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Fall 2019

Quantum Chemical Methods: Its history and future

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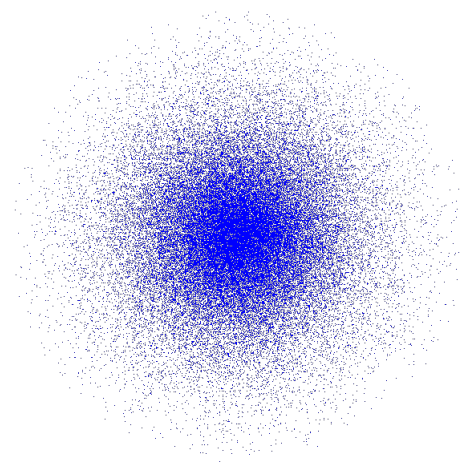
Its history and future

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December 12, 2019

Introduction

Computational quantum chemistry combines the power of computation and the foundations of physics to understand chemical problems. The dawn of quantum chemistry coincided with the advent of computing technology as solving many-electron problems could take years if done by hand. Modern day computation comes from the use of nodes and processors to handle large amounts of data typically run through a quantum chemical software package. These quantum chemical methods are the foundation of most theoretical studies of medium to small molecules.

Two theories have driven this approach, wave function theory(WFT) and density functional theory(DFT). Wave function techniques look at each individual electron while density functional theory view the total electron density to explain chemical properties. Each give reasonable solutions that agree with experimental results, but theory did not always match experiment. New and better methods had to be obtained over the years in order to accurately describe the motion of the electrons so that reliability and confidence was reached. This is still the goal of method development today as the many-body problem becomes much more complicated for increasingly challenging cases.

Density Functional Theory

Hohenberg-Kohn Theorems

DFT was founded upon the theorems of Hohenberg and Kohn in their 1964 paper on an inhomogeneous electron gas.[1] The first theorem states that the ground-state electron density, $\rho(r)$, uniquely determines the external potential, $v(r)$. This was proved for a non-degenerate ground-state, Ψ, using *reductio ad absurdum* by assuming that another potential, $v'(r)$ could equal the same electron density, $\rho(r)$, corresponding to the ground-state, Ψ'.[1] Then it could

be shown that for Ψ,

$$
\begin{aligned}
E &= \langle \Psi | \hat{H} | \Psi \rangle \\
&= \int v(r)\rho(r)dr \; + \langle \Psi | (\hat{T} + \hat{V}_{\text{ee}}) | \Psi \rangle
\end{aligned}
\tag{1}
$$

where T and V_{ee} are the kinetic energy and electron-electron repulsion operators. Similarly for Ψ',

$$
\begin{aligned}
E' &= \langle \Psi' | \hat{H}' | \Psi' \rangle \\
&= \int v'(r)\rho(r)dr \; + \langle \Psi' | (\hat{T} + \hat{V}_{\text{ee}}) | \Psi' \rangle \, .
\end{aligned}
\tag{2}
$$

Unless $v'(r)$ equals $v(r)$ plus a constant, then Ψ and Ψ' must be unequal and therefore, since ground-states are energy minima,

$$
\begin{aligned}
E &< \langle \Psi' | \hat{H} | \Psi' \rangle \\
&= \int v(r)\rho(r)dr \; + \langle \Psi' | (\hat{T} + \hat{V}_{\text{ee}}) | \Psi' \rangle \\
&= E' + \int [v(r) - v'(r)]\, n(r)dr
\end{aligned}
\tag{3}
$$

and

$$
\begin{aligned}
E' &\leq \langle \Psi | \hat{H}' | \Psi \rangle \\
&= \int v'(r)\rho(r)dr \; + \langle \Psi | (\hat{T} + \hat{V}_{\text{ee}}) | \Psi \rangle \\
&= E + \int [v'(r) - v(r)]\, n(r)dr \, .
\end{aligned}
\tag{4}
$$

Combining the two gives a contradiction such that

$$
E + E' \; < \; E + E' \, .
\tag{5}
$$

3

Therefore, the first theorem is proved for a non-degenerate ground-state. It can also be expanded to include those with degenerate ground-states.[2]

The second theorem defines that the ground-state electron density can be used to attain the minimum energy of a system by using the variational principle to solve the universal functional, F_{HK}. It can easily be seen in the above equations that the energy is dependent on $\rho(r)$ making it a functional of the density such that

$$E = E_v[\rho(r)]. \tag{6}$$

This can be mathematically proven because the Hamiltonian is dependent upon the number of electrons, N, and $v(r)$, which can both be calculated using $\rho(r)$.[3] Due to this dependence, it can also be shown that the universal functional is dependent on $\rho(r)$ so

$$F_{HK}[\rho(r)] = \langle\Psi|(\hat{T}[\rho(r)] + \hat{V}_{\text{ee}}[\rho(r)])|\Psi\rangle. \tag{7}$$

The energy equation is then

$$E_v[\rho(r)] = \int v(r)\rho(r)dr + F_{\text{HK}}[\rho(r)]. \tag{8}$$

If the exact ground-state electron density can be chosen, then the minimum ground-state energy can be determined. Therefore, by the variational principle, if any other density is used it will be larger than this energy. The optimal $\rho(r)$ is one that does not change the energy upon small variations of the density[3] where

$$\delta(E - \mu\rho(r)) = 0 \tag{9}$$

such that

$$\int \rho(r)dr = N \tag{10}$$

and μ is the Lagrange multiplier.

The variational principle will be more deeply explained in our discussion of Hartree-Fock, but for now we turn our focus to the universal function, $F_{\text{HK}}[\rho(r)]$, more commonly called the Hohenberg-Kohn functional. The emphasis on this functional is expressed here since its form allows the ground-state energy of a system to be solved by using only the ground-state electron density which is a three-dimensional term. Therefore, it would only require the minimization of this three-dimensional term to determine the minimum energy.[1] It also makes DFT an exact theory, because the functional describes motion of all electrons independent of the external potential allowing us to know all information of the system. The problem is that no one knows the form of this functional and its classification as a non-deterministic polynomial-time hard (NP-hard) problem means that no one will probably ever solve it since it would take on such a challenging form.[4] Yet, theoretical chemistry found a way to somewhat resolve this in 1964 by Kohn and Sham.

Kohn-Sham Formalism

The Hohenberg-Kohn functional is then the holy grail of DFT as it makes DFT be an exact theory, but what is more commonly referred to when we are talking about the theory is Kohn-Sham DFT (KS-DFT) which made DFT a viable option. Its sudden increase in popularity was a direct product of its inclusion of orbitals to DFT. These orbitals are similar to those in Hartree-Fock such that each orbital contains one-electron and assumes no interaction of the electrons between each orbital. The density can then be written as a sum of the wave function consisting of those orbitals with

$$\rho(r) = \int \sum_i^N |\phi_i(\mathbf{x})|^2 d\sigma \,, \tag{11}$$

5

where $\mathbf{x}$ is the spatial and spin coordinates. Kohn and Sham then started changing the original DFT energy by writing the Hohenberg-Kohn functional as

$$F_{\mathrm{HK}}[\rho(r)] = T_s[\rho(r)] + J[\rho(r)] + E_{\mathrm{XC}}[\rho(r)], \qquad (12)$$

where $T_{\mathrm{s}}[\rho(r)]$ is the kinetic energy of assuming a non-interacting system, $J[\rho(r)]$ is the Coulombic interaction energy, and $E_{\mathrm{XC}}[\rho(r)]$ includes the exchange and correlation energy of that same system.[3] This third term is the base of KS-DFT with it reintroducing the interaction effects that govern a system.

