



HAL
open science

A Perspective on the so-called Dual Descriptor

Henry Chermette, Lynda Merzoud, Frédéric Guégan, Christophe Morell

► **To cite this version:**

Henry Chermette, Lynda Merzoud, Frédéric Guégan, Christophe Morell. A Perspective on the so-called Dual Descriptor. Pratim Kumar Chattaraj, Debdutta Chakraborty. Chemical Reactivity in Confined Systems, John Wiley & Sons, 2021, 9781119684022. <hal-03933168>

HAL Id: hal-03933168

<https://cnrs.hal.science/hal-03933168v1>

Submitted on 10 Jan 2023

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.



HAL Authorization

A Perspective on the so-called Dual Descriptor

F. Guégan,^{*,†} L. Merzoud,[‡] H. Chermette,[‡] and C. Morell^{*,‡}

[†]*IC2MP UMR 7285, Université de Poitiers – CNRS, 4, rue Michel Brunet TSA
51106–86073 Cedex 9 Poitiers, France.*

[‡]*Université de Lyon, Institut des Sciences Analytiques, UMR 5280, CNRS, Université
Lyon 1, ENS Lyon - 5, rue de la Doua, F-69100 Villeurbanne, France.*

E-mail: frederic.guegan@univ-poitiers.fr; christophe.morell@univ-lyon1.fr

In this chapter, the so-called dual descriptor from conceptual DFT framework is reviewed. the power of the dual descriptor is highlighted by selected examples.

1 Introduction: conceptual DFT

Chemistry can be defined as a science dedicated to the study of the transformations of matter. Its central concern is thus to understand and predict reactivity and selectivity during reactions.^{1,2} Theoretical chemistry offers in this respect a wonderful tool to achieve first-principle rationalisations, and thus it is not surprising that many different theoretical frameworks were proposed over time. Among these one may find Conceptual Density Functional Theory (C-DFT).^{3–8} The basic assumption in C-DFT is that the first Hohenberg-Kohn theorem⁹ is satisfied, and thus that energy is a unique functional of the electron density. This implies that, if all accessible information on the system is contained within the wavefunction, it is

also contained within the electron density. C-DFT then focuses on extracting this information, by the calculation of relevant quantities designed from first principles, often responses of the system to a (chemical) perturbation. The dual descriptor is one example of such descriptors, designed to provide insight on the chemical reactivity of a system.

In the following sections, we will present how it has initially been formulated. This first approach already revealed a strong connection between the dual descriptor and reactivity, which was further established by alternative derivations of this quantity, revealing deeper links with other reactivity descriptors and principles. Then, its efficiency in predicting reactivity and selectivity will be illustrated on simple yet insightful classical reactions in organic chemistry.

2 The Dual Descriptor: fundamental aspects

2.1 Initial formulation

The dual descriptor was first derived in 2005, through a study of the energy variation two reagents undergo when put in interaction.¹⁰ Decomposing this interaction into covalent, electrostatic and polarisation contributions (or, in a HSAB framework, into soft-soft, hard-hard and hard-soft contributions), it could be shown that maximal covalent interaction with a nucleophile (respectively an electrophile) is expected when the quantity

$$\Delta f(\mathbf{r}) = f^+(\mathbf{r}) - f^-(\mathbf{r}) \tag{1}$$

is maximal (respectively minimal). In this expression, f^+ and f^- are, respectively, the electrophilic and nucleophilic Fukui functions¹¹ (right and left derivatives of the electron density with respect to the number of electrons). Since each Fukui Function is normalized

to one, the dual descriptor is also normalized :

$$\int_{\mathbb{R}^3} \Delta f(\mathbf{r}) d\mathbf{r} = 0 \quad (2)$$

Thus, localisation of both the most electrophilic and nucleophilic sites of a given reagent are possible by a simple study of the extrema of a single quantity, Δf , hence the name "dual descriptor".

But beside this search for the most reactive regions, one may expect that Δf will allow to characterise all reactive regions in the system. Indeed, in any electrophilic area, one expects that $f^+(\mathbf{r}) > f^-(\mathbf{r})$, thus $\Delta f(\mathbf{r}) > 0$. Conversely, in nucleophilic regions $f^+(\mathbf{r}) < f^-(\mathbf{r})$ and $\Delta f(\mathbf{r}) < 0$. One may thus approach local philicities by the sign of the dual descriptor, and compare site reactivities by comparing their dual descriptor values. This is illustrated in section 3.

2.2 Alternative formulations

2.2.1 Derivative formulations

Before moving to the illustrations, further arguments can be provided to illustrate the strong connection between Δf and reactivity/selectivity. It can indeed be shown that Δf represents the local variation of hardness η due to a change in the external potential (approach of a reagent) $\delta v(\mathbf{r})$:¹

$$\Delta f(\mathbf{r}) = \left(\frac{\delta \eta}{\delta v(\mathbf{r})} \right)_N. \quad (3)$$

¹Note that, formally, identity between these two quantities is only met if temperature equals 0 K, which is an implicit assumption in most DFT calculations.

From Maxwell identities, it can then be shown that

$$\Delta f(\mathbf{r}) = \left(\frac{\partial^2 \rho(\mathbf{r})}{\partial N^2} \right)_{v(\mathbf{r})}. \quad (4)$$

As one may note, Equation 1 can be retrieved from Equation 4 using finite difference approximation (unitary variation of N). This latter formulation furthermore stresses out an important feature of the dual descriptor: formally, this quantity is a high order response of the system (second order response of the electron density and third order response of the energy). Nevertheless, it presents a significant advantage over the first-order response of ρ : it is uniquely defined, contrarily to the Fukui functions (left and right derivatives being inequivalent). Thus one may catch both nucleophilicity and electrophilicity through a single object, which furthermore may offer deeper insight on local reactivity than the Fukui functions. There may indeed be regions of space where $f^+(\mathbf{r})$ is rather large and $f^-(\mathbf{r})$ too. If one restricts to a study of either Fukui functions, these regions could be deemed rather electrophilic or nucleophilic, while Δf suggests these regions are merely "electron interchanges". One may however note that this deeper insight is offered at a certain expense. Δf is indeed small either when both Fukui functions are large or small. These two situations are chemically inequivalent: in the first case, a marked polarisability or local softness is expected, since electrons are easily mobilised, while in the second case a marked local hardness (or weak polarisability) is expected.

