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REGULAR ARTICLE

# Phenomenological chemical reactivity theory for mobile electrons

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**Abstract** We present herein a model to deal with the chemical reactivity, selectivity and site activation concepts of $\pi$ electron systems derived by merging the classical Coulson–Longuet-Higgins response function theory based on the Hückel molecular orbital (HMO) theory and the conceptual density functional theory. HMO-like expressions for the electronic chemical potential, chemical hardness and softness, including their local counterparts, atomic and bond Fukui functions and non-local response functions are derived. It is shown that sophisticated non-local concepts as site activation may be cast into deeper physical grounds by introducing a simplified version of static response functions. In this way, useful quantities such as self and mutual polarizabilities originally defined through the HMO parameters can be redefined as self and mutual softnesses. The model is illustrated by discussing the classical Hammett free energy relationship describing inductive substituent effects on the reactivity of benzoic acids.

**Keywords** Self and mutual softnesses · Semi-empirical response functions · Phenomenological reactivity theory

## 1 Introduction

The treatment of chemical reactivity has been performed with the aid of electronic structure descriptors from the dawn of theoretical chemistry. Starting from early quantum molecular models such as the Hückel molecular orbital (HMO) theory [1] or the valence bond (VB) approximation [2–4], this approach finds a current example in the conceptual density functional theory (DFT) developed by Parr and Yang [5–7]. In the pioneering paper *On quantum mechanical contribution to the benzene problem* [1], Erich Hückel formulated a model framed on the description of the chemical bond for planar hydrocarbons with a further extension to incorporate heteroatoms. This model, yet very simple, provided an excellent qualitative approach to chemical reactivity. It is, however, worth emphasizing at this point that the HMO theory, as conceived by E. Hückel, was not a methodology to solve the Schrödinger equation, but a simple theory of the chemical bond. HMO can be considered as a double bond theory designed to describe bonding properties in unsaturated planar carbon containing compounds in terms of few aspects of the system, which are often the essential ones. A nice survey about the true philosophy contained in the HMO approach to the bonding and reactivity problems in $\pi$ electron systems is the recent essay written by Werner Kutzelnigg [8].

Towards the end of the 1940s, Coulson and Longuet-Higgins [9–13] extended the HMO model in the frame of a perturbed HMO framework. In a series of five papers on the electronic structure of conjugated systems, these

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authors developed, without making reference to Hückel's fundamental work, the MO–LCAO model using perturbation theory. In their approach the electron density and the bond order appear for the first time as first-order derivatives of the total energy of conjugated systems with respect to Hückel's parameters α (coulomb integral) and β (resonance integral), respectively. Also a set of local and non-local response functions, called polarizabilities, is obtained as second derivatives of the total energy with respect to the parameters α and β, respectively. In this way, the HMO model was reformulated in an elegant format that proved to be very attractive to the chemistry and even to the physics communities. Gosh and Parr, in a later paper [14], proposed a semi-empirical density functional approach to the theory of molecular structure and bonding. Therein, some ideas involving bond electronegativity and bond hardness were introduced and discussed.

Sophisticated non-local concepts as site activation, on the other hand, may be cast into deeper physical grounds by introducing a simplified version of static response functions. For instance, if chemical reactivity is regarded as global responses to a local external perturbation (consider for instance the change in electronic chemical potential or chemical hardness induced by chemical substitution) or non-local responses to local external stimuli (i.e., site activation induced for instance by intramolecular rearrangements or the orientation of chemical reactivity induced by chemical substitution), then chemical interconversion may adequately be described with the aid of static response functions [15–18]. These quantities are well defined in the conceptual DFT of Parr and Yang [5]. However, the analytical interactability of the hardness kernel is a severe limitation for the development of models of chemical reactivity including (regio) selectivity and site activation based on non-local response functions [19, 20]. On the other hand, HMO theory provides simple conceptual tools to deal with response functions, as the ones introduced by Coulson and Longuet-Higgins, namely, atom and bond polarizabilities. These quantities when gathered around a rigorous theory of structure and bonding may provide important clues to board more elaborated concepts in chemistry. In this work, we present a model to deal with chemical reactivity, selectivity and site activation for systems that can appropriately be described within the HMO theory, in terms of the modern concepts of response functions defined in the conceptual DFT.

## 2 Basic HMO and DFT equations

In the HMO, the energy of a conjugated system is given by [9, 21]

$$E = \sum_r q_r \alpha_r + 2\sum_{r<}\sum_s p_{rs}\beta_{rs}, \tag{1}$$

where $\alpha_r$ is the one center Coulomb integral, $\beta_{rs}$ is the two center resonance integral, $q_r$ is the net atomic charge on center $r$ in the molecule and $p_{rs}$ is the bond order between the bonded atoms $r$ and $s$. The set of energy levels and molecular orbitals (MO) are found after solving the secular equation (2)

$$\sum_r c_{j\mu}\left(h^{\mathrm{eff}}_{\mu\nu} - \delta_{\mu\nu}\varepsilon_j\right) = 0, \tag{2}$$

