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Strategies for computing chemical reactivity indices

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Abstract. Two recent articles [(2000) *J Am Chem Soc* 122: 2010, (2001) *J Am Chem Soc* 123: 2007] have explored electron-density-based and external-potential-based chemical reactivity indices. In this article, methods are presented for computing these indices from the output of a Kohn–Sham density functional theory calculation.

Key words: External-potential-based indices – Electron-density-based indices – Hardness kernel – Fukui function

1 Introduction

The abundance of chemical knowledge underscores the need for incisive and inclusive tools for systematizing chemical data. In recent years, much attention has been paid to the insights density functional theory (DFT) [1, 2] can give into chemical reactivity.

In two recent articles [3, 4], DFT was used to provide a "perturbative perspective" on chemical reactivity. In the first article [3], problems associated with charge transfer were explored using functional Taylor series in the electron density and DFT's fundamental variational principles [5], establishing a novel perspective to quantities of established chemical significance, notably the Fukui function [6, 7], local softness [8, 9], chemical hardness [10–12], and softness. In the second article [4], problems associated with changes in the positions of the atomic nuclei were explored using functional Taylor series in the external potential. In analogy to the "electron-density-based" indices of the first article, the second article proposes several "external-potential-based" indices, most notably an approximate potential-energy surface, the stability, the lability, and the proton hardness. The present article enhances the practical utility of these indices by presenting strategies for evaluating them using the output of Kohn–Sham DFT calculations [13].

2 External-potential-based indices

2.1 Canonical ensemble

Suppose that we have performed a Kohn–Sham DFT calculation for an N-electron system with external potential, ${v_0}^{\mathrm{ref}}(\mathbf{r})$. As this system undergoes a chemical reaction, the external potential changes owing to the rearrangement of the atomic nuclei and/or the approach of a reactant molecule. The key external-potential-based reactivity index, $\Upsilon_{\mathrm{N}}[N,\mathrm{v}_0(\mathbf{r})]$, approximates how the energy changes when the external potential changes from ${v_0}^{\mathrm{ref}}(\mathbf{r})$ to $v_0(\mathbf{r})$. For an M-atom molecule, relevant changes in the external potential can always be parameterized by a set of no more than $3M$ coordinates; however, as demonstrated in Ref. [4], a small subset, $\mathbf{X}$, of these parameters usually suffices for qualitative descriptions of chemical reactivity.

Expressing ${v_0}^{\mathrm{ref}}(\mathbf{r})$ and $v_0(\mathbf{r})$ as functions of $\mathbf{X}$ yields, as an approximate expression for the change in energy due to a small change about the reference nuclear configuration, $\mathbf{X}_{\mathrm{ref}}$,

$$\begin{aligned}\Upsilon_N(\mathbf{X}) \equiv{}& \Delta V_{\mathrm{rep}}(\mathbf{X},\mathbf{X}_{\mathrm{ref}}) + \int \rho_{\mathrm{ref}}(r)[v_0(\mathbf{X};\mathbf{r}) - v_0(\mathbf{X}_{\mathrm{ref}};\mathbf{r})]\mathrm{d}\mathbf{r} \\ &+\frac{1}{2}\int\int [v_0(\mathbf{X};\mathbf{r}') - v_0(\mathbf{X}_{\mathrm{ref}};\mathbf{r}')]P_{\mathrm{ref}}(\mathbf{r},\mathbf{r}')[v_0(\mathbf{X};\mathbf{r}) \\ &- v_0(\mathbf{X}_{\mathrm{ref}};\mathbf{r})]\mathrm{d}\mathbf{r}\mathrm{d}\mathbf{r}'. \end{aligned} \tag{1}$$

In Eq. (1), $\Delta \mathrm{V}_{\mathrm{rep}}(\mathbf{X},\mathbf{X}_{\mathrm{ref}})$ represents the change in the nuclear–nuclear repulsion energy when the nuclear configuration is changed from $\mathbf{X}_{\mathrm{ref}}$ to $\mathbf{X}$, $v_0(\mathbf{X};\mathbf{r})$ denotes the external potential associated with the nuclear configuration parameterized by $\mathbf{X}$, $\rho_{\mathrm{ref}}(\mathbf{r})$ is the electron density for the reference nuclear configuration, and

$$P_{\mathrm{ref}}(\mathbf{r},\mathbf{r}') \equiv \left(\frac{\delta\rho_{\mathrm{ref}}(\mathbf{r})}{\delta v_0(\mathbf{r}')}\right)_N \tag{2}$$

is the polarizability kernel at $\mathbf{X}_{\mathrm{ref}}$. Because

$$\Upsilon_N(\mathbf{X}) \approx U(\mathbf{X}) - U(\mathbf{X}_{\mathrm{ref}}), \tag{3}$$

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where $U(\mathbf{X})$ is the total energy (electronic energy plus nuclear–nuclear repulsion energy) associated with the molecular configuration $\mathbf{X}$, $\Upsilon_N(\mathbf{X})$ is small at sites on the potential-energy surface where the molecule is especially stable and is large for high-energy conformations of the molecule. Of particular interest are the properties of the system near the global minimum, $\mathbf{X}_{\min}$, of $\Upsilon_N(\mathbf{X})$. Key properties associated with the global minimum are the stability,

$$\Xi_N \equiv -\Upsilon_N(\mathbf{X}_{\min}), \tag{4}$$

and the lability,

$$\Lambda_N \equiv \frac{\dim(\mathbf{X})}{\operatorname{tr}\{\Phi_{ij}\}}, \tag{5}$$

where $\dim(\mathbf{X})$ denotes the dimension of the vector $\mathbf{X}$, and $\operatorname{tr}\{\mathbf{\Phi}_{ij}\}$ is the trace of the Hessian matrix at global minimum:

$$\begin{aligned}\Phi_{ij} &\equiv \left.\frac{\partial^2 \Upsilon_N(\mathbf{X})}{\partial \mathbf{X}_i \partial \mathbf{X}_j}\right]_{\mathbf{X}=\mathbf{X}_{\min}} \\ &= [\nabla\nabla\Upsilon_N(\mathbf{X})]_{\mathbf{X}=\mathbf{X}_{\min}}.\end{aligned} \tag{6}$$

Given $\Upsilon_N(\mathbf{X})$, both the stability, Ξ_N, and the lability, Λ_N, are readily determined.

Using Eq. (1), $\Upsilon_N(\mathbf{X})$ may be readily determined from the electron density, $\rho_{\text{ref}}(\mathbf{r})$, and polarizability kernel, $P_{\text{ref}}(\mathbf{r},\mathbf{r}')$, of the reference state. The electron density is readily determined from the output of many different computational procedures, including a Kohn–Sham DFT calculation on the reference system [13]:

$$\rho_{\text{ref}}(\mathbf{r}) \equiv \sum_{i=1}^{\infty} n_i |\psi_i(\mathbf{r})|^2, \tag{7}$$

where $\{\psi_i(\mathbf{r})\}_{i=1}^{\infty}$ and $\{n_i\}^{\infty}{}_{i=1}$ are the Kohn–Sham orbitals and orbital occupation numbers for a system with N electrons and external potential $v_0{}^{\text{ref}}(\mathbf{r}) \equiv v_0(\mathbf{X}_{\text{ref}};\mathbf{r})$. However, the polarizability kernel,

$$P_{\text{ref}}(\mathbf{r}_1,\mathbf{r}_2) \equiv 2N^2 \sum_{j=1}^{\infty} \frac{\left\{ \begin{array}{l} \left[\int\cdots\int \Psi_j^*(x_1,\ldots x_N)\Psi_0(x_1,\ldots x_N)\mathrm{d}s_2\mathrm{d}x_1\mathrm{d}x_3\ldots\mathrm{d}x_N\right] \\ \cdot\left[\int\cdots\int \Psi_0^*(x_1,\ldots x_N)\Psi_j(x_1,\ldots x_N)\mathrm{d}s_1\mathrm{d}x_2\ldots\mathrm{d}x_N\right] \end{array} \right\}}{E_0 - E_j}, \tag{8}$$

where Ψ_j and E_j are the wavefunction and energy eigenvalue for the jth excited state of the reference system, is less easily computed. In particular, we note that evaluating Eq. (8) requires not only the ground-state wavefunction and energy eigenvalue, but energy eigenvalues and eigenfunctions for all the excited states as well; hence, Eq. (8) does not represent a practical method for computing $P_{\text{ref}}(\mathbf{r}_1,\mathbf{r}_2)$.

