Softened electrostatic molecular potentials

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ABSTRACT

Electrostatic molecular potentials (EMPs) are studied from two points of view. First, a softened EMP (SEMP) approach is proposed, consisting in the substitution of a positive point charge as the entity with which an electronic density function (DF) interacts electrostatically to generate a classical EMP for a Gaussian charge distribution. Second, the performance of this SEMP approach under the Atomic Shell Approximation (ASA) is described and compared with classical EMP at the same ASA level. Several sample applications are presented to describe the general features of this new method of studying electrostatic interactions in molecules. The net result is a family of SEMPs that encompass EMPs as special cases but do not possess their infinite discontinuities. The features of SEMPs are quite similar to those of EMPs distant from nuclei, and the absence of infinity values makes them good candidates to be employed in molecular similarity calculations.

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1. Introduction

Since Scrocco et al. [1] proposed using the electrostatic molecular potential (EMP)[1] generated by a molecular first-order density function (DF) in front of a positive point charge, EMPs have become an important quantum chemical tool for understanding molecular and biological activity.

A perusal of the relevant literature unequivocally shows that, thousands of papers have been devoted to applications of EMPs since description of EMP in 1970, and most of them concern chemical applications [2,3]. For example, several recent papers describe the role of EMPs in current theoretical and quantum chemistry [4–13]. For more concrete examples of the critical and theoretical interest in EMPs, one can follow the recent work of Gadre on this subject [14–21]. In our laboratory, many studies implementing the EMP approach [22–26], as well as the Atomic Shell Approximation (ASA) DF to obtain reliable EMP descriptions [27] have been performed. Moreover, the possibility of using EMPs for quantum similarity research was proposed some years ago [28,29], but the infinite discontinuities of EMPs in atomic neighborhoods have presented obvious difficulties despite the use of arbitrary grids or other approximations [30,31]. Thus, with respect to treating quantum

similarity, the EMP approach has not evolved to the extent that the DF approach has (see for example [32]).

In contrast, although Weinstein et al. have shown the positive definiteness of EMPs in isolated atoms [33], EMPs were recently studied in our laboratory under the ASA. We demonstrated that a simple promolecular approach of the ASA DF will be positive everywhere for any molecular structure [34]. Thus, the former property was extended to non-spherical quantum objects, and a polarized ASA DF framework was simultaneously proposed to overcome this positive definite behavior. Our interest in the structure and applications of Gaussian functions (GFs) [35–40] is connected to the goals of the present study, in which we proposed to substitute a Gaussian charge distribution for the EMP point charge. Such an alternative for treating atoms was published several years ago by one of the members of our group [41]. This initial work can be considered an attempt to transition from EMPs to a set of similar functions and thus as the first stage of the present approach.

The main purpose of the present study was to show that SEMPs might be essentially the same as EMPs within polarized ASA density representations, except at the nuclei. The SEMP approach provides the added utility of using Gaussian densities instead of point charges in EMP calculations, which can also be considered a first step toward the construction of general algorithms, which allows for quantum similarity comparisons between the EMPs of different quantum objects.

1.1. Nature of the EMP and the present proposal

Exact or approximate, classically computed EMPs present a general drawback: in the neighborhood of an atom within a

given molecule, EMP values become largely repulsive because the nuclear contribution at the atomic positions tends to infinity as the distance between the charge position and any atomic location becomes smaller. Such a feature makes several aspects of potential EMP applications difficult and certainly restricts the comparison of two functions to those belonging to different molecular structures.

The aim of the present study was to provide a solution to this asymptotic problem. To this end, a *softened* EMP (SEMP),[2] which is based on the simple idea of replacing the usual EMP positive point charge with a *charge distribution* in the form of a GF multiplied by a constant real charge value, will be described.

1.2. Organization of this study

To describe this modified SEMP, the present paper's main goal is to present the mathematical framework underlying the SEMP approach, particularly under the ASA for practical purposes. From this simplified outline, the ab initio computational framework of the SEMP can be described in a straightforward manner. To address these considerations, the present paper is organized as follows. First, the nature of the ASA density description will be discussed. Then, the form of the classical EMP at the ASA level will be addressed. Similarly, description of the SEMP will be followed by a further section on the potential's ASA form. Next, a discussion on considering a classical EMP as an asymptotic member of a SEMP family will be presented. A discussion of finite values at atomic centers will conclude the theoretical part of this study. Afterward, several examples of applications will be presented.

2. Atomic Shell Approximation (ASA) description

Within the ASA description [42–46], any molecular first-order density function (DF) can be written as a sum of atomic contributions $\{\Gamma^I\}$, and each contribution is written in turn as a linear combination of normalized 1s Gaussian functions (GF):

$$\rho(\mathbf{r}) = \sum_{I \in M} \Gamma^I(\mathbf{r} - \mathbf{R}_I) = \sum_{I \in M} \left(\sum_{\mu \in I} q_\mu^I G_\mu^I(\mathbf{r} - \mathbf{R}_I, \alpha_\mu^I) \right) \quad (1)$$

Hereafter, it is assumed that each GF G is Minkowski normalized to the unit according to the rule:

$$\langle G(\mathbf{r}, \alpha) \rangle = \int_D G(\mathbf{r}, \alpha) \, d\mathbf{r} = 1$$

where

$$G(\mathbf{r}, \alpha) = N_\alpha g(\mathbf{r}, \alpha)$$

and using:

$$g(\mathbf{r}, \alpha) = e^{-\alpha |\mathbf{r}|^2} \rightarrow \langle g(\mathbf{r}, \alpha) \rangle = \left(\frac{\pi}{\alpha} \right)^{3/2}$$

produces a Minkowski normalization factor given by:

$$N_\alpha = \left(\frac{\alpha}{\pi} \right)^{3/2}.$$

Furthermore, a single GF $G(\mathbf{r}, \alpha)$ can be considered to be an oversimplified DF, so that through multiplication by a real constant: Θ, it can be associated to a continuous charge distribution fulfilling the following condition:

$$\langle \Theta G(\mathbf{r}, \alpha) \rangle = \Theta.$$

Hence, partial integration of Eq. (1) yields over any atom I the atom's electronic charge Q_I:

$$\forall I \in M : \langle \Gamma^I \rangle = \sum_{\mu \in I} q_\mu^I \langle G_\mu^I(\mathbf{r}, \alpha_\mu^I) \rangle = \sum_{\mu \in I} q_\mu^I = Q_I,$$

such that the full integration of the ASA expression gives Q the total number of electrons of molecule M:

$$\langle \rho(\mathbf{r}) \rangle = \sum_{I \in M} \sum_{\mu \in I} q_\mu^I \langle G_\mu^I(\mathbf{r} - \mathbf{R}_I, \alpha_\mu^I) \rangle = \sum_{I \in M} \left(\sum_{\mu \in I} q_\mu^I \right) = \sum_{I \in M} Q_I = Q$$

Additionally, one can see that for every atom I, the set of coefficients $\{q_\mu^I\}$ represents the manner in which the atomic charge Q_I has been distributed among the GF set $\{G_\mu^I\}$.

