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A COMPUTATIONAL EVALUATION OF STRUCTURES AND PROPERTIES OF NUCLEIC ACID BASE – WATER COMPLEXES

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Abstract

Electronic properties, electron affinity and ionization potential, binding energies, and conformational changes of neutral, cationic, and anionic DNA base-water complexes, [Base $(H_2O)_n$] $^{(0,+)}$ (n = 0, 4, 8, 14) have been investigated in gas and aqueous phases using the DFT/M06-2X hybrid functional method with 6-31++g(d,p) basis set implemented in the Gaussian09 software package. We find that the electronic properties of DNA bases are strongly influenced by implicit and explicit solvation. While purines show high electron affinity, pyrimidines show the greatest ionization potential at the hydration levels observed. Data also reveals that binding energy lowers in implicit solvation. Additionally, the molecular electrostatic potential surfaces of each compound were calculated to identify the most favorable sites for water binding. The ESP charges, derived from the electron density, indicate that regions of the highest electronegativity do not always correspond to the lowest charge, suggesting complex interactions in the solvation processes. These results provide significant insight into the effects of hydration on the electrostatic properties of DNA nucleobases.

Keywords: DNA bases; DFT study; electron affinity; ionization potential; binding energy; hydration shell; radiation

КОМП'ЮТЕРНА ОЦІНКА СТРУКТУР І ВЛАСТИВОСТЕЙ КОМПЛЕКСІВ ОСНОВА НУКЛЕЇНОВОЇ КИСЛОТИ – ВОДА

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Анотація

За допомогою гібридного функціонального методу DFT/M06-2X з набором базисів 6-31++g(d,p), реалізованого в програмному пакеті Gaussian09 [Base (H2O)n] (0,+) (n = 0, 4, 8, 14) досліджені електронні властивості, електронна спорідненість та потенціал іонізації, енергії зв'язку та конформаційні зміни нейтральних, катіонних та аніонних комплексів основ ДНК з водою в газовій та водній фазах. Ми виявили, що на електронні властивості основ ДНК сильно впливає неявна та явна сольватація. У той час як пурини демонструють високу електронну спорідненість, піримідини показують найбільший потенціал іонізації на спостережуваних рівнях гідратації. Дані також показують, що енергія зв'язку знижується в разі неявної сольватації. Додатково було розраховано молекулярні поверхні електростатичного потенціалу кожної сполуки для виявлення найсприятливіших місць для зв'язування води. Заряди ESP, отримані з електронної густини, вказують на те, що ділянки з найвищою електронегативністю не завжди відповідають найнижчому заряду, що свідчить про складні взаємодії в процесах сольватації. Ці результати дають суттєве розуміння впливу гідратації на електростатичні властивості нуклеотидів ДНК.

Ключові слова: ДНК; DFT дослідження; електронна спорідненість; енергія іонізації; енергія зв'язку; гідратаційна оболонка; радіація.

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Introduction

The molecular-level analysis of nucleic acid bases holds immense significance in comprehending the mechanisms of proton transfer, base tautomerism, and radiation-induced damage [1–5]. At the molecular scale, ionizing radiation in biological systems causes a range of modifications to DNA bases, ionization of DNA components, and production of radical species in aqueous media [4–10]. The initial step of radiation damage in DNA involves the generation of radicals within the strand, leading to the attachment of ions to DNA bases, resulting in the creation of nucleic acid base anions and cations [10–12]. These charged species can induce bond cleavage, causing single and double strand breaks and leading to a considerable amount of oxidative damage [1]. Oxidative damage to crucial cellular structures can trigger the onset of various diseases, including cancer, diabetes, metabolic diseases, and cardiovascular diseases [13]. Direct ionization events can result in a range of base modifications, such as the formation of DNA-ion radicals (DNA+) [14]. DNA base modification is the main cause of genomic instability and, ultimately, cellular dysfunction. DNA base modification plays a role in the process of charge transport, and electron and exciton migration in different DNA components.

Previous studies show that after high-energy radiation sources pass through biological components, low-energy radiation is produced [15–18]. However, it is challenging for scientists to determine the level of radiation that causes epigenetic and carcinogenic effects, making it impossible to determine a threshold for these radiation effects. This leads to a significant number of uncertainties regarding projected cancer risk estimates and connections to acute and chronic biological effects, hindering the development of effective countermeasures [15]. A comprehensive understanding of radiation mechanisms is essential to provide insights into the correlation between DNA alterations and observed biological effects in organisms. It has been established that the electronic properties of single and paired DNA bases play a crucial role in understanding the charge transport mechanisms at the molecular level [1–2]. Understanding those mechanisms is necessary for studying exciton migration, identifying trends in electron binding and selectivity of DNA binding sites, and determining the potential applications of DNA in electronics [2; 5; 11; 19–22].

