

Fast Geometry Optimization in Self-Consistent Reaction Field Computations on Solvated Molecules

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The free energy gradient or Hessian of a molecule interacting with a liquid represented by a dielectric continuum is derived in the self-consistent reaction field formalism. An *ellipsoidal approximation* of the cavity is proposed with an algorithm to automatically define the ellipsoid from the nuclear coordinates of the atoms. With this approximation, geometry optimization of the solvated molecule becomes very fast. This method has been implemented in some standard *ab initio* or semiempirical computational codes. As a first test of the method, full geometry optimization of formamide in a high dielectric constant medium reveals that the CPU time needed for one optimization cycle is less than 3% longer for a solvated species than for the corresponding free molecule.

INTRODUCTION

Theoretical studies of molecular structure in the liquid state are becoming increasingly popular. Owing to the difficulty of a full treatment of a molecular liquid from first principles, simplified models are used and a wide variety of approaches is available. The problems connected with molecular electronic structure or reactivity require a description of the molecule at the quantum mechanical level. Therefore, the models allowing quantum chemical computations in the liquid state necessarily introduce a rather large degree of simplification in the description of the molecular surroundings.

In the self-consistent reaction field (SCRF)¹ approach, the solvent is assimilated to a dielectric continuum and the solute is assumed to be placed in a cavity. The polarization of the boundary between the cavity and the continuum by the solute's charge distribution creates a nonuniform electric field that interacts with the solute. The key feature of the model is the computation of this interaction. Several techniques have been proposed previously^{2,3} corresponding to different strategies in this computation. Geometry optimization, which is of major importance, has already been considered but to date the only available algorithms deal either with an oversimplified spherical cavity⁴ or with purely numerical techniques⁵ that may become exceedingly time consuming.

In the present approach, the charge distribution is represented by a multipole expansion. We shall use the spherical tensor formalism⁶ in which the

multipole of order l has $2l + 1$ independent components denoted M_l^m . Such a multipole is coupled with the l th derivatives of the electric potential, which are often called the "reaction field" components and which we shall denote R_l^m so that the energy of interaction between the molecule and the reaction field can be written:

$$\mathcal{K} = - \sum_{l=0}^{\infty} \sum_{m=-l}^l R_l^m M_l^m \quad (1)$$

In the rest of this article, we shall adopt the convention that the repeated indices correspond to a sum over all their possible values so that a shorthand expression of eq. (1) becomes:

$$\mathcal{K} = -R_l^m M_l^m \quad (2)$$

The reaction field represents a response of the surroundings to the charge distribution of the solute. Within the limits of the linear response approximation, one may write a proportionality relationship:

$$R_l^m = f_{ll'}^{mm'} M_{l'}^{m'} \quad (3)$$

Here, the reaction field factors $f_{ll'}^{mm'}$ only depend on the geometry of the cavity and on the dielectric permittivity ϵ of the solvent.

The shape of the cavity then plays a major role in the model. We proposed earlier to define the cavity by an electronic isodensity surface chosen in such a way that the volume of the cavity is equal to the partial molecular volume. It happens that this surface has some features in common with the van der Waals surface on the molecule, especially if the spheres are given a radius slightly larger than the van der Waals radius.³

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The cavity being defined, the reaction field factors can be computed numerically by verifying the electrostatic boundary conditions.⁷ The presence of the reaction field perturbs the electronic structure of the molecule and the equilibrium position of the nuclei. The averaged structure of the solute corresponds to the minimum of the free energy of the system, i.e., the energy of the molecule and the free energy of solvation, which is given by⁸:

$$\Delta A_e = -\frac{1}{2} M_l^m f_{ll'}^{mm'} M_{l'}^m \quad (4)$$

The minimization of the free energy of the system allows us to derive a set of self-consistent field equations in which $F_{\mu\nu}$, the $(\mu\nu)$ element of the Hartree-Fock operator, is deduced from the corresponding element $F_{\mu\nu}^0$ in the case of an isolated molecule by the equation:

$$F_{\mu\nu} = F_{\mu\nu}^0 + M_l^m f_{ll'}^{mm'} \langle \mu | M_{l'}^{m'} | \nu \rangle \quad (5)$$

Here, $M_{l'}^{m'}$ denotes the electronic part of the quantum mechanical operator associated with the m' th element of the multipole of rank l' .