Overall, Δf appears to be a suitable descriptor for the characterisation of local reactivity and selectivity, but not for local polarisability/softness. Actually, the definition of local softness and hardness were quite recently revisited (*vide infra*) and show, as expected from the previous discussion, an explicit dependence over both the dual descriptor and the Fukui functions (thus regaining information relative to their magnitude).

2.2.2 Link with Frontier Molecular Orbital theory

The strong insight on reactivity Δf offers is further stressed out by a common working approximation. Using finite differentiation, Equation 4 rewrites :

$$\Delta f(\mathbf{r}) \approx \rho_{N+1}(\mathbf{r}) + \rho_{N-1}(\mathbf{r}) - 2\rho_N(\mathbf{r}) \quad (5)$$

with ρ_j the electron density of the system with j electrons (at constant geometry). If orbitals are frozen, that is they remain unchanged by addition or subtraction of electrons, one obtains

$$\Delta f(\mathbf{r}) \approx \rho_{LU}(\mathbf{r}) - \rho_{HO}(\mathbf{r}) \quad (6)$$

with ρ_{HO} and ρ_{LU} , respectively, the highest occupied and lowest unoccupied Molecular Orbital densities. This result is in line with the Frontier Molecular Orbital approximation of Fukui.^{12,13} In this framework, electrophilic regions correspond to places where the LUMO develops, while nucleophilic areas are characterised by the HOMO. This is quite obviously retrieved here, since $\Delta f(\mathbf{r}) > 0$ where the LUMO develops and $\Delta f(\mathbf{r}) < 0$ where the HOMO develops.

2.2.3 State specific development

So far, we did not discuss the "computability" of the dual descriptor, and only focused on formal expressions and approximations for this quantity. Yet, there may be cases where our previous expressions cannot be computed, or at least cannot afford a satisfactory picture. For instance, when the FMO theory is known to fail (which is expected when orbital relaxation plays an important role), or when frontier orbitals are (quasi)-degenerate, equation 6 can hardly provide a clear and relevant insight on reactivity.

In such cases, one could still rely on equation 5, but issues can also arise. In the case

of anionic systems for instance, it is not always possible to attach an additional electron, and thus ρ_{N+1} cannot be computed. Furthermore, in the case of transition-metal containing systems, the proper spin-state of the N+1/N-1 species is often not trivially guessed.

From this, it appeared necessary to propose alternative ways to compute Δf , or generalisation of this quantity. In 2013,¹⁴ a formulation relying on excited states was proposed. One may note that Pearson already proposed in 1988 to analyse the ground state reactivity of molecules through a careful analysis of their first excitation.¹⁵ The central idea was that one could express the ground state electron density of a chemical system undergoing a perturbation as an expansion on the set of ground and excited state electron densities,

$$\rho_{pert}(\mathbf{r}) = \sum_i \alpha_i \rho_i(\mathbf{r}), \quad \sum_i \alpha_i = 1 \quad (7)$$

i indexing the electronic states (0 meaning ground state). From this, the ground state electron density reshuffling under perturbation can be expressed as

$$\Delta\rho(\mathbf{r}) = \rho_{pert}(\mathbf{r}) - \rho_0(\mathbf{r}) = \sum_{i>0} \alpha_i (\rho_i(\mathbf{r}) - \rho_0(\mathbf{r})) = \sum_{i>0} \alpha_i \Delta f_i(\mathbf{r}) \quad (8)$$

In the previous equation, Δf_i is called the i th state specific dual descriptor. It may indeed be shown, under the frozen orbital hypothesis, that Δf_1 equals the FMO approximation of the dual descriptor. The sum over all excited states is then called an "extended dual descriptor".

Now a central question remains: how can one express the weighting parameters α_i ? So far, no formula could be proposed, but in line with the sum-over-states formula one may encounter for instance in the expression of the molecular static polarisabilities, it may be surmised that α_i decays with excitation energies. Thus, it seems reasonable to restrict the calculation to the first few excited states, which are expected to convey most information on the ground state reactivity. This approach has been successfully applied to some organic

reactions whose outcome cannot be predicted by Frontier Molecular Orbital Theory¹⁴ and to the trans effect in octahedral transition metal complexes.¹⁶

2.2.4 MO degeneracy

The state specific development offers a solution for the computation of the dual descriptor when classical approximations are impossible to use, especially when the addition of one electron is impossible (self-ionizing anion) or when a near-degeneracy is observed around the Fermi level. However in this latter case computations are still rather cumbersome, since no algebraic formula can be provided for the weighting parameters in equation 8; at best, one may expect here to reach a qualitative level of description, but no quantification is at hand...

J. Martinez-Araya proposed in 2016 a way to address the problem of orbital degeneracy.¹⁷ More specifically, he proposed a general operational formula for Δf in closed-shell molecules presenting q-fold degenerate HOMO and p-fold degenerate LUMO. This proposal relies on equation 1, in which f^+ and f^- are reformulated to take the orbital degeneracy into account. Let us take the example of f^+ . Usually, addition of one electron in a chemical system results in addition of a supplementary molecular orbital in the Slater determinant describing its ground state wavefunction (addition of the newly occupied LUMO). However if the LUMO is p-fold degenerate, p different determinants can be build, corresponding to addition of the electron into a given LUMO. All these determinants should offer an equally valid representation of the state of the anion. Thus one should consider a linear combination of all these determinants as ground-state wavefunction. Obviously this is a tedious task for large p values. J. Martinez-Araya thus proposed a simplification: instead of considering p configurations associated to a one-electron addition, one could consider a unique configuration associated to the addition of p electrons at once (one electron per LUMO).

