

The Fukui Potential and the Capacity of Charge and the Global Hardness of Atoms

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ABSTRACT: In the course of a reaction it is the shape of the Fukui potential that guides a distant reagent toward the site where an electrophile/nucleophile is willing to accept/donate charge. In this paper we explore the mathematical characteristics of the Fukui potential and demonstrate its relationship to the hardness and the ability of an atom in a molecule to change its charge. The Fukui potential not only determines the active site for electron transfer, but it also approximates the distribution of hardness of a molecule: it is the Coulomb contribution to the frontier local hardness. The Fukui potential at the position of the nuclei is equal to the variation of the chemical potential with the nuclear charge and therefore measures the sensitivity of the system to changes in atom type. In the specific case of atoms and slightly charged ions, the Fukui potential at the nucleus measures the hardness. The strong correlation between the hardness and the Fukui potential at the nucleus suggests that the Fukui potential at the nucleus is an alternative definition for the chemical hardness.

$$v_f(\mathbf{r}) \Big|_{\mathbf{r}=\mathbf{0}} = \int \frac{f(\mathbf{r}')}{|\mathbf{r}-\mathbf{r}'|} d\mathbf{r}' \propto \eta$$

I. INTRODUCTION

The strategy of using the mathematical formulation of density functional theory (DFT) to formulate models for chemical reactivity started with the work of Parr and his collaborators in the late 1970s and early 1980s.^{1–7} Nowadays, the importance and interpretation of most of the basic DFT-based chemical reactivity indicators—electronegativity,¹ hardness,^{2,8} Fukui function,^{3,4,9–12} local softness,^{9,13} etc.—is well-established. Many open questions remain, however, both to improve the predictive power of existing models and to extend the DFT-based formalism to a greater diversity of chemical reactions. This work is designed to explore the properties of one of the most fundamental, rarely explored, and in our opinion underutilized reactivity indicators in DFT: the Fukui potential.^{14,15} In this paper, we explore the mathematical characteristics of the Fukui potential and discuss its usefulness for characterizing regioselectivity preferences in electrophile–nucleophile reactions and its link with chemical hardness.

Although it is customary to classify reactions as being controlled by either electron-transfer (i.e., frontier molecular orbital) or electrostatic (i.e., charge) effects, there is a continuum of intermediate cases where both effects are important. This was first pointed out, in the context of molecular orbital theory, in the seminal work by Klopman and Salem^{16,17} and was later extended to DFT-based chemical reactivity indicators by Anderson et al.¹⁵ There are many cases where either electron-transfer or electrostatic effects predominate so that only one effect need be considered. Electron-transfer-controlled reactions usually feature neutral molecules with slightly charged active sites. This corresponds to the interaction of soft molecules and the breaking and

formation of covalent bonds. Electrostatically controlled reactions usually feature highly charged species and ionic-bond transformations. Though the electronic interaction energy between electron donors (i.e., nucleophiles) and electron acceptors (i.e., electrophiles) was formulated in the DFT context long ago,^{2,14} to account for all the interactions that drive chemical reactions one must include the nuclear–nuclear repulsion.^{15,18,19} The key DFT-based expression for the change in the energy of an electrophile upon attack by a nucleophile is thus^{7,15}

$$\Delta W_{e\text{-phile}} = \mu_{e\text{-phile}}^+ \Delta N - \int \left(\sum_{\alpha \in e\text{-phile}} Z_{\alpha} \delta(\mathbf{r} - \mathbf{R}_{\alpha}) - \rho_{e\text{-phile}}(\mathbf{r}) - \Delta N f_{e\text{-phile}}^+(\mathbf{r}) \right) \delta v_{N\text{-phile}}(\mathbf{r}) d\mathbf{r} \quad (1)$$

where N-phile and e-phile stand for properties of the nucleophile and electrophile and the charge and position of the nuclei are indexed by α . The right-hand chemical potential, μ^+ , is equal to minus the electron affinity. ΔN is the number of electrons transferred from the nucleophile to the electrophile. $\delta v_{N\text{-phile}}(\mathbf{r})$ is the change in the external potential of the electrophile due to the presence of the nucleophile. $\delta(\mathbf{r} - \mathbf{R}_{\alpha})$ is the Dirac δ function centered at the position of the nucleus α , which accounts for the electrostatic interaction between the nuclei of both species, which are considered point charges. The second term in the integral corresponds to a classical electrostatic interaction of the nucleophile with the electron density of the

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acceptor. This term, together with the first (point charge) term, plays the decisive role for electrostatic control of the reaction.

