WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
Coden USA: WJPRAP Impact Factor 8.63
Volume 15, Issue 16, 952-966. Research Article ISSN 2277–7105

SEQUENCE-DEPENDENT THERMODYNAMIC AND QUANTUM-CHEMICAL DESCRIPTORS OF DNA DINUCLEOTIDES: AN AM1/MOPAC2016 COMPUTATIONAL STUDY

***Dr. Bojja Rajeshwar Rao**

Senior Chemist (Retired), Chemical Division, Kakatiya Thermal Power Project (O&M), Chelpur-506 170, Telangana State, India.

Article Received on 16 July 2026,
Article Revised on 06 August 2026,
Article Published on 16 August 2026,

https://doi.org/10.5281/zenodo.21916479

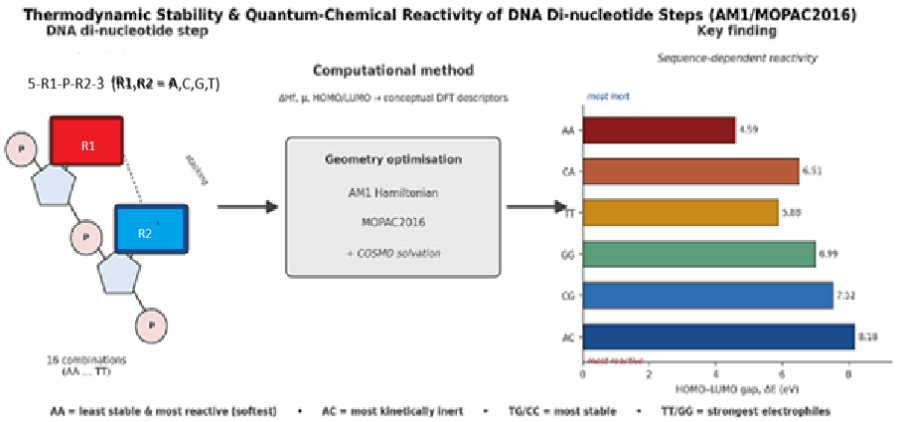
***Corresponding Author**

Dr. Bojja Rajeshwar Rao

Senior Chemist (Retired), Chemical Division, Kakatiya Thermal Power Project (O&M), Chelpur-506 170, Telangana State, India.

How to cite this Article: *Dr. Bojja Rajeshwar Rao*. (2026). Sequence-Dependent Thermodynamic And Quantum-Chemical Descriptors Of Dna Dinucleotides: An Am1/Mopac2016 Computational Study (r2). World Journal of Pharmaceutical Research, 15(16), 952–966.

GRAPHICAL ABSTRACT



ABSTRACT

The thermodynamic stability and quantum chemical properties of all sixteen possible DNA dinucleotides (5′-R^1R^2-3′; R^1, R^2 = A, C, G, and T) were investigated using the semi-empirical Austin Model-1 (AM1) Hamiltonian as implemented in MOPAC2016. For each fully optimized dinucleotide, the heat of formation, dipole moment, frontier molecular orbital (HOMO and LUMO) energies, and COSMO-derived solvent-accessible surface area and molecular volume were calculated. These electronic properties were further employed to derive conceptual density functional theory (DFT)-based global reactivity descriptors, including the HOMO–LUMO energy gap, ionization potential, electron affinity, electronegativity, global hardness, global softness, and chemical potential, and electrophilicity index.

The results indicate that purine-initiated dinucleotides, particularly AA, are the least thermodynamically stable and exhibit the greatest electronic reactivity, characterized by the smallest HOMO–LUMO energy gap, lowest global hardness, and lowest electrophilicity index. In contrast, AC and CG possess the largest energy gaps and highest ionization potentials, reflecting enhanced kinetic stability and reduced chemical reactivity. Dinucleotides such as TG and CC are thermodynamically the most stable, whereas TT and GG exhibit the highest electron affinity and electrophilicity index, identifying them as comparatively stronger electrophiles. Molecular size, as represented by COSMO molecular volume and molecular weight, is governed primarily by purine content rather than by sequence order. Overall, these findings provide a quantitative framework for understanding sequence-dependent variations in the thermodynamic stability, electronic structure, and chemical reactivity of DNA dinucleotides, thereby establishing a useful reference for studies of DNA stability, molecular recognition, and nucleic acid–based therapeutic design.

KEYWORDS: DNA di-nucleotides; AM1 method; MOPAC2016; HOMO-LUMO gap; COSMO; Global hardness; Electrophilicity index; Semi-empirical quantum chemistry.