Following the same line of argument in the case of the q-fold degenerate HOMO (one

configuration associated to the loss of q electrons), he then proposed that :

$$\Delta f(\mathbf{r}) = \frac{q \cdot \rho_{N+p}^{p+1}(\mathbf{r}) - (p+q) \cdot \rho_N^1(\mathbf{r}) + p \cdot \rho_{N-q}^{q+1}(\mathbf{r})}{pq} \quad (9)$$

where the subscripts indicate the total number of electrons and the superscript the spin multiplicity to consider in the calculation (as suggested by Hund's rule). Quite obviously, if $q=p=1$ one retrieves equation 5. This operational formula then proved very efficient in the rationalisation of the chemical properties of molecular systems displaying a genuine MO degeneracy.

2.2.5 Quasi degeneracy

However, it may be surmised that the same approach will provide a less accurate picture in the case of near-degeneracy. Let us consider here the case of a system displaying an occupied MO close in energy to the HOMO, but not exactly degenerate with it, and a vacant MO close to the LUMO but here also not degenerate with it. In such case, the FMO approximation is expected to fail, as both the frontier and "near frontier" levels should contribute to reactivity. Yet these contributions should be quantitatively different, and thus equation 9 (which implicitly assumes all contributions are equivalent) is not expected to perform well either.

Qualitatively, one may expect that the further away a MO is from the frontier levels, the less it will contribute to the ground state reactivity. Following this idea, R. Pino-Rios and co-workers recently proposed a MO-weighted dual-descriptor, which may be seen as an extension of the FMO approximation of Δf .¹⁸

More specifically, they proposed to define orbital-weighted Fukui functions:

$$f_w^-(\mathbf{r}) = \sum_{i=1}^{HOMO} \omega_i^- \rho_i(\mathbf{r}), \quad \omega_i^- = \frac{\exp\left[-\left(\frac{\mu-\epsilon_i}{\Delta}\right)^2\right]}{\sum_{i=1}^{HOMO} \exp\left[-\left(\frac{\mu-\epsilon_i}{\Delta}\right)^2\right]} \quad (10)$$

$$f_w^+(\mathbf{r}) = \sum_{i=LUMO}^{N'} \omega_i^+ \rho_i(\mathbf{r}), \quad \omega_i^+ = \frac{\exp\left[-\left(\frac{\mu-\epsilon_i}{\Delta}\right)^2\right]}{\sum_{i=LUMO}^{N'} \exp\left[-\left(\frac{\mu-\epsilon_i}{\Delta}\right)^2\right]} \quad (11)$$

where i indexes a MO (assuming the system is represented by N' MO), μ is the chemical potential (average of the HOMO and LUMO energy in the FMO approximation), ϵ_i is the MO energy, ρ_i the associated electron density, and Δ a width parameter. From these weighted Fukui functions, they then proposed to design a weighted dual descriptor as

$$\Delta f_w(\mathbf{r}) = f_w^+(\mathbf{r}) - f_w^-(\mathbf{r}). \quad (12)$$

As one may note from f_w^- and f_w^+ definitions, contributions from all occupied and vacant MOs are taken into account. Nevertheless, the further away from the frontier levels, the lower the contribution, as a consequence of the Gaussian weighting. It may also be noted that perfect degeneracy can still be taken into account here, resulting as expected in similar weights for the degenerate levels.

Equation 12 thus provides an interesting way to evaluate Δf in various situations, noticeably when degeneracy is present. Yet, it must be noted the Gaussian weighting scheme is an ansatz (since it does not stem from a first principle derivation). Thus, even though it presents desirable features, especially regarding normalisation and convergence, it is not theoretically motivated. Additionally, the choice of the width parameter Δ is also not trivial from first principles, and thus calculations of Δf_w may be quite cumbersome in the general case.

2.2.6 Spin polarisation

Up to now, we have made only limited mention of the problem of the spin-state and spin polarisation in the calculation of Δf , and we have especially implicitly assumed the system under study bears a closed shell. This is of course often the case for organic compounds, but not in coordination or organometallic chemistry.

It is an understatement to say that extension of reactivity models to open-shell systems is not trivial: new concepts should indeed be developed, to account for the peculiar properties of unpaired electrons.² In the frame of C-DFT, this can be achieved by a study of the responses of the system to a change in the spin number N_S , or equivalently to a change in the total number of α and β spins, and to variations an external magnetic field $\mathbf{B}(\mathbf{r})$.

Thus, several different descriptors can be derived from the dual descriptor in spin-polarised DFT.¹⁹ Recalling that

$$\rho(\mathbf{r}) = \left(\frac{\delta E}{\delta v(\mathbf{r})} \right)_{\mathbf{B}(\mathbf{r}), N, N_S}, \quad \rho_S(\mathbf{r}) = \left(\frac{\delta E}{\delta \mathbf{B}(\mathbf{r})} \right)_{v(\mathbf{r}), N, N_S} \quad (13)$$

with ρ_S the spin-density, in analogy with equation 4 one may derive 6 different spin-polarised

²One cannot expect to describe a unique electron as being halfway between an electron pair and a vacancy, as is unfortunately implicitly assumed in some approaches, such as in the definition of the radical Fukui function $f^0 = \frac{1}{2}(f^+ + f^-)$.

dual descriptors:

$$\Delta f_{N,NN}(\mathbf{r}) = \left(\frac{\partial^2 \rho(\mathbf{r})}{\partial N^2} \right)_{N_S, v(\mathbf{r}), \mathbf{B}(\mathbf{r})} \quad (14)$$

$$\Delta f_{N_S, N_S N_S}(\mathbf{r}) = \left(\frac{\partial^2 \rho_S(\mathbf{r})}{\partial N_S^2} \right)_{N, v(\mathbf{r}), \mathbf{B}(\mathbf{r})} \quad (15)$$

$$\Delta f_{N, N_S N_S}(\mathbf{r}) = \left(\frac{\partial^2 \rho(\mathbf{r})}{\partial N_S^2} \right)_{N, v(\mathbf{r}), \mathbf{B}(\mathbf{r})} \quad (16)$$

$$\Delta f_{N_S, NN}(\mathbf{r}) = \left(\frac{\partial^2 \rho_S(\mathbf{r})}{\partial N^2} \right)_{N_S, v(\mathbf{r}), \mathbf{B}(\mathbf{r})} \quad (17)$$

$$\Delta f_{N, NN_S}(\mathbf{r}) = \left(\frac{\partial^2 \rho(\mathbf{r})}{\partial N \partial N_S} \right)_{v(\mathbf{r}), \mathbf{B}(\mathbf{r})} \quad (18)$$

$$\Delta f_{N_S, NN_S}(\mathbf{r}) = \left(\frac{\partial^2 \rho_S(\mathbf{r})}{\partial N \partial N_S} \right)_{v(\mathbf{r}), \mathbf{B}(\mathbf{r})} \quad (19)$$