The last term in eq 1, where the right-hand Fukui function is involved, accounts for the stabilization of the electrophile after electron transfer from the nucleophile takes place. It captures how the electrostatic interactions between the reagents change upon charge transfer, when ΔN electrons are transferred from the nucleophile. Clearly, this term captures information about the electron-transfer control of the reaction. It is important to note that eq 1 is rigorously valid only at 0 K and for small perturbations in the external potential, where higher-order contributions from $\delta v_{N\text{-phile}}(\mathbf{r})$ are, if not quantitatively small, at least qualitatively unimportant.

Although the effective external potential that the electrophile feels from the presence of the nucleophile can, in principle, be calculated exactly,^{20,21} when the reagents are far apart electrostatic interactions dominate, so^{20,21}

$$\delta v_{N\text{-phile}}(\mathbf{r}) \approx -\Phi_{N\text{-phile}}(\mathbf{r}) + \Delta N \int \frac{f_{N\text{-phile}}^-(\mathbf{r}')}{|\mathbf{r}' - \mathbf{r}|} d\mathbf{r}' \quad (2)$$

The second term, which involves the nucleophilic Fukui function of the nucleophile, is a correction to the molecular electrostatic potential (MEP), $\Phi(\mathbf{r})$. This correction explains the change in the MEP of the donor after ΔN electrons are transferred to the acceptor. Analogous equations to eqs 1 and 2 hold for the nucleophile in the presence of an electrophilic reagent. The only changes are the permutation of the indexes N-phile and e-phile and the sign of ΔN . Adding together $\Delta W_{N\text{-phile}}$ and $\Delta W_{e\text{-phile}}$ and subtracting a correction for the double counting of interactions yields the following approximation for the total interaction energy between substrate and reagent:^{19,22,23}

$$\begin{aligned} \Delta W_{\text{int}} = & (A_{e\text{-phile}} - I_{N\text{-phile}})\Delta N + \int \left(\sum_{\alpha \in N\text{-phile}} Z_{\alpha} \delta(\mathbf{r} - \mathbf{R}_{\alpha}) \right. \\ & - \rho_{N\text{-phile}}(\mathbf{r})\Phi_{e\text{-phile}}(\mathbf{r}) d\mathbf{r} + \Delta N \int (f_{e\text{-phile}}^+(\mathbf{r})\Phi_{N\text{-phile}}(\mathbf{r}) \\ & \left. - f_{N\text{-phile}}^-(\mathbf{r})\Phi_{e\text{-phile}}(\mathbf{r}) d\mathbf{r} - (\Delta N)^2 \int \int \frac{f_{N\text{-phile}}^-(\mathbf{r})f_{e\text{-phile}}^+(\mathbf{r}')}{|\mathbf{r}' - \mathbf{r}|} d\mathbf{r} d\mathbf{r}' \right) \quad (3) \end{aligned}$$

The first term is independent of the orientation of the molecule and does not play a role in regioselectivity. The second term is a pure electrostatic interaction, and it is generally negative because the reactive sites of electrophiles and nucleophiles are, respectively, usually positively and negatively charged. The third term is the correction to the electrostatic interaction because of the electron transfer between both molecules. This term is usually positive: electron transfer weakens the strength of the electrostatic interaction because electron flow from the nucleophile to the electrophile tends to equalize the charges of the reactive sites. Finally, the integrand in the last term is usually positive because the Fukui function is positive, with some exceptions only in small regions around the nuclei of molecules with nodes of the frontier orbitals in the nuclear positions.²⁴ This term, then, is stabilizing and depends entirely on the relative orientation between the "frontier" densities of the molecules; this term is decisive for explaining the regioselectivity of slightly charged species, where electrostatic interactions are negligible. The last term is a purely electron-transfer contribution and is, thus, most important for

