

## 3D Structure Based Atomic Charge Calculation for Molecular Mechanics and Molecular Dynamics Simulations

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### Abstract

We propose a new charge equilibration approach that depends upon molecular 3D structure. Nishimoto – Mataga equation is used to express the shielding effect. With the present approach, it is not necessary to iterate simultaneous equations for evaluating charge equilibration, although that is required in the QEq method. Atomic charge calculations were carried out for several organic molecules. Calculated charge distributions are in good agreement with experimental values.

**Key Words:** Atomic Charge, Charge Equilibration method, 3D structure, Molecular Mechanics, Molecular Dynamics, Dipole Moment

**Area of interest:** Molecular Computation

## 1. Introduction

Generally, a non-bonded interaction is represented by the following formula:

$$E_{\text{non-bonded}} = E_{\text{short+middle}} + E_{\text{electrostatic}} \quad (1)$$

A serious problem is that conventional molecular mechanics and molecular dynamics simulations use fixed charges that cannot represent the relaxation of charge distribution that depends upon changing molecular structure, which is essential to evaluate the appropriate electrostatic energies

for biopolymer simulations like the prediction of protein folding. We propose a new charge equilibration approach that depends upon geometry, apply the method to a number of molecules, and compare our results with the experimental or ab initio MO method.

## 2. Method

Rappé and Goddard have proposed the charge equilibration (QEq) approach for predicting charge distribution that depends upon molecular geometry [1]. They derived the following formula (2) between atomic chemical potential  $\chi_A$  and atomic charge  $Q_A$ :

$$\chi_A(Q_1 \wedge Q_N) = \chi_A^0 + J_{AA}^0 Q_A + \sum_{B \neq A} J_{AB} Q_B \quad (2)$$

$$\chi_A^0 = \frac{1}{2}(IP + EA) \quad (3)$$

$$J_{AA}^0 = IP - EA \quad (4)$$

where  $IP$  and  $EA$  denote the ionization potential and electron affinity and  $J_{AB}$  is the Coulomb integral between atoms A and B.

The atomic chemical potentials equilibrium conditions

$$\chi_1 = \chi_2 = \dots = \chi_N \quad (5)$$

and the condition on total charge

$$Q_{total} = \sum_{i=1}^N Q_i \quad (6)$$

lead to a total of  $N$  simultaneous equations

$$\mathbf{CQ} = \mathbf{D} \quad (7)$$

where

$$C_{1j} = 1 \quad (8)$$

$$C_{ij} = J_{1j} - J_{ij} \quad \text{for } i \geq 2$$

and

$$D_1 = Q_{total} \quad (9)$$

$$D_i = \chi_i^0 - \chi_1^0 \quad \text{for } i \geq 2.$$

To express the shielding effect, we have chosen the Nishimoto – Mataga equation [2] (10) for evaluating Coulomb integrals.

$$J_{AB} = \frac{1}{R_{AB} + \gamma} \quad (\text{a.u.}) \quad (10)$$

$$\gamma = 2[J_{AA}^0 + J_{BB}^0]^{-1}$$

where  $R_{AB}$  is the distance between A and B. Since the Nishimoto – Mataga equation (10) does not contain the atomic charges  $Q_A$ , it is not necessary to iterate simultaneous equations for evaluating charge equilibration, although that is required in the QEq method [1].

In addition to calculating atomic charges, the derivative of atomic charges with respect to nuclear coordinates  $X, \partial Q_j / \partial X$ , can be calculated by the following simultaneous equations (11). Taking the derivative of the charge equilibrium equation (7) with respect to  $X$  leads to the simultaneous equations (11):

$$\sum_j \frac{\partial Q_j}{\partial X} = 0 \quad \text{for } i = 1 \quad (11)$$

$$\sum_j c_{ij} \frac{\partial Q_j}{\partial X} = - \sum_j \left\{ \frac{\partial J_{1j}}{\partial X} - \frac{\partial J_{ij}}{\partial X} \right\} Q_j \quad \text{for } i \geq 2.$$

In the following calculation, we used the atomic parameters  $\chi_A^0$  and  $J_{AA}^0$  that are independent of molecules in reference [1].

### 3. Results and discussion

Atomic charge calculations were carried out for the following molecules: formaldehyde, acetaldehyde, formamide, formic acid, acetic acid, propane, methylamine, methanol, ethanol, methanethiol, dimethyl sulfide, toluene, phenol, and (Ala)<sub>5</sub> conformers. Molecular structures of small molecules are taken from HF/6-31G\*\* optimized geometries. (Ala)<sub>5</sub> conformers are modeled with the MSI InsightII molecular modeling system [4]. The semi-empirical AM1 and ab initio molecular orbital (MO) calculations were carried out on a DELL Precision 610 workstation (Pentium II Xeon 450MHz) with the Gaussian 98 program system [5]. The calculated dipole moments are listed in Table 1, and Figure 1 shows the correlation between the present results and the experimental values. The calculated dipole moments of (Ala)<sub>5</sub> conformers are listed in Table 2.