Previous experimental and theoretical studies report molecular structure, stability, and electronic properties of isolated nucleic acid bases and base pairs [22–55]. Shukla and Leszczynski [22] studied guanine and its interaction with water molecules, including $(H_2O)_3$ and $(H_2O)_{5–13}$, at the ground and single ππ* excited state using ab initio methods in the gas phase. Their results show that guanine-water complexes at the ground state exhibit planarity due to the interaction of the water molecules with the hydrogen molecules on the amino group. In contrast, isolated guanine in the s1 (ππ*) excited state was characterized as non-planar. Sadr-Arani et al. [23] investigated the fragmentation processes of ionized adenine, cytosine, and guanine in the gas phase, and their results indicated a consistent dissociation of the HNCO molecule in cytosine and guanine, followed by further instances of fragmentation in the nucleobases. Khistyaev et al. [24] presented the various conformations of micro-hydrated thymine $[T(H_2O)_{1–3}]$ in the gas phase. They observed a decrease in adiabatic ionization energy (AIE) with the addition of water molecules, changes that were strictly dependent on conformation and ionization state.

It is understood that hydrogen bonding between DNA components plays a crucial role in maintaining its double-helical structure [22], and manipulation of this network can impact its structure and function [25]. Crystallographic and nuclear magnetic resonance (NMR) investigations of DNA have confirmed that the degree of hydration plays a significant role in helix stabilization and the function of DNA components [25]. The presence of water molecules is suggested to largely govern the transition of DNA into various structural forms, and there is a strict relationship between the conformation of DNA and the number of water molecules per nucleotide [25]. Investigating the interactions of DNA components with explicit water molecules can provide insight into the intermolecular interactions that contribute to helix destabilization and conformational transitions of DNA [26; 27]. However, there are limited studies on the combined effects of hydration and ionization on nucleobase structure and function, especially when the hydration level exceeds $(H_2O)_3$. The purpose of this study is to fill that gap by performing a systematic study on the ionization energies and conformational changes of isolated DNA nucleobases in both hydrated and non-hydrated environments. A better understanding of the behavior of isolated

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hydrated and non-hydrated DNA nucleobases as well as the analysis of electron affinity and ionization energies in nucleobases may provide significant insight into the improvement of radiation therapies, radiation risk estimation in terrestrial and cosmic environments, as well as other DNA-related fields.

Theoretical Method

Calculations of Vertical and Adiabatic Electronic Properties. In the present study, we aimed to calculate the adiabatic and vertical ionization energies of DNA-water complexes by utilizing the latest advancements in computational chemistry. The ground state conformers were employed as templates, and ionization was induced implicitly utilizing the Gaussian09 software package and the Minnesota density functional, M06-2X [56], combined with the highly accurate 6-31++ G (d, p) basis set [57; 58].

Electronic properties, electron affinity and ionization potential, are derived from energy differences between different molecular states. The ionization potential, represented by equation 1, is obtained by subtracting the Hartree-Fock (HF) energy of the neutral molecule from that of the cation, while the electron affinity, represented by equation 2, is calculated by subtracting the HF energy of the neutral molecule from that of the anion.

$$IP = E_{HF}(\text{cation}) - E_{HF}(\text{neutral}) \quad \text{(Eq. 1)}$$

$$EA = E_{HF}(\text{neutral}) - E_{HF}(\text{anion}) \quad \text{(Eq. 2)}$$

These calculations reflect the energy required to remove or add an electron to the system, based on the Hartree-Fock approximation. Adiabatic electron affinity (AEA), represented by equation 3, has been calculated as the energy difference between the optimized neutral molecule and its optimized radical anion. Vertical electron affinity (VEA), represented by equation 4, shows the difference between the optimized neutral molecule and the radical anion calculated at the geometry of the neutral molecule. Calculated adiabatic ionization potential (AIP), is represented by equation 5, which includes the energy difference between the optimized radical cation and its optimized neutral molecule. Finally, the vertical ionization potential (VIP), represented by equation 6, provides the difference between the radical cation calculated at the geometry of the neutral molecule and the optimized neutral molecule [7].

$$AEA = E_{gas/aq}(O) - E_{gas/aq}(X^-) \quad \text{(Eq. 3)}$$

$$VEA = E_{gas/aq}(O) - E_{gas/aq}(X^{-*}) \quad \text{(Eq. 4)}$$

$$AIP = E_{gas/aq}(X^+) - E_{gas/aq}(O) \quad \text{(Eq. 5)}$$

$$VIP = E_{gas/aq}(X^{+*}) - E_{gas/aq}(O) \quad \text{(Eq. 6)}$$

The energy of the neutral molecule ($E_{gas/aq}$ (O)), the energy of the radical anion ($E_{gas/aq}$ (X^{-*})), the energy of the radical anion optimized using the geometry of the neutral molecule ($E_{gas/aq}$ (X^-)), the energy of the radical cation ($E_{gas/aq}$ (X^{+*})), and the energy of the radical cation optimized using the geometry of the neutral molecule ($E_{gas/aq}$ (X^+)) were all calculated and employed in the aforementioned equations [7]. Binding energy (E_{Bind}), shown in equation 7, is the energy difference between the optimized dimer and optimized isolated monomers.

