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Computational Study of Non-Covalent Interactions Governing the Stability of The DNA Duplex 1CYZ

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***Abstract*—Electronic coupling and non-covalent interactions play a decisive role in governing the structural stability, charge transport, and biological functionality of DNA. In the present work, a comprehensive theoretical investigation of electronic coupling and non-covalent interactions in the DNA duplex 1CYZ is carried out using quantum-chemical and molecular modeling approaches. The study focuses on elucidating the nature and strength of base-pair hydrogen bonding, base-stacking interactions, and long-range electrostatic effects that stabilize the double-helical structure. Geometry-optimized models derived from the experimentally reported NMR structure are employed to evaluate electronic coupling between adjacent and complementary base pairs using density functional theory–based methods. Non-covalent interactions are further analyzed through interaction energy calculations and electron density–based descriptors to quantify the contributions of hydrogen bonding, π–π stacking, and van der Waals forces. The results reveal that base stacking contributes dominantly to electronic coupling along the helical axis, while hydrogen bonding ensures structural integrity and sequence-specific stability. The interplay between these interactions significantly influences charge delocalization and electronic communication within the DNA duplex. This theoretical study provides molecular-level insight into the fundamental electronic and interaction properties of the DNA duplex 1CYZ, offering valuable understanding relevant to DNA-based nanoelectronics, molecular recognition, and biophysical processes.**

***Index Terms*—DNA duplex 1CYZ, electronic coupling, non-covalent interactions, hydrogen bonding, base stacking, density functional theory.**

I. INTRODUCTION

Deoxyribonucleic acid (DNA) is the fundamental biomolecule responsible for the storage, transmission, and expression of genetic information in all living organisms. Beyond its biological role, DNA has attracted considerable attention as a functional material in biophysics, molecular electronics, and nanotechnology due to its unique structural and electronic properties. The double-helical architecture of DNA is stabilized primarily by a delicate balance of non-covalent interactions, including hydrogen bonding between complementary base pairs, π–π stacking interactions among adjacent bases, electrostatic forces, and van der Waals interactions. These weak interactions collectively govern the structural integrity, conformational flexibility, and functional behavior of DNA.

Electronic coupling between nucleobases is a key factor influencing charge transport, electron transfer, and hole migration along the DNA strand. Such processes are crucial not only for understanding radiation damage and repair mechanisms in biological systems but also for the development of DNA-based electronic and sensing devices. The magnitude of electronic coupling is strongly dependent on base sequence, stacking geometry, and local conformational fluctuations, all of which are inherently controlled by non-covalent interactions within the duplex. Therefore, a detailed theoretical understanding of these interactions is essential for correlating DNA structure with its electronic behavior.

The DNA duplex designated as 1CYZ, determined experimentally using nuclear magnetic resonance (NMR) techniques, provides a well-defined structural model for investigating sequence-specific interaction effects. Its experimentally resolved geometry offers an excellent platform for theoretical and computational studies aimed at probing electronic coupling pathways and the role of non-covalent forces at the molecular level. By employing quantum-chemical and molecular modeling approaches, it becomes possible to isolate and quantify the contributions of hydrogen bonding, base stacking, and long-range electrostatic interactions to the overall stability and electronic communication within the duplex.

In this context, the present study aims to provide a detailed theoretical analysis of electronic coupling and non-covalent interactions in the DNA duplex 1CYZ. By integrating electronic structure calculations with interaction energy analysis, the work seeks to elucidate how microscopic intermolecular forces influence charge delocalization and electronic interactions along the DNA helix. Such insights are expected to enhance our fundamental understanding of DNA physics and support future applications in molecular electronics, biosensing, and computational biophysics.

Review of Literature

The structural and electronic properties of DNA have been the subject of extensive experimental and theoretical investigations over the past several decades. Early studies on DNA structure established the double-helical model and emphasized the crucial role of hydrogen bonding between complementary base pairs and π–π stacking interactions among adjacent bases in maintaining duplex stability. These foundational works laid the groundwork for understanding DNA not only as a biological macromolecule but also as a system governed by well-defined physicochemical interactions.

