Bader's and Reactivity Descriptors' Analysis of DNA Base Pairs

R. Parthasarathi, R. Amutha, V. Subramanian,* Balachandran Unni Nair, and T. Ramasami

Chemical Laboratory, Central Leather Research Institute, Adyar, Chennai 600 020, India

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The characterization of hydrogen bonds (H bonds) present in various canonical and noncanonical base pairs of DNA in terms of the electron density ($\rho(r_c)$), Laplacian of electron density ($\nabla^2\rho(r_c)$), and integrated atomic properties of hydrogen atoms involved in hydrogen bonding has been made. The existence of hydrogen bond critical points (HBCP) and the values of $\rho(r_c)$ and $\nabla^2\rho(r_c)$ at HBCP indicate the presence of hydrogen bonding and the closed-shell kind of interactions governing DNA base pairing. It has been observed that the calculated total $\rho(r_c)$ at HBCPs of the base pairs varies linearly with their interaction energy. The total $\nabla^2\rho(r_c)$ also exhibits a similar trend with the interaction energy. Integrated atomic properties such as charge, energy, volume, the first moment of the H-bonded hydrogen atoms in the DNA bases and in the H-bonded base pairs, and the change (Δ) in the corresponding properties arising upon pairing have also been calculated and compared. The calculated global chemical hardness of various DNA bases and DNA base pairs has been used to establish a linear relation with interaction energy. The charge transfer involved in the formation of DNA base pairs has also been qualitatively determined using Parr's formula and also from AIM-derived charges.

Introduction

Studies on hydrogen-bonding interactions in several model systems have been performed with a view toward understanding various chemical and biochemical processes in real life systems. Because the hydrogen-bonding (H-bonding) interaction is the one of the important factors in the stabilization of the DNA double helix, numerous theoretical and experimental investigations have been carried out on the strength of the hydrogen-bonding interaction between DNA bases.[1−16] Sponer and Hobza have carried out a detailed survey of the theoretical calculations on DNA bases, bases pairs, and stacked dimers.[17] It is noteworthy to mention here that Sponer et al.[18] have studied the geometries, interaction energies, and relative roles of various energy contributions of hydrogen-bonded DNA base pairs using higher-level nonempirical ab initio techniques.

The theory of atoms in molecules (AIM) allows one to look at the concept of the chemical bond and the bond strength in terms of an electron density distribution function.[19,20] The AIM theory exploits the topological features of electron density and thereby provides a definition of chemical bonding through the bond path and bond critical point (BCP). A BCP (a point at which the gradient vector vanishes, $\nabla\rho(r) = 0$) is found between the two nuclei of the molecule in equilibrium geometry, which is considered to be connected by a chemical bond. Bader and his group have pioneered the theory and applications of the AIM approach.[19] Similarly, Popelier and co-workers have also made significant contributions to the development of AIM theory and its applications to various chemical issues.[21−23] Bone and Bader performed an AIM analysis on several configurations of van der Waals complexes of Ar with CO_2, C_2H_2, OCS, and SO_2 molecules.[24] Several criteria based on AIM theory were proposed to characterize the hydrogen bonds and were applied to the study of conventional H bonds as well as nonconventional H bonds.[25] The cooperative enhancement of inter- and intramolecular H-bonding interactions in a variety of molecular clusters has been described using the AIM approach.[26−32] AIM theory has also been used to investigate blue-shifting hydrogen bonds.[33] The topological descriptors obtained from AIM theory and the electron localization function can be successfully employed to distinguish weak, medium, and strong H bonds in various molecular systems.[24−33] Grabowski used ab initio and Bader's theory to unravel the hydrogen bonding in R−C−N···HF and R−C−N···HCl complexes.[34] Subramanian et al. have applied AIM theory to understand the interactions of He, Ne, and Ar with HF and HCl.[35] Bader-type analysis has been carried out for dihydrogen-bonded complexes in the framework of high-level post-Hartree−Fock theory. [36,37] Prompted by these wide applications and the success of AIM theory, a systematic study has been initiated on various canonical and noncanonical DNA pairs to characterize the hydrogen-bonding interaction using Bader's approach.

Similar to AIM theory, conceptual density functional theory has been widely used to probe various chemical problems. The electronegativity and hardness are two important concepts that have been extensively used in various situations to understand stability and chemical reactivity.[38] Pearson introduced the concept of chemical hardness through his hard−soft acids and bases principle (HSAB) and maximum hardness principle (MHP).[39,40] Parr, Pearson, and co-workers have provided simple working equations for the calculation of global hardness and chemical potential and local quantities such as Fukui functions.[38−43] These descriptors in combination with Pearson's principle of HASB have been used in understanding various aspects of chemical reactivity in organic chemistry, inorganic chemistry, and biochemistry.[39−41] The applications of the global and local reactivity descriptors have been recently reviewed.[42] Parr and Chattraj provided the formal proof for the maximum hardness principle (MHP).[44] MHP compliments the minimum-energy criterion for the stability of atoms and molecules.

* To whom correspondence should be addressed. E-mail. subuchem@hotmail.com. Fax: +91 44 24911589, +91 44 24411630.

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The generalized electronegativity equalization procedure has also been employed to probe chemical binding. Recently, Sanderson's geometric mean equalization principle for electronegativity has been used to estimate global electronic properties and bond energies of hydrogen-bonded complexes.[45] It is evident from several earlier studies that maximum hardness and minimum polarizability complement the minimum-energy criteria for the stability of molecular aggregates.[41−46] Hence, the connection between energy and hardness through MHP motivated us to investigate the relationship between the interaction energy of H-bonded DNA pairs and their respective hardness. When two fragments are brought into contact, electrons will flow from the one of higher chemical potential (μ) to the one of lower chemical potential, the amount of flowing charge being proportional to the difference in the chemical potential of the fragments.[38] As a consequence, the interaction energy is proportional to the charge transfer between two DNA base pairs. Hence, the charge transfer (ΔN) in the DNA base paring has also been qualitatively assessed using chemical reactivity descriptors.

In this work, we have employed the theory of AIM and the application of various reactivity descriptors to characterize the hydrogen-bonding interaction in the DNA base pairs. An attempt has also been made to establish a relationship between the interaction energy of various DNA base pairs with the electron density at the HBCP, the Laplacian of electron density at the HBCP, and other integrated properties of hydrogen bond donor atoms that participate in H bonding. Similarly, we have also explored the possible relationship between calculated chemical hardness and interaction energy.