where $c_{j\mu}$ are the coefficients of the atomic center $\mu$ in the $j$th MO, $h^{\mathrm{eff}}_{\mu\mu}$ are the Coulomb integrals α, defined by $h^{\mathrm{eff}}_{\mu\mu} = \langle\varphi_\mu|h^{\mathrm{eff}}_j|\varphi_\mu\rangle$ and $hs^{\mathrm{eff}}_{\mu\nu}$ are the resonance integrals, defined by $h^{\mathrm{eff}}_{\mu\nu} = \langle\varphi_\mu|h^{\mathrm{eff}}_j|\varphi_\nu\rangle = \beta_{\mu\nu}$, if the centers $\mu$ and $\nu$ are bonded, or $h^{\mathrm{eff}}_{\mu\nu} = \langle\varphi_\mu|h^{\mathrm{eff}}_j|\varphi_\nu\rangle = 0$, if the centers $\mu$ and $\nu$ are not bonded. $\varepsilon_j$ is the one electron energy of the $j$th MO. These constrains lead to the introduction of the adjacency and identity matrixes, **A** and **I**, respectively, as follows:

$$(\alpha - \varepsilon)\boldsymbol{I} + \beta\boldsymbol{A} = 0. \tag{3}$$

Thus, if Eq. 3 is divided by $\beta$, the problem of finding the energy levels referred to α is reduced to calculate directly the eigenvalues $x_i = (\alpha - \varepsilon_j)/\beta$ of the adjacency matrix to the molecular system [22].

On the other hand, within the DFT of Parr and Yang [5], the ground state energy of an atomic or molecular system is a function of the number of electrons $N$ and a functional of the external potential $v(\boldsymbol{r})$ due to the compensating nuclear charges in the system: $E = E[N, v(\boldsymbol{r})]$.

The first-order variation of the ground state energy

$$\mathrm{d}E = \mu \mathrm{d}N + \int \mathrm{d}\boldsymbol{r}\rho(\boldsymbol{r})\delta v(\boldsymbol{r}) \tag{4}$$

introduces the electronic potential $\mu$ of the system:

$$\mu = \left[\frac{\partial E}{\partial N}\right]_{v(\boldsymbol{r})}, \tag{5}$$

subject to the condition,

$$\left[\frac{\delta E}{\delta v(\boldsymbol{r})}\right]_N = \rho(\boldsymbol{r}), \tag{6}$$

$\rho(\boldsymbol{r})$ is the ground state electron density of the system. A second variation in the ground state energy (or a first variation in the electronic chemical potential) yields:

$$\mathrm{d}\mu = \eta \mathrm{d}N + \int \mathrm{d}\boldsymbol{r} f(\boldsymbol{r})\delta v(\boldsymbol{r}), \tag{7}$$

thereby introducing the global hardness $\eta = \left[\frac{\partial^2 E}{\partial N^2}\right]_{v(\boldsymbol{r})}$ and its inverse, the chemical softness $S = 1/\eta$.

Within the second-order energy variation described in Eq. 7, the Fukui function (FF) is introduced:

$$f(\boldsymbol{r}) = \left[\frac{\delta\mu}{\delta v(\boldsymbol{r})}\right]_N = \left[\frac{\partial\rho(\boldsymbol{r})}{\partial N}\right]_{v(\boldsymbol{r})}. \tag{8}$$

The FF plays a key role in the DFT of chemical reactivity because, apart from being a local reactivity index by itself, it is generally used to project global properties onto atoms or fragments within a molecule. A recent study on proton transport catalysis emphasizes this property well [23]. Other applications of the FF as a distribution function have been reviewed [24, 25].

Another pertinent non-local quantity is the static density response function:

$$\chi(\boldsymbol{r},\boldsymbol{r}') = \left[\frac{\delta\rho(\boldsymbol{r})}{\delta v(\boldsymbol{r}')}\right]_N \tag{9}$$

obeying the condition

$$\int \mathrm{d}\boldsymbol{r}\chi(\boldsymbol{r},\boldsymbol{r}') = 0. \tag{10}$$

Physically, the quantity $\chi(\boldsymbol{r},\boldsymbol{r}')$ represents the change of the electron density at any point $\mathbf{r}$ in space produced by the variation of a spin independent external perturbation at a different point $\mathbf{r}'$, and therefore it can be considered as a suitable reactivity index to describe site activation in chemistry. The relevance of the static density response function as a non-local reactivity index has already been shown to correctly account for site activation promoted by chemical substitution [26, 27], preferential solvent effects [28] and recently in enzymatic catalysis [29].