INTRODUCTION

Deoxyribonucleic acid (DNA) is composed of four canonical nucleobases—adenine (A), cytosine (C), guanine (G), and thymine (T). The sequential arrangement of these nucleobases into dinucleotide steps plays a fundamental role in determining the local electronic, structural, and thermodynamic properties of the DNA double helix.[1] Sequence-dependent base-stacking interactions between adjacent nucleotides significantly influence DNA stability, conformational flexibility, groove geometry, charge-transport characteristics, and susceptibility to oxidative damage.[2] Consequently, understanding the intrinsic physicochemical properties of individual dinucleotide steps is essential for elucidating the relationship between DNA sequence and molecular function.[3]

Qu1antum chemical methods provide valuable insights into the electronic structure and reactivity of nucleic acid systems. In particular, frontier molecular orbital (FMO) theory, based on the energies of the highest occupied molecular orbital (HOMO) and the lowest unoccupied molecular orbital (LUMO), has been widely employed to investigate sequence-dependent electronic behaviour. The HOMO–LUMO energy gap serves as an important indicator of kinetic stability, chemical hardness, and charge-transfer capability, thereby offering a quantitative framework for assessing the relative stability and reactivity of different DNA

dinucleotide sequences.[4]

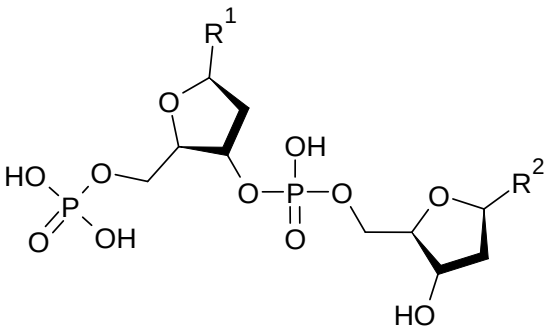


Figure - 1: - Four DNA nucleobases (A,G - purines; C,T - pyrimidines) that combine pairwise to generate the sixteen 5'-R^1,R^2-3' di-nucleotides

Conceptual density functional theory (CDFT), as developed by Parr and co-workers, provides a powerful theoretical framework for describing molecular reactivity through a set of global descriptors, including electronegativity (χ), chemical hardness (η), global softness (S), Chemical potential (μ), and the electrophilicity index (ω). Within Koopmans' approximation[5], these descriptors can be readily estimated from the energies of the highest occupied molecular orbital (HOMO) and the lowest unoccupied molecular orbital (LUMO). Owing to their strong correlation with electron-donating and electron-accepting tendencies, these descriptors have been widely employed to investigate the stability and reactivity of biomolecules, drug-like compounds, nucleobases, and their analogues.[6,7]

The semi-empirical Austin Model-1 (AM1) Hamiltonian, implemented in the MOPAC2016 package, provides an efficient and computationally economical approach for investigating the electronic structure of relatively large biomolecular systems. Despite its relatively low computational cost, in continuous of research work,[8] AM1 yields reliable estimates of molecular geometries, heats of formation, dipole moments, and frontier molecular orbital energies, making it well suited for comparative studies of nucleic acid fragments.[9]

In the present study, all sixteen possible DNA dinucleotides were fully optimized at the AM1 level using MOPAC2016. The heat of formation, dipole moment, HOMO and LUMO energies, and COSMO-derived solvent-accessible surface area and molecular volume were calculated for each optimized structure (Table - 1). These electronic properties were subsequently used to derive a complete set of conceptual DFT global reactivity descriptors, including the HOMO–LUMO energy gap, ionization potential, electron affinity, electronegativity, global

hardness, global softness, chemical potential, and electrophilicity index (Table - 2). The primary objective of this investigation is to elucidate sequence-dependent variations in thermodynamic stability, molecular polarity, molecular size, and electronic reactivity among the sixteen DNA dinucleotide steps, and to examine how these properties are influenced by base composition (purine versus pyrimidine content) and sequence identity.

MATERIALS AND METHODS

Initial geometries of all sixteen possible DNA dinucleotides (5′-R^1R^2-3′; R^1,R^2= A, C, G, and T)

were constructed and fully optimized without imposing any symmetry constraints using the semi-empirical Austin Model-1 (AM1) Hamiltonian[10] as implemented in **MOPAC2016** (Version 22.234w).[11] Geometry optimizations were performed using the eigenvector-following (EF) algorithm until the default gradient convergence criterion was satisfied, and the optimized structures were confirmed to correspond to local minima on the potential energy surface. Schematic representation of a generic DNA di-nucleotide step, 5′-R^1-p-R^2-3′, showing the sugar-phosphate backbone linking Base R^1 and Base R^2 (Figure – 1). For each optimized dinucleotide, the heat of formation (ΔH_f), dipole moment, frontier molecular orbital energies (HOMO and LUMO), and molecular weight were obtained directly from the MOPAC2016 output. Solvation effects were evaluated using the Conductor-like Screening Model (COSMO)[12], from which the solvent-accessible molecular surface area and molecular volume were determined. These calculated properties provided the basis for evaluating the thermodynamic stability, electronic structure, molecular polarity, and size of each DNA dinucleotide.