Fortunately, one can express $P_{\text{ref}}(\mathbf{r},\mathbf{r}')$ in terms of the orbitals and orbital eigenvalues of an independent-particle model for the reference system.[1] In the Kohn–Sham model N, noninteracting electrons interact with an effective external potential [13]

$$v_{\text{K-S}}^{\text{ref}}(\mathbf{r}) \equiv v_0^{\text{ref}}(\mathbf{r}) + v_{\text{J}}^{\text{ref}}(\mathbf{r}) + v_{\text{xc}}^{\text{ref}}(\mathbf{r}). \tag{9}$$

Here both the classical electrostatic potential,

$$v_{\text{J}}^{\text{ref}}(\mathbf{r}) \equiv \int \frac{\rho_{\text{ref}}(\mathbf{r}')}{|\mathbf{r}-\mathbf{r}'|}\mathrm{d}\mathbf{r}', \tag{10}$$

and the exchange correlation potential, $v_{\text{xc}}{}^{\text{ref}}(\mathbf{r})$, are functionals of $\rho_{\text{ref}}(\mathbf{r})$, while $v_0{}^{\text{ref}}(\mathbf{r})$, which was held fixed during the Kohn–Sham calculation, is the external potential for which $\rho_{\text{ref}}(\mathbf{r})$ is the ground-state density. Hence $v_0{}^{\text{ref}}(\mathbf{r})$ may also be considered to be a functional of $\rho_{\text{ref}}(\mathbf{r})$ [5].

The functional derivative of $v_{\text{K-S}}{}^{\text{ref}}(\mathbf{r})$ with respect to the density,

$$\left.\frac{\delta v_{\text{K-S}}(\mathbf{r})}{\delta\rho(\mathbf{r}')}\right]_{\rho=\rho_{\text{ref}}} \equiv \left.\frac{\delta v_0(\mathbf{r})}{\delta\rho(\mathbf{r}')}\right]_{\rho=\rho_{\text{ref}}} + \left.\frac{\delta v_{\text{J}}(\mathbf{r})}{\delta\rho(\mathbf{r}')}\right]_{\rho=\rho_{\text{ref}}} + \left.\frac{\delta v_{\text{xc}}(\mathbf{r})}{\delta\rho(\mathbf{r}')}\right]_{\rho=\rho_{\text{ref}}}, \tag{11}$$

is the inverse of the polarizability kernel for the noninteracting reference system,

$$P_{\text{ref}}^{\text{K-S}}(\mathbf{r},\mathbf{r}') \equiv \left.\left(\frac{\delta\rho(\mathbf{r})}{\delta v_{\text{K-S}}(\mathbf{r}')}\right)_N\right]_{\rho=\rho_{\text{ref}}}, \tag{12}$$

and hence

$$\int \left(\frac{\delta\rho_{\text{ref}}(\mathbf{r})}{\delta v_{\text{K-S}}(\mathbf{r}')}\right)_N \cdot \frac{\delta v_{\text{K-S}}^{\text{ref}}(\mathbf{r}')}{\delta\rho(\mathbf{r}'')}\mathrm{d}\mathbf{r}' = \delta(\mathbf{r}-\mathbf{r}''). \tag{13}$$

In Sect. 3, we will see that Eq. (13), as here stated, is not valid. For the purposes of this derivation, it suffices to note that eliminating nonphysical variations in the Kohn–Sham effective potential allows Eq. (13) to be recovered. Equation (13) introduces compact notation for specifying that the functional derivatives are to be evaluated at $\rho(\mathbf{r}) = \rho_{\text{ref}}(\mathbf{r})$. The Kohn–Sham polarizability kernel can be evaluated in terms of the Kohn–Sham orbitals, $\{\psi_i(\mathbf{r})\}_{i=0}^{\infty}$, orbital occupation numbers, $\{n_i\}^{\infty}{}_{i=0}$, and orbital energies, $\{\varepsilon_i\}^{\infty}{}_{i=0}$ [15]:

$$P_{\text{ref}}^{\text{K-S}}(\mathbf{r},\mathbf{r}') = \sum_{i=0}^{\infty}\sum_{j\neq i}^{\infty} \frac{(n_j - n_i)}{\varepsilon_j - \varepsilon_i} \cdot \psi_i^*(\mathbf{r})\psi_j(\mathbf{r})\psi_j^*(\mathbf{r}')\psi_i(\mathbf{r}'). \tag{14}$$

Equation (14) suggests that we seek a method for expressing the polarizability kernel of the interacting system in terms of the Kohn–Sham polarizability kernel.

To derive a formula linking $\left(\frac{\delta\rho_{\text{ref}}(\mathbf{r})}{\delta v_{\text{K-S}}(\mathbf{r}')}\right)_N$ to $\left(\frac{\delta\rho_{\text{ref}}(\mathbf{r})}{\delta v_0(\mathbf{r}')}\right)_N$, we start with the identity:

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[1] There are several alternative methods for computing the polarizability kernel [14].

$$\left(\frac{\delta\rho_{\mathrm{ref}}(\mathbf{r})}{\delta v_0(\mathbf{r}')}\right)_N - \left(\frac{\delta\rho_{\mathrm{ref}}(\mathbf{r})}{\delta v_{\mathrm{K-S}}(\mathbf{r}')}\right)_N \equiv \int \left(\frac{\delta\rho_{\mathrm{ref}}(\mathbf{x}')}{\delta v_0(\mathbf{r}')}\right)_N \delta(\mathbf{r}-\mathbf{x}')\mathrm{d}\mathbf{x}' - \int \delta(\mathbf{r}'-\mathbf{x})\left(\frac{\delta\rho_{\mathrm{ref}}(\mathbf{r})}{\delta v_{\mathrm{K-S}}(\mathbf{x})}\right)_N \mathrm{d}\mathbf{x}. \tag{15}$$

By inserting Eq. (13) and its analogue for interacting systems and applying the definitions of the polarizability kernels, one obtains

$$P_{\mathrm{ref}}(\mathbf{r},\mathbf{r}') - P_{\mathrm{ref}}^{\mathrm{K-S}}(\mathbf{r},\mathbf{r}') = \int\int \left(\frac{\delta\rho_{\mathrm{ref}}(\mathbf{x}')}{\delta v_0(\mathbf{r}')}\right)_N \left[\left(\frac{\delta\rho_{\mathrm{ref}}(\mathbf{r})}{\delta v_{\mathrm{K-S}}(\mathbf{x})}\right)_N \cdot \frac{\delta v_{\mathrm{K-S}}^{\mathrm{ref}}(\mathbf{x})}{\delta\rho(\mathbf{x}')}\right]\mathrm{d}\mathbf{x}\mathrm{d}\mathbf{x}' - \int\int \left[\frac{\delta v_0^{\mathrm{ref}}(\mathbf{x})}{\delta\rho(\mathbf{x}')} \cdot \left(\frac{\delta\rho_{\mathrm{ref}}(\mathbf{x}')}{\delta v_0(\mathbf{r}')}\right)_N\right]\left(\frac{\delta\rho_{\mathrm{ref}}(\mathbf{r})}{\delta v_{\mathrm{K-S}}(\mathbf{x})}\right)_N \mathrm{d}\mathbf{x}'\mathrm{d}\mathbf{x}, \tag{16}$$

which simplifies to

$$P_{\mathrm{ref}}(\mathbf{r},\mathbf{r}') - P_{\mathrm{ref}}^{\mathrm{K-S}}(\mathbf{r},\mathbf{r}') = \int\int P_{\mathrm{ref}}^{\mathrm{K-S}}(\mathbf{r},\mathbf{x})\left(\frac{\delta v_{\mathrm{K-S}}^{\mathrm{ref}}(\mathbf{x})}{\delta\rho(\mathbf{x}')} - \frac{\delta v_0^{\mathrm{ref}}(\mathbf{x})}{\delta\rho(\mathbf{x}')}\right)P_{\mathrm{ref}}(\mathbf{x}',\mathbf{r}')\mathrm{d}\mathbf{x}\mathrm{d}\mathbf{x}'. \tag{17}$$