The exchange-correlation functional, $E_{\mathrm{XC}}[\rho(r)]$, is now the only part of the energy formula that is unknown. This functional includes the more challenging quantum effects of electron interaction. Part of it is the examination of the exchange energy which deals with the exchange of two identical fermions, specifically electrons, and the antisymmetric properties that must be satisfied. Another part is the correlation energy which describes the interaction of electrons with each other such as attraction and repulsion. This differs from the classical Coulombic energy because it takes into account that we cannot know both the position and momentum of an electron simultaneously due to the Heisenberg uncertainty principle. Furthermore, it covers both the effects of the instantaneous electron-electron repulsions and the degeneracies of a system.

Approximate Exchange-Correlation Functionals

For the same reasons that the Hohnenberg-Kohn functional is unsolvable, the exchange-correlation functional is most likely to never be solved. Describing the quantum effects of how all the electrons interact is still a goal for chemical theorists but due to the Kohn-Sham formalism, solving the equations of Kohn and Sham can lead us to what is called the Hartree-Fock limit. This limit assumes a non-interacting system and for simple molecules can give reasonable energies, but when the exchange-correlation energy is added it can greatly increase

chemical accuracy. The exchange-correlation energy is found using approximate functionals that simplify how we calculate for the quantum effects. They are used extensively throughout all fields of chemistry and can help point chemists toward the correct way of understanding things mechanistically. The approximate functionals are so commonplace that they are commonly just referred to as the functional itself. For brevity, when the word functional is used, it is implied that it is of the approximate form.

Localized-Spin Density Approximation

The first approximations made were local such that they relied on the spin densities, spin-orbitals, and their derivatives at a point of the energy density.[4] The simplest of the local methods is the localized spin-density approximation where the density is split into α and β spins, so that the energy is dependent upon them so that

$$E = T_{\mathrm{S}}[\rho_\alpha, \rho_\beta] + \int dr\, v_{ext}(r)\rho(r) + J(\rho) + E_{\mathrm{XC}}[\rho_\alpha, \rho_\beta]\,. \tag{13}$$

This approximation is exact for a uniform electron gas as solved numerically using quantum Monte Carlo methods.[5]

The two most common types to be used are the Vosko, Wilk, and Nusair functional and the Perdew And Wang functional. The VWN method slightly changes the spin-polarization term such that

$$\epsilon_{\mathrm{c}}^{\mathrm{VWN}}(r_s, \zeta) = \epsilon_c(r_s, 0) + \epsilon_a(r_s)\left[\frac{f_2(\zeta)}{f_2''(0)}\right](1 - \zeta^4) + [\epsilon_c(r_s, 1) - \epsilon_c(r_s, 0)]f_2(\zeta)\zeta^4 \tag{14}$$

and

$$f_2(\zeta) = \frac{f_1(\zeta) - 2}{2^{1/3} - 1}\,. \tag{15}$$

The Perdew-Wang method parameterizes much differently with

$$\epsilon_{\mathrm{c/a}}^{\mathrm{PW}}(x) = -2\alpha\rho(1 + \alpha x^2)ln\left(1 + \frac{1}{2\alpha(\beta_1 x + \beta_2 x^2 + \beta_3 x^3 + \beta_4 x^4)}\right). \qquad (16)$$

The difference between the two equations of the methods within the same category of localized spin-density approximation shows the complexity of creating one of them, but these still depend upon a strict simplification. LSDA can be used to solve exactly for a uniform electron gas. This method then works by assuming a uniform electron gas which is untrue for all chemical systems of interest. This shows that the LSDA method is insufficient since it underestimates the correlation energy by approximately 10%.[6]

Generalized Gradient Approximation

The generalized gradient approximation makes major improvements upon LSDA by having the energy dependent upon the gradients of the spin densities. Using the gradients as well as the spin densities allows flexibility such that we are no longer approximating a uniform electron gas and are instead looking at a slowly varying electron gas.[7] This is still not a perfect picture but greatly improved the results of LSDA, with its form for the exchange energy being quite simple,

$$E_{\mathrm{x}}^{\mathrm{GGA}}[\rho, x] = \int \rho^{4/3} F(x) dr, \qquad (17)$$

where $F(x)$ can be changed depending on the functional used.

The functionals work by separately solving for the exchange energy and the correlation energy. Two popular methods that use a GGA approach is by the Perdew-Burke-Ernzerhof functional (PBE) and Becke's functional (B88) from 1988. For the exchange term, the two vary in the parameterization of the $F(x)$ function with the energy of PBE being

$$E_{\mathrm{x}}^{\mathrm{PBE}} = -\int \rho^{4/3}\left[\frac{3}{4}\left(\frac{3}{\pi}\right)^{1/3} + \frac{\mu s^2}{1 + \frac{\mu s^2}{\kappa}}\right] dr, \qquad (18)$$

and the energy of Becke's exchange being

$$E_x^{B88} = \sum_{\sigma=\alpha,\beta} \int \rho_\sigma^{4/3} \left[\frac{3}{4} \left(\frac{6}{\pi} \right)^{1/3} + \frac{\beta x_\sigma^2}{1 + 6\beta x_\sigma \sinh^{-1} x_\sigma} \right] dr \,. \tag{19}$$

PBE has its own correlation functional that traditionally goes with its exchange term also. It works by fitting its parameters not to empirical data but to some conditions of functionals themselves. One of these is that the correlation potential will show asymptotic behavior corresponding to the function, $-\frac{1}{2}\alpha r^{-4}$, where α is polarizability.[6] This differs greatly from the widely used Lee, Yang, and Parr correlation functional which was parameterized using experimental data from helium atoms. It is worth noting and writing out this equation given its frequent occurence in DFT where

$$\epsilon_c^{LYP} = -4a \frac{\rho_\alpha \rho_\beta}{\rho^2 \left(1 + d\rho^{-1/3} \right)} -$$
$$\left\{ \frac{\rho_\alpha \rho_\beta}{18} \left[144(2^{2/3}) C_F \left(\rho_\alpha^{8/3} + \rho_\beta^{8/3} \right) + (47 - 7\delta)|\nabla\rho|^2 - \right. \right.$$
$$(45 - \delta) \left(|\nabla\rho_\sigma|^2 + |\nabla\rho_\beta|^2 \right) + 2\rho^{-1}(11 - \delta) \left(\rho_\sigma|\nabla\rho_\sigma|^2 + \rho_\beta|\nabla\rho_\beta|^2 \right) \Big]$$
$$\left. + \frac{2}{3}\rho^2 \left(|\nabla\rho_\sigma|^2 + |\nabla\rho_\beta|^2 - |\nabla\rho|^2 \right) - \left(\rho_\alpha^2|\nabla\rho_\beta|^2 + \rho_\beta^2|\nabla\rho_\alpha|^2 \right) \right\} \tag{20}$$

such that

$$\omega = \frac{\exp{-c\rho^{-1/3}}}{\rho^{14/3} \left(1 + d\rho^{-1/3} \right)}$$

and

$$\delta = c\rho^{-1/3} + \frac{d\rho^{-1/3}}{\left(1 + d\rho^{-1/3} \right)} \,.$$