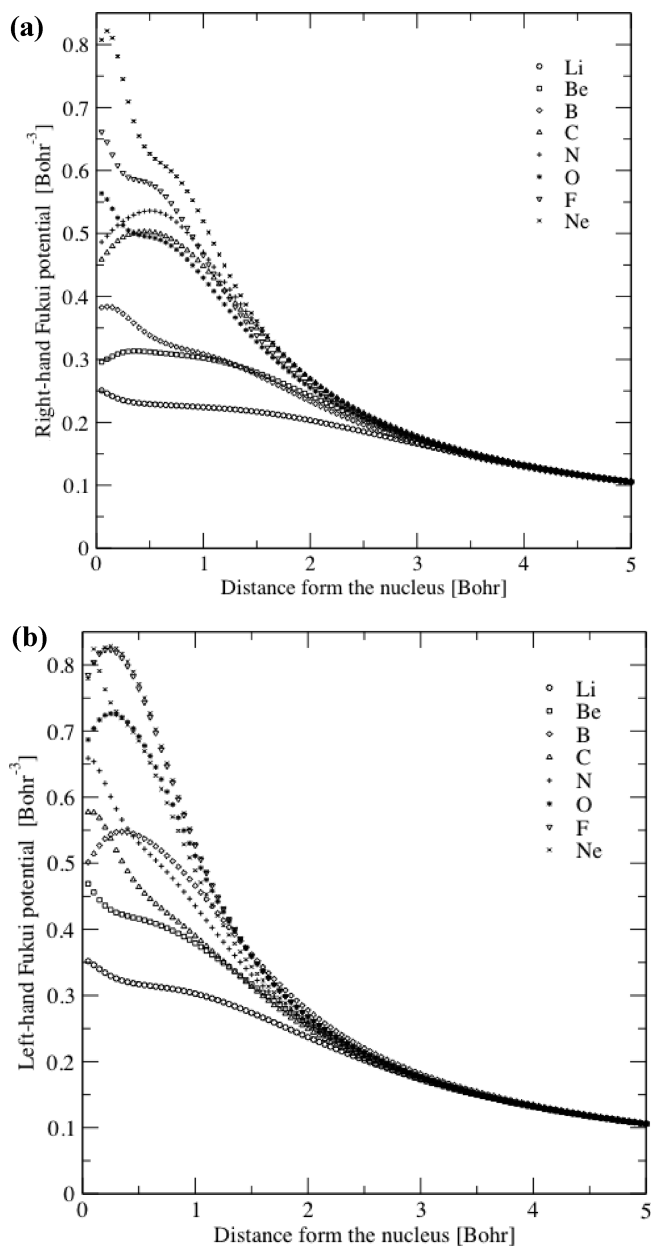


Figure 1. Fukui potential $v_f(\mathbf{r})$ of all the atoms of the second period. (a) $v_f^+(\mathbf{r})$ was computed from the MEP of the neutral and anion, $v_f^+(\mathbf{r}) = -(\phi^{\text{Anion}}(\mathbf{r}) - \phi^{\text{Neutral}}(\mathbf{r}))$. (b) $v_f^-(\mathbf{r})$ was computed from the MEP of the neutral and cation, $v_f^-(\mathbf{r}) = -(\phi^{\text{Neutral}}(\mathbf{r}) - \phi^{\text{Cation}}(\mathbf{r}))$. The MEP was calculated at the HF/6-31G(+) level.

soft reagents. However, as we shall show, this term is also related to local hard–hard interactions.

II. FUKUI POTENTIAL

The Fukui potential is defined as^{11,14}

$$v_f^{+/-}(\mathbf{r}) = \int \frac{f^{+/-}(\mathbf{r}')}{|\mathbf{r}' - \mathbf{r}|} d\mathbf{r}' \quad (4)$$

This is the electrostatic potential due to a distribution of charge equal to the Fukui function.

To show the key role of the Fukui potential for selectivity, reconsider how the fourth term of eq 3 depends on the Fukui

potential of the electrophile, $v_{f,e\text{-phile}}^{+/-}(\mathbf{r}')$. Suppose that the substrate and reagent are far from each other and that the nucleophile has only one active site, α . From the point of view of the electrophile, the Fukui function of the partner can be condensed to a pointwise distribution centered on the reactive site, α , and the integral can be approximated by

$$f_{N\text{-phile},\alpha}^- \int \frac{f_{e\text{-phile}}^+(\mathbf{r}')}{|\mathbf{r}' - \mathbf{r}|} d\mathbf{r}' = f_{N\text{-phile},\alpha}^- v_{f,e\text{-phile}}^+(\mathbf{r}) \quad (5)$$

where $f_{N\text{-phile},\alpha}^-$ is a condensed representation of the Fukui function.^{21,25–28} Hence, the nucleophile will approach the electrophile at a site where the Fukui potential of the electrophile is big because this maximizes its energetic stability. It is the shape of the Fukui potential that guides a distant reagent to the place in the electrophile that is most willing to accept electrons.

It is the value of the Fukui potential, more than the value of the Fukui function itself, that determines the reactive site. One might argue that the sites where the Fukui function and the Fukui potential are large coincide, but this is not strictly true. There are often local maxima of both the Fukui function and the Fukui potential at the nuclear positions, but this is not necessary true—sometimes the Fukui function/potential is a minimum here. Because of the cusp condition, the Fukui function is always either a maximum or a minimum at each nucleus.¹¹ Certainly the local maxima of the Fukui function are not necessarily always at the position of nuclei and the maxima of the Fukui function can be very broad.²⁹ Regioselectivity is mostly controlled by the value of the Fukui potential on a “reactive surface” associated with the initial contact between two molecules. At this stage the reagents are usually separated by a distance greater than the sum of their van der Waals radii, and approximating the Fukui and the electrostatic potentials of the reagents as being generated by point charges (as in eq 5) is a reasonable approximation. This suggests that the energy expression in eq 3 is not very sensitive to the values of the Fukui function and the Fukui potential at the atomic nuclei.

