

Molecular dynamics study on glycolic acid in the physiological salt solution

S Matsunaga

National Institute of Technology, Nagaoka College, 940-8532 Nagaoka, Japan

E-mail: matsu@nagaoka-ct.ac.jp

Abstract. Molecular dynamics (MD) study on glycolic acid in the physiological salt solution has been performed, which is a model of a biofuel cell. The structure and charge distribution of glycolic acid in aqueous solution used in MD is beforehand optimized by Gaussian09 utilizing the density functional theory. MD is performed in the NTV constant condition, *i.e.* the number of particles, temperature, and volume of MD cell are definite. The structure difference of the glycolic acid and oxalic acid is detected by the water distribution around the molecules using the pair distribution functions, $g_{ij}(r)$, and the frequency dependent diffusion coefficients, $D_i(v)$. The anomalous dielectric constant of the solution, *i.e.* about 12 times larger than that of water, has been obtained, which may be attributed to the ion pair formation in the solution.

1. Introduction

Recently much attention has been riveted on the biodegradable polymers. They are used in the broad area, especially in the medical treatment, *e.g.* surgical suture, cartilage support, and capsules carrying drugs to the affected part. Poly glycolic acid (PGL) is one of the promising candidates which can be produced from biological origin resources. The degradation process of PGL by hydrolysis has been examined by experiment and molecular dynamics (MD). However, the physical properties of resolved PGL, or glycolic acid in the physiological salt solution is not sufficiently investigated [1].

Besides, according to the recent experimental reports of the CREST (Core Research for Evolutionary Science and Technology) project, a sort of rechargeable biofuel cell has been constructed using glycolic acid and oxalic acid aqueous solution without CO₂ emission [2]. Although the extensive experimental and *ab initio* studies have been reported regarding this system, the detailed structure and transport coefficients related to electric properties have not been examined yet by classical MD on the stand point of multi-component organic molecular solutions, to the best of our knowledge. Out of these motives, we perform the MD study on the glycolic acid in NaCl aqueous solution to simulate a physiological salt solution in a human body.

2. Simulation procedure and results

As mentioned in the previous section, the electric power circulation method based on the glycolic acid (HOOC-CH₂OH) and oxalic acid ((COOH)₂) redox couple has been proposed. The electric power charge has been achieved using TiO₂ in the potential region of -0.5 to -0.7 V vs. the reversible hydrogen electrode (RHE). The reaction in the cell is summarized as,





Although, these reactions are formed in alkaline solutions, we perform MD in a physiological salt solution to examine the hydration of glycolic acid and oxalic acid in detail. The optimized structure and charges of used molecules have been prepared using Gaussian09 by the density functional theory (DFT) in advance. The calculations are carried out at the B3LYP/6-311++G(d,p) level of the theory in a cavity in the IEF-PCM solvent field. The obtained molecules and ions are shown in figures 1(a)-1(d).

