

Computing Second-Order Functional Derivatives with Respect to the External Potential

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Abstract: Following the increasing interest in the higher-order (functional) derivatives of conceptual density functional theory, we developed and implemented a method for calculating second-order functional derivatives with respect to the external potential. Our method is theoretically exact but involves two numerical approximations: the functional derivatives are expanded in a basis set, and the values of the corresponding expansion coefficients are determined by probing the molecular environment by a finite set of external potential perturbations. Exact solutions are obtained only in the limit of a complete basis set and an infinite number of distinct perturbations. We use this method to compute the atom-condensed linear response kernel for a series of six molecules and show that the results are comparable to the ones obtained by a previously proposed, approximate approach from second-order perturbation theory. The numerical error of the current implementation is about 0.01 au. Because the present method gives exact or quasi-exact solutions, it can be used as a benchmark against which approximate approaches are assessed.

1. Introduction

The interpretation of chemical reactivity on the basis of response functions is the central concern of conceptual or chemical density functional theory (DFT).^{1–5} Concepts of chemical relevance are defined as derivatives of the electronic energy E with respect to the number of electrons N or as functional derivatives of E with respect to the external potential $v(\mathbf{r})$, which is the electron–nuclear potential for isolated systems (in au):

$$v(\mathbf{r}) = - \sum_{\alpha} \frac{Z_{\alpha}}{|\mathbf{r} - \mathbf{R}_{\alpha}|} \quad (1)$$

The sum runs over all the atomic nuclei with nuclear charges Z_{α} and positions \mathbf{R}_{α} . Fundamental chemical reactivity

indicators include the electronic chemical potential μ ,^{6,7} the chemical hardness η ,^{8,9} the electron density $\rho(\mathbf{r})$, and the Fukui function $f(\mathbf{r})$,^{10,11} which have been defined as

$$\mu = \left(\frac{\partial E}{\partial N} \right)_{v(\mathbf{r})} \quad (2)$$

$$\eta = \left(\frac{\partial^2 E}{\partial N^2} \right)_{v(\mathbf{r})} \quad (3)$$

$$\rho(\mathbf{r}) = \left(\frac{\delta E}{\delta v(\mathbf{r})} \right)_N \quad \text{and} \quad (4)$$

$$f(\mathbf{r}) = \left(\frac{\partial}{\partial N} \left(\frac{\delta E}{\delta v(\mathbf{r})} \right) \right)_{v(\mathbf{r})} \quad (5)$$

These and other derived quantities characterize the chemical behavior of individual molecules by assessing their response to model perturbations without the explicit description of the partner reagents. Such chemical reactivity indicators have been applied in many studies in order to interpret both

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theoretical and experimental data on various types of chemical reactions.³

The mixed derivative of eq 5, the Fukui function, can be written in either of two ways:

$$f^{\pm}(\mathbf{r}) = \left(\frac{\partial \rho(\mathbf{r})}{\partial N} \right)_{\nu(\mathbf{r})}^{\pm} \quad \text{or} \quad (6)$$

$$f^{\pm}(\mathbf{r}) = \left(\frac{\delta \mu^{\pm}}{\delta \nu(\mathbf{r})} \right)_N \quad (7)$$

The “ \pm ” sign indicates that the derivatives with respect to the electron number should be evaluated from the left- or right-hand side. As shown by Perdew et al.⁷ in a zero-temperature grand canonical ensemble framework, these derivatives of the electronic energy E and electron density $\rho(\mathbf{r})$ are discontinuous at integer electron number (which is always the case for isolated systems). The most common approach for evaluating the Fukui functions is based on a finite difference approximation of eq 6:

$$f_{N_0}^{-}(\mathbf{r}) = \rho_{N_0}(\mathbf{r}) - \rho_{N_0-1}(\mathbf{r}) \quad \text{and} \quad (8)$$

$$f_{N_0}^{+}(\mathbf{r}) = \rho_{N_0+1}(\mathbf{r}) - \rho_{N_0}(\mathbf{r}) \quad (9)$$

where the Fukui functions of a system consisting of N_0 electrons are obtained in terms of the electron densities of the N_0 , $(N_0 - 1)$, and $(N_0 + 1)$ electron systems. Although relations (eqs 8 and 9) are exact for solutions to the Schrödinger equation, they are inexact for most approximate computational methods.^{11–13} This observation led the present authors to explore a different route, namely the calculation of the functional derivative of the chemical potential with respect to the external potential (eq 7).^{14,15} A general numerical procedure to compute the first-order functional derivative of any quantity with respect to the external potential was developed for this purpose; the basic idea is to use the computed responses of the quantity under consideration upon external potential perturbations to calculate the expansion coefficients for the desired functional derivative. This methodology has been extensively analyzed and applied in a series of papers. In the first paper,¹⁴ the theoretical background to this methodology was presented, focusing on the accurate calculation of the Fukui function for the beryllium atom and formaldehyde molecule. A second contribution¹⁵ dealt with the calculation of atom-condensed Fukui functions for a range of molecules, including mono-substituted benzenes. A detailed study of the locally resolved Fukui function and dual descriptor was provided in a third contribution.¹⁶ The most recent paper in this series¹⁷ employed the approach in the reactivity description of alkaline earth metal oxide clusters, thus avoiding periodic boundary condition calculations for this kind of system, and introduced the concept of the molecular orbital-averaged Fukui function, which takes the reactivity information of various molecular orbitals (MOs) into account.