On substituting Eq. (11) into Eq. (17), we find

$$P_{\mathrm{ref}}(\mathbf{r},\mathbf{r}') - P_{\mathrm{ref}}^{\mathrm{K-S}}(\mathbf{r},\mathbf{r}') = \int\int P_{\mathrm{ref}}^{\mathrm{K-S}}(\mathbf{r},\mathbf{x})\left(\frac{\delta v_{\mathrm{J}}^{\mathrm{ref}}(\mathbf{x})}{\delta\rho(\mathbf{x}')} + \frac{\delta v_{\mathrm{xc}}^{\mathrm{ref}}(\mathbf{x})}{\delta\rho(\mathbf{x}')}\right)P_{\mathrm{ref}}(\mathbf{x}',\mathbf{r}')\mathrm{d}\mathbf{x}\mathrm{d}\mathbf{x}'. \tag{18}$$

To further simplify Eq. (18), note

1. $\frac{\delta v_{\mathrm{xc}}^{\mathrm{ref}}(\mathbf{x})}{\delta\rho(\mathbf{x}')} = \frac{\delta E_{\mathrm{xc}}(\rho_{\mathrm{ref}})}{\delta\rho(\mathbf{x}')\rho(\mathbf{x})}$, where $E_{\mathrm{xc}}(\rho)$ is an appropriate approximation to the exchange–correlation energy density functional.
2. It follows from from Eq. (10) that $\frac{\delta v_{\mathrm{J}}^{\mathrm{ref}}(\mathbf{x})}{\delta\rho(\mathbf{x}')} = \frac{1}{|\mathbf{x}-\mathbf{x}'|}$.

On substituting these results into Eq. (18), we obtain [15]

$$P_{\mathrm{ref}}(\mathbf{r},\mathbf{r}') - P_{\mathrm{ref}}^{\mathrm{K-S}}(\mathbf{r},\mathbf{r}') = \int\int P_{\mathrm{ref}}^{\mathrm{K-S}}(\mathbf{r},\mathbf{x})\left(\frac{1}{|\mathbf{x}-\mathbf{x}'|} + \frac{\delta^2 E_{\mathrm{xc}}(\rho_{\mathrm{ref}})}{\delta\rho(\mathbf{x}')\rho(\mathbf{x})}\right)P_{\mathrm{ref}}(\mathbf{x}',\mathbf{r}')\mathrm{d}\mathbf{x}\mathrm{d}\mathbf{x}'. \tag{19}$$

Equation (19) is an integral equation for $\mathrm{P}_{\mathrm{ref}}(\mathbf{r},\mathbf{r}')$ in terms of quantities accessible from a Kohn–Sham DFT calculation on the reference system.

Equations (7), (14), and (19) provide the apparatus for deriving all the quantities necessary to compute $\Upsilon_{\mathrm{N}}(\mathbf{X})$ using Eq. (1). Once $\Upsilon_{\mathrm{N}}(\mathbf{X})$ is known, the stability and lability are readily computed from their definitions (Eqs. 4, 5, respectively).

2.2 Grand canonical ensemble

Analogous to $\Upsilon_{\mathrm{N}}(\mathbf{X})$ and Eq. (1) in the canonical ensemble, in the grand canonical ensemble we have

$$\Upsilon_{\mu}(\mathbf{X}) \equiv \Delta V_{\mathrm{rep}}(\mathbf{X},\mathbf{X}_{\mathrm{ref}}) + \int \rho_{\mathrm{ref}}(\mathbf{r})[v_0(\mathbf{X};\mathbf{r}) - v_0(\mathbf{X}_{\mathrm{ref}};\mathbf{r})]\mathrm{d}\mathbf{r} - \frac{1}{2}\int\int [v_0(\mathbf{X};\mathbf{r}') - v_0(\mathbf{X}_{\mathrm{ref}};\mathbf{r}')] \times s_{\mathrm{ref}}(\mathbf{r},\mathbf{r}')[v_0(\mathbf{X};\mathbf{r}) - v_0(\mathbf{X}_{\mathrm{ref}};\mathbf{r})]\mathrm{d}\mathbf{r}\mathrm{d}\mathbf{r}', \tag{20}$$

where $s_{\mathrm{ref}}(\mathbf{r},\mathbf{r}')$, the softness kernel for the reference system, is defined by

$$s_{\mathrm{ref}}(\mathbf{r},\mathbf{r}') \equiv -\left(\frac{\delta\rho_{\mathrm{ref}}(\mathbf{r})}{\delta v_0(\mathbf{r}')}\right)_{\mu} = -\left(\frac{\delta^2\Omega}{\delta v(\mathbf{r}')\delta v(\mathbf{r})}\right)_{\mu}, \tag{21}$$

where

$$\Omega[\mu, v_0(\mathbf{r})] \equiv E[N, v_0(\mathbf{r})] - \mu N \tag{22}$$

is the grand potential and [1, 16]

$$\mu \equiv \left(\frac{\partial E[N, v_0(\mathbf{r})]}{\partial N}\right)_{v_0(\mathbf{r})} \tag{23}$$

is the chemical potential.

Just as computing $\Upsilon_{\mathrm{N}}(\mathbf{X})$ requires an efficient method for computing the polarizability kernel, computing $\Upsilon_{\mu}(\mathbf{X})$ requires an efficient method for computing the softness kernel. However, Kohn–Sham DFT calculations are generally performed for a fixed number of electrons, N, instead of at a constant electronic chemical potential, μ; hence Kohn–Sham DFT does not provide a direct approach to computing the softness kernel.

Towards solving this problem, we begin by examining the grand potential at zero temperature. At zero temperature, plots of electronic energy versus particle number consist of straight line segments, interpolating the values of the energies for integer numbers of electrons (Fig. 1a) [17–19]. Corresponding to this result, the plot of $\Omega[\mu,v(\mathbf{r})]$ versus μ consists of a sequence of straight line segments with slopes given by

$$\left(\frac{\partial\Omega}{\partial\mu}\right)_{v(\mathbf{r})} \equiv -N \ . \tag{24}$$

(Fig. 1b.) $N[\mu,v(\mathbf{r})]$ is discontinuous when $-\mu$ is equal to one of the system's successive ionization potentials or electron affinities (the marked points in Fig. 1b). Elsewhere, the global softness,

$$S \equiv \frac{1}{\eta} = \left(\frac{\partial N}{\partial\mu}\right)_{v(\mathbf{r})} = -\left(\frac{\partial^2\Omega}{\partial\mu^2}\right)_{v(\mathbf{r})} = \int\int s(\mathbf{r},\mathbf{r}')\mathrm{d}\mathbf{r}\mathrm{d}\mathbf{r}' \ , \tag{25}$$

where η is the chemical hardness, is zero.