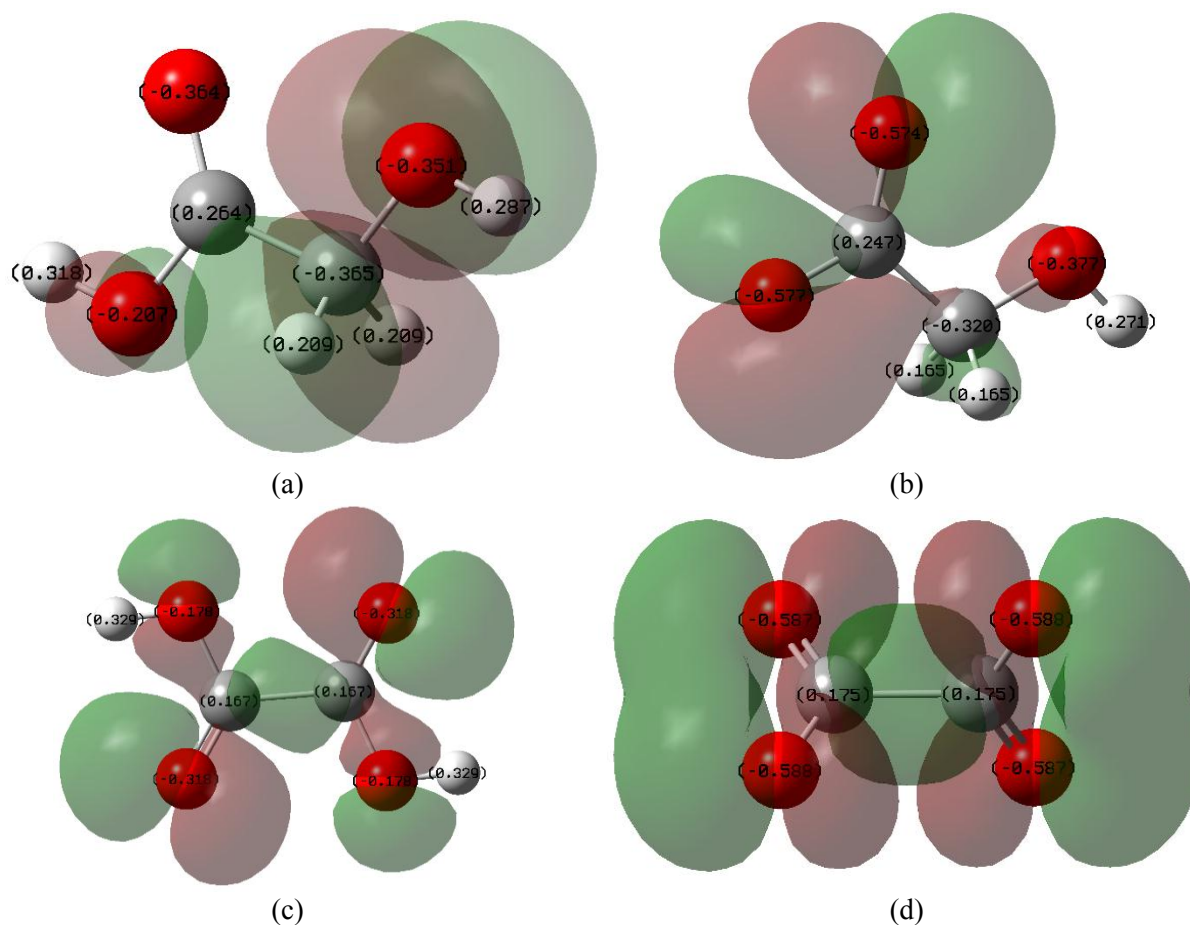


Figure 1. (a) Glycolic acid, (b) Glycolic acid anion, (c) Oxalic acid and (d) Oxalic acid anion.

In MD calculation, glycolic acid and oxalic acid are assumed to be ionized in the solution, i.e. they are in the form of anion. Therefore the constituents of MD are glycolic acid anion, oxalic acid anion, Na^+ , Cl^- , and water molecule.

The procedure of MD simulation is same as our previous works [3-5]. We briefly give outline below. The rigid body water model, TIP4P, is used. The charged Lennard-Jones (L-J) type potentials are used for the potential function for water molecules as [6,7],

$$\phi_{ij}(r) = \frac{z_i z_j e^2}{r} + 4\epsilon \left\{ \left(\frac{\sigma}{r} \right)^{12} - \left(\frac{\sigma}{r} \right)^6 \right\} \quad (4)$$

From now on, the symbols i and j in the equations stand for the constituent ions; z_i is the charge for the constituent ions i ; and e is the elementary charge. The parameters of equation (4) are taken from the literature. The interactions between Na^+ - Na^+ , Na^+ - Cl^- , Cl^- - Cl^- , TIP4P - Na^+ , and TIP4P - Cl^- are

described as [8],

$$\phi_{ij}(r) = \frac{z_i z_j e^2}{r} + \frac{C}{r^9} - \frac{D}{r^6} \quad (5)$$

The softness of the interactions is represented by the power 9 of the second repulsive term. MD is performed in the NPT constant condition, using about 2100 molecules, i.e. 1.5 wt% glycolic acid anion and 1.8 wt% oxalic acid anion in a physiological salt solution, at 1atm, 310 K. The one timestep is 0.2 fs. Ewald method is used for charge interaction. SEIGRESS package (Fujitsu) is used for calculation [9].