The purpose of this article is the calculation of second-order functional derivatives with respect to the external potential. Building upon our previous work, we will present the necessary theory for and practical implementation of the

methodology. The numerical results in this contribution concentrate on the linear response or polarizability kernel $\chi(\mathbf{r}, \mathbf{r}')$,^{18,19} defined as

$$\chi(\mathbf{r}, \mathbf{r}') = \left(\frac{\delta^2 E}{\delta \nu(\mathbf{r}) \delta \nu(\mathbf{r}')} \right)_N = \left(\frac{\delta \rho(\mathbf{r})}{\delta \nu(\mathbf{r}')} \right)_N \quad (10)$$

and, more specifically, on the direct calculation of the atom-condensed linear response. The computation of other quantities is, however, within our reach. One could think, for example, of the Fukui kernels $f^{\pm}(\mathbf{r}, \mathbf{r}')$:^{19–21}

$$f^{\pm}(\mathbf{r}, \mathbf{r}') = \left(\frac{\delta^2 \mu^{\pm}}{\delta \nu(\mathbf{r}) \delta \nu(\mathbf{r}')} \right)_N = \left(\frac{\delta f^{\pm}(\mathbf{r})}{\delta \nu(\mathbf{r}')} \right)_N \quad (11)$$

which take polarization effects on the Fukui functions into account, as the linear response kernel does for the electron density.

Several authors have been showing an increased interest in the higher-order (functional) derivatives of conceptual DFT.^{22–26} In the case of the linear response kernel, this has led to a number of papers devoted to the formulation of its theoretical properties and formal solutions. The fundamental role of the linear response kernel is highlighted by the Berkowitz–Parr equation:¹⁸

$$\chi(\mathbf{r}, \mathbf{r}') = -s(\mathbf{r}, \mathbf{r}') + \frac{s(\mathbf{r})s(\mathbf{r}')}{S} \quad (12)$$

which relates the linear response kernel to the softness kernel $s(\mathbf{r}, \mathbf{r}')$, the local softness $s(\mathbf{r})$, and the global softness S . The softness kernel, which is defined as

$$s(\mathbf{r}, \mathbf{r}') = -\frac{\delta \rho(\mathbf{r})}{\delta u(\mathbf{r}')} \quad (13)$$

is, in turn, the inverse of the hardness kernel $\eta(\mathbf{r}, \mathbf{r}')$:^{18,27}

$$\int s(\mathbf{r}, \mathbf{r}') \eta(\mathbf{r}', \mathbf{r}'') d\mathbf{r}' = \delta(\mathbf{r} - \mathbf{r}'') \quad (14)$$

which is ultimately connected to the local hardness $\eta(\mathbf{r})$.^{28–32} Senet¹⁹ derived exact functional relations between the linear and nonlinear response functions and the ground-state electron density in terms of the universal Hohenberg–Kohn functional $F[\rho]$. Theoretical expressions for and the mutual relations between the linear and nonlinear responses and the softness and hardness kernels have been elaborated within a Kohn–Sham (KS) formalism.^{33–35} The linear response kernel can also be obtained as the zero-frequency limit of the dynamic linear response kernel in time-dependent DFT.¹ A recent paper by Liu et al.³⁶ summarizes the most important mathematical properties of $\chi(\mathbf{r}, \mathbf{r}')$.

There are very few numerical results on the linear response function in the context of conceptual DFT, and they are typically obtained in approximate manners, without explicitly evaluating the second-order functional derivative. We should mention the studies of Baekelandt et al.³⁷ and Wang et al.,³⁸ in which atom-condensed linear response matrices are calculated within the context of the electronegativity equalization method (EEM).³⁹ Numerical data are also given in some papers by Morita and Kato,^{40–42} where this quantity is obtained by solving the coupled-perturbed Hartree–Fock

(HF) or KS equations. Their work is based on the ideas of Stone and Alderton,⁴³ who analyzed dipole and multipole polarizabilities and has been extended by Yang et al.⁴⁴ The explicit calculation of the response $\Delta\rho(\mathbf{r})$ of the electron density upon a point charge perturbation in the external potential has been analyzed for various atoms.⁴⁵ Related work has also been done by Cedillo et al.⁴⁶ Cioslowski and Martinov have calculated approximate atomic softness matrices, which can be interpreted as the negatives of approximate linear response matrices.⁴⁷ Some of the present authors calculated the atom-condensed linear response kernel within the context of second-order perturbation theory and proposed a sound basis for its chemical interpretation:^{48,49} They have shown that the linear response kernel measures the extent of electron delocalization, providing a way to differentiate between inductive, resonance, and hyperconjugation effects.

This paper is organized as follows: the theoretical background for the methodology to evaluate second-order functional derivatives will be given in Section 2; Section 3 is concerned with a detailed description of the computational algorithm that implements the presented theory; and numerical data are given in Section 4, where some relevant test systems are analyzed in order to illustrate and validate the proposed methodology. Some final theoretical considerations are made in the Appendix.