$$E_{Bind} = E[Base(H_2O)_n]^+ - E_{Base} + E(H_2O)_n \quad \text{(Eq. 7)}$$

where $E[Base(H_2O)_n]^{\pm}$, is the optimized energy of the DNA base – water complex, E_{Base} is the optimized energy of the DNA base, and $E(H_2O)_n$, is the energy of the water cluster size, where n = 0, 4, 8, 14.

Modeling of Hydration Shells. Previous theoretical and experimental studies on hydrated DNA bases, base pairs, and nucleic acids have revealed various water-binding sites. Stupar et al. [28] demonstrated hydration sites in canonical base pairs. Adenine and guanine primarily exhibited water binding at their nitrogen groups (N2, N3, and N7), while cytosine and thymine displayed binding to the keto and amino groups. Sundaralingam et al. [29] investigated the hydration sites of DNA and RNA base pairs (G-C, G-U, and U-U) in oligonucleotides. The hydration sites for G-C were consistent with prior findings, while G-U displayed water binding at sites N2, N3, N7, C2, and the keto group. U-U exhibited water binding on the keto groups of both bases, with double hydration at the nitrogen group of only one base. Schneider et al. [30] presented numerous variations in hydration sites for DNA bases in A, B, and Z-DNA structures.

The Molecular Electrostatic Potential Surfaces (MEPS) of non-hydrated nucleobases (Fig.1.) have been calculated by mapping the electrostatic potential onto the electron density surfaces of the nucleobases observed. Blue areas of MEPS, denoting areas of positive electrostatic potential, typically attract negatively charged groups or lone pairs, such as those on the oxygen atoms of water molecules. Positive potential indicates an electron deficiency, making these areas appealing to electron-rich entities. Conversely, red regions, indicating negative potentials, tend to repel the electron-rich oxygen of a water molecule. Thus, blue regions on MEPS generally facilitate water binding, as they are inclined to attract the oxygen

atom of a water molecule, which carries a partial negative charge.

The detailed analysis of MEPS reveals two potential water-binding sites of adenine, both adjacent to the amino groups. Cytosine displays the highest positive potential near the amino and carbonyl groups. Guanine displays potential water-binding sites near the amino group. Thymine exhibits potential sites for water interaction near both carbonyl groups. The amino group positioned between these carbonyl groups is in a negatively charged region, whereas the amino group bonded to the methyl group forms the most likely region for water bonding. Primary water-binding sites are typically near hydrogen atoms, facilitating the formation of hydrogen bonds between carbonyl groups and X-H, where X can be either nitrogen or carbon. Additionally, carbonyl groups can bond to hydrogen to form, O-HOH. This additional binding potential highlights the complex interplay of electrostatic potential in nucleobase hydration. An exception is noted in cytosine, where the amino group possesses a very high positive potential due to the significant negative charge on the nitrogen atom. This charge significantly influences the positive charges on the adjacent hydrogen atoms, thereby inhibiting effective hydrogen bonding. Additionally, the oxygen atom in guanine is not a favorable site due to the closely located nitrogen atom, which lacks hydrogen shielding; hence, a positive potential is evident near both atoms.

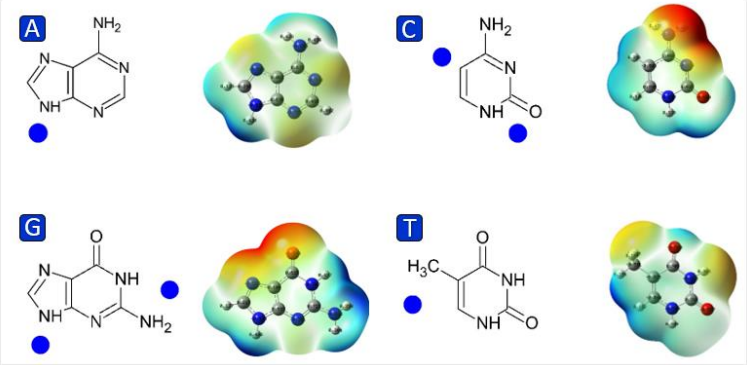

Fig. 1. Molecular Electrostatic Potential Surfaces and binding sites of Adenine (A), Guanine (G), Cytosine (C), and Thymine (T)

We modeled the first hydration shell using binding sites identified in the MEPS. To account for the explicit hydration shell surrounding the nucleobases, a deviation from the conventional mono-solvation scheme was adopted, as described by Pullman [27; 31]. In this model, the first solvation shell of the neutral, anionic, and cationic geometries of [Base $(H_2O)_n$] $^{(0,\pm)}$ (n = 0, 4, 8, 14) was composed of four explicitly hydrogen-bonded water molecules directly to the ground state conformer, with varying binding sites by nucleobase (Fig. 2). The second solvation shell was built by hydrogen bonding water molecules to the first solvation shell until the desired hydration level was reached. The Conductor-like Polarizable Continuum Model (CPCM) solvation model with water as the solvent was used for these calculations.