It is then possible to determine the electronic structure of a solvated molecule in the Born-Openheimer approximation and at the Hartree-Fock level. The equilibrium geometry corresponds to the minimum of the free energy with respect to the position of the nuclei. The minimization can be efficiently performed if the derivatives of the free energy with respect to the nuclear coordinates are known. These are usually obtained numerically and the computation may be pretty lengthy. Since this approach is based on a model with no pretention of being realistic, one may look for further simplifications allowing a substantial gain in computational time. It happens that in the case of small molecules this cavity can often be approximated with good accuracy by some regularly shaped surface such as an ellipsoid, a spheroid, or even a sphere. Then, the reaction field factors have an analytical expression^{8,9} that makes the SCF computations almost as fast as for a free molecule and the derivatives of the free energy can be efficiently computed as well, as we shall now show.

ENERGY GRADIENT AND HESSIAN FOR A SOLVATED MOLECULE

The SCRF formalism rests on the assumption that there is no entropy variation during the variational procedure to compute the molecular wave function so that the modified SCF equations (5) are obtained by minimizing the quantity:

$$\Delta A = E_0 - \frac{1}{2} R_l^m M_l^m \quad (6)$$

in which E_0 is the Hartree-Fock energy obtained with the wave function of the solvated molecule.

Similarly, the search for a critical point on the potential energy surface of the system can be performed under the same assumption, although some corrections may be necessary *in fine* due, for instance, to the disappearance or the emergence of a symmetry property that may affect the partition function. This limitation should be kept in mind for the following considerations. Therefore, we shall deal with the derivatives of the free energy variation ΔA defined by (6) with respect to the atomic coordinates.

Following a convention used earlier,^{10,11} we shall denote by $\partial_k B$ the partial derivative of any quantity B with respect to an atomic coordinate q_k , C_j an eigenvector of the Hartree-Fock operator (5) in the basis of atomic orbitals, C_j^+ its transposed vector, and n_j its occupation number. In addition, we shall denote by H^c the core hamiltonian and G the electron-electron interaction operator so that the Hartree-Fock matrix is written:

$$F = H^c + \sum_j n_j C_j^+ (G + R_l^m M_l^m) C_j \quad (7)$$

in which M_l^m is the operator associated with the multipole moment component M_l^m . The Hartree-Fock-Roothaan equations take the form:

$$F C_i = e_i S C_i \quad (8)$$

in which e_i is the eigenvalue and S the overlap matrix.

The free energy variation is defined by:

$$\Delta A = \sum_i n_i C_i^+ \left[H^c + \frac{1}{2} \left(\sum_{n_j} C_j^+ G C_j + R_l^m M_l^m \right) \right] C_i - \sum_{(AB)} \frac{Z_A Z_B}{R_{AB}} - \frac{1}{2} \sum_A R_l^m Z_A M_l^m(\mathbf{R}_A) \quad (9)$$

in which $\Sigma_{(AB)}$ stands for a sum over the pairs of nuclei AB , R_{AB} is the distance between these nuclei, \mathbf{R}_A the radius vector of nucleus A , and Z_A its charge in atomic units.