Hybrid Functionals

Equations 19 and 20 form the precursor to the most popular functional in all chemistry, B3LYP. B3LYP stands for Becke 3-parameter Lee, Yang, Parr, and it is a hybrid functional composed of the B88 exchange term and the LYP correlation term so that the full exchange-

correlation energy can be given by

$$E_{\text{XC}}^{\text{B3LYP}} = (1 - a)E_{\text{x}}^{\text{LSDA}} + aE_{\text{x}}^{\text{exact}} + b\Delta E_{\text{x}}^{\text{B88}} + (1 - c)E_{\text{c}}^{\text{LSDA}} + cE_{\text{c}}^{\text{LYP}}, \qquad (21)$$

where experimental data determines what a, b, and c will be.

Hybrid functionals have become quite popular over the years as they help with the self-interaction error which is part of the static correlation deficiencies in KS-DFT. The beginnings of hybrids start with the Adiabatic Connection Formula (ACF) as its base. This formulation allows us to connect energies of an interacting system with energies of a noninteracting system.[8] Part of this is the introduction of the λ term which is a coupling constant that can range from zero to one.[9] The addition of this term makes the exchange-correlation energy an integral

$$E_{\text{XC}} = \int_0^1 \langle \Psi_\lambda | V_{\text{XC}}^{\text{hole}}(\lambda) | \Psi_\lambda \rangle d\lambda \qquad (22)$$

where the variation of λ causes the electron-electron interactions to be "turned on".[6]

The best aspect of hybrids is then their ability to mix some Hartree-Fock exchange with DFT. One of the first attempts at mixing the two is the half-and-half approach which, as the name explains, calculates the exchange energy with half of the exact exchange energy and half the combination of the exchange and correlation energy computed using LSDA,

$$E_{\text{XC}}^{\text{H+H}} = \frac{1}{2}E_{\text{x}}^{\text{exact}} + \frac{1}{2}\left(E_{\text{x}}^{\text{LSDA}} + E_{\text{c}}^{\text{LSDA}}\right). \qquad (23)$$

Typically this enhances the equations such that the results are closer to the experimental values than without the addition of Hartree-Fock exchange, but caution must be taken when adding this exchange to DFT. Certain amounts of the exchange work better for different functionals where PBE0, similar to PBE, includes 25% Hartree-Fock exchange and another method called TPSSh (Tao-Perdew-Staroverov-Scuseria) only uses approximately 10%.

Meta Functionals

The use of second-order derivatives of the electron density create a class of functionals called meta functionals. These will use either the Laplacian of the density ($\nabla^2 \rho$) and/or the density of the kinetic energy (τ). The two are related due to both using the same orbitals and effective potential.[10] Although, the kinetic energy density is more popular and takes on the form

$$\tau(r) = \frac{1}{2} \sum_i^{occ} |\nabla \phi_i(r)|^2 \,. \tag{24}$$

The popularity of $\tau(r)$ over the Laplacian is in its numerical stability and the kinetic energy density's ability to recognize one-electron character by its relation to the von Weizsäcker kinetic energy,

$$\tau_W(r) = \frac{|\nabla \rho(r)|^2}{8\rho(r)} \,. \tag{25}$$

TPSS, created in 2003, is one example of a meta-GGA.[11]

As new advances have been made in calculating the exchange-correlation energy a new class has emerged called the hybrid meta functionals. These include many of the popular Minnesota functionals, including the well-known M06-2X functional . This particular functional is specifically good at calculating main-group thermochemistry, kinetics, noncovalent interactions, and electronic excitation energies to valence and Rydberg states.[12] Although not as popular as B3LYP, M06-2X has become a staple in the computational community for a variety of systems performing well during rigorous testing against multiple databases.[10]

Applications of DFT

Density functional theory is elegant and complex due to the variety of functionals available. Bringing the discussion back to a more tangible representation of DFT, an example of its application is presented.
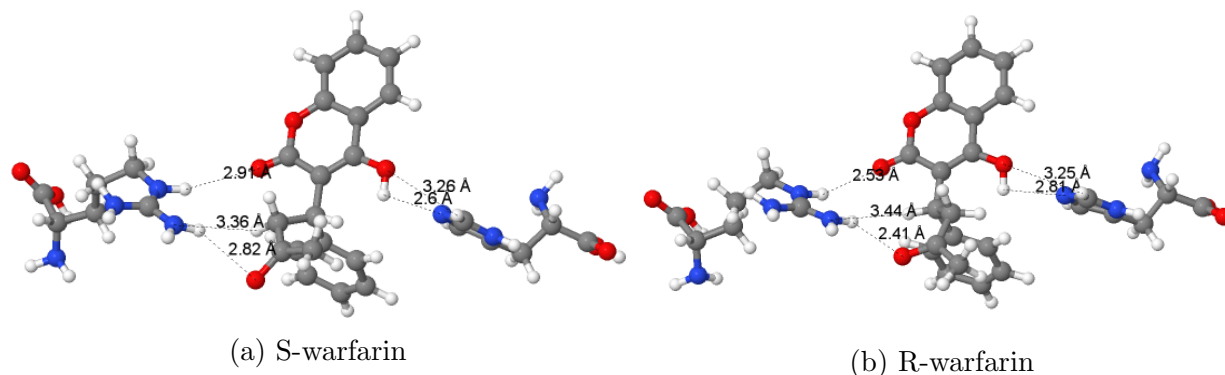
Figure 1: *S*- and *R*- warfarin optimized structures using M06-2X/aug-cc-pVTZ. Annotated lines show the hydrogen bonds between the warfarin and the two amino acids. For each figure, on the left is the arginine-222 and on the right is the histidine-242.

Warfarin

A study of *S*- and *R*- warfarin was done using the hybrid meta-GGA, M06-2X. The project was collaborative with experimental work done at Belhaven University and computational work done at Taylor University. The experiment consisted of adding halogens (F, Cl, or Br) to the phenyl ring of the warfarin to be identified using fluorescent spectroscopy. The motivation of the project was to create better pharmaceuticals by testing the binding of warfarin to blood serum albumin. The computational side of the study was done to confirm experimental results and to compute the possibility of different halogens at differing positions having an impact on binding energy.

The initial calculations were done in gas phase, then the polarizable continuum model was used to replicate the dielectric constant of water simulating a solvent environment. Warfarin binds specifically to three amino acids within a pocket of the blood serum albumin and these are arginine-222, histidine-242, and tryptophan-214. Only arginine-22 and histidine-242 were studied initially so compiled data is only shown for the binding interactions between the warfarin and Arg222 and His242. Binding energies for tryptophan have been done and do not show significant changes from the calculations without it. Therefore, the values in Fig. 2 are still deemed acceptable for comparison with experiment.

