On the Quality of the Hardness Kernel and the Fukui Function to Evaluate the Global Hardness

MIQUEL TORRENT-SUCARRAT,[1] PEDRO SALVADOR,[2] PAUL GEERLINGS,[1] MIQUEL SOLÀ[2]

[1]*Eenheid Algemene Chemie, Faculteit Wetenschappen, Vrije Universiteit Brussel (VUB),
Pleinlaan 2, Brussels, Belgium*
[2]*Institut de Química Computacional and Departament de Química, Universitat de Girona,
E-17071 Girona, Catalonia, Spain*

Abstract: An approximated hardness kernel, which includes the second derivative with respect to the density of the kinetic energy, the electron–electron coulomb repulsion, and the exchange density functionals, has been tested for the calculation of the global hardness. The results obtained for a series of 40 cations and neutral systems and 16 anions represent in most cases an improvement of the results obtained using the HOMO-LUMO gap approach and indicate the viability of this approach to evaluate global hardness. In addition, the relevance of the Fukui function approximation and the role of the three components of the hardness kernel in the evaluation of the global hardness have been analyzed.

© 2006 Wiley Periodicals, Inc.   J Comput Chem 28: 574–583, 2007

Key words: density functional theory (DFT); conceptual DFT; hardness; hardness kernel; local hardness; Fukui function

Introduction

Density functional theory (DFT) has revolutionized the theoretical study of chemical reactivity in many areas, varying from inorganic to organic chemistry and from materials science to biochemistry.[1,2] An important branch of the DFT has been developed since the late 1970s and early 1980s, called conceptual DFT[2–5] by its protagonist, R. G. Parr. On the basis of the idea that the electron density is the fundamental quantity for describing atomic and molecular ground states, Parr and coworkers were able to give sharp definitions for chemical concepts which were already known and had been in use for many years in various branches of chemistry (e.g., electronegativity and chemical hardness), allowing for their calculation and quantitative use.[2]

The central quantities of conceptual DFT are the response functions. These functions are the response of the chemical system to perturbations in its number of electrons, N, and/or the external potential, $v(\vec{r})$, which is the potential acting on an electron at position $\vec{r}$ due to the nuclear attraction plus other external forces that may be present. Assuming differentiability of the electronic energy, E, with respect to N and $v(\vec{r})$, a series of response functions emerge, probably the most important being the electronic chemical potential, μ,[6] the hardness, η,[7] and the Fukui function, $f(\vec{r})$.[8] It is worth noticing that the properties obtained from differentiation with respect to N have a global character (describe the characteristic of a molecule as a whole, e.g., η), whereas differentiation with respect to $v(\vec{r})$ introduces a local character to the property (establishing the regioselectivity aspects of molecular reactivity, e.g., $f(\vec{r})$). Associated with these properties, important chemical reactivity principles have been rationalized within the framework of conceptual DFT like the hard and soft acids and bases principle,[9–13] the Sanderson electronegativity equalization principle,[14,15] the maximum hardness principle,[9,16–19] and the minimum polarizability principle.[20]

Correspondence to: M. Torrent-Sucarrat; e-mail: mtorrent@vub.ac.be

A fundamental problem arises when evaluating properties like η and $f(\vec{r})$, as they involve differentiation of the energy and electron density with respect to the number of electrons of the system (necessarily an integer number for isolated atoms, molecules, etc.).[21–23] The larger part of the research devoted to these properties has been carried out within the finite difference approach.[4,5] This approach may bring about difficulties that might be quite important when adding and/or subtracting one electron leads to metastable species. For this reason, it is very important to explore new ways to compute more accurately these chemical reactivity indexes.[19,24–29] An alternative methodology is to evaluate the hardness starting from the second functional derivative of the Hohenberg–Kohn universal density functional, $F[\rho(\vec{r})]$, with respect to the density, i.e., the hardness kernel, $\eta(\vec{r}, \vec{r}')$.[30,31] There have been few attempts of exploring this avenue. So far, it has been only applied either to atoms[32–36] or to molecules[37,38] with highly simplified models for the hardness kernel. Particular attention should be given to the study of Liu et al.,[32] who have shown that the simple model for the hardness kernel $\eta(\vec{r}, \vec{r}') \cong 1/\|\vec{r} - \vec{r}'\| + C$, where C is a constant, generates good results for the global hardness of neutral atoms ($Z = 1 \rightarrow 54$). To our knowledge, the only η values for molecules reported in the literature starting from hardness kernels have been reported by some of the present authors[37,38] using as approximated hardness kernels $1/\|\vec{r} - \vec{r}'\|$ and $\delta(\vec{r}, \vec{r}')$. Finally, Ayers[39] proposed an interesting external-potential-based hardness kernel, which, however, as far as we know, has never been tested yet.

This work is the first attempt to implement and evaluate the global hardness for polyatomic molecules using a hardness kernel, which includes the second derivative with respect to the density of the kinetic energy, $T[\rho(\vec{r})]$, the electron–electron coulomb repulsion, $J[\rho(\vec{r})]$, and the exchange density functionals, $E_x[\rho(\vec{r})]$.

Theoretical Background

The response functions can be split into three groups: global, local, and nonlocal reactivity indices. Examples of global reactivity indices are μ and η

$$\mu = \left(\frac{\partial E}{\partial N}\right)_{v(r)} \tag{1}$$

and

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

The electronic chemical potential characterizes the escaping tendency of electrons from the molecular system while the global hardness represents the resistance of a chemical species to change its electronic configuration.[2,9] Applying the finite difference approximation and Koopmans' theorem,[40] one obtains the operational equations for μ and η

$$\mu_1 = -\frac{1}{2}(I + A), \tag{3}$$

$$\mu_2 = \frac{1}{2}(\varepsilon_{\text{HOMO}} + \varepsilon_{\text{LUMO}}), \tag{4}$$

$$\eta_1 = I - A, \text{ and} \tag{5}$$

$$\eta_2 = \varepsilon_{\text{LUMO}} - \varepsilon_{\text{HOMO}}, \tag{6}$$

where I and A are the first vertical ionization potential and electron affinity of the neutral molecule, respectively, and $\varepsilon_{\text{LUMO}}$ and $\varepsilon_{\text{HOMO}}$ are the energies of the lowest unoccupied and the highest occupied molecular orbitals, respectively.

On the other hand, the Fukui function, $f(\vec{r})$,[8] and the local hardness, $\eta(\vec{r})$,[41,42] are local reactivity indices, which have become very useful predicting the regioselectivity of chemical reactions.[43–47] The Fukui function is a normalized function that describes the local variation in the electron density of the system due to a change in the global number of electrons

$$f(\vec{r}) = \left(\frac{\partial^2 E}{\partial N \delta v(\vec{r})}\right) = \left(\frac{\partial \rho(\vec{r})}{\partial N}\right)_{v(r)}. \tag{7}$$

The evaluation of this property is also affected by the technical problem of a differentiation with respect to an integer, and some authors approximate it as simply $\rho(\vec{r})/N$.[24,35,48,49] Alternatively, Parr and Yang have defined the left ($f^-(\vec{r})$), right ($f^+(\vec{r})$), and central ($f^0(\vec{r})$) derivatives of eq. (7).[8] Applying a finite difference approximation and the frontier-electron theory of reactivity, these three Fukui approximations can be written as

$$f^+(\vec{r}) \cong \rho_{N+1}(\vec{r}) - \rho_N(\vec{r}) \cong \rho_{\text{LUMO}}(\vec{r}), \tag{8}$$

$$f^-(\vec{r}) \cong \rho_N(\vec{r}) - \rho_{N-1}(\vec{r}) \cong \rho_{\text{HOMO}}(\vec{r}), \text{ and} \tag{9}$$

$$f^0(\vec{r}) \cong \frac{1}{2}[\rho_{N+1}(\vec{r}) - \rho_{N-1}(\vec{r})] \cong \frac{1}{2}[\rho_{\text{LUMO}}(\vec{r}) + \rho_{\text{HOMO}}(\vec{r})]. \tag{10}$$