Therefore, the partial derivatives of ΔA can be written:

$$\begin{aligned} \partial_k \Delta A = & \sum_i n_i C_i^+ \\ & \times \left[\partial_k H^c + \frac{1}{2} \sum_j n_j C_j^+ \partial_k G C_j + R_l^m \partial_k M_l^m \right] C_i \\ & + 2 \sum_i n_i \partial C_i^+ \left[H^c + \sum_j^{occ} n_j C_j^+ (G + R_l^m M_l^m) C_j \right] C_i \\ & - \sum_{(AB)} \frac{Z_A Z_B}{R_{AB}^2} \partial_k R_{AB} - R_l^m \sum_A Z_A \partial_k M_l^m(\mathbf{R}_A) \\ & - \frac{1}{2} M_l^m \partial_k f_{ll'}^{mm'} M_{l'}^{m'} \end{aligned} \quad (10)$$

In this equation, we made use of eq. (3) relating R to M . We notice that the coefficient of $\partial_k C_i^+$ is the right-hand side of eq. (8) defined by eq. (7) and by making use of the normalization condition:

$$C_i^+ \mathbf{S} C_i = 1 \quad (11)$$

which is derived as:

$$2\partial_k C_i^+ \mathbf{S} C_i + C_i^+ \partial_k \mathbf{S} C_i = 0 \quad (12)$$

Equation (10) reduces to:

$$\begin{aligned} \partial_k \Delta A = & \sum_i n_i C_i^+ \\ & \times \left[\partial_k \mathbf{H}^c + \frac{1}{2} \sum_j n_j C_j^+ \partial_k \mathbf{G} C_j + R_l^m \partial_k \mathbf{M}_l^m - e_i \partial_k \mathbf{S} \right] \\ & \times C_i - \sum_{(AB)} \frac{Z_A Z_B}{R_{AB}^2} \partial_k R_{AB} - R_l^m \sum_A Z_A \partial_k \mathbf{M}_l^m(\mathbf{R}_A) \\ & - \frac{1}{2} M_l^m \partial_k f_{ll'}^{mm'} M_{l'}^m \end{aligned} \quad (13)$$

The important point in this equation is the fact that the first derivatives of the free energy do not depend on the derivatives of the eigenvectors or, equivalently, of the density matrix. The derivatives of \mathbf{H}^c and \mathbf{G} are usually computed in modern quantum chemistry packages. The derivatives of R_{AB} and of the nuclear contributions to the multipole moments $\mathbf{M}_l^m(\mathbf{R}_A)$ do not raise any difficulty; the only problem arises from the derivation of the reaction field factors $f_{ll'}^{mm'}$ that, in general, has to be performed numerically after the definition of the boundary of the cavity and the numerical procedure to compute these factors.

The Hessian matrix is obtained by a second derivation performed on eq. (13). The second derivatives of the previous quantities, as well as the first derivatives of the eigenvectors, occur in the results. An efficient procedure to compute the derivatives of the eigenvectors has been proposed in ref. 10 and 11. Again, the only new problem comes from the second derivatives of the reaction field factors. We introduce in the next paragraph the so-called *ellipsoidal approximation* in which the cavity is fitted to an ellipsoid whose shape is modified according to the geometry variations of the solute. This approximation allows an analytical definition of the first and second derivatives and, therefore, a very efficient algorithm to optimize the geometry of a molecule interacting electrostatically with a liquid solvent.

ELLIPSOIDAL APPROXIMATION

Many small molecules fit an ellipsoidal cavity pretty well, provided that this cavity has been carefully defined. In our approach, we always constrain the cavity to have a volume V equal to the

average molecular volume in the liquid state at the temperature of the study.⁸ This volume may be deduced from the van der Waals volume V , but it is known to be significantly larger.³ In the case of the ellipsoidal approximation, we only have to define the relative lengths of the axes. We again relate these quantities to the van der Waals surface by considering that this surface be the external boundary of a solid of uniform density, which we call the van der Waals solid. Let $\bar{X}_1 \bar{X}_2 \bar{X}_3$ be the three principal axes of inertia of this solid, corresponding to the three principal moments $I_1 I_2 I_3$. The ellipsoid is defined such that $\bar{X}_1 \bar{X}_2 \bar{X}_3$ are its axes and that its principal moments of inertia are proportional to $I_1 I_2 I_3$, the proportionality factor being fixed by the condition on the volume. Therefore, for any of the semiaxes a_i :

$$a_i = \left(\frac{3V}{4\pi} \right)^{1/3} \times \frac{(I_{i'} + I_{i''} - I_i)^{1/2}}{[(I_2 + I_3 - I_1)(I_3 + I_1 - I_2)(I_1 + I_2 - I_3)]^{1/3}} \quad (14)$$

in which the triad, i, i', i'' corresponds to any order of 1, 2, 3.