The partial pair distribution functions, $g_{ij}(r)$, are obtainable from the simulation data, which represents configurations of ions in the solution, defined as [10],

$$n_{ij}(r) = \sum_{n < r/\Delta r} (N_j/V) g_{ij}(n \cdot \Delta r). \quad (6)$$

where $n_{ij}(r)$ stands the integrated coordination number. The obtained $g_{ij}(r)$'s are shown in figures 2(a)-2(b). The disparities of $g_{ij}(r)$'s reflect the structural difference between glycolic acid anion and oxalic acid anion, and the water distribution around them. In figure 2(a), $g_{ij}(r)$ for C(glycolic acid anion) - O(water) and C(glycolic acid anion) - H(water) have plateaus around 3.9 Å and 4.5 Å, respectively.

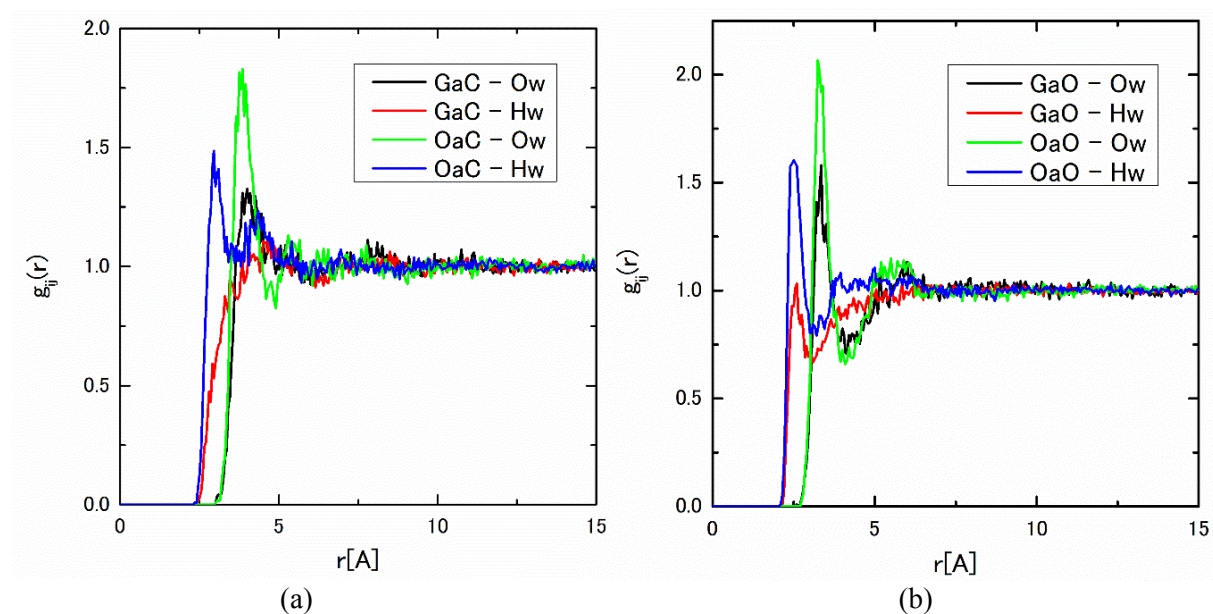


Figure 2. (a) $g_{ij}(r)$ for C(glycolic acid anion) - O(water), C(glycolic acid anion) - H(water), C(oxalic acid anion) - O(water), and C(oxalic acid anion) - H(water), and (b) $g_{ij}(r)$ for O(glycolic acid anion) - O(water), O(glycolic acid anion) - H(water), O(oxalic acid anion) - O(water), and O(oxalic acid anion) - H(water).