The local hardness, $\eta(\vec{r})$, is the local counterpart of the global hardness and its analytical definition was first proposed by Ghosh and Berkowiz as[41]

$$\eta(\vec{r}) = \left(\frac{\delta \mu}{\delta \rho(\vec{r})}\right)_{v(r)}. \tag{11}$$

It can be connected with η through the subsequent chain rule

$$\eta = \left(\frac{\partial \mu}{\partial N}\right)_{v(r)} = \int \left(\frac{\delta \mu}{\delta \rho(\vec{r})}\right)_{v(r)} \left(\frac{\partial \rho(\vec{r})}{\partial N}\right)_{v(r)} d\vec{r} =$$
$$\int \eta(\vec{r}) f(\vec{r}) d\vec{r}. \tag{12}$$

Last but not least, the hardness kernel[30,31] represents an example of a nonlocal reactivity index, and it is simply defined as

$$\eta(\vec{r}, \vec{r}') = \frac{\delta^2 F[\rho(\vec{r})]}{\delta \rho(\vec{r}) \delta \rho(\vec{r}')}, \tag{13}$$

where $F[\rho(\vec{r})]$ stands for the exact form of the Hohenberg–Kohn universal density functional. Since the exact functional is unknown, approximations are necessary for practical calculations, this being

the major drawback of this methodology. The hardness kernel is connected to the local and global hardness through the Fukui function by the following equations

$$\eta(\vec{r}) = \int \eta(\vec{r}, \vec{r}')f(\vec{r}')d\vec{r}', \text{ and} \qquad (14)$$

$$\eta = \int \eta(\vec{r})f(\vec{r})d\vec{r}. \qquad (15)$$

As has been argued, the dependence between the density and the external potential in the definition of local hardness [eq. (11)] and the replacement of the Fukui function by other functions, which integrate to unity, have cast some doubts about the correct definition of these reactivity indexes.[19,30,34,47,50,51] For instance, Harbola et al.[50] proposed that $\eta(\vec{r})$ is constant and equal to the global hardness in all the positions of the space. According to our opinion, the local hardness and its relation with the hardness kernel is still one of the most vexing yet fascinating problems in the field of conceptual DFT. Additional work on this subject is presently in progress in our laboratory.

Hence, it is possible to calculate the local and global hardnesses from the hardness kernel and the Fukui function. Considering the Thomas–Fermi,[52,53] and Dirac[54] approximations for the kinetic and exchange energies, respectively, $F[\rho(\vec{r})]$ can be approximated as

$$F[\rho(\vec{r})] \cong \frac{1}{2}\int\int\frac{\rho(\vec{r})\rho(\vec{r}')}{|\vec{r}-\vec{r}'|}d\vec{r}d\vec{r}' + C_T\int\rho^{5/3}(\vec{r})d\vec{r}$$
$$- C_X\int\rho^{4/3}(\vec{r})d\vec{r}, \qquad (16)$$

where $C_T = (3/10)(3\pi^2)^{2/3}$ and $C_X = (3/4)(3/\pi)^{1/3}$. Then, an analytical expression for the hardness kernel can be obtained by derivation of each term of the previous expression twice with respect to the electron density

$$\eta(\vec{r}, \vec{r}') \cong \left[\frac{10}{9}C_T\rho(\vec{r})^{-1/3} - \frac{4}{9}C_X\rho(\vec{r})^{-2/3}\right]\delta(\vec{r}-\vec{r}')$$
$$+ \frac{1}{\|\vec{r}-\vec{r}'\|}. \qquad (17)$$

One of the problems of the Thomas–Fermi theory is the non-binding theorem, which states that in the Thomas–Fermi model molecular systems are unstable relative to dissociation into constituent fragments.[55–57] However, in the present work we have applied the Thomas–Fermi model to the electron densities obtained with the B3LYP method. More involved expressions for the exact kinetic energy, exchange, and correlation functionals exist and could be used, too. However, as it was shown by different authors,[32,34,49] the main contribution to the global hardness comes from the Coulomb term. Hence, we believe that the use of more sophisticated kinetic[58] and exchange-correlation functionals[59–61] will probably not change meaningfully our global hardness values.

Now, approximate expressions for the Fukui function are necessary. A crude model, sometimes used in the literature consist of using the density per particle function, $\rho(\vec{r})/N$. In this case, from eqs. (14), (15), and (17), simple analytical equations for global and local hardnesses that only depend on $\rho(\vec{r})$ are obtained,

$$\eta(\vec{r}) \cong \frac{1}{N}\left[\frac{10}{9}C_T\rho(\vec{r})^{2/3} - \frac{4}{9}C_X\rho(\vec{r})^{1/3} + \int\frac{\rho(\vec{r}')}{\|\vec{r}-\vec{r}'\|}d\vec{r}'\right] \text{ and} \qquad (18)$$

$$\eta \cong \frac{1}{N^2}\left[\frac{10}{9}C_T\int\rho(\vec{r})^{5/3}d\vec{r} - \frac{4}{9}C_X\int\rho(\vec{r})^{4/3}d\vec{r} + \int\int\frac{\rho(\vec{r})\rho(\vec{r}')}{\|\vec{r}-\vec{r}'\|}d\vec{r}d\vec{r}'\right]. \qquad (19)$$

The global hardness can be written in a more compact way as

$$\eta[\rho(\vec{r})/N] \cong \eta_T[\rho(\vec{r})/N] + \eta_X[\rho(\vec{r})/N] + \eta_J[\rho(\vec{r})/N], \qquad (20)$$

where the expression between brackets is the approximation used to evaluate the Fukui function.

A more elaborated approximation for the Fukui function based on the frontier-electron theory is given by the density of the HOMO orbital, $\rho_{\text{HOMO}}(\vec{r})$. Following the same procedure but using the latter approximation to the Fukui function, one gets

$$\eta(\vec{r}) \cong \frac{10}{9}C_T\rho_{\text{HOMO}}(\vec{r})\rho(\vec{r})^{-1/3} - \frac{4}{9}C_X\rho_{\text{HOMO}}(\vec{r})\rho(\vec{r})^{-2/3}$$
$$+ \int\frac{\rho_{\text{HOMO}}(\vec{r}')}{\|\vec{r}-\vec{r}'\|}d\vec{r}' \qquad (21)$$

and

$$\eta \cong \frac{10}{9}C_T\int\rho_{\text{HOMO}}^2(\vec{r})\rho(\vec{r})^{-1/3}d\vec{r} - \frac{4}{9}C_X\int\rho_{\text{HOMO}}^2(\vec{r})\rho(\vec{r})^{-2/3}d\vec{r}$$
$$+ \int\int\frac{\rho_{\text{HOMO}}(\vec{r})\rho_{\text{HOMO}}(\vec{r}')}{\|\vec{r}-\vec{r}'\|}d\vec{r}d\vec{r}', \qquad (22)$$

or, more compactly

$$\eta[\rho_{\text{HOMO}}(\vec{r})] \cong \eta_T[\rho_{\text{HOMO}}(\vec{r})] + \eta_X[\rho_{\text{HOMO}}(\vec{r})] + \eta_J[\rho_{\text{HOMO}}(\vec{r})]. \qquad (23)$$

Likewise, it is possible to obtain similar expressions for the local and global hardnesses using $\rho_{\text{LUMO}}(\vec{r})$ and $1/2(\rho_{\text{HOMO}}(\vec{r}) + \rho_{\text{LUMO}}(\vec{r}))$ as approximations to the Fukui function.

An alternative way to express the Hohenberg–Kohn universal density functional is the independent particle approximation, where the exchange-correlation energy contains part of the kinetic energy. In that framework, the only terms that would contribute to the hardness are the coulombic and the exchange-correlation ones, because the contribution of the noninteracting kinetic energy to the hardness is null.[34,62]

The aim of this work is to examine the validity of eqs. (19) and (22) to calculate the global hardness and to analyze the importance of the three terms (kinetic, exchange, and coulombic) in the evaluation of η.