Examining Fig. 1b in more detail, let us consider the value of the chemical potential selected by the arrow, μ_0. At such points,

$$-\left(\frac{\partial\Omega[\mu_0, v(\mathbf{r})]}{\partial\mu}\right)_{v(\mathbf{r})} = N = -\left(\frac{\partial\Omega[\mu_0, v(\mathbf{r}) + \Delta v(\mathbf{r})]}{\partial\mu}\right)_{v(\mathbf{r})}, \tag{26}$$

and hence, at zero temperature, infinitesimal changes in the external potential at fixed chemical potential do not

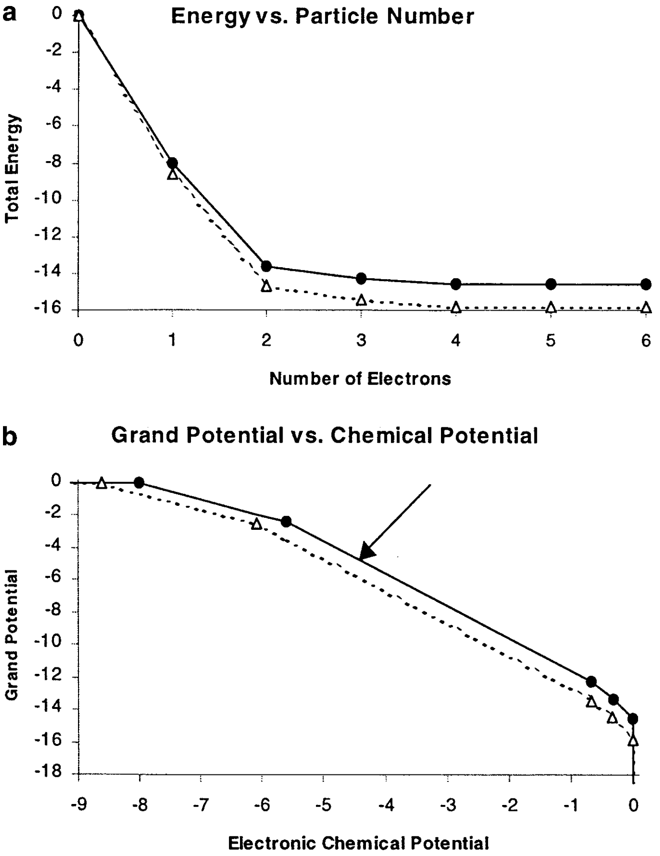

Fig. 1. **a** $E[N,v(\mathbf{r})]$ versus N (*solid line*) and $E[N,v(\mathbf{r})+\Delta v(\mathbf{r})]$ versus N (d*otted line*) at zero temperature. Places where the chemical potential, $\mu = \left(\frac{\partial E}{\partial N}\right)_{v(\mathbf{r})}$, is discontinuous are marked with *points*. **b** $\Omega[N,v(\mathbf{r})]$ versus μ (*solid line*) and $\Omega[N,v(\mathbf{r})+\Delta v(\mathbf{r})]$ versus μ (*dotted line*) at zero temperature. Places where the electron number, $N = -\left(\frac{\partial \Omega}{\partial \mu}\right)_{v(\mathbf{r})}$, is discontinuous are marked with *points*

change the number of electrons in the system.[2] Accordingly, the local softness,

$$s(\mathbf{r}) \equiv -\left(\frac{\delta N}{\delta v(\mathbf{r})}\right)_{\mu_0} = \left(\frac{\partial \rho(\mathbf{r})}{\partial \mu}\right)_{v(r)} = Sf(\mathbf{r}) = \int s(\mathbf{r},\mathbf{r}')\mathrm{d}\mathbf{r}\mathrm{d}\mathbf{r}' \ , \tag{27}$$

where $f(\mathbf{r})$ is the Fukui function, is identically zero except at the points of discontinuity in N (where the local softness, like the global softness, is infinite). Moreover, because infinitesimal changes in the external potential at fixed chemical potential do not result in changes in the number of electrons, functional derivatives with respect to the external potential at constant chemical potential, μ_0, are equivalent to the same functional derivatives performed at constant N $[\mu_0,v(\mathbf{r})]$. Applying this general result, we obtain the formula of Cohen, et al. [20, 21] for the zero-temperature softness kernel:

$$\begin{aligned} -s_{\beta\to\infty}(\mathbf{r},\mathbf{r}') &\equiv \left(\frac{\delta \rho(\mathbf{r})}{\delta v(\mathbf{r})}\right)_{\mu,\beta\to\infty} = \left(\frac{\delta \rho(\mathbf{r})}{\delta v(\mathbf{r})}\right)_{N,\beta\to\infty} \\ &\equiv P_{\beta\to\infty}(\mathbf{r},\mathbf{r}') \ , \end{aligned} \tag{28}$$

where the notation indicates that Eq. (28) holds only in the limit of zero temperature $\left(\beta \equiv \frac{1}{kT}\right)$. Equation (28) implies that $\Upsilon_{\mu}(\mathbf{X})$ (Eq. 20) and $\Upsilon_{\mathrm{N}}(\mathbf{X})$ (Eq. 1) are equal at zero temperature.

In as much as the external-potential-based indices evaluated at constant N and constant μ are equal at zero temperature, in order to differentiate between the two approaches we must consider $T>0$. In order to find a relationship between the finite-temperature polarizability kernel, $\mathrm{P}^{\beta}{}_{\mathrm{ref}}(\mathbf{r},\mathbf{r}')$ might be computed, for instance, from a finite-temperature Kohn–Sham DFT calculation [13, 22],

$$P^{\beta}(\mathbf{r},\mathbf{r}') \equiv \frac{\sum\limits_{k=0}^{\infty} P_k(\mathbf{r},\mathbf{r}')\exp(-\beta E_k)}{\sum\limits_{k=0}^{\infty} \exp(-\beta E_k)} \ , \tag{29}$$

where $P_{\mathrm{k}}(\mathbf{r},\mathbf{r}')$ is the polarizability kernel for the kth excited state of the reference system, and the finite temperature softness kernel, $s^{\beta}(\mathbf{r},\mathbf{r}')$, we apply the identity for functional derivatives that is analogous to

$$\left(\frac{\partial z}{\partial x}\right)_w \equiv \left(\frac{\partial z}{\partial x}\right)_y + \left(\frac{\partial z}{\partial y}\right)_x \left(\frac{\partial y}{\partial x}\right)_w \ , \tag{30}$$

thereby attaining

$$\left(\frac{\delta \rho(\mathbf{r})}{\delta v_0(\mathbf{r}')}\right)_{N,\beta} \equiv \left(\frac{\delta \rho^{\mathrm{ref}}(\mathbf{r})}{\delta v_0(\mathbf{r}')}\right)_{\mu,\beta} + \left(\frac{\partial \rho(\mathbf{r})}{\partial \mu}\right)_{v_0^{\mathrm{ref}}(\mathbf{r}),\beta} \left(\frac{\delta \mu}{\delta v_0(\mathbf{r}')}\right)_{N,\beta} . \tag{31}$$

Substituting Eqs. (21), (25), and (27) into Eq. (31) yields the Berkowitz–Parr relation [9],

$$P^{\beta}_{\mathrm{ref}}(\mathbf{r},\mathbf{r}') = s^{\beta}_{\mathrm{ref}}(\mathbf{r}) f^{\beta}_{\mathrm{ref}}(\mathbf{r}') - s^{\beta}_{\mathrm{ref}}(\mathbf{r},\mathbf{r}') \ , \tag{32}$$

or, equivalently,

$$P^{\beta}_{\mathrm{ref}}(\mathbf{r},\mathbf{r}') = \frac{s^{\beta}_{\mathrm{ref}}(\mathbf{r}) s^{\beta}_{\mathrm{ref}}(\mathbf{r}')}{s^{\beta}_{\mathrm{ref}}} - s^{\beta}_{\mathrm{ref}}(\mathbf{r},\mathbf{r}') \ . \tag{33}$$

Note that because the local softness is zero when $T=0$, Eq. (32) reduces to Eq. (28) in the limit of zero temperature. For computational purposes, it is convenient to rewrite Eq. (33) (using Eqs. 25, 27) as an integral equation for the softness kernel:

$$\begin{aligned} 0 &= \left[P^{\beta}_{\mathrm{ref}}(\mathbf{r},\mathbf{r}') + s^{\beta}_{\mathrm{ref}}(\mathbf{r},\mathbf{r}')\right] \int\int s^{\beta}_{\mathrm{ref}}(\mathbf{x},\mathbf{x}')\mathrm{d}\mathbf{x}\mathrm{d}\mathbf{x}' \\ &\quad - \int\int s^{\beta}_{\mathrm{ref}}(\mathbf{r},\mathbf{x}) s^{\beta}_{\mathrm{ref}}(\mathbf{x}',\mathbf{r}')\mathrm{d}\mathbf{x}\mathrm{d}\mathbf{x}' \\ 0 &= \int\int \left\{ \left[P^{\beta}_{\mathrm{ref}}(\mathbf{r},\mathbf{r}') + s^{\beta}_{\mathrm{ref}}(\mathbf{r},\mathbf{r}')\right] s^{\beta}_{\mathrm{ref}}(\mathbf{x},\mathbf{x}') \right. \\ &\quad \left. - s^{\beta}_{\mathrm{ref}}(\mathbf{r},\mathbf{x}) s^{\beta}_{\mathrm{ref}}(\mathbf{x}',\mathbf{r}') \right\} \mathrm{d}\mathbf{x}\mathrm{d}\mathbf{x}' \ . \end{aligned} \tag{34}$$

Equation (34) represents the generalization of Eq. (28) to nonzero temperature. Along with Eq. (28),

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[2] Actually, the change in external potential represented in Fig. 1b is fairly large, representing the effect of changing an atom's nuclear charge from $Z = 4$ (the solid line is constructed from data on beryllium) to $Z = 4.15$.