In Figure 1, parts a and b, the Fukui potentials of atoms of the second period are depicted. The forms of the curves closely resemble the plots by Chattaraj et al.,³⁰ which are the only plots of atomic Fukui potentials we are aware of. The Fukui potential exhibits a maximum close to the nuclear position and decays with the distance. The asymptotic form of the Fukui potential is $-1/r$ plus correction terms. The asymptotic decay of the exchange-correlation potential is, in fact, dominated by the Fukui potential.³¹

Since the Fukui function can have negative values, it is striking that the Fukui potentials for these atoms do not show negative values. This arises because the Fukui potential at \mathbf{r} (cf. eq 4) has contributions from the Fukui function over the entire range of \mathbf{r}' , and the Fukui function is rarely negative except in small regions where the highest occupied molecular orbital (HOMO) (for f^-) or the lowest unoccupied molecular orbital (LUMO) (for f^+) have nodal surfaces.^{24,32,33} The HOMO has a node at the origin for boron–neon, but not for lithium–beryllium.³² Therefore the f^- is negative near the origin for boron–neon. This explains why, in Figure 1b, the Fukui potentials have a local maximum for lithium and beryllium but local minima for the p-block elements. A similar argument can be used to explain the near-nuclear behavior of $v_f^-(\mathbf{r})$ using Figure 1a, but the trends sometimes are contrary to what would be expected (local minimal for Be–F; local maxima for Li and Ne). This is probably because it is very

hard to perform accurate calculations on these atomic anions, some of which (Be, N, Ne) are unstable; it is also true that orbital relaxation effects are much larger when the ionization potential is small (as it is for an anion),³⁴ and this makes it more difficult to make theoretical predictions about the negative regions of the Fukui function.

One can also use the Fukui potential to address the much more controversial issue of whether there should be negative values for the condensed Fukui functions.^{32,33,35–40} Negative values of the condensed Fukui functions are indisputable if the Fukui potential is negative at any point on or outside van der Waals surface of the molecule. In such cases, negative atom-condensed Fukui functions are needed to reproduce reactivity patterns that are predicted by the Fukui potential. The last term in eq 3 could be positive when one or both of the reagents have negative condensed Fukui functions, but this is still unlikely because the reagents will tend to orient themselves so that this term is negative (energy-lowering).

The Fukui potential clearly plays a decisive role in the regioselectivity aspects of electron-transfer-controlled reactions, as well as a fundamental role in DFT more broadly. This motivated us to study the formal mathematical properties of the Fukui potential and to characterize it numerically for simple systems. Before we do this, however, we wish to comment on the extent to which the Fukui potential might be useful not only for reactions between soft reagents but also for reactions between hard reagents. Specifically, we shall show that the Fukui function is closely related to the local hardness.

III. FUKUI POTENTIAL AND LOCAL HARDNESS

The local hardness is ambiguous in the sense that there are infinitely many ways of defining it^{41–46}

$$\eta(\mathbf{r}) = \int \eta(\mathbf{r}, \mathbf{r}') \omega(\mathbf{r}') d\mathbf{r}' \quad (6)$$

where $\omega(\mathbf{r})$ is any continuous charge density with total charge $+1$. $\eta(\mathbf{r}, \mathbf{r}')$ is the hardness kernel^{47,48}

$$\eta(\mathbf{r}, \mathbf{r}') \equiv \frac{\delta^2 F[\rho(\mathbf{r})]}{\delta \rho(\mathbf{r}) \delta \rho(\mathbf{r}')} \quad (7)$$

with $F[\rho]$ the universal functional in the Hohenberg and Kohn energy functional.^{47,49}

The ambiguity resides in the arbitrariness in choosing $\omega(\mathbf{r})$. Different choices provide different definitions.⁴⁶ When shape function,^{50–52} $\sigma(\mathbf{r})$ [$\sigma(\mathbf{r}) = \rho(\mathbf{r})/N$], is used, the “total local hardness” arises:

$$\eta(\mathbf{r}) = \int \eta(\mathbf{r}, \mathbf{r}') \frac{\rho(\mathbf{r}')}{N} d\mathbf{r}' = \int \eta(\mathbf{r}, \mathbf{r}') \sigma(\mathbf{r}') d\mathbf{r}' \quad (8)$$

If $\omega(\mathbf{r})$ is chosen to be the Fukui function, the local hardness (“frontier local hardness”) is the same everywhere in the space and equal to the global hardness:^{12,30,53–56}

$$\eta_f(\mathbf{r}) = \eta = \int \eta(\mathbf{r}, \mathbf{r}') f(\mathbf{r}') d\mathbf{r}' \quad (9)$$