The corresponding 3D and 6D integrations have been evaluated using the Becke multicenter numerical integration scheme,[63] which encompasses a decomposition of the 3D space using "fuzzy" Voronoi polyhedra. This decomposition is similar to the successful and basis set independent "stockholders" scheme used by Hirshfeld[64] for calculating effective atomic charges in molecules. This molecular partitioning of space in eq. (15) leads to atomic or condensed

hardnesses, the sum of all giving the global hardness. In contrast to the traditional methods to evaluate the hardness [eqs. (5) and (6)], the present methodology yields information about the local (atomic or condensed hardness) and global (molecular hardness) reactivity at the same time. In this work, we have only focused on the global hardness and its behavior as compared with the traditional methods, whereas in near future work the features of the condensed hardness and their possible applications in reactivity will be highlighted.

Computational Details

For the evaluation of the different integrals required in eqs. (19) and (22) we have implemented Becke's method of multicenter numerical integration,[63] in a program for which the only input is a formatted checkpoint file obtained from Gaussian 03 package.[65]

This method decomposes the integration of a function $F(\vec{r})$ over the 3D space into a sum of integrations over single-atom components using a weight function, $w_n(\vec{r})$, for nucleus n in the system at every point of the space $\vec{r}$ in such a way that

$$\sum_n w_n(\vec{r}) = 1. \tag{24}$$

In this scheme the numerical integration of a quantity I is determined as a sum of atomic contributions, I_n

$$I \cong \sum_n I_n = \sum_n \int w_n(\vec{r}) F(\vec{r}) d\vec{r}, \tag{25}$$

where $w_n(\vec{r})$ has the value 1 in the vicinity of its own nucleus, but vanishes in a continuous and well-behaved manner near any other nucleus, resulting in the so-called "fuzzy" atoms. The $w_n(\vec{r})$ used in this work are the fuzzy Voronoi polyhedra proposed by Becke, taking into account the Bragg–Slater radius[66] and the Becke's recipe[63] suggesting to increase the radius of hydrogen to 0.35 Å. Each atom is integrated using Chebyshev's integration for the radial part and Lebedev's quadrature[67] for the angular part. The routine for the Lebedev quadrature has been downloaded from ref. 68.

Under the approximation of eq. (19), the two-electron contribution of the hardness kernel to the global hardness is simply twice the coulombic electron–electron repulsion divided by N^2. In the case of eq. (22), it can be obtained also analytically by a four-index transformation of the two-electron integrals over the atomic orbitals. We have used a modified version of the HONDO package[69] to obtain the two-electron integrals necessary to compute the coulomb contribution analytically. However, the program uses a nondirect algorithm and it has an internal limitation on the number of basis functions (255 maximum). In the light of this, we have decided to compute both the one- and two-electron contributions by numerical integration using Becke's scheme.[63] With a grid consisting of 40 radial and 146 angular points for each atom, we have achieved a typical accuracy for the one-electron contribution of $\cong 10^{-5}$ a.u. For the two-electron integrations we have used two identical grids for each atom that were slightly rotated to achieve better accuracy, as described in ref. 70. In this manner we could obtain an acceptable accuracy for the two-electron contribution ($\cong 10^{-3}$ a.u.) using the same atomic grid.

The numerical evaluation of the coulomb term is obviously the bottleneck of the calculation. Nevertheless, the computational cost of the global hardness calculations, eqs. (19) and (22), is similar to that for a single point energy calculation.

In this work, the Gaussian 03 package[65] has been used to perform the geometry optimizations and to obtain $\varepsilon_{\text{LUMO}}$, $\varepsilon_{\text{HOMO}}$, $\rho(\vec{r})$, $\rho_{\text{HOMO}}(\vec{r})$, and $\rho_{\text{LUMO}}(\vec{r})$ at the B3LYP/6-311++G(2d,2p) level of theory.[71–73] In addition, all calculations of this work were also carried out at the HF/6-31+G(d), B3LYP/6-31+G(d), and HF/6-311++G(2d,2p) levels of theory, yielding qualitatively the same results and tendencies.

Results and Discussion

All calculated hardness values reported in Tables 1–3 and Figures 1–3 have been obtained using eqs. (6) and (22), with Thomas–Fermi and Dirac approximations for the kinetic and exchange energies in the hardness kernel, respectively, and with $\rho_{\text{HOMO}}(\vec{r})$ as an approximation of the Fukui function. Although other approximations of the Fukui function have been tested, the corresponding values are not included in the present work. When using $\rho(\vec{r})/N$ as the simplest approximation for the Fukui function [eq. (19)], characteristic soft systems such as H_2S and PH_3 were predicted to be harder than classical hard systems like H_2O and NH_3, showing the importance of the use of an accurate Fukui function to obtain reliable results. According to the variational principle for determining the Fukui function and chemical hardness of Chattaraj et al.,[30] the best Fukui function will give the smallest (and best) hardness values. The results obtained in this work show that $\eta[\rho(\vec{r})/N]$ always present higher values than $\eta[\rho_{\text{HOMO}}(\vec{r})]$, emphasizing the quality of the $\eta[\rho_{\text{HOMO}}(\vec{r})]$ values.

The equivalents of eq. (22) using $\rho_{\text{LUMO}}(\vec{r})$ and $1/2(\rho_{\text{HOMO}}(\vec{r}) + \rho_{\text{LUMO}}(\vec{r}))$ as approximations of the Fukui function have also been used to calculate $\eta[\rho_{\text{LUMO}}(\vec{r})]$ and $\eta[1/2(\rho_{\text{HOMO}}(\vec{r}) + \rho_{\text{LUMO}}(\vec{r}))]$ values. Even though the results obtained are pretty reasonable, particularly the $\eta[1/2(\rho_{\text{HOMO}}(\vec{r}) + \rho_{\text{LUMO}}(\vec{r}))]$ ones, spurious values have been obtained for some systems. This problem comes from the fact that in the single-reference SCF procedure only the occupied orbitals enter in the expression of the Fock operator and they are the only orbitals really optimized. In addition, the GGA functional sometimes produces unreliable and defective LUMO orbitals.[76] In particular, when using large basis sets, especially including diffuse functions, it is possible to obtain spurious LUMO, resembling *s* type orbitals, which leads to unphysical higher values of the global hardness when determined from eq. (22). It is worth noting that these spurious LUMOs have a large impact on the shape of the $\rho_{\text{LUMO}}(\vec{r})$, however, this effect is less relevant in the $\varepsilon_{\text{LUMO}}$, where their values in most of the cases are close to zero, the anions being the only exception. Thus, we have kept $\varepsilon_{\text{LUMO}}$ in the calculations of η_2. In the following paragraphs, the discussion will only be based on the results obtained for η_2 and $\eta[\rho_{\text{HOMO}}(\vec{r})]$.

The evaluation of the global hardness from eq. (5) has not been considered in this study as we are mainly interested in the comparison between the hardness kernel and the traditional methods for computing hardness values, but using in both cases the same level of theory and approximations. Then, since the hardness of eq. (22) has been obtained with the information of a single point calculation and using the unrelaxed approach for the Fukui function, the reference approach in the traditional method to calculate the hardness must be that of eq. (6) with the Koopmans'

Table 1. Calculated and Experimental Hardnesses for Cations and Neutral Molecules Studied in This Work.

