

Effect of hydration on properties of glucose using explicit and implicit solvent models

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Abstract. *The interplay between carbohydrates and water molecules is fundamental to understanding the intricate metabolic processes in biological systems. This study employs density-functional theory calculations to examine the structural and electronic properties of hydrated β -glucose, $G(H_2O)_n$, where $0 \leq n \leq 15$, using the explicit and implicit solvent models. Explicit (implicit) model reveals that the average length of the H-bond reaches a minimum of 1.76 (1.79) Å when the hydration shell is filled with nine water molecules. Stepwise hydration energies remain negative for all of n , indicating a thermodynamically favorable hydration process. However, the inconsistency between the two models when n is either small ($n \leq 3$) or large ($n \geq 13$) emphasizes the need for careful selection of the solvent model. For the two models, the trend in the highest occupied molecular orbital energies is an increase up to $n = 10$, followed by a decrease. The energy gap between the highest occupied and lowest unoccupied molecular orbitals is highly sensitive to n for the explicit model. In contrast, it is less sensitive in the implicit model for $n \geq 6$. These findings highlight the explicit inclusion of water molecules even when an implicit model is utilized.*

Keywords: β -glucose; explicit solvent model; implicit solvent model; density-functional theory.

Classification numbers: 31.15.A-; 31.70.Dk; 31.15.E-.

1. Introduction

Carbohydrates are essential biomolecules that function as both a primary energy source and a fundamental structural component in biological systems. Among carbohydrates, glucose is the most common monosaccharide, which is involved in various life processes such as the formation of cellulose or glycogen [1]. As a hydrophilic compound, glucose can form intricate H-bond networks with surrounding water molecules. Through H-bonding, water molecules reshape the

molecular geometry and alter the electronic properties and thermodynamic stability of the glucose [1–3]. The water-glucose interactions are therefore critical for biological processes such as glycolysis, cellular signaling, and energy metabolism [4]. Gaining a detailed understanding of glucose hydration at the molecular level is vital for fields ranging from biochemistry and pharmacology to food science.

Numerous experimental and theoretical studies have been conducted to elucidate the hydration mechanism of glucose. Infrared and Raman spectra of various glucose aqueous solutions reveal that the reduced amount of free hydroxyl groups increases H-bonds [5]. Neutron diffraction experiments provide some indication of slow migration and an enhancement of water densities at specific sites surrounding the sugar molecule [6–11]. In addition, little water structure-breaking has been observed even at high sugar concentrations [6–11].

Complementary to that, theoretical methods have helped uncover the structural, electronic, and vibrational features of hydrated glucose systems [3, 12–14]. Using random conformational search and density-functional theory calculation, Song and coworkers find that hydrate sites for water molecules change dynamically with the increase of water molecules [15]. Momany and Schnupf suggest that water molecules rapidly migrate around glucose, leaving no single site occupied for a significant period of several picoseconds [16].

Although these approaches consider water molecules explicitly (explicit models), they are limited to gas-phase studies. A key question remains: how would these results change in a dielectric medium like water? To incorporate solvent effects, implicit models such as the conductor-like screening model [17] or solvation models based on density [18] are often employed. Despite that, limited attempts have been made to compare and combine the two models [19, 20].

This study investigates the structural and electronic properties of hydrated β -glucose using explicit and implicit models. Our findings show that the average H-bond length is shortest when the hydration shell contains nine water molecules in both models. The consistent negativity of stepwise hydration energies confirms that the hydration process is thermodynamically favorable at all hydration numbers. Nevertheless, the models diverge significantly when the number of water molecules (n) is either small ($n \leq 3$) or large ($n \geq 13$), underscoring the critical need for a suitable solvent model. For both models, the highest occupied molecular orbital (HOMO) energy increases until $n = 10$ and then decreases. In addition, the energy gap between the highest occupied and lowest unoccupied molecular orbitals is highly sensitive to n in the explicit model. The dependency is less in the implicit model when $n \geq 6$. These discrepancies suggest that explicitly including some water molecules is critical, even when using an implicit model.

