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Theoretical
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Perspective

Perspective on "Density functional approach to the frontier-electron theory of chemical reactivity"

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Abstract. The Fukui function, $f(\vec{r})$, was proposed as a tool for deducing the relative reactivity of different positions in a molecule by Parr and Yang in 1984. Herein we sketch the theory of the Fukui function, with special emphasis on its logical motivation, interpretation, qualitative characteristics, and practical computation. We conclude with some words about the Fukui function's extensions, limitations, and importance.

Key words: Fukui function – Site reactivity – Chemical potential – Hardness-softness

1 Introduction

Chemistry is the study of how atoms and molecules act when exposed to external stimuli (other electronic systems, lasers, electrodes, Bunsen burners, etc.). Theoretical chemistry is tasked with both the explanation of existing chemical data and the prediction of new results. Even the former of these tasks is formidable; perusal of a chemical catalog or one of the many handbooks of chemistry will convince one that separate theoretical treatment of each cataloged molecule and chemical reaction is neither possible nor desirable. What we desire are "primitive patterns of understanding" [1] – general principles that both impart order to the chemical storehouse of knowledge and help to predict which molecules and chemical reactions are the most likely to achieve some desired goal.

One such principle is provided by the Fukui function, proposed by Parr and Yang in 1984 as a tool for understanding and predicting the relative reactivity of different sites in a molecule [2]. This paper provides a perspective on the Fukui function through the lens of 15 years of subsequent developments.

2 Theoretical background

We start by asking the following question. Given a molecule, A, how does it react with another molecule, B? When addressing this problem, it is convenient to work with the three-dimensional ground-state electron density, $\rho(\vec{r})$. With the use of $\rho(\vec{r})$, the total energy is given through

$$E_{v_0}[\rho] = F[\rho] + \int \rho(\vec{r}) v_0(\vec{r}) \mathrm{d}\vec{r} \quad , \tag{1}$$

where F is either the original Hohenberg–Kohn functional for nondegenerate ground states or its later extension to degenerate ground states. F is the sum of the kinetic energy functional, T, and the electron–electron repulsion energy functional, V_{ee} [3, 4].

The electron density not only determines the total energy, but also how the total energy changes as the number of electrons, N, and the external potential, $v_0(\vec{r})$, change. To see this, start with the expression for the first-order change in the energy [5]:

$$\mathrm{d}E[N, v_0(\vec{r})] = \left(\frac{\partial E}{\partial N}\right)_{v_0(\vec{r})} \mathrm{d}N + \int \left(\frac{\delta E}{\delta v_0(\vec{r})}\right)_N \delta v_0(\vec{r}) \mathrm{d}\vec{r} \quad . \tag{2}$$

Using Eq. (1) to derive

$$\left(\frac{\delta E}{\delta v_0(\vec{r})}\right)_N = \rho(\vec{r}) \quad , \tag{3}$$

defining the chemical potential through

$$\mu \equiv \left(\frac{\partial E}{\partial N}\right)_{v_0(\vec{r})} \quad , \tag{4}$$

Correspondence to: P. W. Ayers and M. Levy and substituting Eqs. (3) and (4) into Eq. (2) gives the working equation [3]

$$\mathrm{d}E[N, v_0(\vec{r})] = \mu\,\mathrm{d}N + \int \rho(\vec{r})\delta v_0(\vec{r})\mathrm{d}\vec{r} \ . \tag{5}$$

It has been shown by Perdew et al. [6] that μ is discontinuous at integer values of N.

The identification of $(\partial E/\partial N)_{v_0(\vec{r})}$ as an electronic chemical potential gives several insights into reactivity. First of all, μ can be regarded as measuring the escaping tendency of electrons from a system; electrons flow from places with high chemical potential to places with low chemical potential until μ is constant throughout the molecule [3]. So μ is related to the negative of the electronegativity [3, 7]. (Indeed, Mulliken's electronegativity scale is simply the finite difference approximation to $-\mu$ [7, 8].) The principle of electronegativity equalization follows from the fact that μ is a global property of the molecule [7, 9–12]. The second term of Eq. (5) is just the Hellmann-Feynman [13] expression in density functional theory (DFT).

To get more detailed information about reactivity we must consider the second-order change in the energy due to changes in electron number and external potential. These effects are carried in the first-order changes of the chemical potential and the density [14]:

$$\mathrm{d}\mu[N, v_0(\vec{r})] = \left(\frac{\partial\mu}{\partial N}\right)_{v_0(\vec{r})} \mathrm{d}N + \int \left(\frac{\delta\mu}{\delta v_0(\vec{r})}\right)_N \delta v_0(\vec{r})\mathrm{d}\vec{r} \tag{6}$$

$$\delta\rho[N, v_0(\vec{r});\vec{r}] = \left(\frac{\partial\rho(\vec{r})}{\partial N}\right)_{v_0(\vec{r})} \mathrm{d}N + \int \left(\frac{\delta\rho(\vec{r})}{\delta v_0(\vec{r}')}\right)_N \delta v_0(\vec{r}')\mathrm{d}\vec{r}' \ . \tag{7}$$

The first term in Eq. (6) has been identified as the absolute hardness, η [15]:

$$\eta \equiv \left(\frac{\partial\mu}{\partial N}\right)_{v_0(\vec{r})} = \left(\frac{\partial^2 E}{\partial N^2}\right)_{v_0(\vec{r})} \ . \tag{8}$$

This identification has paved the way for enhanced understanding of the hard/soft acid/base principle [15–18] and the maximum hardness principle [19–23]. The second term in Eq. (7) is called the linear response function [3, 24, 25]

$$\omega(\vec{r}, \vec{r}') \equiv \left(\frac{\delta\rho(\vec{r})}{\delta v_0(\vec{r}')}\right)_N \ ; \tag{9}$$

$\omega(\vec{r}, \vec{r}')$ measures the way the density changes when the external potential changes.