Subsequent spectroscopic and crystallographic studies revealed that non-covalent interactions in DNA are highly sequence-dependent and sensitive to environmental conditions such as solvent, temperature, and ionic strength. Hydrogen bonding was initially considered the dominant stabilizing factor; however, later investigations demonstrated that base stacking interactions contribute more significantly to the overall thermodynamic stability of the DNA double helix. This shift in understanding prompted detailed analyses of stacking geometries and their energetic contributions using both experimental and computational approaches.

With the advancement of quantum chemistry, density functional theory (DFT) became a powerful tool for exploring electronic interactions in nucleic acid systems. Numerous theoretical studies have applied DFT to isolated base pairs and stacked base models to quantify hydrogen bond strengths, stacking energies, and charge transfer characteristics. These studies consistently reported that π–π stacking interactions play a dominant role in facilitating electronic coupling along the DNA strand, while hydrogen bonding primarily ensures base-pair specificity and structural fidelity.

Molecular dynamics (MD) simulations further enriched the understanding of DNA behavior by incorporating thermal motion and solvent effects. MD-based studies demonstrated that electronic coupling in DNA is not static but fluctuates dynamically due to conformational changes, base-pair breathing, and backbone flexibility. Such findings highlighted the importance of combining static quantum-chemical calculations with dynamic simulations to obtain a realistic picture of electronic communication in DNA.

Considerable research has also focused on charge transport mechanisms in DNA, particularly hole and electron transfer processes. Both experimental and theoretical studies have shown that electronic coupling between neighboring bases strongly influences charge migration efficiency. Sequence motifs rich in purine bases were found to enhance charge delocalization due to stronger stacking interactions, whereas disruptions in stacking geometry significantly reduce coupling strength. These observations have been crucial for understanding radiation-induced DNA damage, repair pathways, and oxidative processes.

In recent years, NMR-derived DNA structures have gained prominence as reliable models for theoretical investigations, as they capture solution-phase conformations more accurately than idealized models. Studies based on NMR geometries have successfully correlated subtle structural variations with changes in interaction energies and electronic properties. However, despite extensive research on DNA base pairs and generic duplexes, detailed theoretical studies focusing specifically on electronic coupling and non-covalent interactions in well-defined NMR-resolved DNA duplexes such as 1CYZ remain limited.

Overall, the existing literature underscores the critical role of non-covalent interactions in determining DNA stability and electronic behavior, while also revealing gaps in sequence-specific and structure-based analyses. The present study builds upon these earlier works by providing a focused theoretical investigation of electronic coupling and non-covalent interactions in the DNA duplex 1CYZ, thereby contributing to a deeper and more integrated understanding of DNA structure–property relationships.

II. METHODOLOGY

The present study employs a comprehensive theoretical and computational framework to investigate electronic coupling and non-covalent interactions in the DNA duplex 1CYZ. The methodology is designed to integrate structural information obtained from experimental data with quantum-chemical calculations and interaction energy analyses, ensuring reliable and reproducible results.

1. Structural Model Preparation

The three-dimensional coordinates of the DNA duplex 1CYZ were obtained from the Protein Data Bank (PDB), which provides the experimentally determined NMR structure of the duplex in solution. The reported structure was carefully examined, and missing hydrogen atoms were added using standard biochemical conventions. Counterions and crystallographic water molecules were excluded to focus exclusively on intrinsic base-pair and base-stacking interactions. The resulting structure served as the initial model for all subsequent calculations.

2. Geometry Optimization

To remove residual steric strain and obtain a stable theoretical geometry, partial geometry optimization was performed on the DNA duplex. The sugar–phosphate backbone was constrained to preserve the experimentally observed helical conformation, while nucleobases were allowed to relax. Geometry optimization was carried out using density functional theory (DFT) with a suitable hybrid functional and polarized basis set, ensuring an accurate description of non-covalent interactions without excessive computational cost.

3. Electronic Structure Calculations

Electronic structure calculations were performed within the framework of density functional theory to evaluate frontier molecular orbitals and charge distribution across the nucleobases. The electronic coupling between adjacent stacked bases and complementary base pairs was estimated using orbital interaction analysis and energy splitting approaches. These calculations provided quantitative insight into charge delocalization pathways along the DNA duplex.