The HOMO and LUMO energies were subsequently employed to calculate a series of conceptual density functional theory (CDFT) global reactivity descriptors within Koopmans' approximation. The ionization potential (IP) and electron affinity (EA) were estimated as:

Ionization potential, $IP = -E_{HOMO}$

Electron affinity, $EA = -E_{LUMO}$

From which the electronegativity (χ), chemical potential (μ), global hardness (η), global softness (S), and electrophilicity index (ω) were calculated using the standard expressions:

HOMO–LUMO gap, $\Delta E = E_{LUMO} - E_{HOMO}$

Electronegativity, $\chi = (IP + EA)/2$

Chemical hardness, $\eta = (IP - EA)/2 = \Delta E/2$

Softness, $S = 1/\eta$

Chemical potential, $\mu = -\chi$

Electrophilicity index, $\omega = \mu^2/2\eta$

The HOMO–LUMO energy gap ($\Delta E = E_{LUMO} - E_{HOMO}$) was used as an indicator of kinetic stability and chemical reactivity, with larger energy gaps corresponding to greater electronic stability and lower chemical reactivity. The calculated thermodynamic, electronic, and reactivity parameters were subsequently analyzed to identify sequence-dependent trends among the sixteen DNA dinucleotide steps.

The general architecture of a DNA dinucleotide, consisting of two nucleobases connected through a deoxyribose–phosphate backbone, is illustrated schematically in **Figure - 1**. The frontier orbital energies were used to derive the conceptual DFT reactivity descriptors following the Koopmans'-theorem-based were calculated for each di-nucleotide in the standard manner.[5] These descriptors provide complementary information on the electron-donating and electron-accepting abilities, chemical stability, and overall reactivity of the DNA dinucleotides, thereby enabling a systematic comparison of sequence-dependent electronic properties.

RESULTS AND DISCUSSION

Heat of formation and thermodynamic stability

The calculated heats of formation (ΔH_f) for the sixteen DNA dinucleotides are summarized in **Table - 1** and span a wide range from **–294.59 kcal mol^{-1}** for **AA** to **–551.47 kcal mol^{-1}** for **TG**, representing a variation of more than **250 kcal mol^{-1}** among the dinucleotides (**Figure - 3**). More negative values of ΔH_f indicate greater thermodynamic stability of the optimized structures. Among the sequences investigated, **TG** (–551.47 kcal mol^{-1}), **CC** (–525.19 kcal mol^{-1}), and **GT** (–522.13 kcal mol^{-1}) are the most thermodynamically stable, whereas **AA** (–294.59 kcal mol^{-1}), **AG** (–357.55 kcal mol^{-1}), and **GA** (–373.18 kcal mol^{-1}) are the least stable.

A clear sequence-dependent trend is evident from these results. Dinucleotides containing consecutive purine bases, particularly adenine-rich sequences, exhibit comparatively less negative heats of formation, reflecting reduced thermodynamic stability. In contrast, dinucleotides containing pyrimidines or mixed purine–pyrimidine combinations, especially those incorporating thymine and cytosine, display substantially more negative ΔH_f values

and are therefore thermodynamically more stable. These observations suggest that both nucleobase composition and sequence order significantly influence the intrinsic stability of DNA dinucleotide steps, most likely through differences in base–based electronic interactions and the overall molecular geometry established during structural optimization.

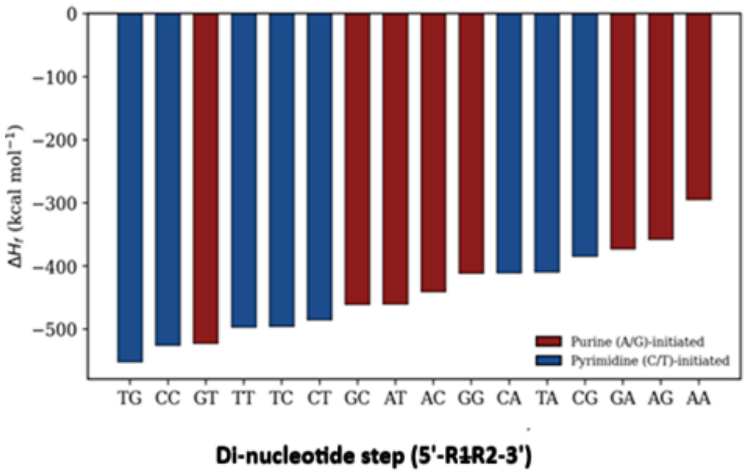


Figure 3: AM1 heats of formation (ΔHf) of the sixteen DNA di-nucleotides, ranked from least to most negative. Red bars: purine (A/G)-initiated steps; blue bars: pyrimidine (C/T)-initiated steps.