The Maxwell relation for Eq. (5) is used to define the Fukui function [2]:

$$f(\vec{r}) \equiv \left(\frac{\partial\rho(\vec{r})}{\partial N}\right)_{v_0(\vec{r})} = \left(\frac{\delta\mu}{\delta v_0(\vec{r})}\right)_N \ . \tag{10}$$

Substitution of Eqs. (8)–(10) simplifies Eqs. (6) and (7), yielding the working equations

$$\mathrm{d}\mu[N, v_0(\vec{r})] = \eta\,\mathrm{d}N + \int f(\vec{r})\delta v_0(\vec{r})\mathrm{d}\vec{r} \tag{11}$$

$$\delta\rho[N, v_0(\vec{r});\vec{r}] = f(\vec{r})\mathrm{d}N + \int \omega(\vec{r}, \vec{r}')\delta v_0(\vec{r}')\mathrm{d}\vec{r}' \ . \tag{12}$$

3 Interpreting the Fukui function

We return to a consideration of the chemical reaction

$$A + B \rightarrow A - B \ . \tag{13}$$

Equations (5), (11), and (12) do much to explain this reaction. For instance, consideration of the chemical potentials μ_{A} and μ_{B} and the hardnesses η_{A} and η_{B} not only allows one to predict whether or not reaction Eq. (13) will occur, but if the reaction occurs it allows one to estimate the binding energy of the product molecule, A-B [3, 12, 15, 17]. Consideration of the linear response function for the reactant molecules allows one to approximate the change in the density associated with reaction Eq. (13). However, because μ and η are global constants they contain no information on site reactivity. It is precisely information about site reactivity that is contained in the Fukui function.

Consider the case where the chemical potential of reactant B is much higher than that of reactant A. Then, in accord with the principle of electronegativity equalization, molecule B transfers electrons to molecule A. Hence, for reaction Eq. (13), $\Delta N_{\mathrm{A}} > 0$ and $\Delta N_{\mathrm{B}} < 0$. Now, consider the change in ρ_{A} due to an increase in the number of electrons, N_{A}:

$$f_{\mathrm{A}}^{+}(\vec{r}) \equiv \left(\frac{\partial\rho_{\mathrm{A}}(\vec{r})}{\partial N_{\mathrm{A}}}\right)^{+}_{v_{0,\mathrm{A}}(\vec{r})} \ . \tag{14}$$

In Eq. (14) the superscript "+" on the derivative indicates that the derivative is taken from above. We conclude that molecule A readily accepts electrons into regions where $f_{\mathrm{A}}^{+}(\vec{r})$ is large.

Now consider the change in ρ_{B} upon loss of electrons:

$$f_{\mathrm{B}}^{-}(\vec{r}) \equiv \left(\frac{\partial\rho_{\mathrm{B}}(\vec{r})}{\partial N_{\mathrm{B}}}\right)^{-}_{v_{0,\mathrm{B}}(\vec{r})} \ . \tag{15}$$

We conclude that molecule B readily donates electrons from regions where $f_{\mathrm{B}}^{-}(\vec{r})$ is large.

We expect that when the product, A-B, forms, B will have donated electrons to molecule A from those regions where $f_{\mathrm{B}}^{-}(\vec{r})$ is large and A will have accepted electrons from molecule B into regions where $f_{\mathrm{A}}^{+}(\vec{r})$ is large. Accordingly, we expect chemical bonds to form between atom(s) in fragment A where $f_{\mathrm{A}}^{+}(\vec{r})$was large and atom(s) in fragment B where $f_{\mathrm{B}}^{-}(\vec{r})$ was large.

What happens if the chemical potentials of molecules A and B are similar, so that

$$\Delta N_{\mathrm{A}} \approx \Delta N_{\mathrm{B}} \approx 0 \ . \tag{16}$$

In this case we suspect that reactant A will both accept electrons from and donate electrons to reactant B. So here we need the true derivative (as opposed to the one-sided derivatives of Eqs. 14 and 15):

$$f^0(\vec{r}) \equiv \underbrace{\lim}_{\varepsilon\to 0} \frac{\rho[N+\varepsilon, v_0(\vec{r})] - \rho[N-\varepsilon, v_0(\vec{r})]}{2\varepsilon} \quad . \tag{17}$$

Unfortunately, since ρ has slope discontinuities at integer numbers of electrons [2, 6, 26–28] (see Eq. 29), the limit in Eq. (17) does not exist. But defining $f^0(\vec{r})$ as the average of $f^+(\vec{r})$ and $f^-(\vec{r})$ makes good sense, as is seen from the following analysis:

$$\begin{aligned} f^0(\vec{r}) &\equiv \underbrace{\lim}_{\varepsilon\to 0} \frac{\rho[N+\varepsilon, v_0(\vec{r})] - \rho[N-\varepsilon, v_0(\vec{r})]}{2\varepsilon} \\ &= \underbrace{\lim}_{\varepsilon\to 0} \left\{ \begin{array}{c} \dfrac{(\rho[N+\varepsilon, v_0(\vec{r})] - \rho[N, v_0(\vec{r})])}{2\varepsilon} \\ + \dfrac{(\rho[N, v_0(\vec{r})] - \rho[N-\varepsilon, v_0(\vec{r})])}{2\varepsilon} \end{array} \right\} \\ &= \underbrace{\lim}_{\varepsilon\to 0} \frac{(\rho[N+\varepsilon, v_0(\vec{r})] - \rho[N, v_0(\vec{r})])}{2\varepsilon} \\ &\quad + \underbrace{\lim}_{\varepsilon\to 0} \frac{(\rho[N, v_0(\vec{r})] - \rho[N-\varepsilon, v_0(\vec{r})])}{2\varepsilon} \\ &= \frac{f^+(\vec{r}) + f^-(\vec{r})}{2} \quad . \end{aligned} \tag{18}$$