Explicit expressions for the hardness kernel and frontier local hardness are straightforwardly deduced from the definition of $F[\rho]$ and eq 9

$$\eta(\mathbf{r}, \mathbf{r}') = \frac{1}{|\mathbf{r} - \mathbf{r}'|} + \frac{\delta^2}{\delta\rho(\mathbf{r})\delta\rho(\mathbf{r}')} (T_s[\rho(\mathbf{r})] + \varepsilon_{\text{XC}}[\rho(\mathbf{r})]) \quad (10)$$

and

$$\begin{aligned} \eta_f(\mathbf{r}) = \int \frac{f(\mathbf{r}')}{|\mathbf{r} - \mathbf{r}'|} d\mathbf{r}' + \int f(\mathbf{r}') \frac{\delta^2}{\delta\rho(\mathbf{r})\delta\rho(\mathbf{r}')} (T_s[\rho] \\ + \varepsilon_{\text{XC}}[\rho]) d\mathbf{r}' = v_f(\mathbf{r}) + \eta^{T+\text{XC}}(\mathbf{r}) \end{aligned} \quad (11)$$

where $T_s[\rho(\mathbf{r})]$ is the noninteracting kinetic energy of the Kohn–Sham reference system and $\varepsilon_{\text{XC}}[\rho(\mathbf{r})]$ is the exchange–correlation energy.⁵⁷ The last equation allows us to interpret the Fukui potential as the Coulomb contribution to the frontier local hardness. When approximate hardness kernels are used, it is observed that the Coulomb term in eq 11 makes the largest contribution to the local hardness.⁴⁴ Then, the Fukui potential is representative of the “distribution” of the hardness of a molecule. It seems contradictory that the Fukui potential is an indicator of the willingness of a site to donate/accept electrons but, at the same time, measures the distribution of the local hardness. Hardness and local hardness are usually thought as a descriptor of hard–hard (mostly electrostatic) interactions. Recently, Torrent-Sucarrat et al.⁴⁶ have argued that the local softness (ergo the Fukui function) and the local hardness contain the same information. They say that “the local hardness and local softness are functions that measure the ‘local abundance’ or ‘concentration’ of the corresponding global properties,” and that the difference is that the former integrates to hardness and the latter to the softness, which are authentically inverse properties. Then, eqs 3 and 11 seem to conciliate the authors’ approach as the Fukui function (and local softness) is at the same time an indicator of the soft–soft and hard–hard interactions. Nevertheless, the association of Fukui potential to a density of hardness seems circumstantial as this association/relationship is only true for one definition of the local hardness (the frontier local hardness, evaluated with a specific approximation to the hardness kernel). Not all mathematical definitions of the local hardness are equivalent, but it has been argued that the frontier local hardness is particularly appropriate because it is the minimum-norm choice.⁵³

IV. ELECTRON ACCEPTOR POWER, EXPANSION ON $Z^{1/3}$, AND HARDNESS

The previous two sections reveal that the Fukui potential is a key reactivity indicator related to both electron transfer (softness) controlled reactivity and the local hardness. We would now like to derive formal properties of the Fukui potential. We will restrict ourselves to atoms and atomic ions, because it is only in these cases that simple analytic results can be obtained. We will also focus our attention on the value of the Fukui potential at the nuclear positions, because (a) the asymptotic $-1/r$ decay of the Fukui potential is universal, and therefore not very interesting, and (b) parts a and b of Figure 1 show that the Fukui potential has different (therefore interesting) behavior at the nuclei for different atoms even though the long-range form is very similar. In particular, we will show that the Fukui potential at the nuclear positions measures the variation of the chemical potential with the nuclear charge, which can be interpreted as the willingness of an atom to changes in its total charge. Then, to reinforce our proposal that the Fukui potential measures hardness, we show

that, for atoms, the value of the Fukui potential can be considered a measure of the global hardness.

IV.a. Atoms and Ions. Using the Hellmann–Feynman theorem, the derivative of the energy of a nondegenerate atom or ion with respect to the nuclear charge at fixed electron number is^{58–61}

$$\begin{aligned} \left(\frac{\partial E_N}{\partial Z} \right)_N &= \left\langle \Psi_N \left| \frac{\partial \hat{H}}{\partial Z} \right| \Psi_N \right\rangle = \int \frac{\rho(\mathbf{r})}{|\mathbf{r}|} d\mathbf{r} \\ &= -\langle r^{-1} \rangle = \phi_e(r=0) \end{aligned} \quad (12)$$

This classical result says that the negative of the expected value of r^{-1} is exactly equal to the electronic contribution to the MEP, $\phi_e(\mathbf{r})$, at the position of the nucleus.