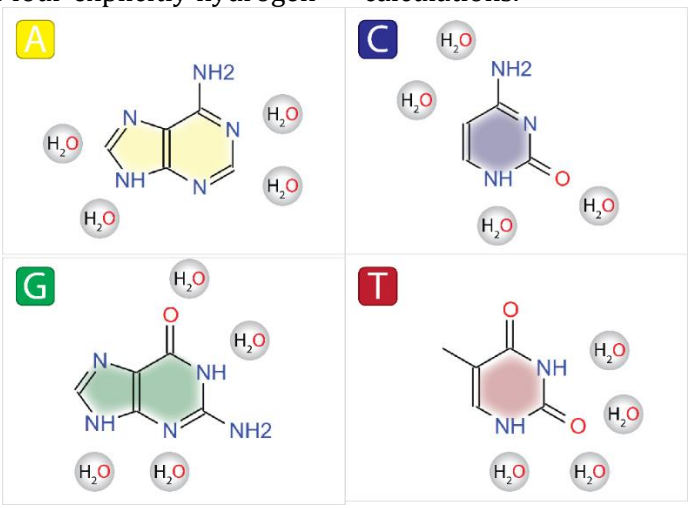

Fig. 2. The scheme of the first solvation shell (4 water molecules) for Adenine (A), Guanine (G), Cytosine (C), and Thymine (T)

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Results and Discussion

Quantitative Evaluation of Electron Affinity and Ionization Potential of Nucleic Acid Bases. Calculated electron affinity values of nucleic acid bases, VEA and AEA, are reported in Table 1. When analyzing electron affinity values, it is important to note that negative integers indicate electron affinity. Alternatively, positive integers indicate electron resistance. VEA values show a trend of majority negative integers in the gas phase and positive integers in the aqueous phase, suggesting that implicit solvation lowers electron affinity. In the gas phase, adenine shows a significant decrease in electron affinity as it becomes increasingly hydrated. This suggests that as water molecules surround adenine, they destabilize its ability to accept electrons, reducing its electron affinity overall. Guanine exhibits an initial increase in VEA as it transitions from $(H_2O)_0$ to $(H_2O)_4$ (3.66 kcal/mol), indicating electron uptake. However, it follows with a steady decrease, meaning it becomes difficult for guanine to accept electrons after more hydration. The total change from $(H_2O)_0$ to $(H_2O)_{14}$ suggests that hydration lowers guanine's resistance to electron acceptance. Although adenine and guanine are classified as purines, they show distinct trends in electron receptivity, with adenine exhibiting the lowest energy response at hydration level $(H_2O)_4$ and guanine at hydration level $(H_2O)_{14}$.

In the gas phase, pyrimidines, cytosine and thymine, show a continuous decrease in electron affinity with increasing hydration levels, indicating that hydration decreases their ability to accept electrons. The change is more gradual compared to purines, but the trend is consistent—the greater presence of water molecules makes it harder for these bases to gain electrons. The VEA values in the gas phase remain relatively low for cytosine and thymine, but the introduction of solvation dramatically shifts the dynamics.

There is a contrasting energy response of VEA values observed between adenine and guanine values in solvation. Adenine reaches its most stable point at $(H_2O)_8$ before starting to increase again, while the energy of guanine continues to decrease throughout. Cytosine and thymine show similar behaviors, with cytosine experiencing a significant drop from $(H_2O)_8$ to $(H_2O)_{14}$ and thymine following a steady decline. These trends suggest that hydration stabilizes the nucleobases differently based on their molecular structure. Hydration seems to help cytosine and thymine resist electrons more easily, while the response in adenine and guanine is more complex, possibly due to their purine ring structures.

The significant difference between hydration levelshighlights the opposing energy responses in purines.