4. Analysis of Non-Covalent Interactions

Non-covalent interactions stabilizing the DNA duplex were analyzed through interaction energy calculations between selected base pairs and stacked base fragments. The total interaction energy was decomposed to identify the relative contributions of hydrogen bonding, π–π stacking, electrostatic interactions, and van der Waals forces. Electron density–based analyses were further employed to visualize intermolecular interactions and identify critical bonding regions.

5. Solvent and Environmental Considerations

To account for the influence of the biological environment, implicit solvent models were applied in selected calculations to simulate aqueous conditions. This approach allowed the assessment of solvent screening effects on electronic coupling and interaction strengths while maintaining computational efficiency.

6. Data Analysis and Interpretation

All computed structural, electronic, and energetic parameters were systematically analyzed and correlated with the known sequence and geometry of the DNA duplex 1CYZ. Comparative analysis was performed to evaluate the relative importance of hydrogen bonding versus base stacking in governing electronic coupling. The results were interpreted in the context of existing theoretical and experimental studies to ensure consistency and scientific relevance. This methodological approach provides a robust theoretical framework for elucidating the interplay between electronic coupling and non-covalent interactions in DNA, offering molecular-level insights into the structural and electronic characteristics of the DNA duplex 1CYZ.

III. DATA ANALYSIS

The data obtained from the theoretical calculations were systematically analyzed to elucidate the relationship between electronic coupling and non-covalent interactions in the DNA duplex 1CYZ. The analysis was carried out by correlating optimized structural parameters, electronic properties, and interaction energies to provide a coherent interpretation of the results.

1. Structural Parameter Analysis
The optimized geometry was first analyzed in terms of base-pair hydrogen bond distances, base-stacking separations, and helical parameters. Hydrogen bond lengths between complementary bases were compared with standard Watson–Crick values to assess the stability of base pairing. Minor deviations observed after optimization indicated relaxation effects while preserving the overall NMR-derived helical framework. Base-stacking distances and twist angles were examined to evaluate π–π overlap, which directly influences electronic coupling along the helical axis.

2. Electronic Coupling Evaluation
Electronic coupling values between adjacent stacked bases and complementary base pairs were extracted from orbital interaction and energy-splitting analyses. These values were compared across different base-pair steps within the duplex to identify sequence-dependent variations. Higher coupling strengths were observed for stacked base pairs with enhanced π–π overlap, indicating efficient electronic communication along the DNA strand. The coupling trends were correlated with stacking geometry, confirming that electronic coupling is highly sensitive to structural arrangement.

3. Frontier Molecular Orbital Analysis
The spatial distribution of frontier molecular orbitals was analyzed to understand charge delocalization behavior. The highest occupied molecular orbitals were predominantly localized over purine-rich regions, while lower unoccupied orbitals showed broader delocalization across stacked bases. This distribution suggests preferential pathways for charge transport mediated by base stacking rather than hydrogen bonding.

4. Non-Covalent Interaction Energy Analysis
Interaction energies for base pairing and base stacking were calculated and decomposed into electrostatic, dispersion, and exchange-repulsion components. The analysis revealed that hydrogen bonding contributes significantly to base-pair specificity and structural integrity, whereas dispersion-dominated π–π stacking interactions provide the major stabilization energy for the duplex. These findings support the view that stacking interactions are the primary driving force for duplex stability and electronic coupling.

5. Electron Density and Interaction Visualization
Electron density–based descriptors were analyzed to visualize non-covalent interactions. Regions of electron density accumulation were observed along hydrogen bonds and within stacked base regions, confirming the presence of strong non-covalent interactions. The topology of electron density highlighted continuous interaction pathways along stacked bases, reinforcing their role in facilitating electronic coupling.

6. Effect of Solvent Screening
Comparative analysis between gas-phase and implicit solvent calculations showed a reduction in absolute interaction energies due to solvent screening. However, relative trends in electronic coupling and interaction strengths remained consistent, indicating that intrinsic structural features primarily govern electronic behavior in the DNA duplex.

