

## Necessary Conditions for the Calculation of Useful Electrostatic Isopotential Maps from CNDO/INDO Wavefunctions

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The calculation of reliable electrostatic isopotential maps from CNDO or INDO wavefunctions while preserving the ZDO approximation fails because the individual atoms are treated as if they were spherical charge distributions. The resulting potential maps could be adequately interpreted on the basis of classical electrostatics. Approaches to the determination of useful maps include (a) the use of localized orbitals with a ZDO approximation applied among the localized orbitals as long as the localization procedure is defined with respect to the connectivity of the molecule and has no reference to a set of laboratory coordinates or (b) relaxation of the ZDO approximation in the determination of the potential by including the 3-center potential integrals. In either case, the preservation of rotational invariance takes paramount importance.

**Key words:** Electrostatic isopotential maps – ZDO approximation – Rotational invariance.

The calculation of electrostatic isopotential maps has been a useful tool in the study of chemical reactions [1]. The application of electrostatic isopotential maps has emphasized the use of *ab initio* wavefunctions. Although the *ab initio* wavefunctions have been calculated and electrostatic isopotential maps have been drawn for some molecules of fairly respectable size, the expense involved in an activity of this sort can become prohibitive quite easily. The problem of expense is aggravated when the study of the effect of solvation on solute properties is attempted.

In a recent study of the effect of solvation on the barrier to internal rotation of formamide [2], the calculation of the electrostatic potentials and fields generated by a solute molecule from an *ab initio* STO-3G wavefunction were used to generate charges on the walls of a cavity in a polarizable medium treated as a continuum [3]. The induced charges polarize the solute wavefunctions, and both the charges on the cavity walls and the solute wavefunctions are calculated iteratively until overall self-consistency is achieved. In this model of solvation, there is a definite need for a good representation of electrostatic potentials and fields in this approach to solvation.

Included in this same study was a comparison of this cavity model in which an *ab initio* wavefunction for the solute had been used with a previously developed solvation model of solvation employed in the context of a CNDO/2 method of calculation [4]. Although both methods reproduced the experimental trend of increasing rotational barrier of formamide with increasing solvent dielectric constant, the extension of either method to larger molecules (particularly molecules of biological interest) would cause problems. The cavity model with *ab initio* wavefunctions is costly to use. The solvation model suffers from ambiguities in the generation of solvations and the possibility of problems associated with wavefunction polarization. It would be desirable to combine the best features of both methods (the cavity inside of a polarizable medium and the ease of use of semiempirical calculations) to examine the effect of solvation on the properties of larger molecules.

There are problems associated with the calculation of electrostatic isopotential maps using CNDO wavefunctions [5, 6, 7]. Approximations I, II, and III in the Giessner-Prettre and Pullman papers include the ZDO approximation. They fail to dispose regions of strong negative potential to where lone pairs of electrons can be expected. Rather, in the case of formaldehyde, each approximation has a single region of strong negative potential on the C—O bond axis. The approximations predict quite different magnitudes for the potentials and fields.

Electrostatics can be used to provide an explanation why potential wells are predicted to be on the C—O bond axis when approximations based on ZDO are used. In ZDO, all charge distributions are centered at the atoms and each distribution is treated as if it were spherically symmetrical. For instance, consider the oxygen and carbon atoms in formaldehyde as if they were spheres or point charges with net charges from a CNDO calculation. The oxygen bears a small negative charge and the carbon a small positive charge. A potential map associated with these two points will show a minimum on the C—O bond axis on the side of the oxygen opposite to the carbon. This is the same as found from the CNDO wavefunctions. One should not be surprised to discover that any potential calculation including the ZDO approximation and the assumption of spherical averaging will give an identical orientation of the potential well with the only differences being the depth of the well and its distance from the atom.

If the molecule has low symmetry, there may be superficial differences in the potentials calculated which may give the illusion of a recognition of molecular

geometry or lone pairs. This behavior is an artifact of the details of the addition of the spherically disposed contributions to the potential from the different atoms of the molecule with the values depending on the particular approximation used to calculate the overall potential at a given point.