M06–2X/aug–cc–pVTZ (kcal mol^{-1})				
Fluorine Substitution	Binding Energy		Binding Energy in Water	
	R	S	R	S
No Substitution	−29.98	−22.12	−4.11	−1.49
Ortho (Arg222)	−31.99	−24.01	−4.17	−1.61
Meta (Arg222)	−29.83	−22.16	−4.12	−4.48
Para	−29.29	−21.55	−4.24	−1.82
Meta (His242)	−29.28	−21.55	−4.53	−1.56
Ortho (His242)	−28.49	−19.66	−1.92	−0.01

Figure 2: Table of the binding energy of fluorinated warfarin derivatives using M06-2X/aug-cc-pVTZ.

The results were promising using the density functional M06-2X with the large basis set aug-cc-pVTZ. From the data, Fig. 2, it can be shown R-warfarin has a stronger binding affinity which is in agreement with experimental work done at room temperature, where R-warfarin is bound 1-3 kcal mol^{-1} greater than S-warfarin. For the derivatives, the -ortho position nearest His242 has the weakest binding affinity due to increased repulsion of the fluorine with the nitrogen on histidine. Then, the -ortho position nearest Arg222 has the strongest binding affinity due to increased attraction with the nitrogen system on arginine. Solvation with water agrees with expected behavior since it is a high dielectric constant solvent. This causes charge stabilization of the dipole moments of the amino acids, especially the electron deficient nitrogen system of Arg222. Overall, the study of warfarin to blood serum albumin shows one application in which DFT may be used successfully with complementary results from experiment confirming this.

Wave Function Theory

Hartree-Fock Theory

The base of all wave function theory is Hartree-Fock (HF). HF was created by Douglas Hartree and Vladimir Fock and is an approximate method for calculating atomic and molecular properties.[13] The approximation comes from the fact that only one-electron systems, such as the hydrogen atom, may be solved analytically. Consider helium, a two-electron system, where the Schrödinger equation is

$$
\left(-\frac{\hbar^2}{2M}\nabla^2 - \frac{\hbar^2}{2m_e}\nabla_1^2 - \frac{\hbar^2}{2m_e}\nabla_2^2 \right) \psi(\mathbf{R}, \mathbf{r}_1, \mathbf{r}_2) \quad +
$$
$$
\left(-\frac{2e^2}{4\pi\epsilon_o|\mathbf{R} - \mathbf{r}_1|} - \frac{2e^2}{4\pi\epsilon_o|\mathbf{R} - \mathbf{r}_2|} + \frac{e^2}{4\pi\epsilon_o|\mathbf{r}_1 - \mathbf{r}_2|} \right) \psi(\mathbf{R}, \mathbf{r}_1, \mathbf{r}_2)
$$
$$
= \quad E\psi(\mathbf{R}, \mathbf{r}_1, \mathbf{r}_2) , \quad (26)
$$

and under the Born-Oppenheimer approximation which fixes the nucleus at the origin of the chosen coordinate system, Eq. 26 becomes

$$
-\frac{\hbar^2}{2m_e}(\nabla_1^2 + \nabla_2^2)\psi(\mathbf{r}_1, \mathbf{r}_2) - \frac{2e^2}{4\pi\epsilon_o}\left(\frac{1}{r_1} + \frac{1}{r_2} \right)\psi(\mathbf{r}_1, \mathbf{r}_2)
$$
$$
+ \frac{e^2}{4\pi\epsilon_o|\mathbf{r}_1 - \mathbf{r}_2|}\psi(\mathbf{r}_1, \mathbf{r}_2) = E\psi(\mathbf{r}_1, \mathbf{r}_2) . \quad (27)
$$

There is a term in Eq. 28 called the interelectronic repulsion term, $\frac{1}{|\mathbf{r}_1-\mathbf{r}_2|}$, that appears in all many-electron systems and is the reason the Schrödinger equation cannot be solved. The distance between the electrons cannot be quantified since their motions are correlated, therefore, the value cannot be determined.[6] Hartree and Fock bypass this conundrum by approximating the electrons such that there is no electron correlation. The theory puts an electron into a one-electron molecular orbital, then places the orbital into the average effective potential created by all the other electrons. This method is done to every electron in the

system and allows the problem to be converted from a many-body problem into multiple two-body problems.

Before explaining HF theory further, the creation of a many-electron wave function will be briefly explained. Although not mentioned in depth in this paper, the start to building molecular orbitals is by choosing a basis set which contains the atomic orbitals. Atomic orbitals are typically Gaussian functions and the linear combination of them makes molecular orbitals such that

$$\phi = \sum_i^n c_i \chi_i \ . \tag{28}$$

From the molecular orbitals, a Hartree product(HP) can be made,

$$\Phi_{\mathrm{HP}}(\mathbf{r}_1, \mathbf{r}_2, \dots, \mathbf{r}_N) = \phi_1(\mathbf{r}_1)\phi_2(\mathbf{r}_2)...\phi_N(\mathbf{r}_N) \ , \tag{29}$$

but a more proper way to arrange the orbitals would be in a Slater determinant (Φ_{SD}),

$$\Phi_{\mathrm{SD}}(\mathbf{r}_1, \mathbf{r}_2, \dots, \mathbf{r}_N) = \frac{1}{\sqrt{N!}} \begin{vmatrix} \phi_1(\mathbf{r}_1) & \phi_2(\mathbf{r}_1) & \dots & \phi_N(\mathbf{r}_1) \\ \phi_1(\mathbf{r}_2) & \phi_2(\mathbf{r}_2) & \dots & \phi_N(\mathbf{r}_2) \\ \vdots & \vdots & \ddots & \vdots \\ \phi_1(\mathbf{r}_N) & \phi_2(\mathbf{r}_N) & \dots & \phi_N(\mathbf{r}_N) \end{vmatrix} . \tag{30}$$

Slater determinants (SDs) are preferred since they are properly antisymmetrized meaning that under the exchange of any two electrons the sign of the determinant will flip. Different types of wave functions can be created using SDs. If a single configuration (SC) wave function is made, then only one SD is used while if a multiconfigurational (MC) wave function is made, then a linear combination of SDs is used. In HF theory, a SC wave function is forced,

$$\Psi_{\mathrm{SC}} = \Phi_{\mathrm{SD}} \ . \tag{31}$$

Now that the basics of a wave function are understood as linear combinations of atomic

orbitals and molecular orbitals, the self-consistent nature of the Hartree equations may be discussed [1] . As stated earlier, HF places one-electron as if it is feeling the average effective potential of all the other electrons. In mathematical form, the average interactions are carried out by the Fock operator,

$$\hat{F}_i = \hat{h}_i + \sum_{j}^{N_{\text{elec}}} (\hat{J}_j - \hat{K}_j) \ . \tag{32}$$

The Fock operator is an effective one-electron energy operator that describes the electronic kinetic energy and the attraction of the nuclei through the $\hat{h}_i$ operator and also describes the repulsion to all the other electrons through the $\hat{J}$ and $\hat{K}$ operators.[6] The $\hat{J}$ and $\hat{K}$ operators have a much more thorough derivation, but the importance of them is not forgotten as they represent the classical repulsions between two charge distributions, the Coulomb integral, and the correlated motion of electrons, the exchange integral, respectively.