2. Computational approach

Density-functional theory calculations are executed via the GPAW package [21] and Atomic Simulation Environment [22]. Perdew-Burke-Ernzerhof generalized gradient approximation is used to describe the electron-electron interaction [23]. A real-space finite-difference formalism [24] is employed, and a grid spacing of 0.20 Å is chosen. Further reduction of the grid spacing to 0.14 Å yields energies (energy levels) that change by less than 15 (6) meV, which do not affect our conclusions. Explicit and implicit solvent models (ESM and ISM) are utilized to simulate the solvation effects on glucose.

For explicit model, water molecules are added to the β -glucose to form the sugar-water complex $G(H_2O)_n$, with $0 \leq n \leq 15$. Lowest-energy configurations, identified through exhaustive

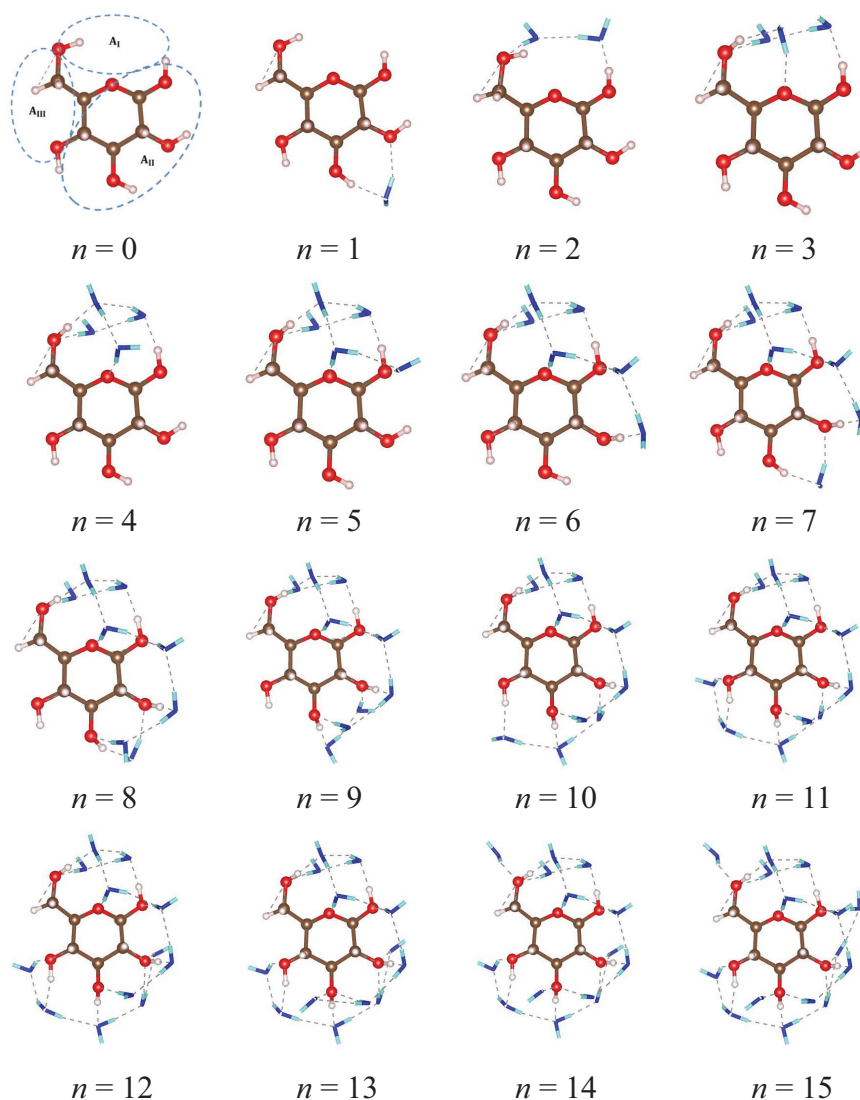


Fig. 1. Optimized geometries of the $G(\text{H}_2\text{O})_n$ with n from 0 to 15. Water molecules are colored differently for better visualization.