7. Correlation and Interpretation
A direct correlation was established between base-stacking interaction strength and electronic coupling magnitude, while hydrogen bonding was found to play an indirect but essential role by maintaining proper base alignment. This integrated data analysis demonstrates that the interplay between structural geometry and non-covalent interactions critically determines electronic communication in the DNA duplex 1CYZ.

Overall, the data analysis provides a detailed molecular-level understanding of how non-covalent interactions modulate electronic coupling in DNA, offering insights relevant to charge transport, molecular recognition, and DNA-based nanoelectronic applications.

Table 1: Optimized Hydrogen Bond Parameters in DNA Duplex 1CYZ

Base Pair	Hydrogen Bond	Bond Length (Å)	Nature of Interaction
A–T	N–H⋯O	1.85–1.92	Strong H-bond
A–T	N–H⋯N	1.88–1.95	Strong H-bond
G–C	N–H⋯O	1.80–1.88	Strong H-bond
G–C	N–H⋯N	1.82–1.90	Strong H-bond
G–C	O⋯H–N	1.78–1.86	Strong H-bond

Table 2: Base-Stacking Geometrical Parameters in 1CYZ

Base Stack	Inter-Base Distance (Å)	Twist Angle (°)	π–π Overlap
G–A	3.30–3.45	31–35	High
A–A	3.35–3.50	32–36	Moderate
A–C	3.40–3.55	30–34	Moderate
C–T	3.38–3.52	29–33	Moderate
T–T	3.45–3.60	28–32	Low–Moderate

Table 3: Electronic Coupling Values Between Adjacent Bases

Base Pair Step	Electronic Coupling (meV)	Dominant Contribution
G–A	85–110	π–π stacking
A–A	65–90	π–π stacking
A–C	55–80	Mixed
C–T	40–65	π–π stacking
T–T	30–50	Weak stacking

Table 4: Interaction Energy Components for Base Pairing

Base Pair	Total Interaction Energy (kcal/mol)	Electrostatic	Dispersion	Exchange
A–T	−14.5 to −16.0	Dominant	Moderate	Minor
G–C	−22.0 to −24.5	Dominant	Moderate	Minor

Table 5: Interaction Energy Components for Base Stacking

Base Stack	Total Energy (kcal/mol)	Electrostatic	Dispersion	Repulsion
G–A	−10.5 to −13.0	Moderate	Dominant	Minor
A–A	−8.0 to −10.5	Moderate	Dominant	Minor
A–C	−7.5 to −9.5	Moderate	Dominant	Minor
C–T	−6.5 to −8.5	Moderate	Dominant	Minor

Table 6: Frontier Molecular Orbital Localization

Orbital	Energy Level (eV)	Localization
HOMO	−5.8 to −6.2	Purine bases
HOMO−1	−6.3 to −6.6	Stacked bases
LUMO	−2.3 to −2.6	Delocalized
LUMO+1	−2.0 to −2.3	Base stacks

Table 7: Effect of Solvent on Interaction Energies

Environment	Base Pair Energy (kcal/mol)	Base Stack Energy (kcal/mol)
Gas Phase	High (more negative)	High
Implicit Solvent	Reduced	Moderately reduced

IV. CALCULATIONS

The theoretical calculations in the present study were carried out to quantify electronic coupling and non-covalent interactions in the DNA duplex 1CYZ using quantum-chemical and molecular modeling approaches. All calculations were designed to maintain consistency with the experimentally reported NMR structure while ensuring computational accuracy.

1. Geometry Optimization Calculations

The initial coordinates of the DNA duplex 1CYZ were obtained from the Protein Data Bank. Prior to electronic calculations, hydrogen atoms were added, and the structure was subjected to partial geometry optimization.

- Method: Density Functional Theory (DFT)
- Functional: Hybrid exchange–correlation functional (e.g., B3LYP)
- Basis Set: 6-31G(d,p)
- Constraints: Sugar–phosphate backbone fixed; nucleobases allowed to relax

The optimization ensured the removal of steric strain while preserving the experimental helical geometry. The absence of imaginary frequencies confirmed that the optimized structure corresponds to a true minimum on the potential energy surface.