In taking the derivative of $(\partial E_N / \partial Z)_N$ with respect to the number of electrons, the discontinuity of the derivative of energy with respect to N must be respected.^{62–68} Therefore, instead of one derivative there are two one-sided derivatives, one for electron removal and another one for electron addition

$$\begin{aligned} \left(\frac{\partial E_N}{\partial Z_A} \right)_N - \left(\frac{\partial E_{N+1}}{\partial Z_A} \right)_N &= - \left(\frac{\partial \mu^+}{\partial Z} \right) \\ &= \int \frac{\rho^{N+1}(\mathbf{r}) - \rho^N(\mathbf{r})}{|\mathbf{r}|} d\mathbf{r} \\ &= \int \frac{f^+(\mathbf{r})}{|\mathbf{r}|} d\mathbf{r} = \langle r^{-1} \rangle_{f^+} \\ &= v_f^+(r=0) \end{aligned} \quad (13)$$

and

$$\begin{aligned} \left(\frac{\partial E_{N-1}}{\partial Z_A} \right)_N - \left(\frac{\partial E_N}{\partial Z_A} \right)_N &= - \left(\frac{\partial \mu^-}{\partial Z} \right) \\ &= \int \frac{\rho^N(\mathbf{r}) - \rho^{N-1}(\mathbf{r})}{|\mathbf{r}|} d\mathbf{r} \\ &= \int \frac{f^-(\mathbf{r})}{|\mathbf{r}|} d\mathbf{r} = \langle r^{-1} \rangle_{f^-} \\ &= v_f^-(r=0) \end{aligned} \quad (14)$$

These equations reveal that the Fukui potential at the nuclear position measures the variation of the chemical potential with the nuclear charge, which can be interpreted as the willingness of an atom to accept/donate electrons.

In the limit of large atomic number, Z , and large electron number, N , one is in a quasiclassical situation, and the derivative discontinuity with respect to electron number can be neglected. In the high- Z limit, increasing Z is similar to decreasing N , since both perturbations make the system more positive. The leading term in a (Z, N) expansion of the chemical potential of a neutral atom ($N/Z = 1$) depends on both N and Z as the inverse of the cubic root, that is⁶⁹

$$\mu_{\text{neutral}} \propto N^{-1/3} \propto Z^{-1/3} \quad (15)$$

The ability of a system to accept electrons is determined by its chemical potential. A species will accept electrons until its chemical potential equals the chemical potential of its surroundings (the bath, or reservoir, of electrons).^{53,70,71} Hence, as the chemical potential

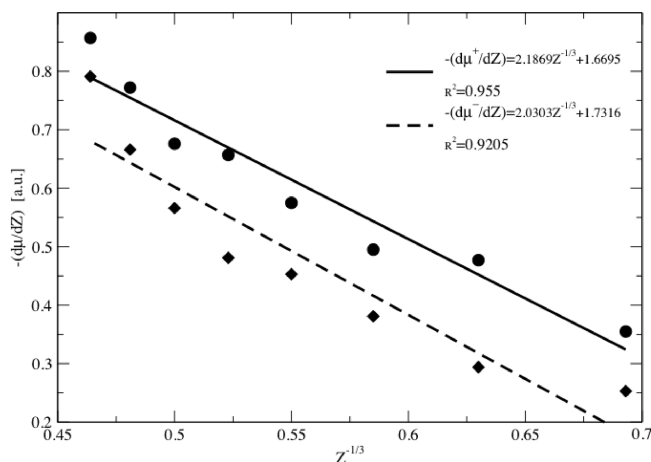


Figure 2. Correlation between $-(\partial\mu^{+/-}/\partial Z)_N$ and $Z^{-1/3}$. $-(\partial\mu/\partial Z)_N$ was calculated from values of the MEP at the nucleus. For details see the caption in Figure 1. The same method of calculation as in Figure 1 was used.

increases (becomes less negative) the capacity of the system for additional electrons decreases, and vice versa. Therefore, the smaller $-(\partial\mu/\partial Z)$ is, the easier it is to ionize the system. This is only true for small changes of charge. In the next section it will be shown that $-(\partial\mu/\partial Z)$ is proportional to the atomic hardness. The hardness is also a measure of resistance of a system to change its state of charge through changes in the number of electrons. Summarizing, the Fukui potential at the position of the nucleus measures the capacity of an atom or ion to change its state of charge.

It is straightforward to extend eq 14 to molecules. The result is essentially the same; minus the derivative of the chemical potential respect to the charge of the nucleus α is the Fukui potential at the position of that nucleus

$$\begin{aligned} -\left(\frac{\partial\mu}{\partial Z_{\alpha}}\right) &= \int \frac{f^{+/-}(\mathbf{r})}{|\mathbf{r}-\mathbf{R}_{\alpha}|} d\mathbf{r} = \langle (\mathbf{r}-\mathbf{R}_{\alpha})^{-1} \rangle_{f^{+/-}} \\ &= v_f^{+/-}(\mathbf{r}=\mathbf{R}_{\alpha}) \end{aligned} \quad (16)$$

The interpretation is the same: the Fukui potential at nuclear positions measures the capacity of an atom in a molecule to change its state of charge.