Molecule	$\eta_T[\rho_{HOMO}(\vec{r})]^a$	$\eta_X[\rho_{HOMO}(\vec{r})]^a$	$\eta_J[\rho_{HOMO}(\vec{r})]^a$	$\eta[\rho_{HOMO}(\vec{r})]^a$	$\eta_2{}^b$	$\eta_1{}^{exp\,c}$
Li^+	49.2	−4.3	44.7	89.7	57.0	70.2
Na^+	25.1	−2.0	33.9	56.9	32.0	42.2
K^+	7.2	−1.1	18.6	24.8	20.5	27.3
Be^{2+}	93.2	−5.9	61.8	149.1	115.7	135.7
Mg^{2+}	33.7	−2.4	39.5	70.9	51.8	65.1
Ca^{2+}	9.2	−1.2	21.1	29.1	30.4	39.0
B^{3+}	150.9	−7.5	78.8	222.2	194.5	221.4
Al^{3+}	43.5	−2.7	45.1	85.9	75.3	91.5
Ga^{3+}	22.4	−1.3	34.4	55.4	20.6	34.0
Ti^{2+}	7.2	−0.9	18.4	24.7	1.9	13.9
Ge^{2+}	2.7	−0.8	12.4	14.3	10.7	18.3
Sc^{3+}	11.4	−1.3	23.5	33.6	35.8	48.7
V^{3+}	10.4	−1.1	22.3	31.6	2.2	17.4
HF	12.7	−1.4	23.8	35.1	10.9	22.0
HCl	4.3	−0.8	14.2	17.6	8.5	16.0
H_2O	9.1	−1.2	19.9	27.8	8.2	19.0
H_2S	3.3	−0.8	12.4	15.0	6.8	12.4
NH_3	6.5	−1.1	16.8	22.2	7.0	16.4
PH_3	2.8	−0.7	11.4	13.4	7.3	12.0
AsH_3	2.2	−0.6	10.4	12.1	7.2	12.2
CO	5.7	−1.2	15.9	20.4	9.4	15.8
CH_3F	5.9	−0.7	14.8	20.0	9.5	18.8
CH_3Cl	3.6	−0.7	12.8	15.7	7.8	15.0
CH_3OH	6.4	−0.9	15.7	21.2	7.4	17.0
CH_3OCH_3	5.6	−0.7	14.3	19.2	7.0	16.0
CH_3SCH_3	2.8	−0.6	11.3	13.5	5.8	12.0
NH_2CH_3	5.3	−0.9	14.6	19.1	6.3	14.4
$N(CH_3)_3$	4.5	−0.7	12.8	16.6	5.7	12.6
C_2H_4	3.0	−0.7	12.2	14.5	7.4	12.4
BF_3	5.0	−0.5	12.8	17.2	11.5	13.4^d
BCl_3	1.7	−0.3	8.1	9.5	6.8	11.2
F_2	8.1	−0.9	17.8	25.1	7.1	12.6
Cl_2	2.5	−0.5	10.5	12.6	4.7	9.2
CO_2	5.3	−0.7	13.8	18.4	10.0	17.6
SO_3	3.9	−0.5	11.3	14.7	6.6	11.0
SO_2	3.4	−0.5	11.4	14.3	5.6	11.2
H_2	7.6	−1.7	17.9	23.7	12.4	17.4
CS	4.7	−1.0	14.0	17.7	6.1	11.6
N_2	5.3	−0.8	15.0	19.5	11.1	17.8
HCN	4.3	−0.8	14.5	18.0	9.9	16.0

All units are eV.
^{a}Hardness values calculated from eq. (22).
${}^b\eta_2$ is obtained using eq. (6).
^{c}From ref. 74.
^{d}Electron affinity is obtained from ref. 75.

approximation. In addition, it is important to remark that the experimental hardnesses, η_1^{exp}—usually, the experimental hardness results show an arbitrary factor ½ in the definition of eq. (5), which will be omitted in the present work—are obtained from eq. (5) using the experimental vertical values of I and A,[74] whose experimental determination in some cases is not trivial, e.g., the electron affinity of anions. In these situations, the importance of designing new methodologies to evaluate the hardness emerges, in particular when the traditional methods [eqs. (5) and (6)] fail.

The experimental hardnesses, the hardness values obtained with eqs. (6) and (22), and the three components (kinetic, exchange-correlation, and coulombic) of the latter for 40 cations and neutral systems are given in Table 1.

Figures 1 and 2 display a good correlation between η_1^{exp} and $\eta[\rho_{HOMO}(\vec{r})]$ and η_2 with r^2 of 0.970 and 0.996, respectively. When the cationic species and the HF and F_2 molecules (*vide infra*) are not included in the comparison, the correlations become worse, although the general tendency is conserved, particularly in the case of $\eta[\rho_{HOMO}(\vec{r})]$ (r^2 of 0.696). It is also interesting to look at the evolution of the slope along the linear correlations of Figures 1 and 2. For instance, the slope values for the correlations of Figure 2 are 0.896 and 0.475, indicating that the experimental

Table 2. Calculated Hardnesses for the Anions Studied in This Work.

Molecule	$\eta_T[\rho_{\text{HOMO}}(\vec{r})]^a$	$\eta_X[\rho_{\text{HOMO}}(\vec{r})]^a$	$\eta_J[\rho_{\text{HOMO}}(\vec{r})]^a$	$\eta[\rho_{\text{HOMO}}(\vec{r})]^a$	η_2^b
F^-	11.1	−1.3	21.9	31.7	10.1
Cl^-	3.7	−0.8	13.2	16.2	6.5
Br^-	2.7	−0.6	11.6	13.7	5.3
OH^-	7.5	−1.1	17.9	24.4	3.3
CH_3O^-	6.0	−0.8	15.0	20.2	2.5
SH^-	2.7	−0.7	11.3	13.3	3.8
CH_3S^-	2.7	−0.6	11.0	13.0	2.8
NH_2^-	4.7	−0.9	14.1	17.9	2.3
CH_3NH^-	4.4	−0.8	13.2	16.8	1.5
$CH_3NCH_3^-$	3.8	−0.6	11.7	14.8	1.8
PH_2^-	1.9	−0.6	9.3	10.6	2.9
NO_3^-	4.0	−0.5	11.8	15.3	5.7
NO_2^-	3.5	−0.5	12.0	15.0	5.0
CH_3^-	3.1	−0.7	11.2	13.5	2.0
SiH_3^-	1.8	−0.6	9.0	10.2	3.4
H^-	3.3	−1.1	10.9	13.1	4.6

All units are eV.
[a]Hardness values calculated from eq. (22).
[b]η_2 is obtained using eq. (6).

values for the cations species are properly reproduced with η_2, although for the neutral systems (inner plot of the Fig. 2) a clear underestimation is observed (slope value of 0.475). In contrast, $\eta[\rho_{\text{HOMO}}(\vec{r})]$ values are slightly overestimated for the neutral systems (slope value of 1.207, inner plot of Fig. 1), although an improvement over the results obtained from the HOMO-LUMO gap approach is clearly noticed, i.e., higher r^2 value and the slope and y-intercept becoming closer to 1.0 and 0.0, respectively. When the cations and the HF and F_2 molecules are taken into account, the tendencies of the Figures 1 and 2 become very close.

Finally, the results displayed in the Figure 1 clearly indicate that $\eta[\rho_{\text{HOMO}}(\vec{r})]$ can be used as a good alternative to evaluate the global hardness, not just to correlate but to reproduce the experimental results.

The improvement of the $\eta[\rho_{\text{HOMO}}(\vec{r})]$ results with respect to η_2 hardnesses can be also appreciated from the values of Table 1. For neutral molecules, $\eta[\rho_{\text{HOMO}}(\vec{r})]$ shows two critical cases, HF and F_2, where the predicted $\eta[\rho_{\text{HOMO}}(\vec{r})]$ values are 13.1 and 12.5 eV, respectively, larger than the experimental results. These incorrect performances are also present at the HF/6-31+G(d), HF/6-

Table 3. Hardness Classification of the Different Anionic Lewis Bases According to the Calculated Hardnesses in Table 2 for the Different Methods Studied[a].