In the ellipsoidal approximation, the cavity is then defined by six independent parameters: the three semiaxes $a_1 a_2 a_3$ and the three parameters $\omega_1 \omega_2 \omega_3$ (the Euler angles for instance), which define the orientation of the axes in the reference frame.

The variation of any nuclear coordinate q_k modifies the six quantities and the derivative of $f_{ll'}^{mm'}$ with respect to this coordinate may be written:

$$\partial_k f_{ll'}^{mm'} = \sum_i \frac{\partial f_{ll'}^{mm'}}{\partial a_i} \partial_k a_i + \sum_j \frac{\partial f_{ll'}^{mm'}}{\partial \omega_j} \partial_k \omega_j \quad (15)$$

The derivatives $\partial_k a_i$ and $\partial_k \omega_j$ are related to the modifications of the van der Waals tensor of inertia due to the variation of q_k . According to the method of computation of this tensor detailed in the Appendix, we only have to consider the displacement of the sphere associated to the atom bearing the coordinate q_k with respect to those relative to the atoms sharing a chemical bond with the former. The variation of the tensor of inertia is readily obtained and by the diagonalization of this tensor one obtains the derivatives of interest.

Finally, the derivatives $\partial f_{ll'}^{mm'}/\partial a_i$ and $\partial f_{ll'}^{mm'}/\partial \omega_j$ are obtained by analytical derivation of the formulae defining these factors^{9,12} and the corresponding multipole moments.

IMPLEMENTATION AND TEST OF THE METHOD

This fast optimization procedure has been implemented in the GEOMOS package¹³ to work at the

Table I. Bond lengths, $r(\text{\AA})$, and bond angles, $\theta(^{\circ})$ of the isolated and the solvated molecule of planar formamide.

Internal coordinate	Isolated	Solvated
r_{CN}	1.3485	1.3360
r_{CO}	1.1929	1.2052
r_{CH}	1.0908	1.0874
r_{NH1}	0.9955	0.9975
r_{NH2}	0.9929	0.9946
θ_{NCO}	125.00	125.03
θ_{NCH}	112.69	113.19
θ_{CNH1}	119.26	120.49
θ_{CNH2}	121.83	121.19

semiempirical level. Links for Gaussian 86¹⁴ and HONDO¹⁵ packages have been programmed.*

To illustrate the possibilities of the method, full geometry optimization of the formamide molecule in the standard 6-31G* basis set with the Gaussian 86 package working on a IBM RISC 6000/530 workstation has been performed in the isolated state and in a solvent with a high dielectric constant ($\epsilon = 78$). The geometric parameters are given in Table I. The fit between the ellipsoidal cavity and the van der Waals surface of the molecule can be appreciated in Figure 1.

The efficiency of the algorithm can be measured by the ratio of the CPU time needed by one cycle of the geometry optimization process for a molecule in solution and in the free space, respectively. In this example, the ratio is less than 1.03 and this result appears to be more or less constant in a series of other cases. Therefore, full geometry optimization of a molecule in a situation that simulates a liquid surroundings becomes readily accessible.