Theoretical Background

Theory of Atoms in Molecules (AIM). The molecular electron density distribution $\rho(r)$ can be extracted from the corresponding many-particle wave function $\psi(x_1, x_2...x_N)$ as

$$\rho(r) = N\sum_{\sigma}\int \psi(x, x_2,.., x_N)|^2 \, \mathrm{d}^3r_2...\mathrm{d}^3r_N \qquad (1)$$

Here, the summation runs over all spin coordinates, integration is over all but one spatial coordinate (x stands for position and spin), and N is the total number of electrons. Within the simplest Hartree−Fock framework wherein the wave function ψ is expressed in the form of a Slater determinant constructed from molecular orbitals (which are, in turn, expressed as linear combinations of the basis functions $\{\phi_i\}$), $\rho(r)$ assumes the form

$$\rho(r) = \sum_{\mu v} P_{\mu v}\phi_{\mu}(r)\phi^*_{v}(r) \qquad (2)$$

where P stands for the charge density−bond order matrix satisfying the idempotency condition. Properties such as $\rho(r_c)$, the trajectories of the gradient vector field of charge density ($\nabla\rho$), critical points (at which $\nabla\rho$ vanishes, $\rho(r_c)$), and the second derivative of charge density or the Laplacian ($\nabla^2\rho_(r_c)$) are used to characterize the intermolecular interactions present in H-bonded, van der Waals, and ionic species.

Bader and Essen have made the first study of the observed categories of critical points.[47] They concluded that the hallmark of "shared" (i.e., covalent) interactions is a high value of the charge density at BCP on the order of $>10^{-1}$ au. The curvatures of the charge density are usually large. The Laplacian of the electron density ($\nabla^2\rho(r_c)$) is a measure of local concentrations of density and may be positive or negative, on the order of ρ-(r_c). A negative Laplacian denotes electron concentration at a particular point whereas a positive Laplacian implies depletion of charge. It is evident from the previous AIM analysis that in hydrogen-bonded systems, noble-gas dimers, and ionic systems, $\rho(r_c)$ is quite small ($\sim 10^{-2}$ au or less and 10^{-3} au in van der Waals complexes) and the Laplacian is positive. These two observations are indicative of a closed-shell interaction.

Definition of Chemical Reactivity Descriptors. The chemical hardness (η) has been shown to be a useful global index of reactivity in atoms, molecules, and clusters.[38,39] The theoretical definition of chemical hardness has been provided by density functional theory as the second derivative of electronic energy with respect to the number of electrons, N, for a constant external potential $v(\vec{r})$

$$\eta = \frac{1}{2}\left(\frac{\partial^2 E}{\partial N^2}\right)_{V(\vec{r})} = \frac{1}{2}\left(\frac{\partial \mu}{\partial N}\right)_{V(\vec{r})} \qquad (3)$$

where E is the total energy, N is the number of electrons of the chemical species, and μ is the chemical potential, which is identified as the negative of the electronegativity (χ) as defined by Iczkowski and Margrave.[48] By applying the finite difference approximation to eq 3 and Koopman's theorem,[38] we get the operational definition for η as

$$\eta = \frac{\mathrm{IP} - \mathrm{EA}}{2} \qquad (4)$$

where IP and EA are the ionization potential and electron affinity of the atom or molecule.

$$\mathrm{IP} = -\epsilon_{\mathrm{HOMO}} \qquad \text{and} \qquad \mathrm{EA} = -\epsilon_{\mathrm{LUMO}} \qquad (5)$$

if ϵ_{HOMO} and ϵ_{LUMO} are the energies of the highest occupied and lowest unoccupied molecular orbitals, respectively

The global interactions between the DNA base pairs have been determined using the parameter ΔN, which represents the fractional number of electrons transferred from system A to system B, and is represented by[38,43]

$$\Delta N = \frac{\mu_{\mathrm{B}} - \mu_{\mathrm{A}}}{2(\eta_{\mathrm{A}} + \eta_{\mathrm{B}})} \qquad (6)$$

Computational Details

The geometrical parameters of the various canonical and noncanonical base pairs have been taken from Sponer et al.,[18] and the same nomenclature has been used for both DNA bases and base pairs. All of the canonical and noncanonical base pairs are bonded such that the imino group of the base forms an H bond either with a N atom or with an O atom of the other base. To predict the topography of the electron density of the various complexes, wave functions have been generated using the WFN option in the Gaussian 98W package[49] employing the single-point MP2/6-31G*(0.25) level of calculation. 6-31G*(0.25) represents the standard spilt-valence 6-31G basis set augmented by a set of diffuse d-polarization functions with an exponent of 0.25 added to the second-row elements. The density = current option is used to get the wave function for AIM analysis. Using the wave function, the topological parameters of electron density and the Laplacian of electron density of various intermolecular complexes have been determined. All AIM calculations have been made using AIM 2000 software.[50] The sum of the electron density as well as the Laplacian of electron density at the HBCPs have been plotted against the interaction energy to establish the relationship between the topological parameter and hydrogen bonding. The MP2/6-31G*(0.25) method has been used to