By using a SD that is diagonalized, a set of pseudo-eigenvalue equations such that

$$\hat{F}_i|\phi_i\rangle = \varepsilon_i|\phi_i\rangle \tag{33}$$

where ε_i is the energy of the orbital, ϕ_i. Self-consistency is then attained because a specific Fock orbital can only be determined if all the occupied orbitals are known and each one of those orbitals are at an energy minimum.[6] Figure 3 shows how Eq. 33 is used self-consistently in a computation. From the geometry of a molecule, coordinates can be obtained to create the initial molecular orbitals. These one-electron MOs are used to create the Fock matrix,

---

[1]The equations from this point will be written in Dirac's *bra-ket* notation where

$$|\Psi_{\text{SC}}\rangle = \Psi_{\text{SC}}$$
$$\langle\Psi_{\text{SC}}| = \Psi_{\text{SC}}^*$$
$$\langle\Psi_{\text{SC}}|\Psi_{\text{SC}}\rangle = \int \Psi_{\text{SC}}^* \Psi_{\text{SC}} d\mathbf{r}$$
$$\langle\Psi_{\text{SC}}|\hat{A}|\Psi_{\text{SC}}\rangle = \int \Psi_{\text{SC}}^* \hat{A} \Psi_{\text{SC}} d\mathbf{r}$$

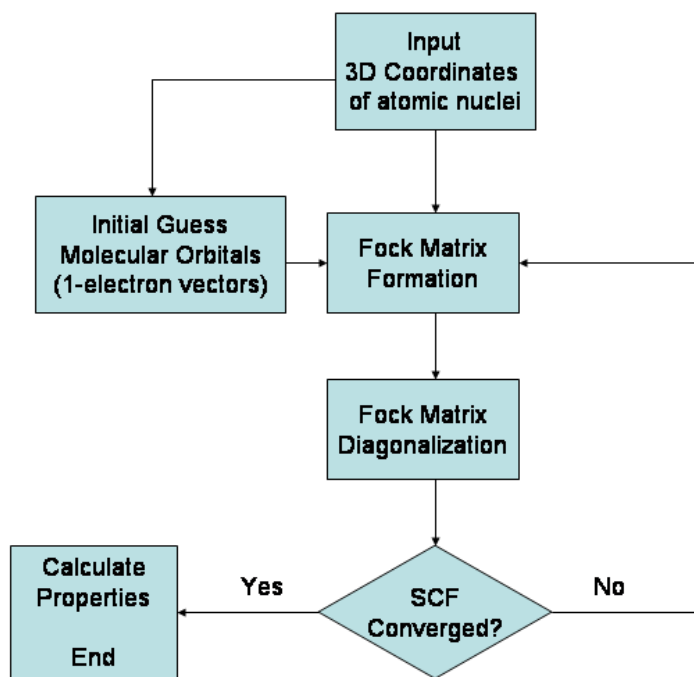and $\hat{A}$ is any operator such as the Hamiltonian, $\hat{H}$.

Figure 3: Flow chart of HF self-consistent equations in a computation.

Eq. 33, which is then diagonalized and the orbital energies are compared to the energies from the set before. If the energy is not within a certain threshold of the last one, then the new MOs from diagonalizing the matrix are used in the next iteration. If the energy is within the threshold, then the solution is considered to be converged and the molecular orbitals produced may be used to calculate the properties of interest for the system. Figure 4 shows the output from the Psi4 quantum chemistry program[2] where the H_2 molecule was solved for using the scheme in Fig. 3.

Hartree-Fock theory works as a good initial calculation to get the molecular orbitals for higher levels of wave function theory, such as coupled-cluster and configuration interaction, but is not recommended to report values due to its neglect of electron correlation. Electron

[2]Psi4 1.1: An Open-Source Electronic Structure Program Emphasizing Automation, Advanced Libraries, and Interoperability", R. M. Parrish, L. A. Burns, D. G. A. Smith, A. C. Simmonett, A. E. DePrince III, E. G. Hohenstein, U. Bozkaya, A. Yu. Sokolov, R. Di Remigio, R. M. Richard, J. F. Gonthier, A. M. James, H. R. McAlexander, A. Kumar, M. Saitow, X. Wang, B. P. Pritchard, P. Verma, H. F. Schaefer III, K. Patkowski, R. A. King, E. F. Valeev, F. A. Evangelista, J. M. Turney, T. D. Crawford, and C. D. Sherrill, J. Chem. Theory Comput., 13(7) 3185–3197 (2017).

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SCF Guess: Superposition of Atomic Densities via on-the-fly atomic UHF.

