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Fractional Electron Number, Temperature, and Perturbations in Chemical Reactions

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We provide a perspective on the role of non-integer electron number in the density functional theory approach to chemical reactivity (conceptual DFT), emphasizing that it is important to not only treat reagents as open systems, but also as non-isolated systems, in contact with their surroundings. The special case of well-separated reagents is treated in some detail, as is the case where reagents interact strongly. The resulting expressions for the chemical potential of an acid, $\mu_{\text{acid}} = -(\alpha I + A)/(1+\alpha)$, and a base, $\mu_{\text{base}} = -(I + \alpha A)/(1+\alpha)$, elucidate and generalize the assumptions inherent in the chemical potential models of Mulliken (α=1) and Gazquez, Cedillo, and Vela (α=3). In the strongly-interacting limit, it is appropriate to model the effects of the environment as a state-specific effective temperature, thereby providing a rigorous justification for the phenomenological effective-temperature model one of the authors previously proposed. The framework for the strongly interacting limit subsumes our model for weakly-interacting subsystems at nonzero temperature, the case of open but otherwise noninteracting subsystems, and the zero-temperature limit.

1. Introduction

The study of chemical reactivity is today, and it will likely remain, one of the most active areas of research in chemistry. In contrast to the purely empirical nature of this field in the distant past, chemists can now probe deeper and reveal the intricacies of chemical reactions, using the fundamental principles of quantum mechanics. That is why, in concert with the

development of more precise and powerful experimental techniques, there is great interest in sharpening the theoretical tools we need to understand and predict the behavior of chemical reagents. To this end one can identify two broad classes of theoretical approaches, those that pursue a quantitative description (typically using state-of-the-art computer software and hardware) and those that aim for a qualitative understanding (often using simplified models and broad chemical principles). In this work we will analyze a popular approach that lies in the thin overlapping region between these two families: conceptual density functional theory (DFT), also known as chemical reactivity theory within DFT, DFT for chemical reactivity, and density functional reactivity theory.[1-7]

One of the simplest ways to present conceptual DFT is through the perturbative expansion:[7]

$$\Delta E = \left(\frac{\partial E}{\partial N}\right)_{v(\mathbf{r})}\Delta N + \int\left(\frac{\delta E}{\delta v(\mathbf{r})}\right)_{N}\Delta v(\mathbf{r})\,d\mathbf{r} + \frac{1}{2}\left(\frac{\partial^2 E}{\partial N^2}\right)_{v(\mathbf{r})}\Delta N^2 + \int\left(\frac{\delta^2 E}{\delta v(\mathbf{r})\partial N}\right)\Delta N\Delta v(\mathbf{r})\,d\mathbf{r} + \frac{1}{2}\int\left(\frac{\delta^2 E}{\delta v(\mathbf{r})\delta v(\mathbf{r}')}\right)_{N}\Delta v(\mathbf{r}')\Delta v(\mathbf{r})\,d\mathbf{r}d\mathbf{r}' + \ldots \quad (1)$$

The simple idea behind Eq. (1) is that any molecular system can be characterized by its number of electrons, N, and its external potential, $v(\mathbf{r})$. Accordingly, a chemical process can be described by its respective ΔN and $\Delta v(\mathbf{r})$ variations. Therefore, the change of any state function (e.g. the energy) associated to this process could be calculated as in Eq. (1).

From a mathematical point of view, Eq. (1) is nothing more than an attempt to calculate (or at least approximate), the value of a function in one point in function space, $E\left[N+\Delta N, v(\mathbf{r})+\Delta v(\mathbf{r})\right]$, starting from another point of its domain (from now on referred to as the "initial state" or "initial point"), $E\left[N, v(\mathbf{r})\right]$. This could seem like an unnecessarily indirect approach for computing the difference $\Delta E = E\left[N+\Delta N, v(\mathbf{r})+\Delta v(\mathbf{r})\right] - E\left[N, v(\mathbf{r})\right]$, but the main attraction of conceptual DFT does not rest in the quantitative accuracy of such expressions. The great advantage of an approach based on Eq. (1) lies in the possibility of working with the coefficients of the expansion, namely, the (functional) derivatives $\frac{\delta^a E}{\delta^b v(\mathbf{r})\partial^{a-b}N}$ (which can in principle be calculated using any quantum chemical method).[2] These coefficients, which depend only on the molecular system being studied and not on the properties of its reaction partner,[7] are

widely regarded as reactivity descriptors, and there is a great body of work supporting the fact that they can be used to quantify a variety of chemical concepts, such as the electronegativity[8-10] and the chemical hardness.[11-16] In this way it is easy to understand why Eq. (1) has played such an important role in the modern study of chemical reactivity. A chemical reaction can be viewed as a change in its reactants, and the change in the reactants can be modeled using the partial derivatives in Eq. (1) evaluated at the initial stage of the reaction. These partial derivatives determine how the molecule's energy changes in response to a perturbation, and therefore whether a specific change is favorable (or less unfavorable). Then, the more favorable (or less unfavorable) responses will indicate which reactions are more likely to occur.[2] It is important to note that usually one does not need to evaluate many of the coefficients (descriptors) appearing in Eq. (1), which is usually truncated at second order.[7] If in the reaction of interest charge transfer effects are predominant over the purely electrostatic changes, then one can consider only the terms associated with the ΔN changes (e.g. $\left(\frac{\partial E}{\partial N}\right)_{v(\mathbf{r})}$, $\left(\frac{\partial^2 E}{\partial N^2}\right)_{v(\mathbf{r})}$ and perhaps $\left(\frac{\delta^2 E}{\delta v(\mathbf{r})\partial N}\right)$). The converse is true if electrostatic interactions predominate. Finally, while we have centered our discussion on the energy of the system, the above formalism can be reformulated for other state functions.[2, 10, 17-19] This allows one to include, for example, solvent effects and entropic contributions.

This elegant mathematical framework, together with the great number of applications using conceptual DFT, support the use of Eq. (1) as an attractive and powerful method for studying chemical reactivity. However, as straightforward and clear as this procedure might appear, there are a number of essential issues that must be addressed in order to provide it with a strong physical justification. For example: How should one select the initial state/point at which the perturbative expansion is centered? Is there a way to justify the presence of derivatives with respect to the number of electrons, since this requires considering non-integer numbers of particles? Do the descriptors appearing in Eq. (1) depend solely on a given reactant? What are the possible working expressions for the descriptors? These, and other similar questions, will be our main concern in the present work, as we intend to go deeper into the physical foundations of conceptual DFT than usual. Our primary focus will be the problem of the variation of the molecular properties with respect to the number of electrons, and especially variations in the energy (e.g. the *E* vs. *N* problem). This is a fundamental problem in conceptual DFT due to the

presence of the derivatives with respect to N in the descriptors presented above, since the precise mathematical definition of these quantities requires working with systems with non-integer numbers of particles. In the next section we will discuss the general results concerning this problem when formulated for isolated reagents at 0 Kelvin, showing the inadequacy of that approach for chemical reactivity studies. Then we explore the natural generalizations of this procedure, pointing out the necessity of taking into account both finite temperatures and the interaction with the molecular surroundings in order to properly describe reacting species. Throughout this paper, we will focus on the chemical potential, leaving the detailed analysis of other conceptual DFT descriptors for subsequent work.