3. Classical EMP in terms of an ASA expression

Given a molecular DF $\rho(\mathbf{r})$, the classical [1] EMP $V^c(\mathbf{R})$ can be expressed as the sum of two electrostatic contributions, namely the electronic:

$$V_e^c(\mathbf{R}) = - \int_D \rho(\mathbf{r}) |\mathbf{R} - \mathbf{r}|^{-1} \, d\mathbf{r}$$

and the nuclear:

$$V_N^c(\mathbf{R}) = \sum_{I \in M} Z_I |\mathbf{R} - \mathbf{R}_I|^{-1}$$

such that $V^c(\mathbf{R}) = V_N^c(\mathbf{R}) + V_e^c(\mathbf{R})$.

If a molecular DF is expressed according to the ASA framework, as in Eq. (1), the classical ASA-EMP expression becomes:

$$V^c(\mathbf{R}) = \sum_{I \in M} Z_I |\mathbf{R} - \mathbf{R}_I|^{-1}$$
$$- \sum_{I \in M} \sum_{\mu \in I} q_\mu^I \int_D G_\mu^I(\mathbf{r} - \mathbf{R}_I, \alpha_\mu^I) |\mathbf{R} - \mathbf{r}|^{-1} \, d\mathbf{r} \quad (2)$$

The integration in Eq. (2) involves simple nuclear attraction-like integrals over 1s-type GFs, which are obtained using straightforward analytical forms [47]:

$$\int_D G(\mathbf{r} - \mathbf{R}, \alpha) |\mathbf{A} - \mathbf{r}|^{-1} \, d\mathbf{r} = N_\alpha \int_D g(\mathbf{r} - \mathbf{R}, \alpha) |\mathbf{A} - \mathbf{r}|^{-1} \, d\mathbf{r}$$
$$= N_\alpha \frac{2\pi}{\alpha} F_0(\alpha |\mathbf{A} - \mathbf{R}|^2)$$

In the above equation, the incomplete gamma function $F_0(t)$ has been described in many references (see for instance Saunders [47] or Abramowitz [48]). Additionally, the integral generating $F_0(t)$ can be easily related to the error function by means of the following identity:

$$F_0(x) = \int_0^1 e^{-xt^2} \, dx = \frac{1}{2} \sqrt{\frac{\pi}{x}} erf \left(\sqrt{x} \right).$$

Then, in this manner, the basic needed integral can also be readily written as follows:

$$\int_D G(\mathbf{r} - \mathbf{R}, \alpha) |\mathbf{A} - \mathbf{r}|^{-1} \, d\mathbf{r} = |\mathbf{A} - \mathbf{R}|^{-1} erf(\alpha^{1/2} |\mathbf{A} - \mathbf{R}|)$$
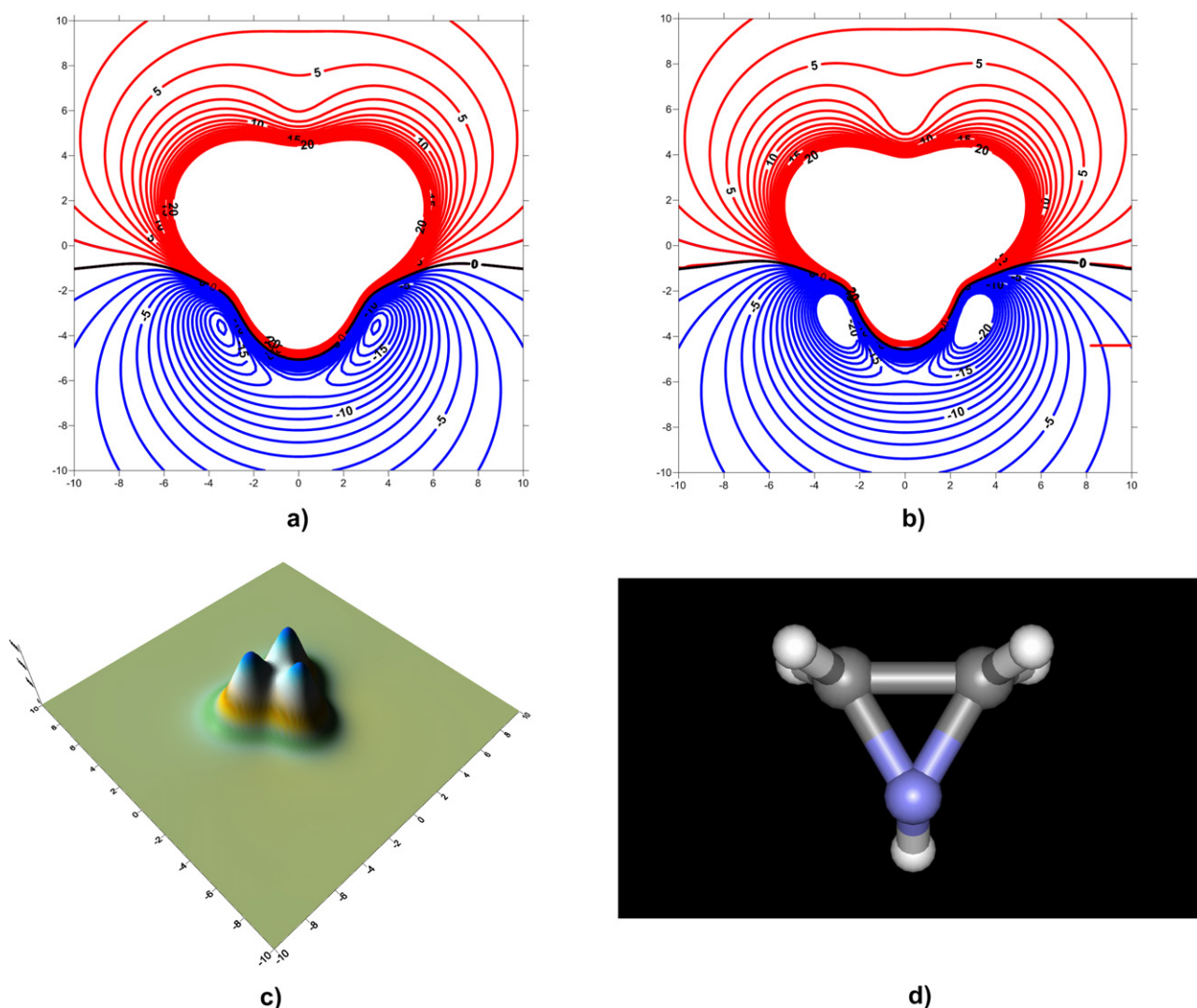

Fig. 1. The SEMP and classical EMP maps generated using the ASA approach for $(CH_2)_2NH$ (aziridine). From left to right and top to bottom: (a) SEMP (ASA) contours, (b) classical (ASA) contours, (c) SEMP (ASA) 3D view and (d) aziridine molecule.

By rearranging the terms in Eq. (2), the classical ASA-EMP can be ultimately expressed with the aid of linear combinations of atomic centered error functions:

$$V^c(\mathbf{R}) = \sum_{I \in M} Z_I |\mathbf{R} - \mathbf{R}_I|^{-1} - \sum_{I \in M} |\mathbf{R} - \mathbf{R}_I|^{-1} \sum_{\mu \in I} q_\mu^I erf((\alpha_\mu^I)^{1/2} |\mathbf{R} - \mathbf{R}_I|)$$

$$= \sum_{I \in M} |\mathbf{R} - \mathbf{R}_I|^{-1} \left[Z_I - \sum_{\mu \in I} q_\mu^I erf((\alpha_\mu^I)^{1/2} |\mathbf{R} - \mathbf{R}_I|) \right] \qquad (3)$$

As mentioned in Section 1, the principal disadvantage of the classical EMP at any approximation level, and therefore also in the final expression (3), is that the EMP becomes infinite at the nuclear centers, i.e., at the points where $\mathbf{R} = \mathbf{R}_I$, and consequently can also possess extremely large values in the neighborhood of atomic positions. This property greatly limits the capabilities of the classical EMP approach when used for certain applications for instance (1) when post-integration procedures, such as drawing or mapping EMPs, have to be performed or (2) when quantum similarity measures are planned to be evaluated between the electrostatic maps

of two or more molecules [28–31]. Extra care must be taken with artificial truncation around the atomic centers in the first case, and in the second, smoothing must be performed to avoid integration poles.

