

Why is the dual descriptor a more accurate local reactivity descriptor than Fukui functions?

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Abstract A mathematical analysis reveals that dual descriptor is a more accurate tool than nucleophilic and electrophilic Fukui functions. Although Fukui function has the capability of revealing nucleophilic and electrophilic regions on a molecule, the dual descriptor is able to unambiguously expose truly nucleophilic and electrophilic regions, but along with the latter, dual descriptor is less affected by the lack of relaxation terms than the Fukui function when the frontier molecular orbital approximation is applied. This implies that the dual descriptor can be considered a more reliable descriptor to measure local reactivity than Fukui function. This statement is demonstrated in the present work.

Keywords Dual descriptor · Nucleophilic Fukui function · Electrophilic Fukui function · Local reactivity descriptor

1 Introduction

A local reactivity descriptor (LRD) that reveals, preferably and without ambiguity both nucleophilic and electrophilic sites on a molecule, has been proposed by Morrell et al. [1, 2] and it has been called dual descriptor. This LRD is defined in terms of a derivative of $f(\mathbf{r})$, the Fukui function [3–7], with respect to N , the number of electrons, thus meaning it is a partial derivative of second order of the electronic density $\rho(\mathbf{r})$ with

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respect to the number of electrons N . Through a Maxwell relation, the same descriptor is interpreted as the variation of molecular hardness, η , with respect to the external potential, $v(\mathbf{r})$; molecular hardness measures the resistance to charge transfer. The definition of $f^{(2)}(\mathbf{r})$ is shown as indicated by Morell et al. [1,2]:

$$f^{(2)}(\mathbf{r}) = \left(\frac{\partial^2 \rho(\mathbf{r})}{\partial N^2} \right)_{v(\mathbf{r})} = \left(\frac{\partial f(\mathbf{r})}{\partial N} \right)_{v(\mathbf{r})} = \left[\frac{\delta \eta}{\delta v(\mathbf{r})} \right]_N. \quad (1)$$

An operational equation for $f^{(2)}(\mathbf{r})$ is written as the difference between nucleophilic and electrophilic Fukui functions leading to the finite difference approximation (FDA) of second order [1]:

$$f^{(2)}(\mathbf{r}) \approx f^+(\mathbf{r}) - f^-(\mathbf{r}) = \rho_{N+1}(\mathbf{r}) - 2\rho_N(\mathbf{r}) + \rho_{N-1}(\mathbf{r}). \quad (2)$$

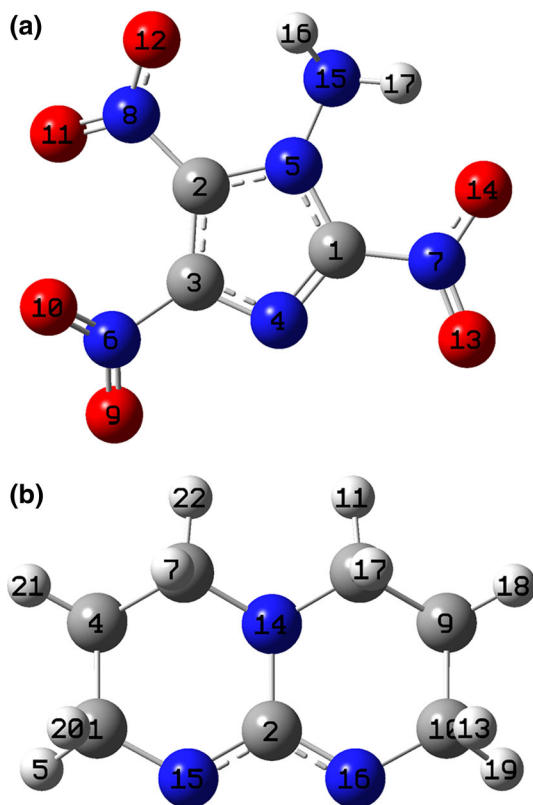
In terms of densities of frontier molecular orbitals (frontier molecular orbital approximation, FMOA), Eq. (2) turns into Eq. (3) as follows:

$$\begin{aligned} f^{(2)}(\mathbf{r}) &\approx |\psi_{\text{LUMO}}(\mathbf{r})|^2 - |\psi_{\text{HOMO}}(\mathbf{r})|^2 \\ &\approx \rho_{\text{LUMO}}(\mathbf{r}) - \rho_{\text{HOMO}}(\mathbf{r}), \end{aligned} \quad (3)$$

As written, this expression indicates that the electronic densities of frontier molecular orbitals are responsible of the local reactivity of the molecule while the electronic densities of the remaining occupied molecular orbitals are not taking part of the chemical reaction, meaning that relaxation effects are excluded per se.