So, in this case we use

$$f_{\mathrm{A}}^0(\vec{r}) \equiv \frac{f_{\mathrm{A}}^-(\vec{r}) + f_{\mathrm{A}}^+(\vec{r})}{2} \tag{19}$$

and

$$f_{\mathrm{B}}^0(\vec{r}) \equiv \frac{f_{\mathrm{B}}^-(\vec{r}) + f_{\mathrm{B}}^+(\vec{r})}{2} \tag{20}$$

to predict site reactivity. Extension of our previous result leads us to conclude that for reactions in which $\mu_{\mathrm{A}} \approx \mu_{\mathrm{B}}$, bonds form between atom(s) in fragment A where $f_{\mathrm{A}}^0(\vec{r})$ was large and atom(s) in fragment B where $f_{\mathrm{B}}^0(\vec{r})$ was large [29].[1]

In summary, $f^+(\vec{r})$ (Eq. 14) measures the reactivity of a site in a molecule relative to nucleophilic attack; $f^-(\vec{r})$ (Eq. 15) measures the reactivity of a site relative to electrophilic attack; and $f^0(\vec{r})$ (Eqs. 19, 20) measures the reactivity of a site relative to neutral (or radical) attack [2].

We note that one can obtain the same conclusions when one considers [2]

$$f(\vec{r}) \equiv \left(\frac{\delta\mu}{\delta v_0(\vec{r})}\right)_N \quad . \tag{21}$$

In this formulation the key realization is that $d\mu$ represents the extent of a chemical reaction and hence that "$|d\mu|$ big is good" [2, 3]. One-sided functional derivatives are once again required since $\mu[N, v_0(\vec{r})]$ is discontinuous at integer values of N [6, 26–28]. Use of the definitions

$$\mu^{+/-} = \left(\frac{\partial E}{\partial N}\right)_{v_0(\vec{r})}^{+/-} \tag{22}$$

$$f_{\mathrm{A}}^+(\vec{r}) \equiv \left(\frac{\delta\mu_{\mathrm{A}}^+}{\delta v_{0,\mathrm{A}}(\vec{r})}\right)_{N_{\mathrm{A}}} \tag{23}$$

$$f_{\mathrm{B}}^-(\vec{r}) \equiv \left(\frac{\delta\mu_{\mathrm{B}}^-}{\delta v_{0,\mathrm{B}}(\vec{r})}\right)_{N_{\mathrm{B}}} \tag{24}$$

and the "$|d\mu|$ big is good" rule leads to the recovery of our previous results [2].

4 Qualitative properties of the Fukui function

Before attempting to accurately compute a quantity it is useful to know something about its qualitative behavior. Here we consider some results of this type for the Fukui function.

1. Normalization. The Fukui function is normalized to unity [3]:

$$\int f(\vec{r})d\vec{r} = 1 \quad . \tag{25}$$

In proving this result we introduce the shape function, $\sigma(\vec{r}) \equiv \rho(\vec{r})/N$; note that σ is normalized to unity [30, 31]. Then

$$\begin{aligned} \int f(\vec{r})d\vec{r} &= \int \left(\frac{\partial\rho(\vec{r})}{\partial N}\right)_{v_0(\vec{r})} d\vec{r} = \left(\frac{\partial\left[\int N\sigma(\vec{r})d\vec{r}\right]}{\partial N}\right)_{v_0(\vec{r})} \\ &= \left(\frac{\partial\left[N\int \sigma(\vec{r})d\vec{r}\right]}{\partial N}\right)_{v_0(\vec{r})} = 1 \quad . \end{aligned} \tag{26}$$

2. Cusp condition. In a molecule, the density has cusps at each nuclear position, $\vec{R}_\alpha$. These cusps satisfy the relation

$$\underbrace{\lim}_{|\vec{r}-\vec{R}_\alpha|\to 0} \left(\frac{(\vec{r}-\vec{R}_\alpha)}{|\vec{r}-\vec{R}_\alpha|} \frac{\vec{\nabla}_{\vec{r}-\vec{R}_\alpha}\rho(\vec{r})}{\rho(\vec{r})}\right) = -2Z_\alpha \quad , \tag{27}$$

where Z_α is the nuclear charge of the nucleus at the point $\vec{R}_\alpha$ and the notation indicates that the initial point of the vectors is $\vec{R}_\alpha$ [32–35]. Chattaraj et al. [36] showed that Eq. (27) implies that the Fukui function also satisfies the cusp condition

$$\underbrace{\lim}_{|\vec{r}-\vec{R}_\alpha|\to 0} \left(\frac{(\vec{r}-\vec{R}_\alpha)}{|\vec{r}-\vec{R}_\alpha|} \frac{\vec{\nabla}_{\vec{r}-\vec{R}_\alpha}f(\vec{r})}{f(\vec{r})}\right) = -2Z_\alpha \quad . \tag{28}$$

3. Asymptotic decay. If one uses the zero-temperature limit of the grand canonical ensemble to interpolate between integer numbers of electrons, then

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[1] Berkowitz shows that during chemical reaction (Eq. 13), the amount of charge transfer between the two molecular fragments A and B increases as

$$J_f \equiv \iint \frac{f_{\mathrm{A}}(\vec{r})f_{\mathrm{B}}(\vec{r}\,')}{|\vec{r}-\vec{r}\,'|} d\vec{r}d\vec{r}\,'$$

increases. This result suggests that the Fukui potentials,

$$v_{f_{\mathrm{A/B}}}(\vec{r}) \equiv \int \frac{f_{\mathrm{A/B}}(\vec{r}\,')}{|\vec{r}-\vec{r}\,'|} d\vec{r}\,' \quad ,$$

indicate favorable orientations for the reacting fragments. Since the Fukui potentials are large where $f_{\mathrm{A/B}}$ is large, Berkowitz's conclusions agree with those in the text

$$\rho[N+\varepsilon, v_0;\vec{r}] = (1-\varepsilon)\rho[N, v_0;\vec{r}] + \varepsilon\rho[N+1, v_0;\vec{r}] \ , \tag{29}$$

where ε is between zero and one, inclusive [6, 26–28]. Then

$$f^+(\vec{r}) \equiv \left(\frac{\partial\rho(\vec{r})}{\partial N}\right)^+_{v_0} = \underbrace{\lim}_{\varepsilon\to 0^+}\left\{\frac{\rho[N+\varepsilon, v_0;\vec{r}] - \rho[N, v_0;\vec{r}]}{\varepsilon}\right\}$$
$$= \rho[N+1, v_0;\vec{r}] - \rho[N, v_0;\vec{r}] \tag{30}$$
$$f^-(\vec{r}) \equiv \left(\frac{\partial\rho(\vec{r})}{\partial N}\right)^-_{v_0} = \underbrace{\lim}_{\varepsilon\to 0^+}\left\{\frac{\rho[N, v_0;\vec{r}] - \rho[N-\varepsilon, v_0;\vec{r}]}{\varepsilon}\right\}$$
$$= \rho[N, v_0;\vec{r}] - \rho[N-1, v_0;\vec{r}] \ . \tag{31}$$