4. Softened EMP

Here, we propose and describe an alternative EMP-like function: SEMP. SEMPs operate much like EMPs but without the above-described atomic asymptotic property. As mentioned in Section 1, a SEMP replaces the implicit point charge probe of a typical EMP with a charge density Q_γ, which is defined by a normalized GF (representing a fuzzy unit charge) featuring a parametric exponent factor γ:

$$G(\mathbf{R}; \gamma) = Q_\gamma N_\gamma g(\mathbf{R}; \gamma).$$

Within this context, SEMPs can also be defined as the sum of nuclear and electronic contributions:

$$V(\mathbf{R}, \gamma) = V_N(\mathbf{R}, \gamma) + V_e(\mathbf{R}, \gamma)$$
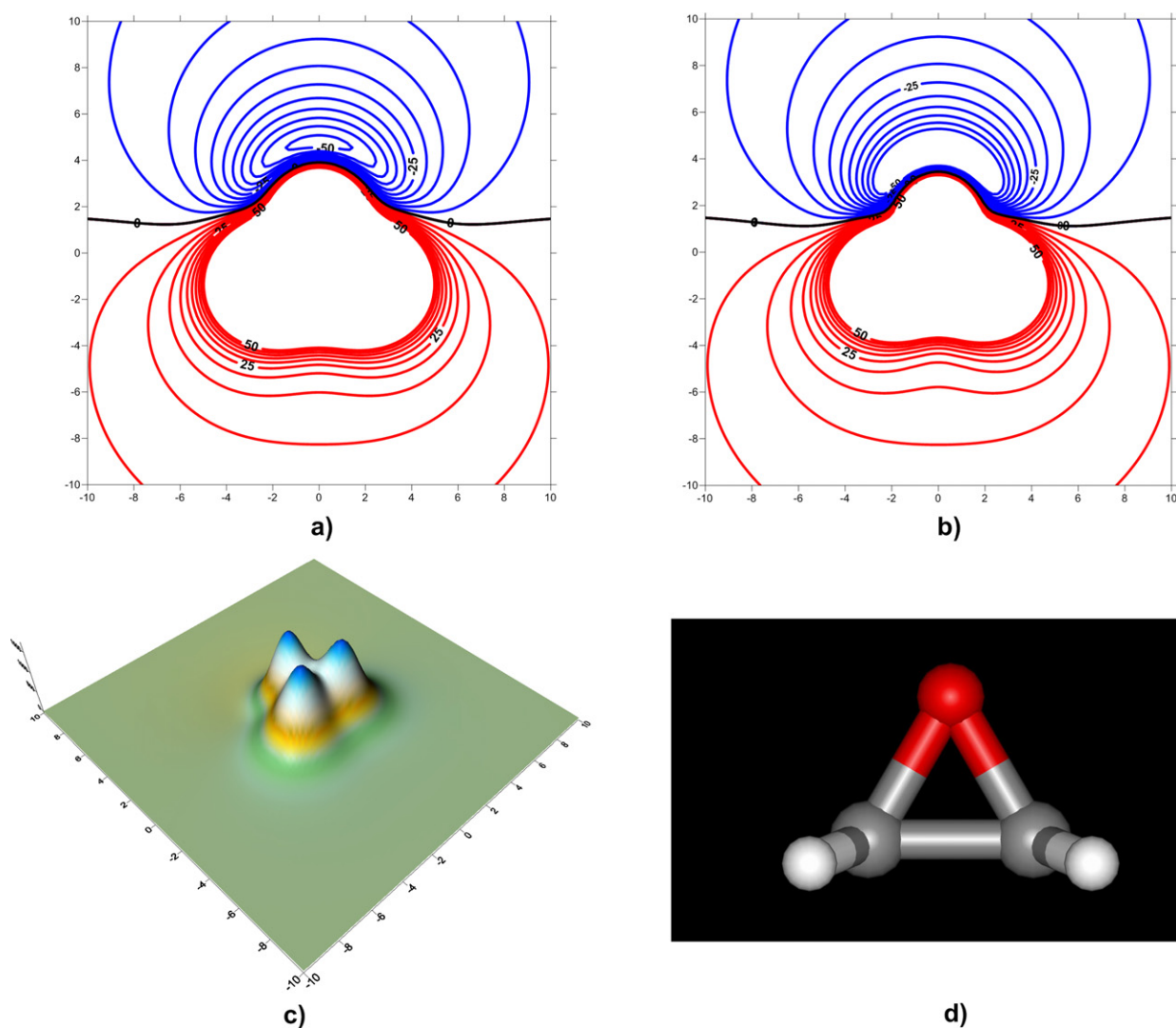
Fig. 2. The SEMP and classical EMP maps generated using the ASA approach for $(CH_2)_2O$ (oxirane). From left to right and top to bottom: (a) SEMP (ASA) contours, (b) classical (ASA) contours, (c) SEMP (ASA) 3D view and (d) oxirane molecule.

Each contribution in turn is written as follows:

$$V_N(\mathbf{R}, \gamma) = Q_\gamma N_\gamma \sum_{I \in M} Z_I \int_D g(\mathbf{r} - \mathbf{R}, \gamma) |\mathbf{R}_I - \mathbf{r}|^{-1} \, d\mathbf{r}$$

and

$$V_e(\mathbf{R}, \gamma) = -Q_\gamma N_\gamma \int_D \int_D \rho(\mathbf{r}) g(\mathbf{r}' - \mathbf{R}, \gamma) |\mathbf{r} - \mathbf{r}'|^{-1} \, d\mathbf{r} \, d\mathbf{r}'$$

When studying the nuclear part, the relevant integral possesses the general form:

$$A_N(\mathbf{R}, \gamma) = \int g(\mathbf{r} - \mathbf{R}, \gamma) |\mathbf{A} - \mathbf{r}|^{-1} \, d\mathbf{r},$$

which constitutes a nuclear attraction integral readily computed [47] and expressed as follows:

$$A_N(\mathbf{R}, \gamma) = \frac{2\pi}{\gamma} F_0(\gamma |\mathbf{R} - \mathbf{A}|^2) = \left(\frac{\pi}{\gamma}\right)^{3/2} |\mathbf{R} - \mathbf{A}|^{-1} erf\left(\sqrt{\gamma} |\mathbf{R} - \mathbf{A}|\right)$$

in such a manner, the nuclear contribution to SEMP can finally be written as:

$$V_N(\mathbf{R}, \gamma) = Q_\gamma \sum_{I \in M} Z_I |\mathbf{R} - \mathbf{R}_I|^{-1} erf\left(\sqrt{\gamma} |\mathbf{R} - \mathbf{R}_I|\right).$$