Standard deviations were 0.57D, 0.37D, and 0.15D in the present method, HF/AM1, and HF/6-31G\*\* calculations, respectively. Although the error is larger than the MO calculations, the trend that for corresponds well, and the present calculations give charge distributions close those of the MO calculations. The calculated dipole moments of (Ala)<sub>5</sub> alpha helix and extended conformations are good agreements with those of HF/AM1 and HF/STO-3G calculations. The computation time of the present method is about 10<sup>3</sup> times faster than the AM1 method and 10<sup>4</sup> times faster than the HF/6-31G\*\* method.

By using the Nishimoto-Mataga equation to estimate a coulomb potential, the present method can calculate the atomic charge just by solving a simultaneous equation once. It will be possible to simulate the change of charge distribution by a change in the molecule structure, by incorporating this method to the molecular dynamics and molecular mechanics calculations. We believe that this approach will be useful for simulating biomolecules as an important non-bonded interaction.

Table 1  
Calculated Dipole Moments (in D)

Compound	Present	HF/AM1	HF/6-31G**	Expt. <sup>a)</sup>
Formaldehyde	2.6753	3.4159	2.6628	2.3315
Acetaldehyde	3.3224	2.4338	2.9948	2.750
Formamide	2.8887	3.4159	4.0931	3.711
Formic acid	1.1678	1.2861	1.6254	1.4214
Acetic acid	2.7363	1.5778	1.8286	1.70
Propane	0.0355	0.0076	0.0600	0.0841
Methylamine	0.7736	1.5745	1.4735	1.27
Methanol	1.9274	1.5908	1.8334	1.66
Ethanol	1.8991	1.5039	1.7037	1.441
Methanethiol	2.1832	1.8584	1.7828	1.26
Dimethyl sulfide	2.2570	1.7379	1.8060	1.554
Toluene	0.3218	0.2850	0.2932	0.375
Phenol	2.2711	1.1751	1.4293	1.224

a) Ref. [3].

Table 2  
Calculated Dipole Moments of (Ala)<sub>5</sub> Conformers (in D)

Conformation	Present	HF/AM1	HF/STO-3G
Alpha helix	10.4269	14.5816	11.0891
Beta strand	6.1815	2.3141	2.5459
Extended	5.3545	6.1192	5.6600

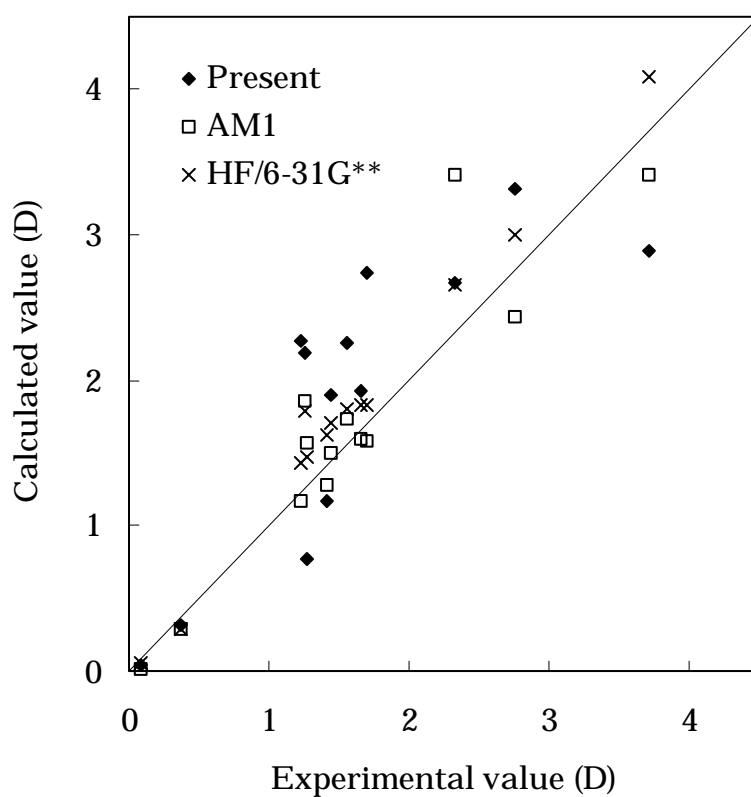


Figure 1 Comparison between experimental and calculated values of dipole moments

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## 分子力学および分子動力学シミュレーションのための3次元構造に基づいた原子電荷の計算

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### 要旨

分子の3次元構造に基づいた原子電荷の計算方法を開発した。この方法は、Goddardらの電荷平衡法を基に、クーロンポテンシャルの計算に西本 - 又賀の式を用い、連立一次方程式の反復計算を不要にし、計算時間の大幅な短縮を実現した。この方法で計算された原子電荷から分子の双極子モーメントを計算し、AM1法、ab initio 分子軌道法による計算値および実験値との比較を行い、よい一致を得た。この方法を分子力学および分子動力学計算に組み込むことにより、分子構造の変化による電荷分布の変化をシミュレーションに取り込むことが可能になり、タンパク質のような非結合相互作用が重要な系の解析に有用であると考えられる。

**キーワード:** 原子電荷、電荷平衡法、3次元構造、西本 - 又賀の式、双極子モーメント、分子力学、分子動力学、非結合相互作用

**領域区分:** 分子計算