These quantities were first proposed in 2008 by E. Chamorro and co-workers, and the chemical meaning of the four first ones examined.²⁰

The first quantity, $\Delta f_{N,NN}(\mathbf{r})$, is rather straightforward: it is the "usual" dual descriptor, that is, second-order response of the electron density to a change in the number of electrons, but *at fixed total spin*. As one may note, this constraint was not implemented in the previously mentioned approximations of Δf .

The fourth quantity, $\Delta f_{N_S,NN}(\mathbf{r})$, is also a descriptor associated to a response at fixed total spin, but this time of the spin density function. It is thus expected to provide information about the rearrangement of the unpaired electrons in space under a nucleophilic or electrophilic attack, but with a constant total spin.

The second and third quantities, $\Delta f_{N_S, N_S N_S}(\mathbf{r})$ and $\Delta f_{N, N_S N_S}(\mathbf{r})$, however provide information about the reorganisation of the spin-density and electron density under a change in the total spin of the molecule, at fixed total number of electrons. Said otherwise, they allow to map the reorganisation of spin and electron density of a system when it changes its spin multiplicity. They were coined "twofold spin-polarisation descriptors", and are ex-

pected to display negative values in regions where electron (for $\Delta f_{N,N_S N_S}(\mathbf{r})$) or spin (for $\Delta f_{N_S, N_S N_S}(\mathbf{r})$) density vary under a decrease in the spin multiplicity. Similarly, they should display positive values in regions where the electron or spin density vary under an increase in the spin multiplicity. Thus these quantities afford a description of the electron (or spin) density reshuffling under a change in the electronic state, as is for instance happening in singlet-triplet conversion.

2.2.7 Grand canonical ensemble derivation

Up to now, all derivations we presented were conducted within the canonical statistical ensemble, that is, electronic configuration are determined by the total number of electrons N and external potential $v(\mathbf{r})$.

Because of this choice of statistical ensemble, limited transferability is granted to Δf : one cannot compare (quantitatively) systems with different N . In order to afford complete transferability, one should thus shift to a statistical ensemble in which N is allowed to fluctuate: the grand-canonical ensemble, defined by the external potential $v(\mathbf{r})$ and the chemical potential μ (conjugate of N).

In line with equation 4, we may express the second-order response of the electron density with respect to μ :

$$\left(\frac{\partial^2 \rho(\mathbf{r})}{\partial \mu^2} \right)_{v(\mathbf{r})} = \frac{\Delta f(\mathbf{r})}{\eta^2} + \frac{\gamma}{\eta^3} f(\mathbf{r}) \quad (20)$$

with γ the canonical hyperhardness (third order response of energy to a change in N). Even though hyperhardness values are not necessarily negligible, one may expect that the ratio γ/η^3 will be quite small compared to $1/\eta^2$, and thus the second term in the previous equation is usually neglected. As a consequence, the grand-canonical equivalent of the dual descriptor can be directly approximated from the canonical function, by a simple weighting by the

square of hardness. Hence the problem of transferability can be reduced to a simple scaling of Δf .¹⁶

2.3 Real-space partitioning

As one may note, so far we only evaluated reactivity and selectivity through a local analysis of the dual descriptor (local meaning in that case "point by point in real space"). However in chemistry one often reasons in a semi-local approach, comparing the reactivity of atoms or groups of atoms.

Conciliation of both approaches can be achieved by real-space partitioning, that is, division of whole space into non-overlapping volumes and integration within these volumes. For instance, one may obtain atomic dual descriptor values by integration of Δf into atomic basins, defined for instance in a Hirshfeld or AIM partitioning method. From equation 5, if we assume the atomic basins only marginally vary under the addition or subtraction of one electron to the whole molecule, we have

$$\Delta f(A) \approx -2q_N(A) + q_{N+1}(A) + q_{N-1}(A) \quad (21)$$

for a given atom A.

But one may also consider integrating Δf into any real-space function domains, as long as these domains span \mathbb{R}^3 . This is noteworthy the case of Δf , which may then be partitioned into domains of constant sign.²¹ This affords in principle a partition into reactive domains (electrophilic versus nucleophilic). Nevertheless, examples have shown that often all nucleophilic (resp. electrophilic) basins merge into a single one, and thus very limited insight is gained. A possible solution is then to exclude regions in space exhibiting Δf values lower than a given cut-off. This indeed often allows to separate reactive regions, but at the expense of an approximation in the calculated values. In this respect, the zero integration

over all space (Equation 2) affords a certain degree of control on the approximation. Indeed, one may check how much the chosen cut-off induces a strong error by comparing the sum of the integrated values to zero.

2.4 Dual descriptor and chemical principles

Beyond its intrinsic value, the dual descriptor can also be used or retrieved in the development of other quantities of interest and principles.

2.4.1 Principle of Maximum Hardness

For instance, from Equation 3, it appears that interaction between reagents is optimal when their hardness variation is also optimum. This is rather reminiscent of the Principle of Maximum Hardness (PMH) of Pearson, Parr and Chattaraj.^{22,23} Actually, if the incoming reagent is an electrophile, one may expect $\delta v(\mathbf{r}) < 0$ (interaction with an electron-poor species). Thus in order to minimise $\Delta f(\mathbf{r})$, $\delta\eta$ must be positive: hardness is indeed increasing. Similarly, interaction with a nucleophile should result in $\delta v(\mathbf{r}) > 0$, and thus $\delta\eta > 0$ is expected if one wants to maximise $\Delta f(\mathbf{r})$. Thus it appears that optimum (local) interactions between reagents translates in a tendency of hardness to increase.