Evaluation of the electronic SEMP contribution requires the computation of electron–electron repulsion-like integrals. Despite this slight complication, the next section describes how the application of the ASA-EMP approximation leads to the computation of simple integrals involving only 1s-type functions. This feature simplifies the problem, and again, only calculation of the error function is required.
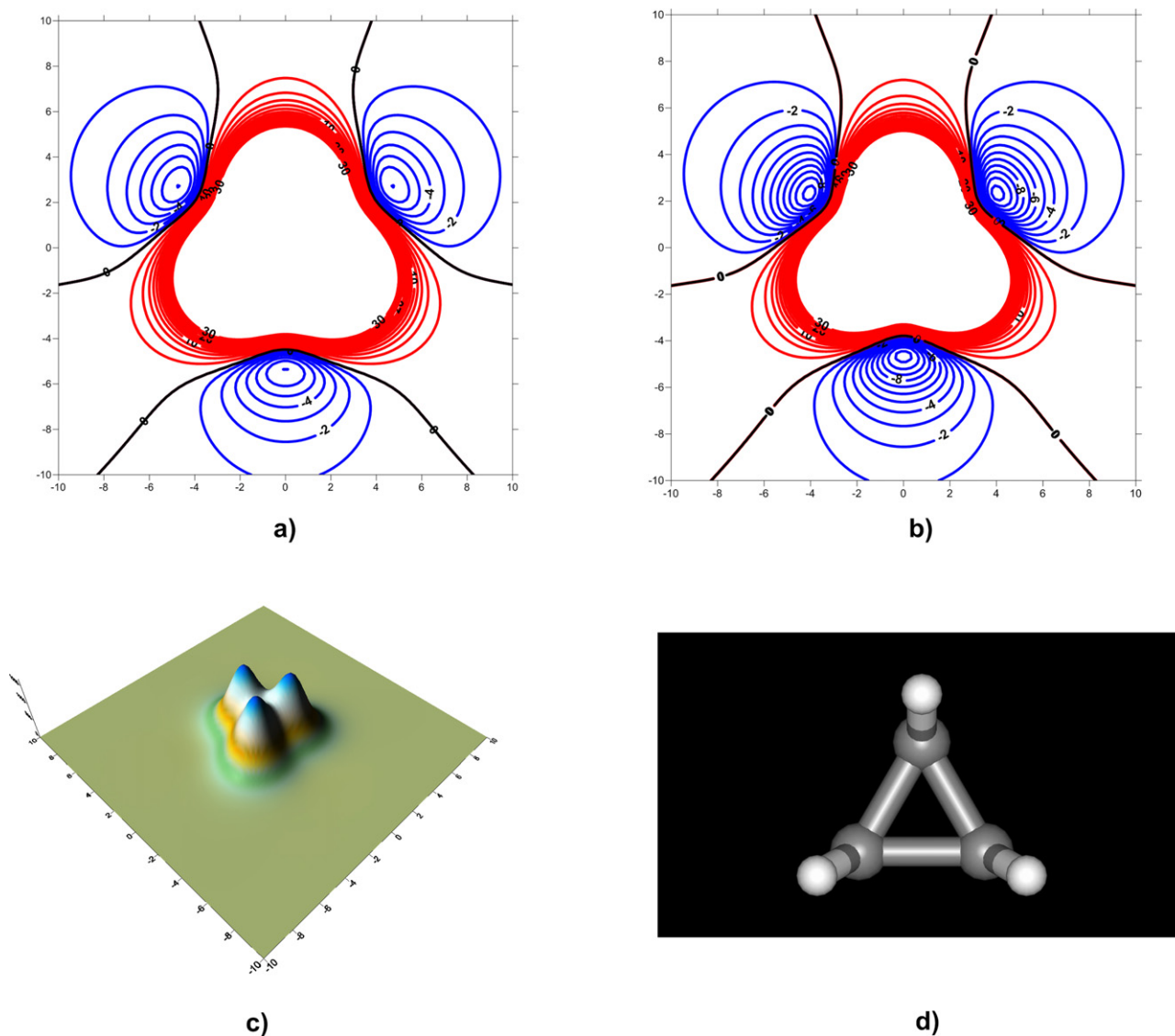
Fig. 3. The SEMP and classical EMP maps generated using the ASA approach for $(CH_2)_3$ (cyclopropane). From left to right and top to bottom: (a) SEMP (ASA) contours, (b) classical (ASA) contours, (c) SEMP (ASA) 3D view and (d) cyclopropane molecule.

5. Classical EMP as a limiting case of SEMP

It can be demonstrated that the definition of SEMPs encompasses that of classical EMPs as a special case. In SEMPs, the classical point charge probe is replaced by the function

$$G(\mathbf{R}; \gamma) = Q_\gamma N_\gamma g(\mathbf{R}; \gamma);$$

explicitly, it can be written as follows:

$$G(\mathbf{R}; \gamma) = Q_\gamma \left(\frac{\gamma}{\pi}\right)^{3/2} e^{-\gamma|\mathbf{R}|^2}$$

$$= Q_\gamma \left(\frac{\gamma}{\pi}\right)^{1/2} e^{-\gamma|R_x|^2} \left(\frac{\gamma}{\pi}\right)^{1/2} e^{-\gamma|R_y|^2} \left(\frac{\gamma}{\pi}\right)^{1/2} e^{-\gamma|R_z|^2}.$$

It can be easily seen how the point charge probe paradigm invoked in the classical EMP approach can be recovered if the exponential parameter tends to infinity:

$$\lim_{\gamma \to +\infty} G(\mathbf{R}; \gamma)$$

$$= Q_\gamma \lim_{\gamma \to +\infty} \left\{ \left(\frac{\gamma}{\pi}\right)^{1/2} e^{-\gamma|R_x|^2} \left(\frac{\gamma}{\pi}\right)^{1/2} e^{-\gamma|R_y|^2} \left(\frac{\gamma}{\pi}\right)^{1/2} e^{-\gamma|R_z|^2} \right\};$$

then, from the formal integral normalized representation of the Dirac delta function

$$\delta(R) = \lim_{a \to +\infty} \left(\frac{a}{\pi}\right)^{1/2} e^{-aR^2}$$

the following can be obtained:

$$\lim_{\gamma \to +\infty} G(\mathbf{R}; \gamma) = Q_\gamma \delta(R_x)\delta(R_y)\delta(R_z) = Q_\gamma \delta(\mathbf{R}).$$