Equations (30) and (31) are remarkable since they indicate that the finite difference approximation to Eqs. (14) and (15) with $\Delta N \leq 1$ is exact (for exact DFT).

Far from any finite system, the electron density decays exponentially according to

$$\rho(\vec{r}) \xrightarrow{\text{big } |\vec{r}|} A\mathrm{e}^{-\sqrt{8\mathrm{IP}}\, r} \ , \tag{32}$$

where A is a constant of proportionality and IP is the ionization potential of the system [37–44]. Due to the empirically observed convexity of E versus N [3, 6],

$$\mathrm{IP}[N, v_0(\vec{r})] > \mathrm{IP}[N+1, v_0(\vec{r})] \tag{33}$$

as long as the $N+1$st electron is bound. When the $N+1$st electron is unbound, $\rho[N, v_0(\vec{r})] = \rho[N+1, v_0(\vec{r})]$ and hence the Fukui function is a generalized function which is zero everywhere but which is normalized to 1 (as the $\alpha \to 0^+$ limit of the function $\frac{\alpha^3}{8\pi}\cdot \mathrm{e}^{-\alpha r}$).

Equations (30)–(33) reveal that at long range the dominant contribution to the Fukui function is from the density with the greatest number of electrons (as the contribution from the other density decays exponentially faster). Hence

$$f^+(\vec{r}) \xrightarrow{\text{big } |\vec{r}|} A[N+1, v_0]\mathrm{e}^{-\sqrt{8\mathrm{EA}}\, r} \tag{34}$$

and

$$f^-(\vec{r}) \xrightarrow{\text{big } |\vec{r}|} A[N, v_0]\mathrm{e}^{-\sqrt{8\mathrm{IP}}\, r} \ , \tag{35}$$

where EA and IP denote the electron affinity and ionization potential of the N-electron system. Restating Eqs. (34) and (35) and including higher-order terms [37–44] one finds that

$$\left[\frac{\partial \ln(f^+(\vec{r}))}{\partial r}\right] \xrightarrow{\text{big } r} -\sqrt{8\,\mathrm{EA}} + 2\left(\frac{(Z_{\mathrm{total}} - N)}{\sqrt{2\,\mathrm{EA}}} - 1\right)\left(\frac{1}{r}\right) + \left(\text{higher powers of } \frac{1}{r}\right) \tag{36}$$

$$\left[\frac{\partial \ln(f^-(\vec{r}))}{\partial r}\right] \xrightarrow{\text{big } r} -\sqrt{8\,\mathrm{IP}} + 2\left(\frac{[Z_{\mathrm{total}} - (N-1)]}{\sqrt{2\,\mathrm{IP}}} - 1\right)\left(\frac{1}{r}\right) + \left(\text{higher powers of } \frac{1}{r}\right) \ , \tag{37}$$

where Z_{total} is the sum of all the nuclear charges.

It should be noted that Eqs. (30) and (31) also provide an alternative derivation of the cusp condition for the Fukui function. This can be seen by substituting Eqs. (30) and (31) into Eq. (28) and using Eq. (27) to simplify the result.

5 Computing the Fukui function

In Sect. 3 we showed that the Fukui function should be useful for predicting site reactivity. How do we calculate it? One possibility is to use Eqs. (30) and (31). The first problem with doing this is that it requires us to do ab initio calculations not only for the neutral system, but also for the cation and the anion. Having to perform three calculations is difficult enough; the fact that one of these calculations is for an anion complicates matters still further. Another problem is that Eq. (29) is valid only for the exact theory; approximate density functionals do not satisfy this condition and hence Eqs. (30) and (31) are only approximately true for DFT calculations performed with approximate density functionals. Indeed, one sometimes obtains qualitatively incorrect answers if Eq. (30) is applied when Eq. (29) is not valid [45].

A different approach is to perform a gradient expansion of the Fukui function. For an atom, Chattaraj et al. proposed the expansion

$$f(\vec{r}) = \frac{\rho(\vec{r})}{N} + \frac{\alpha}{N\rho^{\frac{2}{3}}(0)}\left\{\left[\left(\frac{\rho(0)}{\rho(\vec{r})}\right)^{\frac{2}{3}} - 1\right]\nabla^2\rho(\vec{r}) - \frac{2}{3}\left(\frac{\rho(0)}{\rho(\vec{r})}\right)^{\frac{2}{3}}\frac{\vec{\nabla}\rho(\vec{r})\,\vec{\nabla}\rho(\vec{r})}{\rho(\vec{r})}\right\} \ , \tag{38}$$

where $\rho(0)$ is the value of the density at the nucleus and α is an empirical parameter [36, 46]. Unfortunately, expansions of this type only produce one Fukui function: $f^+(\vec{r})$ and $f^-(\vec{r})$ are not found [36, 46].