conformational sampling from the work of Song *et al.* [15], are taken as initial geometries of the $G(\text{H}_2\text{O})_n$. An open boundary condition is imposed, and a large computational box with 15 Å vacuum in each direction is employed to capture the evanescent waves. Increasing the vacuum space to 20 Å only results in a decrease in total energies of less than 9 meV. In the implicit model, implicit water interactions with the $G(\text{H}_2\text{O})_n$ are treated using the continuum solvation model, as described in Ref. [25]. As implemented in GPAW, solvent parameters for water include fitted potential at the van der Waals radius ($u_0 = 0.18$ eV), water dielectric constant ($\epsilon_\infty = 78.4$), water surface tension ($\gamma = 18.4$ dyn cm⁻¹) at 298 K, and the van der Waals radius of H (1.09 Å). For

both models, geometry optimizations are carried out using the BFGS algorithm until the maximum force on any atom is below 0.05 eV/Å. The H-bonds between water and glucose molecules are identified using the geometric criteria of O $\cdots$ H distance ≤ 2.5 Å and O–H $\cdots$ O angle $\geq 120^\circ$ [3].

3. Results and discussion

3.1. Structural properties

As pointed out by Song and colleagues [15], binding positions of water molecules to the glucose are divided into three hydrate sites: AI site includes the CH₂OH side chain and the hydroxyl group at the anomeric position (C1), representing the most accessible area with ample space for strong H-bondings; AII site includes hydroxyl groups at C2 and C3, which can also form H-bonds effectively but are more influenced by steric hindrance; and AIII site comprises the opposite side (C4–C5), where geometric restrictions limit the formation of optimal H-bonds.

Figure 1 plots the optimized geometries of the G(H₂O)_{*n*}, with $0 \leq n \leq 15$, using the ESM. The spatial occupation order AI $\rightarrow$ AII $\rightarrow$ AIII is clearly observed. Water molecules first prefer to bind at AI and AII hydrate sites. The AIII sites are occupied only when the AI and AII sites are saturated. Geometries obtained by the ISM do not significantly differ from those by the ESM and are not shown here.

The average length of H-bonds between water and glucose molecules, $\bar{d}_{O\cdots H}$, in the G(H₂O)_{*n*} is shown in Fig. 2. Both the ESM and ISM show similar trends. As *n* increases from 1 to 9, the $\bar{d}_{O\cdots H}$ tends to decrease and reaches a minimum of 1.76 (1.79) Å, obtained by the ESM (ISM). In this region, adding water molecules helps stabilize the H-bonds. The water-glucose interaction is strongest at *n* = 9, corresponding to the saturation of the AI and AII hydrate sites. As *n* increases from 10 to 15, water molecules start occupying the less favorable AIII site and the already saturated AII site. The $\bar{d}_{O\cdots H}$ increases and the water-glucose interaction is weakened. The average difference in $\bar{d}_{O\cdots H}$ calculated by the two models is 0.02 Å. The difference is minimal when *n* is either small (≤ 3) or large (≥ 14).

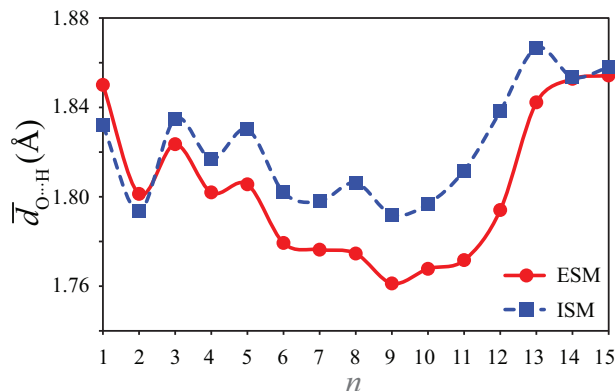


Fig. 2. (Color online) Changes in the $\bar{d}_{O\cdots H}$ of the G(H₂O)_{*n*} with respect to *n*. The red solid (blue dashed) curve indicates the results obtained by the ESM (ISM).

3.2. Energetic properties

Figure 3 plots the stepwise hydration energy, E_{hyd} , defined as

$$\Delta E_{hyd} = E_n - E_{n-1} - E_{H_2O}, \quad (1)$$

where, E_n , E_{n-1} , and E_{H_2O} are the total energies, calculated by the ESM and ISM, of the G(H₂O)_{*n*}, the G(H₂O)_{*n*-1}, and a water molecule, respectively. In both ESM and ISM calculations, the ΔE_{hyd}

remains negative, indicating that the hydration process is thermodynamically favorable as each water molecule is added.