Substituting this limit into the SEMP expression and recalling the integration properties of the Dirac delta function, the following is
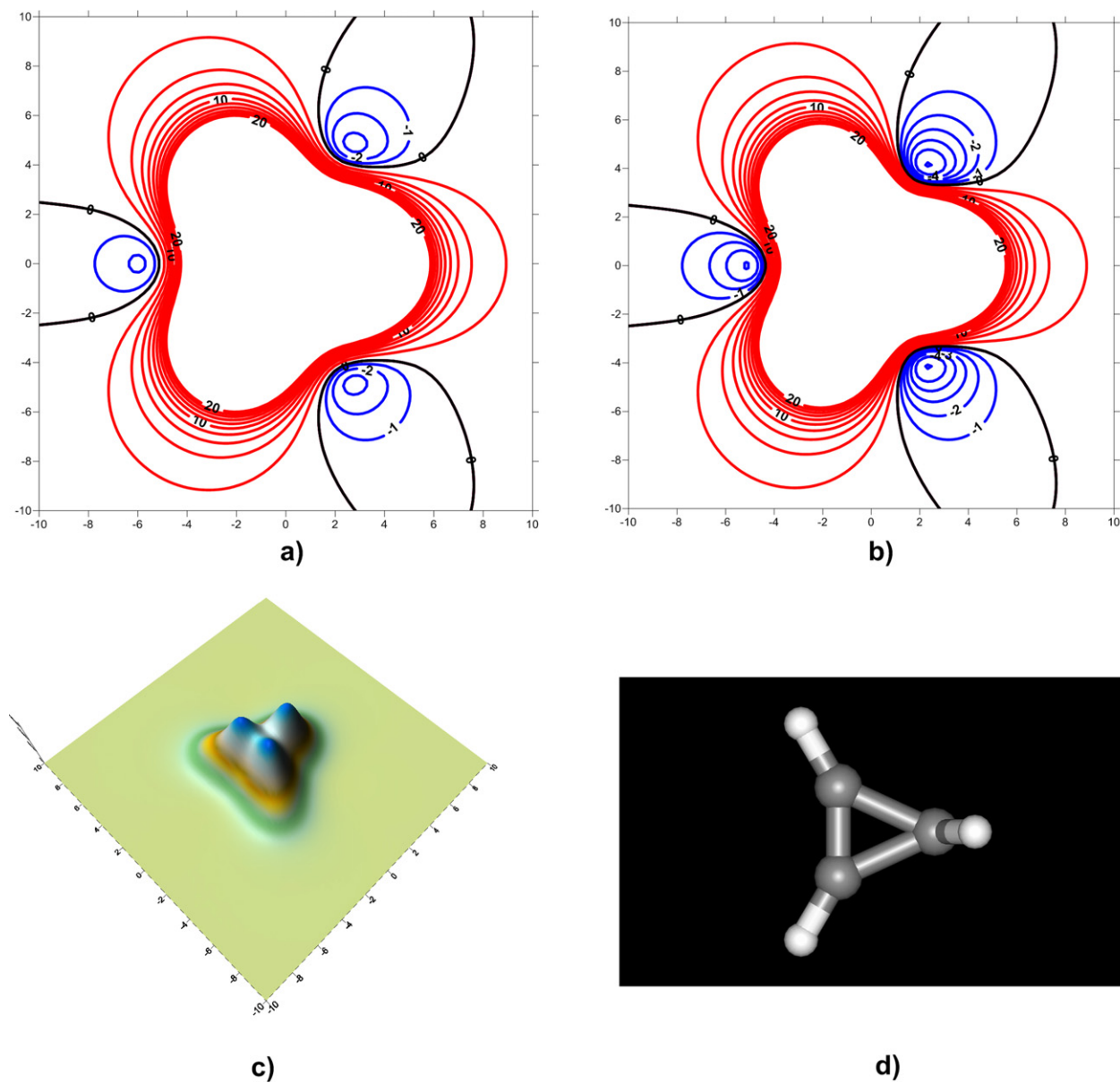
Fig. 4. The SEMP and classical EMP maps generated using the ASA approach for $(CH)_2CH_2$ (cyclopropene). From left to right and top to bottom: (a) SEMP (ASA) contours, (b) classical (ASA) contours, (c) SEMP (ASA) 3D view and (d) cyclopropene molecule.

obtained for the nuclear part:

$$\lim_{\gamma \to +\infty} V_N(\mathbf{R}, \gamma) = Q_\gamma \lim_{\gamma \to +\infty} N_\gamma \sum_{I \in M} Z_I \int_D g(\mathbf{r} - \mathbf{R}, \gamma)|\mathbf{R}_I - \mathbf{R}|^{-1} \, d\mathbf{r}$$

$$= Q_\gamma \sum_{I \in M} Z_I \int_D \delta(\mathbf{r} - \mathbf{R})|\mathbf{R}_I - \mathbf{r}|^{-1} \, d\mathbf{r}$$

$$= Q_\gamma \sum_{I \in M} Z_I |\mathbf{R}_I - \mathbf{R}|^{-1}$$

Similarly, the following is obtained for the electronic part:

$$\lim_{\gamma \to +\infty} V_e(\mathbf{R}, \gamma) = -Q_\gamma \lim_{\gamma \to +\infty} N_\gamma \int_D \int_D \rho(\mathbf{r})g(\mathbf{r}' - \mathbf{R}, \gamma)|\mathbf{r} - \mathbf{r}'|^{-1} \, d\mathbf{r} \, d\mathbf{r}'$$

$$= -Q_\gamma \int_D \int_D \rho(\mathbf{r})\delta(\mathbf{r}' - \mathbf{R})|\mathbf{r} - \mathbf{r}'|^{-1} \, d\mathbf{r} \, d\mathbf{r}'$$

$$= -Q_\gamma \int_D \rho(\mathbf{r})|\mathbf{r} - \mathbf{R}|^{-1} \, d\mathbf{r}.$$

Hence, for a unit charge ($Q_\gamma = 1$) probe distribution, the SEMP limit yields the classical EMP definition:
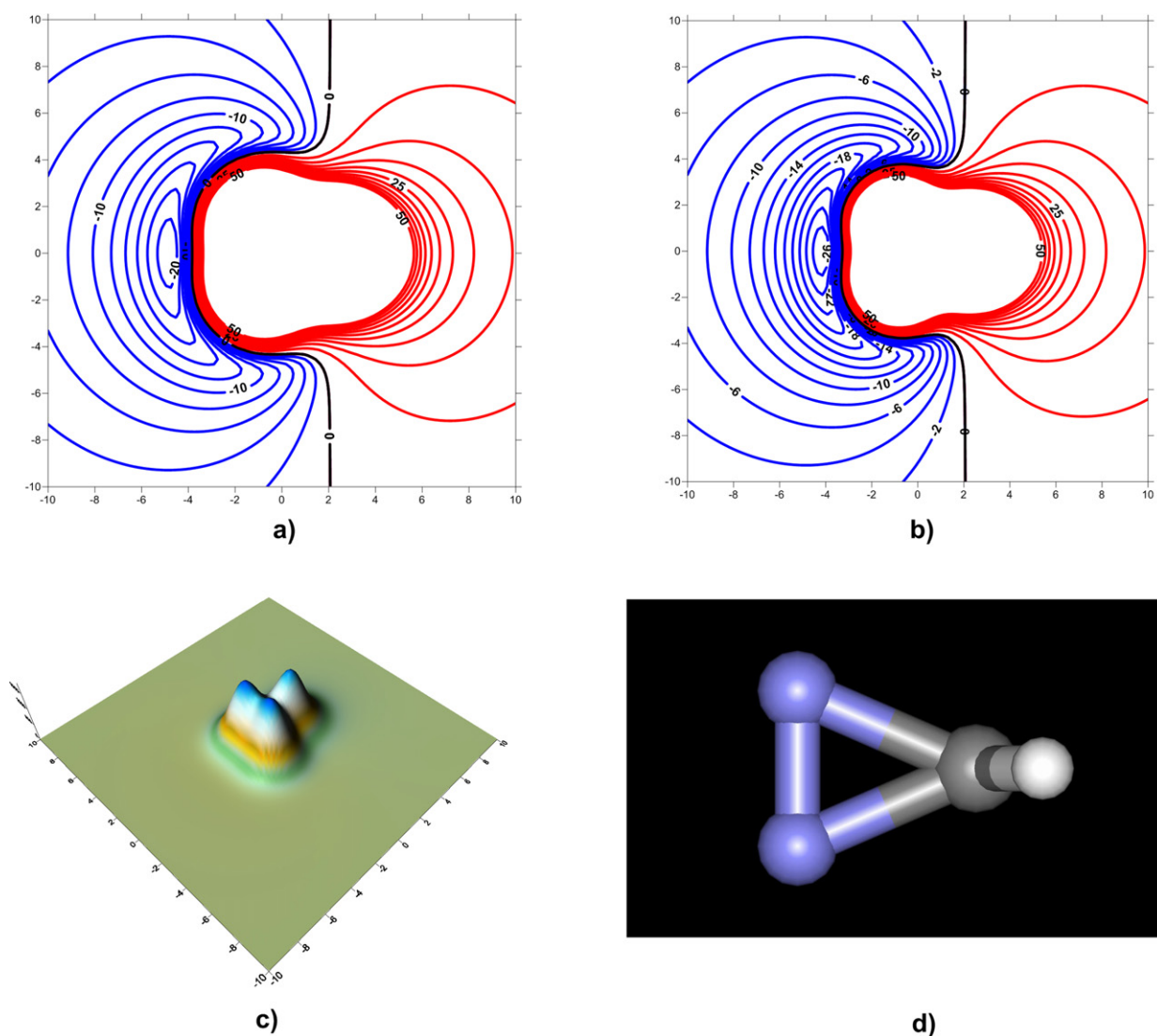
Fig. 5. The SEMP and classical EMP maps generated using the ASA approach for the cyclic structure N_2CH_2 (3H-diazirine). From left to right and top to bottom: (a) SEMP (ASA) contours, (b) classical (ASA) contours, (c) SEMP (ASA) 3D view and (d) 3H-diazirine molecule.