## 3 The model

The link between the HMO and DFT involving the static response functions is the main object of the present work because it embodies the whole set of global and local reactivity descriptors in both formalisms. The key quantities here are the static electron density response function of DFT, and the self and mutual polarizabilities defined in the context of Coulson–Longuet-Higgins (CLH) theory of reactivity for mobile electrons. The link between both theories is however not immediate due to the lack of a physical meaningful representation of the self polarization quantity in the static density response function defined in Eq. 9. In fact, if we write the explicit form of the static density response function, namely [30]

$$\chi(\boldsymbol{r},\boldsymbol{r}') = \left[\frac{\delta\rho(\boldsymbol{r})}{\delta v(\boldsymbol{r}')}\right]_N = -s(\boldsymbol{r},\boldsymbol{r}') + \frac{s(\boldsymbol{r})s(\boldsymbol{r}')}{S}. \tag{11}$$

The meaning of $\chi(\boldsymbol{r},\boldsymbol{r}')$ for the case $\mathbf{r} = \mathbf{r}'$ is not obvious. Note that this case would correspond to a situation where the response is being probed at the same point in space where the external local perturbation is being applied. The isomorphism between the meaning of the external potential in DFT and the HMO parameters is not obvious either. However, progress can be made if we reason in the opposite direction, namely, from the HMO perturbation theory towards the reactivity, selectivity and site activation concepts defined in the conceptual DFT. The starting point is the definition of the self and mutual polarizabilities given by Coulson and Longuet-Higgin [9]. These quantities appear as charge derivatives with respect to $\alpha$ and $\beta$ HMO parameters. Thus, changes in the charge distribution in a $\pi$ electron system due to a perturbation $\delta\alpha$ of $\alpha$ at site $s$ can be described with the aid of atom–atom polarizabilities defined by [9]

$$\pi_{rs} = \frac{\partial q_r}{\partial \alpha_s}. \tag{12}$$

Even though this quantity is condensed to atoms $r$ and $s$ one, its non-local (or semi-local) nature is immediate: it measures the change in the electron population at atom $r$ when the Coulomb integral, representing the valence electronegativity of atom $s$ is varied. As stated before, an isomorphism between the external potential appearing in the definition of the static density response defined in Eq. 9 and the atomic valence electronegativity cannot a priori be established. However, we may simplify the problem if we use the chain rule in Eq. 12 and write:

$$\pi_{rs} = \frac{\partial q_r}{\partial \alpha_s} = \frac{\partial q_r \partial N}{\partial N \partial \alpha_s} = f_r \frac{\partial N}{\partial \alpha_s}, \tag{13}$$

where $f_r$ is the FF condensed to atom $r$. In the process of review of the manuscript a referee call our attention stating that the change rule applied in Eq. 13 was incomplete because the contribution of changes in external potential was lacking. These contributions are related to molecular structure changes. Geometry changes cannot be assessed within HMO theory, and this limitation must be considered. However the effect on the calculated $\pi_{rs}$ for molecules bearing the same number of $\pi$ electrons but differing in the type of atoms (heteroatoms) is taken into account by the $\alpha_s$ and $\beta_{rs}$ HMO parameters and therefore they will display different values of $\pi_{rs}$.

Having in mind that the Coulomb integral represents atomic valence electronegativity $\chi_s$ [14], we can further write:

$$\frac{\partial N}{\partial \alpha_s} = \frac{\partial q_r}{\partial \chi_s} = -\frac{\partial N}{\partial \mu_s} = -\eta_s^{-1}, \tag{14}$$

where the relationship $\chi_s = -\mu_s$ has been used. $\mu_s$ and $\eta_s$ have been defined as the valence atom electronic chemical potential and the atomic hardness in the semi-empirical

DFT of Parr and Ghosh [14]. Substitution of Eq. (14) into Eq. (13) yields:

$$\pi_{rs} = -f_r \eta_s^{-1}. \tag{15}$$

A more useful form for this equation can be obtained using the inverse relationship between the condensed to atom regional softness and hardness given by Contreras et al. [31]. These authors showed that for a model external potential, the regional softness and hardness are at least inversely proportional to each other

$$s_s \eta_s \cong \frac{\Delta N_s}{\Delta N}, \tag{16}$$

with the normalization condition $\sum_s s_s \eta_s = 1$, which is the discrete form of inverse relationship $\int s(\boldsymbol{r})\eta(\boldsymbol{r})d\boldsymbol{r} = 1$. Having this result in mind, and replacing $N_r$ by $q_r$ in HMO theory, it follows that

$$s_s \eta_s \cong \frac{\Delta N_s}{\Delta N} = \frac{\Delta q_s}{\Delta N} \approx f_s. \tag{17}$$

A result suggesting that within the HMO framework, the condensed to atom hardness and softness are related by

$$\eta_s^{-1} = \frac{1}{f_s} s_s \tag{18}$$

Substitution of Eq. 18 into Eq. 15 yields the desired result, namely:

$$\pi_{rs} = -f_r \frac{s_s}{f_s} = -f_r S'; \quad r \neq s, \tag{19}$$

where

$$S' = \sum_{s \neq r}^{n} s_s. \tag{20}$$

Note that the quantity $\pi_{rs}$ embodies the interaction of site $r$ with the remaining $n-1$ atomic center in the $\pi$ conjugated system in a form which is consistent with the second-order perturbation theory expression of the static dipole polarizability. Equation 20 also shows that the HMO response function represented by the self and mutual polarizabilities appears connected to a non-correlated model response function having the simple form $h(\boldsymbol{r},\boldsymbol{r}') = k(\boldsymbol{r})g(\boldsymbol{r}')$ instead of the explicit static density response function $\chi(\boldsymbol{r},\boldsymbol{r}')$ defined in Eq. 11. The charm of the empirical expression (19) is that it opens the possibility of defining an atomic self-polarizability with a nice physical meaning. For instance, if we put $r = s$ in Eq. 19 we immediately get:

$$\pi_{rr} = -f_r \frac{s_r}{f_r} = -s_r, \tag{21}$$

that corresponds to the diagonal elements of an atom–atom polarizability matrix $\boldsymbol{\Pi}$, describing the regional valence softness of atom $r$ in the molecule. Moreover, taking the trace of the matrix $\boldsymbol{\Pi}$, we immediately obtain an additional useful result, namely

$$Tr\boldsymbol{\Pi} = \sum_r \pi_{rr} = -\sum_r s_r = -S, \tag{22}$$

a result suggesting that the sum of the diagonal elements of the atom–atom self and mutual polarizability matrices $\boldsymbol{\Pi}$ yields directly the global softness of the $\pi$ electron system. Note that both the atomic and global softness are semi-positive definite quantities because they are given in $\beta^{-1}$ units within the HMO theory ($\beta < 0$). The HMO softness additivity rule expressed in Eq. 22 has interesting implications such as allowing the definition of group or fragment softness of functional groups in $\pi$-conjugated systems.

An additional pertinent remark is worth making. The atomic FF, apart from being a reactivity (selectivity) index by itself, has often been used in DFT as a suitable quantity to project global properties onto atoms or fragments in a molecule. If we use the results obtained up to now, we may further write:

$$f_r = \frac{s_r}{S} = \frac{\pi_{rr}}{Tr\boldsymbol{\Pi}} = \frac{\pi_{rr}}{\sum_r \pi_{rr}}, \tag{23}$$

which shows that within the Coulson–Longuett-Higgins theory, the condensed to atom FF (a) is a positive definite quantity [32, 33] and (b) it has the form of a distribution function, and therefore it is a suitable quantity to project global properties onto atoms or fragments within a conjugated $\pi$ system.

A final consideration that closes the comparison between the static density response function of DFT, and the self and mutual polarizabilities within the Coulson–Longuet-Higgins theory is related to the sum rule:

$$\sum_r \pi_{rs} = \pi_{rr} + \sum_{s\,>\,r} \pi_{rs} = 0, \tag{24}$$

which is the HMO counterpart of the sum rule of the static density response function $\int d\boldsymbol{r}\chi(\boldsymbol{r},\boldsymbol{r}') = 0$ described in Eq. 10. The corresponding model *static polarizability response function* associated with the $N \times N\boldsymbol{\Pi}$ matrix in the HMO that fulfills condition (24) is then given by:

$$\boldsymbol{\Pi}(r,s) = \sum_s \pi_{rs}\delta_{rs} + \frac{s_s}{f_s} f_r, \tag{25}$$

where $\delta_{rs} = 0$ for $r \neq s$ and $\delta_{rs} = 1$ for $r = s$. Expression 25, when summed over the atomic centers $r$ does yield the sum rule (24). This empirical static density response function, as expected, is not related to the exact function $\chi(\boldsymbol{r},\boldsymbol{r}')$ given in Eq. 11. One of the reasons for this may be related to the fact that the HMO quantities are directly expressed in terms of condensed to atom and condensed to bond quantities, and therefore they are one integration step ahead. There is however the possibility of relating the *static polarizability response function* associated with the

$\mathbf{\Pi}$ matrix in the HMO with an empirical static response function in DFT that may incorporate a local component related to the self polarizability contribution. A good candidate that fulfills this condition is the locally approximated static density response function proposed by Vela and Gázquez [34]:

$$\begin{aligned}\chi(\mathbf{r},\mathbf{r}') &= \left[\frac{\delta\rho(\mathbf{r})}{\delta v(\mathbf{r}')}\right]_N \\ \chi(\mathbf{r},\mathbf{r}') &= -Sf(\mathbf{r})\delta(\mathbf{r}-\mathbf{r}') + Sf(\mathbf{r})f(\mathbf{r}'),\end{aligned} \tag{26}$$

which leads to the following expression for the induced electron density $\delta\rho(\mathbf{r})$:

$$\delta\rho(\mathbf{r}) = Sf(\mathbf{r})\left[\int \mathrm{d}\mathbf{r}' f(\mathbf{r}')\delta v(\mathbf{r}') + \delta v(\mathbf{r}')\right]. \tag{27}$$

It may be seen now that the electronic polarization bears a non-local component given by the first term of Eq. 27, and a local contribution given by the second term, namely, $-Sf(\mathbf{r})\delta v(\mathbf{r}) = -s(\mathbf{r})\delta v(\mathbf{r})$ that determines the change in electron density at point **r** when the external potential is changed at the same point in space. This is exactly the part of the static density response function which is related to the self-atom polarizability in the Coulson–Longuet-Higgins theory of mobile electrons. Note further that the locally approximated static density response function given in Eq. 27 directly yields:

$$\left[\frac{\delta\rho(\mathbf{r})}{\delta v(\mathbf{r})}\right]_N = -s(\mathbf{r}), \tag{28}$$

which consistently compares with the local term of the static polarizability response function $\pi_{rr} = -s_r$, associated with the $\mathbf{\Pi}$ polarizability matrix of the CLH theory given by Eq. 21.