Dipole Moment

The calculated dipole moments of the sixteen DNA dinucleotides are presented in **Table 1** and range from **3.16 D** for **AC** to **11.93 D** for **CA**, demonstrating a substantial dependence of molecular polarity on nucleotide sequence. Among the dinucleotides examined, **CA** (11.93 D), **CG** (10.38 D), and **AG** (10.38 D) exhibit the highest dipole moments, indicating pronounced charge separation within their optimized structures. In contrast, **AC** (3.16 D) and **TT** (3.48 D) possess the lowest dipole moments and are therefore comparatively less polar. The considerable variation in dipole moment among the sixteen sequences reflects the sensitivity of molecular polarity to the spatial arrangement of nucleobases and the orientation of the deoxyribose–phosphate backbone. Because the dipole moment is determined by the overall distribution of electronic charge, even dinucleotides with identical base composition but different sequence order (e.g., AC versus CA) exhibit markedly different values. This observation highlights the important role of sequence-dependent molecular geometry in governing the electrostatic properties of DNA.

Variations in molecular polarity are expected to influence several biologically relevant

properties, including solvent interactions, hydration, intermolecular recognition, and electrostatic interactions with proteins, metal ions, and small-molecule ligands. Consequently, the calculated dipole moments provide useful insight into how local sequence composition modulates the electrostatic environment and molecular recognition characteristics of DNA dinucleotide steps.

Frontier Molecular Orbitals and Electronic Stability

The frontier molecular orbital energies of the sixteen DNA dinucleotides are summarized in **Table 2**. The HOMO energies range from **–9.007 eV** for **CG** to **–5.934 eV** for **AA**, indicating substantial sequence-dependent variation in electron-donating ability. The HOMO–LUMO energy gap (ΔE), a widely accepted indicator of kinetic stability and chemical reactivity, spans from **4.593 eV** for **AA** to **8.182 eV** for **AC** (**Figure 4**). A smaller energy gap generally corresponds to higher electronic reactivity, greater charge-transfer capability, and lower kinetic stability, whereas a larger gap signifies enhanced electronic stability and reduced chemical reactivity.

Among the sixteen dinucleotides, **AA** exhibits the highest HOMO energy together with the smallest HOMO–LUMO energy gap, identifying it as the most electronically reactive and kinetically least stable sequence. In contrast, **AC** and **CG** possess the largest energy gaps (8.182 and 7.518 eV, respectively), indicating greater resistance to electronic excitation and charge transfer, and consequently higher kinetic stability.

An interesting correlation emerges when these electronic properties are compared with the thermodynamic results discussed. The **AA** dinucleotide is not only the least thermodynamically stable, as evidenced by its least negative heat of formation, but also the most electronically reactive owing to its high HOMO energy and narrow HOMO–LUMO gap. Conversely, dinucleotides with larger energy gaps generally exhibit greater thermodynamic stability. This agreement between thermodynamic and electronic descriptors suggests that sequence-dependent stability in DNA dinucleotides is governed by complementary energetic and electronic factors, with frontier molecular orbital analysis providing a valuable framework for interpreting differences in molecular reactivity and charge-transfer behavior.

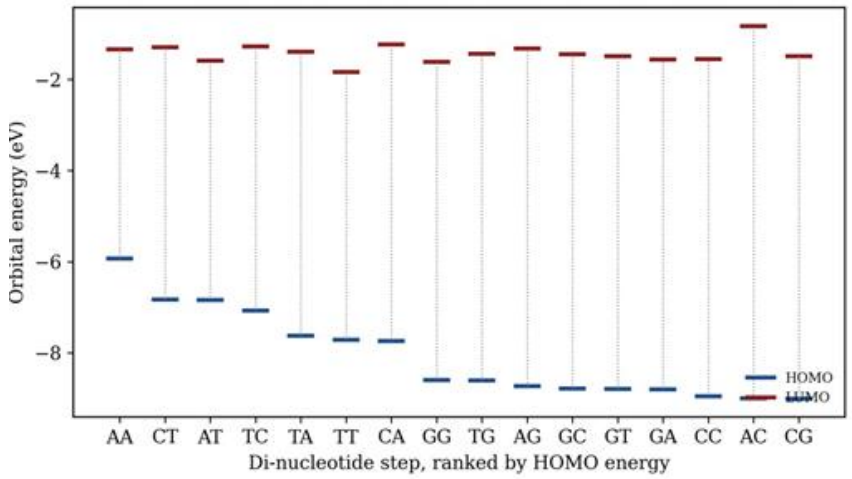


Figure 4: AM1 frontier molecular orbital (HOMO/LUMO) energy-level diagram for the sixteen di-nucleotide steps, ranked by HOMO energy.