IV.b. Expansion on Z/N of $v_f(r=0)$. *IV.b.1. Neutral Atoms.* March and White showed that the total energy of an atom and ion can be exactly written as a series in Z/N :^{69,72}

$$E(N, Z) = \sum_{n=0}^{\infty} F_n \left(\frac{N}{Z}\right) Z^{(7-n)/3} \quad (17)$$

from which the chemical potential is readily computed:⁶⁹

$$\mu = \sum_{n=0}^{\infty} Z^{(4-n)/3} F'_n \left(\frac{N}{Z}\right) \quad (18)$$

where $F'_n(N/Z)$ is the derivative of the expansion coefficient respect to N/Z . When the number of electrons is significantly greater than Z ($N/Z \rightarrow \infty$), the electrons are unbound and both the ionization potential and the electron affinity (and therefore the chemical potential, hardness, and all higher derivatives) must be zero. This asymptotic limit forces the first five coefficients in eq 18 to be zero.

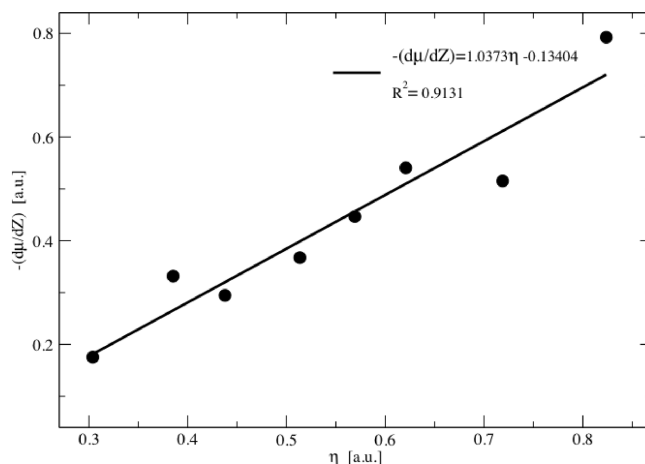


Figure 3. Correlation between $-(\partial\mu/\partial Z)_N$ and experimental values of the hardness (ref 74). $-(\partial\mu/\partial Z)_N$ was evaluated as the average value of $-(\partial\mu^{+}/\partial Z)_N$ and $-(\partial\mu^{-}/\partial Z)_N$. The same computational method as in Figure 1 was used.

Consider first the case of a neutral atom, $N/Z = 1$. According to eq 14, the value of the Fukui potential at the nucleus can be obtained by differentiating the chemical potential with respect to Z in eq 18. This gives the following expansion for $v_f(r=0)$:

$$\begin{aligned} -\left(\frac{\partial\mu}{\partial Z}\right)_N &= v_f(r=0) = -\sum_{n=5}^{\infty} \frac{1}{3} (4-n) Z^{-1 + [(4-n)/3]} F'_n(1) \\ &+ \sum_{n=0}^{\infty} Z^{(1-n)/3} F''_n(1) = \frac{F''_2(1)}{Z^{1/3}} + \frac{F''_3(1)}{Z^{2/3}} + \frac{F''_4(1)}{Z} \\ &+ \frac{1/3 F'_5(1) + F''_5(1)}{Z^{4/3}} + \frac{2/3 F'_6(1) + F''_6(1)}{Z^{5/3}} + \dots \end{aligned} \quad (19)$$

$F''_2(N/Z)$ is the leading coefficient. Tal and Bartolotti⁷³ showed that (a) $F_2(N/Z)$ decreases with N/Z , (b) $F'_2(N/Z)$ is negative of order $O(1)$, and (c) $F''_2(N/Z)$ is negative of order $O(10^{-1}$ to 10). These results are supported by Figure 2, which shows the correlation between $-(\partial\mu^{+/-}/\partial Z)_N$ and $Z^{-1/3}$. The correlation is surprisingly good if one considers the low level of calculation (HF/6-31G(+)) and the fact these atoms are far from the asymptotic limit.

IV.b.2. Slightly Charged Ions. The charge capacity of ions is different from that of neutral atoms. Anions are less prone to gain electrons than cations, whereas cations are less prone to lose electrons than anions. To derive the Z expansion of $v_f(r=0)$ of an ion of charge q (with $N = Z - q$) in terms of the expansion coefficient of the neutral ($N/Z = 1$), take the derivative of eq 18 with respect to Z and expand this derivative in a Taylor expansion around $N/Z = 1$. The final expression at first order in N/Z is

$$\begin{aligned} -\left(\frac{\partial\mu}{\partial Z}\right)_N &= v_f(r=0) \\ &= \frac{F''_2[1]}{Z^{1/3}} + \frac{F''_3[1] - qF''_0[1]}{Z^{2/3}} + \frac{F''_4[1] - qF''_1[1]}{Z} \dots \end{aligned} \quad (20)$$

Note that the proportionality between $v_f(r=0)$ and $Z^{1/3}$ persists: the correction due to charge occurs only at $O(Z^{-2/3})$. The charge capacity of slightly charged ions is similar to that of the

neutral atom. This is not surprising: changing the charge state of an atom should not change the value of the Fukui potential *at the nucleus* very strongly, partly because the charge distribution defined by the Fukui function is concentrated in the valence regions of the atom.