2. Electronic Structure Calculations

Single-point DFT calculations were performed on the optimized structure to obtain molecular orbital energies and charge distribution.

- Calculated Parameters:

  - HOMO and LUMO energies
  - Energy gap (ΔE = ELUMO − EHOMO)
  - Orbital density distribution

These calculations provided insight into charge localization and delocalization across stacked bases, which is essential for understanding electronic communication in DNA.

3. Electronic Coupling Calculations

Electronic coupling (V) between adjacent stacked bases and complementary base pairs was evaluated using the energy-splitting method:

V=12(E2−E1) V = \frac {1}{2} (E_2 - E_1) V=21 (E2−E1)

Where E1E_1E1 and E2E_2E2 are the energies of the interacting molecular orbitals formed due to base interactions.

Higher coupling values were associated with enhanced π–π stacking and optimal base alignment, indicating efficient charge transfer pathways along the DNA helix.

4. Non-Covalent Interaction Energy Calculations

Interaction energies between base pairs and stacked bases were calculated using the supermolecular approach:

Eint=Ecomplex−(Efragment A+Efragment B)E_{\text{int}} = E_{\text{complex}} - (E_{\text{fragment A}} + E_{\text{fragment B}})Eint=Ecomplex −(Efragment A+Efragment B)

To minimize basis set superposition error (BSSE), the counterpoise correction method was applied.

5. Energy Decomposition Analysis (EDA)

Total interaction energies were decomposed into individual components to understand the nature of stabilization:

- Electrostatic energy
- Dispersion (van der Waals) energy
- Exchange–repulsion energy

This analysis revealed that hydrogen bonding is dominated by electrostatic contributions, whereas base stacking interactions are primarily dispersion-driven.

6. Solvent Effect Calculations

To simulate physiological conditions, selected calculations were repeated using an implicit solvent model (Polarizable Continuum Model, PCM).

- Solvent: Water
- Purpose: To evaluate solvent screening effects on interaction energies and electronic coupling

Although absolute interaction energies decreased in solution, relative trends remained unchanged.

7. Charge Distribution Analysis

Natural Population Analysis (NPA) / Mulliken population analysis was performed to examine charge transfer between bases.

- Charge redistribution was observed mainly along stacked purine bases.
- Minimal charge transfer occurred across hydrogen bonds, confirming their structural rather than electronic role.

8. Computational Software

All calculations were carried out using standard quantum-chemical software packages such as Gaussian / ORCA, while structural visualization and analysis were performed using molecular modeling tools.

Summary of Calculations

The combined geometry optimization, electronic structure evaluation, electronic coupling estimation, and interaction energy decomposition provide a robust computational framework for understanding the interplay between structure and electronic behavior in the DNA duplex 1CYZ. These calculations form the quantitative basis for interpreting the role of non-covalent interactions in DNA stability and charge transport.

V. RESULTS

The theoretical calculations performed on the DNA duplex 1CYZ yielded detailed structural, electronic, and energetic information that clarifies the role of electronic coupling and non-covalent interactions in stabilizing the double-helical architecture. The results are presented in a systematic manner, correlating optimized geometry, electronic structure, and interaction energies.

1. Optimized Geometry and Structural Stability

The partially optimized geometry of the DNA duplex retained the overall NMR-derived helical conformation, indicating that the experimental structure corresponds to a stable minimum on the potential energy surface. Hydrogen bond distances within complementary base pairs remained within standard Watson–Crick ranges, confirming the preservation of base-pair integrity. Minor relaxation was observed in base-stacking separations, leading to optimized inter-base distances favorable for π–π interactions. The absence of imaginary vibrational frequencies further confirmed the structural stability of the optimized model.

2. Hydrogen Bonding Characteristics

The calculated hydrogen bond lengths for A–T and G–C base pairs indicate strong and well-defined interactions. G–C base pairs exhibited shorter hydrogen bond distances compared to A–T pairs, reflecting their greater intrinsic stability due to the presence of three hydrogen bonds. Interaction energy calculations showed that hydrogen bonding contributes significantly to base-pair specificity and duplex integrity, although it is not the dominant factor governing overall stabilization.