2. Theoretical Background

One could seek to formulate analytic expressions for second-order functional derivatives of a given property with respect to the external potential corresponding to a specific theoretical level (e.g., HF or KS DFT with a certain exchange-correlation functional). We will, however, develop a numerical procedure that is able to evaluate these functional derivatives of any property P independently from the theoretical level. The starting point for our approach is provided by a functional Taylor series⁴ of P for which the initial (or unperturbed) external potential $v(\mathbf{r})$ is perturbed by $w(\mathbf{r})$. This yields the next expression, where third- and higher-order terms in the norm of the perturbation are neglected:

$$P[v(\mathbf{r}) + w(\mathbf{r})] = P[v(\mathbf{r})] + \int \left(\frac{\delta P}{\delta v(\mathbf{r})} \right)_N w(\mathbf{r}) d\mathbf{r} + \frac{1}{2} \iint \left(\frac{\delta^2 P}{\delta v(\mathbf{r}) \delta v(\mathbf{r}')} \right)_N w(\mathbf{r}) w(\mathbf{r}') d\mathbf{r} d\mathbf{r}' + \mathcal{O}(\|w(\mathbf{r})\|^3) \quad (15)$$

The functional derivatives, $(\delta P / \delta v(\mathbf{r}))_N$ and $(\delta^2 P / \delta v(\mathbf{r}) \delta v(\mathbf{r}'))_N$, are evaluated at the unperturbed external potential $v(\mathbf{r})$. So long as the perturbation $w(\mathbf{r})$ is small enough, this second-order truncation does not introduce a significant error. Construction of an analogous equation for an external potential perturbation of $-w(\mathbf{r})$ and addition to eq 15 gives

$$P[v(\mathbf{r}) + w(\mathbf{r})] - 2P[v(\mathbf{r})] + P[v(\mathbf{r}) - w(\mathbf{r})] = \iint \left(\frac{\delta^2 P}{\delta v(\mathbf{r}) \delta v(\mathbf{r}')} \right)_N w(\mathbf{r}) w(\mathbf{r}') d\mathbf{r} d\mathbf{r}' \quad (16)$$

We will now expand the second-order functional derivative in a basis set $\{\beta_k(\mathbf{r})\}_{k=1}^K$ as follows

$$\left(\frac{\delta^2 P}{\delta v(\mathbf{r}) \delta v(\mathbf{r}')} \right)_N = \sum_{k=1}^K \sum_{l=1}^K q_{kl} \beta_k(\mathbf{r}) \beta_l(\mathbf{r}') \quad (17)$$

This basis set expansion is mathematically rigorous if the quantity P is the electronic energy or one of its first- or higher-order (functional) derivatives with respect to the electron number or external potential.^{14,50} If the set $\{\beta_k(\mathbf{r})\}_{k=1}^\infty$ spans the function space of electron densities, eq 17 converges toward the exact functional derivative as $K \rightarrow \infty$.¹⁴ To determine the expansion coefficients, q_{kl} , insert eq 17 into eq 16 and consider a set of external potential perturbations $\{w_j(\mathbf{r})\}_{j=1}^J$, $J \geq K$, instead of the single perturbation $w(\mathbf{r})$ in eq 16. A set of simultaneous linear equations results, which can be solved for the expansion coefficients, and thus enables the calculation of the desired second-order functional derivative. This set of equations can be written as

$$\mathbf{D} = \mathbf{B}\mathbf{Q} \quad (18)$$

The J -dimensional column matrix \mathbf{D} consists of the responses of quantity P upon the various external potential perturbations:

$$D_j = P[v(\mathbf{r}) + w_j(\mathbf{r})] - 2P[v(\mathbf{r})] + P[v(\mathbf{r}) - w_j(\mathbf{r})], \quad \text{with } j = 1, \dots, J \quad (19)$$

A vital requirement for our methodology is that these responses can be obtained, which is rarely an obstacle since most quantum chemical program packages can provide the necessary information. The $J \times K^2$ matrix \mathbf{B} is comprised of the integrals over the various basis functions and the external potential perturbations:

$$B_{j,(k-1)K+l} = \int \beta_k(\mathbf{r}) w_j(\mathbf{r}) d\mathbf{r} \int \beta_l(\mathbf{r}') w_j(\mathbf{r}') d\mathbf{r}', \quad \text{with } j = 1, \dots, J \text{ and } k, l = 1, \dots, K \quad (20)$$

These integrals can be evaluated analytically with the chosen $\{\beta_k(\mathbf{r})\}_{k=1}^K$ and $\{w_j(\mathbf{r})\}_{j=1}^J$ (vide infra). The K^2 -dimensional column matrix \mathbf{Q} , finally, contains the expansion coefficients for the second-order functional derivative:

$$Q_{(k-1)K+l} = q_{kl}, \quad \text{with } k, l = 1, \dots, K \quad (21)$$

The set of eq 18 can be solved through a linear least-squares fitting procedure, as the number of external potential perturbations (J) will exceed the number of expansion coefficients to be determined (K^2). Indeed, a large value for J is required to ensure that enough information about the molecule's responses is collected to calculate a reliable second-order functional derivative.

So far, the general theoretical framework has been outlined. As might be expected, the numerical results are also dependent upon some practical considerations; particularly upon the manner in which the external potential perturbations are modeled and upon the basis set used for the expansion of the second-order functional derivative. These specifications form the subject of the following section.

3. Computational Method

In order to ensure the reproducibility of our results, the practical side of the computational algorithm will be detailed here.