Eq. (34) provides a method for computing the softness kernel of the reference system, and hence $\Upsilon_{\mu}(\mathbf{X})$ (Eq. 20). Once $\Upsilon_{\mu}(\mathbf{X})$ is computed, the grand canonical stability,

$$\Xi_{\mu} \equiv -\Upsilon_{\mu}(X_{\min}) \ , \tag{35}$$

and lability,

$$\Lambda_{\mu} \equiv \frac{\dim(\mathbf{X})}{\mathrm{tr}\{\mathscr{F}_{ij}\}} \ , \tag{36}$$

can be obtained. (In Eq. 36, $\mathscr{F}_{ij}$ is the Hessian matrix for $\Upsilon_{\mu}(\mathbf{X})$ at $\mathbf{X}_{\min}$.)

2.3 Brönstead–Lowry acids and bases and the proton hardness

As a specific example of external-potential-based indices, consider the changes in external potential

$$v_0(\mathbf{R};\mathbf{r}) - v_0(\mathbf{R}_{\mathrm{ref}};\mathbf{r}) \equiv -\int n_{+}(\mathbf{R},\sigma;\mathbf{r}')\frac{1}{|\mathbf{r}-\mathbf{r}'|}\mathrm{d}\mathbf{r}' \ , \tag{37}$$

$$v_0(\mathbf{R};\mathbf{r}) - v_0(\mathbf{R}_{\mathrm{ref}};\mathbf{r}) \equiv -\int n_{-}(\mathbf{R},\sigma;\mathbf{r}')\frac{1}{|\mathbf{r}-\mathbf{r}'|}\mathrm{d}\mathbf{r}' \ , \tag{38}$$

where

$$n_{\pm}(\mathbf{R},\sigma;\mathbf{r}') \equiv \pm\frac{1}{\pi^{\frac{3}{2}}\sigma^{3}}\exp\left[-\left(\frac{\mathbf{r}'-\mathbf{R}}{\sigma}\right)^{2}\right] \ . \tag{39}$$

Substituting Eq. (37) into Eq. (1) defines $\Upsilon^{+,\sigma}{}_{N}(\mathbf{R})$, which models the site reactivity of a molecule relative to a cationic reagent of unit charge and characteristic size σ. Similarly, substituting Eq. (38) into Eq. (1) defines $\Upsilon^{-,\sigma}{}_{N}(\mathbf{R})$, which models the site reactivity of a molecule relative to an anionic reagent of unit charge and characteristic size σ. Of particular interest is the limit $\sigma \to 0$; $\Upsilon^{+,\sigma=0}{}_{N}(\mathbf{R})$ and $\Upsilon^{-,\sigma=0}{}_{N}(\mathbf{R})$, denoted $\Upsilon_{\text{BL-base}}(\mathbf{R})$ and $\Upsilon_{\text{BL-acid}}(\mathbf{R})$, respectively, in Ref. [4], are appropriate reactivity indices for considering the protonation and deprotonation of Brönstead–Lowry bases and Brönstead–Lowry acids, respectively. In particular, $\Upsilon^{+,\sigma=0}{}_{N}(\mathbf{R})$ represents the change in molecular energy that results from placing a proton at the point R. When evaluated at the position of a proton, $\mathbf{R}_{\mathrm{H}}$, $\Upsilon^{-,\sigma=0}{}_{\mathrm{N}}(\mathbf{R}_{\mathrm{H}})$ represents the change in molecular energy that results from removing that proton from the system. Therefore, the proton(s) where $\Upsilon^{-,\sigma=0}{}_{\mathrm{N}}(\mathbf{R}_{\mathrm{H}})$ is smallest is(are) the most acidic proton(s) in the molecule (in the gas phase). The value of $\Upsilon^{-,\sigma=0}{}_{\mathrm{N}}(\mathbf{R}_{\mathrm{H}})$ at the most acidic proton is labeled $-\Xi_{\text{BL-acid}}$; large values of $\Xi_{\text{BL-acid}}$ are associated with strong Brönstead–Lowry acids. The value of $\Upsilon^{+,\sigma=0}{}_{N}(\mathbf{R})$ at its global minimum models the proton affinity of the molecule and is labeled $-\Xi_{\text{BL-base}}$; large values of $\Xi_{\text{BL-base}}$ are associated with strong Brönstead–Lowry bases.

Reference [4] defines the proton hardness as

$$\Pi_{N} \equiv \frac{1}{\Xi_{\mathrm{BL-acid}} + \Xi_{\mathrm{BL-base}}} \ . \tag{40}$$

For a given acid (base) strength, a small value of the proton hardness indicates that the molecule is an unusually good Brönstead–Lowry base (acid). A molecule with a small proton hardness, then, may be expected to act as a Brönstead–Lowry acid in certain conditions and as a Brönstead–Lowry base in other conditions.

3 Electron-density-based reactivity indices

The external-potential-based indices from Sect. 2 are most appropriate for reactions which are well described as a change in the number, kind, or positions of the atomic nuclei. For reactions, like those between Lewis acids and bases, that are best described as a change in the electronic structure of the reactants, the electron-density-based indices considered in Ref. [3] are more appropriate.

In Ref. [3], three key electron-density-based indices are considered: the chemical potential, μ; the chemical hardness, $\eta \equiv \frac{1}{S}$; and the Fukui function, $f(\mathbf{r}) = \frac{s(\mathbf{r})}{S}$. These quantities were introduced in Sect. 2.2 in the context of the grand canonical ensemble for $T > 0$. For integer numbers of particles at $T = 0$, however, derivatives of the energy with respect to particle number do not exist, and each electron-density-based descriptor is replaced by two descriptors, one in which the derivative is taken from above and one in which the derivative is taken from below (Fig. 1a).[3] For instance, corresponding to Eq. (23), one now has two chemical potentials, one where the derivative is taken from above,

$$\mu^{+} \equiv \left(\frac{\partial E[N, v_0(\mathbf{r})]}{\partial N}\right)^{+}_{v_0(\mathbf{r})} = -A \ , \tag{41}$$

and one where the derivative is taken from below,

$$\mu^{-} \equiv \left(\frac{\partial E[N, v_0(\mathbf{r})]}{\partial N}\right)^{-}_{v_0(\mathbf{r})} = -I \ ; \tag{42}$$

where I and A denote the ionization potential and electron affinity, respectively. Likewise, there are now two Fukui functions,

$$f^{+}(\mathbf{r}) \equiv \left(\frac{\partial \rho(\mathbf{r})}{\partial N}\right)^{+}_{v_0(\mathbf{r})} = \left(\frac{\delta \mu^{+}}{\delta v_0(\mathbf{r})}\right)_{N} = \rho_{N+1}(\mathbf{r}) - \rho_{N}(\mathbf{r}) \tag{43}$$

and

$$f^{-}(\mathbf{r}) \equiv \left(\frac{\partial \rho(\mathbf{r})}{\partial N}\right)^{-}_{v_0(\mathbf{r})} = \left(\frac{\delta \mu^{-}}{\delta v_0(\mathbf{r})}\right)_{N} = \rho_{N}(\mathbf{r}) - \rho_{N-1}(\mathbf{r}) \ , \tag{44}$$

where $\rho_{\mathrm{N}}(\mathbf{r})$ denotes the electron density for the N-electron system with external potential $v_0(\mathbf{r})$. At zero temperature, the hardness,

$$\eta \equiv \left(\frac{\partial^{2} E[N, v_0(\mathbf{r})]}{\partial N^{2}}\right)_{v_0(\mathbf{r})} \ , \tag{45}$$

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[3] A more detailed derivation of these results is found in the appendix of Ref. [3].

is zero when the derivatives are taken from above or below and is infinite when a central difference formula is used. For this reason, it is most useful to define η with the finite-difference approximation to Eq. (45) (with $\Delta N = 1$):

$$\eta = \mu^+ - \mu^- = I - A \ . \tag{46}$$

The chemical potentials and the chemical hardness are related to the ionization potential and the electron affinity and are known for many atoms and molecules [23]. By contrast, finding accurate methods for computing the Fukui function is an area of active research [20, 21, 24–31] (Ref [7] reviews recent progress). We now present a method for computing the Fukui functions from the output of a Kohn-Sham DFT calculation [13].