Molecular Size and COSMO Solvation Parameters

The COSMO-derived solvent-accessible surface area and molecular volume of the sixteen DNA dinucleotides are summarized in **Table 1**. Both parameters exhibit a strong positive correlation with molecular weight and are governed primarily by the purine content of the dinucleotide rather than by sequence order (**Figure 5**). Dinucleotides containing two purine bases, such as **AG**, **GA**, and **GG**, possess the highest molecular weights (approximately **660–676 g mol^{-1}**) and the largest COSMO molecular volumes (**700–709 Å^3**). In contrast, pyrimidine–pyrimidine sequences, including **CC**, **CT**, and **TC**, exhibit lower molecular weights (**596–611 g mol^{-1}**) and correspondingly smaller molecular volumes (**653–684 Å^3**).

This trend is readily explained by the intrinsic structural differences between the nucleobases. Adenine and guanine are bicyclic purines, which contribute greater molecular mass and steric volume than the monocyclic pyrimidines, cytosine and thymine. Consequently, dinucleotides enriched in purine bases occupy a larger solvent-accessible volume and present a greater molecular surface area than pyrimidine-rich sequences.

The relatively small differences observed between reverse sequence pairs (e.g., **AG** versus **GA** or **CT** versus **TC**) further indicate that molecular size is influenced predominantly by nucleobase composition rather than by nucleotide order. Although sequence orientation can affect molecular geometry and electronic properties, its contribution to the overall molecular dimensions is comparatively minor. These findings demonstrate that COSMO-derived molecular surface area and volume are primarily structural descriptors reflecting the size and

composition of the constituent nucleobases, providing a useful basis for understanding sequence-dependent differences in solvation, molecular packing, and intermolecular interactions.

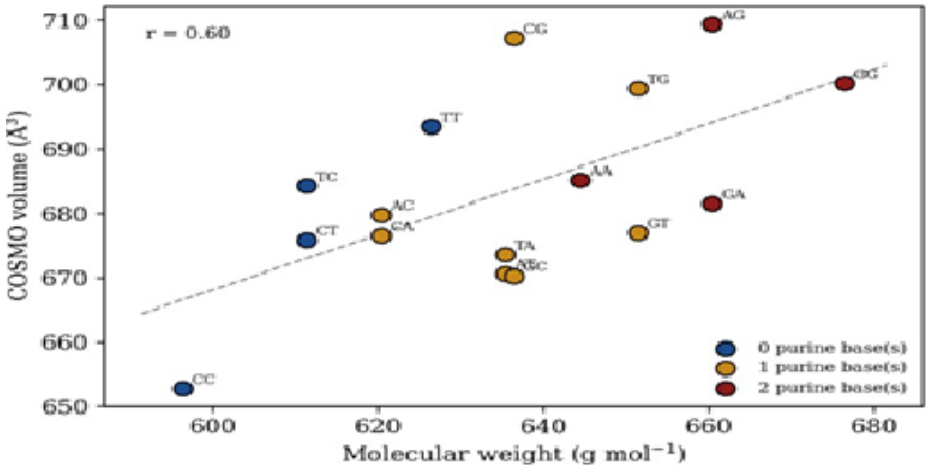


Figure 5: Correlation between molecular weight and COSMO volume for the sixteen di-nucleotide steps, grouped by purine content (0, 1 or 2 purine bases per step).

Quantum chemical reactivity descriptors

The conceptual density functional theory (CDFT) global reactivity descriptors derived from the frontier molecular orbital energies are summarized in **Table 2**. These descriptors provide complementary information on the electron-donating and electron-accepting abilities, chemical stability, and overall reactivity of the sixteen DNA dinucleotides.

The ionization potential (IP), which is directly related to the negative of the HOMO energy, ranges from **5.934 eV** for **AA** to **9.007 eV** for **CG**. The high IP values of **CG** (9.007 eV) and **AC** (9.006 eV) indicate a greater resistance to electron removal, whereas the markedly lower IP of **AA** confirms that it is the most readily ionized dinucleotide and therefore the strongest electron donor among the sequences investigated.

The calculated electron affinity (EA) varies substantially with sequence composition. **TT** (1.836 eV) and **GG** (1.611 eV) exhibit the highest EA values, indicating the greatest tendency to accept an additional electron, while **AC** (0.824 eV) possesses the lowest electron affinity and is therefore the weakest electron acceptor.

The electronegativity (χ) and chemical potential ($\mu = -\chi$) display consistent sequence-dependent trends. **CC** (5.256 eV) and **CG** (5.248 eV) are the most electronegative

dinucleotides, reflecting a strong tendency to attract electron density, whereas **AA** (3.638 eV) is the least electronegative and consequently exhibits the greatest electron-donating character. The corresponding chemical potential values mirror this behavior, with more negative values indicating enhanced electron-accepting capability.