2. Isolated reagents at absolute zero

Though it may seem that the notion of "a fraction of an electron" lacks any physical meaning, it can be provided with a sound theoretical basis for this idea by considering quantum open systems.[10, 20, 21] Specifically, if a system is allowed to exchange particles (i.e. electrons) with its surroundings, then the average number of such particles can be an arbitrary (non-negative) real number. (Formally, the states of these systems do not necessarily have to be eigenstates of the number of particles and so, in the following, when we talk about the number of electrons/particles in the system we will be referring to the average number of particles.) This fits naturally with our interest in chemical reactivity, since in virtually every chemical reaction electrons flow between the molecular reagents, between the reagents and their surroundings, and even between different regions of the same reagent.

Quantum open systems can be described using the grand-canonical (GC) formalism.[10, 21-23] In this framework, quantum states are described not by a state function, but by a density matrix (DM), which has the general form:

$$D = \sum_{M} \sum_{k} {}^{M}\omega_k \left| {}^{M}\Psi_k \right\rangle \left\langle {}^{M}\Psi_k \right| \tag{2}$$

In this expression the microcanonical density matrices $\left| {}^{M}\Psi_k \right\rangle \left\langle {}^{M}\Psi_k \right|$ represent pure states where the index k runs over a complete basis for every number of particles $M \in \mathbb{N}$. The coefficients ${}^{M}\omega_k$ are just statistical weights, and as such they satisfy normalization ($\sum_{M} \sum_{k} {}^{M}\omega_k = 1$) and non-negativity ($\forall M, k : 0 \leq {}^{M}\omega_k$) constraints. In full analogy with the wave

function in the closed system picture, knowledge of the DM is all we need to calculate the average value, Q, of any observable $\hat{Q}$:

$$Q = \mathrm{Tr}\left(\hat{Q}D\right) \tag{3}$$

where $\mathrm{Tr}\left(\hat{B}\right)$ indicates the trace of operator $\hat{B}$.

The next step is to determine the values of ${}^{M}\omega_k$ that are chemically relevant for studying chemical systems and their changes. For chemical reactions and molecular rearrangements occurring on the ground-state potential energy surface, it is natural to consider the ground state of the system. The ground state can be determined invoking the variational principle,[10, 24] which can be stated in two different (but entirely equivalent) ways. Either we find the minimum of the expectation value of the Hamiltonian, $\mathrm{Tr}\left(\hat{H}D\right)$, over all GC-DMs corresponding to the given number of particles:

$$E\left(N\right)_0 = \underbrace{\min}_{\left\{D\middle|\mathrm{Tr}\left(D\hat{N}\right)=N\right\}} \mathrm{Tr}\left(\hat{H}D\right), \tag{4}$$

where $\mathrm{Tr}\left[D\hat{N}\right] = N$ constrains the number of particles to be correct and $\hat{N}$ is the number operator. Or, on the other hand, we perform an unconstrained minimization with respect to the number of particles, imposing this condition via a Lagrange multiplier, μ:

$$\delta\left\{\mathrm{Tr}\left(\hat{H}D\right) - \mu\mathrm{Tr}\left(D\hat{N}\right)\right\} = 0 \tag{5}$$

where μ is chosen so that $\mathrm{Tr}\left(D\left(N\right)_0\hat{N}\right) = N$, where $D\left(N\right)_0$ denotes the solution of Eq. (5) (and hence also of Eq. (4)). This Lagrange multiplier can be shown to be the chemical potential of the system,[9]

$$\mu = \frac{\partial E}{\partial N} \tag{6}$$

Here, and in the following, we dropped the sub-index indicating that the partial derivative must be taken at constant external potential $v(\mathbf{r})$.

One key feature of the chemical potential is that for the ground state of any system, it is a global constant, and does not depend on position in space or on the specific molecular fragment in a supersystem.[1, 9, 25] This is easily proved by noting that, in the ground state, there is no net

transfer between different regions in the system and it is the mathematical statement of Sanderson's principle of electronegativity equalization.[26]

If the ground state energy is a convex function of the number of particles (there are no known exceptions for isolated Coulomb systems like molecules), the solution to Eqs. (4) and (5) can be stated explicitly,[20, 27-29]

$$D\left(N=M+x\right)_0 = x\left|{}^{M+1}\Phi\right\rangle\left\langle{}^{M+1}\Phi\right| + \left(1-x\right)\left|{}^{M}\Phi\right\rangle\left\langle{}^{M}\Phi\right| \tag{7}$$

where $0 \le x \le 1$ and $\left|{}^{M}\Phi\right\rangle$ represents the ground state of the (closed) system with M electrons. As it has been remarked before, this solution relies in the fact that the corresponding integer-particle states are not degenerate (an assumption we will make in the following). Another consequence of the convexity of E is that its Legendre transform is well defined,[2, 30] so we can equivalently study the same system using the new state function:

$$G = E - \mu N \tag{8}$$

The variational principle in terms of G is just Eq. (5). Now, the independent variables necessary to describe the state of the system are μ and $v(r)$. This opens the possibility of analyzing a perturbative expansion analogous to Eq. (1), replacing E with G and N with μ. This is known as the "open system picture" (as opposed to the "closed system picture" of Eq. (1)) in the traditional conceptual DFT terminology.[2] However, it must be noticed that both "pictures" are based on states given by Eq. (2). Then, in the sense of Malek and Balawender[30] (MB from now on), we could consider that both pictures correspond to open systems (following their nomenclature, the closed picture will correspond to partially-open systems); they only differ in the independent variables chosen to describe the states and their changes. This is a natural (and, as argued previously, necessary) consideration, since is the only way to physically account for non-integer numbers of particles. This terminology indicates that the nature of the quantum open systems we consider are determined by the way we describe their states (e.g., their DMs), rather than by the state functions (which are determined by the selected independent variables). As MB pointed out, the difference with the usual thermodynamical approach relies on the fact that classical closed (canonical) systems are supposed to have a constant, integer, number of particles, while in this picture, a partially open system is one where there are no fluctuations of N, but N can nonetheless be any non-negative real number.[30]