==> Iterations <==

                             Total Energy          Delta E       RMS |[F,P]|

 @DF-RHF iter SAD:     -0.84147163895715    -8.41472e-01    0.00000e+00
 @DF-RHF iter   1:     -1.13004917344409    -2.88578e-01    4.08028e-03 DIIS
 @DF-RHF iter   2:     -1.13286582891487    -2.81666e-03    8.26398e-04 DIIS
 @DF-RHF iter   3:     -1.13298977901196    -1.23950e-04    6.44151e-05 DIIS
 @DF-RHF iter   4:     -1.13299026642392    -4.87412e-07    2.78200e-06 DIIS
 @DF-RHF iter   5:     -1.13299026717485    -7.50930e-10    1.87139e-07 DIIS
Energy and wave function converged.
```

Figure 4: SCF iteration for the H_2 molecule.

correlation energy is what is missing in HF calculations and therefore it is defined as the difference between the exact non-relativistic Born-Oppenheimer energy of a system minus the HF limit,

$$E_{\text{exact}} - E_{\text{HF}} = E_{\text{corr}} . \tag{34}$$

The correlation energy is split into static and dynamic due to our limited understanding of how electrons interact, but complete separation of the two is impossible because they are inherently related. The separation is imposed by defining static correlation as a more permanent repulsion that arises due to near-degeneracies while dynamic correlation is defined by the instantaneous electron-electron repulsions. HF despite neglecting the correlation energy is about 99% accurate at predicting the energy, so different methods typically build upon its base such as adding more determinants where the wave function is

$$\Psi_{MC} = c_0 \Phi_{HF} + \sum_{i=1}^{N} c_i \Phi_i . \tag{35}$$

Multiconfigurational Self-Consistent Field Theory

Multiconfigurational self-consistent field (MCSCF) is one method which uses multiple Slater determinants to describe systems in which a single electron configuration is no longer

an adequate way to represent the system's character. This is because of the orbitals are changing as bonds are changing along the intrinsic reaction coordinate (IRC).[6] As a bond is broken, the orbitals it forms can change occupation and therefore, electronic configurations which can result in degeneracies. If the number of configurations is equal to one, then MCSCF is equal to a Hartree-Fock (HF) method but if it is larger than one, then multireference character becomes more pronounced and its effects cannot be assumed insignificant.

For example, consider the dissociation of the H_2 molecule. As the distance increases, the electrons can either pair together into one orbital or separate with one electron in each orbital. In HF, the electrons are forced into double occupation neglecting the single-electron occupation possible because it uses a single SD, one electron configuration. Using MCSCF, we are able to use both electron configurations, two SDs, giving flexibility to our wave function and representing the chemical system more accurately.
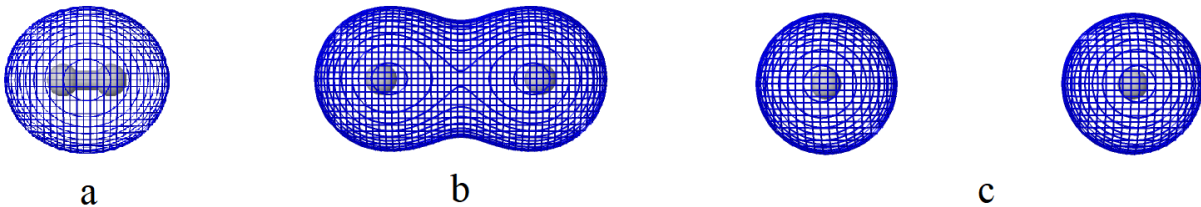

a   b   c

Figure 5: First MO of H_2 at various bond lengths a) 0.734 Å, b) 2.500 Å, c) 5.000 Å.

Mathematically, MCSCF linearly combines the SDs into a configuration interaction (CI) wave function,

$$\Psi_{\text{MCSCF}} = \sum_i^N c_i \Phi_i \ , \tag{36}$$

where the coefficients in front of the determinants and the molecular orbitals (MO) are both optimized by the variational principle.[14] The linear variation method takes the coefficients of the basis functions and minimizes them by taking the derivative of the energy with respect to the coefficients creating the MOs. Unique to MCSCF methods, the MO coefficients, c_i, are changed in the active space while the coefficients relating to the contribution of the

19

determinants to the wave function are also changing. This allows us to look at different arrangements of the electron configuration in varying MOs, therefore including the multi-configurational energy contributions. When two configurations have about the same energy and both contribute to the wave function of a system, we call them near-degenerate. Then, MCSCF is really good at accounting for near-degeneracies which correspond to static correlation. To include the effect of dynamic correlation, a separate calculation is normally performed after running a MCSCF calculation.
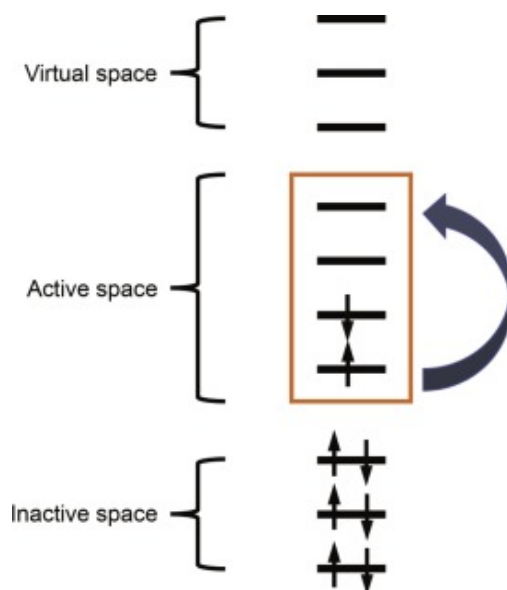

Figure 6: Separation of the molecular orbitals into inactive, active, and virtual spaces according to the complete active space self-consistent field method.

A key component of MCSCF is selecting an active space and one way to do this is using the complete active space self-consistent field method (CASSCF) which separates the MOs into inactive, active, and virtual spaces. The inactive orbitals will always be doubly occupied while the virtual orbitals will be unoccupied. The active space contains what we call "active" electrons because it is the space where all the excitations will occur, and the optimization of the MO coefficients will take place only for these orbitals. The flexibility of the MOs in the active space allows the orbitals to be partially occupied as shown in Fig. 6. The problem with choosing the active space is that as the number of electrons and orbitals are