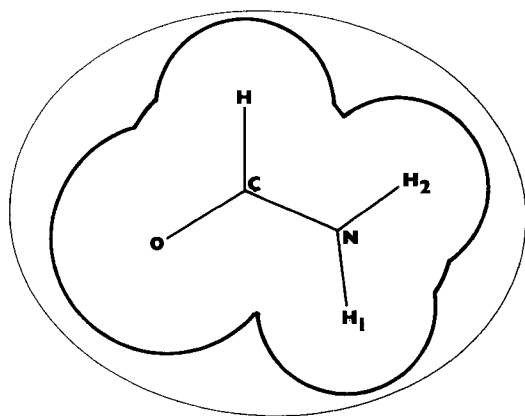


Figure 1. Intersection with the plane containing the nuclei of the van der Waals surface and the ellipsoid of formamide.

*A copy of the programs may be obtained from the authors on request.

CONCLUSION

In this article, we showed that the ellipsoidal approximation is very powerful in simplifying the algorithms devised to perform quantum chemical computations on molecules interacting with a liquid.

At first glance, one may be reluctant to use such an approximation instead of a more realistic shape of the cavity and obviously the use of this approach is not universal. Nevertheless, one must bear in mind that the continuum models are still a rather naive picture and that in the center of the cavity the electrostatic potential differences from one shape of cavity to another are often less than the error bars on the same quantity computed with a Monte Carlo averaging of a model system in which the liquid is represented as an ensemble of discrete molecules.¹⁶

This approximation appears to be good for most small molecules. It ceases to be valid when the distance of one atom to the ellipsoid is smaller than ca. 90% of its van der Waals radius. This failure is usually characterized by a divergence of the multipole expansion of the solute-solvent energy of interaction.

This method therefore appears to be a useful tool for the study of the basic problems raised by the physical effects of a solvent on the structure and reactivity of a molecular solute on selected model solutes that meet the geometrical conditions imposed by the ellipsoidal approximation. It can be further used as a first step in a computation using a more sophisticated shape of cavity, either to optimize the geometry that will be used subsequently to reevaluate the energy of interaction or to provide a realistic starting point for a geometry optimization in a more complex procedure.

APPENDIX: DEFINITION OF THE CAVITY

The van der Waals volume of a pair of bonded atoms I and J with van der Waals radii r_i and r_j and a bond length d can be defined by:

$$V_{IJ} = V_I + V_J - V_{I \cap J} \quad (16)$$

in which V_I and V_J represent the volumes of the atomic van der Waals spheres and $V_{I \cap J}$ the volume of their intersection. The plane of the intersection of the spheres splits this intersection into two portions whose volume can be computed by simple geometric considerations (Fig. 2).

If V_{IS} is the volume of the portion of the sphere I belonging to $V_{I \cap J}$, one obtains:

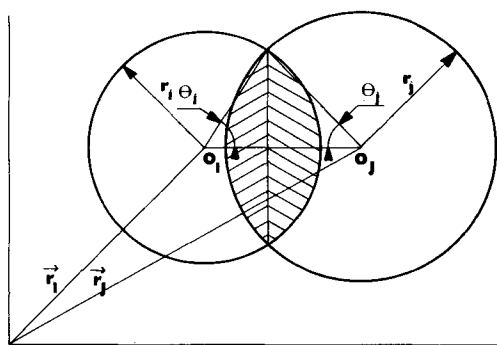


Figure 2. Intersection of two van der Waals spheres.

$$V_{IS} = \frac{\pi}{3} r_i^3 (2 - 3 \cos \theta_i + \cos^3 \theta_i) \quad (17)$$

with $\cos \theta_i = r_i^2 - r_i^2 + d^2/2dr_i$.

The same definition holds *mutatis mutandis* for V_{JS} and

$$V_{IJ} = V_{IS} + V_{JS} \quad (18)$$

This result is easily extended to polyatomic molecules, in which the above computation refers to pairs of bonded atoms.