On the other hand, $g_{ij}(r)$ for C(oxalic acid anion) - O(water) and C(oxalic acid anion) - H(water) have pronounced peaks at 3.7 Å and 3.0 Å, respectively. The difference of the peak heights of $g_{ij}(r)$'s around a glycolic acid anion and an oxalic acid anion might be attributed to the difference of charges of anions, i.e. a glycolic acid anion -1, an oxalic acid anion -2. The four C in an oxalic acid anion attract H of water most, which causes the peak of $g_{ij}(r)$ for C(oxalic acid anion) - H(water) at 3.0 Å. In figure 2(b), the difference of the peak heights of $g_{ij}(r)$'s around a glycolic acid anion and an oxalic acid anion are also attributed to the difference of charges of anions. Regarding the peak positions, $g_{ij}(r)$ for O(glycolic acid anion) - O(water) and O(glycolic acid anion) - H(water) have peaks at 3.4 Å and 2.6 Å, respectively. On the other hand, $g_{ij}(r)$ for O(oxalic acid anion) - O(water) and O(oxalic acid anion) -

H(water) have high peaks at 3.2Å and 2.5Å, respectively. Therefore, the structural difference between glycolic acid anion and oxalic acid anion are detected most by the distribution of H in water around them.

Next we examine the transport properties, i.e. the shear viscosity and the diffusion coefficients. The major advantages of the biofuel cell are its safety and small size. To design a small sized cell, the transport properties are particularly important, because the small sized fluid is treated in the cell. Therefore, on the stand point of physical properties, the similar transport features as water are desirable.

The shear viscosity is calculated using the Green-Kubo's formula as [11],

$$\eta = \frac{V}{k_B T} \int_0^\infty \langle \sigma^{xz}(t) \sigma^{xz}(0) \rangle dt. \quad (7)$$

where $\sigma^{xz}(t)$ and $\sigma^{xz}(0)$ are the off diagonal elements of the stress tensor; k_B is the Boltzmann's constant; V is the volume of the system. The estimated shear viscosity is 1.72 cP at 1atm, 310 K, which is about 2 times larger than that of pure water 0.89 cP at 1atm 298 K.

The diffusion coefficient for i -th constituent can be estimated using the mean square displacement (MSD) as,

$$D_i = \lim_{t \rightarrow \infty} \frac{1}{6t} \langle |\mathbf{r}_i(t) - \mathbf{r}_i(0)|^2 \rangle. \quad (8)$$

The calculated diffusion coefficients for constituents are listed in table 1. The obtained D_i 's values for glycolic acid and water are comparable to those in literatures [12,13]. D_i for oxalic acid anion is much smaller than that of glycolic acid and water.

Table 1. Diffusion coefficients estimated from MSD.

constituent	$D_i (\times 10^{-5} \text{ cm}^2/\text{s})$
glycolic acid anion	3.04
oxalic acid anion	1.87
Na ⁺	2.63
Cl ⁻	2.34
water	4.68

The dynamical properties of glycolic acid anion and oxalic acid anion are estimated by the frequency dependent diffusion coefficient $D_i(\nu)$, which is expressed as [10],

$$D_i(\nu) = \frac{1}{3} \int_0^\infty \langle \mathbf{v}_i(t) \cdot \mathbf{v}_i(0) \rangle \cos(2\pi\nu t) dt, \quad (9)$$

where $\langle \mathbf{v}_i(t) \cdot \mathbf{v}_i(0) \rangle$ stands for the velocity auto-correlation function (VAF) for the i^{th} atom species.