Recall that the hardness kernel is defined through [9]

$$\begin{aligned}\eta(\mathbf{r},\mathbf{r}') &\equiv \frac{\delta F(\rho)}{\delta\rho(\mathbf{r}')\delta\rho(\mathbf{r})} \\ &= \frac{\delta T_{\mathrm{s}}(\rho)}{\delta\rho(\mathbf{r}')\delta\rho(r)} + \frac{\delta J(\rho)}{\delta\rho(\mathbf{r}')\delta\rho(\mathbf{r})} + \frac{\delta E_{\mathrm{xc}}(\rho)}{\delta\rho(\mathbf{r}')\delta\rho(\mathbf{r})} \ ,\end{aligned} \tag{47}$$

where $F(\rho)$ is the Hohenberg–Kohn functional, $T_{\mathrm{s}}(\rho)$ is the noninteracting kinetic energy,

$$J(\rho) \equiv \frac{1}{2}\int\int \frac{\rho(\mathbf{r}')\rho(\mathbf{r})}{|\mathbf{r}-\mathbf{r}'|}\mathrm{d}\mathbf{r}\mathrm{d}\mathbf{r}' \tag{48}$$

is the electrostatic repulsion energy, and $E_{\mathrm{xc}}(\rho)$ is the exchange–correlation energy density functional. Many electron-density-based indices, including the Fukui function, can be derived from the hardness kernel [9].

To obtain an equation for the Fukui function in terms of the hardness kernel, we use the fact that the hardness kernel is the inverse of the softness kernel to obtain

$$\begin{aligned}1 &= \int \delta(\mathbf{r}-\mathbf{r}'')\mathrm{d}\mathbf{r}'' \\ &= \int\int \eta(\mathbf{r},\mathbf{r}')s(\mathbf{r}',\mathbf{r}'')\mathrm{d}\mathbf{r}'\mathrm{d}\mathbf{r}'' \\ &= \int \eta(\mathbf{r},\mathbf{r}')\int s(\mathbf{r}',\mathbf{r}'')\mathrm{d}\mathbf{r}''\mathrm{d}\mathbf{r}' \\ &= \int \eta(\mathbf{r},\mathbf{r}')\cdot Sf(\mathbf{r}')\mathrm{d}\mathbf{r}' \ ,\end{aligned} \tag{49}$$

where the last step follows from Eq. (27). By applying the definition of the softness (Eq. 25) it follows that

$$\eta = \int f(\mathbf{r}')\eta(\mathbf{r},\mathbf{r}')\mathrm{d}\mathbf{r}' \ . \tag{50}$$

Equation (50) is a known result and can also be derived from the chain rule for functional derivatives [27, 32] and the variational principle for the Fukui function [3, 27].

For integer numbers of electrons at zero temperature, Eq. (50) becomes two integral equations, one for the Fukui function from above,

$$\eta^+ = \int f^+(\mathbf{r}')\eta^+(\mathbf{r},\mathbf{r}')\mathrm{d}\mathbf{r}' \ , \tag{51}$$

and one for the Fukui function from below,

$$\eta^- = \int f^-(\mathbf{r}')\eta^-(\mathbf{r},\mathbf{r}')\mathrm{d}\mathbf{r}' \ . \tag{52}$$

While $\eta^+ = \eta^- = 0$ for exact DFT, this is not generally true for hardness kernels computed with approximate exchange–correlation functionals. If we can compute the one-sided hardness kernels from the results of a Kohn–Sham calculation, then we may compute the Fukui functions by solving integral Eqs. (51) and (52).

We approach the one-sided hardness kernels through Eq. (47). In particular, note that we can compute $\delta^2 E_{\mathrm{xc}}(\rho)/\delta\rho(\mathbf{r}')\delta\rho(\mathbf{r})$ for any approximate exchange–correlation energy density functional, while

$$\frac{\delta^2 J(\rho)}{\delta\rho(\mathbf{r}')\delta\rho(\mathbf{r})} = \frac{1}{|\mathbf{r}-\mathbf{r}'|} \ . \tag{53}$$

What is required, then, is a method for computing the one-sided functional derivatives of the Kohn–Sham kinetic energy, $\left(\delta^2 T_{\mathrm{s}}(\rho)/\delta\rho(\mathbf{r}')\delta\rho(\mathbf{r})\right)^+$ and $\left(\delta^2 T_{\mathrm{s}}(\rho)/\delta\rho(\mathbf{r}')\delta\rho(\mathbf{r})\right)^-$. These functional derivatives can be expressed in terms of Kohn–Sham DFT quantities, as is now shown.

We start by recalling that

$$\frac{\delta T_{\mathrm{s}}(\rho)^{+/-}}{\delta\rho(\mathbf{r})} = \varepsilon_{\mathrm{LUMO/HOMO}} - v_{\mathrm{K-S}}(\rho;\mathbf{r}) \ . \tag{54}$$

(This result for noninteracting systems is analogous to the equation

$$\left(\frac{\delta F(\rho)}{\delta\rho(\mathbf{r})}\right)^{+/-} = \mu^{+/-} - v(\rho;\mathbf{r}) \ ,$$

which holds for interacting systems.)

By taking the functional derivative of Eq. (54) with respect to the density, we obtain

$$\left(\frac{\delta T_{\mathrm{s}}(\rho)}{\delta\rho(\mathbf{r}')\delta\rho(\mathbf{r})}\right)^{+/-} = \frac{\delta\left[\varepsilon_{\mathrm{LUMO/HOMO}}(\rho)\right]}{\delta\rho(\mathbf{r}')} - \frac{\delta v_{\mathrm{K-S}}(\rho;\mathbf{r})}{\rho(\mathbf{r}')} \ . \tag{55}$$

To compute $\frac{\delta\left[\varepsilon_{\mathrm{LUMO/HOMO}}(\rho)\right]}{\delta\rho(\mathbf{r}')}$, use the relation

$$\begin{aligned}&\varepsilon_{\mathrm{LUMO/HOMO}}(\rho) \equiv \\ &\left\langle \psi_{\mathrm{LUMO/HOMO}}(r) \middle| -\frac{1}{2}\nabla^2 + v_{\mathrm{K-S}}(\rho;\mathbf{r}) \middle| \psi_{\mathrm{LUMO/HOMO}}(\mathbf{r}) \right\rangle \ ,\end{aligned} \tag{56}$$

to obtain

$$\begin{aligned}&\frac{\delta\left[\varepsilon_{\mathrm{LUMO/HOMO}}(\rho)\right]}{\delta\rho(\mathbf{r}')} \\ &= \left\langle \psi_{\mathrm{LUMO/HOMO}}(\mathbf{r}) \middle| -\frac{1}{2}\nabla^2 + v_{\mathrm{K-S}}(\rho;\mathbf{r}) \middle| \frac{\delta\psi_{\mathrm{LUMO/HOMO}}(\mathbf{r})}{\delta\rho(\mathbf{r}')} \right\rangle \\ &+ \left\langle \frac{\psi_{\mathrm{LUMO/HOMO}}(\mathbf{r})}{\delta\rho(\mathbf{r}')} \middle| -\frac{1}{2}\nabla^2 + v_{\mathrm{K-S}}(\rho;\mathbf{r}) \middle| \psi_{\mathrm{LUMO/HOMO}}(\mathbf{r}) \right\rangle \\ &+ \left\langle \psi_{\mathrm{LUMO/HOMO}}(\mathbf{r}) \middle| \frac{\delta\left(-\frac{1}{2}\nabla^2 + v_{\mathrm{K-S}}(\rho;\mathbf{r})\right)}{\delta\rho(\mathbf{r}')} \middle| \psi_{\mathrm{LUMO/HOMO}}(\mathbf{r}) \right\rangle \ .\end{aligned} \tag{57}$$