Substituting Eq. (7) into Eq. (3) gives an expression for how any observable varies with the number of electrons for a system in its ground state. The only thing that remains to be specified before the perturbative series (Eq. (1)) can be evaluated, then, is the initial state. One could argue that states with integer numbers of electrons are the most convenient. First, reagents have an integer number of electrons before the reaction starts, and second, the vast majority of the computational quantum chemistry methods perform poorly (if they are even defined!) for systems with non-integer N.[31, 32] However, choosing an N to be an integer has an apparent drawback. Since Eq. (7) is, by construction, consistent with a GC formulation and leads to:

$$ {}^{M}E = \left\langle {}^{M}\Phi \middle| \hat{H} \middle| {}^{M}\Phi \right\rangle = E(M) = \mathrm{Tr}\left(D(M)_0 \hat{H} \right) \tag{9} $$

when M is an integer, a recently proven theorem implies that either (a) the chemical potential is zero for every M or (b) this model is not differentiable at integer numbers of particles[33]. While both possibilities are problematic, the former is actually more devastating. Since the negative of the chemical potential can be identified with the tendency of a system to gain electrons (e.g. $-\mu$ is a measure of a system's electronegativity),[9, 10] a constant, zero value, of μ for every integer electron number is in clear disagreement with experimental facts. Fortunately, this is not the case, and it is well known that the model derived from Eq. (7) is nondifferentiable at integer N. Instead, at these points we will have one-sided derivatives, which can be easily calculated as:

$$ {}^{M}\mu^{+} = \lim_{x\to 0^{+}} \frac{E(M+x)-E(M)}{x} = {}^{M+1}E - {}^{M}E = -A \tag{10} $$

$$ {}^{M}\mu^{-} = \lim_{x\to 0^{-}} \frac{E(M+x)-E(M)}{x} = {}^{M}E - {}^{M-1}E = -I \tag{11} $$

where I and A stand for the ionization potential and electron affinity of the M-electron system.

Similarly, one can define higher-order one-sided derivatives, and rewrite the perturbative series in Eq. (1) as two formulas, one appropriate for electron-acceptance and one appropriate for electron donation:

$$ \Delta E = E[M+\Delta N] - E[M] = {}^{M}\mu^{+}\Delta N + \sum_{k>1} \frac{1}{k!} \left(\frac{\partial^k E}{\partial N^k} \right)^{+}_{N=M} (\Delta N)^k \text{ if } \Delta N > 0 \tag{12} $$

$$ \Delta E = E[M+\Delta N] - E[M] = {}^{M}\mu^{-}\Delta N + \sum_{k>1} \frac{1}{k!} {}^{M} \left(\frac{\partial^k E}{\partial N^k} \right)^{-}_{N=M} (\Delta N)^k \text{ if } \Delta N < 0 \tag{13} $$

While these equations are mathematically correct (notice that we have not made any assumptions), their chemical relevance merits further discussion. To this end, consider a simple chemical process where two reagents, *X* and *Y*, combine to form a product *XY*. First, note that—independently of the sign of ΔN—every partial derivative $\frac{\partial^k E}{\partial N^k}$ with $k>1$ is identically equal to 0, which is not surprising considering the linear nature of the model shown in Eq. (7). This implies that chemical descriptors such as the hardness, $\eta = \frac{\partial^2 E}{\partial N^2}$, play no role in the analysis of Eqs. (12) and (13).[34, 35]

Second, note that in order to apply Eqs. (12) and (13), we must first know the direction of net charge transfer. In principle, this can be easily done by considering both possibilities: net electron flow from *X* to *Y* $\left(X \to Y\right)$ and net electron flow from *Y* to *X* $\left(Y \to X\right)$, then choosing the most energetically favorable. For example, if the process of moving $\Delta N > 0$ electrons from *X* to *Y* is more favorable than moving them from *Y* to *X* we must have:

$$\Delta^{X\to Y}E < \Delta^{Y\to X}E \tag{14}$$

where:

$$\Delta^{X\to Y}E = \Delta^{X\to Y}E_X + \Delta^{X\to Y}E_Y \tag{15}$$

$$\begin{aligned}\Delta^{X\to Y}E_X &= -\mu_X^-\Delta N \\ \Delta^{X\to Y}E_Y &= \mu_Y^+\Delta N\end{aligned} \tag{16}$$

with equivalent expressions holding for the $\Delta^{Y\to X}E$ change. (For simplicity, we have omitted for the supra-indexes in the chemical potentials indicating that they are calculated for integer numbers of particles, *M*). Substituting Eqs. (10), (11), (15) and (16) in Eq. (14) we thus obtain the criteria for electrons to go from *X* to *Y*, namely:

$$I_X - A_Y < I_Y - A_X \tag{17}$$

Now it is easy to see another problem with this procedure. Since the largest atomic electron affinities are lower than the lowest atomic ionization energies, neither charge transfer process will be energetically favored. Therefore, as noted by Perdew, Parr, Levy and Balduz, this model predicts that there will be no electron transfer in any neutral diatomic molecule.[20] This result is a mere consequence of the initial assumptions considered in this section—isolated systems at absolute zero temperature—and indeed it is the only reasonable outcome in this situation. This

strongly suggests that we should consider other frameworks as our starting point for studying chemical reactivity.

3. Finite temperature

Since the consideration of GC states of isolated systems at 0 Kelvin is not suitable for studying chemical reactivity, we must look for generalizations of these conditions. As we cannot renounce the GC description of the states, the next logical step is to look for a formulation that explicitly accounts for the role of temperature.[21, 30, 36-38] This brings a qualitative difference with respect to the previous case, because now the most adequate states to describe our system and its changes are not the ground but equilibrium states.[10] In complete analogy with the zero-temperature case, we can determine such states using either of two state functions: the Helmholtz free energy, A, or the grand-potential (or thermodynamic potential), Ω:[10, 30]

$$\mathrm{A} = E - TS \tag{18}$$

$$\Omega = E - TS - \mu N \tag{19}$$

where S represents the (electronic) entropy. As in the previous section, minimization of Eq. (18) must be performed over the set of GC-DMs having the correct number of electrons, while in Eq. (19) we can use any GC-DM.

In fact, both variational principles can be shown to follow from a general, maximum entropy, principle that has a similar form to Eq. (5):[30]

$$\delta\left\{S(D) - \beta\left[\mathrm{Tr}\left(\hat{H}D\right) - \mu\mathrm{Tr}\left(D\hat{N}\right)\right]\right\} = 0 \tag{20}$$

Here, $\beta = 1/T$ and the entropy is a function of the DM of the state, which has the familiar form:

$$S(D) = -\mathrm{Tr}\left(D\ln D\right) \tag{21}$$

(Following MB we are working with temperatures expressed in energy units, thus the absence of Boltzmann's constant in the previous expressions.)