The dual descriptor allows one to obtain simultaneously the preferably sites for nucleophilic attacks ($f^{(2)}(\mathbf{r}) > 0$) and the preferably sites for electrophilic attacks ($f^{(2)}(\mathbf{r}) < 0$) over the system at point \mathbf{r} . This LRD has demonstrated to be a robust tool revealing true nucleophilic and electrophilic sites on a molecular system [8–17]. For instance, the 2,4,5-trinitro-1*H*-imidazol-1-amine [18] molecule has been geometrically optimized at the B3LYP/6-311(d,p) level of theory and it is depicted by Fig. 1a. Its local reactivity can be analyzed by means of Fukui functions and dual descriptor. According to the FMOA given by Fig. 2, Fukui functions [$f^+(\mathbf{r})$ and $f^-(\mathbf{r})$] indicate that some atoms are susceptible to be attacked by nucleophiles and others, by electrophiles. But some confusion could arise, for instance, atoms number 7 and 8 can be attacked by some nucleophilic species only, as depicted by $f^+(\mathbf{r})$. On the contrary, atoms number 1 and 3 can be attacked either by some nucleophilic or electrophilic species because these both Fukui functions are favoring these atoms either from an behavior of electrophilic or nucleophilic type, respectively, thus meaning an ambiguity that prevents revealing the real nature of atoms number 1 and 3. What is the most likely behavior of these two last atoms? the answer is given by the dual descriptor [$f^{(2)}(\mathbf{r})$] which indicates that these atoms are going to be preferably attacked by an electrophilic species and not by a nucleophilic species. In this context, the doubt is cleared because dual descriptor reveals that atoms number 1 and 3 are more susceptible to be attacked by an electrophilic species. Along with that, in this molecular system the

Fig. 1 Optimized molecular structure of **a** 2,4,5-trinitro-1*H*-imidazol-1-amine, an energetic molecule and **b** anion of 1,3,4,6,7,8 hexahydro-2*H*-pyrimido[1,2-*a*]pyrimidine (bearing a -1 net charge) and that is used as a ligand



relaxation terms seem to be not too much important because scalar fields (3D figures) given by the FDA are very similar to those that have been generated by the FMOA. In fact, reader can notice that 3D maps of dual descriptors generated either by the use of FDA or FMOA (Fig. 2), are almost identical, thus indicating that the relaxation effects can be neglected. Cases like this validate the use of the FMOA.

But a criticism might arise since this analysis is based on the use of the FMOA and not by means of the FDA which defines the more accurate working equations for Fukui functions and dual descriptor. Then, along with the energetic molecule aforementioned, a second molecule where relaxation effects have proven to be not negligible is analyzed. This is the anion of 1,3,4,6,7,8-hexahydro-2*H*-pyrimido[1,2-*a*]pyrimidine [19] (or simply hpp^-) that is shown in Fig. 1b. It was geometrically optimized at the B3LYP/6-311G(d,p) level of theory. Like the case of the energetic molecule, FDA and FMOA were used in order to generate 3D maps of the $f^+(\mathbf{r})$, $f^-(\mathbf{r})$ and $f^{(2)}(\mathbf{r})$ as depicted by Fig. 3. In this case, it is observed that $f^+(\mathbf{r})$ shows a zone that is more susceptible to be attacked by nucleophilic species than other zones, either via FDA or FMOA; on the contrary, $f^-(\mathbf{r})$ computed by FDA differs from that computed by FMOA because the latter tells us that close to the hydrogen atoms 7, 11, 17 and 22 there is a region that is the most susceptible to be attacked by nucleophilic

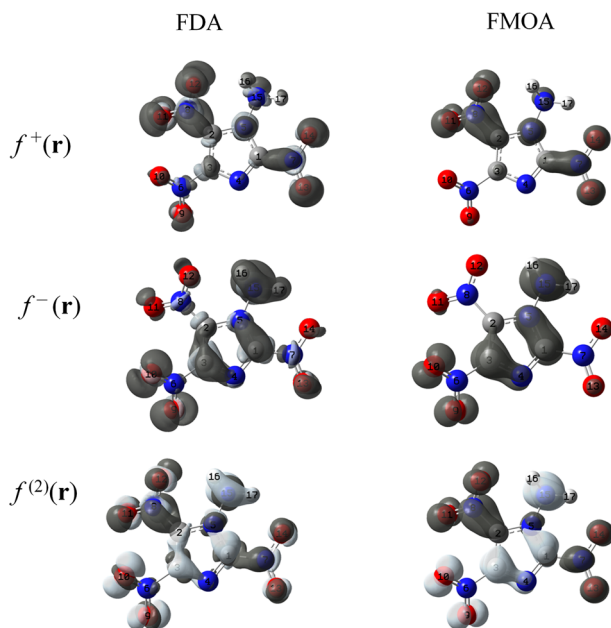


Fig. 2 Nucleophilic Fukui function, electrophilic Fukui function and dual descriptor were generated by both the finite difference (FDA) and the frontier molecular orbital approximations (FMOA) for 2,4,5-trinitro-1H-imidazol-1-amine. *Scalar fields* nucleophilic Fukui function $f^+(\mathbf{r})$; electrophilic Fukui function $f^-(\mathbf{r})$ and dual descriptor $f^{(2)}(\mathbf{r})$. Fukui functions are monophasic functions (*dark-colored lobes* only), being positive and reveal site of electrophilic and nucleophilic behavior, respectively. Dual descriptor is a biphasic function, so that *dark-colored lobes* indicate electrophilic behavior, meaning $f^{(2)}(\mathbf{r}) > 0$, meanwhile *white-colored lobes* reveal nucleophilic behavior, meaning $f^{(2)}(\mathbf{r}) < 0$. All isosurfaces are generated at a 0.0025 a.u. at the (U)B3LYP/6-311G(d,p) level of theory

species, however this zone of maximum electrophilic behavior does not exist in the dual descriptor described by the FDA.