As seen in figure 3, the lower frequency distribution in the infrared region is attributed to the cage effect by the surrounding water molecules. The structural difference between glycolic acid anion and oxalic acid anion is observed most in middle and higher frequencies. Although the bond length is fixed and only bending is allowed in these molecules in MD, the high frequency distributions around 900 [1/cm] are obtained. These results may be yielded by the interaction between atoms in the different molecules, i.e. the inter molecular interaction. In figure 3, the frequency distribution of water and glycolic acid are mainly in lower region, and the higher frequencies are seen most in oxalic acid anion, which may prevent the diffusion of oxalic acid anion. These facts suggest that the cell should be operated in glycolic acid rich region around 3 wt%.

Finally, we would like to refer to the static dielectric constant of the solution estimated by MD, ϵ , which is defined as [11],

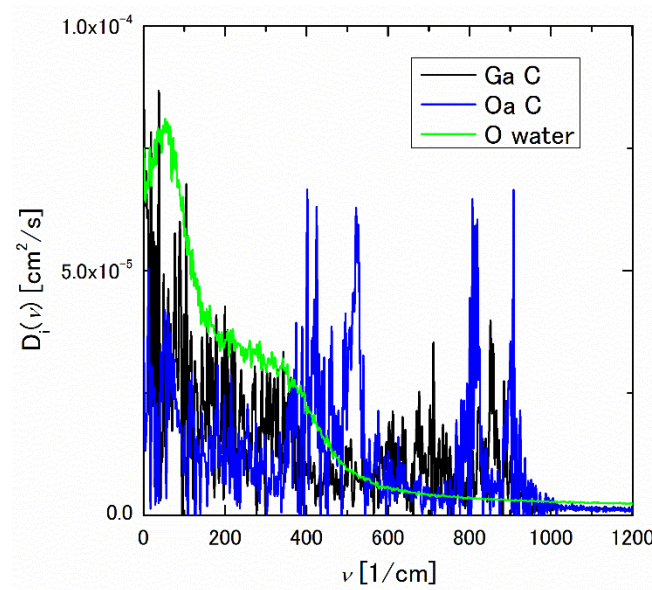


Figure 3. $D_i(\nu)$ for C(glycolic acid anion), C(oxalic acid anion) and O(water).

$$\frac{1}{\varepsilon - 1} = \frac{3k_B\varepsilon_0TV}{M^2} - \frac{1}{2\varepsilon_s + 1} \quad (10)$$

where k_B is the Boltzmann's constant, ε_0 is the static dielectric constant in a vacuum, T is the temperature, V is the volume of the MD cell. The term M^2 is expressed as,

$$M^2 = \langle |\sum_{i=1}^N \vec{\mu}_i|^2 \rangle. \quad (11)$$

where $\vec{\mu}_i$ stands for the dipole moment of the i -th molecule. The static dielectric constant, ε_s , on the outside of the cell is assumed to be infinity under the periodic boundary condition. Then, ε is expressed as,

$$\varepsilon = \frac{M^2}{3k_B\varepsilon_0TV} + 1 \quad (12)$$

The estimated static dielectric constant of the solution is 9.6×10^2 , which is about 12 times larger than that of pure water. According to the experiment, for example, alkali halides water solution yields decrease in ε by the formation of hydration shell around ions, which prevents creating the effective dipole moments in the solution. On the other hand, in the case of onium salts (e.g. Bu_4NBr etc.) water solution, ε increases as the concentration of solute increases, because the ions may associate to form ion pairs [14]. The present results of increasing ε also might be explained by the large dipole moment formation by ion pairs in the solution. If the relation of ε and the concentration of solute, c , follows the Onsager's equation, $d\varepsilon/dc$ is anticipated to be proportional to M^2 [15]. However, the detailed analysis is left for further study.

3. Conclusion

MD simulations have been performed on the glycolic acid and oxalic acid in NaCl aqueous solution as a model of human body. The obtained $g_{ij}(r)$'s suggest that oxalic acid anions attract water molecule around them to form a hydration shell. The transport properties for glycolic acid anion and oxalic acid anion are quite different, which may be attributed to the structural difference. The anomalous dielectric constant has been obtained. This fact may be explained by the large dipole moment formation in the solution, however the further analysis are left for the future study.

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