Substitution of the Kohn–Sham equations,

$$\left(-\frac{1}{2}\nabla^2 + v_{\mathrm{K-S}}(\rho;\mathbf{r})\right)\psi_{\mathrm{LUMO/HOMO}}(\mathbf{r})$$
$$= \varepsilon_{\mathrm{LUMO/HOMO}}\cdot\psi_{\mathrm{LUMO/HOMO}}(\mathbf{r}) \ , \tag{58}$$

into Eq. (57) yields

$$\begin{aligned}
&\frac{\delta\left[\varepsilon_{\mathrm{LUMO/HOMO}}(\rho)\right]}{\delta\rho(\mathbf{r}')} \\
&= 2\varepsilon_{\mathrm{LUMO/HOMO}}\cdot\frac{\delta}{\delta\rho(\mathbf{r}')} \\
&\quad\times\left\langle\psi_{\mathrm{LUMO/HOMO}}(\mathbf{r})\middle|\psi_{\mathrm{LUMO/HOMO}}(\mathbf{r})\right\rangle \\
&\quad+\left\langle\psi_{\mathrm{LUMO/HOMO}}(\mathbf{r})\middle|\frac{\delta v_{\mathrm{K-S}}(\rho;\mathbf{r})}{\delta\rho(\mathbf{r}')}\middle|\psi_{\mathrm{LUMO/HOMO}}(\mathbf{r})\right\rangle \\
&= 2\varepsilon_{\mathrm{LUMO/HOMO}}\cdot\frac{\delta(1)}{\delta\rho(\mathbf{r}')} \\
&\quad+\left\langle\psi_{\mathrm{LUMO/HOMO}}(\mathbf{r})\middle|\frac{\delta v_{\mathrm{K-S}}(\rho;\mathbf{r})}{\delta\rho(\mathbf{r}')}\middle|\psi_{\mathrm{LUMO/HOMO}}(\mathbf{r})\right\rangle \\
&= \int\left|\psi_{\mathrm{LUMO/HOMO}}(\mathbf{r})\right|^2\frac{\delta v_{\mathrm{K-S}}(\rho;\mathbf{r})}{\delta\rho(\mathbf{r}')}\mathrm{d}\mathbf{r} \ .
\end{aligned}\tag{59}$$

Identifying $\varepsilon_{\mathrm{LUMO}}$ with $-A$ and $\varepsilon_{\mathrm{HOMO}}$ with $-I$ reveals that Eq. (59) represents an approximate formula for the local hardness, $\eta(\mathbf{r})$.[4] Combining Eqs. (55) and (59) yields an expression for the second functional derivative of the Kohn–Sham kinetic energy:

$$\left(\frac{\delta T_{\mathrm{s}}(\rho)}{\delta\rho(\mathbf{r}')\delta\rho(\mathbf{r})}\right)^{+/-} = \int\left|\psi_{\mathrm{LUMO/HOMO}}(\mathbf{r})\right|^2\frac{\delta v_{\mathrm{K-S}}(\rho;\mathbf{r})}{\delta\rho(\mathbf{r}')}\mathrm{d}\mathbf{r} - \frac{\delta v_{\mathrm{K-S}}(\rho;\mathbf{r})}{\delta\rho(\mathbf{r}')} \ . \tag{60}$$

Then, combining this last result with Eqs. (47) and (53) gives an expression for the one-sided hardness kernels:

$$\eta^{+/-}(\mathbf{r},\mathbf{r}') = \int\left|\psi_{\mathrm{LUMO/HOMO}}(\mathbf{r})\right|^2\frac{\delta v_{\mathrm{K-S}}(\rho;\mathbf{r})}{\delta\rho(\mathbf{r}')}\mathrm{d}\mathbf{r} - \frac{\delta v_{\mathrm{K-S}}(\rho;\mathbf{r})}{\delta\rho(\mathbf{r}')} + \frac{1}{|\mathbf{r}-\mathbf{r}'|} + \frac{\delta^2 E_{\mathrm{xc}}(\rho)}{\delta\rho(\mathbf{r}')\delta\rho(\mathbf{r})} \ . \tag{61}$$

Because the zero of energy is arbitrary, $v_{\mathrm{K\text{-}S}}(\mathbf{r})$ is only defined up to an arbitrary constant; therefore, $\delta v_{\mathrm{K-S}}(\rho;\mathbf{r})/\delta\rho(\mathbf{r}')$ is only defined up to a constant. However, because the Kohn–Sham orbitals are normalized to unity, the expressions for $(\delta T_{\mathrm{s}}(\rho)/\delta\rho(\mathbf{r}')\delta\rho(\mathbf{r}))^{+/-}$ (Eq. 60) and $\eta^{+/-}$ (Eq. 61) are invariant with respect to arbitrary constants in $\delta v_{\mathrm{K-S}}(\rho;\mathbf{r})/\delta\rho(\mathbf{r}')$.

When combined with a method for computing, and the integral equations for the Fukui functions (Eqs. 51, 52), Eq. (61) allows us to compute the Fukui functions from the output of a Kohn–Sham calculation. Alternatively, Eq. (61) could be used in the variational principle for the Fukui function [3, 27].

Now we discuss methods for computing $\delta v_{\mathrm{K-S}}(\rho;\mathbf{r})/\delta\rho(\mathbf{r}')$.[5] Consider that

$$\int\left(\frac{\delta\rho(\mathbf{r}')}{\delta v_{\mathrm{K-S}}(\mathbf{r})}\right)_N\mathrm{d}\mathbf{r} = \int\left(\frac{\delta\rho(\mathbf{r}')}{\delta v_{\mathrm{K-S}}(\mathbf{r})}\right)_N\mathrm{d}\mathbf{r}' = 0 \ , \tag{62}$$

a result that follows directly from Eq. (14). Physically, Eq. (62) reflects the fact that shifting the Kohn–Sham potential by a constant only shifts the zero of energy and does not change the density. Equation (62) reveals that $(\delta\rho(\mathbf{r}')/\delta v_{\mathrm{K-S}}(\mathbf{r}))_N$ possesses a zero eigenvalue and hence has no inverse; however, $\delta v_{\mathrm{K-S}}(\rho;\mathbf{r})/\delta\rho(\mathbf{r}')$ may be regarded as a generalized inverse of $(\delta\rho(\mathbf{r}')/\delta v_{\mathrm{K-S}}(\mathbf{r}))_N$ since

$$\int\frac{\delta v_{\mathrm{K-S}}(\rho;\mathbf{r})}{\delta\rho(\mathbf{r}')}\left(\frac{\delta\rho(\mathbf{r}')}{\delta v_{\mathrm{K-S}}(\mathbf{r}'')}\right)_N\mathrm{d}\mathbf{r}' = \delta(\mathbf{r}-\mathbf{r}'') \ . \tag{63}$$

In order to find a generalized inverse of $(\delta\rho(\mathbf{r}')/\delta v_{\mathrm{K-S}}(\mathbf{r}''))_N$, we must remove the "infinite wavelength" variations, which correspond to shifting $v_{\mathrm{K\text{-}S}}(\mathbf{r})$ by a constant.[6] One may accomplish this by performing a singular value decomposition. One starts by expanding $(\delta\rho(\mathbf{r}')/\delta v_{\mathrm{K-S}}(\mathbf{r}''))_N$ in a basis set, thereby obtaining a matrix, $\mathbf{P}^{\mathrm{K\text{-}S}}{}_{i,j}$. On diagonalizing the matrix, one obtains an expression for $(\delta\rho(\mathbf{r}')/\delta v_{\mathrm{K-S}}(\mathbf{r}''))_N$ in terms of its eigenvalues, λ_{i}, and eigenvectors, $\mathscr{L}_i(\mathbf{r})$,

$$\left(\frac{\delta\rho(\mathbf{r}')}{\delta v_{\mathrm{K-S}}(\mathbf{r}'')}\right)_N \equiv \sum_{i=0}^{\infty}\lambda_i\mathscr{L}_i(\mathbf{r}')\mathscr{L}_i(\mathbf{r}''). \tag{64}$$

The generalized inverse is then

$$\frac{\delta v_{\mathrm{K-S}}(\rho;\mathbf{r})}{\delta\rho(\mathbf{r}')} = {\sum_i^{\infty}}'\left(\frac{1}{\lambda_i}\right)\mathscr{L}_i(\mathbf{r}')\mathscr{L}_i(\mathbf{r}'') \ , \tag{65}$$

where the prime on the summation symbol indicates that the sum excludes i for which $\lambda_{\mathrm{i}} = 0$.[7] The analogue of this procedure for periodic systems has been explored by many authors [33–35].