$$\lim_{\gamma \to +\infty} V(\mathbf{R}, \gamma) = \lim_{\gamma \to +\infty} V_N(\mathbf{R}, \gamma) + \lim_{\gamma \to +\infty} V_e(\mathbf{R}, \gamma)$$

$$= \sum_{I \in M} Z_I |\mathbf{R}_I - \mathbf{R}|^{-1} - \int_D \rho(\mathbf{r})|\mathbf{r} - \mathbf{R}|^{-1} \, d\mathbf{r}$$

$$= V_N^c(\mathbf{R}) + V_e^c(\mathbf{R}) = V^c(\mathbf{R}).$$

6. SEMP within the ASA context

Under the ASA framework, the electronic part of the SEMP is expressed as follows:

$$V_e(\mathbf{R}, \gamma) = -Q_\gamma N_\gamma \sum_{I \in M} \sum_{\mu \in I} q_\mu^I N_{\alpha_\mu^I} \int_D \int_D g(\mathbf{r} - \mathbf{R}_I, \alpha_\mu^I)$$

$$\times g(\mathbf{r}' - \mathbf{R}, \gamma)|\mathbf{r} - \mathbf{r}'|^{-1} \, d\mathbf{r} \, d\mathbf{r}'$$

which is equivalent to an electron repulsion integral of the generic form

$$A_e(\mathbf{R}, \alpha, \gamma) = \int \int g(\mathbf{r} - \mathbf{A}, \alpha)g(\mathbf{r}' - \mathbf{R}, \gamma)|\mathbf{r} - \mathbf{r}'|^{-1} \, d\mathbf{r} \, d\mathbf{r}'$$

which corresponds to the following equivalent expressions [47,49,50]:

$$A_e(\mathbf{R}, \alpha, \gamma) = \frac{2\pi^{5/2}}{\alpha\gamma(\alpha + \gamma)^{1/2}} F_0\left(\frac{\alpha\gamma}{\alpha + \gamma}|\mathbf{R} - \mathbf{A}|^2\right)$$

$$= \frac{\pi^3}{(\alpha\gamma)^{3/2}}|\mathbf{R} - \mathbf{A}|^{-1} erf\left(\sqrt{\frac{\alpha\gamma}{\alpha + \gamma}}|\mathbf{R} - \mathbf{A}|\right).$$

By rearranging the terms of the expression above, the final form of the electronic SEMP contribution is readily obtained:

$$V_e(\mathbf{R}, \gamma) = -Q_\gamma \sum_{I \in M} |\mathbf{R} - \mathbf{R}_I|^{-1} \sum_{\mu \in I} q_\mu^I erf\left(\sqrt{\frac{\alpha_\mu^I \gamma}{\alpha_\mu^I + \gamma}}|\mathbf{R} - \mathbf{R}_I|\right).$$
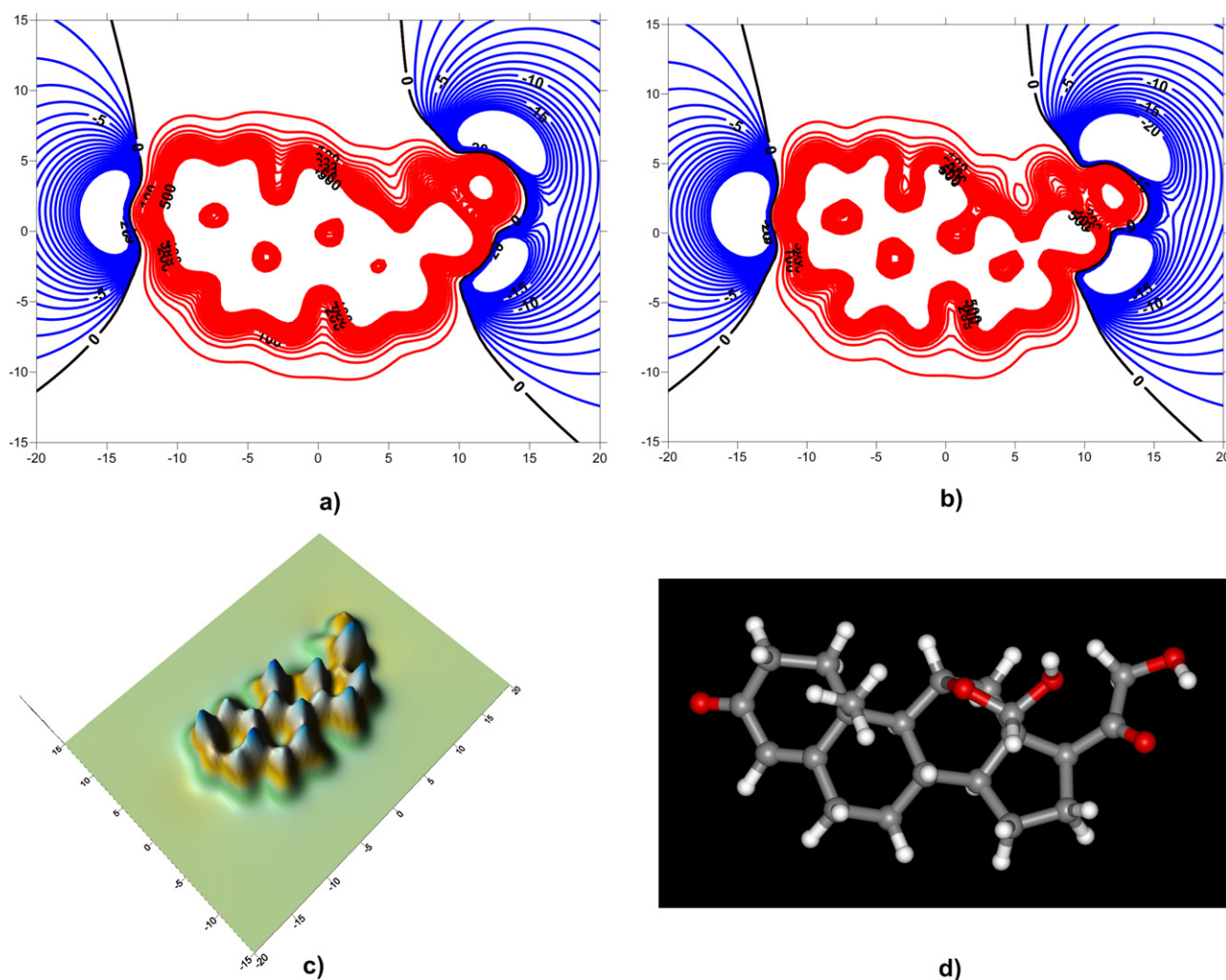
Fig. 6. The SEMP and classical EMP maps generated using the ASA approach for the aldosterone molecule. From left to right and top to bottom: (a) SEMP (ASA) contours, (b) classical (ASA) contours, (c) SEMP (ASA) 3D view and (d) aldosterone molecule.