Global hardness (η), which measures resistance to charge transfer and electronic deformation, is highest for **AC** (4.091 eV), followed closely by **CG**, indicating that these dinucleotides are electronically the most stable and least reactive. In contrast, **AA** exhibits the lowest hardness (2.297 eV), consistent with its small HOMO–LUMO energy gap and high electronic reactivity. As expected, global softness (S), the reciprocal of hardness, follows the opposite trend. The highest softness values are observed for **TT** (2.624 eV^{-1}) and **AA** (2.584 eV^{-1}), suggesting that these sequences are more readily polarized and can undergo electronic redistribution more easily than harder dinucleotides.

The electrophilicity index (ω), which combines electronegativity and hardness into a single measure of electrophilic character, further distinguishes the relative reactivity of the DNA dinucleotides. **TT** (3.879 eV), **GG** (3.730 eV), and **CC** (3.729 eV) exhibit the highest electrophilicity indices, indicating the strongest propensity to accept electron density during chemical interactions. Conversely, **AA** (2.881 eV) and **AC** (2.952 eV) possess the lowest electrophilicity values, reflecting comparatively weaker electrophilic character (**Figure - 6**).

Overall, the CDFT descriptors reveal a clear sequence dependence in the electronic properties of DNA dinucleotides. **AA** is characterized by low ionization potential, low electronegativity, low hardness, and a narrow HOMO–LUMO energy gap, identifying it as the most electronically reactive and kinetically least stable sequence. In contrast, **AC** and **CG** display high ionization potentials, large HOMO–LUMO energy gaps, and high hardness values, indicating enhanced electronic stability. Meanwhile, **TT**, **GG**, and **CC** exhibit the greatest electrophilic character owing to their relatively high electron affinity and electrophilicity index. These results demonstrate that conceptual DFT descriptors provide a comprehensive framework for understanding sequence-dependent variations in the electronic structure and chemical reactivity of DNA dinucleotides.

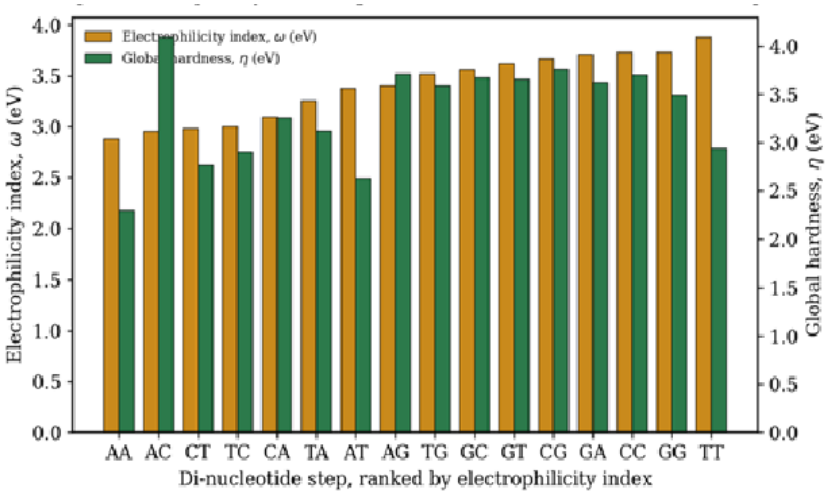


Figure 6: Electrophilicity index (ω) and global hardness (η) of the sixteen di-nucleotide steps, ranked by electrophilicity index.

Taken together, the results presented in **Tables - 1 and - 2** reveal distinct sequence-dependent trends in the thermodynamic stability and electronic reactivity of the sixteen DNA dinucleotides. Among all the sequences examined, **AA** emerges as a clear outlier, exhibiting the least negative heat of formation, the smallest HOMO–LUMO energy gap, the lowest ionization potential, the lowest global hardness, and one of the lowest electrophilicity indices. These characteristics identify **AA** as the softest, most readily ionized, and most electronically reactive DNA dinucleotide, indicating both reduced thermodynamic stability and enhanced kinetic reactivity.

In contrast, **AC** combines the largest HOMO–LUMO energy gap, a high ionization potential, and the highest global hardness, establishing it as the most electronically stable and kinetically inert dinucleotide among the sixteen sequences. **TT** and **GG**, on the other hand, are distinguished by their high electron affinities and electrophilicity indices, indicating a comparatively greater propensity to accept electron density during intermolecular interactions and chemical reactions.

Overall, these results demonstrate that both nucleobase composition and sequence identity strongly influence the intrinsic physicochemical properties of DNA dinucleotides. While adenine-rich and purine-initiated sequences generally exhibit enhanced electronic reactivity, G/C-rich and mixed-base sequences tend to possess greater kinetic stability and reduced charge-transfer propensity. The observed trends are consistent with the established understanding that sequence-dependent base-stacking interactions and electronic structure

govern the stability and reactivity of DNA. Consequently, the present AM1/MOPAC2016 calculations provide a quantitative framework for interpreting sequence-dependent variations in DNA electronic properties and furnish a useful reference for future studies of DNA charge transport, oxidative damage, molecular recognition, and nucleic acid-based drug design.