Table 1

Vertical and adiabatic electron affinity (kcal/mol) calculations and statistical parameters

Vertical Electron Affinity									
NAB	Experiment[a]	gas				solvation			
		$(H_2O)_0$	$(H_2O)_4$	$(H_2O)_8$	$(H_2O)_{14}$	$(H_2O)_0$	$(H_2O)_4$	$(H_2O)_8$	$(H_2O)_{14}$
A	21.85	–15.4	–2.27	–20.2	–3.71	24.0	23.9	29.5	25.4
G	34.73	–9.24	–12.9	–1.40	–0.29	17.8	21.3	22.2	25.3
C	12.88	–17.4	–15.2	–11.0	–2.40	30.9	36.7	32.5	33.5
T	18.17	–12.2	–10.9	–7.23	–1.84	33.4	36.5	37.2	34.2
R[1]		0.849	0.082	0.497	0.633	–0.899	–0.861	–0.851	–0.782
A[2]		2.20	0.13	0.59	4.16	–1.19	–0.98	–1.26	–1.48
B[3]		51.76	23.30	27.75	30.48	53.42	51.00	60.13	65.71
Adiabatic Electron Affinity									
NAB	Experiment	gas				solvation			
		$(H_2O)_0$	$(H_2O)_4$	$(H_2O)_8$	$(H_2O)_{14}$	$(H_2O)_0$	$(H_2O)_4$	$(H_2O)_8$	$(H_2O)_{14}$
A		–14.9	0.57	3.96	*	30.8	33.2	41.1	42.2
G		–7.91	–10.2	2.32	8.87	20.7	32.7	33.4	37.6
C		–5.44	–3.81	–8.89	7.00	41.6	47.6	46.7	20.7
T		–1.99	10.4	7.65	25.6	42.7	47.2	51.7	51.5
R[1]		–0.289	–0.560	0.408	–0.197	–0.941	–0.810	–0.862	0.279
A[2]		–0.49	–0.60	0.53	–0.22	–0.85	–0.90	–1.02	0.20
B[3]		18.19	21.44	21.24	24.95	50.66	58.19	66.06	14.27

1 – R: correlation coefficient; 2 – A: slope; 3 – B: intercept; * the structure failed to converge; a – Ref [32].

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In the gas phase, as hydration increases, the AEA of adenine decreases. This suggests that hydration destabilizes the ability of adenine to accept electrons. The interaction between water molecules and adenine's polar regions might disrupt the delocalization of charge in the anionic form, reducing its overall stability. The trend in hydration from $(H_2O)_0$ to $(H_2O)_{14}$ shows that AEA drops significantly around 13 kcal/mol initially, then stabilizes. As hydration increases, adenine's ability to capture electrons weakens due to solvation effects around the purine ring system. This decrease may reflect the interactions of hydration with specific functional groups of adenine, such as the amine group and nitrogen atoms in the purine ring. In the aqueous phase, AEA of adenine is likely to decrease further, indicating that it is much harder for adenine to capture and stabilize an additional electron in a fully hydrated environment. The stabilization from explicit solvation in water competes with the intrinsic charge stabilization of the anionic form.

In the gas phase, guanine initially shows higher resistance to electron uptake compared to adenine, but hydration causes a slight increase in AEA up to $(H_2O)_4$. The increase of AEA at the initial hydration stage suggests that the first few water molecules destabilize guanine's structure, possibly through hydrogen bonding or interaction with the oxygen and nitrogen atoms. The trend in hydration from $(H_2O)_4$ to $(H_2O)_{14}$ in AEA shows a steady decrease, indicating that beyond a certain point, guanine's ability to accept electrons decreases with more hydration. This stabilization at higher hydration levels implies that guanine's interaction with water molecules eventually decreases the electron affinity, especially due to solvation at specific reactive sites like the carbonyl group (C=O) or amino group (-NH_2) at the purine ring. In a fully aqueous phase, guanine's AEA could remain positive but much closer to zero. The solvation shell around guanine likely enhances stabilization around the nitrogen atoms and carbonyl group, leading to a smaller but still positive AEA.

Cytosine is relatively reactive in gas form, and the introduction of hydration seems to further stabilize its anionic form. Water molecules likely interact with the nitrogen and oxygen atoms in the pyrimidine ring, stabilizing the negative charge that forms upon electron acceptance. This suggests that hydration enhances the electron-capturing ability of cytosine. In the aqueous phase, cytosine would likely show a significant decrease in AEA values, potentially becoming negative, as hydration further stabilizes the anionic form. The pyrimidine ring of cytosine, particularly the oxygen and nitrogen atoms, forms favorable hydrogen bonds with water, leading to increased stabilization in the aqueous environment. This added solvation can help cytosine accept and stabilize extra electrons.

Thymine starts with the lowest AEA value of the four nucleobases in the gas phase. Hydration results in a gradual decrease in AEA. The carbonyl and methyl groups may influence its behavior. Thymine's lower initial AEA suggests that it is relatively stable even in an anionic form. The steady decrease in AEA indicates that hydration progressively hinders thymine's ability to accept electrons. The interaction with water likely stabilizes thymine's structure, particularly around the carbonyl groups, which might be involved in hydrogen bonding with water. In the aqueous phase, thymine's AEA is expected to further decrease. The carbonyl groups in thymine play a crucial role in interacting with water molecules, forming strong hydrogen bonds. These solvation interactions further stabilize thymine's structure, making it more difficult to stabilize an additional electron, as the water shell may compete with or disrupt the electron distribution within the molecule.