Using Eqs. 12 and 27, the following expression for the electronic polarization at site $r$ of the $\pi$ conjugated system may be obtained:

$$\Delta q_r^L = \pi_{rr}\Delta\alpha_s = s_r\Delta\mu_s \tag{29}$$

and

$$\begin{aligned}\Delta q_r^{\mathrm{NL}} &= \sum_{r\neq s}\pi_{rs}\Delta\alpha_s \\ \Delta q_r^{NL} &= -\sum_{r\neq s}\frac{f_r s_s}{f_s}\Delta\alpha_s = S\sum_{r\neq s} f_r\Delta\mu_s,\end{aligned} \tag{30}$$

in terms of a local contribution given by Eq. 29 and a non-local one given by Eq. 30. Note the similarity of Eqs. 29 and 30 to their DFT counterparts given in Eq. 27.

In summary, within the Coulson–Longuet-Higgins reactivity theory, the static response function is represented by the self and mutual atom–atom polarizability matrix, whose diagonal elements $\pi_{rr}$ are the condensed to atom regional softness and whose trace is the global softness of the $\pi$ electron system. Moreover, the self and mutual atom–atom polarizability matrices has an associated model static density response function that may be related to a locally approximated static density response within the DFT framework. This result permits the definition of the self atom polarizability, in terms of the valence state atomic softness.

The bond FFs is also useful to define further polarizability quantities that involve an atomic center and a bond. For instance, in the context of the CLH theory, there are two additional non-local response functions. One of them is the bond–atom polarizability defined by Coulson and Longuet-Higgins [9]

$$\pi_{rs,t} = \frac{\partial p_{rs}}{\partial \mu_t}, \tag{31}$$

the other one is the atom–bond polarizability $\pi_{t,rs}$ defined by

$$\pi_{t,rs} = \frac{\partial q_r}{\partial \beta_{rs}}, \tag{32}$$

both response functions are related by

$$\pi_{t,rs} = 2\pi_{rs,t} \tag{33}$$

and satisfying the sum rule:

$$\sum_t \pi_{rs,t} = 0. \tag{34}$$

Following a procedure similar to that leading to the atom–atom self and mutual softnesses $\pi_{rr}$ and $\pi_{rs}$ we may use the chain rule in Eq. 31 to write:

$$\pi_{rs,t} = \frac{\partial p_{rs}}{\partial \alpha_t} = \frac{\partial p_{rs}\partial N}{\partial N\,\partial \alpha_t} = f_{rs}\frac{\partial N}{\partial \alpha_t}. \tag{35}$$

This quantity also has the dimension of softness. Note, however, that this time it is associated with the bond FF and the softness of the site where the perturbation is being applied. Using Eq. 14, we may write, for the bond–atom polarizability:

$$\pi_{rs,t} = -f_{rs}\eta_t^{-1}. \tag{36}$$

Using the empirical inverse relationship for the condensed to atom softness and hardness given in Eq. 18 for center $t$, we may further write:

$$\pi_{rs,t} = -f_{rs}\frac{s_t}{f_t} = f_{rs}\frac{\pi_{tt}}{f_t}, \tag{37}$$

this equation cast the bond–atom polarizability in terms of the bond FF involving the atom $r$ and $s$, the self polarizability of atom $t$ and the FF condensed to atom $t$. Following the same procedure to derive an expression for $\pi_{rs,t}$ it is possible to find an expression for $\pi_{t,rs}$, in terms of the FF and the bond hardness, $\eta_{rs}$. There results:

$$\pi_{t,rs} = -f_t \eta_{rs}^{-1}, \tag{38}$$

The quantity $\pi_{t,rs}$ in Eq. 38 also represents softness. Furthermore $\eta_{rs}$ may be defined as $\eta_{rs} = \frac{\partial \mu_{rs}}{\partial N}$, where $\mu_{rs}$ is the bond chemical potential that corresponds to the negative of the resonance integral $\beta_{rs}$ [13]. The inverse of the bond hardness $\eta_{rs}$ can be considered as a measure of the bond softness between atoms $r$ and $s$.

By replacing Eq. 33 into Eq. 38, we may further relate the bond–atom polarizability with the bond hardness as follows:

$$\pi_{t,rs} = -\frac{1}{2} f_t \eta_{rs}^{-1}. \tag{39}$$

Bond–atom and atom–bond polarizabilities are expected to be useful tools for the study of chemical reactivity involving the interaction of a reagent with the atomic centers and bonds of a $\pi$-conjugated system. The haptotropic walk observed in the interaction of a metallic cation with polycyclic aromatic hydrocarbons (PAHs) [35] may be a suitable benchmark system to test the usefulness and reliability of the self and mutual softnesses and the bond–atom polarizabilities, in a language that simultaneously integrates the conceptual DFT and the classical HMO theory.

The expression for the electronic polarization at bond $rs$ of the conjugated system may be obtained as follows:

$$\Delta p_{rs} = \pi_{rs,t} \Delta \alpha_t = f_{rs} \frac{s_t}{f_t} \Delta \mu_t \tag{40}$$

or

$$\Delta p_{rs} = \frac{1}{2} \pi_{t,rs} \Delta \alpha_t = \frac{1}{2} \eta_{rs}^{-1} f_t \Delta \mu_t. \tag{41}$$

Equation 41 shows that the electronic polarization of the bond is proportional to its bond softness.