A variational method for obtaining the Fukui function has been devised [47]. Define the hardness kernel as [3, 24]

$$\eta(\vec{r}, \vec{r}\,') = \frac{\delta^2 E_{v_0}[\rho]}{\delta\rho(\vec{r})\delta\rho(\vec{r}\,')} = \frac{\delta^2 F[\rho]}{\delta\rho(\vec{r})\delta\rho(\vec{r}\,')} = \frac{\delta(\mu - v_0(\vec{r}))}{\delta\rho(\vec{r}\,')} \ . \tag{39}$$

Then minimize the functional

$$\eta[g] \equiv \int\int g(\vec{r})g(\vec{r}\,')\eta(\vec{r}, \vec{r}\,')\mathrm{d}\vec{r}\,\mathrm{d}\vec{r}\,' \tag{40}$$

with respect to $g(\vec{r})$ which obey the normalization constraint

$$\int g(\vec{r})\mathrm{d}\vec{r} = 1 \ . \tag{41}$$

The Fukui function, $f(\vec{r})$, is the function which minimizes Eq. (40) and $\eta[f] = \eta$, the absolute hardness from Eq. (8) [47]. If one enforces the normalization constraint (Eq. 41) with a Lagrange multiplier, λ, one finds that $\lambda = 2\eta$ and that [47, 48]

$$\eta = \int f(\vec{r})\eta(\vec{r},\vec{r}\,')\mathrm{d}\vec{r}\,' \ . \tag{42}$$

Equation (42) is remarkable because the integration is only over one set of coordinates.

While the gradient expansion approach (Eq. 38) does not give results for the one-sided Fukui functions, $f^{+}(\vec{r})$ and $f^{-}(\vec{r})$ may be obtained from the variational approach by using the one-sided hardness kernels, $\eta^{+/-}(\vec{r},\vec{r}\,')$, in Eqs. (40) and (42) [47]. If we use the one-sided hardness kernels obtained from the zero-temperature limit of the grand canonical ensemble [6], then $\eta^{+} = \eta^{-} = 0$; hence, the one-sided hardness kernels have no inverse.

It seems that this variational method should be the method of choice for generating the Fukui function. Unfortunately, accurate determination of the hardness kernel is complicated by the lack of an accurate explicit kinetic energy functional, $T[\rho]$. Nonetheless, Eq. (40) has been applied to the Hückel model [49] and Eq. (42) has been applied to the Thomas–Fermi–Dirac–Weizsäcker approximation of $F[\rho]$ [47].

Since most modern DFT calculations use the Kohn–Sham method, it seems desirable to use the information available from a solution of the Kohn–Sham equations to determine the Fukui function. To this end, Cohen and coworkers [50–52] showed that one can relate the Fukui function to the frontier orbital densities of Kohn–Sham theory through

$$f^{+/-}(\vec{r}) = \int \left[\left(\frac{\delta v_0(\vec{r}\,')}{\delta v_{\mathrm{eff}}(\vec{r})}\right)_{\mu}\right]^{-1} \times \sum_{\mathrm{spin}} \left|\phi^{\mathrm{LUMO/HOMO}}(\vec{r}\,',s)\right|^2 \mathrm{d}\vec{r}\,' \ . \tag{43}$$

Here $[(\delta v_0(\vec{r}\,')/\delta v_{\mathrm{eff}}(\vec{r}))_{\mu}]^{-1}$ is the inverse of the transpose of the potential–potential response function, $(\delta v_0(\vec{r})/\delta v_{\mathrm{eff}}(\vec{r}\,'))_{\mu}$, v_{eff} is the Kohn–Sham effective potential, and ϕ^{LUMO} (ϕ^{HOMO}) is the lowest unoccupied (highest occupied) Kohn–Sham orbital. Fortunately, one can express $(\delta v_0(\vec{r})/\delta v_{\mathrm{eff}}(\vec{r}\,'))_{\mu}$ in terms of quantities from a Kohn–Sham DFT equation:

$$\left(\frac{\delta v_0(\vec{r})}{\delta v_{\mathrm{eff}}(\vec{r}\,')}\right)_{\mu} = \delta(\vec{r}\,' - \vec{r}) - \int \left[\left(\frac{\delta \rho(\vec{r}\,'')}{\delta v_{\mathrm{eff}}(\vec{r})}\right)_{\mu} \cdot \left(\frac{1}{|\vec{r}\,'' - \vec{r}\,'|} + \frac{\delta v_{\mathrm{xc}}(\vec{r}\,')}{\delta \rho(\vec{r}\,'')}\right)\right] \mathrm{d}\vec{r}\,'' , \tag{44}$$

where v_{xc} is the exchange–correlation potential [53]. Ignoring the second term in Eq. (44), recovers the "frozen orbital" approximation of Parr and Yang [2]. Accordingly, the second term in Eq. (44) must represent the effects of orbital relaxation.

We encounter problems when we decide to compute the effects of orbital relaxation. Consider, for a moment, just the problems associated with computing $\delta v_{\mathrm{xc}}(\vec{r}\,')/\delta \rho(\vec{r}\,'')$. While $\delta v_{\mathrm{xc}}(\vec{r}\,')/\delta \rho(\vec{r}\,'')$ is indeed readily computed from a given approximation of E_{xc}, it is probably not accurately modeled by approximate functionals which were designed to reproduce energetic data (and not the exchange–correlation potential, much less the functional derivative thereof).

Another approach to computing the Fukui function was provided by Yang et al. [12, 54]:

$$f^{+}(\vec{r}) = \left|\phi_{N+1}(\vec{r})\right|^2 + \sum_{i=1}^{N} \left(\frac{\partial |\phi_i(\vec{r})|^2}{\partial N}\right)^{+}_{v_0(\vec{r})} \tag{45}$$

$$f^{-}(\vec{r}) = |\phi_N(\vec{r})|^2 + \sum_{i=1}^{N-1} \left(\frac{\partial |\phi_i(\vec{r})|^2}{\partial N}\right)^{-}_{v_0(\vec{r})} \ . \tag{46}$$

Here N is the number of electrons in the system and the ϕ_i are Kohn–Sham spin orbitals. It is apparent that if one neglects the relaxation of the core orbitals (the frozen core approximation), Eqs. (45) and (46) reduce to

$$f^{+}(\vec{r}) \approx \rho_{\mathrm{LUMO}}(\vec{r}) \ , \tag{47}$$

$$f^{-}(\vec{r}) \approx \rho_{\mathrm{HOMO}}(\vec{r}) \ , \tag{48}$$

and hence (from Eq. 19)

$$f^{0}(\vec{r}) \approx \frac{\rho_{\mathrm{HOMO}}(\vec{r}) + \rho_{\mathrm{LUMO}}(\vec{r})}{2} \ . \tag{49}$$

Equations (47)–(49) are precisely the densities of the frontier molecular orbitals; hence, in a frozen core approximation the (exact) theory of the Fukui function reverts to an essential element of the approximate frontier molecular orbital theory of Fukui [55–57].