Ionization potential energy values, VIP and AIP, are reported in Table 2. The VIP values of purines range from 181–205 kcal/mol, indicating a lower threshold for ionization compared to pyrimidines. This is attributed to their more stable aromatic structures, which allow for greater electron delocalization. The VIP values of pyrimidines range from 203–213 kcal/mol, suggesting they require more energy to ionize possibly due to less delocalization. From $(H_2O)_0$ to $(H_2O)_4$, adenine shows a decrease of 7.55 kcal/mol in VIP, suggesting an initial stabilization effect as hydration increases. From $(H_2O)_4$ to $(H_2O)_8$, there is a substantial increase of 16.25 kcal/mol, indicating that further hydration destabilizes the base, making it easier to ionize. Finally, from $(H_2O)_8$ to $(H_2O)_{14}$, there's a slight decrease of 5.91 kcal/mol, possibly reflecting a return to some stabilization with additional water molecules. In the aqueous phase, the initial hydration stabilizes the electron density of adenine. The solvation allows for better stabilization of the charge, thus lowering the VIP.

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Table 2

Vertical and adiabatic ionization potential (kcal/mol) calculations and statistical parameters

Vertical Ionization Potential

NAB	Experiment[a]	gas				solvation			
		$(H_2O)_0$	$(H_2O)_4$	$(H_2O)_8$	$(H_2O)_{14}$	$(H_2O\}_0$	$(H_2O)_4$	$(H_2O)_8$	$(H_2O)_{14}$
A	195.09	196.22	188.67	204.92	199.01	152.20	152.71	157.54	152.22
G	191.41	190.51	187.64	181.47	183.37	145.97	147.46	146.50	149.49
C	205.24	206.67	206.26	205.29	202.90	160.48	167.01	165.17	167.50
T	211.47	212.87	213.72	207.93	203.24	161.70	164.69	165.20	163.46
R[1]		0.997	0.990	0.744	0.809	0.962	0.927	0.898	0.890
A[2]		0.91	0.70	0.55	0.79	1.20	0.91	0.94	0.94
B[3]		17.13	60.93	90.02	44.22	15.20	57.42	52.35	51.36

Adiabatic Ionization Potential

NAB	Experiment[b]	gas				solvation			
		$(H_2O)_0$	$(H_2O)_4$	$(H_2O)_8$	$(H_2O)_{14}$	$(H_2O)_0$	$(H_2O)_4$	$(H_2O)_8$	$(H_2O)_{14}$
A	190.48	190.46	169.77	185.34	159.48	144.97	145.24	145.92	143.46
G	179.18	180.49	173.19	167.30	158.41	138.03	138.22	136.96	137.87
C	200.17	203.57	185.35	194.67	178.34	155.80	152.47	152.87	153.71
T	204.55	206.02	190.63	194.32	169.01	154.97	150.14	153.95	147.47
R[1]		0.994	0.844	0.969	0.773	0.976	0.951	0.993	0.851
A[2]		0.94	0.96	0.85	0.93	1.29	1.70	1.43	1.44
B[3]		10.18	20.44	35.76	38.27	1.70	–55.55	–16.98	–15.59

1 – R: correlation coefficient; 2 – A: slope; 3 – B: intercept; a – Refs [33–40]; b – Ref [34].

In the gas phase, guanine shows a steady decrease in VIP values. Guanine exhibits a steady decrease of 9.04 kcal/mol from $(H_2O)_0$ to $(H_2O)_8$, similar to adenine, indicating hydration enhances stability up to this point. A slight increase of 2.20 kcal/mol from $(H_2O)_8$ to $(H_2O)_{14}$ shows a trend of destabilization as hydration continues. This pattern shows that guanine becomes more stable upon initial hydration, but the presence of water can introduce competitive interactions that may hinder ionization at higher hydration levels. This could be due to the electron-donating nature of its oxygen and nitrogen atoms. These atoms destabilize the neutral state and make guanine more prone to losing an electron, thus requiring less energy for ionization.

In the gas phase, the VIP energy values of cytosine, suggest that electrons are held more tightly. Its simpler structure means the electrons are more localized. The amine group and the electron-withdrawing carbonyl affect the stability of the electrons, but they don't create as much delocalization as in purines. In solvation, there is an increase in VIP which indicates that solvation aids in destabilizing cytosine, but is ultimately less likely to be ionized in the aqueous phase compared to its gas phase behavior.