At a first glance, it seems to be a big problem, but not too much. After adding diffuse functions, but using the geometrically structures obtained by means of the original level of theory, meaning (U)B3LYP/6-311G(d,p) and by the use of the energy computed at the new level of theory, (U)B3LYP/6-311++G(d,p), results are depicted by Fig. 4. As observed, inasmuch as this structure is an anion, it is expected that $f^+(\mathbf{r})$ has a very tiny scalar field described either by FDA or FMOA. On the contrary, $f^-(\mathbf{r})$ presents a well extended scalar field because the anion hpp^- would have a more trend for donating electrons instead of capturing them. In consequence, the dual descriptor is mainly dependant of $f^-(\mathbf{r})$ along with its relaxation orbital terms, however, there is a consistency in the local reactivity because, either by FMOA or FDA, electrophilic attacks might occur preferably over atoms 15 and 16 as indicated by $f^{(2)}(\mathbf{r})$ in Fig. 4.

In reference to the couple of examples that have been just described, there had not been a simple explanation that allows one understand the high accuracy of dual descriptor for describing nucleophilic and electrophilic interactions in comparison with Fukui functions. It is important to mention that the case of hpp^- is one of the more “pathological” systems that have been broached from this perspective, hence

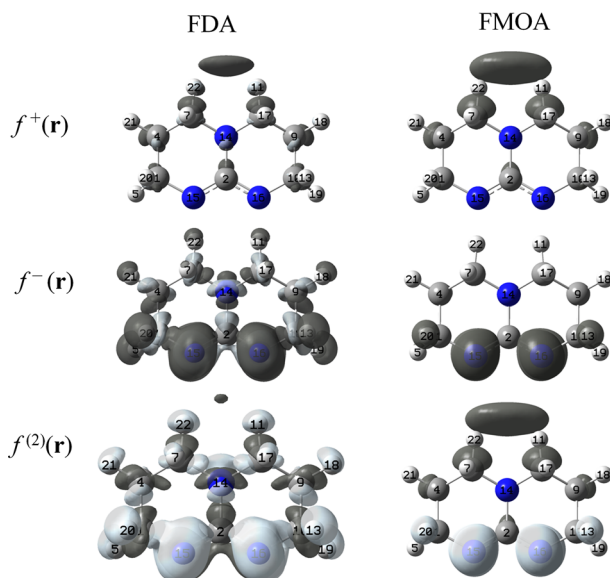


Fig. 3 Nucleophilic Fukui function, electrophilic Fukui function and dual descriptor were generated by both the finite difference (FDA) and the frontier molecular orbital approximations (FMOA) for the anion of 1,3,4,6,7,8 hexahydro-2H-pyrimido[1,2-a]pyrimidine. *Scalar fields* nucleophilic Fukui function $f^+(\mathbf{r})$; electrophilic Fukui function $f^-(\mathbf{r})$ and dual descriptor $f^{(2)}(\mathbf{r})$. Fukui functions are monophasic functions (*dark-colored lobes* only), being positive and reveal site of electrophilic and nucleophilic behavior, respectively. Dual descriptor is a biphasic function, so that *dark-colored lobes* indicate electrophilic behavior, meaning $f^{(2)}(\mathbf{r}) > 0$, meanwhile *white-colored lobes* reveal nucleophilic behavior, meaning $f^{(2)}(\mathbf{r}) < 0$. All isosurfaces are generated at a 0.0025 a.u. at the (U)B3LYP/6-311G(d,p) level of theory

the FMOA is not a proper approximation when a big accurate is required. Even so, the qualitative information is provided correctly. Other cases can be cited: there is evidence that *s*-electrons are dominant in relaxation effect for *p*-block atoms [20] and for conjugated organic molecules, the dominant orbital relaxation is attributable to the σ -framework [21–23].

The purpose of this article is to reveal than instead of using nucleophilic and electrophilic Fukui functions, the use of the dual descriptor should be fostered because this LRD is able to unambiguously describe the nucleophilic and electrophilic behavior on several sites of a molecule from a perspective of covalent interactions. The reader can recall that nucleophilic Fukui function, $f^+(\mathbf{r})$, can be written in terms of densities of all of occupied molecular orbitals and the density of LUMO as follows [3,24]:

$$f^+(\mathbf{r}) \approx |\psi_{\text{LUMO}}(\mathbf{r})|^2 + 2 \sum_{i=1}^{\text{HOMO}} \left(\frac{\partial |\psi_i(\mathbf{r})|^2}{\partial N} \right)^+, \quad (4)$$

when i runs from 1 to $N/2 + 1$ (LUMO), passing through $N/2$ (HOMO). Similarly, electrophilic Fukui function, $f^-(\mathbf{r})$, can be written in terms of densities of all occupied molecular orbitals including the density of HOMO as follows [3,24]:

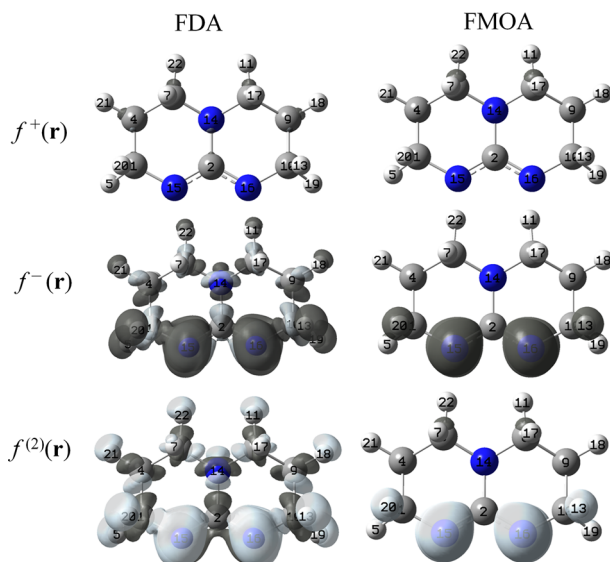


Fig. 4 Nucleophilic Fukui function, electrophilic Fukui function and dual descriptor were generated by both the finite difference (FDA) and the frontier molecular orbital approximations (FMOA) for the anion of 1,3,4,6,7,8 hexahydro-2H-pyrimido[1,2-a]pyrimidine. *Scalar fields* nucleophilic Fukui function $f^+(\mathbf{r})$; electrophilic Fukui function $f^-(\mathbf{r})$ and dual descriptor $f^{(2)}(\mathbf{r})$. Fukui functions are monophasic functions (*dark-colored lobes* only), being positive and reveal site of electrophilic and nucleophilic behavior, respectively. Dual descriptor is a biphasic function, so that *dark-colored lobes* indicate electrophilic behavior, meaning $f^{(2)}(\mathbf{r}) > 0$, meanwhile *white-colored lobes* reveal nucleophilic behavior, meaning $f^{(2)}(\mathbf{r}) < 0$. All isosurfaces are generated at a 0.0025 a.u. at the (U)B3LYP/6-311++G(d,p)/(U)B3LYP/6-311G(d,p) level of theory

$$f^-(\mathbf{r}) \approx |\psi_{\text{HOMO}}(\mathbf{r})|^2 + 2 \sum_{i=1}^{\text{HOMO}} \left(\frac{\partial |\psi_i(\mathbf{r})|^2}{\partial N} \right)^- \quad (5)$$

The Eqs. (4) and (5) [24–28] correspond to the working equations in terms of all occupied molecular orbitals.

This article is organized as follows: The present Introduction section provides the motivation which has given rise to this work along with the theoretical background that exposes the basic knowledge associated to the dual descriptor within the framework of the conceptual density functional theory to the non specialized reader, the Discussion section is the second section where the higher accuracy of dual descriptor is revealed in terms of densities of molecular orbitals and to finish the Concluding remarks section gives the conclusions concerning the analysis that has been exposed here.

2 Discussion

Note that HOMO and LUMO correspond always to molecular orbitals number $N/2$ and $N/2 + 1$, respectively, of the closed-shell system containing N electrons, under the assumption that N is an even number. In order to emphasize that the systems with

N , $N + 1$ and $N - 1$ electrons are being used, the N , $N + 1$ and $N - 1$ subscripts are used too as will be seen throughout the present work.

The information concerning to the $N/2$ -th molecular orbital, $|\psi_{N/2}(\mathbf{r})|_N^2$, it is interpreted as follows: “the absolute value of HOMO raised to the square, for a system with N electrons”. According to the latter, $|\psi_{N/2}(\mathbf{r})|_N^2 \equiv |\psi_{\text{HOMO}}(\mathbf{r})|_N^2 \equiv |\psi_{\text{HOMO}}(\mathbf{r})|^2$. The N subscript can be dropped once we realize that we are referring to the original system with N electrons.

In case of the system with $N + 1$ and $N - 1$ electrons, the respective subscripts must be conserved in order to recall that we have begun the analysis starting from the original system with N electrons.

Similarly, information concerning to the following molecular orbital $|\psi_{N/2}(\mathbf{r})|_{N+1}^2$, it is interpreted like “the absolute value of the $N/2$ -th molecular orbital raised to the square for a system with $N + 1$ electrons (it is an anion if the original system with N electrons is electrically neutral)”. And in consequence, that information concerning to the $|\psi_{N/2}(\mathbf{r})|_{N-1}^2$ molecular orbital is interpreted like “the absolute value of the $N/2$ -th molecular orbital raised to the square for a system with $N - 1$ electrons (it is a cation if the original system with N electrons is electrically neutral)”.

The electronic density is expressed in terms of electronic densities of the occupied molecular orbitals:

$$\rho_N(\mathbf{r}) = \sum_{i=1}^{N/2} 2 |\psi_i(\mathbf{r})|_N^2, \quad (6)$$

where the subscript N indicates that all of molecular orbitals are associated to the system containing N electrons; a 2 factor corresponds to the double occupancy in every orbital, counting from HOMO down to the very first occupied molecular orbital and the N -th orbital corresponds to the HOMO.