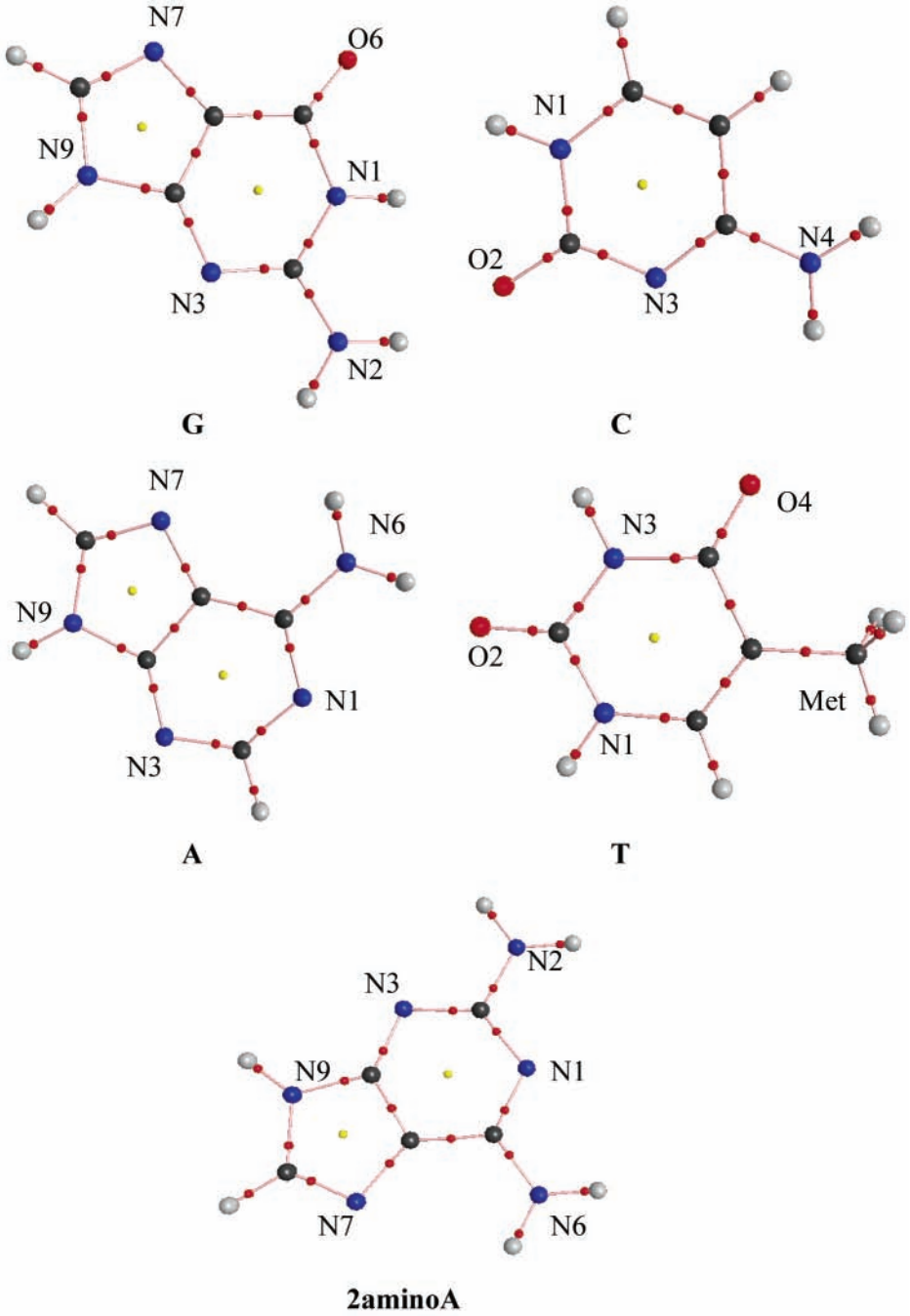
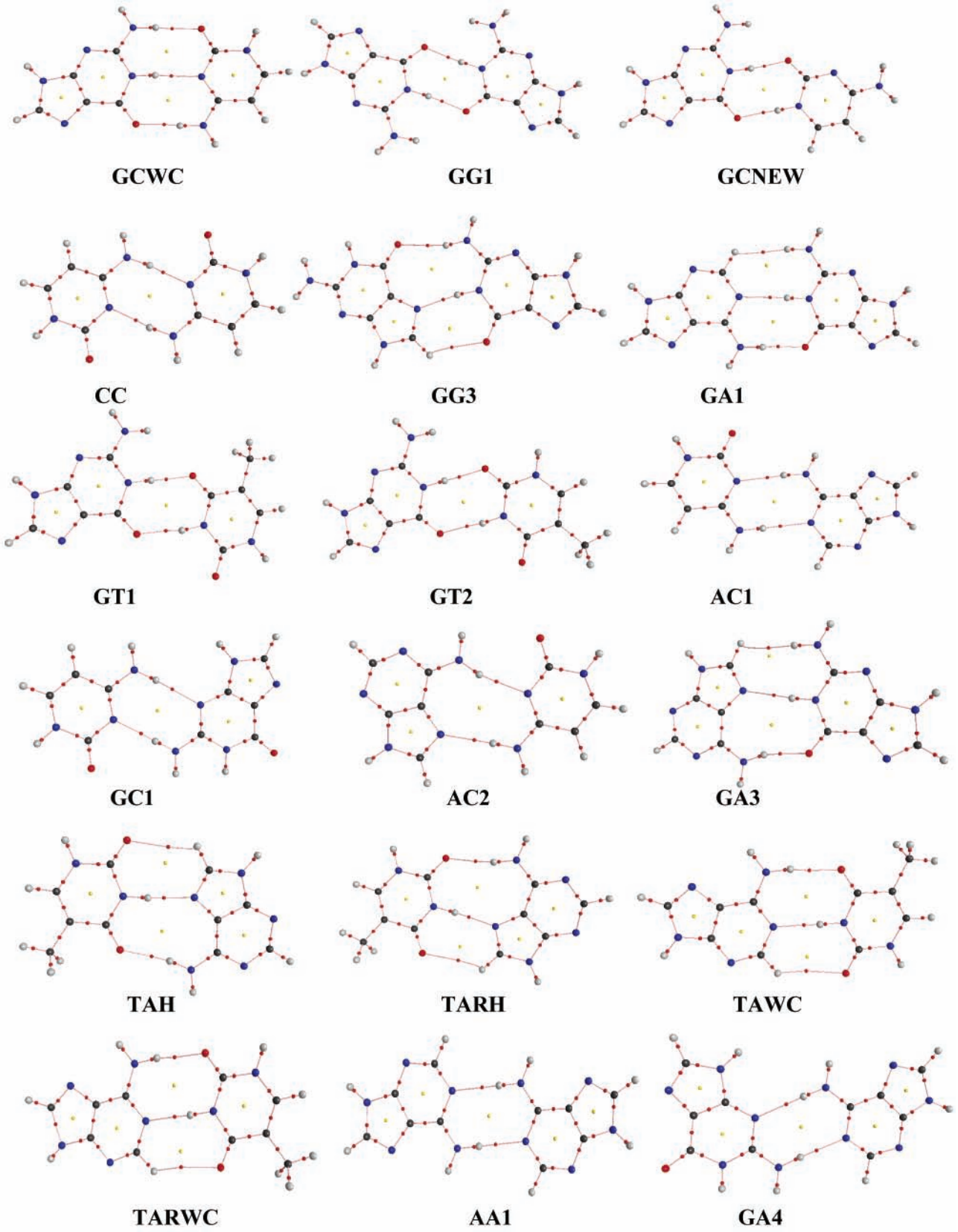


Figure 1. Molecular graphs of DNA bases obtained from theoretical charge density. Bond critical points are denoted by red dots, and yellow dots denote the ring critical points.

compute the chemical hardness and chemical potential of various molecular systems using Koopman's approximation.[38] The interaction energy (calculated at MP2/6-31 G*(0.25)) for various base pairs has been taken from the earlier work of Sponer, Lesczynski, and Hobza.[18]