Michelak et al. [45] have computed the Fukui function using a variety of the methods previously described as well as some more sophisticated approximate approaches. Specifically, they considered the finite difference approximation to the derivative with $\Delta N = 1$ and $\Delta N = 0.01$, a modified finite difference formula in which only terms linear in orbital changes and occupation number changes are retained, the frozen core approximation (Eqs. 47, 48) and an approximation to Eq. (46).

Their approximation to Eq. (46) deserves further comment. If one differentiates the Kohn–Sham equations with respect to the particle number at constant external potential, one obtains

$$\left(-\frac{\nabla^2}{2} + v_0(\vec{r}) + \int \frac{\rho(\vec{r}\,')}{|\vec{r} - \vec{r}\,'|}\mathrm{d}\vec{r}\,' + v_{\mathrm{xc}}(\vec{r}) - \varepsilon_i\right) \times \left(\frac{\partial \phi_i(\vec{r})}{\partial N}\right)_{v_0(\vec{r})} + \left[\int \frac{f(\vec{r}\,')}{|\vec{r} - \vec{r}\,'|}\mathrm{d}\vec{r}\,' + \left(\frac{\partial v_{\mathrm{xc}}(\vec{r})}{\partial N}\right)_{v_0(\vec{r})} - \left(\frac{\partial \varepsilon_i}{\partial N}\right)_{v_0(\vec{r})}\right]\phi_i(\vec{r}) = 0 \ , \tag{50}$$

One can then get the Fukui function by combining Eqs. (50) and (46). By omitting the derivative of the v_{xc} with respect to N (a term which is approximated to questionable accuracy by existing functionals), one may eliminate all the integrals except those which were already calculated in the course of the Kohn–Sham calculation (which provides an advantage over methods using Eqs. 43, 44).

The results of Michelak et al. [45] indicate that while the frontier molecular orbital approximation is sometimes qualitatively different from the other methods of computing the Fukui function, all the other methods usually give qualitatively similar results. Since the Fukui function is used to make qualitative judgements about site reactivity, these results suggest that one may compute the effects of orbital relaxation on the Fukui function in whatever reasonable manner one finds most convenient.

6 Miscellany

There are numerous other applications and extensions of the Fukui function. For instance, we have not included the extension of the Fukui function formalism to conductors (where there are "bands" of occupied states rather than occupied orbitals) [58, 59]. One can also fruitfully consider "condensed Fukui functions" [12, 45, 60–64], where one affixes a Fukui "index" to each atomic center (by partitioning the molecule into regions in either real space or function space and integrating the Fukui function over that region). The relationships between the Fukui function and the grand canonical ensemble of DFT and the relationships between the Fukui function and the softness kernel and local softness are also important [24, 51, 65].

In Sect. 2 we hinted at some of the Fukui function's shortcomings. The Fukui function measures the change in the density of a system when the number of electrons changes at constant external potential. As such, the Fukui function accurately reflects the component of chemical reactivity that is conveyed through the transfer of charge between systems; however, the Fukui function explicitly ignores the effects of the approaching reagent's external potential, assuming, in effect, that the transfer of charge between reactant molecules occurs at such large distances that charge distributes itself in a reactant molecule exactly as it would were the molecule isolated. This assumption may be good when the transition state occurs very early along the reaction coordinate (equivalently, when the transition state more strongly resembles the reactants than the products) because in this case the "point of no return" which determines how the reactant molecules will bind to each other is encountered before the external potentials (hence the density, hence the Fukui function) of the reactants are significantly different from those of the isolated molecules. Of course, the Fukui potential response [66], $(\delta f(\vec{r})/\delta v_0(\vec{r}'))_N$, enters into the energy expression in the third order and includes these effects [51]. For cases in which more than one electron is transferred, the discontinuities in the Fukui function at integer N cause further complications.

Similar to the previous caveat is the following observation: the Fukui function is generally computed for an isolated reactant molecule (using one of the approximations from Sect. 4). When the reactant is placed into solution, however, the external potential felt by the molecule changes, and both the ground-state density and the Fukui function can be expected to differ appreciably from their values in vacuo. Viewed in this context, it is remarkable that the frontier molecular orbital theory does as good a job at predicting reactivity in solution as it does – especially when one considers the ability of solvents to stabilize and destabilize charges on molecules.

One can rationalize the success of the gas-phase Fukui functions in solution by noting that the chemical potential, μ, is relatively insensitive to solvent effects [67]. If this insensitivity carries through to the Fukui function (which is a functional derivative of μ – see Eq. 21) then the use of gas-phase Fukui functions is placed on a more solid footing. Alternatively, consider the argument of Dewar and Storch [68]: if the solvent is pushed out of the "reacting region" as the reactant molecules approach each other then solvent effects may be small enough for the gas-phase reactivity indices to make qualitatively correct predictions. Further exploration of the gas-phase Fukui function's success in solution is needed.

To the extent that the Fukui function is a qualitative index, solvent effects and the way $f(\vec{r})$ changes with $v_0(\vec{r})$ and N are unimportant whenever such effects do not change the ordering of site reactivities (as in this case the predicted site reactivity preferences of the molecule are unchanged from the gas phase). Certainly we are not always so fortunate. For instance, the site at which an ambidentate ligand binds to a substrate will generally depend both on the solvent in which the reaction is conducted and on the identity of the substrate. Inasmuch as gas-phase Fukui functions predict that one of the two possible binding sites is preferable in all circumstances, the gas-phase Fukui function fails to predict the correct results whenever circumstances conspire to make the other binding site preferable. (Contreras et al. [69] have recently considered such a case, discovering that including the effects of the Fukui response was sufficient to give the correct site reactivity predictions for acetaldehyde enolate.)