The very last term of the sum can be released:

$$\rho_N(\mathbf{r}) = 2 |\psi_{N/2}(\mathbf{r})|_N^2 + \sum_{i=1}^{N/2-1} 2 |\psi_i(\mathbf{r})|_N^2, \quad (7)$$

When the molecular system with N electrons releases one electron from HOMO, as a consequence of an electrophilic attack, an orbital relaxation occurs, thus meaning that there is no reason to assume that molecular orbitals will be the same as they were written before, in fact they have to change and then the following expression can be written:

$$\rho_{N-1}(\mathbf{r}) = |\psi_{N/2}(\mathbf{r})|_{N-1}^2 + \sum_{i=1}^{N/2-1} 2 |\psi_i(\mathbf{r})|_{N-1}^2, \quad (8)$$

The arithmetic difference between Eqs. (7) and (8) along with the respective division by $\Delta N = (N) - (N - 1) = 1$ leads to the electrophilic Fukui function:

$$f^-(\mathbf{r}) = \frac{\rho_N(\mathbf{r}) - \rho_{N-1}(\mathbf{r})}{\Delta N} \equiv \rho_N(\mathbf{r}) - \rho_{N-1}(\mathbf{r})$$

$$\begin{aligned}
 &= 2 |\psi_{N/2}(\mathbf{r})|_N^2 + \sum_{i=1}^{N/2-1} 2 |\psi_i(\mathbf{r})|_N^2 - |\psi_{N/2}(\mathbf{r})|_{N-1}^2 - \sum_{i=1}^{N/2-1} 2 |\psi_i(\mathbf{r})|_{N-1}^2 \\
 &= 2 |\psi_{N/2}(\mathbf{r})|_N^2 - |\psi_{N/2}(\mathbf{r})|_{N-1}^2 + \sum_{i=1}^{N/2-1} 2 \left\{ |\psi_i(\mathbf{r})|_N^2 - |\psi_i(\mathbf{r})|_{N-1}^2 \right\}
 \end{aligned}$$

After adding and subtracting the $|\psi_{N/2}(\mathbf{r})|_{N-1}^2$ term on the right-hand side, we obtain:

$$f^-(\mathbf{r}) = |\psi_{N/2}(\mathbf{r})|_{N-1}^2 + \sum_{i=1}^{N/2} 2 \left\{ |\psi_i(\mathbf{r})|_N^2 - |\psi_i(\mathbf{r})|_{N-1}^2 \right\} \quad (9)$$

Under the assumption that $|\psi_{N/2}(\mathbf{r})|_{N-1}^2 \approx |\psi_{N/2}(\mathbf{r})|_N^2 \equiv |\psi_{\text{HOMO}}(\mathbf{r})|_N^2 \equiv |\psi_{\text{HOMO}}(\mathbf{r})|^2$ along with $|\psi_i(\mathbf{r})|_N^2 = |\psi_i(\mathbf{r})|_{N-1}^2$, Eq. (9) turns into:

$$\begin{aligned}
 f^-(\mathbf{r}) &\approx |\psi_{N/2}(\mathbf{r})|_{N-1}^2 + \sum_{i=1}^{N/2} 2 \left\{ |\psi_i(\mathbf{r})|_N^2 - |\psi_i(\mathbf{r})|_{N-1}^2 \right\} \\
 &\approx |\psi_{N/2}(\mathbf{r})|_{N-1}^2 \\
 &\approx |\psi_{N/2}(\mathbf{r})|_N^2 \\
 &\approx |\psi_{\text{HOMO}}(\mathbf{r})|_N^2 \equiv |\psi_{\text{HOMO}}(\mathbf{r})|^2
 \end{aligned} \quad (10)$$

When returning to the the formal definition given by:

$$\begin{aligned}
 \left(\frac{\partial |\psi_i(\mathbf{r})|_N^2}{\partial N} \right)^- &= \lim_{\Delta N \rightarrow 0} \frac{|\psi_i(\mathbf{r})|_N^2 - |\psi_i(\mathbf{r})|_{N-1}^2}{\Delta N} \implies |\psi_{N/2}(\mathbf{r})|_{N-1}^2 \approx |\psi_{N/2}(\mathbf{r})|_N^2 \\
 &\equiv |\psi_{\text{HOMO}}(\mathbf{r})|^2
 \end{aligned}$$

the Eq. (9) can be re-written as it is well-known:

$$\begin{aligned}
 f^-(\mathbf{r}) &\approx |\psi_{N/2}(\mathbf{r})|_N^2 + \sum_{i=1}^{N/2} 2 \left(\frac{\partial |\psi_i(\mathbf{r})|_N^2}{\partial N} \right)^- \\
 &\approx |\psi_{\text{HOMO}}(\mathbf{r})|^2 + \sum_{i=1}^{\text{HOMO}} 2 \left(\frac{\partial |\psi_i(\mathbf{r})|_N^2}{\partial N} \right)^-
 \end{aligned}$$

On the other hand, when one electron arrives to the molecular system with N electrons, that extra arriving electron has to be located at the LUMO under the assumption that

the most likely unoccupied molecular orbital to be filled is the $N/2 + 1$ th-orbital, meaning LUMO precisely.

$$\rho_{N+1}(\mathbf{r}) = |\psi_{N/2+1}(\mathbf{r})|_{N+1}^2 + \sum_{i=1}^{N/2} 2|\psi_i(\mathbf{r})|_{N+1}^2. \quad (11)$$

After using the definition for nucleophilic Fukui function along with establishing the arithmetic difference between Eqs. (11) and (6), a division by $\Delta N = (N + 1) - (N) = 1$ must be performed as follows:

$$\begin{aligned} f^+(\mathbf{r}) &= \frac{\rho_{N+1}(\mathbf{r}) - \rho_N(\mathbf{r})}{\Delta N} \equiv \rho_{N+1}(\mathbf{r}) - \rho_N(\mathbf{r}) \\ &= |\psi_{N/2+1}(\mathbf{r})|_{N+1}^2 + \sum_{i=1}^{N/2} 2|\psi_i(\mathbf{r})|_{N+1}^2 - \sum_{i=1}^{N/2} 2|\psi_i(\mathbf{r})|_N^2 \\ &= |\psi_{N/2+1}(\mathbf{r})|_{N+1}^2 + \sum_{i=1}^{N/2} 2 \left\{ |\psi_i(\mathbf{r})|_{N+1}^2 - |\psi_i(\mathbf{r})|_N^2 \right\} \end{aligned} \quad (12)$$