chosen, the number of SDs increase factorially which is computationally expensive. Then, the chosen electrons and orbitals are the ones that will recover the most changes that occur in the correlation energy for the predicted process, so that all the electron correlation in the active space will be computed.

Applications of MCSCF

The focus on strongly correlated systems has increased over the years since these systems are a much better representation of transition states, transition metal and actinide chemistry, systems with partially broken bonds, and electronically excited states.[15]

Benzvalyne

One application of the CASSCF method is the study of transition states, specifically the transition states (TSs) between benzvalyne, Fig. 7a, and benzyne, Fig. 7b. This reaction path was surveyed by looking at both the conrotatory and disrotatory TSs according to the Woodward-Hoffmann rules. The rules govern that for this system, 8 π electrons, the conrotatory path would be allowed while the disrotatory path would be forbidden.[16]
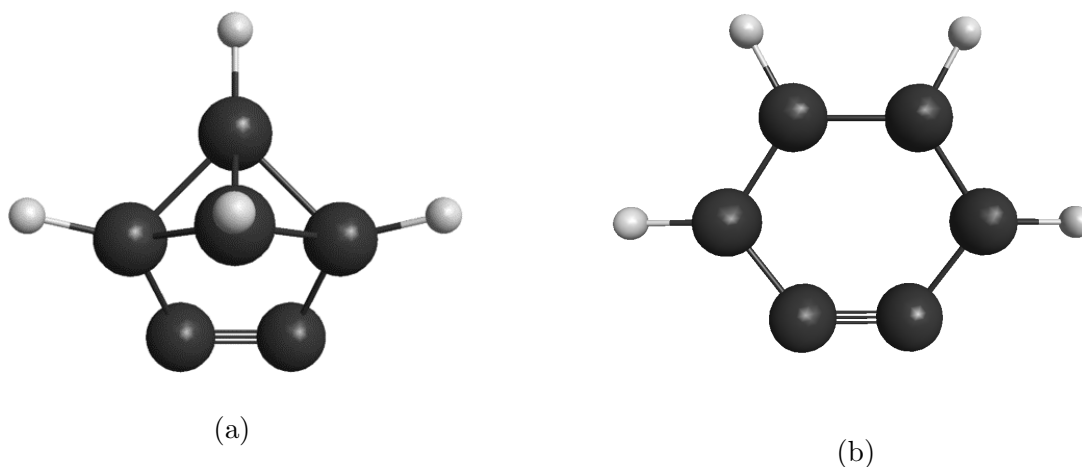

(a)

(b)

Figure 7: a) Benzvalyne, an isomer of benzyne. b) Benzyne, an intermediate in some organic chemistry reactions.

Conrotatory means that the bonds breaking are twisting the same direction while disrotatory means they are twisting opposite.

In order to search for the TSs, CASSCF was used by putting 10 active electrons in 10 active orbitals to make a CAS(10,10). This method was chosen because of the high multiconfigurational character of benzvalyne and the breaking of multiple bonds along the reaction coordinate as it reached the transition states. The CASSCF energies, Fig. 8, were then used as a starting point to analyze the different response properties of the system, including: chemical potential (μ), chemical hardness (η), electrophiliciy (ω), and polarizability (α).
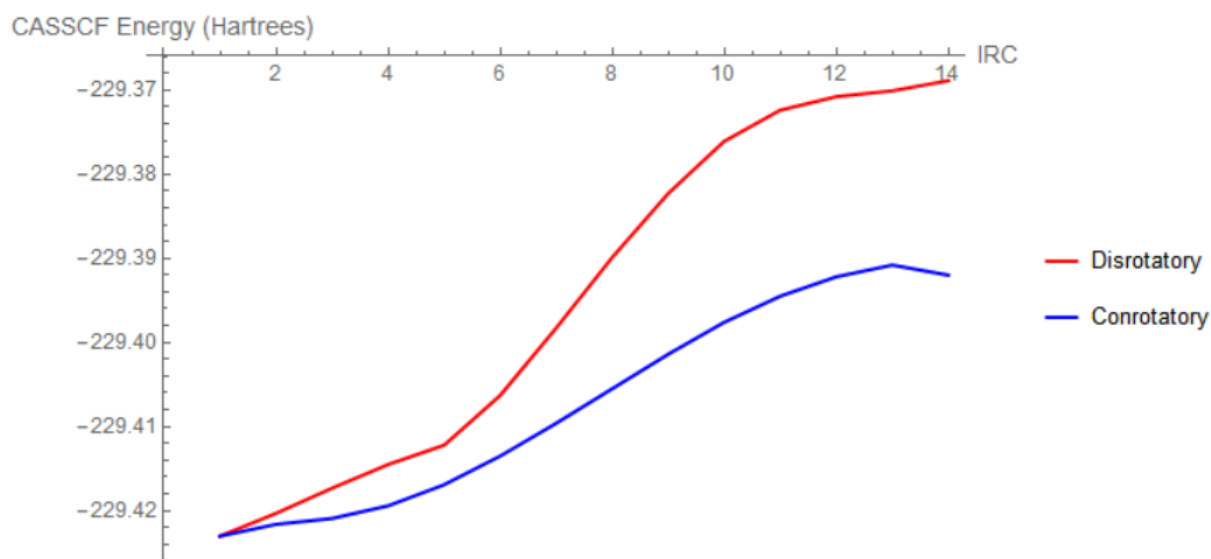

Figure 8: Plot showing the energy change from reactant, benzvalyne, to transition state with the conrotatory path in blue and the disrotatory path in red.

The overall results showed that the CASSCF energies provided a good framework to qualitatively understand the relationship between energy and hardness through a conceptual DFT vantage point.

Combining the Two

Wave function techniques and density functional methods seem to have a give and take relationship in terms of their advantages and disadvantages with one's weakness being the

other's strength. Therefore, the attempt to combine the two was a natural approach to fix the gaps in each theory.

Multiconfiguration Pair-Density Functional Theory

Multiconfiguration pair-density functional theory (MC-PDFT) combines multiconfiguration wave functions with density functional theory by using the multiconfiguration kinetic energy, total density, and on-top pair density to calculate the energy of a system[17] so

$$E = V_{nn} + \langle \Psi_{MCSCF} | \hat{T} + \hat{V}_{ne} | \Psi_{MCSCF} \rangle + V_C[\rho] + E_{ot}[\rho(r), \Pi(r)] \ . \tag{37}$$

It is similar in form to Kohn-Sham density functional theory but rather than having the exchange-correlation energy functional be dependent upon only the total density, a new functional called the on-top pair density functional is used which is dependent on both the total density and the pair density. The on-top pair density , $\Pi(r)$, is used to look at the probability of two electrons of opposing spin to be found within the wave function.

The total density and pair density require only the one-body, D_{pq}, and two-body, d_{pqrs}, density matrices to be constructed,

$$\rho(r) = \sum_{pq} \phi_p(\mathbf{r})\phi_q(\mathbf{r})D_{pq} \tag{38}$$

and

$$\Pi(r) = \sum_{pqrs} \phi_p(\mathbf{r})\phi_q(\mathbf{r})\phi_r(\mathbf{r})\phi_s(\mathbf{r})d_{pqrs} \ . \tag{39}$$

The two denisty matrices can then be used to calculate the on-top functional. This functional takes on a form similar to the original exchange-correlation energy by translating the GGA

such that

$$
E_{\text{ot}}[\rho(r), \Pi(r)] = E_{\text{XC}} \left[\rho(r), \begin{cases} \rho(r)(1-R)^{1/2}, & R \leq 1 \\ 0, & R > 1 \end{cases}, \rho'(r), \begin{cases} \rho'(r)(1-R)^{1/2}, & R \leq 1 \\ 0, & R > 1 \end{cases} \right]
$$
(40)

where

$$
R = \frac{4\Pi(r)}{\rho(r)^2} ,
$$
(41)

but R can become complicated with multireference systems since R is not necessarily unitary.[18]