Looking towards the future, designing better ways to compute the Fukui function is still a priority. In this regard, the search for accurate, explicit, kinetic energy functionals (so that Eq. 40 or 42 represents a viable alternative to Kohn–Sham-based methods like Eqs. 45, 46) is of great importance. Of course, finding an accurate kinetic energy functional would also revolutionize DFT by providing a simple alternative to solving the Kohn–Sham equations. In the more immediate future, it is anticipated that the recent progress in computing the Fukui function from a single Kohn–Sham calculation will continue, with more and more reliable approximations being made, while concurrent progress is made in increasing the methods' computational efficiency.

As we deepen our understanding of the zero-temperature limit of the grand canonical ensemble [6, 26–28] and other possible schemes for interpolating between integer numbers of electrons we may gain new insights into the Fukui function and its associated reactivity measures.

Recently there has been some interest in the Fukui responses, which, we argued, may be important for systems in which the charge transfer between reactants only occurs once the reactants are too close together for either reactant's Fukui function to resemble its value in isolation [25, 69]. As efficient methods for computing Fukui responses become available we may see first-order corrections to the Fukui function routinely included in many calculations.

Finally, recent work by Chattaraj and coworkers [70, 71] has focussed on extending the conceptual tools of the ground-state DFT to excited states. These studies have the potential to significantly deepen our understanding of excited-state chemistry.

We close with some additional words on the significance of the Fukui function. The Fukui function shores up the theoretical foundations of frontier molecular orbital theory. Equations (43)–(46) reveal that the site reactivity indices of frontier molecular orbital theory (Eqs. 47–49) may be regarded as the frozen orbital approximation to the Fukui function. The Fukui function is the zeroth-order index for site reactivity; various functional derivatives of the Fukui function represent higher-order corrections to the zeroth-order site reactivity map provided by the Fukui function. For instance, the first-order correction to the Fukui function is

$$\begin{aligned}\delta f^{+/0/-}[N, v_0(\vec{r}); \vec{r}] &= \left(\frac{\partial f^{+/0/-}(\vec{r})}{\partial N}\right)_{v_0(\vec{r})} \mathrm{d}N \\ &\quad + \int \left(\frac{\delta f^{+/0/-}(\vec{r})}{\delta v_0(\vec{r}\,')}\right)_N \delta v_0(\vec{r}\,')\mathrm{d}\vec{r}\,' \ .\end{aligned} \qquad (51)$$

Hence, frontier molecular orbital theory may be considered as an approximation to the theory of the Fukui function, which is itself an approximation (since it is corrected by Eq. 51 and higher-order corrections) to the exact site reactivity map of a molecule.

Also significant is the fact that the Fukui function can be used to provide an "aufbau principle" for DFT. To see this, find $f_{\mathrm{B}}^{-}(\vec{r})$ and subtract this from $\rho(\vec{r})$ to get the $N-1$ electron density $\rho_{N-1}(\vec{r})$ (see Eqs. 30, 31). Continuing this process until all the electrons have been removed, one finds that

$$\begin{aligned}\rho(\vec{r}) &= \sum_{n=1}^{N} f_n^{-}(\vec{r}) \\ &= \sum_{n=1}^{N} \int_{n-1}^{n} f_k^{-}(\vec{r})\,\mathrm{d}k \ ,\end{aligned} \qquad (52)$$

where $f_n^{-}(\vec{r})$ is the Fukui function from below for the n-electron system. The second equality in Eq. (52) extends this "aufbau principle" to approximate density functionals (where Eqs. 30, 31 are invalid). Equation (52) has considerable potential as a conceptual tool since it allows one to build an N-electron density from one-electron densities just as one might build an N-electron wavefunction from orbitals.

7 Conclusion

We started this review by indicating that we should strive for general principles that explain a wide range of chemical phenomena. The use of the Fukui function provides one such principle [2, 3, 12, 72–75]. While the Fukui function may give erroneous results in situations where the first- and higher-order corrections thereto are important, it is the leading-order term in an exact theory of the site reactivity of a molecule.

The Fukui function successfully predicts relative site reactivities for most chemical systems. As such it provides a method for understanding and categorizing chemical reactions. More importantly, the Fukui function can be used to predict what the products of a given reaction will be. As computing the Fukui function becomes faster and easier, its predictive ability might be routinely used to winnow the list of potentially useful reagents, catalysts, etc. before performing the types of experiments or calculations necessary to fully characterize a chemical reaction. This predictive ability renders the Fukui function an important tool of the chemist.