$\eta_T[\rho_{\text{HOMO}}(\vec{r})]$	$|\eta_X[\rho_{\text{HOMO}}(\vec{r})]|$	$\eta_J[\rho_{\text{HOMO}}(\vec{r})]$	$\eta[\rho_{\text{HOMO}}(\vec{r})]$	η_2
F^-	F^-	F^-	F^-	F^-
OH^-	OH^-	OH^-	OH^-	Cl^-
CH_3O^-	H^-	CH_3O^-	CH_3O^-	NO_3^-
NH_2^-	NH_2^-	NH_2^-	NH_2^-	Br^-
CH_3NH^-	CH_3O^-	Cl^-	CH_3NH^-	NO_2^-
NO_3^-	CH_3NH^-	CH_3NH^-	Cl^-	H^-
$CH_3NCH_3^-$	Cl^-	NO_2^-	NO_3^-	SH^-
Cl^-	CH_3^-	NO_3^-	NO_2^-	SiH_3^-
NO_2^-	SH^-	$CH_3NCH_3^-$	$CH_3NCH_3^-$	OH^-
H^-	Br^-	Br^-	Br^-	PH_2^-
CH_3^-	$CH_3NCH_3^-$	SH^-	CH_3^-	CH_3S^-
SH^-	CH_3S^-	CH_3^-	SH^-	CH_3O^-
Br^-	SiH_3^-	CH_3S^-	H^-	NH_2^-
CH_3S^-	PH_2^-	H^-	CH_3S^-	CH_3^-
PH_2^-	NO_2^-	PH_2^-	PH_2^-	$CH_3NCH_3^-$
SiH_3^-	NO_3^-	SiH_3^-	SiH_3^-	CH_3NH^-

[a]The hardness decreases in going down through a column. The cells in dark grey correspond to hard molecules according to the qualitative classification given by Pearson[9] while those in light grey and white represent borderline and soft molecules, respectively.
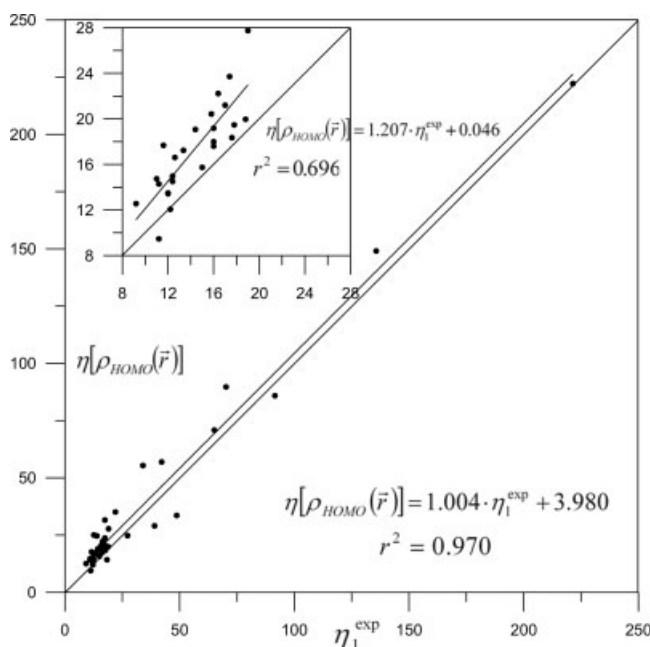
Figure 1. Correlation between the experimental hardness and the global hardness calculated from eq. (22) for the cations and neutral molecules studied in this work. The correlation for the neutral molecules, except F_2 and HF, is also given (inner plot). All values are given in eV.

On the other hand, $\eta_T[\rho_{HOMO}(\vec{r})]$ and $\eta_J[\rho_{HOMO}(\vec{r})]$ also present reasonable tendencies with respect to η_1^{exp} for the neutral species with r^2 values of 0.661 and 0.682, respectively (including HF and F_2, r^2 becomes 0.611 and 0.651, respectively). It is important to remark that the $\eta_T[\rho_{HOMO}(\vec{r})]$ contribution is computationally much cheaper than the $\eta_J[\rho_{HOMO}(\vec{r})]$ and $\eta[\rho_{HOMO}(\vec{r})]$ ones. Taking into account the reasonable correlation of $\eta_T[\rho_{HOMO}(\vec{r})]$ with η_1^{exp}, we can suggest that $\eta_T[\rho_{HOMO}(\vec{r})]$, although being generally a relatively small term in $\eta[\rho_{HOMO}(\vec{r})]$, may become an interesting alternative for a fast qualitative evaluation of the hardness. Furthermore, the importance of $\eta_T[\rho_{HOMO}(\vec{r})]$ in $\eta[\rho_{HOMO}(\vec{r})]$ is reflected in the linear tendencies as can be seen in the graphics of Figures 1 and 3. Despite of the fact that r^2 is very similar for both correlations the introduction of the kinetic and exchange contributions produces data closer to the $y = x$ line and a slope and intercept becoming closer to 1.0 (1.004 and 0.352 in Figs. 1 and 3, respectively) and 0.0 values (3.980 and 10.153 in Figs. 1 and 3, respectively), respectively. In addition, the inner plots of the Figures 1 and 2 display similar features.

Table 1 shows that a hard molecule presents high values of $\eta_J[\rho_{HOMO}(\vec{r})]$ and $\eta_T[\rho_{HOMO}(\vec{r})]$, increasing the global value of $\eta[\rho_{HOMO}(\vec{r})]$. The respective $\eta_X[\rho_{HOMO}(\vec{r})]$ values are also larger for hard molecules but negative. Hence, the effect of $\eta_X[\rho_{HOMO}(\vec{r})]$ is always to reduce the global hardness value.
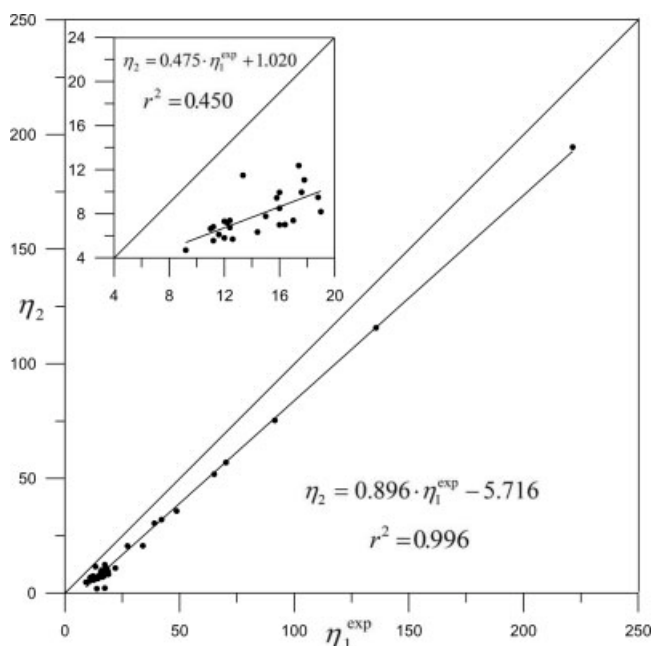
311++G(2d,2p), and B3LYP/6-31+G(d) levels of theory, and one can conclude that the origin of this error must be in the approximations used in the hardness kernel and/or Fukui functions and, at least for F_2, to the need of a better treatment of electron correlation.[77–79] HF and F_2 have not been included in the zoom of the neutral species in Figures 1–3.

In addition to the study of the validity of $\eta[\rho_{HOMO}(\vec{r})]$ as a measure of hardness, we were also interested in the analysis of the behavior and importance of its three components, namely, $\eta_T[\rho_{HOMO}(\vec{r})]$, $\eta_X[\rho_{HOMO}(\vec{r})]$, and $\eta_J[\rho_{HOMO}(\vec{r})]$. By inspection of Table 1, it is clear that $\eta_J[\rho_{HOMO}(\vec{r})]$ represents in most cases the main contribution to $\eta[\rho_{HOMO}(\vec{r})]$, although for some cations the kinetic contribution can be as important as the coulombic term and for neutral molecules the contribution of $\eta_T[\rho_{HOMO}(\vec{r})]$ is smaller but not negligible. For instance, although for neutral molecules the $\eta_T[\rho_{HOMO}(\vec{r})]$ contribution is smaller than 35% of the total, for cationic species it can represent more than 50% (e.g., Li$^+$ 54.9%, Be^{2+} 62.5%, and B^{3+} 67.9%). In contrast, the contribution of $\eta_X[\rho_{HOMO}(\vec{r})]$ is always smaller than 6.0% of the total, indicating the minor effect of this term in the global hardness. Nevertheless, its contribution in the "exact" Hohenberg–Kohn universal functional case could be more important because of the simple approximation used in our work to evaluate the exchange contribution. It is important to remark that Liu et al.[32] have arrived at similar conclusions for the neutral atoms ($Z = 1 \rightarrow 54$), i.e., coulombic term is the major component of the hardness kernel and the inclusion of the kinetic and exchange-correlation contributions does not provide significant improvements of the global hardness. However, our results show that the kinetic contribution for some systems can be as important as the coulombic term.