Again, the original approximation implies that no relaxation effects occurs in molecular orbitals, so that $|\psi_i(\mathbf{r})|_{N+1}^2 = |\psi_i(\mathbf{r})|_N^2$. As a consequence, Eq. (12) turns into:

$$\begin{aligned} f^+(\mathbf{r}) &\approx \sum_{i=1}^{N/2} 2 \left\{ |\psi_i(\mathbf{r})|_{N+1}^2 - |\psi_i(\mathbf{r})|_N^2 \right\} + |\psi_{N/2+1}(\mathbf{r})|_{N+1}^2 \\ &\approx |\psi_{N/2+1}(\mathbf{r})|_{N+1}^2 \\ &\approx |\psi_{N/2+1}(\mathbf{r})|_N^2 \\ &\approx |\psi_{\text{LUMO}}(\mathbf{r})|_N^2 \equiv |\psi_{\text{LUMO}}(\mathbf{r})|^2 \end{aligned} \quad (13)$$

The original expression of the nucleophilic Fukui written in terms of the squared molecular orbitals according to Eq. (12) along with using the formal definition of partial derivatives leads to:

$$\begin{aligned} \left(\frac{\partial |\psi_i(\mathbf{r})|_N^2}{\partial N} \right)^+ &= \lim_{\Delta N \rightarrow 0} \frac{|\psi_i(\mathbf{r})|_{N+1}^2 - |\psi_i(\mathbf{r})|_N^2}{\Delta N} \implies |\psi_{N/2+1}(\mathbf{r})|_{N+1}^2 \\ &\approx |\psi_{N/2+1}(\mathbf{r})|_N^2 \equiv |\psi_{\text{LUMO}}(\mathbf{r})|^2 \end{aligned}$$

The latter allows one to obtain the original definition written in terms of molecular orbitals from Eq. (12):

$$f^+(\mathbf{r}) \approx |\psi_{N/2+1}(\mathbf{r})|_N^2 + \sum_{i=1}^{N/2} 2 \left(\frac{\partial |\psi_i(\mathbf{r})|_N^2}{\partial N} \right)^+$$

$$\approx |\psi_{\text{LUMO}}(\mathbf{r})|^2 + \sum_{i=1}^{\text{HOMO}} 2 \left(\frac{\partial |\psi_i(\mathbf{r})|_N^2}{\partial N} \right)^+$$

Note that Eqs. (9) and (12) correspond to exact definitions written in terms of electronic densities of all occupied molecular orbitals. While Eqs. (10) and (13) are the classic approximations for electrophilic and nucleophilic Fukui functions. And as dual descriptor is given by the arithmetic difference between $f^+(\mathbf{r})$ and $f^-(\mathbf{r})$, the expected approximation for dual descriptor is obtained as depicted by Eq. (3). Dual descriptor has been described as a robust reactivity descriptor because it reveals unambiguously nucleophilic and electrophilic sites on a molecule. For instance, nucleophilic Fukui function, $f^+(\mathbf{r})$, can show us sites on a molecular that are susceptible for nucleophilic attacks. Additionally, electrophilic Fukui function, $f^-(\mathbf{r})$, shows us sites that are susceptible for electrophilic attacks. However, some nucleophilic sites on a molecule, according to $f^+(\mathbf{r})$, overlaps with some electrophilic sites according to $f^-(\mathbf{r})$, so the question is: what about that intersection region, is it nucleophilic or electrophilic? The answer is given by dual descriptor which allows to disambiguate between $f^+(\mathbf{r})$ and $f^-(\mathbf{r})$.

3 Dual descriptor allows one additional approximation that makes it more accurate to describe local reactivity

Now, a different level of approximation should lead to understand the characteristic of dual descriptor for revealing true nucleophilic and electrophilic sites on a molecule. By taking Eqs. (9) and (12), we recall that every partial derivative symbolizes the following arithmetic differences:

$$\left(\frac{\partial |\psi_i(\mathbf{r})|_N^2}{\partial N} \right)^- \approx |\psi_i(\mathbf{r})|_N^2 - |\psi_i(\mathbf{r})|_{N-1}^2 \quad (14)$$

and

$$\left(\frac{\partial |\psi_i(\mathbf{r})|_N^2}{\partial N} \right)^+ \approx |\psi_i(\mathbf{r})|_{N+1}^2 - |\psi_i(\mathbf{r})|_N^2 \quad (15)$$

Then, after replacing in Eqs. (9) and (12), the following expressions are obtained:

$$f^-(\mathbf{r}) \approx |\psi_{N/2}(\mathbf{r})|_{N-1}^2 + \sum_{i=1}^{N/2} 2 \left(\frac{\partial |\psi_i(\mathbf{r})|_N^2}{\partial N} \right)^- \quad (16)$$

$$f^+(\mathbf{r}) \approx |\psi_{N/2+1}(\mathbf{r})|_{N+1}^2 + \sum_{i=1}^{N/2} 2 \left(\frac{\partial |\psi_i(\mathbf{r})|_N^2}{\partial N} \right)^+ \quad (17)$$