Results and Discussions

The electron density and Laplacian of the electron density at HBCP for the hydrogen-bonded base pairs GCWC, GG1, GCNEW, CC, GG3, GA1, GT1, GT2, AC1, GC1, AC2, GA3, TAH, TARH, TAWC, TARWC, AA1, GA4, TC2, TC1, AA2, TT2, TT1, TT3, GA2, GG4, AA3, and 2aminoAT of DNA have been calculated. Figure 1 shows the molecular topography of DNA bases, and Figure 2 shows the DNA base pairs obtained from electron density. BCPs are denoted by red dots, and yellow dots represent the ring CPs. The $\rho(r_c)$ and $(\nabla^2\rho(r_c))$ at each H bond present in each base pair are given in Table 1. Calculated chemical reactivity descriptors for various DNA bases and base pairs are shown in Table 2 along with their respective interaction energies.[18] All of the base pairs studied possess a N−H- - -Y type of hydrogen bond, where Y is the general representation for atoms N and O. The BCPs have been observed between one of the H atoms of the imino group and the Y atom. Two BCPs have been observed for those base pairs bonded by two H bonds, and three bond critical points have been identified for the base pairs bonded through three hydrogen bonds. All of the bases are paired by two hydrogen bonds except for GCWC and 2aminoAT, which have three H bonds between them. It is


GCWC
GG1
GCNEW
CC
GG3
GA1
GT1
GT2
AC1
GC1
AC2
GA3
TAH
TARH
TAWC
TARWC
AA1
GA4

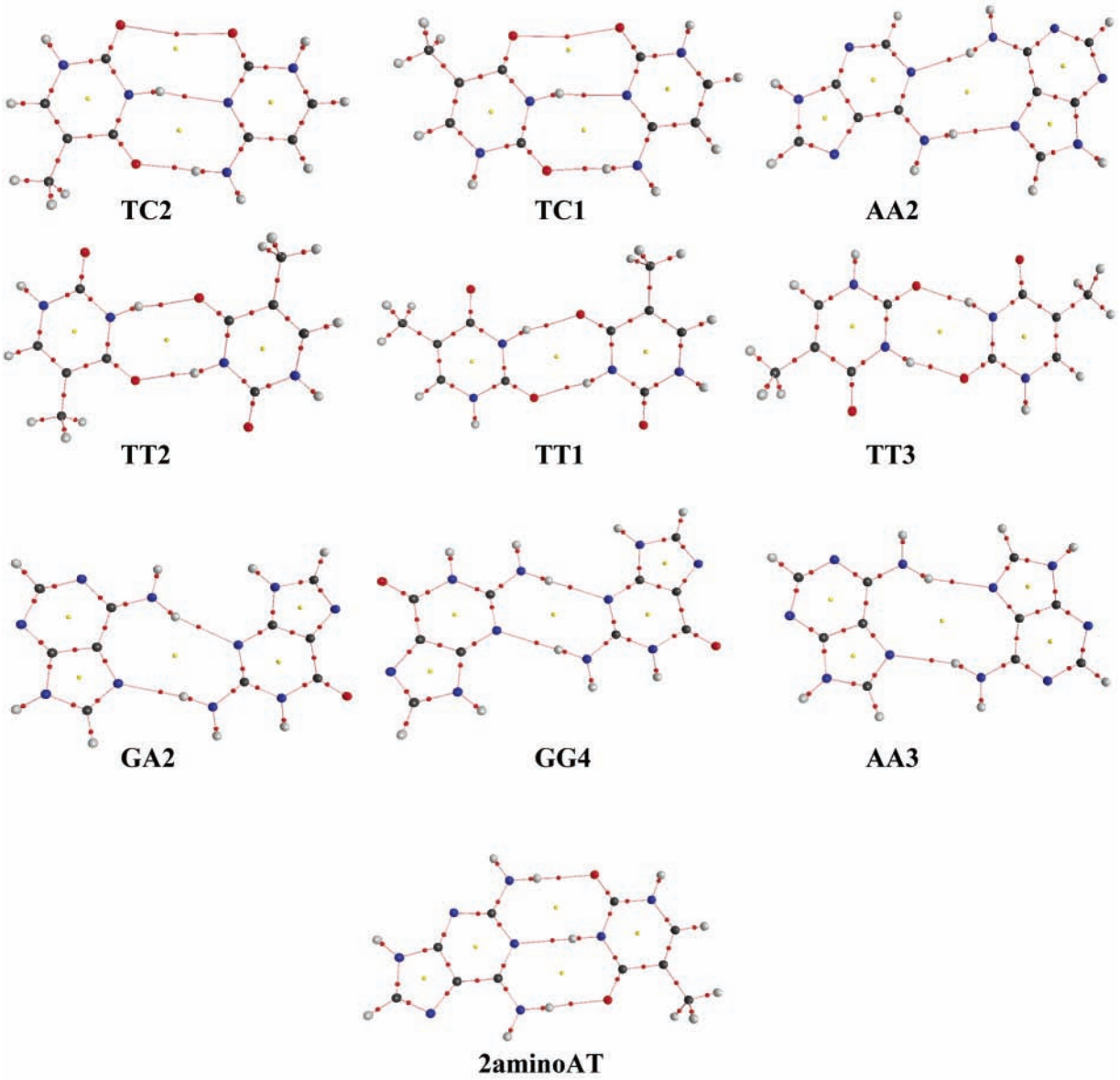


Figure 2. Molecular topography of DNA base pairs obtained from theoretical charge density. Bond critical points are denoted by red dots, and yellow dots denote the ring critical point.

evident from Table 1 that the calculated values of $\rho(r_c)$ and the positive signature of $\nabla^2\rho(r_c)$ for various DNA base pairs indicate the presence of the closed-shell kind of interaction between the two bases.

Secondary Interactions in Various DNA Base Pairs. Although it is recognized that the triply hydrogen-bonded base pairs are invariably more stable than the doubly hydrogen-bonded ones, a simple count of the hydrogen bonds does not necessarily provide insight into the stability of biomolecular systems. The further rigorous analysis of the stability of biomolecules led to the secondary interaction hypothesis (SIH).[51] Short-range and cross interactions between the base pairs have been considered as possible secondary interactions. Mohan and Yathindra have carried out a systematic analysis of the cross-strand hydrogen bonding in DNA base pairs.[52] The results showed that a limited number of combinations of adjacent base pairs that would facilitate bifurcated cross-strand hydrogen bonds. Recently, Popelier et al. have elucidated the atomic rationale for DNA base pair stability and have analyzed the importance of secondary interactions in DNA base pairs.[53] In the earlier study, Sponer et al. have obtained geometrical parameters for various DNA base pairs using HF/6-31G**-level calculations.[18] From the optimum intermolecular geometries, it is possible to identify the primary hydrogen-bonding interaction. In addition, they have identified distances to some other groups that would influence the stabilities of the base pairs. These interactions are called secondary interactions in DNA base pairs. Possible primary interactions and secondary interactions in various DNA base pairs are presented in Table 1. Using the AIM theory, the existence of BCP in the secondary interaction regions has been probed. It is possible to obtain BCP in the secondary interaction regions in the case of GG3, GA1, TAH, TARH, TAWC, TARWC, TC2, and TC1 for which HF/6-31G**-level calculations[18] have also supported the presence of secondary interactions. It is interesting to note from Table 1 and Figure 2 that the presence of a third weak interaction stabilizes different AT pairs. In addition, the presence of secondary interactions is evident in the case of GA3, for which there is no information based on distance criteria.[18] Even though the same study[18] showed the existence of secondary interactions in the cases of GG1, GCNEW, GT1, and GT2; electron density

