with the NEO-DFT/epc17-2 and NEO-DFT/no-epc methods are presented in Table 1. For comparison, Table 1 also includes experimentally measured values, as well as previously published computed proton affinities obtained using second-order proton propagator theory (PP2),[38] a Green's function-based propagator method that uses the NEO-HF wave function as a reference state. The calculated NEO-DFT/epc17-2 proton affinities agree well with the experimentally measured values, exhibiting a mean unsigned error (MUE) of 0.06 eV relative to the experimental values. The NEO-DFT/epc17-2 method performs similarly across all classes of molecules in this study, with the MUE ranging from 0.05 eV for amines to 0.10 eV for aromatics. Table 1 demonstrates the importance of electron–proton correlation in NEO-type methods for the calculation of energy-based properties such as proton affinities, which require accurate ZPEs. Specifically, the overall MUE for the NEO-DFT/no-epc method is an order of magnitude larger than that for the NEO-DFT/epc17-2 method. Moreover, the NEO-DFT/epc17-2 proton affinities agree better with experiment than do the PP2 proton affinities, with the overall average MUE more than twice as large for the PP2 method. Note that the epc17-2 functional was parametrized to reproduce a balance of the HCN and FHF$^-$ energies and was subsequently used to calculate the proton affinities in Table 1 without any further parametrization. The agreement with experiment for a range of different types of molecules illustrates the transferability of this functional.

In addition to being more accurate than the PP2 method for proton affinities, the NEO-DFT/epc17-2 method includes electron–electron correlation, which is lacking in this implementation of the PP2 method, and has better computational scaling than the PP2 method. The NEO-DFT/epc17 method scales identically to conventional electronic DFT (N^3 or N^4, depending on the electronic exchange–correlation functional, with N related to the number of basis functions),

Table 1. Proton Affinities Measured Experimentally and Calculated with the NEO-DFT/epc17-2, PP2, and NEO-DFT/no-epc Methods[a]

molecule	PA (eV)			
	expt[b]	epc17-2	PP2[c]	no-epc
Amines				
NH$_3$	8.85	8.89	8.79	8.12
CH$_3$NH$_2$[d]	9.32	9.37	9.31	8.60
CH$_3$CH$_2$NH$_2$[d]	9.45	9.52	9.48	8.75
CH$_3$CH$_2$CH$_2$NH$_2$	9.51	9.58	9.51	8.81
(CH$_3$)$_2$NH	9.63	9.67	9.64	8.90
(CH$_3$)$_3$N	9.84	9.85	9.82	9.08
MUE		0.05	0.02	0.72
Aromatics				
C$_6$H$_5$NH$_2$	9.15	9.16	9.31	8.39
C$_6$H$_5$COO$^-$	14.75	14.53	15.07	13.75
C$_6$H$_5$O$^-$	15.24	15.17	15.53	14.39
MUE		0.10	0.26	0.87
Inorganics				
CN$^-$[e]	15.31	15.21	14.80	14.45
HS$^-$	15.31	15.27	14.82	14.51
NO$_2^-$	14.75	14.84	14.77	14.06
MUE		0.07	0.34	0.79
Carboxylates				
HCOO$^-$	14.97	14.95	14.86	14.17
CH$_3$COO$^-$[d]	15.11	15.12	15.22	14.34
CH$_3$CH$_2$COO$^-$[d]	15.07	15.10	15.17	14.32
CH$_3$CH$_2$CH$_2$COO$^-$	15.03	15.08	15.23	14.30
CH$_3$CH$_2$CH$_2$CH$_2$COO$^-$	15.01	15.08	15.24	14.30
CH$_3$COCOO$^-$	14.46	14.43	14.60	13.65
CH$_2$FCOO$^-$	14.71	14.66	14.65	13.88
CHF$_2$COO$^-$	14.32	14.33	14.19	13.55
CF$_3$COO$^-$	13.99	14.06	13.85	13.28
ClCH$_2$COO$^-$	14.58	14.53	14.63	13.75
ClCH$_2$CH$_2$COO$^-$	14.78	14.64	14.68	13.87
MUE		0.05	0.12	0.78
overall MUE		0.06	0.14	0.78