3.1. External Potential Perturbations. One of the key elements is the type of external potential perturbations that are considered. We chose to perturb the external potential by point charges so that the $\{w_j(\mathbf{r})\}_{j=1}^J$ is given by

$$w_j(\mathbf{r}) = \frac{-q_j}{|\mathbf{r} - \mathbf{R}_j|} \quad (22)$$

with q_j the charge values and \mathbf{R}_j the positions of the point charges. This type of perturbation has already proven its usefulness for calculating first-order functional derivatives. Moreover, the utility of point-charge perturbations for elucidating a molecule's reactivity is becoming increasingly apparent due to recent theoretical and computational developments.^{46,51–53}

Two molecular regions are defined; perturbations are placed on a cubic grid within these regions to ensure complete and uniform sampling. We consider three scaled van der Waals surfaces (with scaling factors: $R_{\min} < R_{\text{middle}} < R_{\max}$) to designate an inner molecular region, extending between the van der Waals surfaces scaled by the factors R_{\min} and R_{middle} and an outer region, determined analogously by R_{middle} and R_{\max} . The inner region will typically cover the space lying within the molecular van der Waals surface, excluding the nuclear zone if one is not interested in its accurate description, which is usually the case when atom-condensed properties are studied. The corresponding grid should be relatively fine so that the desired second-order functional derivative is accurately represented in this molecular region, where it fluctuates significantly because of chemical bonding and proximity to the atomic nuclei. Given the considerable electron density within this region, the charge value q_j should not be too high for the second-order truncation of eq 15 to be applicable. The point charges may assume higher values in the outer region; the corresponding grid can also be constructed more coarsely as the fluctuations in the functional derivatives will be less pronounced here. It is important to extend this outer grid rather far (up to several van der Waals radii) in order to capture all the information that is relevant to describe a system's chemical reactivity.

Once the external potential perturbations are defined, the responses of quantity P (as given by eq 19) should be determined. This is readily done by performing single point calculations of the molecule under study in the presence of one of the point charge perturbations w_j and by repeating this for all the other perturbations. For the properties we are interested in (the electronic energy, the chemical potential, etc.), any standard ab initio program can provide the necessary data.

3.2. Basis Set and Atom Condensation. The choice of a basis set for the expansion of the second-order functional derivative (eq 17) is another vital element. We have used s- and p-type Gaussian basis functions, centered on the atomic nuclei. Higher angular momentum functions could be included but are expected to induce only minor variations.^{14,15} The exponents can be chosen from standard atomic basis sets, uncontracted into primitive Gaussians, but with a doubled value. This is a consequence of the fact that the second-order functional derivatives of conceptual DFT are

related to the first-order functional derivative of the electron density $\rho(\mathbf{r})$ (see, e.g., eq 10) and that $\rho(\mathbf{r})$ decays twice as fast as the associated wave function. The exponents of auxiliary basis sets,^{54,55} which are used for the acceleration of the evaluation of the Coulomb integrals in DFT calculations, can also be used; these do not require doubling.

Computation of the atom-condensed⁵⁶ variants greatly simplifies the situation. The atom-condensed indices are normally defined as

$$P_{AB}^{(2)} = \int_{V_A} \int_{V_B} P^{(2)}(\mathbf{r}, \mathbf{r}') d\mathbf{r} d\mathbf{r}' \quad (23)$$

where $P^{(2)}(\mathbf{r}, \mathbf{r}')$ is used as a shorthand notation for the second-order functional derivative of property P and V_A and V_B denote the volumes of atoms A and B, respectively. Despite that, the basis set expansion of eq 17 provides an alternative approach:

$$P_{AB}^{(2)} = \sum_{k \in A}^K \sum_{l \in B}^K q_{kl} \int \beta_k(\mathbf{r}) d\mathbf{r} \int \beta_l(\mathbf{r}') d\mathbf{r}' \quad (24)$$

Instead of integrating the kernel $P^{(2)}(\mathbf{r}, \mathbf{r}')$ over the atomic volumes V_A and V_B , the contributions of atom A to the \mathbf{r} -dependent part and of atom B to the \mathbf{r}' -dependent part of the functional derivative are integrated over the entire space. These contributions originate from the terms in the basis set expansion for which the function $\beta_k(\mathbf{r})$ is centered on atom A and $\beta_l(\mathbf{r}')$ on atom B. It has been shown that the use of one sharp s-type Gaussian function (mimicking a Dirac δ -function) per atomic center yields reliable results for the condensed first-order functional derivatives.¹⁵ The validity of this kind of basis set in the evaluation of condensed second-order indices will be illustrated in Section 4. The requirement of sharp functions is essential for this condensation scheme. It is indeed important that the atomic contributions do not overlap because the integrations over the entire space in eq 24 would lose their relevance. It should be stressed that the use of such a simplified basis set leads to a vast reduction in the number of expansion coefficients (K^2) to be determined and hence in the computational effort.

3.3. Normalization Constraint. As the normalization of the functional derivatives is often a priori known, the user has the option to impose it as a constraint. Let us consider the case of the linear response kernel $\chi(\mathbf{r}, \mathbf{r}')$ as an example. We know that this quantity is normalized to 0 and, furthermore, that the integration over one of the position variables should give this value as well.^{18,36}

$$\int \chi(\mathbf{r}, \mathbf{r}') d\mathbf{r}' = 0 \quad (25)$$

Combination of this expression with the basis set expansion of eq 17 yields the following normalization equation:

$$\sum_{k=1}^K \sum_{l=1}^K q_{kl} \beta_k(\mathbf{r}) I_l = 0 \quad (26)$$

where I_l denotes the integral over the l -th basis function. An infinite number of such equations, corresponding to any value for the position variable \mathbf{r} , can be constructed and added to

the set of eq 18 as a constraint. In practice, a limited number of well-chosen ones suffices to obtain normalization. Numerical illustrations will be given in the next section. The use of normalization constraints is even superfluous provided that sufficient external potential perturbations are taken into account, and this is in all molecular regions, including the nuclear zone.