TABLE 1: Charge Density $\rho(r_c)$ and Laplacian of Charge Density ($\nabla^2\rho(r_c)$) of Various DNA Base Pairs

H-bonded pairs	primary H bonds	charge density (e/a_o^3)	Laplacian of charge density (e/a_o^5)	secondary H bonds	charge density (e/a_o^3)	Laplacian of charge density (e/a_o^5)
GCWC	N2(H)−O2	0.023006	0.01776			
	N1(H)−N3	0.026608	0.01837			
	O6−(H)N4	0.02824	0.02205			
GG1	N1(H)−O6	0.03304	0.02493			
	O6−(H)N1	0.03286	0.02476			
GCNEW	N1(H)−O2	0.03674	0.02876			
	O6−(H)N1	0.02919	0.02173			
CC	N3−(H)N4	0.03462	0.02411			
	N4(H)−N3	0.03457	0.02406			
GG3	N1(H)−N7	0.0303	0.02157	O6−H(C8)	0.007147	0.00677
	N2(H)−O6	0.01236	0.01041			
GT1	O6−(H)N3	0.02453	0.01882			
	N1(H)−O4	0.03042	0.02395			
GT2	O6−(H)N3	0.02367	0.01841			
	N1(H)−O2	0.02975	0.0237			
GC1	N2(H)−N3	0.01822	0.01243			
	N3−(H)N4	0.02726	0.01912			
GA1	O6−(H)N6	0.02624	0.02057	H(N2)−H(C2)	0.00361	0.00406
	N1(H)−N1	0.02015	0.01318			
2aminoAT	N6(H)−O2	0.01941	0.01549			
	N1−(H)N3	0.0253	0.01616			
	N2(H)−O4	0.02122	0.0166			
AC1	N6(H)−N3	0.02347	0.01646			
	N1−(H)N4	0.02196	0.01468			
AC2	N7−(H)N4	0.02267	0.01619			
	N6(H)−N3	0.02033	0.01393			
GA3	O6−(H)N6	0.02476	0.02017	H(N1)−H(C8)	0.0032	0.0039
	N1(H)−N7	0.01778	0.01208			
TAH	O4−(H)N6	0.01667	0.01345	O2−H(C8)	0.00411	0.00429
	N3(H)−N7	0.03137	0.02173			
TARH	O2−(H)N6	0.01639	0.01346	O4−H(C8)	0.00427	0.00438
	N3(H)−N7	0.03148	0.02173			
TAWC	O4−(H)N6	0.01936	0.01513	O2−H(C8)	0.00351	0.00354
	N3(H)−N1	0.03001	0.02005			
TARWC	O2−(H)N6	0.019	0.01502	O4−H(C2)	0.00359	0.00357
	N3(H)−N1	0.02999	0.0201			
TC2	O4−(H)N4	0.02566	0.02091	O2−O2	0.00177	0.00267
	N3(H)−N3	0.01713	0.01203			
TC1	O2−(H)N4	0.02552	0.02101	O4−O2	0.00179	0.00268
	N3(H)−N3	0.01689	0.01189			
TT1	N3(H)−O4	0.02345	0.01919			
	O2−(H)N3	0.02304	0.01868			
TT3	O2−(H)N3	0.02303	0.01887			
	N3(H)−O2	0.02314	0.01898			
TT2	O4−(H)N3	0.02342	0.01892			
	N3(H)−O4	0.02342	0.01892			
GA4	N2(H)−N1	0.02321	0.01563			
	N3−(H)N6	0.01912	0.01319			
AA1	N6(H)−N1	0.02076	0.01404			
	N1−(H)N6	0.02079	0.01406			
AA2	N1−(H)N6	0.01893	0.0131			
	N6(H)−N7	0.02005	0.01395			
GA2	N2(H)−N7	0.01649	0.01171			
	N3−(H)N6	0.02178	0.01512			
GG4	N2(H)−N3	0.02078	0.01423			
	N3−(H)N2	0.02072	0.01418			
AA3	N6(H)−N7	0.0174	0.01249			
	N7−(H)N6	0.01744	0.01252			

topography does not provide necessary information about the BCP in the respective DNA pairs.

Integrated Atomic Properties Related to the H Atom Involved in the H Bonding of DNA Base Paring. A topological atom is defined according to the theory of AIM as a region in space consisting of a bundle of the electron density gradient path attracted to a nucleus. Because of firm theoretical footing in quantum mechanics, AIM can be considered to be a partitioning scheme to understand the properties of atoms in molecules. Hence, AIM can be used to probe the properties of atoms after intermolecular complexation. In this study, the properties of hydrogen atoms have been used to understand the hydrogen bonding in various DNA base pairs. Cubero et al. have used AIM theory to address hydrogen bonding versus anti-hydrogen bonding and have provided an atomic rationale for the blue shifting.[54] The results presented in that study[54] showed that H-bonded criteria based on AIM are satisfied for conventional H bonding, nonconventional C−H···H H bonding, and dihydrogen bonding and provide a basis by which to distinguish these interactions from van der Waals interactions. However, they found that to differentiate H bonding and antibonding it is necessary to supplement Popelier's criteria with information on

TABLE 2: Calculated Chemical Reactivity Descriptors for Various DNA Base Pairs and Interaction Energy of DNA Base Pairing[a]

	chemical hardness (ev)	chemical potential (ev)	interaction energy[a] (E^T)(kcal/mol)
A	6.064	−2.31	
T	6.351	−3.175	
G	6.16	−1.839	
C	6.231	−2.932	
GCWC	5.188	−2.292	−23.8
GG1	6.08	−1.918	−22.2
GCNEW	5.501	−2.22	−19.9
CC	6.129	−2.998	−17.5
GG3	5.538	−1.807	−17
GT1	5.41	−2.383	−14.1
GT2	5.526	−2.273	−14.1
GC1	5.371	−2.414	−13.9
GA1	5.779	−2.15	−13.5
2aminoAT	5.249	−2.152	−13.5
AC1	5.66	−2.403	−13.4
AC2	5.563	−2.4	−13.2
GA3	5.834	−2.204	−13.1
TAH	5.72	−2.475	−12.7
TARH	5.719	−2.483	−12.6
TAWC	5.755	−2.468	−11.8
TARWC	5.886	−2.542	−11.7
TC2	6.208	−2.792	−11
TC1	6.256	−2.818	−10.7
TT1	6.315	−3.029	−10.7
TT3	6.372	−2.997	−10.7
TT2	6.3	−3.033	−10.3
GA4	6.158	−2.105	−10
AA1	6.033	−2.242	−10
AA2	6.004	−2.278	−9.9
GA2	5.732	−2.295	−9.6
GG4	6.158	−2.105	−9.3
AA3	6.01	−2.318	−9.2