Because the expression for $\delta v_{\mathrm{K-S}}(\rho;\mathbf{r})/\delta\rho(\mathbf{r}')$ is derived from information about the constant N system, a more accurate notation for the result of Eq. (65) is $(\delta v_{\mathrm{K-S}}(\rho;\mathbf{r})/\delta\rho(\mathbf{r}'))_N$. As shown by Parr and Bartolotti [36], functional derivatives at constant N differ from unrestricted functional derivatives by an arbitrary additive constant. For $(\delta v_{\mathrm{K-S}}(\rho;\mathbf{r})/\delta\rho(\mathbf{r}'))_N$ and $\delta v_{\mathrm{K-S}}(\rho;\mathbf{r})/\delta\rho(\mathbf{r}')$, this poses no problem, as it merely reflects the invariance of Kohn–Sham calculations

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[4] In order to make this identification, it is necessary that one constrain $v_{\mathrm{K\text{-}S}}(\rho;\mathbf{r})$ to approach zero (rather than some other constant) asymptotically. This amounts to fixing the zero of energy. Reference [9] establishes that the local hardness is not uniquely defined in DFT. The present definition is useful in the context of Ref. [3].

[5] The Hohenberg–Kohn theorem, as applied to a system of noninteracting electrons, ensures that $\delta v_{\mathrm{K-S}}(\mathbf{r})/\delta\rho(\mathbf{r}')$ exists whenever both $\rho(\mathbf{r})$ and $\rho(\mathbf{r}) + \delta\rho(\mathbf{r})$ are noninteracting-v-representable.

[6] Especially for periodic systems, it is often easier to subtract out the effects of zero-wavenumber variations in $v_{\mathrm{K\text{-}S}}(\mathbf{k})$. Conseqently, one takes the Fourier transform of $(\delta\rho(\mathbf{r}')/\delta v_{\mathrm{K-S}}(\mathbf{r}))_N$ and removes the zero-wavenumber "modes", thereby obtaining a polarizability kernel, $(\delta\rho(\mathbf{k}')/\delta v_{\mathrm{K-S}}(\mathbf{k}))_N^0$ that does not include the effects of constant shifts in $v_{\mathrm{K\text{-}S}}(\mathbf{r})$ [33–35]. Inverting this matrix and performing the inverse Fourier transform yields a generalized inverse, $\delta v_{\mathrm{K-S}}(\rho;\mathbf{r})/\rho(\mathbf{r}')$.

[7] In practice, one omits all λ_{i} whose absolute value is sufficiently close to zero.

to constant shifts of $v_{\text{K-S}}(\rho;\, \mathbf{r})$. From this perspective, the computational procedure of Eq. (65) represents a method for fixing the value of this constant. This causes no problems: returning to the discussion following Eq. (61), it is clear that the particular value assumed by this constant does not alter the results of Eqs. (60) or (61).

4 Conclusion

This article shows how key electron-density-based and external-potential-based reactivity indices may be computed from the output of a Kohn–Sham DFT calculation. This does not suggest that these indices are necessarily easily computed in this fashion, or that the methods proposed here are optimal. For the Fukui function in particular, methods which combine satisfactory accuracy with suitable computational ease are available [7, 25]. In general, however, the methods proposed here should be no more costly than obtaining the original solution to the Kohn–Sham equations.

Many of the results contained within the treatment have been previously derived in other contexts; as such, the primary contribution of this article consists of combining these results to form a plausible scheme for computing the reactivity indices of interest to chemistry. For instance, the time- and frequency-dependent analogues to Eq. (19) are important tools in the time-dependent DFT approach to excitation energies [15]. While Eqs. (28) and (32) have been previously presented in the context of DFT reactivity theory [9, 20, 21], the present derivations are more straightforward. Similarly, though Eq. (50) is a known result [3, 27, 28, 32], the present derivation is new. Finally, the expressions for the second functional derivative of $T_s(\rho)$ (Eq. 60) and the hardness kernel (Eq. 61) in terms of Kohn–Sham DFT quantities are, to the best of the author's knowledge, original to the present work. As developed in Ref. [9] and emphasized in Refs. [20, 21], the hardness kernel is the fundamental DFT reactivity index; hence, Eq. (61) has many potential applications. Likewise, there has recently been renewed interest in the kinetic energy kernel, $\delta T_s(\rho)/\delta\rho(\mathbf{r}')\delta\rho(\mathbf{r})$ [37–39]. It is expected that the exact Eq. (60) will be helpful for both formal studies and also applications. In particular, Eq. (60) may prove useful for the DFT-based embedding method of Govind et al. [38], where both $(\delta T_s(\rho)/\delta\rho(\mathbf{r}))^{+/-}$ (Eq. 54) and the way $(\delta T_s(\rho)/\delta\rho(\mathbf{r}))^{+/-}$ changes as electron density is transferred between the "bulk" and "cluster" subsystems,

$$\left(\frac{\delta T_s(\rho)}{\delta\rho(\mathbf{r})}\right)^{+/-} = \int \left(\frac{\delta T_s(\rho)}{\delta\rho(\mathbf{r}')\delta\rho(\mathbf{r})}\right)^{+/-} \delta\rho(\mathbf{r}')\,d\mathbf{r}' \ , \qquad (66)$$

are of interest.

We conclude with a few words concerning the successful application of the reactivity indices considered in this article. The derivations in Refs. [3, 4] emphasize that the reactivity indices of DFT represent "response functions" to perturbations in the electron number (electron-density-based indices) or the external potential (external-potential-based indices). As such, they will be most reliable when the perturbation is small, so that higher-order effects are negligible. Consequently, the reactivity indices of DFT are most appropriate for describing geometries in which the reactants are well separated, so that the perturbations under consideration are relatively weak. This suggests that one consider the values the local reactivity indices, $\Upsilon_{N/\mu}(\mathbf{X})$ and $f(\mathbf{r})$, assume on the molecular van der Waals surface. For reactions where the transition state is reached while the reactants are still well separated (that is, the transition state is positioned early along the reaction coordinate), large values of $f(\mathbf{r})$ (small values of $\Upsilon_{N/\mu}(\mathbf{X})$) should indicate enhanced site reactivity. In practice, plots of reactivity indices on molecular van der Waals surfaces may correctly predict the products of reactions even when the transition state is not especially early; for such reactions, however, higher-order response functions may significantly influence reactivity patterns and, hence, the types of reactivity indices considered here may prove unreliable.

Concerning the definition of the "van der Waals surface" of a molecule, the isodensity surfaces, $\rho(\mathbf{r}) = k$ (generally $0.001 \le k \le 0.002$), have been successfully employed for studies of chemical reactivity using the Fukui function and molecular electrostatic potential [40]. Perhaps more appropriate to Kohn–Sham DFT, however, is the surface

$$v_{\text{K-S}}(\mathbf{r}) = \varepsilon_{\text{HOMO}} \ , \qquad (67)$$

where $\varepsilon_{\text{HOMO}}$ is the orbital energy of the highest occupied molecular orbital, which corresponds to the classical turning point for the noninteracting electrons in the Kohn–Sham reference system. This surface strongly resembles van der Waals surfaces generated by other criteria [41] and is expected to strongly resemble the accurate classical turning point surface [42].

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