3.1 The original approximation implying that relaxation effects on molecular orbitals are not included

The following approximations are often applied on Eqs. (16) and (17):

$$\left(\frac{\partial |\psi_i(\mathbf{r})|_N^2}{\partial N}\right)^- \approx |\psi_i(\mathbf{r})|_N^2 - |\psi_i(\mathbf{r})|_{N-1}^2 \approx 0 \quad (18)$$

and

$$\left(\frac{\partial |\psi_i(\mathbf{r})|_N^2}{\partial N}\right)^+ \approx |\psi_i(\mathbf{r})|_{N+1}^2 - |\psi_i(\mathbf{r})|_N^2 \approx 0 \quad (19)$$

and therefore:

$$|\psi_{N/2}(\mathbf{r})|_{N-1}^2 \approx |\psi_{N/2}(\mathbf{r})|_N^2 \equiv |\psi_{\text{HOMO}}(\mathbf{r})|^2$$

and

$$|\psi_{N/2+1}(\mathbf{r})|_{N+1}^2 \approx |\psi_{N/2+1}(\mathbf{r})|_N^2 \equiv |\psi_{\text{LUMO}}(\mathbf{r})|^2$$

In consequence, the typical working equation for dual descriptor in terms of densities of frontier molecular orbitals is obtained:

$$\begin{aligned} f^{(2)}(\mathbf{r}) &= f^+(\mathbf{r}) - f^-(\mathbf{r}) \approx |\psi_{N/2+1}(\mathbf{r})|_{N+1}^2 - |\psi_{N/2}(\mathbf{r})|_{N-1}^2 \\ &\approx |\psi_{\text{LUMO}}(\mathbf{r})|^2 - |\psi_{\text{HOMO}}(\mathbf{r})|^2 \end{aligned}$$

Note that approximations given by Eqs. (18) and (19) imply that $N/2$ terms in Eq. (16) and $N/2$ terms in Eq. (17) are deleted.

3.2 An alternative approximation implying that relaxation effects on molecular orbitals are included

This second approximation is less dramatic and it can only be performed in the definition of dual descriptor and not on every definition of Fukui function. First, the mathematical expression for dual descriptor is written as the arithmetic difference between the nucleophilic and electrophilic Fukui functions, thus meaning Eq. (17) minus Eq. (16), thus meaning that $f^{(2)}(\mathbf{r}) \approx f^+(\mathbf{r}) - f^-(\mathbf{r})$:

$$\begin{aligned} f^{(2)}(\mathbf{r}) &\approx |\psi_{N/2+1}(\mathbf{r})|_{N+1}^2 + \sum_{i=1}^{N/2} 2 \left(\frac{\partial |\psi_i(\mathbf{r})|_N^2}{\partial N}\right)^+ - |\psi_{N/2}(\mathbf{r})|_{N-1}^2 - \sum_{i=1}^{N/2} 2 \left(\frac{\partial |\psi_i(\mathbf{r})|_N^2}{\partial N}\right)^- \\ &\approx |\psi_{N/2+1}(\mathbf{r})|_{N+1}^2 - |\psi_{N/2}(\mathbf{r})|_{N-1}^2 + \sum_{i=1}^{N/2} 2 \left\{ \left(\frac{\partial |\psi_i(\mathbf{r})|_N^2}{\partial N}\right)^+ - \left(\frac{\partial |\psi_i(\mathbf{r})|_N^2}{\partial N}\right)^- \right\} \end{aligned}$$

Now, the reader can notice there is no need that all partial derivatives tend to zero, because it is sufficient that the following less dramatic approximation be established:

$$\left(\frac{\partial |\psi_i(\mathbf{r})|_N^2}{\partial N}\right)^- \approx \left(\frac{\partial |\psi_i(\mathbf{r})|_N^2}{\partial N}\right)^+ \quad (20)$$

along with:

$$\left(\frac{\partial |\psi_i(\mathbf{r})|_N^2}{\partial N}\right)^- \neq 0 \quad \wedge \quad \left(\frac{\partial |\psi_i(\mathbf{r})|_N^2}{\partial N}\right)^+ \neq 0$$

This alternative approximation given by Eq. (20) can only be applied on dual descriptor definition. It leads to:

$$\begin{aligned} f^{(2)}(\mathbf{r}) &\approx |\psi_{N/2+1}(\mathbf{r})|_{N+1}^2 - |\psi_{N/2}(\mathbf{r})|_{N-1}^2 + \sum_{i=1}^{N/2} 2 \left\{ \left(\frac{\partial |\psi_i(\mathbf{r})|_N^2}{\partial N}\right)^+ - \left(\frac{\partial |\psi_i(\mathbf{r})|_N^2}{\partial N}\right)^- \right\} \\ f^{(2)}(\mathbf{r}) &\approx |\psi_{N/2+1}(\mathbf{r})|_{N+1}^2 - |\psi_{N/2}(\mathbf{r})|_{N-1}^2 \end{aligned} \quad (21)$$