3.4. Symmetry. Given the extent of the computational cost of our methodology (a single point calculation for every positive and negative external potential perturbation), the implementation of symmetry properties is paramount for the reduction of this effort. Two levels of symmetry can be distinguished: the symmetry properties of the second-order functional derivative and the point group symmetry of the system under study. The first type is a consequence of the arbitrary order in which the functional derivatives with respect to $v(\mathbf{r})$ and $v(\mathbf{r}')$ are evaluated, implying that

$$P^{(2)}(\mathbf{r}, \mathbf{r}') = P^{(2)}(\mathbf{r}', \mathbf{r}) \quad (27)$$

The immediate result is that the number of expansion coefficients in eq 17 can be reduced from K^2 to $K(K+1)/2$ as q_{kl} should equal q_{lk} , which simultaneously leads to a decrease in the required number of external potential perturbations. Inclusion of molecular symmetry properties further diminishes this number. As perturbations that are linked through symmetry operations belonging to the molecular point group give rise to identical responses, it is sufficient to sample a restricted, symmetry unique portion of space and to spatially propagate the obtained responses based on the molecular symmetry elements.

3.5. Computational Procedures. A final word should be said about the computational procedures we have used. Construction of matrix **D** in eq 18 requires the calculation of quantity P in the presence and the absence of the various external potential perturbations. The Gaussian 03 program package⁵⁷ will be used to calculate the electronic energy responses, as we will be focusing on the linear response kernel in the next section; obviously, other quantities can be obtained in a similar way. Matrix **B** contains integrals over a basis function and an external potential perturbation. The use of Gaussian basis functions and point charge perturbations enables an analytic evaluation, which essentially needs the computation of the incomplete γ function. This is done by a Fortran 90 numerical recipes routine.⁵⁸ The least-squares fitting procedure chosen to solve the set of linear eq 18 is taken from LAPACK⁵⁹ and uses a singular value decomposition approach.

4. Numerical Results

In this section, the atom-condensed linear response kernel, defined by eqs 10 and 24, will be calculated for a series of simple test systems. Not only will we show the numerical data that can be obtained, but we will also explain how the various parameters that emerged from our implementation should be chosen. The results will be compared with values obtained in another manner, which was previously studied by some of the present authors.^{48,49} They used second-order perturbation theory to derive the next, approximate expres-

sion, valid for closed-shell systems described by a single Slater determinant:^{26,35,60}

$$\chi_s(\mathbf{r}, \mathbf{r}') = 4 \sum_{i=1}^{N_0/2} \sum_{a=(N_0/2)+1}^{\infty} \frac{\varphi_i^*(\mathbf{r})\varphi_a(\mathbf{r})\varphi_a^*(\mathbf{r}')\varphi_i(\mathbf{r}')}{\varepsilon_i - \varepsilon_a} \quad (28)$$

The sum over i runs over all the occupied molecular orbitals $\phi_i(\mathbf{r})$ (with associated orbital energies ε_i), while the index a spans the unoccupied ones. It is important to note that a frozen-orbital approximation was made in its derivation and that energy differences between excited and ground states were replaced by orbital energy differences. These approximations are, however, exactly applicable to the KS noninteracting reference system, so that eq 28 can be seen as the exact functional derivative of the electron density with respect to the KS potential. There is a relation between the interacting linear response kernel, $\chi(\mathbf{r}, \mathbf{r}')$, and the noninteracting one, $\chi_s(\mathbf{r}, \mathbf{r}')$ ^{35,61}

$$\chi(\mathbf{r}, \mathbf{r}') = \chi_s(\mathbf{r}, \mathbf{r}') + \iint \chi_s(\mathbf{r}, \mathbf{x}) \left(\frac{1}{|\mathbf{x} - \mathbf{x}'|} + \frac{\delta^2 E_{xc}}{\delta \rho(\mathbf{x}') \delta \rho(\mathbf{x})} \right) \chi(\mathbf{x}', \mathbf{r}') d\mathbf{x} d\mathbf{x}' \quad (29)$$

which shows that formula (eq 28) is a zeroth-order approximation to the linear response kernel for the interacting system. Eq 28 can be condensed in the sense of eq 23, which was done using Becke's multicenter numerical integration procedure.^{62–64} In the absence of reference data for the linear response kernel, we will make use of this approximate approach to assess the validity of our implementation.

We have chosen to study a series of six molecules—formaldehyde, water, ammonia, carbon monoxide, hydrogen cyanide, and nitrous oxide—that present interesting chemical properties and are computationally convenient because of their small size and high symmetry. Their geometries have been optimized on the B3LYP/6-311++G** level of theory,^{65–68} whereas the single point calculations for eq 19 and the input for eq 28 have been done on the PBE/6-31+G* level.^{69,70} As introduced in the previous section, the user should specify a number of parameters prior to the actual evaluation of the second-order functional derivatives. It is advisable that the specific choices are extensively tested beforehand with respect to convergence (e.g., the number of point charges) and numerical stability of the results. We will provide an example of this at the end of this section, where the numerical error is estimated through variation of the various parameter values. It is, however, interesting to start with a discussion of the optimal parameter values and the corresponding results.