Figure 2. Correlation between the experimental hardness and the global hardness calculated from eq. (6) for the cations and neutral molecules studied in this work. The correlation for the neutral molecules, except F_2 and HF, is also given (inner plot). All values are given in eV.
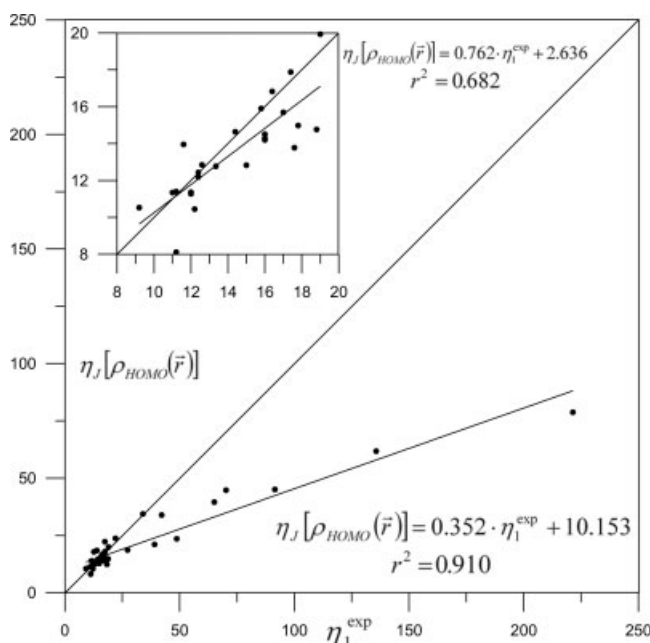
Figure 3. Correlation between the experimental hardness and the electron–electron coulombic contribution to the global hardness calculated from eq. (22) for the cations and neutral molecules studied in this work. The correlation for the neutral molecules, except F_2 and HF, is also given (inner plot). All values are given in eV.

On the basis of the expected chemical behavior of atomic hardnesses through the periodic table,[9,80,81] one can expect the following trends

$$
\begin{aligned}
&i)\ \ \eta(\text{HF}) > \eta(\text{HCl}) \\
&ii)\ \ \eta(\text{H}_2\text{O}) > \eta(\text{H}_2\text{S}) \\
&iii)\ \ \eta(\text{NH}_3) > \eta(\text{PH}_3) > \eta(\text{AsH}_3) \\
&iv)\ \ \eta(\text{HF}) > \eta(\text{H}_2\text{O}) > \eta(\text{NH}_3) \\
&v)\ \ \eta(\text{HCl}) > \eta(\text{H}_2\text{S}) > \eta(\text{PH}_3) \\
&vi)\ \ \eta(\text{Li}^+) > \eta(\text{Na}^+) > \eta(\text{K}^+) \\
&vii)\ \ \eta(\text{Be}^{2+}) > \eta(\text{Mg}^{2+}) > \eta(\text{Ca}^{2+}) \\
&viii)\ \ \eta(\text{B}^{3+}) > \eta(\text{Al}^{3+}) > \eta(\text{Ga}^{3+}) \\
&ix)\ \ \eta(\text{B}^{3+}) > \eta(\text{Be}^{2+}) > \eta(\text{Li}^+) \\
&x)\ \ \eta(\text{Al}^{3+}) > \eta(\text{Mg}^{2+}) > \eta(\text{Na}^+) \\
&xi)\ \ \eta(\text{F}_2) > \eta(\text{Cl}_2).
\end{aligned}
\tag{26}
$$

These 11 relationships are followed by $\eta_T[\rho_{\text{HOMO}}(\vec{r})]$, $|\eta_X[\rho_{\text{HOMO}}(\vec{r})]|$, $\eta_J[\rho_{\text{HOMO}}(\vec{r})]$, $\eta[\rho_{\text{HOMO}}(\vec{r})]$, and η_2, with the exceptions of $\eta(\text{NH}_3) > \eta(\text{PH}_3)$ for η_2 and $\eta(\text{H}_2\text{S}) > \eta(\text{PH}_3)$ for $\eta_J[\rho_{\text{HOMO}}(\vec{r})]$ and η_2 (see Table 1). It is worth noting that the experimental value of the hardness for PH$_3$ is 0.2 eV smaller than for AsH$_3$, contrary to the chemical intuition. This is in agreement with previous calculations reported by Chattaraj et al.[82,83] In addition, Giju et al.[80] recently presented a similar situation in the theoretical and experimental hardness sequence for the isolated atoms of the neighboring group IV elements (C > Pb > Si > Ge > Sn), which is opposed to the trends of decreasing hardness when going down in the Periodic Table.

Another interesting effect to consider is that the electron-donating character ($+I$) of the alkyl substituents makes the oxygen atom of methanol richer in electrons than the oxygen atom of water. Thus, the oxygen atom of methanol will more easily transfer its electrons (small ionization potential), and as a consequence, methanol should be softer than water. Consequently, one can expect the following trends, which are supported by experimental results[9]

$$
\begin{aligned}
&i)\ \ \eta(\text{HF}) > \eta(\text{CH}_3\text{F}) \\
&ii)\ \ \eta(\text{H}_2\text{O}) > \eta(\text{CH}_3\text{OH}) > \eta(\text{CH}_3\text{OCH}_3) \\
&iii)\ \ \eta(\text{HCl}) > \eta(\text{CH}_3\text{Cl}) \\
&iv)\ \ \eta(\text{H}_2\text{S}) > \eta(\text{CH}_3\text{SCH}_3) \\
&v)\ \ \eta(\text{NH}_3) > \eta(\text{NH}_2\text{CH}_3) > \eta(\text{N}(\text{CH}_3)_3).
\end{aligned}
\tag{27}
$$

All methods used in Table 1 fulfill the relations given by eq. (27), showing the capability of these methodologies to quantify the electron-donating effect in the hardness.

The ethylene molecule (a soft Lewis Base with η_1^{exp} of 12.4 eV)[74] represents an interesting test to evaluate the efficiency of the different hardness methodologies. For instance, η_2 yields a hardness for ethene higher than (or similar to) typical hard systems (e.g. NH$_3$, NH$_2$CH$_3$, and CH$_3$OCH$_3$). In contrast, $\eta[\rho_{\text{HOMO}}(\vec{r})]$ correctly predicts C$_2$H$_4$ as a soft Lewis base and just deviates by 2.1 eV from the experimental value. Other appealing tests are the SO$_3$ and SO$_2$ molecules, because their experimental hardness values are very similar (11.0 and 11.2 eV,[74] respectively). While η_2 yields a difference of 1.0 eV between the two systems, $\eta[\rho_{\text{HOMO}}(\vec{r})]$ predicts a difference less than 0.4 eV.

Finally, it is interesting to note that the hardness of some of the 40 neutral molecules and cations had been previously studied by some of us.[37,38] We obtained similar estimations as in the present work even though the approximations applied for the hardness kernel and Fukui functions were different. While more simplified hardness kernels ($(1/\|\vec{r} - \vec{r}'\|$ and $\delta(\vec{r} - \vec{r}'))$ were taken into account, the approximated Fukui functions were, in principle, of "better" quality ($f^-(\vec{r}) \cong \rho_N(\vec{r}) - \rho_{N-1}(\vec{r})$). This suggests that a methodology that includes both the kinetic and exchange-correlation contribution and the finite difference Fukui functions will likely provide better results than those of our previous and present works. The difference between the calculations of our previous works[37,38] and the present ones lies in the way to evaluate the integrals of eqs. (14) and (15). While the integrals required in the former could be analytically calculated with the MESSEM program,[84,85] most of the integrals required in eqs. (19) and (22) must be evaluated numerically. In addition, our present implementation of eqs. (19) and (22) is currently restricted to closed-shell wavefunctions. Since the finite difference approximation ($f^-(\vec{r}) \cong \rho_N(\vec{r}) - \rho_{N-1}(\vec{r})$) involves the density of an open-shell species, we have been compelled to use $\rho_{\text{HOMO}}(\vec{r})$ as approximation for the Fukui function. Additional work on the improvement of the Fukui functions and the kinetic and exchange-correlation contributions is presently in progress in our laboratory.