As in the past section, the independent variables for A are N and $v(r)$, while for Ω we change the number of particles using the chemical potential. Then, the equilibrium state determined by means of A (Ω), will correspond to the system under the constraint of constant N (μ). (As it is well known from Statistical Mechanics, both descriptions are equivalent in the

thermodynamic limit.) In this context however, the chemical potential is not defined as in Eq. (6) , but instead as:[10]

$$\mu = \frac{\partial \mathrm{A}}{\partial N} \tag{22}$$

There are several advantages related to this definition, which Kaplan argued is the only appropriate choice.[39] First, since we are basing our study in the state functions shown in Eqs. (18) and (19) it is natural to replace the perturbative series Eq. (1) by their analogues in terms of the new state functions, namely:

$$\begin{aligned}\Delta \mathrm{A} = &\left(\frac{\partial \mathrm{A}}{\partial N}\right)_{v(r)} \Delta N + \int \left(\frac{\delta \mathrm{A}}{\delta v(r)}\right)_N \Delta v(r)\, dr + \frac{1}{2}\left(\frac{\partial^2 \mathrm{A}}{\partial N^2}\right)_{v(r)} \Delta N^2 + \\ &\int \left(\frac{\delta^2 \mathrm{A}}{\delta v(r) \partial N}\right) \Delta N \Delta v(r)\, dr + \frac{1}{2}\int \left(\frac{\delta^2 \mathrm{A}}{\delta v(r) \delta v(r')}\right)_N \Delta v(r') \Delta v(r)\, dr dr' + \ldots\end{aligned} \tag{23}$$

and

$$\begin{aligned}\Delta \Omega = &\left(\frac{\partial \Omega}{\partial \mu}\right)_{v(r)} \Delta \mu + \int \left(\frac{\delta \Omega}{\delta v(r)}\right)_\mu \Delta v(r)\, dr + \frac{1}{2}\left(\frac{\partial^2 \Omega}{\partial \mu^2}\right)_{v(r)} \Delta \mu^2 + \\ &\int \left(\frac{\delta^2 \Omega}{\delta v(r) \partial \mu}\right) \Delta \mu \Delta v(r)\, dr + \frac{1}{2}\int \left(\frac{\delta^2 \Omega}{\delta v(r) \delta v(r')}\right)_N \Delta v(r') \Delta v(r)\, dr dr' + \ldots\end{aligned} \tag{24}$$

These equations allow us to redefine all the traditional reactivity indicators in an equivalent way but now, since we are working at finite temperatures, these descriptors include not only energetic, but also entropic effects. It is easy to see that all the well-known relationships between reactivity descriptors (*e.g.* the Berkowitz-Parr relation)[40] automatically hold, since the mathematical structure of the theory remains unaltered. If, on the other hand, we had chosen to retain Eq. (6) as the definition of the chemical potential, many of these relations would be lost, even the simple inverse relation between the hardness and the softness.[1, 37, 41] While the retention of these sorts of identities is convenient, the principal reason to adopt Eq. (22) as the definition of the chemical potential is because only in this way we can recover Sanderson's principle,[1, 26] which is the most important property of the chemical potential.

Another qualitative difference between the energy-based approach (section 1) and the approach based on the free energy or the grand potential is that the variational principle, Eq. (20) , contains a non-linear dependence on the DM in the form of the entropy. This equilibrium DMs likewise vary nonlinearly (Eq. (7) is no longer true) with the number of particles, as do other

observables. Specifically, the equation for the equilibrium GC-DM of a system with chemical potential μ and temperature T, is:[10, 30]

$$D(\mu)_T = \frac{\exp\left[-\beta\left(\hat{H}-\mu\hat{N}\right)\right]}{\mathrm{Tr}\left\{\exp\left[-\beta\left(\hat{H}-\mu\hat{N}\right)\right]\right\}} = \frac{\sum_{M,i}\left|{}^{M}\Phi_i\right\rangle\left\langle{}^{M}\Phi_i\right|\exp\left[-\beta\left({}^{M}E_i-\mu M\right)\right]}{\sum_{M,i}\exp\left[-\beta\left({}^{M}E_i-\mu M\right)\right]} \tag{25}$$

where the sub index i labels the different excited states of the system. This DM also corresponds to a given number of electrons, N, which can be determined by applying Eq. (3):

$$N(\mu) = \frac{\sum_{M,i} M\exp\left[-\beta\left({}^{M}E_i-\mu M\right)\right]}{\sum_{M,i}\exp\left[-\beta\left({}^{M}E_i-\mu M\right)\right]} \tag{26}$$

It is convenient to rewrite Eq. (25) as a function of N, instead of μ. Because the state functions we consider are strictly convex, the function $N(\mu)$ is invertible. Inserting its inverse into Eq. (25) gives an expression for the N-electron GC-DM,

$$D(N)_T = \frac{\exp\left[-\beta\left(\hat{H}-\mu(N)\hat{N}\right)\right]}{\mathrm{Tr}\left\{\exp\left[-\beta\left(\hat{H}-\mu(N)\hat{N}\right)\right]\right\}} \tag{27}$$

Until now we have not made any assumptions, but to explore practical applications of this model we need to restrict the allowed states so that the sum-over-states in Eqs. (25)-(27) has a tractable number of terms. If we restrict ourselves to systems at temperatures that are low compared to the spacing between energy levels, and to the situation where the number of electrons is in the vicinity of a specified integer M, then we can neglect the excited states and deal only with the ground states of the systems with M, $M+1$, and $M-1$ electrons. This greatly simplifies the equations, and the results can be conveniently expressed in terms of the ionization potential, I, and electron affinity, A. For example, the expression for the (average) number of electrons is:

$$N = M + \frac{\exp\left[\beta(A+\mu)\right]-\exp\left[-\beta(I+\mu)\right]}{1+\exp\left[-\beta(I+\mu)\right]+\exp\left[\beta(A+\mu)\right]} \tag{28}$$

As discussed previously, it is sensible to choose systems with integer N as the initial states for the perturbative expansions. In contrast to the treatment in section 2, however, differentiation with respect to the number of electrons at integer N is now unproblematic. In particular, from Eq. (28) is easy to verify that:

$$\mu(M) = -\frac{I + A}{2} \tag{29}$$

It is also clear that the chemical potential is an increasing function of the number of electrons, *i.e.*,

$$\Delta\mu = \mu(N) - \mu(M) > 0 \Rightarrow \Delta N = N - M > 0 \ . \tag{30}$$

We can also derive expressions for other reactivity descriptors. For example, assuming again the simplified 3-state model constructed from the ground states of the M, M–1, and M+1 electron systems, the second derivative of the Helmholtz free energy, called the hardness and denoted η, can be evaluated as:

$$\left(\frac{\partial^2 \mathrm{A}}{\partial N^2}\right) = \eta = (P + Q)^{-1} \tag{31}$$

with

$$P = \frac{\beta\left\{\exp\left[\beta\left(A + \mu(N)\right)\right] + \exp\left[-\beta\left(I + \mu(N)\right)\right]\right\}}{1 + \exp\left[\beta\left(A + \mu(N)\right)\right] + \exp\left[-\beta\left(I + \mu(N)\right)\right]} \tag{32}$$

$$Q = -\frac{\beta\left\{\begin{matrix}\exp\left[\beta\left(A + \mu(N)\right)\right] \\ +\exp\left[-\beta\left(I + \mu(N)\right)\right]\end{matrix}\right\}\left\{\begin{matrix}\exp\left[\beta\left(A + \mu(N)\right)\right] \\ -\exp\left[-\beta\left(I + \mu(N)\right)\right]\end{matrix}\right\}}{\left\{1 + \exp\left[\beta\left(A + \mu(N)\right)\right] + \exp\left[-\beta\left(I + \mu(N)\right)\right]\right\}^2} \tag{33}$$

Here we have used the fact that, due to the convexity of the involved state functions, there is a one-to-one mapping between N and μ. Therefore, as in the previous equations, $\mu(N)$ is taken as a function of the number of particles (e.g. the inverse of the function given in Eq. (26)).