The trends obtained by the two models are in agreement for $4 \leq n \leq 12$ and in disagreement otherwise. As n increases from 4 to 12, the ΔE_{hyd} increases, and the ISM values are overestimated by 0.23 eV compared to the ESM values. For $1 \leq n \leq 3$, where the AI site is not yet saturated, an increment of n should raise the stepwise energy. However, the ΔE_{hyd} calculated by the ESM decreases as n increases. Similarly, for $13 \leq n \leq 15$, the ΔE_{hyd} calculated by the ISM is lowered, although water molecules occupy the unfavorable AIII site and the already saturated AII site. Therefore, usage of both models when n is either small or large should be taken with caution. The inclusion of zero-point energies is expected to yield little change in the trend of the ΔE_{hyd} . Specifically, zero-point correction increases the ΔE_{hyd} for $n = 1, 9$, and 15 increases by 0.10 (0.10), 0.05 (0.05), and 0.08 (0.15) eV in the ESM (ISM), respectively. Furthermore, as literature on the thermodynamic properties of hydrated glucose is limited, future investigations of finite-temperature contributions are promising.

Variation of the highest occupied molecular orbital (HOMO) energy with the number of water molecules reflects the redistribution of electronic charge induced by the formation and development of the H-bond network. In addition, the minus value of the HOMO energy can approximate the ionization potential, according to the ionization potential theorem [26, 27]. Therefore, we plot in Fig. 4 the HOMO energy of the $G(H_2O)_n$ with respect to n . Two distinct regimes appear with a clear transition at $n = 10$.

For $0 \leq n \leq 10$, the HOMO energy increases by c.a. 0.40 (0.14) eV as found by the ESM (ISM). The rise is highly nonlinear rather than monotonic. The increasing tendency correlates with the progressive formation of a stable H-bond network at the preferred AI and AII hydrate sites. Water molecules primarily act as H-bond acceptors, interacting with hydroxyl donor groups on the glucose backbone. This interaction redistributes electrons from the

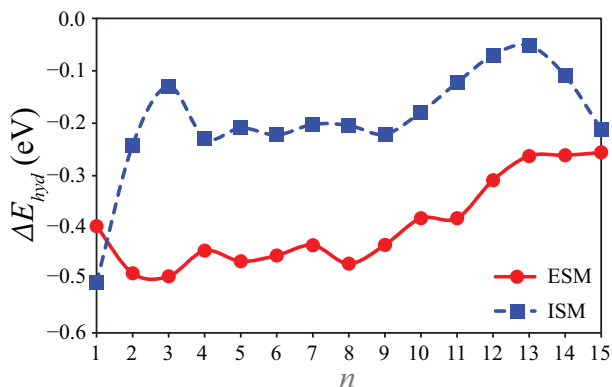


Fig. 3. (Color online) ΔE_{hyd} of the $G(H_2O)_n$ as a function of n . The red solid (blue dashed) curve indicates the results obtained by the ESM (ISM).

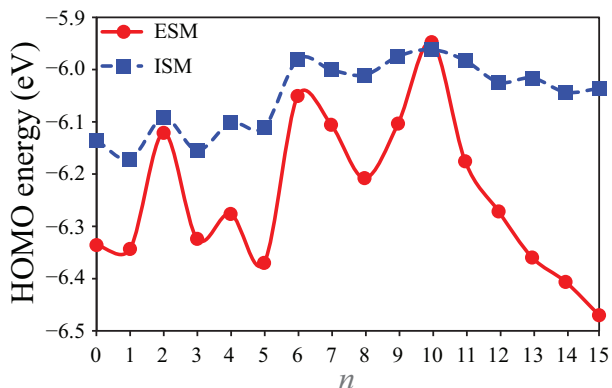


Fig. 4. (Color online) HOMO energy of the $G(H_2O)_n$ with respect to n . The red solid (blue dashed) curve indicates the results obtained by the ESM (ISM).

glucose molecule towards the outer hydration shell, weakening the binding of those electrons to the glucose framework. As the electrons become less tightly bound, the HOMO energy is lifted.