[a] Taken from the study of Sponer et al.[18] at the MP2/6-31G*(0.25) level.

the changes in the electron density and other properties of the donor X−H bond occurring upon complexation.[54] The Popelier criteria[23,37] used to gain insight into hydrogen bonds include (1) the correct topological pattern (bond critical point and gradient path), (2) appropriate values of electron density at BCP, (3) a proper value of the Laplacian of electron density at the BCP, and (4) the mutual penetration of hydrogen and acceptor atoms. The criteria pertaining to integrated properties of hydrogen atoms involve (5) an increase in net charge, (6) an energetic destabilization, (7) a decrease in dipolar polarization, and finally (8) a decrease in atomic volume. The values of the net charge, energy, first moment, and volume of hydrogen bond donor atoms in the isolated DNA bases and in the DNA base pairs as well as their difference (Δ) are shown in Tables 3−6, respectively.

Increase in the Net Charge of Hydrogen Atoms. The loss of charge of hydrogen atoms has been used as one of the criteria for hydrogen bonding. Charges of hydrogen atoms in isolated bases and also in base pairs have been calculated. The charges of hydrogen atoms have been computed by integrating the electron density in the appropriate hydrogen region partitioned by the AIM theory. The values of charge for the hydrogen atoms in the isolated DNA bases and base pairs, which are involved in H bonding, are shown in Table 3. From the charges, it is evident that the hydrogen atoms are descreened upon the formation of hydrogen bonds. The magnitude of this effect ranges from 0.02e to 0.0697e for all of the DNA base pairs. Similar variations have been observed in previous studies on hydrogen-bonded complexes.[54]

TABLE 3: Atomic Charges of the Hydrogen Atoms Involved in H Bonding of DNA Bases and Base Pairs and the Change (Δ) Arising upon Pairing

		charge (au)		
H-bonded pairs	H atom in pair	DNA base	DNA pair	Δ
GCWC	N2(H)−O2	0.44216	0.4995	0.05734
	N1(H)−N3	0.45093	0.49967	0.04873
	O6−(H)N4	0.4667	0.52509	0.05839
GG1	N1(H)−O6	0.45093	0.50498	0.05405
	O6−(H)N1	0.45093	0.50215	0.05121
GCNEW	N1(H)−O2	0.45093	0.51286	0.06192
	O6−(H)N1	0.46036	0.51808	0.05772
CC	N3−(H)N4	0.4667	0.53062	0.06392
	N4(H)−N3	0.4667	0.53383	0.06713
GG3	N1(H)−N7	0.45093	0.49758	0.04664
	N2(H)−O6	0.44216	0.4712	0.02904
GT1	O6−(H)N3	0.46666	0.4941	0.02743
	N1(H)−O4	0.45093	0.52058	0.06965
GT2	O6−(H)N3	0.46666	0.49568	0.02902
	N1(H)−O2	0.45093	0.5203	0.06936
GC1	N2(H)−N3	0.46563	0.51251	0.04688
	N3−(H)N4	0.4667	0.49626	0.02955
GA1	O6−(H)N6	0.45485	0.50886	0.054
	N1(H)−N1	0.44216	0.48353	0.04137
2aminoAT	N6(H)−O2	0.45485	0.48576	0.03091
	N1−(H)N3	0.46666	0.51228	0.04561
	N2(H)−O4	0.45485	0.47732	0.02247
AC1	N6(H)−N3	0.45485	0.51092	0.05606
	N1−(H)N4	0.4667	0.50514	0.03844
AC2	N7−(H)N4	0.4667	0.50333	0.03663
	N6(H)−N3	0.46703	0.50188	0.03485
GA3	O6−(H)N6	0.45976	0.50037	0.04061
	N1(H)−N7	0.45093	0.47976	0.02882
TAH	O4−(H)N6	0.45976	0.4893	0.02954
	N3(H)−N7	0.46666	0.5147	0.04803
TARH	O2−(H)N6	0.45976	0.48861	0.02885
	N3(H)−N7	0.46666	0.51601	0.04934
TAWC	O4−(H)N6	0.45976	0.49245	0.03268
	N3(H)−N1	0.46666	0.51432	0.04765
TARWC	O2−(H)N6	0.45976	0.4948	0.03504
	N3(H)−N1	0.46666	0.51208	0.04541
TC2	O4−(H)N4	0.4667	0.51239	0.04569
	N3(H)−N3	0.46666	0.51574	0.04907
TC1	O2−(H)N4	0.4667	0.5142	0.0475
	N3(H)−N3	0.46666	0.51688	0.05021
TT1	N3(H)−O4	0.46666	0.52092	0.05425
	O2−(H)N3	0.46666	0.5134	0.04673
TT3	O2−(H)N3	0.46666	0.52093	0.05426
	N3(H)−O2	0.46666	0.51853	0.05186
TT2	O4−(H)N3	0.46666	0.51909	0.05242
	N3(H)−O4	0.46666	0.51553	0.04886
GA4	N2(H)−N1	0.46563	0.49831	0.03268
	N3−(H)N6	0.45485	0.48953	0.03468
AA1	N6(H)−N1	0.45485	0.49284	0.03799
	N1−(H)N6	0.45485	0.49325	0.03839
AA2	N1−(H)N6	0.45485	0.48726	0.03241
	N6(H)−N7	0.45976	0.48601	0.02625
GA2	N2(H)−N7	0.46563	0.49543	0.0298
	N3−(H)N6	0.45976	0.4885	0.02874
GG4	N2(H)−N3	0.46563	0.49852	0.03289
	N3−(H)N2	0.46563	0.49524	0.0296
AA3	N6(H)−N7	0.45976	0.48657	0.02681
	N7−(H)N6	0.45976	0.48729	0.02753

Energetic Destabilization of the Hydrogen Atom. Another property of hydrogen bonding is the energetic destabilization of the hydrogen atom, which can be derived from the differences in the atomic energies of the hydrogen atoms in the isolated DNA bases and base pairs. The results that are presented in Table 4 indicate that this quantity is positive in all cases, varying from 0.001 to 0.04 au. It can be seen that the formation of hydrogen bonds necessarily destabilizes the hydrogen atoms, which are involved in H bonding. The general trend is in