Therefore, within the context of the ASA description, the SEMP may be computed as follows:

$$V(\mathbf{R}, \gamma) = Q_\gamma \sum_{I \in M} |\mathbf{R} - \mathbf{R}_I|^{-1} \left\{ Z_I erf \left(\sqrt{\gamma} |\mathbf{R} - \mathbf{R}_I| \right) \right.$$

$$\left. - \sum_{\mu \in I} q_\mu^I erf \left(\sqrt{\frac{\alpha_\mu^I \gamma}{\alpha_\mu^I + \gamma}} |\mathbf{R} - \mathbf{R}_I| \right) \right\},$$

which involves the differences of linear combinations of error functions. One can see that in the final ASA SEMP form, the Gaussian softened charge Q_γ acts as a scaling factor.

7. Finite values at R = R_I points

As mentioned previously, the SEMP does not possess any asymptotic values. The complications that arise when using the EMP in certain applications are those coinciding with nuclear positions, which are well known, but it can be easily shown that SEMP values are always finite at those particular locations where $\mathbf{R} = \mathbf{R}_I$. Such a

convenient characteristic results from the following property of the error function:

$$\lim_{x \to 0} \frac{erf(ax)}{x} = \frac{2a}{\sqrt{\pi}},$$

which can be easily deduced by taking into account the error function series expansion [48]:

$$erf(x) = \frac{2}{\sqrt{\pi}} \sum_{i=0}^{\infty} (-1)^i \frac{x^{2i+1}}{i!(2i+1)}.$$

Thus, the above limit ensures that all SEMP values are finite.

8. Examples

In the following examples, the softened probe charge and the associated GF exponent were set to 1 because, such a choice allows for the computation of molecular maps surrounding the molecules that are quite similar to the classical ones. Several assorted examples are given below. The molecules were handled with ASA densities computed with Mulliken atomic populations, which were obtained with optimized geometries at the HF computational level
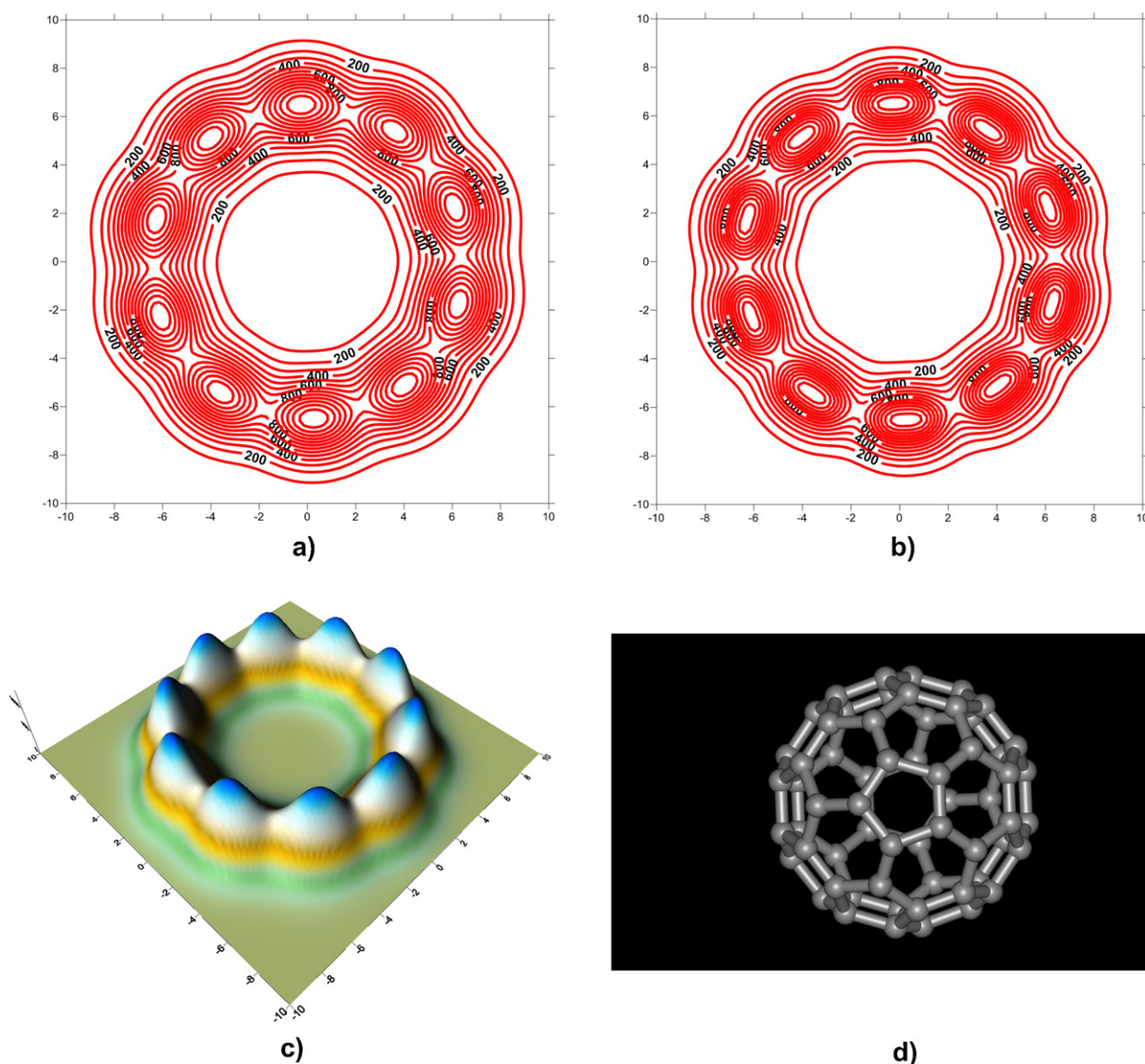
Fig. 7. The SEMP and classical EMP maps generated using the ASA approach for the C_{60} molecule. From left to right and top to bottom: (a) SEMP (ASA) contours, (b) classical (ASA) contours, (c) SEMP (ASA) 3D view and (d) buckminsterfullerene molecule.

using the 3-21G GTO basis set with the Spartan software program [51].