PMH can also be retrieved in the grand-canonical derivation in equation 20: high hardness values should indeed translate in low values for the grand-canonical dual descriptor, and thus low reactivity (which is expected for the end product of a spontaneous reaction in chemistry).

2.4.2 Local hardness descriptors

In the previous paragraph, we discussed the evolution of hardness along a chemical event. Hardness is a central quantity in reactivity, describing the tendency of a system to distort or not its electron density in consequence of a chemical event. Yet, this quantity is global, as it considers the system as a whole.

It then quickly appeared useful to dispose of a local counterpart of hardness, the so-called local hardness descriptor. Though local softness can be straightforwardly derived within the grand canonical ensemble (first order response of electron density to a change in the chemical potential), there is unfortunately no unique definition of local hardness, and thus the concept was heavily debated over time.

Recently, Polanco-Ramirez and co-workers proposed a general strategy to derive local quantities from global descriptors, which they applied to hardness.²⁴⁻²⁶ The central idea in this development is to use chain derivation, to rewrite global derivatives as composed functional derivatives of the electron density:

$$R = \left(\frac{\partial A}{\partial X} \right) = \int \frac{\delta A}{\delta \rho(\mathbf{r})} \left(\frac{\partial \rho(\mathbf{r})}{\partial X} \right) \delta \rho(\mathbf{r}) d\mathbf{r}. \quad (22)$$

The integrand is then considered as the local counterpart of R , $R(\mathbf{r})$. Using this rule in the case of hardness, and by identification of classical C-DFT descriptors, it can ultimately be proposed that

$$\eta(\mathbf{r}) = \mu \Delta f(\mathbf{r}) + \eta f(\mathbf{r}) \quad (23)$$

represents a local hardness descriptor. Thus Δf is not only a valid reactivity descriptor, but it also allow to partially describe local hardness (and thus to convey local information on polarisability).

2.4.3 Local electrophilicity and nucleophilicity

In 1999, Parr, Von Szentpaly and Liu have shown that, at fixed geometry, a molecular system interacting with an electron reservoir can acquire a maximum number of $\Delta N = -\mu/\eta$ electrons, and undergo in this process a stabilisation energy of $-\mu^2/2\eta$.²⁷ In 2014, it could be shown that the same quantity can also be used to characterise nucleophilicity, since in

the grand canonical ensemble, the number of electrons that a system may release when its chemical potential is raised from μ to zero, is equal to $\Delta N = \mu/\eta$.²⁸

Additionally, the maximal variations of the electron number could be used to develop local electrophilicity and nucleophilicity descriptors. Indeed, expanding the electron density variation as a Taylor series on N , one gets at second order that

$$\Delta\rho(\mathbf{r}) = \left(\frac{\partial\rho(\mathbf{r})}{\partial N}\right)_{v(\mathbf{r})} \Delta N + \frac{1}{2} \left(\frac{\partial^2\rho(\mathbf{r})}{\partial N^2}\right)_{v(\mathbf{r})} \Delta N^2. \quad (24)$$

When interacting with a perfect electron reservoir at constant geometry, a molecule will then undergo an electron density variation such that:

$$\Delta\rho_{Elec}(\mathbf{r}) = -\frac{\mu}{\eta} f(\mathbf{r}) + \frac{1}{2} \left(\frac{\mu}{\eta}\right)^2 \Delta f(\mathbf{r}) \quad (25)$$

where we have replaced the previous derivatives by their usual notations (Fukui function and dual descriptor). Similarly, interaction of the molecule with a perfect electron attractor will lead to:

$$\Delta\rho_{Nuc}(\mathbf{r}) = \frac{\mu}{\eta} f(\mathbf{r}) + \frac{1}{2} \left(\frac{\mu}{\eta}\right)^2 \Delta f(\mathbf{r}). \quad (26)$$

As expected, the dual descriptor is involved in these two expressions as a second-order philicity descriptor.

2.4.4 Local chemical potential and excited states reactivity

Finally, it has been shown in 2009 that Δf can also be used to predict reactivity in excited states, and not only in the ground state.²⁹ The principle of the demonstration is the following: let one use an excited state electron density as trial density for the DFT functional. In the general case, the first order response of energy to this density, which in the ground state is

the chemical potential, is a non constant function:

$$\left(\frac{\delta E}{\delta \rho_k(\mathbf{r})} \right)_N = \lambda_k(\mathbf{r}). \quad (27)$$

This local function translates the tendency of electron density to distort from the excited state to the ground state in order to minimise the energy.³⁰ Obviously this local chemical potential can be rewritten as the sum of the ground state (global) chemical potential and a local term

$$\lambda_k(\mathbf{r}) = \mu_0 + V_k(\mathbf{r}). \quad (28)$$

Expressing the excited state density as a distortion of the ground state density, and accordingly the response of energy to this excited state density as a modified response to the ground state density, it could then be shown that for the lowest energy excited states

$$V_k(\mathbf{r}) \approx \int \frac{\Delta f_k(\mathbf{r}')}{|\mathbf{r} - \mathbf{r}'|} d^3 \mathbf{r}' \quad (29)$$

with Δf_k the k-th state specific dual descriptor. The energy change associated to the electron density reshuffling $\delta \rho_k(\mathbf{r})$ towards the ground state configuration can then be expressed as

$$\delta E_k = \mu_0 dN + \int V_k(\mathbf{r}) \delta \rho_k(\mathbf{r}) d^3 \mathbf{r}. \quad (30)$$

At constant number of electron ($dN = 0$), excited states will be stabilised by density variations such that

$$V_k(\mathbf{r}) \delta \rho_k(\mathbf{r}) < 0. \quad (31)$$

This implies that the electron density will be decreasing in regions displaying positive values of Δf_k , and conversely the electron density will increase anywhere Δf_k is negative. Thus meanings of the sign of the state-specific dual descriptors are the opposite of the ones of the ground-state dual descriptor.