TABLE 4: Atomic Energy of the Hydrogen Atoms Involved in H Bonding of DNA Bases and Base Pairs and the Change (Δ) Arising upon Pairing

H-bonded pairs	H atom in pair	energy (au) DNA base	energy (au) DNA pair	Δ
GCWC	N2(H)−O2	−0.4388	−0.4125	0.02629
	N1(H)−N3	−0.4345	−0.4121	0.02236
	O6−(H)N4	−0.4201	−0.3956	0.02456
GG1	N1(H)−O6	−0.4345	−0.4095	0.02501
	O6−(H)N1	−0.4345	−0.4099	0.0246
GCNEW	N1(H)−O2	−0.4345	−0.4058	0.0287
	O6−(H)N1	−0.4209	−0.4021	0.01878
CC	N3−(H)N4	−0.4201	−0.3799	0.04024
	N4(H)−N3	−0.4201	−0.3798	0.04036
GG3	N1(H)−N7	−0.4345	−0.4098	0.02473
	N2(H)−O6	−0.4388	−0.4267	0.01214
GT1	O6−(H)N3	−0.4168	−0.4154	0.00142
	N1(H)−O4	−0.4345	−0.3959	0.03863
GT2	O6−(H)N3	−0.4168	−0.4153	0.00151
	N1(H)−O2	−0.4345	−0.4045	0.02999
GC1	N2(H)−N3	−0.4245	−0.3991	0.02531
	N3−(H)N4	−0.4201	−0.4087	0.01143
GA1	O6−(H)N6	−0.426	−0.4066	0.01942
	N1(H)−N1	−0.4388	−0.4158	0.02305
2aminoAT	N6(H)−O2	−0.426	−0.4186	0.00747
	N1−(H)N3	−0.4168	−0.3914	0.02543
	N2(H)−O4	−0.426	−0.4187	0.00737
AC1	N6(H)−N3	−0.426	−0.4006	0.02541
	N1−(H)N4	−0.4201	−0.4006	0.0195
AC2	N7−(H)N4	−0.4201	−0.4034	0.0167
	N6(H)−N3	−0.4184	−0.4051	0.01333
GA3	O6−(H)N6	−0.4277	−0.413	0.01477
	N1(H)−N7	−0.4345	−0.4175	0.01698
TAH	O4−(H)N6	−0.4277	−0.4168	0.01091
	N3(H)−N7	−0.4168	−0.3971	0.01975
TARH	O2−(H)N6	−0.4277	−0.4178	0.00993
	N3(H)−N7	−0.4168	−0.3941	0.02267
TAWC	O4−(H)N6	−0.4277	−0.4095	0.01822
	N3(H)−N1	−0.4168	−0.3947	0.02216
TARWC	O2−(H)N6	−0.4277	−0.4126	0.01511
	N3(H)−N1	−0.4168	−0.3929	0.02395
TC2	O4−(H)N4	−0.4201	−0.4005	0.01964
	N3(H)−N3	−0.4168	−0.3935	0.02329
TC1	O2−(H)N4	−0.4201	−0.4006	0.01958
	N3(H)−N3	−0.4168	−0.3932	0.0236
TT1	N3(H)−O4	−0.4168	−0.4013	0.01552
	O2−(H)N3	−0.4168	−0.4028	0.01404
TT3	O2−(H)N3	−0.4168	−0.4025	0.01431
	N3(H)−O2	−0.4168	−0.4024	0.01436
TT2	O4−(H)N3	−0.4168	−0.4015	0.01529
	N3(H)−O4	−0.4168	−0.4005	0.01632
GA4	N2(H)−N1	−0.4245	−0.4033	0.02115
	N3−(H)N6	−0.426	−0.415	0.01104
AA1	N6(H)−N1	−0.426	−0.4116	0.01444
	N1−(H)N6	−0.426	−0.4111	0.01491
AA2	N1−(H)N6	−0.426	−0.4109	0.01509
	N6(H)−N7	−0.4277	−0.4141	0.01363
GA2	N2(H)−N7	−0.4245	−0.4077	0.01677
	N3−(H)N6	−0.4277	−0.4147	0.01306
GG4	N2(H)−N3	−0.4245	−0.4077	0.01676
	N3−(H)N2	−0.4245	−0.4081	0.01638
AA3	N6(H)−N7	−0.4277	−0.4172	0.01055
	N7−(H)N6	−0.4277	−0.4177	0.01004

TABLE 5: Atomic First Moment of the Hydrogen Atoms Involved in H Bonding of DNA Bases and Base Pairs and the Change (Δ) Arising upon Pairing