At integer numbers of particles $Q = 0$ and Eq. (31) simplies to

$$\eta(M) = \frac{1 + 2\exp\left(-\frac{1}{2}\beta\tilde{\eta}\right)}{2\beta\exp\left(-\frac{1}{2}\beta\tilde{\eta}\right)} \tag{34}$$

where $\tilde{\eta}_X$ is the Parr-Pearson hardness,[12, 30] defined as:

$$\tilde{\eta}_X = I_X - A_X \tag{35}$$

Notice that, consistent with the derivative discontinuity that occurs in absence of temperature effects, in the zero-temperature limit ($\beta\to\infty$), the expression for the chemical hardness in Eq. (34) diverges,[27, 34, 35, 42]

$$\lim_{\beta\to\infty} \eta(M) = \infty \tag{36}$$

In the zero-temperature case, charge transfer was completely forbidden. (I.e., molecules having integer numbers of electrons in all situations.) To analyze this in the present context let us consider two species, *X* and *Y*, which, according to our initial assumptions, do not interact with each other. From Eq. (30) it follows that if two molecules exchange electrons, the electrons flow from the reagent with larger chemical potential (less electronegativity) to the reagent with lower chemical potential (greater electronegativity). This means that *X* will donate electrons to *Y* if the Mulliken electronegativity[43] of *Y* is greater or, in terms of chemical potentials, if

$$-\frac{I_X + A_X}{2} > -\frac{I_Y + A_Y}{2} \tag{37}$$

In this case, the charge transfer is said to occur indirectly between the molecules, since each of them is only allowed to interact with their corresponding (ideal) electron reservoirs (i.e. the molecules are "externally open but mutually closed").[44] Initially, the reservoirs' chemical potentials correspond to those of the molecule with an integer number of electrons, μ_X and μ_Y, as given in Eq. (29). Then, after the charge transfer takes place, both reservoirs will have the same chemical potential, μ_{XY}. It is important to remark that during this process, *X* and *Y* are in equilibrium with their reservoirs, and their geometries remain unchanged.

To analyze the spontaneity of this process we will consider the overall change in the grand-potential:

$$\Delta\Omega = \Delta\Omega_X + \Delta\Omega_Y \tag{38}$$

with:

$$\Delta\Omega_X = \Omega_X(\mu_{XY}) - \Omega_X(\mu_X) \tag{39}$$

For a given equilibrium state:

$$\Omega(\mu,\beta) = -\frac{1}{\beta}\ln\left(\mathrm{Tr}\left\{\exp\left[-\beta\left(\hat{H}-\mu\hat{N}\right)\right]\right\}\right) \tag{40}$$

So, the charge transfer will take place if:

$$\exp\left(-\beta\Delta\Omega\right)>1 \tag{41}$$

In the specific case of our 3-state model:

$$\begin{aligned}\exp\left(-\beta\Delta\Omega\right)=&\left(\frac{1+\exp\left[\beta\left(A_X+\mu_{XY}\right)\right]+\exp\left[-\beta\left(I_X+\mu_{XY}\right)\right]}{1+\exp\left[\beta\left(A_X+\mu_X\right)\right]+\exp\left[-\beta\left(I_X+\mu_X\right)\right]}\right)\\&\times\left(\frac{1+\exp\left[\beta\left(A_Y+\mu_{XY}\right)\right]+\exp\left[-\beta\left(I_Y+\mu_{XY}\right)\right]}{1+\exp\left[\beta\left(A_Y+\mu_X\right)\right]+\exp\left[-\beta\left(I_Y+\mu_Y\right)\right]}\right)\\&\times\left(\frac{\exp\left\{\beta\left[\mu_{XY}\left(M_X+M_Y\right)\right]\right\}}{\exp\left[\beta\left(\mu_XM_X+\mu_YM_Y\right)\right]}\right)\end{aligned} \tag{42}$$

where M_X indicates the (integer) number of particles of the system with chemical potential μ_X. If we denote $\Delta\mu_X=\mu_{XY}-\mu_X$, this equation can be rewritten in a more elucidative form:

$$\begin{aligned}\exp\left(-\beta\Delta\Omega\right)=&\left(\frac{1+\left[\exp\left(-\beta\Delta\mu_X\right)+\exp\left(\beta\Delta\mu_X\right)\right]\exp\left(-\beta\tilde{\eta}_X/2\right)}{1+2\exp\left(-\beta\tilde{\eta}_X/2\right)}\right)\\&\times\left(\frac{1+\left[\exp\left(-\beta\Delta\mu_Y\right)+\exp\left(\beta\Delta\mu_Y\right)\right]\exp\left(-\beta\tilde{\eta}_Y/2\right)}{1+2\exp\left(-\beta\tilde{\eta}_Y/2\right)}\right)\\&\times\left(\frac{\exp\left\{\beta\left[\mu_{XY}\left(M_X+M_Y\right)\right]\right\}}{\exp\left[\beta\left(\mu_XM_X+\mu_YM_Y\right)\right]}\right)\end{aligned} \tag{43}$$

Since $e^{\alpha}+e^{-\alpha}\geq 2$, with equality only for α = 0, the first two terms of this expression are automatically greater or equal than 1. This means that a sufficient condition for the charge transfer to occur is that:

$$\mu_{XY}\left(M_X+M_Y\right)>\mu_XM_X+\mu_YM_Y \tag{44}$$

To study this inequality in more detail, we employ the traditional conceptual DFT approach to this problem, which uses Taylor series expansion in the (free) energy, truncated at second order. That is, we start from the expressions:

$$\Delta\mathrm{A}_X=\mu_X\Delta N_X+\frac{1}{2}\left(\frac{\partial^2\mathrm{A}_X}{\partial N^2}\right)\left(\Delta N_X\right)^2 \tag{45}$$

$$\Delta \mathrm{A}_Y = \mu_Y \Delta N_Y + \frac{1}{2}\left(\frac{\partial^2 \mathrm{A}_Y}{\partial N^2}\right)\left(\Delta N_Y\right)^2 \tag{46}$$

And then we look for the minimum in free energy by minimizing $\Delta \mathrm{A}_X + \Delta \mathrm{A}_Y$, subject to the constraint that $\Delta N_X = -\Delta N_Y$, where the extent of charge transfer is given by:

$$\Delta N_X = \frac{\exp\left[\beta\left(A_X + \mu_{XY}\right)\right] - \exp\left[-\beta\left(I_X + \mu_{XY}\right)\right]}{1 + \exp\left[-\beta\left(I_X + \mu_{XY}\right)\right] + \exp\left[\beta\left(A_X + \mu_{XY}\right)\right]} \tag{47}$$