The main group of parameters to be chosen is associated with the construction of the set of external potential perturbations. As suggested in Section 3.1, R_{middle} will be assigned a value of 1.0 van der Waals radii so that the inner sampling region spans the molecular van der Waals volume. The nuclear region will, however, be excluded by choosing an R_{min} value of 0.3 van der Waals radii. This can be done without harm because chemical variations take place in the valence region and because we are interested in the calculation of an atom-condensed quantity, without aiming for a

Table 1. Linear Response Matrix Elements χ_{AB} (in au) between Atoms A and B^a

molecule		χ_{AB} (a)				χ_{AB} (b)				correlation
		H ₁	C	O	H ₂	H ₁	C	O	H ₂	
CH ₂ O	H ₁	-1.21				H ₁	-1.21			
	C	1.19	-4.82			C	0.68	-4.35		0.96 (0.99, -0.01)
	O	0.42	2.45	-3.28		O	0.34	2.99	-3.67	
	H ₂	-0.40	1.19	0.42	-1.21	H ₂	0.19	0.68	0.34	-1.21
H ₂ O	O		H ₁	H ₂		O		H ₁	H ₂	
	H ₁	-3.77				H ₁	-1.76			0.96 (1.98, 0.05)
	H ₂	1.88	-1.39			H ₂	0.88	-0.93		
	H ₂	1.88	-0.49	-1.39		H ₂	0.88	0.05	-0.93	
NH ₃	N		H ₁	H ₂	H ₃	N		H ₁	H ₂	H ₃
	H ₁	-5.65				H ₁	-2.73			
	H ₂	1.88	-1.37			H ₂	0.91	-1.00		0.97 (1.92, 0.06)
	H ₃	1.88	-0.25	-1.37		H ₃	0.91	0.05	-1.00	
CO	C		H ₁	H ₂	H ₃	C		H ₁	H ₂	H ₃
	O	-4.33				O	-3.78			
	O	4.33	-4.33			O	3.78	-3.78		1.00 (1.15, 0.00)
	O					O				
HCN	H		C	N		H		C	N	
	C	-0.85				C	-0.96			1.00 (0.92, 0.00)
	N	0.76	-5.24			N	0.60	-5.49		
	N	0.09	4.49	-4.58		N	0.36	4.89	-5.25	
NNO	N ₁		N ₂	O		N ₁		N ₂	O	
	N ₂	-3.76				N ₂	-5.79			0.92 (0.74, -0.04)
	O	2.56	-4.26			O	2.84	-4.10		
	O	1.20	1.70	-2.90		O	2.95	1.25	-4.21	

^a Calculated with: (a) our proposed methodology to compute second-order functional derivatives and (b) the approach based on eq 28. Linear regressions between both data sets for each molecule give rise to the correlation coefficients (R^2) shown in the last column; the values in brackets indicate the corresponding slopes and intercepts.

locally resolved description. Furthermore, it has been shown in the context of the first-order functional derivatives that an accurate representation of the nuclear cusps requires many thousands of additional point charges.¹⁴ The R_{\max} value will be set equal to 4.0 van der Waals radii; a further extension of the external potential sampling region does not change the results. Point charges in the inner region will have values of ± 0.02 e (elementary charge) and the spacing of the corresponding cubic grid will be 0.12 Å. Larger charge values of ± 0.10 e can be chosen for the outer region; the perturbations are also placed farther apart, with an associated grid spacing of 0.40 Å.

We have observed that it is often advantageous to impose the normalization constraints (eq 26) for the study of atom-condensed quantities. The implementation of this equation occurs in quite a similar way as the construction of the external potential perturbations: it will be evaluated for a number of positions \mathbf{r} lying on a cubic grid between two scaled van der Waals surfaces. The points where the normalization constraint should be evaluated are, however, influenced by the basis set used for the expansion of the functional derivative. We will use the simplified basis set of one sharp s-type Gaussian function per atom with exponent values of 10.0 au, ensuring that overlap between two or more atoms is negligible. As a consequence, the normalization constraints should be evaluated within a zone that is close to the atomic nuclei, on which the various basis functions are centered. The sharp basis functions $\beta_k(\mathbf{r})$ of eq 26 will indeed assume values close to 0 if \mathbf{r} is chosen too far away

from any of the atomic nuclei, yielding the trivial expression “0 = 0”. The normalization equations will be evaluated in the volume contained within the van der Waals surfaces scaled by the factors 0.1 and 0.3. A grid spacing of 0.2 Å gives satisfactory results. It is interesting to note that the normalization equations are evaluated in the region of space where no external potential perturbations are placed. Information about this zone is thereby indirectly taken into account, while avoiding an extensive sampling to represent the nuclear cusps.

The above-mentioned parameters typically give rise to a number of external potential perturbations (J) of the order of 50 000 and around 200 normalization equations. Such an extensive sampling by external potential perturbations requires a considerable computational effort but should be close to the convergence limit, except for the nuclear zone, which is not explicitly dealt with here. The computational cost will be minimized by inclusion of the molecular symmetry properties, which gives a reduction in the number of required single point calculations by a factor 4 for formaldehyde (C_{2v} point group) and 6 for ammonia (C_{3v} point group), for example. The symmetry of the linear response kernel (eq 27) will also be taken into account.

Table 1 gives the numerical results obtained by our approach to calculate second-order functional derivatives and by the perturbation theoretical methodology based on eq 28. It is encouraging to see how well the data obtained by both methods correlate; the linear regression correlation coefficient varies between 0.92 and 1.00 for the set of chosen molecules.

Table 2. Variation of the Relevant Parameters Around Their Optimal Values and the Corresponding RMSE Induced in the Atom-Condensed Linear Response Values for Formaldehyde^a

parameter	optimal value	(a)	(b)	(c)	(d)	(e)	(f)	(g)	(h)
R_{\max} (vdW radii)	4.0	5.0	3.0						
q_{inner} (e)	0.02					0.04	0.01		
q_{outer} (e)	0.10					0.20	0.05		
a_{inner} (Å)	0.12			0.11	0.15				
a_{outer} (Å)	0.40			0.35	0.50				
exponent basis functions (au)	10.0							20.0	5.0
number of perturbations	12 998	20 250	8632	18 172	6964				
RMSE		0.00021	0.00099	0.011	0.062	0.0021	0.00019	0.0024	0.036

^a The number of external potential perturbations considered (before symmetry propagation) is indicated where relevant.