As was long time ago discussed in Ref. [27], one cannot expect a perfect ASA reproduction of exact EMP, but a fairly good approximated one. This can be easily checked by comparing Figs. 1–5 with the original Scrocco et al. results of Ref. [1].

First, a set of five small molecules are presented in Figs. 1–5. Such molecular structures were treated in the seminal paper of Scrocco et al. [1], which also details the structures' classical LCAO-SCF-MO EMP maps. The actual EMP maps were computed at the molecular plane ($z = 0$). It can be seen how the classical ASA-EMP and the ASA-SEMP maps provide very similar configurations in the external molecular envelope. In contrast, the classical EMP approach produces the usual asymptotic poles inside the molecules (not shown), whereas the SEMP approach provides a softened and finite pattern as expected, which is depicted in the provided three-dimensional representations of the SEMP for every molecule.

Fig. 6 shows the behavior of a SEMP in a molecule (aldosterone) which is larger than the molecules considered in the previous triatomic cycles. The SEMP and EMP for aldosterone are represented in a plane that lies as close as possible to the atoms of the steroid's four-ring structure, which can be considered here to be the molecular plane. As seen in the previous maps, the functional configuration in the external neighborhood of the molecule is fairly well reproduced in both potentials, and one can conjecture that it will be fairly similar to the ab initio EMP. In addition, the three-dimensional representation of the SEMP shows that every atom has an attached finite repulsive potential hill. Notably, such behavior may be of interest in many applications in which the entire molecular structure of a system must be considered (similarity calculations, map comparisons, etc.). In this case, the SEMP user does not have to be concerned about the possible appearance of repulsion potential poles at the points where atoms are located. Such an advantage might help, for example, to freely execute
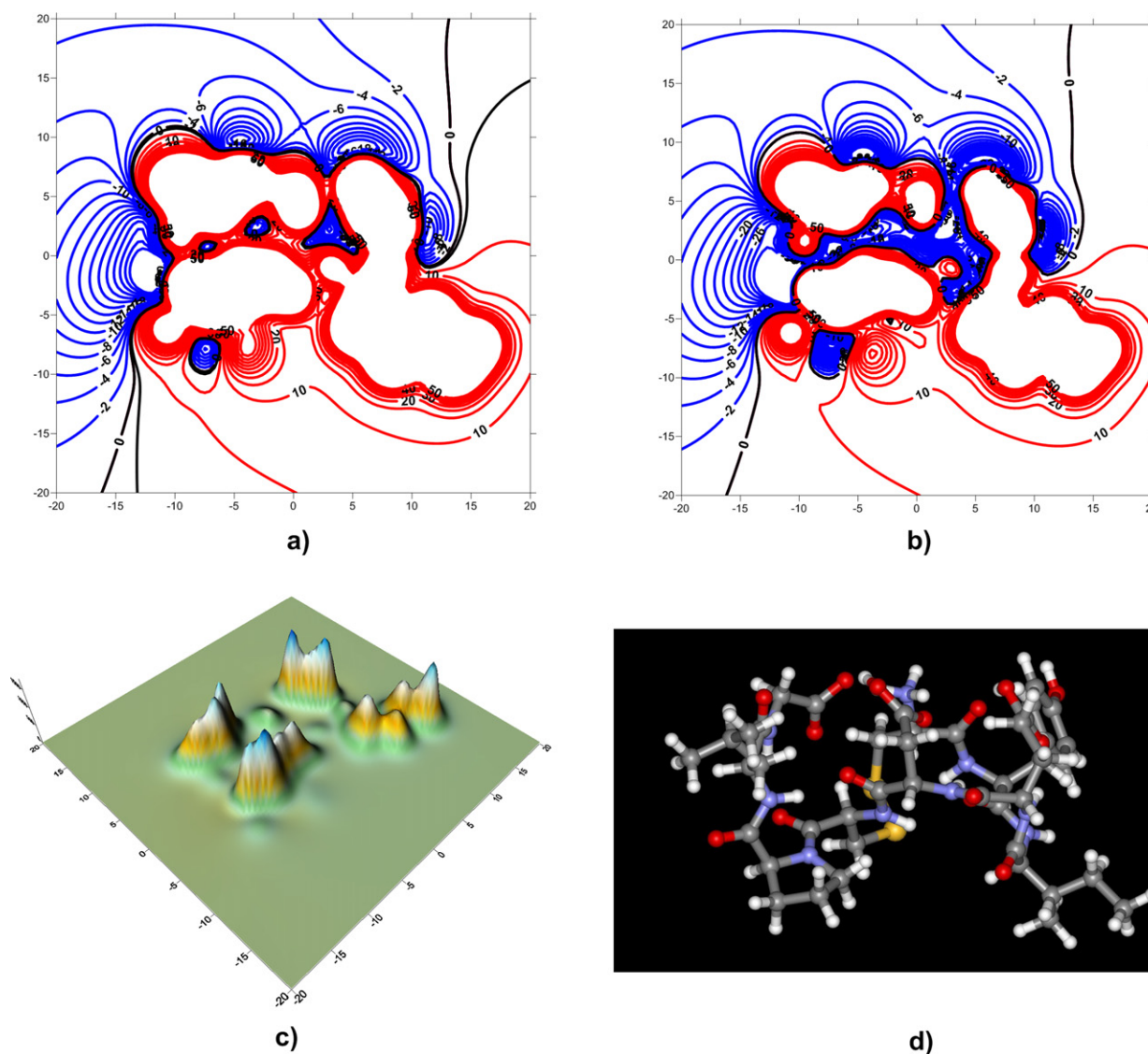
Fig. 8. The SEMP and classical EMP maps generated using the ASA approach for the oxytocin molecule. From left to right and top to bottom: (a) SEMP (ASA) contours, (b) classical (ASA) contours, (c) SEMP (ASA) 3D view and (d) oxytocin molecule.

procedures in which discrete grids are considered in numerical treatments.

The previously mentioned merits of the SEMP approach are also illustrated in Figs. 7 and 8. In Fig. 7, the representation of the C_{60} molecule is shown, with the SEMP and EMP functions drawn at the equatorial plane. In Fig. 8, a larger molecule, oxytocin, a mammalian hormone composed of 132 atoms, has been considered to illustrate the possibilities of using the SEMP approach to study large biological structures. The corresponding figure shows that SEMP calculations can be readily performed using the ASA approach, even for medium and large structures. The oxytocin plane in Fig. 8 is drawn across the molecule, swapping its inner part and some atoms of the complex structure, as shown in the representation of this polypeptide (Fig. 8). Using this plane representation, a visual comparison of Fig. 8a and b reveals how both approaches yield similar results when reproducing the potential along the arbitrary surroundings of the molecule. In addition, Fig. 8c clearly illustrates that infinity map divergences are absent around the selected in-plane atoms when using the SEMP approach.

9. Conclusions

The replacement of the hard positive charge in EMP calculations with a soft charge Gaussian distribution, the hallmark of SEMPs, constitutes a convenient algorithm that produces potential profiles very similar to those produced by EMPs in molecular neighborhoods. However, using the SEMP approach avoids the generation of infinity poles at atomic centers, the principal drawback of the EMP approach. Within the framework of the polarized ASA DF approach, SEMPs can be easily computed for both small and large molecular structures. The salient features of the SEMP approach make it a good candidate for use in quantum similarity calculations to compare different molecular structures.

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