As the Taylor series does not truncate exactly, we should verify that contributions from the third- and higher-order derivatives are negligible; this is true for sufficiently small amounts of charge transfer. Now we can determine the chemical potential after the charge transfer is complete:

$$\mu_{XY} = \frac{\mu_X \eta_Y + \mu_Y \eta_X}{\eta_X + \eta_Y} \tag{48}$$

Substituting this expression in Eq. (44), and, for simplicity, restricting ourselves to the isoelectronic case (e.g. $M_X = M_Y$) we will have:

$$\left(\eta_Y - \eta_X\right)\left(\mu_X - \mu_Y\right) > 0 \tag{49}$$

It is easy to see that the hardness, as expressed in Eq. (34), is a monotonically increasing function of the Parr-Pearson hardness (e.g. $\eta_Y > \eta_X \Leftrightarrow \tilde{\eta}_Y > \tilde{\eta}_X$). Then, the above inequality can be rewritten as:

$$\left(\tilde{\eta}_Y - \tilde{\eta}_X\right)\left(\mu_X - \mu_Y\right) > 0 \tag{50}$$

If we consider that the electron affinity is negligible compared to the ionization potential (which is known to be the case for most neutral organic molecules) we will have:

$$\mu_X \approx -\frac{I_X}{2};\ \tilde{\eta}_X \approx I_X \tag{51}$$

So Eq. (50) reads:

$$\left(I_Y - I_X\right)^2 > 0 \tag{52}$$

which is obviously true.

Once again we remark that the previous discussion only gives sufficient conditions for the charge transfer to be spontaneous, and it may be very well the case that there are other situations where this could happen. What this shows is that, for systems at positive temperature,

there are situations where charge transfer between unlike reagents is spontaneous. In the zero-temperature limit, Eq. (37) correctly predicts the direction of charge transfer, but this is "the right answer for the wrong reason" since, as discussed in conjunction with Eq. (17), at zero temperature fractional electron transfer is forbidden.[20]

By invoking finite temperatures we are able to obtain well-defined expressions for the reactivity descriptors and show that charge transfer is allowed in certain situations; these are appealing features of this formulation. Nonetheless, the tendency for the hardness to be enormous, and the extent of charge transfer to the correspondingly small, at the temperatures that are normally of chemical interest calls the utility of this treatment into question. Aside from this, however, there are other issues. The model predicts, correctly, that there will be no charge transfer between identical species. However it also predicts that there is no chemical potential change upon formation of any aggregate of the form X_n. In other words, this model indicates that atomic Chlorine and its homonuclear diatomic, Cl_2, have the same tendency to gain electrons. It also predicts that all conformers of X_n will have the same chemical potential. The model also predicts the incorrect direction of electron transfer in some molecules, notably heteronuclear diatomic molecules like BF, CF, and CO, where the dipole moment is directed contrary to the expectation one would have from electronegativity considerations alone.[28] This indicates, in fact, that the assumption that a system will have the same chemical response independently of its partner reagent should be reconsidered, and that one should design a framework that allows one to accommodate the peculiarities of different reaction conditions. In the treatment in section 2, such conditions are accommodated in a rudimentary, but useful way by stipulating that a molecule will have different response to nucleophilic and electrophilic attacks (cf. Eqs. (10) and (11)), but that approach forbade fractional electron transfer. The finite-temperature treatment in this section, by contrast, accommodates fractional electron transfer, but loses the ability to distinguish between electrophilic and nucleophilic responses. Such a treatment is adequate for studying the equilibrium between the system and an ideal reservoir of electrons with fixed temperature and chemical potential, with no consideration of any other species. Indeed, as pointed out by Nalewajski,[44] the interaction with other species is not modeled directly (the systems which are mutually closed), but through equilibration of their corresponding reservoirs.

4. Interacting reagents at finite temperature

To overcome these problems, it is necessary to move beyond the description of reagents as isolated systems. We achieve this by considering more general initial states which include some information about the system's environment. The first advantage of this formulation is that charge transfer is immediately allowed between the interacting species. This is a consequence of the fact that the sum of the electron densities of the isolated molecules does not correspond to a stationary state of the combined (interacting) system. The further (spontaneous) relaxation of the electron density (towards the ground or equilibrium state) drives the charge transfer.

Well-separated, weakly-interacting, reagents

Consider, for simplicity, the effects of a small external perturbation upon a given reactant. This can be modeled directly if we center our perturbation series on a point early in the reaction path, where reagents are far apart, but nonetheless already interacting with each other. We assume that we are working at positive temperature, so that the theoretical framework from section 3 is virtually unaltered. In particular, we are still looking for equilibrium states using a maximum entropy principle with the form:

$$\delta\left\{S(D)-\beta\left[\mathrm{Tr}\left(D\hat{H}'\right)-\mu Tr\left(D\hat{N}\right)\right]\right\}=0 \tag{53}$$

with solution (cf. Eq. (25)):

$$D(\mu)_T=\frac{\exp\left[-\beta\left(\hat{H}'-\mu\hat{N}\right)\right]}{\mathrm{Tr}\left\{\exp\left[-\beta\left(\hat{H}'-\mu\hat{N}\right)\right]\right\}} \tag{54}$$

The only difference between these equations and the corresponding ones from the non-interacting case is the presence of a modified Hamiltonian, $\hat{H}'$,

$$\hat{H}'=\hat{H}+\hat{P}_R \tag{55}$$

where $\hat{H}$ is the Hamiltonian of the isolated system and $\hat{P}_R$ is a perturbation that models the (small) interaction between the reagents. We defer specific models for the perturbation to future work, and focus here on the general implications of this revision. To do this, we again employ the three-state model used in the past section, noticing that now Eq. (28) must be rewritten as:

$$N=M+\frac{\exp\left\{-\beta\left[{}^{M+1}E'-\mu(M+1)\right]\right\}-\exp\left\{-\beta\left[{}^{M-1}E'-\mu(M-1)\right]\right\}}{\left(\exp\left\{-\beta\left[{}^{M-1}E'-\mu(M-1)\right]\right\}+\exp\left\{-\beta\left[{}^{M}E'-\mu M\right)\right]\right\}+\exp\left\{-\beta\left[{}^{M+1}E'-\mu(M+1)\right]\right\}\right)} \tag{56}$$

where:

$$^{M}E' = {}^{M}E + {}^{M}\varepsilon \tag{57}$$

are the eigenvalues of $\hat{H}'$ and the assumption of weak interactions means that the first-order perturbation theory expression should be reliable

$$^{M}\varepsilon = \left\langle {}^{M}\Phi \middle| \hat{P}_R \middle| {}^{M}\Phi \right\rangle \tag{58}$$

and that furthermore, for all M, $^{M}\varepsilon \approx 0$. By simplifying Eq. (56), we determine an expression for the chemical potential of the M-electron

$$\mu(M) = -\frac{I + A + \left({}^{M-1}\varepsilon - {}^{M+1}\varepsilon \right)}{2} \tag{59}$$

Here I and A refer to the ionization potential and electron affinity of the unperturbed system. It is interesting that this expression depends only on the perturbed energies of the states with M+1 and M–1 electrons. Equation (59) can be rewritten in terms of a single parameter,

$$\alpha = \frac{I - A + \left({}^{M-1}\varepsilon - {}^{M+1}\varepsilon \right)}{I - A - \left({}^{M-1}\varepsilon - {}^{M+1}\varepsilon \right)} \tag{60}$$

$$\mu(M) = -\frac{\alpha I + A}{1 + \alpha} \tag{61}$$

This expression generalizes the chemical potential expressions previously propounded by Gázquez, Cedillo and Vela (GCV from now on),[45, 46] using quadratic interpolation models. However, in the weakly-interacting limit $\alpha \approx 1$, in contrast to the value ($\alpha = 3$) chosen by GCV for electron-donating species.