Table 2 presents the results for 16 anions for the different methodologies studied. From an experimental point of view it is very difficult to evaluate their electron affinity and hardness because of the instability of these systems when an extra electron

is added. In these systems, the absolute value of the electron affinity can be larger than that of the ionization potential as expected for a molecule that has already an excess of electrons. Similarly to the tendencies of eq. (26), one can expect the following sequences that reflect the patterns of atomic polarizabilities and hardnesses through the periodic table

$$
\begin{aligned}
i)&\ \eta(\mathrm{F}^-) > \eta(\mathrm{Cl}^-) > \eta(\mathrm{Br}^-)\\
ii)&\ \eta(\mathrm{OH}^-) > \eta(\mathrm{SH}^-)\\
iii)&\ \eta(\mathrm{NH}_2^-) > \eta(\mathrm{PH}_2^-)\\
iv)&\ \eta(\mathrm{F}^-) > \eta(\mathrm{OH}^-) > \eta(\mathrm{NH}_2^-) > \eta(\mathrm{CH}_3^-) \quad (28)\\
v)&\ \eta(\mathrm{Cl}^-) > \eta(\mathrm{SH}^-)\\
vi)&\ \eta(\mathrm{PH}_2^-) > \eta(\mathrm{SiH}_3^-)\\
vii)&\ \eta(\mathrm{CH}_3^-) > \eta(\mathrm{SiH}_3^-).
\end{aligned}
$$

These seven relationships are only fulfilled by $\eta_T[\rho_{\mathrm{HOMO}}(\vec{r})]$, while $|\eta_X[\rho_{\mathrm{HOMO}}(\vec{r})]|$, $\eta_J[\rho_{\mathrm{HOMO}}(\vec{r})]$, and $\eta[\rho_{\mathrm{HOMO}}(\vec{r})]$ fail in the vi case. In contrast, η_2 correctly predicts only three of them, indicating the bad behavior of the HOMO-LUMO gap as chemical hardness indicator for anionic systems.

On the other hand, the substitution of a hydrogen atom by an alkyl group produces an electron-withdrawing effect ($-I$), which leads to the delocalization of the electronic density of the central atom into the alkyl group.[37,86] Then, the alkyl group generates a softer system with a more polarizable electronic cloud. Consequently, one can expect the following additional trends

$$
\begin{aligned}
i)&\ \eta(\mathrm{OH}^-) > \eta(\mathrm{CH}_3\mathrm{O}^-)\\
ii)&\ \eta(\mathrm{SH}^-) > \eta(\mathrm{CH}_3\mathrm{S}^-) \quad (29)\\
iii)&\ \eta(\mathrm{NH}_2^-) > \eta(\mathrm{CH}_3\mathrm{NH}^-) > \eta(\mathrm{CH}_3\mathrm{NCH}_3^-).
\end{aligned}
$$

Again, all methods of Table 2 satisfy these relationships except for η_2, which predicts $\eta(\mathrm{CH}_3\mathrm{NCH}_3^-) > \eta(\mathrm{CH}_3\mathrm{NH}^-)$.

All these relationships for anionic species have been summarized in Table 3, which contains the hardness classification of these anions for the different methodologies used. Dark grey cells represent hard systems according to the qualitative classification of Lewis acids and bases put forward by Pearson,[9] while grey and white cells represent borderline and soft species, respectively. The failure of η_2 is obvious. For instance, classical soft systems like H^- and SH^- are predicted harder than classical hard systems like OH^- and NH_2^-. In contrast, the results obtained with $\eta_T[\rho_{\mathrm{HOMO}}(\vec{r})]$, $\eta_J[\rho_{\mathrm{HOMO}}(\vec{r})]$, and $\eta[\rho_{\mathrm{HOMO}}(\vec{r})]$ almost completely reproduce Pearson's qualitative ordering.[9] In fact, the only important failure of $\eta[\rho_{\mathrm{HOMO}}(\vec{r})]$ is the slight overestimation of the $\mathrm{NO}_2{}^-$ hardness with respect to $\mathrm{CH}_3\mathrm{NCH}_3^-$.

Finally, it is worth noting that the same set of anionic molecules were considered in a similar study of some of us where $\delta(\vec{r} - \vec{r}\prime)$ and $f^-(\vec{r}) \cong \rho_N(\vec{r}) - \rho_{N-1}(\vec{r})$ were used as hardness kernel and Fukui function, respectively.[37] In that case, the qualitative ordering of Pearson was perfectly reproduced. Therefore, one can conclude that the quality of the Fukui function seems to be more important than the quality of the hardness kernel itself in the evaluation of global hardness, at least as far as the anionic species is concerned.

Conclusions

In this work we have evaluated for the first time the global hardness for polyatomic molecules by proper numerical integration of a hardness kernel using $\rho_{\mathrm{HOMO}}(\vec{r})$ as approximation for the Fukui function and the Thomas–Fermi and Dirac models as approximations of the kinetic and exchange contributions to the kernel. This methodology has been applied to 40 cations and neutral systems and 16 anions, giving in most cases an improvement of the results obtained using the HOMO-LUMO gap approach for the hardness calculation, especially in the case of the anionic species. We have shown that for neutral systems the coulombic term is the main contribution (more of the 65%) of the global hardness obtained from the hardness kernel although the kinetic contribution must be included too so as to obtain accurate hardness values. In contrast, for some cationic species the kinetic term of the hardness kernel can become the larger contribution to the global hardness. Also, this work shows that the quality of the Fukui function becomes crucial so as to obtain reliable hardness values. Additional work on the improvement of the present methodology and the determination of fragment or atomic contributions by local integration of the hardness kernel are in progress in our laboratory.

References

1. Koch, W.; Holthausen, M. C. Chemist's Guide to Density Functional Theory; Wiley-VCH: Weinheim, 2000.
2. Parr, R. G.; Yang, W. Density-Functional Theory of Atoms and Molecules; Oxford Univesity Press: New York, 1989.
3. Parr, R. G.; Yang, W. T. Annu Rev Phys Chem 1995, 46, 701.
4. Chermette, H. J Comput Chem 1999, 20, 129.
5. Geerlings, P.; De Proft, F.; Langenaeker, W. Chem Rev 2003, 103, 1793.
6. Parr, R. G.; Donnelly, R. A.; Levy, M.; Palke, W. E. J Chem Phys 1978, 68, 3801.
7. Parr, R. G.; Pearson, R. G. J Am Chem Soc 1983, 105, 7512.
8. Parr, R. G.; Yang, W. T. J Am Chem Soc 1984, 106, 4049.
9. Pearson, R. G. Chemical Hardness: Applications from Molecules to Solids; Wiley-VCH: Oxford, 1997.
10. Pearson, R. G. J Chem Edu 1987, 64, 561.
11. Ayers, P. W.; Parr, R. G.; Pearson, R. G. J Chem Phys 2006, 124, 194107.
12. Ayers, P. W. J Chem Phys 2005, 122, 141102.
13. Chattaraj, P. K.; Lee, H.; Parr, R. G. J Am Chem Soc 1991, 113, 1855.
14. Sanderson, R. T. Science 1951, 114, 670.
15. Sanderson, R. T. Science 1955, 121, 207.
16. Pearson, R. G. J Chem Edu 1999, 76, 267.
17. Parr, R. G.; Chattaraj, P. K. J Am Chem Soc 1991, 113, 1854.
18. Zhou, Z. X.; Parr, R. G. J Am Chem Soc 1989, 111, 7371.
19. Ayers, P. W.; Parr, R. G. J Am Chem Soc 2000, 122, 2010.
20. Chattaraj, P. K.; Sengupta, S. J Phys Chem 1996, 100, 16126.
21. Kohn, W.; Becke, A. D.; Parr, R. G. J Phys Chem 1996, 100, 12974.
22. Perdew, J. P.; Parr, R. G.; Levy, M.; Balduz, J. L. Phys Rev Lett 1982, 49, 1691.
23. Nguyen-Dang, T. T.; Bader, R. F. W.; Essen, H. Int J Quantum Chem 1982, 22, 1049.
24. Fuentealba, P. J Mol Struct (THEOCHEM) 1998, 433, 113.
25. Ayers, P. W.; Levy, M. Theor Chem Acc 2000, 103, 353.
26. Senet, P. Chem Phys Lett 1997, 275, 527.