[a]The MUE is the mean unsigned error for each class of molecules for each method with respect to the experimentally measured value. [b]References 39–43. [c]Reference 38. [d]DFT+ZPE calculations were performed on these four molecules with calculated PAs of 9.31, 9.47, 15.09, and 15.07 for the CH$_3$NH$_2$, CH$_3$CH$_2$NH$_2$, CH$_3$COO$^-$, and CH$_3$CH$_2$COO$^-$ systems, respectively. [e]The protonated form of this molecule was used in the parametrization of the functional; the overall MUE without including CN$^-$ is still 0.06 eV.

whereas the PP2 method formally scales as N^4 because it only requires a partial integral transformation. As shown in a footnote of Table 1, for a few of the smaller systems in this study, conventional electronic DFT calculations with the ZPE included using the harmonic approximation (DFT+ZPE) are very accurate, with errors typically less than 0.02 eV. However, the NEO-DFT/epc17 method can be used to include anharmonic effects, which will be important for certain types of systems. Moreover, a computational advantage of the NEO-DFT/epc17 method over the DFT+ZPE method is that the kinetic energy of the proton is included directly in the total energy calculation rather than requiring the computation of the Hessian, as in the DFT+ZPE method. Because of the advantage in computational expense and the reasonably small PA errors, the NEO-DFT/epc17-2 method lends itself to the calculation of proton affinities for larger molecules for which calculating

the Hessian is a large computational expense. The avoidance of calculating the Hessian for ZPEs has similar advantages to a recent study[44] that avoided calculation of the Hessian for computing vibrational frequencies by using finite differences of analytic gradients.

More importantly, the NEO-DFT/epc17 method includes the impact of the nuclear quantum effects of the quantum protons on geometry optimizations for the classical nuclei, as well as the associated minimum energy paths for chemical reactions. These effects are particularly important for hydrogen transfer and proton-coupled electron transfer reactions, where delocalization of the hydrogen nucleus may impact the hydrogen donor–acceptor distance, which plays a critical role in determining the rate constant, and non-Born–Oppenheimer effects between the electrons and the transferring hydrogen nucleus may be significant.[5,45] Because the normal mode procedure for calculating the ZPE through a Hessian calculation is only justified at stationary points on the potential energy surface and treats the ZPE as an energy correction after a geometry optimization, the effects of ZPE and nuclear delocalization on geometry optimizations and reaction paths cannot be included using the standard DFT+ZPE method. Similarly, these effects on optimized geometries and reaction paths cannot easily be incorporated with the PP2 method.

To demonstrate the impact of nuclear quantum effects such as nuclear delocalization and ZPE on the geometry of the classical nuclei, we performed calculations with the NEO-DFT/epc17-2 and no-epc methods on the FHF^- molecule (Figure 1b) as a function of the F–F distance. The calculated energy curves are depicted in Figure 2, and the minimum energy
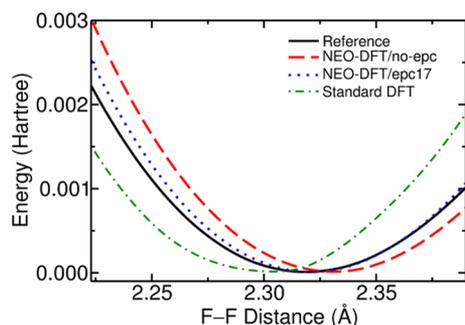
Figure 2. Plot of the energy versus the fluorine–fluorine distance for FHF^-, as obtained with the FGH reference (solid black), NEO-DFT/no-epc (dashed red), NEO-DFT/epc17-2 (dotted blue), and standard DFT (dashed–dotted green) methods. The minimum energy was adjusted to 0.0 hartree for each method.