Departure from the ZDO approximation and the spherical averaging of potentials has been attempted by Giessner-Prettre and Pullman [5] in their Approximation IV and by Caballol, et al. [7].

Giessner-Prettre and Pullman deorthogonalized the ZDO basis by applying the inverse of the Löwdin orthogonalization to the STO basis used which is assumed to have been previously (and hypothetically) orthogonalized by this transformation. The molecular orbital coefficients obtained after this procedure had been employed are used with explicitly calculated 2-center and 3-center potential energy integrals to obtain a potential map. With formaldehyde [5], this procedure was reasonably successful in representing an *ab initio* map. However, for guanine [6], incorrect relative depths for oxygen and nitrogen were predicted in this approximation just as had been predicted when the ZDO approximation and spherical averaging had been retained. The specific problem in the calculation of potential maps for guanine is the overemphasis of the oxygen relative to the nitrogen, and it appears that this is difficult to avoid in the CNDO/2 parameterization.

The Giessner-Prettre and Pullman treatment also suffers from the problem of expense; it is costly to determine orthogonalization matrices and then to calculate 3-center potential energy integrals. A major point in favor of performing CNDO calculations is their inexpensiveness. In addition there is an aesthetic problem related to the treatment of the basis set. Deorthogonalization is performed to undo a transformation which had never been carried out. The supposedly transformed (and delocalized) orbitals are simply STO's localized on the atoms; they would not have been localized had the orthogonalization really been carried out. After deorthogonalization, the basis is supposed to have become changed into a set of atom localized orbitals which is supposed to have been the original nonorthogonal basis; in actuality, the STO orbitals have become transformed into a multicentered set of functions.

The approach of Caballol et al. [7] is supposed to have been successful in that it purports to have calculated a potential map from a CNDO wavefunction for formaldehyde that is quite similar to the *ab initio* map. However, the procedure has failed [6] and is likely to fail because it is not rotationally invariant. Had Giessner-Prettre and Pullman used a different orientation for the guanine with the treatment used by Caballol, they would have obtained a different map.

Preservation of rotational invariance is an old problem [8]. Hase et al. discuss it in terms of density maps, but the particular application is of no consequence. Density maps are one-electron expectation values of the delta function, and potential maps are expectation values of  $r^{-1}$ . Regardless of the type of expectation value,

the first order electron density must be preserved as an invariant independent of the frame of reference.

Having identified these problems, one may state necessary conditions which should be met by an adequate, if not successful, method of calculating electrostatic isopotential maps from semiempirical wavefunctions. Any proposed scheme must preserve rotational invariance and abandon the assumption of a spherical charge densities around atoms.

The use of localized orbitals has been suggested [9] as a way of resolving the problem. In order to preserve rotational invariance, the localized orbitals must be referred to an internal frame in the molecule in a consistent and unbiased manner. In the final analysis, the connectivity of the molecule will govern the localization procedure. In order to move away from spherical charge distributions, a ZDO approximation between different localized orbitals may be made. Otherwise, the localization procedure would accomplish nothing since the localized set of orbitals would be the result of an orthogonal transformation among the original set of orbitals. For application to solvation problems, the localization procedure must possess sufficient flexibility to be able to generate localized orbitals and potentials which reflect the effects of wavefunction polarization induced by solvation.

The inclusion of 3-center integrals which represent contributions to the potential due to overlap distributions was primarily responsible for the partial success of the Giessner-Prettre and Pullman Approximation IV. The deorthogonalization might be nonessential except as a rationalization for the abandonment of the ZDO approximation. The inclusion of overlap charge distributions is a sufficient departure from the assumption of spherical averaging. All that must be done further is to include these overlap distributions in a potential map calculation in such a manner that rotational invariance is preserved.

These approaches are being examined in this laboratory and in a cooperative research effort with the Theoretical Chemistry Group of the Polymer Institute of the Slovak Academy of Sciences.

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