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References

1. Attributed to C.A. Coulson by R. McWeeny in the preface of McWeeny R (1979) Coulson's valence. Oxford University Press, Oxford
2. Parr RG, Yang WT (1984) J Am Chem Soc 106: 4049
3. Parr RG, Yang WT (1989) Density functional theory of atoms and molecules. Oxford University Press, New York
4. Dreizler RM, Gross EKU (1990) Density functional theory. Springer, Berlin Heidelberg New York
5. Nalewajski RF, Parr RG (1982) J Chem Phys 77: 399
6. Perdew JP, Parr RG, Levy M, Balduz JL (1982) Phys Rev Lett 49: 1691
7. Parr RG, Donnelly RA, Levy M, Palke WE (1978) J Chem Phys 68: 3801
8. Mulliken RS (1934) J Chem Phys 2: 782
9. Sanderson RT (1951) Science 114: 670
10. Sanderson RT (1976) Chemical bonds and bond energy. Academic, New York
11. Parr RG, Bartolotti LJ (1982) J Am Chem Soc 104: 3801
12. Chermette H (1999) J Comput Chem 20: 129
13. Feynman RP (1939) Phys Rev 56: 340
14. Liu S, Parr RG (1997) J Chem Phys 106: 5578
15. Parr RG, Pearson RG (1983) J Am Chem Soc 105: 7512
16. Pearson RG (1963) J Am Chem Soc 85: 3533
17. Chattaraj PK, Lee H, Parr RG (1991) J Am Chem Soc 113: 1855
18. Pearson RG (1995) Inorg Chim Acta 240: 93
19. Pearson RG (1987) J Chem Educ 64: 571
20. Parr RG, Chattaraj PK (1991) J Am Chem Soc 113: 1854
21. Chattaraj PK (1996) Proc Indian Natl Sci Acad Part A 62: 513
22. Pearson RG (1993) Acc Chem Res 26: 250
23. Pearson RG (1999) J Chem Educ 76: 267
24. Berkowitz M, Parr RG (1988) J Chem Phys 88: 2554
25. Senet P (1996) J Chem Phys 105: 6471
26. Perdew JP, Levy M (1997) Phys Rev B 56: 16021
27. Chan GK-L (1999) J Chem Phys 110: 4710
28. Zhang Y, Yang WT Theor Chem Acta
29. Berkowitz M (1987) J Am Chem Soc 109: 4823
30. Parr RG, Bartolotti LJ (1983) J Phys Chem 87: 2810
31. Cedillo A (1994) Int J Quantum Chem Symp 28: 231
32. Steiner E (1963) J Chem Phys 39: 2365
33. Kato T (1957) Commun Pure Appl Math 10: 151

34. Handy NC (1996) In: Bicout D, Field M (eds) Quantum mechanical simulation methods for studying biological systems. Springer Berlin Heidelberg New York, p 1
35. Pack RT, Brown WB (1966) J Chem Phys 45: 556
36. Chattaraj PK, Cedillo A, Parr RG (1995) J Chem Phys 103: 10621
37. Morrell MM, Parr RG, Levy M (1975) J Chem Phys 62: 549
38. Levy M, Parr RG (1976) J Chem Phys 64: 2707
39. Katriel J, Davidson ER (1980) Proc Natl Acad Sci USA 77: 4403
40. Hoffmann-Ostenhof M, Hoffmann-Ostenhof T (1977) Phys Rev A 16: 1782
41. Aldrichs R, Hoffmann-Ostenhof M, Hoffmann-Ostenhof T, Morgan JD III (1981) Phys Rev A 23: 2106
42. Levy M, Perdew JP, Sahni V (1984) Phys Rev A 30: 2745
43. Ambladh CO, von Barth U (1985) Phys Rev B 31: 3231
44. Patil SH (1989) J Phys B 22: 2051
45. Michalak A, De Proft F, Geerlings P, Nalewajski RF (1999) J Phys Chem A 103: 762
46. Pacios LF, Gmez PC (1998) J Comput Chem 19: 488
47. Chattaraj PK, Cedillo A, Parr RG (1995) J Chem Phys 103: 7645
48. Ghosh SK (1990) Chem Phys Lett 172: 77
49. Cedillo A, Parr RG (1996) J Chem Phys 105: 9557
50. Cohen MH, Ganduglia-Pirovano MV, Kudrnovsky J (1994) J Chem Phys 101: 8988
51. Cohen MH, Ganduglia-Pirovano MV, Kudrnovsky J (1995) J Chem Phys 103: 3543
52. Cohen MH (1996) In: Nalewajski RF (ed) Topics in current chemistry: density functional theory IV: theory of chemical reactivity. Springer, Berlin Heidelberg New York, pp 143
53. Senet P (1997) J Chem Phys 107: 2516
54. Yang WT, Parr RG, Pucci R (1984) J Chem Phys 81: 2862
55. Fukui K, Yonezawa Y, Shingu H (1952) J Chem Phys 20: 722
56. Fukui K (1973) Theory of orientation and stereoselection. Springer, Berlin Heidelberg New York
57. Fukui K (1982) Science 217: 747
58. Yang W, Parr RG (1985) Proc Natl Acad Sci USA 82: 6723
59. Cohen MH, Ganduglia-Pirovano MV, Kudrnovsky J (1994) Phys Rev Lett 72: 3222
60. Yang W, Mortier W (1986) J Am Chem Soc 108: 5708
61. Langenaeker W, Demel K, Geerlings P (1992) J Mol Struct (THEOCHEM) 259: 317
62. Balawender R, Komorowski L (1998) J Chem Phys 109: 5203
63. De Proft F, Langenaeker W, Geerlings P (1995) Int J Quantum Chem 55: 449
64. Roy RK, Pal S, Hirao K (1999) J Chem Phys 110: 8236
65. Harbola MK, Chattaraj PK, Parr RG (1991) Isr J Chem 31: 395
66. Fuentealba P, Parr RG (1991) J Chem Phys 94: 5559
67. Pearson RG (1986) J Am Chem Soc 108: 6109
68. Dewar MJS, Storch DM (1985) Proc Natl Acad Sci USA 82: 2225
69. Contreras R, Domingo LR, Andrés J, Pérez P, Tapia O (1999) J Phys Chem A 103: 1367
70. Chattaraj PK, Sengupta S (1997) J Phys Chem A 101: 7893
71. Chattaraj PK, Poddar A (1998) J Phys Chem A 102: 9944
72. Nalewajski RF (ed) (1996) Topics in current chemistry: density functional theory IV: theory of chemical reactivity. Springer, Berlin Heidelberg New York; see also Refs [3, 12, 73–75] and references therein
73. Geerlings P, Langenaeker W, De Proft F, Baeten A (1996) In: Murray JS, Sen K (eds) Molecular electrostatic potentials: concepts and applications. Theoretical and computational chemistry, vol. 3. Elsevier, Amsterdam, pp 587
74. Geerlings P, De Proft F, Martin JML (1996) In: Seminario JM (ed) Recent developments and applications of modern density functional theory. Theoretical and computational chemistry, vol 4. Elsevier, Amsterdam, pp 773
75. Parr RG, Yang W (1995) Annu Rev Phys Chem 46: 701