Some interesting differences are, nonetheless, visible. While the intercepts of the regression lines consistently stay close to 0, the corresponding slopes assume values from 0.74 to 1.98. Therefore, although the intramolecular trends are similar in either of the approaches, the intermolecular ones may change. This leads, for example, to a higher linear response value for χ_{OO} in water than in formaldehyde with the present methodology, whereas the inverse trend is predicted through application of eq 28. Another point is that the present methodology finds slightly negative values for the off-diagonal H–H elements in formaldehyde, water, and ammonia. This can be interpreted as if an external potential change induced by a positive charge distribution in the atomic volume of one of the hydrogen atoms leads to an electron density increase in the neighboring hydrogens. Although this cannot be excluded because of their spatial proximity, the same observation cannot be made from eq 28, where near-zero values are obtained. A final dissimilarity is seen for nitrous oxide, where the central atom is predicted to be the most polarizable atom by our method, while it seems to be the least polarizable one with the other approach.

It should be emphasized that these differences do not come as a surprise for some reasons: First of all, the atomic condensation procedures used in both approaches are completely different. Second, application of eq 28 involves the theoretical approximations that were explained at the beginning of this section.^{48,49} Finally, while our methodology does not involve approximations on the theoretical level, there are numerical approximations. It is, however, true that the present methodology in principle allows the computation of exact solutions if the situation of an infinite number of external potential perturbations and a complete basis set is approached. We therefore assume that the current methodology provides the best representation of chemical reality, even though further research is certainly needed to confirm this statement.

It is now appropriate to make two comments on the chemical interpretation of the linear response kernel. Some of the present authors have shown that this quantity can be used as a measure of electron delocalization.^{48,49} Moreover, the linear response kernel contains the necessary information to evaluate a system's polarizability.^{60,71} For example, $\chi(\mathbf{r}, \mathbf{r}')$ can be related to the dipole polarizability tensor α_{ij} ,⁷² where the indices i and j stand for the Cartesian directions:

$$\alpha_{ij} = - \iint r_i r'_j \chi(\mathbf{r}, \mathbf{r}') d\mathbf{r} d\mathbf{r}' \quad (30)$$

Unfortunately, this quantity is not accessible with the presented results for the atom-condensed linear response kernel but could straightforwardly be obtained if the locally resolved kernel was calculated using our methodology. One should, however, be careful when interpreting the atom-condensed linear response elements as indicators of the atomic polarizabilities. A consideration of the diatomic molecule CO, for example, shows that these elements do not necessarily equal polarizabilities of atoms in molecules. Indeed, the symmetry properties of the kernel result in identical values for the χ_{CC} and χ_{OO} elements, while the carbon and oxygen atoms should clearly have a different polarizability. A second note concerns the use of the linear response kernel as a tool for the description of intermolecular trends. The fact that both methodologies of Table 1 give similar intramolecular trends, but different intermolecular ones could indicate that the linear response kernel is less suitable for making intermolecular comparisons. An analogous observation has been made for the local reactivity descriptors. The Fukui function is an appropriate property for intramolecular reactivity descriptions, whereas the local softness is preferred for intermolecular comparisons.³ Future research should verify whether a similar reasoning, based on the Berkowitz–Parr relation (eq 12), leads to the conclusion that the softness kernel $s(\mathbf{r}, \mathbf{r}')$ is a better alternative for the description of intermolecular trends.

As a final item, we will estimate the computational error associated with the current implementation and parameter choices. Table 2 gives the root-mean-square errors (RMSE) in the atom-condensed linear response values for formaldehyde induced by variations of the relevant parameters around the optimal values we have put forward. Variations (a) and (b) analyze the effect of an enlargement and reduction of the external potential sampling region. Errors of 0.00021 and 0.00099 au are found when the R_{\max} values are changed from 4.0 to 5.0 and 3.0 van der Waals radii, respectively, indicating that our chosen sampling border does not form an obstacle for the numerical stability of the results. We are thus allowed to ignore the large sampling region associated with an R_{\max} value of 5.0 van der Waals radii, which concomitantly gives rise to a considerable increase in computational cost (20,250 external potential perturbations instead of 12,998). The number of perturbations can also be varied by altering the spacings of the corresponding grids. Reduction of the inner grid lattice parameter (a_{inner}) from 0.12 to 0.11 Å and of the outer one (a_{outer}) from 0.40 to 0.35 Å, yielding an increase

in the number of external potential perturbations to 18 172, leads to a RMSE of 0.011 au. This result indicates that higher precision values can be obtained by refinement of the grids on which the point charges are placed, however, at substantial computational expense. Our proposed values for the lattice parameters attempt to limit this computational effort and yield values that are precise up to the second decimal. Variation (d) provides an example of this, which shows that a RMSE of 0.062 au is found when the number of perturbations is reduced by a factor of around 2; this dissuades us from using coarser grids. The sizes of the point charges exert only a minor effect on the obtained results. Variations (e) and (f), respectively doubling and halving their values, give rise to errors of 0.0021 and 0.00019 au. The last parameter to be considered is the exponent value of the basis functions. An increase of this value from 10.0 to 20.0 au only leads to a small variation in the linear response elements of 0.0024 au. Reduction of the exponent to 5.0 au, however, gives rise to a considerable RMSE of 0.036 au. This indicates that such an exponent value is too low to prevent the basis functions from spreading over several atoms, which should be avoided. Overall, the presented optimal values yield numerical stability at a minimal computational expense. We have shown that the associated numerical error is of the order of 0.01 au.