3 Illustrations

3.1 Woodward Hoffmann rules in Diels-Alder reactions

In paragraph 2.2.2, a clear link was established between Δf and the Frontier Molecular Orbital theory, through equation 6. Conclusions arising from FMO theory should thus be equally retrieved by a dual descriptor analysis.

This was nicely illustrated by a rederivation of the Woodward-Hoffmann rules.^{31,32} Let us for instance consider the classical Diels-Alder cycloaddition reaction. The HOMO and LUMO of ethylene and butadiene are schematically provided in Figure 1, and the expected shape of Δf in the FMO approximation also depicted.

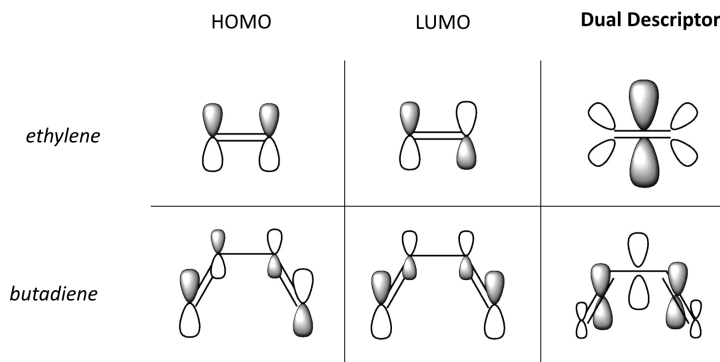


Figure 1: Schematic representation of the HOMO and LUMO of butadiene and ethylene as found in Hückel's theory, and FMO approximation of the dual descriptor.

From these schemes, it is rather plain that suprafacial attack of ethylene on itself will result in a strong repulsion if both molecules are in their ground state, since sites with similar

sign of the dual descriptors are placed in repulsive interaction.

Conversely, reaction of butadiene and ethylene, here also in their ground state, gives rise to overlap between dual descriptor domains with opposite sign, and should thus lead to a certain stabilisation and make the [2+4] addition possible.

Using comparable arguments, it is then possible to show for all other polyenes that [n+m] suprafacial/suprafacial Diels-Alder reactions are thermally possible when n+m equals $4k+2$ ($k \in \mathbb{N}$), in line with Woodward and Hoffmann's rule.

But furthermore, since we observed in paragraph 2.4.4 that the meaning of the sign of Δf is reversed in the excited states, the selectivity rule under photochemical conditions can also be retrieved. For instance, reaction of two ethylene molecules, one in its first excited state and the second in the ground state, leads in that case to a stabilising interaction in the case of a suprafacial/suprafacial attack. Extending this argument to other polyenes, one eventually retrieves Woodward and Hoffmann's rule: photochemical Diels-Alder reactions are possible if n+m equals $4k$.

3.2 Perturbational MO Theory and Dual descriptor

The dual descriptor is an interesting tool to explain the difference in reactivity between ethene and formaldehyde. It should be noted that the formaldehyde double bond reacts easily with nucleophiles whereas ethene does not.

This difference in reactivity can be explained by a detailed study of the dual descriptor shape. Indeed, in the case of ethylene, because of the molecular symmetry the two carbon atoms bear equivalent Δf contributions, with a marked nucleophilicity in the middle of the C=C double bond, while electrophilic areas are equally splitted at the molecule end sites. This is plain when deriving Δf in the frozen orbital scheme, as shown on Figure 2. Thus interaction with an electrophile is "geometrically" favored. On the other hand, in the case of formaldehyde a strong asymmetry is expected in Δf . Once again, this is plain when deriving

the dual descriptor from the frontier orbitals densities, as shown on Figure 2. Electrophilic sites should indeed roughly correspond to the regions in which the LUMO develops most, and thus principally concentrate on the C atom. Because of the anti-bonding character of this orbital, one can furthermore state that the electrophilic basin on C will be pushed away from the C=O bond. Thus maximal interaction with a nucleophile is expected when the attack is performed at a nucleophile-C-O angle larger than 90° . Δf thus allows to retrieve the long known Dunitz-Burgi angle of attack of nucleophiles on carbonyls.³³

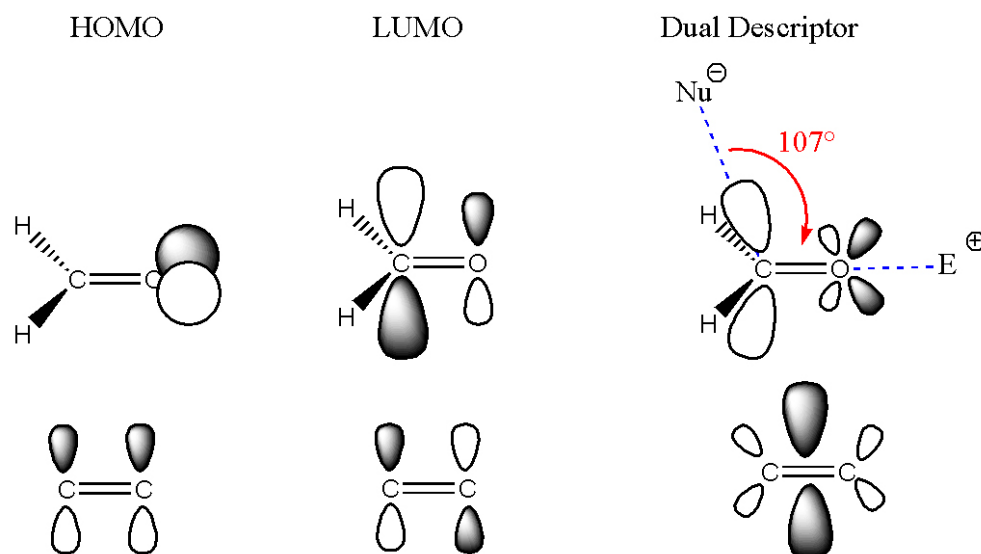


Figure 2: Schematic representation of the HOMO and LUMO of formaldehyde and ethylene and their dual descriptor with the grey lobes are negative region and white lobes are positive region.