Thymine has a relatively high VIP in the gas phase due to the lack of extensive electron delocalization and the electron-withdrawing nature of its two carbonyl groups. These functional groups stabilize the electron density within the base. The electron density is concentrated within a smaller region, which increases its VIP. In solvation, the trend in energy suggests that thymine experiences initial hydration stabilization but becomes less reactive at higher hydration levels.

In the gas phase, purines exhibit a slightly lower range of AIP values (158–191 kcal/mol) compared to pyrimidines (169–206 kcal/mol). Lower AIP values of purines imply that these nucleobases can form a cation with minimal energy input, which can be critical during processes like DNA damage repair or electron transport. The trend of AIP energy of adenine in solvation suggests that the stability of adenine in the ionized state improves with hydration. The close range of AIP values to adenine suggests that guanine can also form cations efficiently, supporting its roles in nucleic acid structure and function. In solvation, the trend in energy indicates that while hydration initially stabilizes guanine, its ability to ionize fluctuates with increasing water molecules, affecting its reactivity.

In the gas phase, the range of AIP values of cytosine and thymine supports its relative

stability and highlights its resistance to ionization. In solvation, the trend in energy of cytosine reflects a complex interaction between hydration and the ability of cytosine to ionize, suggesting that increased hydration stabilizes its structure and lowers its reactivity. The trend of energy of thymine indicates that the ionization potential of thymine is sensitive to hydration, potentially stabilizing its structure but also affecting its reactivity.

Statistical analysis and comparison of the results with experimental data are presented in Table 1 and Table 2. Non-hydrated DNA bases in the gas phase, denoted as [Base $(H_2O)_0$], exhibit the strongest correlation in VEA, VIP, and AIP values. The correlation coefficient values of VEA energy range from 0.089 to 0.899 kcal/mol, while AEA values show an opposing trend with the strongest correlation observed at hydration level $(H_2O)_8$. Weak correlations are found in solvated VIP values and almost all AIP values. Alternatively, IP values show strong correlations in both the gas phase and solvation, with correlation coefficients ranging from 0.744–0.997 kcal/mol in VIP values and 0.773–0.994 kcal/mol in AIP values, suggesting a reasonably good fit between experimental and calculated values. The non-hydrated gas phase yields the most optimal results for both theoretical and experimental values. Fig. 3 illustrates that predicted energy values of non-hydrated nucleobases in the gas phase align well with experimental values, showing relatively strong correlation values of 0.72 kcal/mol for VEA, 0.99 kcal/mol for VIP, and 0.98 kcal/mol for AIP. The trendline equations indicate a positive linear relationship between experimental values and fit values for all electronic properties. The R-squared values suggest that this linear equation explains the relatively high variance in the data, indicating a good fit.

Specifics of water molecule binding and its binding energies. Binding energy values, as listed in Table 3, indicate that DNA base-water complexes exhibit weak binding across all states observed. Results reveal that, in the neutral state, binding energy is weakest compared to cationic and anionic states. In the cationic state, the binding energy is highest, ranging from –224 to –319 kcal/mol in the gas phase and 14.0 to –184 kcal/mol in solvation, signifying stronger binding. A great number of conformational changes are also observed in the cationic state. At hydration level $(H_2O)_{14}$, adenine deprotonates at the N9 binding site, which could lead to hydroxyl radical (OH-) formation, while thymine deprotonates at the N3 binding site. There is a presence of stretched hydrogen bonds which suggest water reorientation. In the anionic state, DNA base-water complexes display moderate binding energy, ranging from –28.3 to 48.3 kcal/mol in the gas phase and –28.7 to 23.0 kcal/mol in solvation. However, binding energy values are the lowest in the solvated state, suggesting that implicit solvation weakens the binding energy of the DNA base-water complexes explored.