Table 1: Computational study on thermodynamic properties of Di-nucleotides by Austin Model-1 (AM1) method using MOPAC2016 (Version: 22.234w)

DNA DI-Nucleotides	ΔHf (Kcal/mol)	Dipole D	HOMO eV	LUMO eV	Cosmo Area (sq ang) (A^2)	Cosmo volume (cu ang) (A^3)	Mol wt
AA	-294.5937	9.3779	-5.934	-1.341	595.09	685.20	644.4333
AC	-440.9169	3.1594	-9.006	-0.824	597.07	679.81	620.4083
AG	-357.5498	10.3765	-8.733	-1.315	642.58	709.40	660.4327
AT	-460.3425	7.5214	-6.845	-1.586	571.41	670.65	635.4199
CA	-410.8395	11.9315	-7.748	-1.234	586.49	676.54	620.4083
CC	-525.1878	10.8768	-8.959	-1.552	563.16	652.82	596.3833
CG	-384.5398	10.3799	-9.007	-1.489	614.24	707.28	636.4077
CT	-484.9681	4.7862	-6.838	-1.295	548.56	675.83	611.3949
GA	-373.1779	5.7133	-8.807	-1.562	604.71	681.52	660.4327
GC	-460.4739	5.2409	-8.788	-1.440	573.14	670.27	636.4077
GG	-411.2003	7.8228	-8.602	-1.611	604.24	700.21	676.4321
GT	-522.1259	7.5589	-8.798	-1.487	591.35	676.98	651.4193
TA	-409.2504	10.1278	-7.626	-1.387	561.54	673.63	635.4199
TC	-495.7862	8.9260	-7.074	-1.274	562.56	684.32	611.3949
TG	-551.4724	9.7549	-8.613	-1.437	623.98	699.39	651.4193
TT	-496.7631	3.4769	-7.716	-1.836	586.37	693.45	626.4065

Table 2: Quantum chemical reactivity descriptors of DNA di-nucleotides derived from AM1 frontier orbital energies.

DNA Di-Nucleotides	HOMO eV	LUMO eV	ΔE eV	IP eV	EA eV	EN eV (χ)	Global Hardness eV(η)	Softness (S)	Chem Pot (μ)	Eletrophilicity Index (ω)
AA	-5.934	-1.341	**-4.593**	**5.934**	**1.341**	**3.638**	**2.297**	**2.584**	**-3.638**	**2.881**
AC	-9.006	-0.824	**-8.182**	**9.006**	**0.824**	**4.915**	**4.091**	**2.201**	**-4.915**	**2.952**
AG	-8.733	-1.315	**-7.418**	**8.733**	**1.315**	**5.024**	**3.709**	**2.355**	**-5.024**	**3.403**
AT	-6.845	-1.586	**-5.259**	**6.845**	**1.586**	**4.216**	**2.630**	**2.603**	**-4.216**	**3.379**
CA	-7.748	-1.234	**-6.514**	**7.748**	**1.234**	**4.491**	**3.257**	**2.379**	**-4.491**	**3.096**
CC	-8.959	-1.552	**-7.407**	**8.959**	**1.552**	**5.256**	**3.704**	**2.419**	**-5.256**	**3.729**
CG	-9.007	-1.489	**-7.518**	**9.007**	**1.489**	**5.248**	**3.759**	**2.396**	**-5.248**	**3.663**
CT	-6.838	-1.295	**-5.543**	**6.838**	**1.295**	**4.067**	**2.772**	**2.467**	**-4.067**	**2.983**
GA	-8.807	-1.562	**-7.245**	**8.807**	**1.562**	**5.185**	**3.623**	**2.431**	**-5.185**	**3.710**
GC	-8.788	-1.440	**-7.348**	**8.788**	**1.440**	**5.114**	**3.674**	**2.392**	**-5.114**	**3.559**
GG	-8.602	-1.611	**-6.991**	**8.602**	**1.611**	**5.107**	**3.496**	**2.461**	**-5.107**	**3.730**

GT	-8.798	-1.487	**-7.311**	**8.798**	**1.487**	**5.143**	**3.656**	**2.407**	**-5.143**	**3.617**
TA	-7.626	-1.387	**-6.239**	**7.626**	**1.387**	**4.507**	**3.120**	**2.445**	**-4.507**	**3.255**
TC	-7.074	-1.274	**-5.800**	**7.074**	**1.274**	**4.174**	**2.900**	**2.439**	**-4.174**	**3.004**
TG	-8.613	-1.437	**-7.176**	**8.613**	**1.437**	**5.025**	**3.588**	**2.401**	**-5.025**	**3.519**
TT	-7.716	-1.836	**-5.880**	**7.716**	**1.836**	**4.776**	**2.940**	**2.624**	**-4.776**	**3.879**