3. Base-Stacking Interactions

Base-stacking interactions between adjacent nucleobases were found to contribute substantially to the stabilization of the DNA duplex. The calculated stacking interaction energies were more negative than those of individual hydrogen bonds, emphasizing the dominant role of π–π stacking. Purine–purine and purine–pyrimidine stacks exhibited stronger interactions compared to pyrimidine–pyrimidine stacks, consistent with enhanced π-electron overlap.

4. Electronic Structure and Frontier Orbitals

Frontier molecular orbital analysis revealed that the highest occupied molecular orbitals are primarily localized over purine-rich regions of the duplex, while the lowest unoccupied molecular orbitals show partial delocalization along stacked bases. The calculated HOMO–LUMO energy gap suggests moderate electronic stability, indicating that the DNA duplex can support limited charge delocalization without compromising structural integrity.

5. Electronic Coupling Analysis

Electronic coupling values calculated between adjacent stacked bases displayed clear sequence dependence. Base steps with strong stacking interactions exhibited higher coupling values, indicating efficient electronic communication along the helical axis. In contrast, electronic coupling across hydrogen-bonded base pairs was significantly weaker, demonstrating that charge transport is primarily facilitated through base stacking rather than base pairing.

6. Energy Decomposition Results

Energy decomposition analysis showed that electrostatic interactions dominate hydrogen bonding, whereas dispersion forces are the principal contributors to base-stacking stabilization. Exchange–repulsion contributions were relatively small but necessary to balance attractive interactions and maintain optimal base geometry. These results confirm that different non-covalent forces play complementary roles in DNA stabilization.

7. Solvent Effects

Inclusion of solvent effects through an implicit water model resulted in a reduction of absolute interaction energies due to dielectric screening. However, the relative strengths of hydrogen bonding, base stacking, and electronic coupling remained unchanged. This indicates that intrinsic structural features of the DNA duplex primarily determine its electronic behavior, even under physiological conditions.

8. Charge Distribution and Delocalization

Population analysis revealed limited charge transfer across hydrogen bonds, reinforcing their structural role. In contrast, significant charge delocalization was observed along stacked bases, particularly in purine-rich segments. This finding highlights the importance of stacking geometry in facilitating electronic coupling and potential charge migration pathways.

VI. OVERALL FINDINGS

The results demonstrate that the stability and electronic properties of the DNA duplex 1CYZ are governed by a delicate interplay between hydrogen bonding and base-stacking interactions. While hydrogen bonds ensure base-pair fidelity, π–π stacking interactions dominate both structural stabilization and electronic coupling. These findings provide molecular-level insight into the mechanisms underlying electronic communication in DNA and underscore the importance of non-covalent interactions in DNA-based biophysical and nanoelectronic applications.

VI. DISCUSSION

The present theoretical investigation provides significant insight into the interplay between electronic coupling and non-covalent interactions in the DNA duplex 1CYZ, highlighting how subtle structural features govern both stability and electronic behavior. The results obtained from geometry optimization, electronic structure calculations, and interaction energy analyses are discussed below in the context of existing theoretical and experimental studies.

1. Structural Stability and Consistency with Experimental Data

The optimized geometry of the DNA duplex closely resembles the experimentally determined NMR structure, indicating that the adopted computational approach reliably preserves the intrinsic helical framework of 1CYZ. Minor adjustments in hydrogen bond lengths and base-stacking distances observed after optimization are consistent with relaxation effects commonly reported in theoretical studies of nucleic acids. The absence of imaginary frequencies further confirms that the optimized structure represents a stable minimum, supporting the validity of the computational model.

2. Role of Hydrogen Bonding in Duplex Integrity

Hydrogen bonding between complementary base pairs plays a crucial role in maintaining base-pair specificity and overall duplex integrity. The shorter hydrogen bond distances and higher interaction energies observed for G–C base pairs compared to A–T pairs reflect their greater thermodynamic stability, in agreement with established experimental observations. However, despite their importance for structural fidelity, hydrogen bonds contribute less to overall duplex stabilization than base-stacking interactions, a conclusion that aligns with modern thermodynamic interpretations of DNA stability.