27. Tozer, D. J.; De Proft, F. J Phys Chem A 2005, 109, 8923.
28. Balawender, R.; Geerlings, P. J Chem Phys 2005, 123, 124102.
29. Balawender, R.; Geerlings, P. J Chem Phys 2005, 123, 124103.
30. Chattaraj, P. K.; Cedillo, A.; Parr, R. G. J Chem Phys 1995, 103, 7645.
31. Berkowitz, M.; Parr, R. G. J Chem Phys 1988, 88, 2554.
32. Liu, S. B.; De Proft, F.; Parr, R. G. J Phys Chem A 1997, 101, 6991.
33. Ghanty, T. K.; Ghosh, S. K. J Phys Chem 1994, 98, 9197.
34. Garza, J.; Robles, J. Int J Quantum Chem 1994, 49, 159.
35. Chattaraj, P. K.; Cedillo, A.; Parr, R. G. J Chem Phys 1995, 103, 10621.
36. Fuentealba, P. J Chem Phys 1995, 103, 6571.
37. Torrent-Sucarrat, M.; Luis, J. M.; Duran, M.; Solà, M. J Mol Struct (THEOCHEM) 2005, 727, 139.
38. Torrent-Sucarrat, M.; Duran, M.; Solà, M. J Phys Chem A 2002, 106, 4632.
39. Ayers, P. W. Theor Chem Acc 2001, 106, 271.
40. Koopmans, T. Physica (Utrecht) 1934, 1, 104.
41. Ghosh, S. K.; Berkowitz, M. J Chem Phys 1985, 83, 2976.
42. Berkowitz, M.; Ghosh, S. K.; Parr, R. G. J Am Chem Soc 1985, 107, 6811.
43. Hirao, H.; Ohwada, T. J Phys Chem A 2005, 109, 816.
44. Morell, C.; Grand, A.; Toro-Labbé, A. J Phys Chem A 2005, 109, 205.
45. Roy, R. K.; Krishnamurti, S.; Geerlings, P.; Pal, S. J Phys Chem A 1998, 102, 3746.
46. Gilardoni, F.; Weber, J.; Chermette, H.; Ward, T. R. J Phys Chem A 1998, 102, 3607.
47. Langenaeker, W.; De Proft, F.; Geerlings, P. J Phys Chem 1995, 99, 6424.
48. Chattaraj, P. K.; Nath, S. Chem Phys Lett 1994, 217, 342.
49. Gázquez, J. L.; Vela, A.; Galván, M. Struct Bond 1987, 66, 79.
50. Harbola, M. K.; Chattaraj, P. K.; Parr, R. G. Isr J Chem 1991, 31, 395.
51. Meneses, L.; Tiznado, W.; Contreras, R.; Fuentealba, P. Chem Phys Lett 2004, 383, 181.
52. Thomas, L. H. Proc Cambridge Philos Soc 1927, 23, 542.
53. Fermi, E. Z Phys 1928, 48, 73.
54. Dirac, P. M. A. Proc Cambridge Philos Soc 1930, 26, 376.
55. Balazs, N. L. Phys Rev 1967, 156, 42.
56. Lieb, E. H.; Simon, B. Adv Math 1977, 23, 22.
57. Lieb, E. H.; Simon, B. Phys Rev Lett 1973, 31, 681.
58. von Weizsäcker, C. F. Z Phys 1936, 96, 431.
59. Wigner, E. P. Phys Rev 1934, 46, 1002.
60. Liu, S.; Sule, P.; LopezBoada, R.; Nagy, A. Chem Phys Lett 1996, 257, 68.
61. Liu, S. B.; Parr, R. G. Phys Rev A 1996, 53, 2211.
62. Garza, J.; Vela, A. Phys Rev A 1998, 58, 3358.
63. Becke, A. D. J Chem Phys 1988, 88, 2547.
64. Hirshfeld, F. L. Theor Chim Acc 1977, 44, 129.
65. Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Montgomery J. A., Jr.; Vreven, T.; Kudin, K. N.; Burant, J. C.; Millam, J. M.; Iyengar, S. S.; Tomasi, J.; Barone, V.; Mennucci, B.; Cossi, M.; Scalmani, G.; Rega, N.; Petersson, G. A.; Nakatsuji, H.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Klene, M.; Li, X.; Knox, J. E.; Hratchian, H. P.; Cross, J. B.; Bakken, V.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Ayala, P. Y.; Morokuma, K.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Zakrzewski, G.; Dapprich, S.; Daniels, A. D.; Strain, M. C.; Farkas, O.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Ortiz, J. V.; Cui, Q.; Baboul, A. G.; Clifford, S.; Cioslowski, J.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Challacombe, M.; Gill, P. M. W.; Johnson, B.; Chen, W.; Wong, M. W.; Gonzalez, C.; Pople, J. A. Gaussian 03; Gaussian: Pittsburgh, PA, 2003.
66. Slater, J. C. J Chem Phys 1964, 41, 3199.
67. Lebedev, V. I.; Laikov, D. N. Dokl Math 1999, 366, 741.
68. Computational Chemistry List (CCL) archives: Available at www.ccl.net/cca/software/SOURCES/FORTRAN/Lebedev-Laikov-Grids/Lebedev-Laikov.F
69. Dupuis, M.; Farazdel, A.MOTECC-91;Center for Scientific and Engineering Computations, IBM Corporation: Kingstom, NY, 1991.
70. Salvador, P.; Mayer, I. J Chem Phys 2004, 120, 5046.
71. Hehre, W. J.; Ditchfield, R.; Pople, J. A. J Chem Phys 1972, 56, 2257.
72. Becke, A. D. J Chem Phys 1993, 98, 5648.
73. Lee, C. T.; Yang, W. T.; Parr, R. G. Phys Rev B 1988, 37, 785.
74. Pearson, R. G. Inorg Chem 1988, 27, 734.
75. Page, F. M.; Goode, G. C. Negative Ions and the Magnetron; Wiley: New York, 1969.
76. Ayers, P. W.; Morrison, R. C.; Parr, R. G. Mol Phys 2005, 103, 2061.
77. Solà, M.; Mestres, J.; Carbó, R.; Duran, M. J Chem Phys 1996, 104, 636.
78. Blomberg, M. R. A.; Siegbahn, P. E. M. Chem Phys Lett 1981, 81, 4.
79. Jonsson, B.; Roos, B. O.; Taylor, P. R.; Siegbahn, P. E. M. J Chem Phys 1981, 74, 4566.
80. Giju, K. T.; De Proft, F.; Geerlings, P. J Phys Chem A 2005, 109, 2925.
81. De Proft, F.; Langenaeker, W.; Geerlings, P. J Phys Chem 1993, 97, 1826.
82. Chattaraj, P. K.; Schleyer, P. V. R. J Am Chem Soc 1994, 116, 1067.
83. Chattaraj, P. K.; Gomez, B.; Chamorro, E.; Santos, J.; Fuentealba, P. J Phys Chem A 2001, 105, 8815.
84. Mestres, J.; Solà, M.; Besalú, E.; Duran, M.; Carbó, R. MESSEM; CAT: Girona, 1993.
85. Besalú, E.; Carbó, R.; Duran, M.; Mestres, J.; Solà, M. In Methods and Techniques in Computational Chemistry (METECC-95); Clementi, E.; Corongiu, G., Eds.; STEF: Cagliari, 1995, p.491.
86. De Proft, F.; Langenaeker, W.; Geerlings, P. Tetrahedron 1995, 51, 4021.