Further developments involving bond–bond polarizabilities defined in the Coulson–Longuett-Higgins theory of mobile electrons, namely, the bond–bond polarizability:

$$\pi_{rs,tu} = \frac{\partial p_{rs}}{\partial \beta_{tu}}, \tag{42}$$

may be of some interest and can be treated within the hybrid HMO–DFT model of chemical reactivity presented here.

The derivation of the condensed to atom and bond FFs may be achieved by writing the electron density of the system in terms of the one-particle density matrix **P** and the overlap matrix **S**:

$$\rho(\boldsymbol{r}) = Tr[\boldsymbol{PS}] \tag{43}$$

The FF can be obtained by differentiating $\rho(\boldsymbol{r})$ with respect to the number, $N$, of $\pi$ electrons as follows:

$$f(\boldsymbol{r}) = \left. \frac{\partial \rho(\boldsymbol{r})}{\partial N} \right|_{v(\boldsymbol{r})} = \sum_{\mu} \frac{\partial P_{\mu\mu}}{\partial N} + \sum_{\mu<\nu} \frac{\partial P_{\mu\mu}}{\partial N}. \tag{44}$$

In deriving Eq. 44 we have used (i) according to the HMO approximations the matrix elements $S_{\mu\nu} = \delta_{\mu\nu}$ and (ii) within the frozen orbital approximation $\frac{\partial S_{\mu\nu}}{\partial N} = 0$, at constant external potential. Then the condensed to atom and condensed to bond FF within HMO theory may be simply expressed in terms of the derivatives of the atomic charge $q_r$ localized at center $r$, and the bond order $p_{rs}$ respectively, as follows:

$$f_k = \frac{\partial q_k}{\partial N} \quad \text{and} \quad f_{kl} = \frac{\partial p_{kl}}{\partial N}. \tag{45}$$

Note that the condensed to atom FF $f_k$ in the HMO framework is exactly the one proposed by Yang and Mortier [6]. However, the FF derived from the variations of the bond orders, a FF we shall call the bond Fukui function (BFF), appears as a new reactivity index which could become a suitable index to describe reactivity for chemical processes involving the attack to a double bond. The practical implementations of both definitions are expressed in terms of the HMO coefficients as:

$$f_r^- = c_{\mathrm{HOMO},r}^2 \quad \text{and} \quad f_r^+ = c_{\mathrm{LUMO},r}^2 \tag{46}$$

for the condensed to atom nucleophilic and electrophilic FFs, and

$$f_{rs}^- = c_{\mathrm{HOMO},r}\, c_{\mathrm{HOMO},s} \tag{47}$$

and

$$f_{rs}^+ = c_{\mathrm{LUMO},r}\, c_{\mathrm{LUMO},s} \tag{48}$$

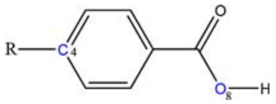
for the bond FFs. In deriving Eqs. 47 and 48 from Eq. 45, Balawender et al.'s [36] approximation for the derivatives of the one particle density matrix with respect to the number of electrons has been used.

An additional remark regarding the HMO FFs is worth making. The sign of the condensed to atom FF has been a matter of debate rather recently [37, 38, 39]. Within the present approach, the condensed to atom FF is a non-negative semi-positive quantity (see Eq. 46). The bond FF admits negative values with physical meaning. For instance, while a positive value of the BFF may be related to an increase of the electron density at the inter-nuclear region a negative value could be related to a decrease of electron density in the internuclear region during an electrophilic/nucleophilic attack. This result deserves further exploration as it may be related to the formation of bonding and anti-bonding states during the reaction in a form described by Berlin's theorem [40]. Note further that the BFFs defined in Eqs. 47 and 48 embodies information about orbital control, defined in the frontier molecular orbital theory of chemical reactions, for an intermolecular process involving systems when the centers *r* and *s* pertain to different interacting molecules. A summary of the complete set of reactivity indexes and their meaning in both the HMO and DFT formalisms is presented in Table 1.

In order to illustrate the reliability and usefulness of some key equations derived herein, we propose to revisit the classical Hammett's free energy relationships model describing inductive substituent effects on the acidity of benzoic acids [41].

The key quantities are the atom–atom mutual softness $\pi_{rs}$ involving the atomic center *r* where the perturbation (chemical substitution) is being applied and the atomic center *s* where the response is being assessed (i.e., the oxygen atom from which the proton detaches, see Table 2 for atom numbering), and the global softness of the $\pi$ system of the reference and substituted benzoic acid derivatives. The values (in $\beta^{-1}$ units) of both quantities are quoted in Table 2 together with the experimental values of constants reported by Hammett for a series of electron releasing and electron acceptor groups. The reference $\pi_{rs}$ value for $R = H$ is 0.0254 in $\beta^{-1}$ units.