IV.c. Relationship between $-(\partial\mu/\partial Z)_N$ and the Hardness of an Atom. There seems to be a proportionality between the global hardness of atoms, $-(\partial\mu/\partial N)_Z$, and $-(\partial\mu/\partial Z)_N$. The expansion of the derivative of the chemical potential for slightly charged ions and atoms with respect to Z , eq 20, and the corresponding expression for the hardness for slightly charged ions and atoms coincide²³

$$-\left(\frac{\partial\mu}{\partial Z}\right)_N = \left(\frac{\partial\mu}{\partial N}\right)_Z = \eta \quad (21)$$

This expresses the fact that the change in chemical potential upon increasing the atomic charge is universal: whether the charge is changed by adjusting the atomic number or adjusting the number of electrons is irrelevant for nearly neutral atoms in the asymptotic limit.

These asymptotic expansions do not account for the discontinuity of the chemical potential at integer values of N and are only valid in the large- Z large- N limits. It is surprising, then, that eq 21 seems to work well even for light atoms. Figure 3 shows the correlation between experimental hardness and $-(\partial\mu/\partial Z)_N$ for the atoms of the second period.⁷⁴ The quality of the correlation, as appraised by the correlation coefficient R^2 , is surprising, especially if one considers the level of calculation (HF/6-31G) and the inaccuracy of the Gaussian basis set close to the nuclei. Note that the constant of proportionality is close to 1, which is not the case when the experimental values of the hardness are compared to computed values of $I - A$. From data of Table 2 in ref 32 it can be shown that $-(\partial\mu/\partial Z)_N$ of cations correlates well with computational values of hardness ($R^2 = 0.97$), whereas the correlation for anions (which are more difficult to compute) is much weaker but still significant ($R^2 = 0.73$).⁷⁵ For neutrals including elements from the main group in the third period and a few transition metal atoms from the third period, the correlation is slightly less strong ($R^2 = 0.73$).⁷⁵ The correlations are so strong that one might suggest using the value of the Fukui potential at the nucleus as an alternative *definition* of the chemical hardness and explore whether this definition is capable of reproducing the important empirical trends associated with the hardness concept.

Equation 21 may be rationalized through the connection between the Fukui potential and the frontier local hardness. The frontier local hardness of eq 11 is exactly equal to the global hardness when the exact kinetic energy and exchange-correlation energy functionals are used, E_{XC} . If we hypothesize that the Coulomb contribution is dominant near the nuclei, then $v_f(\mathbf{r})$ should be a good approximation to the frontier local hardness and thus to the global hardness also.

V. SUMMARY AND CONCLUSIONS

Chemical reactions are normally classified as being either electron-transfer-controlled or electrostatically controlled. However, most chemical reactions actually fall in between these extremes. There are, however, many reactions that are mostly controlled by electrostatics or electron transfer. In the latter case, the regioselectivity is often associated with the distribution of the Fukui function. However, it is the shape of the Fukui potential (eq 4) that guides a distant reagent toward the site where an

electrophile/nucleophile is willing to accept/donate charge. It is, then, the value of the Fukui potential, more than the Fukui function itself, that determines the reactive site. Moreover, the Fukui potential not only determines the active site for electron transfer, it also approximates the distribution of hardness in a molecule. The Fukui potential can be interpreted as the Coulomb contribution to the frontier local hardness, which we believe to be dominant in many cases.

The Fukui potential at the position of the nuclei measures the sensitivity of the system to changes in atom type. Specifically, the Fukui potential at the position of the an atomic nucleus measures the “alchemical” response of the chemical potential to a change in the nucleus’s atomic number. This suggests that the Fukui potential provides valuable guidance for how to select favorable alchemical variations in the chemical space. Understanding molecular responses to alchemical variations is useful for designing molecules with desirable electronic properties.^{76–83}

In the specific case of atoms and slightly charged ions, the Fukui potential at the nucleus measures the hardness. This result arises because, for slightly charged atomic systems, variations in the atomic number and variations in the number of electrons are similar, at least in the asymptotic limit. The correlation between the hardness and the Fukui potential at the nucleus is so strong that we suggest the Fukui potential at the nucleus be used as an alternative definition of the hardness. A necessary next step is to explore whether the Fukui potential at the nucleus is capable of reproducing experimental trends associated with the hardness concept.

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