Additionally, Eq. (20) has the following consequence

$$\begin{aligned} \left(\frac{\partial |\psi_i(\mathbf{r})|_N^2}{\partial N}\right)^- &\approx \left(\frac{\partial |\psi_i(\mathbf{r})|_N^2}{\partial N}\right)^+ \\ |\psi_i(\mathbf{r})|_N^2 - |\psi_i(\mathbf{r})|_{N-1}^2 &\approx |\psi_i(\mathbf{r})|_{N+1}^2 - |\psi_i(\mathbf{r})|_N^2 \\ &\Downarrow \\ 2|\psi_i(\mathbf{r})|_N^2 &\approx |\psi_i(\mathbf{r})|_{N+1}^2 + |\psi_i(\mathbf{r})|_{N-1}^2 \end{aligned}$$

where the

$$\begin{aligned} |\psi_i(\mathbf{r})|_{N+1}^2 &\approx 2|\psi_i(\mathbf{r})|_N^2 - |\psi_i(\mathbf{r})|_{N-1}^2 \\ |\psi_i(\mathbf{r})|_{N-1}^2 &\approx 2|\psi_i(\mathbf{r})|_N^2 - |\psi_i(\mathbf{r})|_{N+1}^2 \end{aligned}$$

From these expressions, the two terms in Eq. (21) are written in the same way:

$$\begin{aligned} |\psi_{N/2+1}(\mathbf{r})|_{N+1}^2 &\approx 2|\psi_{N/2+1}(\mathbf{r})|_N^2 - |\psi_{N/2+1}(\mathbf{r})|_{N-1}^2 \approx |\psi_{N/2+1}(\mathbf{r})|_N^2 \equiv |\psi_{\text{LUMO}}(\mathbf{r})|^2 \\ |\psi_{N/2}(\mathbf{r})|_{N-1}^2 &\approx 2|\psi_{N/2}(\mathbf{r})|_N^2 - |\psi_{N/2}(\mathbf{r})|_{N+1}^2 \approx |\psi_{\text{HOMO}}(\mathbf{r})|^2 \end{aligned}$$

And these terms replace the terms that define the Eq. (21) thus leading exactly to the same working equation given by Eq. (1).

$$f^{(2)}(\mathbf{r}) \approx |\psi_{N/2+1}(\mathbf{r})|_{N+1}^2 - |\psi_{N/2}(\mathbf{r})|_{N-1}^2 \approx |\psi_{\text{LUMO}}(\mathbf{r})|^2 - |\psi_{\text{HOMO}}(\mathbf{r})|^2$$

As can be observed, the working equation of dual descriptor does not imply to neglect the relaxation effect in molecular orbitals because although being relevant or not, its influence in the respective working equation is less important than in working equations given for the nucleophilic and electrophilic Fukui functions. The most simple working equations for nucleophilic and electrophilic Fukui functions can only be expressed by one way of approximation given by Eqs. (18) and (19), while dual descriptor, along with the former dramatic approximations that have been just described, can also be expressed by a second way of approximation given by Eq. (20), thus revealing that the dependence upon relaxation effects on molecular orbitals for dual descriptor is less important than in Fukui functions.

4 Concluding remarks

The analysis exposed in the present work reveals the robust nature of dual descriptor, thus making it a much more useful tool than Fukui function in its nucleophilic and electrophilic versions from the point of view of the frontier molecular orbital approximation so revealing sites of true nucleophilic and electrophilic nature, however this analysis is valid within the framework of the frontier molecular orbital approximation (FMOA), because in some extreme cases like the 1,3,4,6,7,8-hexahydro-2*H*-pyrimido[1,2-*a*]pyrimidine (hpp^-) anion, the relaxation orbital effects are not taken into account very well when using the FMOA, being necessary the use of the finite difference approximation (FDA). But note that the working equation for the dual descriptor based on the FDA does not need the inclusion of diffuse functions in the basis set because there is no a noticeable difference between the 3D map of dual descriptor based on the FDA when the basis set is 6-311G(d,p) and the 3D map of the same descriptor based on FDA when the basis set is 6-311++G(d,p). This statement can be easily confirmed when watching the 3D map of $f^{(2)}(\mathbf{r})$ of hpp^- computed via FDA (Figs. 3 and 4).

In general, the influence of the orbital relaxation is smaller than that one appearing in nucleophilic and electrophilic Fukui functions owing to a partial or total cancellation effect between $\left(\frac{\partial |\psi_i(\mathbf{r})|_N^2}{\partial N}\right)^+$ and $\left(\frac{\partial |\psi_i(\mathbf{r})|_N^2}{\partial N}\right)^-$ thanks to the definition given by Morell et al. for dual descriptor, however there are intrinsic limitations in working equations when they are written in terms of densities of frontier molecular orbitals as demonstrated by the hpp^- anion. Anyway, according to results that are exhibited here, an additional and less dramatic assumption is possible to apply on the working equation for dual descriptor that is not possible to use in the Fukui function definitions. Finally, a comparison among Eqs. (1) and (2) should be always carried out with the aim of assessing the importance of the canceled terms. Anyway, the analysis shown here indicates that dual descriptor is able to totally replace the Fukui functions because

information concerning to the local reactivity is revealed in just one mathematical expression and without including ambiguities. On the contrary, nucleophilic and electrophilic Fukui functions have not this characteristic. To reach the maximum accuracy in describing the local reactivity by the use of dual descriptor, the FDA should be preferred instead of FMOA under the assumption that a good basis set is being used.

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