Beyond the transition point at $n = 10$, the trend reverses and the HOMO energy steadily decreases. Furthermore, the change of 0.52 (0.20) eV is significant (moderate) as observed in the ESM (ISM). This regime marks the saturation of favorable AI and AII hydrate sites, and the occupation of an unfavorable AIII site. The geometric and electronic constraints hinder the formation of optimal H-bonds. Instead of being drawn outward, electrons are redistributed backward to the glucose molecule. This concentration of charge within the glucose molecule leads to electronic stabilization, as reflected by the decrease in HOMO energy

As illustrated in Fig. 4, oscillation of the HOMO energy by the ISM is small (−6.16 to −5.95 eV) compared to that by the ESM (−6.47 to −5.95 eV). The implicit dielectric environment in the ISM partially dampens local electronic perturbations caused by the H-bond network, resulting in smoother changes in the HOMO energy. Although the two methods agree on the general trend, their sensitivities to the HOMO energy are highlighted, and care should be taken when choosing the right solvent model. At $n \geq 6$, the slight shift in the HOMO energy suggests the inclusion of at least six water molecules for the implicit model.

In providing insights into the electronic properties of the system, the gap between HOMO and the lowest unoccupied molecular orbital energies, ΔE_{HL} , is an important feature. As depicted in Fig. 5, separate behaviors of the ΔE_{HL} are marked for the two solvent models. Within the ESM, the ΔE_{HL} demonstrates wide fluctuation, ranging between 4.79 and 5.31 eV, without an apparent asymptotic convergence. The electronic structure is susceptible to the detailed arrangement of the H-bonds. It is noted that the ΔE_{HL} at $n = 15$ by the ESM is not the same as that at $n = 0$ by the ISM. Within the ISM, the ΔE_{HL} rapidly declines from $n = 0$ to 6, followed by a slow convergence to approximately 5.00 eV. The dielectric mean field reduces the sensitivity of frontier orbitals to local structural fluctuations in the H-bond network. Again, at least six explicit water molecules are needed in the ISM for an appropriate approximation of the ΔE_{HL} . When n is large, the ΔE_{HL} obtained by the two models seems to approach each other, with an absolute difference below 0.10 eV.

4. Conclusion

Explicit and implicit models are employed to study the effect of hydration on structural and electronic properties of the β -glucose molecule. The shortest average H-bond length between water and glucose, corresponding to the strongest water-glucose interaction, is reached when the hydration shell contains nine water molecules. The stepwise energies by the two models agree for $4 \leq n \leq 12$ and disagree otherwise. This finding highlights the need for caution when employing

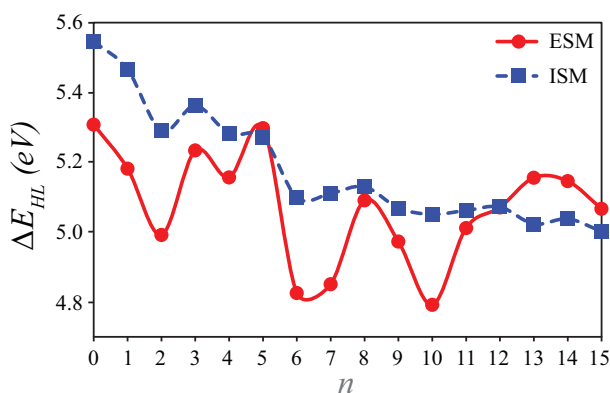


Fig. 5. (Color online) ΔE_{HL} of the $G(H_2O)_n$ as a function of n . The red solid (blue dashed) curve indicates the results obtained by the ESM (ISM).

the explicit model with small n or the implicit model with large n . The HOMO energy generally increases with n up to $n = 10$ and then decreases. The obtained ΔE_{HL} by the ESM largely fluctuates with n , whereas those by the ISM display slow convergence at $n \geq 6$. Inclusion of at least six water molecules is recommended for the calculation of HOMO energy and ΔE_{HL} in the ISM based on our results.

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Authors contributions

Investigation, software, formal analysis, visualization, and writing - original draft: M.N.T.N.; Methodology, project administration, and resources: H.D.N.; Conceptualization, validation, and writing - review and editing: M.N.T.N., H.H.M., and H.D.N..

Conflict of interest

The authors declare that they have no competing financial and non-financial interests.

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