The α coordinate of the center of mass of the same pair of spheres assumed to be filled by a medium having a density of 1 is defined by:

$$g_{IJ}^\alpha = \frac{V_I r_I^\alpha + V_J r_J^\alpha - V_{IJ} g_{IJ}^\alpha}{V_{IJ}} \quad (19)$$

Again, g_{IJ}^α is computed by adding the contribution of the two portions of spheres. In a local frame in which the origin is chosen at the center O_I of sphere I and the z axis is along the $O_I O_J$ direction the z coordinate of the center of mass of the portion of sphere I is g_I' such that:

$$V_{IS} g_I' = \frac{\pi r_i^4}{3} (1 - 2 \cos \theta_i + \cos^4 \theta_i) \quad (20)$$

In the same reference frame, the z coordinate of the center of mass of the portion of sphere J is:

$$V_{JS} g_J' = d V_{JS} + \frac{\pi r_j^4}{3} (1 - 2 \cos \theta_j + \cos^4 \theta_j) \quad (21)$$

and for the intersection:

$$V_{IJ} g_{IJ}' = V_{IS} g_I' + V_{JS} g_J'$$

In the frame of the molecule, the $\vec{O_I O_J}$ vector has three components r_{IJ}^α and if r_i^α is a component of the radius vector of the center of atom I :

$$g_{IJ}^\alpha = r_i^\alpha + g_{IJ}' \frac{r_{IJ}^\alpha}{d} \quad (22)$$

In the case of a polyatomic molecule, eq. (19) is easily generalized to give:

$$g^\alpha = \frac{\sum_I V_I r_I^\alpha - \sum_{(IJ)} V_{IJ} g_{IJ}^\alpha}{V} \quad (23)$$

in which $\sum_{(IJ)}$ stands for a sum over pairs of bonded atoms and V the volume.

In the above reference frame defined by the centers of the spheres, the tensor of the second moments, used to define the tensor of inertia, has two components B^\parallel and B^\perp . The second moments of the portion of sphere I in common with J are defined by:

$$B_I^\perp = \frac{\pi r_i^5}{60} \times (8 - 15 \cos \theta_i + 10 \cos^3 \theta_i - 3 \cos^5 \theta_i) \quad (24)$$

and

$$B_I^\parallel = \frac{\pi r_i^5}{15} (2 - 5 \cos^3 \theta_i + 3 \cos^5 \theta_i) \quad (25)$$

and, in the same reference frame, the second moments of the intersection are:

$$B_{IJ}^\perp = B_I^\perp + B_J^\perp \quad (26)$$

$$B_{IJ}^\parallel = B_I^\parallel + B_J^\parallel - 2g_{IJ}'(g_I' + g_J') + g_{IJ}'^2 V_{IS} + (g_{IJ}' - d)^2 V_{JS} \quad (27)$$

To obtain the corresponding quantities in the general reference frame, one has to rotate the axes and translate the origin. Rotations are performed by the conventional rotation matrices defined by the direction cosines of direction \vec{r}_{ij} , leading to $B_{IJ}^{\alpha\beta}$ tensor components. After the translations of the origin one obtains:

$$B_{IJ}^{\alpha\beta} = B_{IJ}^{\alpha\beta} + V_{IJ} g_{IJ}^\alpha g_{IJ}^\beta \quad (28)$$

The second moments of polyatomic molecule with an origin at the center of mass are given by the general equation:

$$B^{\alpha\beta} = \sum_I \frac{4\pi}{3} r_i^3 \left(r_i^\alpha r_i^\beta + \delta_{IJ} \frac{r_i^2}{5} \right) - \sum_{(IJ)} B_{IJ}^{\alpha\beta} - V g^\alpha g^\beta \quad (29)$$

in which δ_{IJ} is the Kronecker symbol.

The components of the tensor of inertia are readily obtained from these second moments.

There is a linear relationship between the molecular and van der Waals volumes, respectively, V_{mol} and V , given by:

$$V_{mol} = \alpha V + \beta$$

where α and β are constants.

These quantities all depend only on the radius vectors \vec{r}_i and on the cosine of \vec{r}_{IJ} , which are easy to derive with respect to the coordinates of the corresponding atoms.

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