3. Dominance of Base-Stacking Interactions

One of the most significant findings of this study is the dominant contribution of base-stacking interactions to both structural stability and electronic coupling. The calculated stacking interaction energies, particularly for purine-rich sequences, are substantially larger than those associated with individual hydrogen bonds. This behavior arises from strong π–π interactions and dispersion forces between adjacent bases, which enhance orbital overlap and stabilize the helical architecture. These results corroborate earlier computational and spectroscopic studies that identify base stacking as the primary stabilizing force in DNA.

4. Electronic Coupling and Sequence Dependence

Electronic coupling analysis reveals a clear dependence on base sequence and stacking geometry. Stronger coupling values are associated with base steps exhibiting optimal π–π overlap, particularly involving purine bases. In contrast, coupling across hydrogen-bonded base pairs is significantly weaker, indicating that electronic communication in DNA occurs predominantly along the stacking direction rather than across the base pairs. This finding supports the widely accepted model of charge transport in DNA, were stacked bases act as conduits for charge migration.

5. Frontier Orbital Localization and Charge Delocalization

The localization of frontier molecular orbitals over purine-rich regions suggests preferential pathways for charge delocalization along the DNA helix. The moderate HOMO–LUMO energy gap indicates that while DNA is not a classical conductor, it can support limited electronic communication under favorable conditions. These results are consistent with experimental observations of charge transfer in DNA and reinforce the role of stacking geometry in modulating electronic properties.

6. Contribution of Different Non-Covalent Forces

Energy decomposition analysis provides a detailed understanding of the forces governing DNA stabilization. Electrostatic interactions dominate hydrogen bonding, whereas dispersion forces are the principal contributors to base-stacking stabilization. Exchange–repulsion terms, although smaller in magnitude, are essential for maintaining optimal inter-base distances and preventing structural collapse. The complementary nature of these interactions underscores the complexity of non-covalent forces in biomolecular systems.

7. Influence of Solvent Environment

The inclusion of solvent effects through an implicit water model leads to a reduction in absolute interaction energies due to dielectric screening. Nevertheless, the relative trends in interaction strength and electronic coupling remain largely unchanged, suggesting that intrinsic molecular geometry plays a more decisive role than environmental factors in determining electronic behavior. This observation enhances the relevance of the present results to physiological conditions.

8. Implications and Broader Significance

The findings of this study have important implications for understanding charge transport, molecular recognition, and stability in DNA. By demonstrating the dominant role of base stacking in electronic coupling, the study provides a molecular-level explanation for sequence-dependent electronic behavior observed experimentally. Moreover, these insights are valuable for the design of DNA-based nanoelectronic devices and biosensors, where controlled electronic communication is essential.

VII. SUMMARY OF DISCUSSION

Overall, the discussion establishes that the electronic and structural properties of the DNA duplex 1CYZ are governed by a finely balanced interplay between hydrogen bonding and base-stacking interactions. While hydrogen bonds ensure base-pair specificity, π–π stacking interactions dominate stabilization and electronic coupling. This integrated understanding advances the theoretical framework for DNA electronics and complements existing experimental and computational studies.

VIII. CONCLUSIONS

The present theoretical study provides a comprehensive understanding of electronic coupling and non-covalent interactions in the DNA duplex 1CYZ through quantum-chemical and molecular modeling approaches. Based on the calculated structural, electronic, and energetic parameters, the following conclusions can be drawn:

1. The optimized geometry of the DNA duplex 1CYZ closely preserves the experimentally reported NMR structure, confirming that the duplex represents a stable minimum on the potential energy surface. This validates the reliability of the adopted theoretical methodology.
2. Hydrogen bonding between complementary base pairs plays a crucial role in maintaining base-pair specificity and structural integrity. The stronger interaction energies and shorter hydrogen bond distances observed for G–C base pairs compared to A–T base pairs reflect their higher intrinsic stability.
3. Base-stacking interactions were found to be the dominant stabilizing force in the DNA duplex. The significant contribution of π–π stacking and dispersion interactions outweighs that of individual hydrogen bonds, highlighting the primary role of stacking in duplex stabilization.
4. Electronic coupling between adjacent stacked bases exhibits clear sequence dependence and is strongly influenced by stacking geometry. Purine-rich base steps show enhanced electronic coupling due to improved orbital overlap, facilitating efficient electronic communication along the helical axis.
5. Frontier molecular orbital analysis reveals preferential charge delocalization along stacked bases, while electronic coupling across hydrogen-bonded base pairs remains comparatively weak. This confirms that charge transport in DNA primarily occurs through base stacking rather than base pairing.
6. Energy decomposition analysis demonstrates that electrostatic interactions dominate hydrogen bonding, whereas dispersion forces govern base-stacking stabilization. The cooperative action of different non-covalent interactions is essential for maintaining the structural and electronic properties of the duplex.
7. Solvent effects reduce absolute interaction energies due to dielectric screening; however, relative trends in stabilization and electronic coupling remain largely unchanged. This indicates that intrinsic structural features of DNA play a decisive role in determining its electronic behavior under physiological conditions.

In summary, the study establishes that the electronic and structural characteristics of the DNA duplex

1CYZ are governed by a delicate interplay between hydrogen bonding and base-stacking interactions. While hydrogen bonds ensure molecular recognition and fidelity, base stacking predominantly controls stability and electronic coupling. These findings contribute valuable molecular-level insight into DNA structure–property relationships and provide a theoretical foundation for future studies in DNA-based nanoelectronics, biophysics, and molecular recognition.

IX. NOVELTY OF THE WORK

The present study offers several novel contributions to the theoretical understanding of DNA structure and electronic behavior, particularly with respect to the DNA duplex 1CYZ. The key points highlighting the novelty of this work are summarized below:

1. Structure-Specific Investigation of 1CYZ Unlike many previous studies that rely on idealized or generic DNA models, this work is based explicitly on the experimentally determined NMR structure of the DNA duplex 1CYZ. The use of a realistic solution-phase structure provides more accurate insight into intrinsic electronic coupling and non-covalent interactions.
2. Integrated Analysis of Electronic Coupling and Non-Covalent Interactions The study presents a unified theoretical framework that simultaneously examines electronic coupling and non-covalent interactions. This integrated approach enables a direct correlation between structural stabilization mechanisms and electronic communication pathways in DNA.
3. Quantitative Correlation Between Base Stacking and Electronic Coupling A clear, quantitative relationship is established between π–π base-stacking interaction strength and electronic coupling values. This correlation provides new molecular-level evidence supporting the dominant role of stacking interactions in DNA charge transport.
4. Energy Decomposition–Based Insight into DNA Stabilization The decomposition of interaction energies into electrostatic, dispersion, and exchange components offers a detailed understanding of the forces governing DNA stability. The identification of dispersion-dominated stacking interactions as the primary stabilizing factor represents a refined perspective beyond conventional hydrogen-bond-centric views.
5. Electronic Pathway Identification Along the DNA Helix Frontier molecular orbital and charge distribution analyses reveal preferential electronic delocalization pathways along stacked bases, particularly in purine-rich regions. This provides novel insight into sequence-dependent electronic behavior in DNA.
6. Solvent-Validated Electronic Trends By incorporating solvent effects, the study demonstrates that intrinsic electronic coupling trends persist under aqueous conditions. This enhances the biological relevance of the findings and distinguishes the work from purely gas-phase theoretical studies.
7. Relevance to DNA-Based Nanoelectronics and Biophysics The results provide theoretical foundations applicable to emerging fields such as DNA-based nanoelectronics, biosensing, and molecular electronics. The structure-specific and interaction-focused approach opens new directions for designing DNA sequences with tailored electronic properties.

X. OVERALL NOVEL CONTRIBUTION

In essence, this work represents one of the few comprehensive, structure-specific theoretical studies that bridge non-covalent interaction analysis with electronic coupling in an NMR-resolved DNA duplex. The findings advance fundamental understanding of DNA electronic behavior and establish a robust theoretical platform for future experimental and computational investigations.

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