One feature of this approach is that it does not make the usual division of molecular environments into electron-accepting (electrophilic) and electron-donating (nucleophilic) reagents. At least in principle, the introduction of $^{M-1}\varepsilon - {}^{M+1}\varepsilon$ (equivalently, α) allows one to analyze more general responses. The most obvious effect of this modification is the change in the tendency of the system to attract electrons. For example, $\alpha > 1$ corresponds to a perturbed system with greater electronegativity than its isolated counterpart described by Eq. (29). This makes sense: $\alpha > 1$ corresponds to $^{M-1}\varepsilon > {}^{M+1}\varepsilon$, indicating that the perturbation produced by the reagent preferentially stabilizes the M + 1 electron state, making it more energetically accessible than it

was in the idealized "Mulliken" case. Therefore, this perturbation will enhance the tendency of the system to gain electrons.

In their model, GCV give distinct expressions for the chemical potentials of electron acceptors (acids) and electron donors (bases), namely,[45]

$$^{\mathrm{GCV}}\mu(M)_{\mathrm{base}} = -\frac{3I + A}{4} \tag{62}$$

$$^{\mathrm{GCV}}\mu(M)_{\mathrm{acid}} = -\frac{I + 3A}{4} \tag{63}$$

Given the established utility of the GCV model,[46, 47] it is interesting to analyze under what conditions expressions like these might be reliable; i.e., can a given acid/base pair be characterized by chemical potentials of the form

$$\mu(M)_{\mathrm{base}} = -\frac{I + \alpha A}{1 + \alpha} \tag{64}$$

$$\mu(M)_{\mathrm{acid}} = -\frac{\alpha I + A}{1 + \alpha} \tag{65}$$

Motivated by the considerations that led to the GCV model, let us start by assuming that the acid and the base have the same hardness, so that their differential reactivity is governed entirely by their chemical potential. Referring to Eq. (60), it becomes clear that Eqs. (64) and (65) correspond to the assumption that the differential stabilization of the M+1-electron state of the acid is the same as the differential stabilization of the M–1-electron state of the base. That is,

$$^{M-1}\varepsilon_{\mathrm{acid}} - {}^{M+1}\varepsilon_{\mathrm{acid}} = {}^{M+1}\varepsilon_{\mathrm{base}} - {}^{M-1}\varepsilon_{\mathrm{base}} \tag{66}$$

along with the equal-hardness assumption,

$$I_{\mathrm{acid}} - A_{\mathrm{acid}} \approx I_{\mathrm{base}} - A_{\mathrm{base}} \tag{67}$$

leads to Eqs. (64) and (65). Even without these assumptions, one has the model

$$\mu(M)_{Base} = -\frac{\alpha_{Base} I + A}{1 + \alpha_{Base}} \tag{68}$$

$$\mu(M)_{Acid} = -\frac{\alpha_{Acid} I + A}{1 + \alpha_{Acid}} \tag{69}$$

Moreover, based on the reasonable expectation that the electron-accepting states of the acid are stabilized and the electron-donating states of the base are stabilized by their mutual interactions, we may hypothesize

$$\tilde{\eta}_{\text{acid}}\left({}^{M-1}\varepsilon_{\text{base}} - {}^{M+1}\varepsilon_{\text{base}}\right) + \tilde{\eta}_{\text{base}}\left({}^{M-1}\varepsilon_{\text{acid}} - {}^{M+1}\varepsilon_{\text{acid}}\right) \approx 0 \tag{70}$$

and thus

$$\alpha_{\text{base}} \approx \frac{1}{\alpha_{\text{acid}}} \tag{71}$$

Further insight into the behavior of α can be gained if we analyze the Taylor expansion corresponding to Eq. (60):

$$\alpha = 1 + 2\left(\frac{{}^{M-1}\varepsilon - {}^{M+1}\varepsilon}{\tilde{\eta}}\right) + \sum_{k=2}^{\infty}\left(\frac{{}^{M-1}\varepsilon - {}^{M+1}\varepsilon}{\tilde{\eta}}\right)^{k} \tag{72}$$

It is clear that for similar external perturbations, systems with greater values of the Parr-Pearson hardness, $\tilde{\eta}$, will be less affected.

Strongly-interacting reagents

Equations (68) and (69) are appropriate only when the reagents are weakly interacting, and thus only for the early states of a reaction path. There are certainly effects that cannot be described using this approach. For example, when a Boron atom is far from a Fluorine atom, charge flows from Boron to Fluorine, as one would expect. It is only when the reagents are close together and orbital overlap is appreciable that the direction of the dipole moment reverses. Effects like this, and more generally, all reactions with "late" transition states, are often considered to be beyond the domain of conceptual DFT approaches.[48] We wish to establish that this is not the case by extending the previous treatment to strongly-interacting reagents. To do this, we will need to center the perturbation series on a point that is far from the initiation of the chemical process and is, indeed, perhaps closer to the final state. As such, now we not only need a model for the (possibly strong!) external perturbation acting upon a given reagent, but also a method for defining the reagent within the supramolecular reactant complex. There is no unique way to partition a quantum system into subsystem;[49-51] likewise there are several approaches for defining the interactions between the subsystems.[52, 53] However, all of the schemes we are aware of start by determining (or at least approximating) the state of the whole system (in our case, the molecular complex *XY*), and then partition it. This approach is contrary to the spirit of conceptual DFT, where one wishes to find physically grounded, but simple, models that explain chemical reactivity in a reagent-centered way, independent of the fine details of the molecular

environment. For this reason, our approach to strongly interacting reagents is based on direct computation of the state (e.g., the density matrix) of a reagent within a supramolecular entity.