3.3 Markovnikov rule

The regio- and stereoselectivity of the electrophilic additions to asymmetric alkenes are described following the well-known Markovnikov rule.³⁴ Therefore, the acidic proton addition to a double bond proceeds on the least substituted carbon atom. This rule is generalized for all addition reaction to alkenes. Thus, the most stable carbocation adduct is the most favorable electrophile addition product. Regioselectivity explanation based on the Frontier

MOs is not simple. Starting from the MO diagram of ethylene, one would indeed expect that substitution at a C atom by an electron-donating group will end up in a distortion of the HOMO, the unsubstituted C now bearing the largest contribution and thus displaying the largest nucleophilicity. Yet, this distortion appears more than slight when calculating the MO diagram using classical methods (such as DFT) ; it is actually plain only within Hückel's theory. As a matter of fact, computed HOMOs and LUMOs (or equivalently Fukui functions) often suggest both C atoms of the double C=C bond may undergo electrophilic or nucleophilic attack.

However, the dual descriptor successfully translates the expected selectivity, as asymmetric dual lobes are observed. The substituted carbon atom indeed bears a pronounced electrophilic character, whereas the unsubstituted carbon is an electrophile.

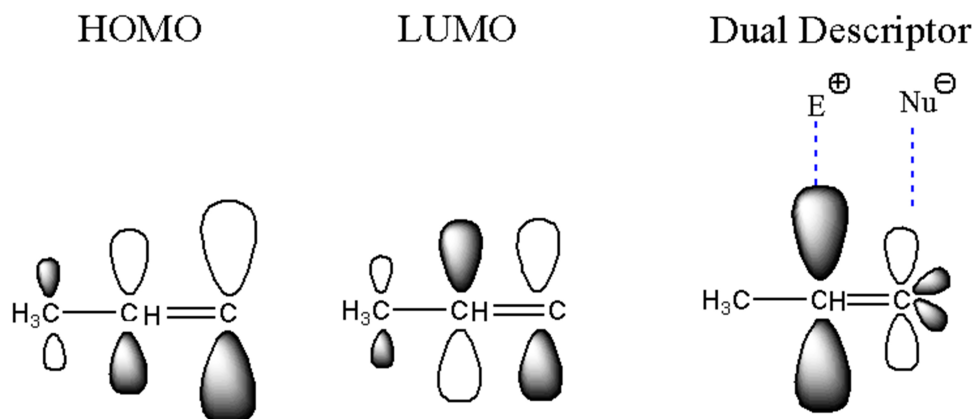


Figure 3: Schematic representation of Markovnikov description with dual descriptor, with the grey lobes are negative region and white lobes are positive region.

The fact that the dual descriptor is successful when both Fukui functions or MOs are not can furthermore be simply accounted for. Indeed, while the asymmetry in the MOs is too slight to be noticed, even on the corresponding MO electron densities (which are approximations of the Fukui functions), by the subtraction in Equation 1 one can expect trends to be amplified. For instance, on the substituted C atom, f^+ will be slightly larger

than on the other C, while at the same time f^- will be smaller, and thus Δf will be more positive. Conversely, on the unsubstituted C atom, Δf is expected to be more negative.

Overall, one retrieves the expected tendency: proton addition on the least substituted C (more nucleophilic), and electrophilic addition on the most substituted C.

4 Conclusions

In this chapter the last fifteen years of development about the so-called dual descriptor are presented. The review starts with the very first definition of the concept and its relations with early theories or concepts such as frontier molecular orbital or chemical hardness. Then, more recent developments pertaining the dual descriptor are shown. Of particular interest, how molecular orbital degeneracy is tackled either through weighted combination of molecular orbital around the Fermi level or using electronic excited states densities. Definitions of dual descriptor counterparts within the grand canonical ensemble or spin polarized description are also recalled. Finally prototypical examples of chemical reactivity and selectivity rationalization are proposed in both ground and excited states. Alternative explanation of chemical rules are put forward using the dual descriptor as principal ingredient. Through this bird's-eye-view, it is plain to see that the dual descriptor is a quite powerful index for understanding chemical reactivity and selectivity. Overtime it might replace with efficiency previous descriptors.

References

- (1) Klopman, G. Chemical Reactivity and the Concept of Charge and Frontier-Controlled reactions. *Journal of American Chemical Society* **1968**, *90*, 223–234.

- (2) Salem, L. Intermolecular Orbital Theory of the Interaction between Conjugated Systems. I. General Theory. *Journal of American Chemical Society* **1968**, *90*, 543–552.
- (3) Geerlings, P.; De Proft, F.; Langenaeker, W. Conceptual Density Functional Theory. *Chem. Rev.* **2003**, *103*, 1793–1874.
- (4) Chermette, H. Chemical reactivity indexes in density functional theory. *Journal of Computational Chemistry* **1999**, *20*, 129–154.
- (5) Parr, R. G.; Yang, W. *Density-Functional Theory of Atoms and Molecules*; International Series of Monographs on Chemistry; Oxford University Press, 1994.
- (6) Gazquez, J.-L. Perspectives on Density Functional Theory of Chemical Reactivity. *J. Mex. Chem. Soc.* **2008**, *52*, 3–10.
- (7) Liu, S.-B. Conceptual Density Functional Theory and Some Recent Developments. *ACTA PHYSICO-CHIMICA SINICA* **2009**, *25*, 590–600.
- (8) Geerlings, P.; Chamorro, E.; Chattaraj, P. K.; De Proft, F.; Gazquez, J.-L.; Liu, S.-B.; Morell, C.; Toro-Labbé, A.; Vela, A.; Ayers, P. W. Conceptual density functional theory: status, prospects, issues. *Theo. Chem. Acc.* **2020**, *193*, 8240–8247.
- (9) Hohenberg, P.; Kohn, W. Inhomogeneous Electron Gas. *Phys. Rev.* **1964**, *136*, 864–871.
- (10) Morell, C.; Grand, A.; Toro-Labbé, A. New Dual Descriptor for Chemical Reactivity. *The Journal of Physical Chemistry A* **2005**, *109*, 205–212, PMID: 16839107.
- (11) Yang, W.; Parr, R. G.; Pucci, R. Electron density, Kohn–Sham frontier orbitals, and Fukui functions. *Journal of Chemical Physics* **1984**, *181*, 2862.
- (12) Fukui, K. Role of Frontier Orbitals in Chemical Reactions. *Science* **1982**, *218*, 747–754.