CONCLUSION

The thermodynamic and quantum chemical properties of all sixteen possible DNA dinucleotides were systematically investigated using the semi-empirical AM1 Hamiltonian implemented in MOPAC2016. The calculated results demonstrate that nucleobase composition and sequence identity exert distinct influences on the physicochemical properties of DNA dinucleotides. Molecular size, as reflected by COSMO-derived surface area, molecular volume, and molecular weight, is governed primarily by the purine–pyrimidine composition of the dinucleotide. In contrast, thermodynamic stability, molecular polarity, and electronic reactivity are strongly dependent on both base identity and sequence order.

Among the sixteen dinucleotides, **AA** consistently exhibits the least negative heat of formation, the smallest HOMO–LUMO energy gap, the lowest ionization potential, and the lowest global hardness, identifying it as the most electronically reactive and kinetically least stable sequence. Conversely, **AC** and **CG** possess the largest HOMO–LUMO energy gaps, highest ionization potentials, and greatest global hardness, indicating enhanced electronic stability and reduced chemical reactivity. The **TG** and **CC** dinucleotides are thermodynamically the most stable, whereas **TT** and **GG** display the highest electron affinities and electrophilicity indices, reflecting a comparatively greater tendency to accept electron density during chemical interactions.

Overall, the present study demonstrates that semi-empirical AM1/MOPAC2016 calculations, combined with conceptual density functional theory descriptors, provide an efficient and reliable framework for characterizing sequence-dependent variations in the thermodynamic stability and electronic properties of DNA dinucleotides. The resulting dataset offers a quantitative reference for understanding DNA charge transport, oxidative damage susceptibility, molecular recognition, and sequence-specific interactions with ligands and therapeutic agents. These findings may also serve as a useful foundation for future computational and experimental investigations of nucleic acid structure, reactivity, and function.

Disclosure statement

No potential conflict of interest was reported by the author.

Funding

The author received no financial support for the research work, and publication of this article.

Author's contribution

The author has participated in conception, design, analysis, interpretation of the data, drafting the article, and approval of the final version.

ACKNOWLEDGEMENT

The author is sincerely grateful to **Dr. D. Rajendra Prasad (Retired), Professor of Education, Kakatiya University, India**, for giving the critical suggestions to carry out this work. The author also acknowledges the assistance of **Claude AI** and **ChatGPT** in improving the presentation of the manuscript. The author takes full responsibility for the scientific content, data analysis, interpretations, and conclusions presented in this article.

REFERENCES

1. Saenger W, Principles of Nucleic Acid Structure (Springer-Verlag, New York), 1984. https://doi.org/10.1007/978-1-4612-5190-3
2. Voityuk A A, Jortner J, Bixon M & Rosch N, J Chem Phys, 2001; 114: 5614. https://doi.org/10.1063/1.1352035
3. Senthilkumar K, Grozema F C, Guerra C F, Bickelhaupt F M & Siebbeles L D A, J Am Chem Soc, 2003; 125: 13658. https://doi.org/10.1021/ja037027d
4. Sponer J, Leszczynski J & Hobza P, Biopolymers, 2002; 61: 3. https://doi.org/10.1002/1097-0282(2001)61:1<3::AID-BIP10048>3.0.CO;2-4
5. Parr R G, Donnelly R A, Levy M & Palke W E, J Chem Phys, 1978; 68: 3801. https://doi.org/10.1063/1.436185
6. Parr R G, Szentpaly L V & Liu S, J Am Chem Soc, 1999; 121: 1922. https://doi.org/10.1021/ja983494x
7. Pearson R G, J Chem Sci, 2005; 117: 369. https://doi.org/10.1007/BF02708340
8. Rajeshwar Rao B, Computational study on the phosphorylation of nucleosides and nucleotides in deoxyribonucleic acid (DNA) by Austin Model-1 Method, *World J Pharmaceutical Research*, **2023;** 12(3): 867-878. www.wjpr.net
9. Dewar M J S, Zoebisch E G, Healy E F & Stewart J J P, J Am Chem Soc, 1985; 107:

3902. https://doi.org/10.1021/ja00299a024

10. Stewart J J P, J Mol Model, 19 (2013) 1https://doi.org/10.1007/s00894-012-1667.
11. Stewart J J P, MOPAC2016 (Stewart Computational Chemistry, Colorado Springs, CO, USA), 2016. http://openmopac.net/
12. Klamt A & Schuurmann G, J Chem Soc Perkin Trans, 1993; 2: 799. https://doi.org/10.1039/P29930000799