To avoid the derivative discontinuity/linearity problems from section 2, we will consider strongly interacting reagents at nonzero temperature. Accordingly, the variational principle retains the form from Eqs. (20) and (53),

$$\delta\left\{S(D)-\beta\left[Tr\left(D\hat{\mathrm{H}}\right)-\mu Tr\left(D\hat{\mathrm{N}}\right)\right]\right\}=0 \tag{73}$$

We have changed the notation for the Hamiltonian and the number operator of the subsystem to indicate, explicitly, that these operators must be revised, and that there is significant freedom in how that is done,

$$\hat{\mathrm{H}}=\hat{H}+\hat{P}_R+\hat{C}_H \tag{74}$$

$$\hat{\mathrm{N}}=\hat{N}+\hat{C}_N \tag{75}$$

There is still the (intrinsic) perturbation due to the environment, $\hat{P}_R$, but this perturbation may not be small. The operators $\hat{C}_H$ and $\hat{C}_N$ are specific to the partitioning method. We will not discuss the possible forms that these operators could take, but focus on the general features of this model. As MB and Kaplan have noticed,[30, 39] it is useful to assume that the energy and particle-number in the subsystem can be measured simultaneously, so we require that these operators commute,

$$\left[\hat{\mathrm{H}},\hat{\mathrm{N}}\right]=0 \tag{76}$$

To impose this constraint, we write the subsystem partitioning method for the energy and number of electrons in terms of an auxiliary operator $\hat{R}$,

$$\hat{\mathrm{H}}=\left(\hat{H}+\hat{P}_R\right)\hat{R} \tag{77}$$

$$\hat{\mathrm{N}}=\hat{N}\hat{R} \tag{78}$$

The operator $\hat{R}$ can be considered a type of subsystem projection operator. Eq. (76) provides a constraint on the types of subsystem partitionings that can be considered. In particular,

$$\left[\hat{R},\hat{N}\right]=\left[\hat{R},\hat{H}+\hat{P}_R\right]=0 \tag{79}$$

This choice is quite general and extremely convenient, but there may be other chemically sensible partitioning methods that do not fit within this framework.

The framework we have selected is convenient because the equilibrium DM for the subsystem has a simple form,

$$D(\mu)_T = \frac{\exp\left[-\beta\hat{R}\left(\hat{H}'-\mu\hat{N}\right)\right]}{\mathrm{Tr}\left\{\exp\left[-\beta\hat{R}\left(\hat{H}'-\mu\hat{N}\right)\right]\right\}} = \frac{\sum_{M,i}\left|{}^{M}\Phi_i'\right\rangle\left\langle{}^{M}\Phi_i'\right|\exp\left[-\beta_M\left({}^{M}E_i'-\mu M\right)\right]}{\sum_{M,i}\exp\left[-\beta_M\left({}^{M}E_i'-\mu M\right)\right]} \tag{80}$$

where:

$$\hat{H}'\left|{}^{M}\Phi_i'\right\rangle = {}^{M}E_i'\left|{}^{M}\Phi_i'\right\rangle \tag{81}$$

$$\beta_M = r_M\beta \tag{82}$$

$$\hat{R}\left|{}^{M}\Phi_i'\right\rangle = r_M\left|{}^{M}\Phi_i'\right\rangle \tag{83}$$

Comparing Eq. (54) for weakly-interacting reagents and Eq. (80) for strongly-interacting reagents, the essential differences are that (a) we no longer may assume we are in the perturbative regime and (b) there is an effective temperature, β_M, that is different for each different (integer) number of electrons. The effective temperature arises because coupling between the operators for the energy and the number of electrons in the subsystem (cf. Eqs. (77) and (78)). An expression like Eq. (80) has been proposed previously, purely heuristically.[54] This derivation provides a rigorous and, in principle, exact mathematical framework that supports that model.

To explore the implications of this model in more detail, we derive the expression for the chemical potential of the M-electron system from the three-state model, namely,

$$\mu = \frac{-\left(r_{M+1}A + r_{M-1}I\right) + {}^{M}E\left(r_{M+1}-r_{M-1}\right) + \left(r_{M+1}\,{}^{M+1}\varepsilon - r_{M-1}\,{}^{M-1}\varepsilon\right)}{r_{M+1}+r_{M-1}+M\left(r_{M+1}-r_{M-1}\right)} \tag{84}$$

The relative complexity of this expression, when compared with Eqs. (29) and (61), reflects the more general nature of the present formalism. This framework not only requires suitable modes for the "intrinsic" interactions of the system with its surroundings (e.g., the changes in the energy eigenvalues of the subsystem, ${}^{M+1}\varepsilon$ and ${}^{M-1}\varepsilon$, which unlike the weakly interacting case need not be especially small), but also models for the partitioning-specific parameters r_{M+1} and r_{M-1}. As

this framework subsumes all the other results in this paper, this model must recover those results in suitable limiting cases. For example, we recognize that the Mulliken formula for the chemical potential, Eq. (29), does not strictly require isolated reagents, but holds whenever one has a "completely symmetric" perturbation/partitioning, such that ${}^{M+1}\varepsilon = {}^{M-1}\varepsilon$ and $r_{M+1} = r_{M-1}$. Similarly, if we consider subsystem partitionings that satisfy the condition

$$ {}^{M}E - \mu M = \frac{r_{M+1}\,{}^{M+1}\varepsilon - r_{M-1}\,{}^{M-1}\varepsilon}{r_{M+1} - r_{M-1}} , \tag{85} $$

one regains a formula that is reminiscent of the weakly interacting limit in Eq. (61), namely

$$ \mu = -\frac{\gamma I + A}{1+\gamma} \tag{86} $$

where the parameter

$$ \gamma = \frac{r_{M-1}}{r_{M+1}} \tag{87} $$

is not necessarily close to one. In the limits $\gamma \to 0$ and $\gamma \to \infty$, Eq. (86) recovers the linear model, Eqs. (10) and (11), respectively.

The framework in Eq. (84) remedies the shortcomings of the noninteracting reagent picture that were discussed at the end of section 3. For example, molecular aggregates will now have different chemical potentials from the isolated atoms and from molecular aggregates with the same composition but different structure because the chemical potentials of the aggregates will change depending on the molecular environment. Similarly, the flexibility of a model like Eq. (84) (and even models like Eqs. (64) and (65)) suffices to describe molecules where the direction of electron transfer is opposed to the prediction from the Mulliken formula.

5. Summary

In this paper, we have explored a hierarchy of models within the grand canonical ensemble. Based on considerations of the zero-temperature grand canonical ensemble, we motivate the introduction of a temperature and electronic chemical potential bath, which allows for fractional electron transfer but still results in a severely oversimplified reactivity model.

This motivated us to shift the expansion point for the perturbation series away from the isolated reagent limit, and consider weakly interacting open systems at nonzero temperature. The

resulting formula for the chemical potential, cf. Eqs. (68)-(71), generalizes and in some sense justifies the model that was previously proposed by Gazquez, Cedillo, and Vela. As the interaction between the subsystems becomes stronger, the chemical potential becomes dependent not only on the subsystems' molecular environment, but on the choice of partitioning method. The framework we present for strongly-interacting reagents, although it is not completely general, is nonetheless general enough to encompass all of the aforementioned limits (the zero-temperature limit, noninteracting subsystems, and weakly interacting subsystems) and, moreover, to validate the viewpoint that the interaction between strongly interacting subsystems can be modeled with an effective temperature.

This work shifts the philosophy of conceptual DFT: no longer do we consider that the reactivity indicators of a reagent are its intrinsic properties, independent of its molecular environment. Nonetheless, while we believe that it is practically useful to retain the approach of looking at a supramolecular complex "one reagent at a time." Our philosophy, then, is to define chemical reactivity parameters for individual reagents, but within a framework that captures the influence of the supramolecular environment. This results in general models (*e.g.*, Eqs. (64), (65) , and (84)) that parameterize the molecular environment in ways that are simple enough to be intuitively useful, but general enough to describe a broad range of chemical processes.

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