Some advantages to this method are that the spin-symmetry is enforced, it provides a more natural representation for strongly correlated systems, and that it includes dynamic correlation without the factorial increase in cost.[15] MC-PDFT is unique in that it includes dynamic correlation unlike CASSCF where many-body perturbations are used at the end. The inclusion of this correlation comes from how the calculation takes place. The algorithm is quite elegant and simple with the initial step optimizing the MCSCF wave function self-consistently. Once optimized, the wave function is used to compute the energy contributions from the nuclear repulsion, kinetic energy, nuclear-electron attraction, and Coulombic interaction energy. The on-top functional is then computed using the total electron density and on-top pair density to calculate the on-top energy. Lastly the combination of the MCSCF energy contributions and the on-top energy give the total MC-PDFT energy.

Applications of MC-PDFT

Despite being young, MC-PDFT is becoming a better known name in the sea of computational theories due to its performance for a variety of applications. These include, but are not limited to, bond energies and potential energy curves, proton affinities, ground and excited state charge transfer, valence and Rydberg excitations of molecules, and barrier heights.[15]
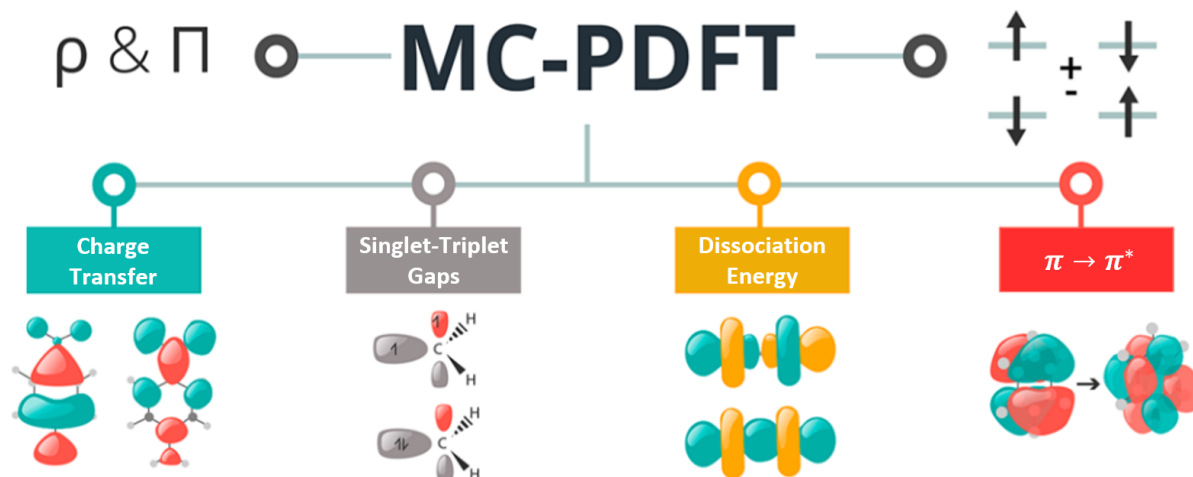
Figure 9: Examples of the applications MC-PDFT has tested for.

Diels-Alder

Although MC-PDFT has been applied to a wide variety of systems, including pericyclic reactants, it has not been used previously for in-depth study of cycloadditions. The simplest cycloaddition is the Diels-Alder reaction of 1,3-butadiene with ethylene, where the transition state can be on either a concerted synchronous path or a diradical stepwise path. After years of study, the reaction path is now known to be a concerted synchronous one, and the prediction of the correct kind of path can serve as a benchmark for testing new methods. This study analyzes the geometries, enthalpies of activation, and reaction enthalpies using complete active space PDFT and compares to the benchmark studies to assess if this method can perform as well as Kohn-Sham DFT and other MC methods.
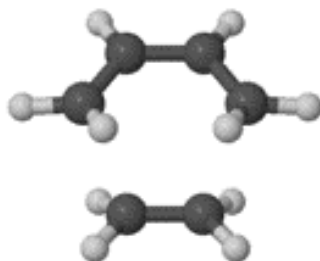

Figure 10: Concerted transition state of the Diels-Alder reaction of 1,3-butadiene and ethylene.

In comparing the concerted synchronous transition state's activation enthalpy across multiple different theories, Fig. 11, it can be confirmed that CAS-PDFT, MC-PDFT with a CASSCF wave function, is more accurate than other methods at calculating the experimental activation energy. course more systems and more properties would need to be computed to have full confidence in the theory as a whole, but the study of the Diels-Alder system is just one more step toward confirming the validity of MC-PDFT.
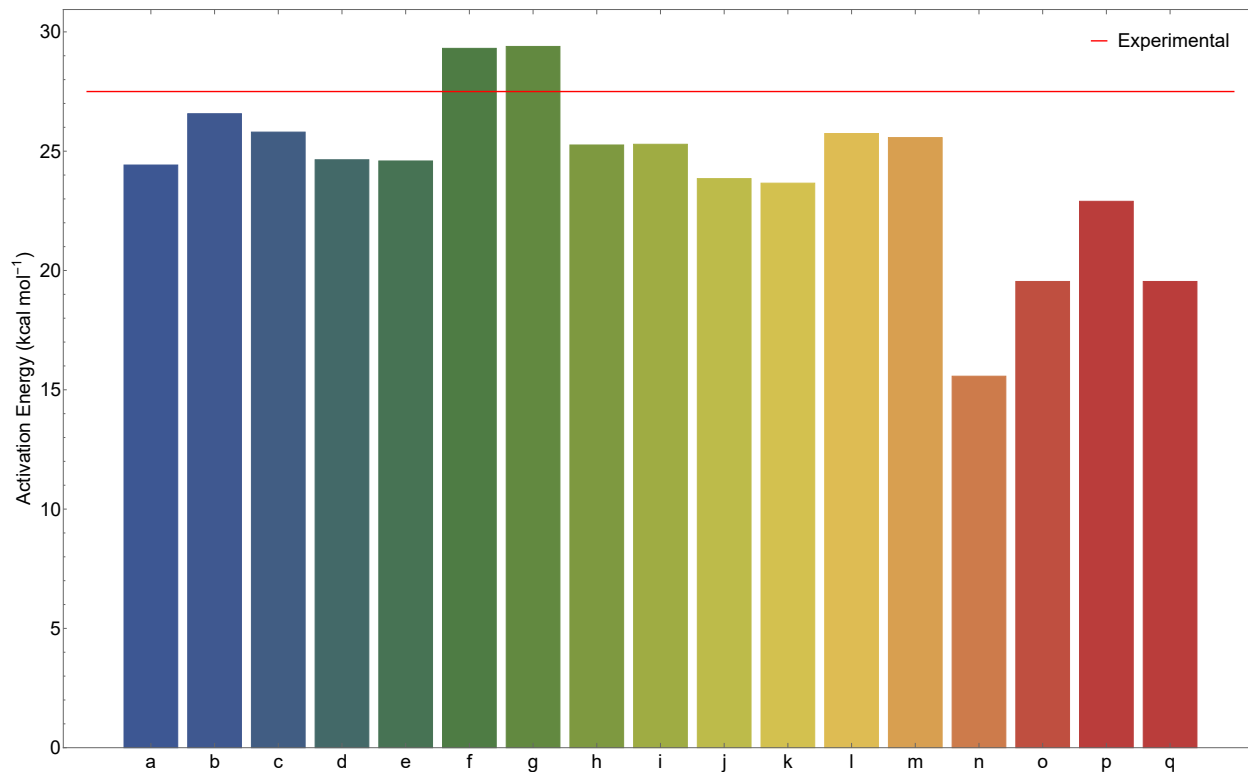

Figure 11: Calculated activation energies of the CTS at various levels of theory: (a) CAS-PDFT/6-31G**, (b) CAS-PDFT/6-311G(2d,p), (c) CAS-PDFT/cc-pVDZ, (d) MN15/ma-TZVP, (e) MN15/aug-cc-pVTZ, (f) B3LYP/ma-TZVP, (g) B3LYP/aug-cc-pVTZ, (h) M06/ma-TZVP, (i) M06/aug-cc-pVTZ, (j) M06-2X/ma-TZVP, (k) M06-2X/aug-cc-pVTZ, (l) revM06/ma-TZVP, (m) revM06/aug-cc-pVTZ, (n) PBE/6-31G**, (o) PBE/aug-cc-pVTZ, (p) PBE0/aug-cc-pVTZ, and (q) UPBE/aug-cc-pVTZ.

Conclusion

Quantum chemical methods are all trying to accomplish the same thing but in different ways. Certain theories perform well for some systems but fail to accurately capture the electron correlation for others. Density functional theory makes the energy a functional of the electron density, but is limited by approximate exchange-correlation functionals and the orbital formalism introduced by Kohn-and Sham. DFT is regularly used in systems with over 50 atoms and is a staple in both periodic systems and biomolecules. Wave function theory calculates the energy from a Slater determinant(s). It is an inexact theory, if Hartree-Fock is used as its base, and requires the addition of more determinants or parameters to reintroduce electron correlation. Multiconfiguration self-consistent filed theory uses the linear combination of Slater determinants to recover static electron correlation, but fails to capture dynamic correlation. Multiconfiguration pair-density functional theory is then the combination of the two. It is similar to Kohn-Sham density functional theory but replaces the exchange-correlation functional with the on-top functional.

Although the numerous amount of theories may seem daunting, quantum chemical methods are constantly being worked on to improve their reliability and expand their range of applications. It is in the best interest of the chemical community to recognize the importance of creating more efficient and accurate ways to compute chemical properties. The advancements in this area can help many different areas of chemistry and even areas within physics. Through understanding quantum chemical methods, a knowledge of the underlying mathematics of chemistry can be gained to help provide a greater context for how chemical phenomena occur.

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