**Table 2** Values of mutual polarizability at centers (4,8), Coulson softness, both in $\beta^{-1}$ units, and substituent constants benzoic acid derivatives



| R | $\pi_{4,8}$ | $Tr\boldsymbol{\Pi}$ | $\sigma$ |
|---|---|---|---|
| $NH_2$ | −0.5201 | 8.8156 | −0.660 |
| $CH_3O$ | −0.3330 | 3.9962 | −0.268 |
| $C_2H_5O$ | −0.230 | 3.8635 | −0.250 |
| $CH_3$ | −0.0250 | 3.0332 | −0.170 |
| H | −0.0254 | 3.0528 | −0.000 |
| F | −0.6249 | 5.3249 | 0.062 |
| Cl | −0.6815 | 5.5238 | 0.227 |
| Br | −0.7828 | 5.7154 | 0.232 |
| I | 1.0050 | 6.5884 | 0.276 |
| $NO_2$ | 1.1046 | 7.7200 | −0.778 |
| CN | 1.2366 | 9.9892 | 1.000 |

The sites of perturbation and response are highlighted in blue

According to Hammett's model, the substituent effect may be assessed after comparing the rate coefficients for the hydrolysis of benzoic acid derivatives with the rate coefficient for the same reaction involving the unsubstituted compounds, namely:

$$log\left(\frac{k}{k_0}\right) = \rho\sigma, \tag{49}$$

where $\rho$ and $\sigma$ are the reaction constant and substituent constant, respectively. We have found that the comparison between the mutual softness $\pi_{rs}$ involving the atomic center $r = 4$ which is the site of substitution and the atomic center $s = 8$ corresponding to the oxygen atom bearing the acidic hydrogen atom yields a qualitative ordering described by the following empirical equation (see Fig. 1):

$$\sigma = 0.7719\pi_{rs} - 0.2330. \tag{50}$$

From this empirical equation, $\sigma$ values for substituent not considered within the series may be predicted. For instance, the mutual softness at sites (4, 8) for $R$ = $–N(CH_3)_2$, $–CH_2CH_3$, $–CH_3S$ and $–C_6H_5$ yields the following predicted values of $\sigma$: −0.2162, −0.2154, −0.2150 and −0.2130. The predicted $\sigma$ value for the reference is −0.2134. This means that substituents $–N(CH_3)_2$, $–CH_2CH_3$, $–CH_3S$ promote deactivating acidity effect while the $–C_6H_5$ group promotes a marginal activating effect, in agreement with the experimental data [41].

The global softness of the $\pi$ electron system calculated as the trace of the mutual polarizability matrix described in Eq. 22 was also analyzed, as substituent effects have been

**Table 1** Relationship between HMO and DFT response functions

| HMO | DFT | Type | Information |
|---|---|---|---|
| ${c^2}_{H/L,r}$ | $f(\boldsymbol{r})$ | Local (regional) | Selectivity |
| $c_{H/L,r}\ c_{H/L,s}$ | $f^{\pm}_{r,s}$ | Non-local | Activation |
| $\pi_{rs}$ | $\frac{f_r}{f_s}s_s$ | Non-local | Activation |
| $\pi_{rr}$ | $s(\boldsymbol{r})$ | Local (regional) | Selectivity |
| $Tr\boldsymbol{\Pi}_{rs}$ | $S$ | Global | Reactivity |
| $\pi_{rs,t} = \frac{1}{2}\pi_{t,rs}$ | $\frac{1}{2}f_r\eta^{-1}_{rs}$ | Non-local | Activation |
| $\Delta q^L_{rs} = \ -s_r\Delta\alpha_s$ | $\delta\rho(\boldsymbol{r}) = -s(\boldsymbol{r})\delta v(\boldsymbol{r})$ | Local (regional) | Polarization |
| $\Delta q^{\mathrm{NL}}_r = \ -S\sum_{r\neq s}f_r\Delta\alpha_s$ | $\delta\rho(\boldsymbol{r}) = Sf(\boldsymbol{r})\left[\int \mathrm{d}\boldsymbol{r}'f(\boldsymbol{r}')\delta v(\boldsymbol{r}')\right]$ | Non-local | Polarization |
| $\Delta p_{rs} = \frac{1}{2}\pi_{t,rs}\Delta\alpha_t$ | $\frac{1}{2}\eta^{-1}_{rs}f_t\Delta\mu_t$ | Non-local | Polarization |
| $\boldsymbol{\Pi}(r,s) = \sum_s \pi_{rs}\delta_{rs} + \frac{s_s}{f_s}f_r$ | $\chi(\boldsymbol{r},\boldsymbol{r}') = -Sf(\boldsymbol{r})\delta(\boldsymbol{r}-\boldsymbol{r}') + Sf(\boldsymbol{r})f(\boldsymbol{r}')$ | Non-local function | Response |