geometry corresponds to the F–F distance at the minimum of each curve. The contributions from nuclear quantum effects on the geometry of the classical nuclei are expected to be larger for molecules with more anharmonicity, but Figure 2 demonstrates that the contribution can be seen even for linear, predominantly harmonic molecules such as FHF^-. To provide a benchmark, Fourier grid Hamiltonian (FGH)[46] calculations were performed with the hydrogen nucleus represented on a three-dimensional grid for each F–F distance. The FGH calculations were performed with DFT/B3LYP and the def2-QZVPP electronic basis set with a three-dimensional grid of 32 grid points per dimension and a maximum grid spacing of 0.03125 Å. For an electronically adiabatic system such as FHF^-, the FGH calculations are numerically exact for a given level of electronic structure theory, such that the FGH minimum

energy F–F distance is the benchmark for a calculation that includes the nuclear quantum effects of only the hydrogen. For comparison, Figure 2 also provides the results from a conventional electronic DFT calculation that treats the hydrogen nucleus as a classical point charge.

Figure 2 indicates that inclusion of the hydrogen nuclear quantum effects increases the equilibrium F–F distance by ∼0.02 Å for the FGH method, which is considered the benchmark, compared to the conventional electronic DFT method. This longer equilibrium distance is physically intuitive as the F–H bonds should contain a small degree of anharmonicity, although the effects of proton delocalization are difficult to predict intuitively because they include a complex balance of attractive and repulsive electrostatic interactions. The NEO-DFT/epc17-2 potential energy curve agrees well with the FGH curve, differing only slightly at smaller F–F distances, but is essentially identical at larger F–F distances and predicts the same equilibrium F–F distance to less than 0.01 Å. Again the inclusion of electron–proton correlation is demonstrated to be important as the NEO-DFT/no-epc equilibrium F–F distance is ∼0.015 Å larger than the FGH and NEO-DFT/epc17-2 equilibrium distances. Note that the epc17-2 functional was parametrized to the energies of HCN and FHF^- at the equilibrium geometries determined by conventional DFT and was subsequently used to generate the curves in Figure 2 without further parametrization, indicating that the form of this functional accurately describes relative energies of nonequilibrium as well as equilibrium geometries. Analytic gradients for this functional are straightforward to derive and are computationally tractable, analogous to such gradients for related electronic functionals. These analytical gradients will enable geometry optimizations of more complex molecules while including the nuclear quantum effects of select protons. Geometry optimizations of the classical and quantum nuclei with the NEO-DFT/epc17 method may also improve the quantitative accuracy of the proton affinities given in Table 1.

The calculations presented in this Letter illustrate that the NEO-DFT/epc17-2 method accurately describes the impact of proton delocalization and ZPE on energetic properties, such as proton affinities, as well as on optimized geometries. The NEO-DFT/epc17-2 method has the same scaling as conventional electronic DFT and therefore is applicable to a wide range of molecular systems. Moreover, many of the tools developed for electronic DFT, such as the inclusion of solvent effects with dielectric continuum theory, are directly applicable to NEO-DFT. The inclusion of solvent effects will allow the NEO-DFT/epc17-2 method to be used for the calculation of pK_a's. In contrast to the standard method for inclusion of the ZPE as a correction to the energy by calculating the Hessian for optimized geometries, the NEO-DFT/epc17-2 method includes nuclear quantum effects associated with the protons during the geometry optimization for the classical nuclei. The simple example of the FHF^- molecule illustrates the increase in the equilibrium F–F distance due to proton delocalization and ZPE effects. Geometry optimizations of larger molecules will require analytic gradients, which are in the process of being implemented for the NEO-DFT/epc17-2 method. The Hessians associated with the classical nuclei will also be implemented and will enable the inclusion of the ZPE associated with the classical nuclei via the standard normal mode analysis. Couplings between the classical and quantum mechanical vibrational modes can also be computed if needed.

In addition, the generation of minimum energy reaction paths and dynamics on the NEO potential energy surface will be possible with analytic gradients.

We emphasize that this Letter represents a proof of concept that multicomponent DFT with the epc17 class of electron−proton correlation functionals is able to predict accurate proton affinities and account for the impact of nuclear quantum effects on optimized geometries. Future functionals will include gradient corrections to enhance the quantitative accuracy and generality of this approach. Thus, this study is only the first step toward a new direction for incorporating nuclear quantum effects of key protons in a wide range of DFT calculations.

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Notes

The authors declare no competing financial interest.

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