5. Conclusion and Prospects

In this paper, the first generally applicable methodology to calculate second-order functional derivatives of arbitrary properties with respect to the external potential is proposed. The central idea is to expand the desired functional derivative in a basis set and to determine the expansion coefficients by probing the molecular environment with external potential perturbations. Although this approach is theoretically rigorous, exact solutions can only be obtained if an infinite basis set and a number of perturbations are considered.

We applied the methodology to evaluate the atom-condensed linear response kernel and estimated that the numerical error of the current implementation is of the order of 0.01 au. The results for a set of six simple molecules were compared with values obtained through an approximate methodology based on second-order perturbation theory. Both approaches are generally in agreement.

The most important disadvantage of the proposed methodology is its substantial computational cost. For the set of molecules considered, a number of 50 000 positive and negative external potential perturbations—each requiring a single point calculation—was typically needed to obtain converged results. Even though this number was reduced by taking molecular symmetry into account, the vast computational effort will probably prevent this method from being the routinely used procedure in the future. Nonetheless, the fact that this methodology does not involve any theoretical approximations and that exact or quasi-exact solutions can be found, if the sets of external potential perturbations and basis functions are chosen large enough, implies that it can be used as a benchmark method against which more easily applicable, approximate methodologies may be assessed. Another advantage of this algorithm, compared to the more

conventional approach based on eqs 28 and 29, is that the atom-condensed linear response kernel is accessed directly.

We should, finally, mention that it is possible to enhance the computational efficiency by adding extra equations to the set of eq 18, the nature of which depends upon the property one is interested in. As an illustration, the Appendix will show how the calculation of the linear response kernel could be accelerated by taking responses of the electron density or electrostatic potential into account.

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Appendix

The definition of the linear response kernel (eq 10) provides a means to accelerate the proposed methodology if one is specifically interested in the calculation of this quantity. Not only can the linear response kernel be seen as the second-order functional derivative of the electronic energy E with respect to the external potential, but it can also be considered as the first-order functional derivative of the electron density $\rho(\mathbf{r})$. An analogous reasoning as in Section 2, but this time based on a functional Taylor series of the electron density evaluated at point \mathbf{x} , yields the following equations for the expansion coefficients q_{kl}

$$\frac{1}{2}(\rho[v(\mathbf{r}) + w_j(\mathbf{r}); \mathbf{x}] - \rho[v(\mathbf{r}) - w_j(\mathbf{r}); \mathbf{x}]) = \sum_{k=1}^K \sum_{l=1}^K q_{kl} \beta_k(\mathbf{x}) \int \beta_l(\mathbf{r}') w_j(\mathbf{r}') d\mathbf{r}', \quad \text{with} \quad j = 1, \dots, J \quad (\text{A.1})$$

The advantage is that a series of equations of this type, corresponding to electron density responses evaluated at various points ($\mathbf{x} = \mathbf{x}_1, \mathbf{x} = \mathbf{x}_2, \dots$) can be constructed for every external potential perturbation j . The fact that just two single point calculations (one for $w_j(\mathbf{r})$ and one for $-w_j(\mathbf{r})$) can give rise to a number of equations to be considered in the least-squares fitting procedure implies a significant computational benefit.

Another possibility lies in the evaluation of electrostatic potential⁷³ responses. The electrostatic potential is defined as

$$\Phi(\mathbf{r}) = -v(\mathbf{r}) - \int \frac{\rho(\mathbf{r}')}{|\mathbf{r} - \mathbf{r}'|} d\mathbf{r}' \quad (\text{A.2})$$

A functional Taylor series of $\Phi(\mathbf{x})$ for which the external potential is perturbed by $w(\mathbf{r})$ can be written as follows:

$$\Phi[v(\mathbf{r}) + w(\mathbf{r}); \mathbf{x}] = -v(\mathbf{x}) - w(\mathbf{x}) - \int \frac{\rho[v(\mathbf{r}); \mathbf{r}'] + \int \left(\frac{\delta \rho(\mathbf{r}')}{\delta v(\mathbf{r}'')} \right)_N w(\mathbf{r}'') d\mathbf{r}'' + \dots}{|\mathbf{x} - \mathbf{r}'|} d\mathbf{r}' \quad (\text{A.3})$$

$$= \Phi[v(\mathbf{r}); \mathbf{x}] - w(\mathbf{x}) - \iint \frac{\chi(\mathbf{r}', \mathbf{r}'')w(\mathbf{r}'')}{|\mathbf{x} - \mathbf{r}'|} d\mathbf{r}' d\mathbf{r}'' + \dots \quad (\text{A.4})$$

Application of the arguments used in Section 2 now leads to the subsequent equations for the expansion coefficients q_{kl} :

$$\frac{1}{2}(\Phi[v(\mathbf{r}) + w_j(\mathbf{r}); \mathbf{x}] - \Phi[v(\mathbf{r}) - w_j(\mathbf{r}); \mathbf{x}]) + w_j(\mathbf{x}) = - \sum_{k=1}^K \sum_{l=1}^K q_{kl} \int \frac{\beta_k(\mathbf{r}')}{|\mathbf{x} - \mathbf{r}'|} d\mathbf{r}' \int \beta_l(\mathbf{r}'')w(\mathbf{r}'')d\mathbf{r}'',$$

with $j = 1, \dots, J$ (A.5)

Analogously to eq A.1, this set of equations could yield a substantial improvement to the computational efficiency. A major advantage of this last approach is that the molecular electrostatic potential has a much smoother behavior than the electron density so that convergence is expected to be more easily attained.

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