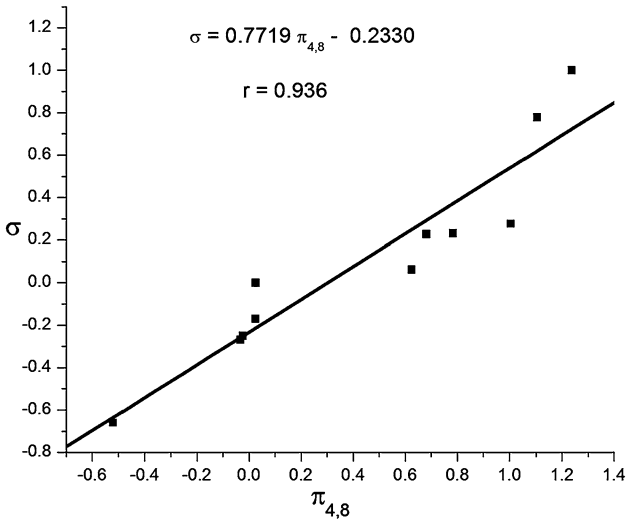


**Fig. 1** Comparison between mutual softness at the perturbation and response sites and experimental Hammett substituent constants

reported to be strongly dependent of the polarizability of the substituent group [42]. We have found that the relative softness is given by:

$$S_{\mathrm{rel}} = \frac{Tr\mathbf{\Pi}}{Tr\mathbf{\Pi}_0}, \tag{51}$$

where $Tr\mathbf{\Pi}_0$ is the global softness of the $\pi$ system of benzoic acid showing an even better correlation with the experimental ($\sigma$) values (see Fig. 2). The best empirical equation is the following:

$$\sigma = 1.5659(-1)^n \log\left[\frac{Tr\mathbf{\Pi}}{Tr\mathbf{\Pi}_0}\right] - 0.0801, \tag{52}$$

where $n$ is a parity constant that fixes the sign for electron releasing groups ($n$ odd) or electron acceptor groups ($n$ even). In order to test the reliability of this empirical equation, predicted values calculated for $R$ = –N(CH$_3$)$_2$, –CH$_2$CH$_3$, –CH$_3$S, and –C$_6$H$_5$ yield the following predicted $\sigma$: −0.2204, −0.1050, −0.0874 and −0.0800, respectively. Predicted $\sigma$ value for the reference is −0.0801. Note that the comparison with the relative global softness is also in qualitative agreement with the experimental order.

In summary, within the present language obtained by merging Coulson–Longuett-Higgings polarizability response function and the conceptual DFT, the inductive substituent effect is explained in the form of a non-local (semi-local) response, the mutual softness, involving the site of perturbation (substitution site) and the site of reaction. The relative global softness of the $\pi$ system on the other hand reinforces this result in a form consistent with Boyd's model [42], where the detachment of the abandoning proton is strongly dependent on the relative polarizability between the substituted and reference acid.

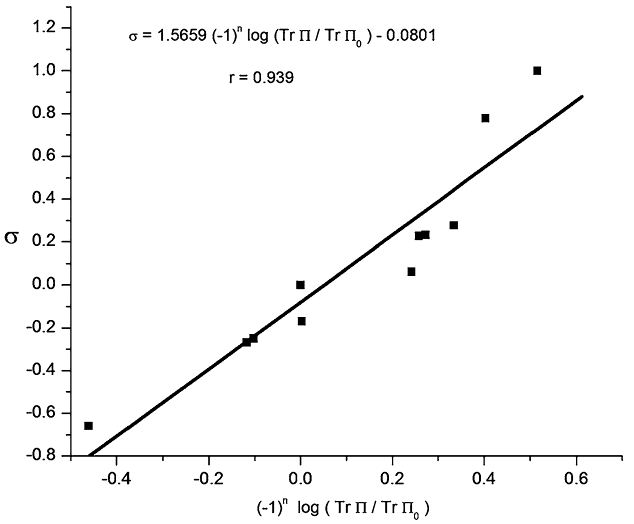


**Fig. 2** Comparison between relative global softness of the system at the perturbation and response sites and experimental Hammett substituent constants

## 4 Concluding remarks

A simple empirical model to deal with chemical reactivity of $\pi$ electron systems derived by merging the classical Coulson–Longuet-Higgins response function theory and the conceptual DFT has been presented. Useful expressions together with their chemical interpretation in both formalisms have been derived. The extensions to condensed to atom and group electrophilicities may be easily obtained from the square of the HMO coefficients, which represents the condensed to atom FF. The derivative of the bond order with respect to the number of $\pi$ electrons defines a new reactivity index, namely, the bond FF. In contrast to the atomic FF, the sign of the BFF bears useful chemical information about activation/deactivation of the $\pi$ bond upon the change in the number of electrons in the system. The self polarizability has been given a clear meaning of a regional atomic softness thereby allowing the global softness of the $\pi$ system to be simply represented as the trace of the self and mutual polarizability matrices. The empirical response function associated with the polarizability matrix yields approximated expressions to deal with the fluctuation of the atomic $\pi$ electron population in terms of a local (regional) term governed by the local softness (self-polarizability), and a non-local contribution described by the mutual polarizabilities (mutual softness). In this way, useful quantities such as self and mutual polarizabilities originally defined through the HMO parameters can be redefined in terms of density functional concepts as self and mutual softnesses. As an illustration, we have revisited the Hammett linear free energy model to assess the inductive substituent effect as a semi-local response described by the mutual softness involving the site of substitution and the site of reaction.

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