- (13) Fukui, K.; Fujimoto, H. An MO-theoretical Interpretation of the Nature of the Chemical Reaction. I. Partitioning Analysis of the Interaction Energy. *Bulletin of the Chemical Society of Japan* **1968**, *41*, 1989–1987.
- (14) Tognetti, V.; Morell, C.; Ayers, P. W.; Joubert, L.; Chermette, H. A proposal for an extended dual descriptor: a possible solution when Frontier Molecular Orbital Theory fails. *Phys. Chem. Chem. Phys.* **2013**, *15*, 14465–14475.
- (15) Pearson, R. G. Electronic spectra and chemical reactivity. *J. Am. Chem. Soc.* **1988**, *110*, 2092–2097.
- (16) Guégan, F.; Tognetti, V.; Joubert, L.; Chermette, H.; Luneau, D.; Morell, C. Towards the first theoretical scale of the trans effect in octahedral complexes. *Phys. Chem. Chem. Phys.* **2016**, *18*, 982–990.
- (17) Martínez-Araya, J. I. A generalized operational formula based on total electronic densities to obtain 3D pictures of the dual descriptor to reveal nucleophilic and electrophilic sites accurately on closed-shell molecules. *Journal of Computational Chemistry* **2016**, *37*, 2279–2303.
- (18) Pino-Rios, R.; Inostroza, D.; Cárdenas-Jirón, G.; Tiznado, W. Orbital-Weighted Dual Descriptor for the Study of Local Reactivity of Systems with (Quasi-) Degenerate States. *The Journal of Physical Chemistry A* **2019**, *123*, 10556–10562, PMID: 31710492.
- (19) Perez, P.; Chamorro, E.; Ayers, P. W. Universal mathematical identities in density functional theory: Results from three different spin-resolved representations. *J. Chem. Phys.* **2008**, *128*, 204108–1–204108–21.
- (20) Chamorro, E.; Pérez, P.; Duque, M.; De Proft, F.; Geerlings, P. Dual descriptors within the framework of spin-polarized density functional theory. *The Journal of Chemical Physics* **2008**, *129*, 064117.

- (21) Tognetti, V.; Morell, C.; Joubert, L. Quantifying electro/nucleophilicity by partitioning the dual descriptor. *Journal of Computational Chemistry* **2015**, *36*, 649–659.
- (22) Pearson, R. G. The principle of maximum hardness. *Accounts of Chemical Research* **1993**, *26*, 250–255.
- (23) Parr, R. G.; Chattaraj, P. K. Principle of maximum hardness. *Journal of the American Chemical Society* **1991**, *113*, 1854–1855.
- (24) Polanco-Ramírez, C. A.; Franco-Pérez, M.; Carmona-Espíndola, J.; Gázquez, J. L.; Ayers, P. W. Revisiting the definition of local hardness and hardness kernel. *Phys. Chem. Chem. Phys.* **2017**, *19*, 12355–12364.
- (25) Guégan, F.; Lamine, W.; Chermette, H.; Morell, C. Comment on “Revisiting the definition of local hardness and hardness kernel” by C. A. Polanco-Ramirez, M. Franco-Pérez, J. Carmona-Espíndola, J. L. Gázquez and P. W. Ayers, *Phys. Chem. Chem. Phys.*, 2017, *19*, 12355. *Phys. Chem. Chem. Phys.* **2018**, *20*, 9006–9010.
- (26) Franco-Pérez, M.; Polanco-Ramírez, C. A.; Gázquez, J. L.; Ayers, P. W. Reply to the ‘Comment on “Revisiting the definition of local hardness and hardness kernel”’ by C. Morell, F. Guégan, W. Lamine, and H. Chermette, *Phys. Chem. Chem. Phys.*, 2018, *20*, DOI: 10.1039/C7CP04100D. *Phys. Chem. Chem. Phys.* **2018**, *20*, 9011–9014.
- (27) Parr, R. G.; Szentpály, L. v.; Liu, S. Electrophilicity Index. *Journal of the American Chemical Society* **1999**, *121*, 1922–1924.
- (28) Morell, C.; Gázquez, J. L.; Vela, A.; Guégan, F.; Chermette, H. Revisiting electroaccepting and electrodonating powers: proposals for local electrophilicity and local nucleophilicity descriptors. *Phys. Chem. Chem. Phys.* **2014**, *16*, 26832–26842.

- (29) Morell, C.; Labet, V.; Grand, A.; Ayers, P. W.; De Proft, F.; Geerlings, P.; Chermette, H. Characterization of the Chemical Behavior of the Low Excited States through a Local Chemical Potential. *Journal of Chemical Theory and Computation* **2009**, *5*, 2274–2283.
- (30) Morell, C.; Ayers, P. W.; Grand, A.; Chermette, H. Application of Electron Density Force to Chemical Reactivity. *Phys. Chem. Chem. Phys* **2011**, *13*, 9601–9608.
- (31) Ayers, P. W.; Morell, C.; De Proft, F.; Geerlings, P. Understanding the Woodward-Hoffmann rules by using changes in electron density. *Chem. Eur. J.* **2007**, *13*, 8240–8247.
- (32) Geerlings, P.; Ayers, P. W.; Toro-Labbé, A.; Chattaraj, P. K.; De Proft, F. The Woodward-Hoffmann Rules Reinterpreted by Conceptual Density Functional Theory. *Eur. Chem. J.* **2007**, *13*, 8240–8247.
- (33) Bürgi, H. B.; Dunitz, J. D.; Lehn, J.-M.; Wipff, G. *Tetrahedron* **1974**, *30*, 1563–1572.
- (34) Markownikoff, W. I. Ueber die Abhängigkeit der verschiedenen Vertretbarkeit des Radicalwasserstoffs in den isomeren Buttersäuren. *Justus Liebigs Annalen der Chemie* **1870**, *153*, 228–259.