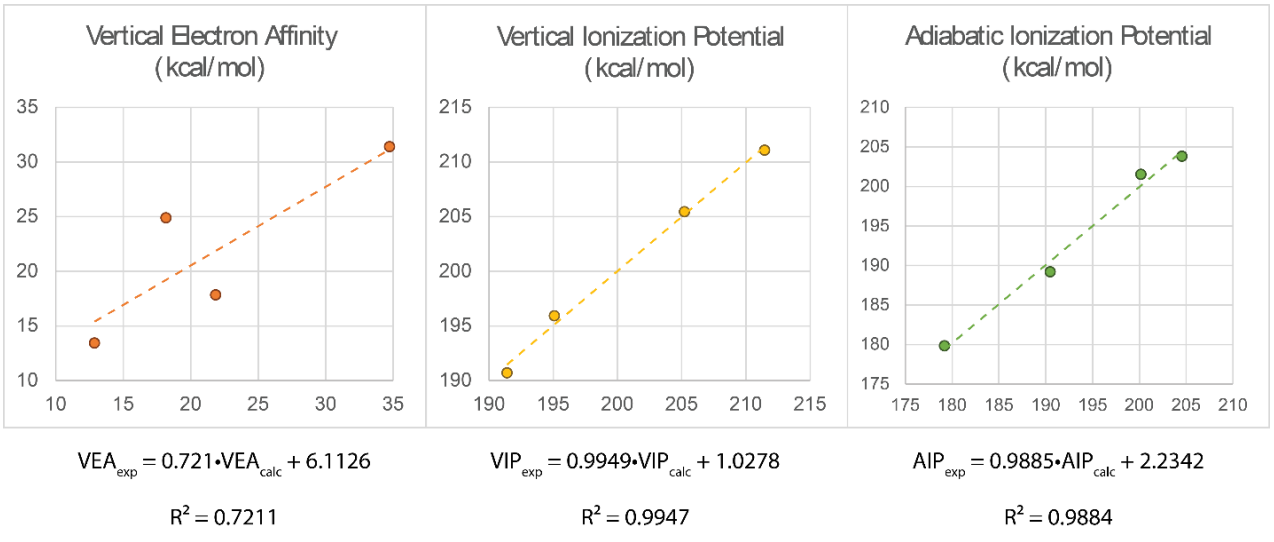

Fig. 3. Correlation plots between experimental data and calculated values

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Table 3

Calculations of binding energy (kcal/mol) in neutral and ionic states

Neutral						
		gas			solvation	
NAB	$(H_2O)_4$	$(H_2O)_8$	$(H_2O)_{14}$	$(H_2O)_4$	$(H_2O)_8$	$(H_2O)_{14}$
A	–0.64	11.9		–1.77	8.71	
G	–20.6	–5.73	–8.71	–11.7	2.02	0.69
C	–12.8	17.1	–17.3	–6.71	–6.64	–5.64
T	–11.2	2.28		–6.93	4.21	
Cation						
		gas			solvation	
NAB	$(H_2O)_4$	$(H_2O)_8$	$(H_2O)_{14}$	$(H_2O)_4$	$(H_2O)_8$	$(H_2O)_{14}$
A	–242	–233		–177	–164	
G	–249	–243	–224	–47.3	–33.3	–33.4
C	–319	–245	–237	–184	–182	–180
T	–250	–243		–30.6	–14.1	
Anion						
		gas			solvation	
NAB	$(H_2O)_4$	$(H_2O)_8$	$(H_2O)_{14}$	$(H_2O)_4$	$(H_2O)_8$	$(H_2O)_{14}$
A	–45.8	–27.0		10.8	18.8	
G	–48.3	–35.2	–32.6	–9.43	21.7	12.2
C	–44.4	–28.6	–37.0		13.1	–28.7
T	–39.3	–37.0		1.20	23.9	

Conclusion

The electronic properties of single and paired DNA bases play a crucial role in understanding charge transport mechanisms, DNA base modifications, ionization of DNA components, and radical species generation in aqueous media at the molecular level. These insights may have significance in elucidating the role of water molecules in DNA-protein interactions, the connection between DNA alterations and biological effects in organisms, and the design of novel DNA-based materials. We calculated the electronic properties, specifically electron affinity (EA) and ionization potential (IP), of DNA base-water complexes. Our data indicates that water molecules strongly influence the electronic properties of DNA bases. In the gas phase, pyrimidines exhibit the highest ionization potential, while purines display elevated electron affinity values and lower ionization potential values. This stark contrast in ionization potential between the gas and aqueous phases of DNA-water complexes emphasizes the impact of water molecules on the ionization process. In the gas phase, the higher ionization potential suggests that DNA bases in a vacuum are more prone to ionization when surrounded by explicit water molecules. This is due to the stabilizing effect

of explicit water molecules on charged species, reducing the energy required for DNA base ionization. Positive EA values associated with DNA-water complexes in implicit solvation imply that solvation may hinder

ionization. Our data further indicates that implicit solvation enhances binding energy across all observed states. While the data for the neutral state suggests relatively weak binding between water molecules and nucleobases alone, DNA base-water complexes in the cationic state exhibit the highest binding energy in the gas phase among all molecules considered. Regarding conformational changes, in the cationic state, adenine and thymine undergo conformational changes at the greatest hydration level explored. Hydrogen bonds in the water network are stretched in some ionic states, suggesting water reorientation. While exploring the electronic properties of cationic and anionic DNA base-water complexes provides insights into the interactions of water and ions with nucleobases, these calculations illustrate insights into nucleobase-water interactions in the neutral state. Our results offer critical insights into the ionization processes within DNA-water complexes and contribute to ongoing efforts to unravel the underlying mechanisms of these essential processes.

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Declaration of Competing Interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Supporting Information

Cartesian coordinates and structures of all the optimized DNA–water complexes are provided.

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