H-bonded pairs	H atom in pair	first moment (au) DNA base	first moment (au) DNA pair	Δ
GCWC	N2(H)−O2	0.17945	0.14361	−0.03584
	N1(H)−N3	0.17831	0.14645	−0.03186
	O6−(H)N4	0.17507	0.13695	−0.03812
GG1	N1(H)−O6	0.17831	0.14215	−0.03616
	O6−(H)N1	0.17831	0.14147	−0.03684
GCNEW	N1(H)−O2	0.17831	0.13347	−0.04484
	O6−(H)N1	0.17798	0.13705	−0.04094
CC	N3−(H)N4	0.17507	0.13226	−0.0428
	N4(H)−N3	0.17507	0.1308	−0.04426
GG3	N1(H)−N7	0.17831	0.14474	−0.03356
	N2(H)−O6	0.17945	0.15991	−0.01954
GT1	O6−(H)N3	0.17585	0.14238	−0.03348
	N1(H)−O4	0.17831	0.14055	−0.03776
GT2	O6−(H)N3	0.17585	0.14225	−0.03361
	N1(H)−O2	0.17831	0.14323	−0.03507
GC1	N2(H)−N3	0.17365	0.14422	−0.02943
	N3−(H)N4	0.17507	0.15386	−0.02121
GA1	O6−(H)N6	0.1804	0.14554	−0.03487
	N1(H)−N1	0.17945	0.15724	−0.02221
2aminoAT	N6(H)−O2	0.1804	0.15179	−0.02861
	N1−(H)N3	0.17585	0.14822	−0.02763
	N2(H)−O4	0.1804	0.15192	−0.02848
AC1	N6(H)−N3	0.1804	0.1485	−0.0319
	N1−(H)N4	0.17507	0.15202	−0.02304
AC2	N7−(H)N4	0.17507	0.15465	−0.02041
	N6(H)−N3	0.17621	0.15211	−0.02409
GA3	O6−(H)N6	0.17345	0.14573	−0.02772
	N1(H)−N7	0.17831	0.16247	−0.01583
TAH	O4−(H)N6	0.17345	0.15282	−0.02063
	N3(H)−N7	0.17585	0.14002	−0.03583
TARH	O2−(H)N6	0.17345	0.15296	−0.02049
	N3(H)−N7	0.17585	0.13928	−0.03657
TAWC	O4−(H)N6	0.17345	0.14226	−0.03119
	N3(H)−N1	0.17585	0.1413	−0.03455
TARWC	O2−(H)N6	0.17345	0.14844	−0.02501
	N3(H)−N1	0.17585	0.14448	−0.03137
TC2	O4−(H)N4	0.17507	0.14248	−0.03259
	N3(H)−N3	0.17585	0.15238	−0.02347
TC1	O2−(H)N4	0.17507	0.14091	−0.03415
	N3(H)−N3	0.17585	0.14909	−0.02676
TT1	N3(H)−O4	0.17585	0.13949	−0.03636
	O2−(H)N3	0.17585	0.14178	−0.03408
TT3	O2−(H)N3	0.17585	0.13939	−0.03646
	N3(H)−O2	0.17585	0.13984	−0.03601
TT2	O4−(H)N3	0.17585	0.14033	−0.03552
	N3(H)−O4	0.17585	0.14143	−0.03442
GA4	N2(H)−N1	0.17365	0.15377	−0.01988
	N3−(H)N6	0.1804	0.15679	−0.02361
AA1	N6(H)−N1	0.1804	0.15581	−0.02459
	N1−(H)N6	0.1804	0.15654	−0.02387
AA2	N1−(H)N6	0.1804	0.1595	−0.0209
	N6(H)−N7	0.17345	0.15755	−0.0159
GA2	N2(H)−N7	0.17365	0.15467	−0.01898
	N3−(H)N6	0.17345	0.15909	−0.01436
GG4	N2(H)−N3	0.17365	0.15572	−0.01793
	N3−(H)N2	0.17365	0.15621	−0.01744
AA3	N6(H)−N7	0.17345	0.1594	−0.01405
	N7−(H)N6	0.17345	0.15845	−0.015

agreement with the destabilization observed in other hydrogen-bonded interactions.[23,29,37]

Decrease in Dipolar Polarization of the Hydrogen Atom. Popelier has also proposed that the first moment of the hydrogen atom decreases upon the formation of hydrogen bonds. The first moment of the hydrogen atom in the isolated DNA base and base pairs has been calculated using the AIM integration. The calculated results are tabulated in Table 5. It is possible to note from the results that the hydrogen bonding of two base pairs leads to a decrease in the first moment of hydrogen atoms, which again reinforces the hydrogen bonding in DNA base pairs. The decrease in the dipolar polarization of the hydrogen atom ranges from 0.014 to 0.0448 au. Again, this decrease is in accordance with the earlier findings.[23,37]

Decrease in Atomic Volume of the Hydrogen Atom. The decrease in atomic volume upon the formation of hydrogen bonding has also been used as a criterion for understanding hydrogen bonding. The atomic volume corresponding to the

TABLE 6: Atomic Volumes of the Hydrogen Atoms Involved in H Bonding of DNA Bases and Base Pairs and the Change (Δ) Arising upon Pairing

H-bonded pairs	H atom in pair	volume (au) DNA base	volume (au) DNA pair	Δ
GCWC	N2(H)−O2	26.6585	18.1012	−8.55734
	N1(H)−N3	24.8152	16.8245	−7.99065
	O6−(H)N4	25.2025	16.5018	−8.70077
GG1	N1(H)−O6	24.8152	16.1827	−8.63248
	O6−(H)N1	24.8152	16.3506	−8.46463
GCNEW	N1(H)−O2	24.8152	14.4133	−10.4019
	O6−(H)N1	25.6447	16.0806	−9.56414
CC	N3−(H)N4	25.2025	15.4373	−9.76522
	N4(H)−N3	25.2025	15.1894	−10.0131
GG3	N1(H)−N7	24.8152	16.5739	−8.24127
	N2(H)−O6	26.6585	22.915	−3.74352
GT1	O6−(H)N3	26.7227	16.6531	−10.0697
	N1(H)−O4	24.8152	17.9556	−6.85961
GT2	O6−(H)N3	26.7227	16.9799	−9.74278
	N1(H)−O2	24.8152	17.2112	−7.60397
GC1	N2(H)−N3	25.2565	16.8827	−8.37379
	N3−(H)N4	25.2025	18.9728	−6.2297
GA1	O6−(H)N6	26.5596	17.3045	−9.25505
	N1(H)−N1	26.6585	19.6153	−7.04322
2aminoAT	N6(H)−O2	26.5596	19.5221	−7.03744
	N1−(H)N3	26.7227	18.6465	−8.07622
	N2(H)−O4	26.5596	19.6167	−6.94292
AC1	N6(H)−N3	26.5596	18.0594	−8.50022
	N1−(H)N4	25.2025	18.9204	−6.28214
AC2	N7−(H)N4	25.2025	18.8771	−6.32542
	N6(H)−N3	26.7004	18.3078	−8.39259
GA3	O6−(H)N6	25.8557	18.208	−7.64772
	N1(H)−N7	24.8152	21.29	−3.52519
TAH	O4−(H)N6	25.8557	19.7512	−6.10447
	N3(H)−N7	26.7227	16.0736	−10.6491
TARH	O2−(H)N6	25.8557	19.9964	−5.85928
	N3(H)−N7	26.7227	16.4681	−10.2546
TAWC	O4−(H)N6	25.8557	20.4595	−5.39624
	N3(H)−N1	26.7227	16.9202	−9.80252
TARWC	O2−(H)N6	25.8557	18.9331	−6.92256
	N3(H)−N1	26.7227	17.3328	−9.38986
TC2	O4−(H)N4	25.2025	17.1502	−8.05229
	N3(H)−N3	26.7227	20.0574	−6.66529
TC1	O2−(H)N4	25.2025	17.204	−7.99856
	N3(H)−N3	26.7227	18.7072	−8.01548
TT1	N3(H)−O4	26.7227	17.2241	−9.49857
	O2−(H)N3	26.7227	18.0918	−8.63089
TT3	O2−(H)N3	26.7227	17.3308	−9.39189
	N3(H)−O2	26.7227	17.9008	−8.82193
TT2	O4−(H)N3	26.7227	17.6792	−9.04352
	N3(H)−O4	26.7227	18.3552	−8.36748
GA4	N2(H)−N1	25.2565	18.7173	−6.53923
	N3−(H)N6	26.5596	19.2629	−7.29669
AA1	N6(H)−N1	26.5596	20.0105	−6.54909
	N1−(H)N6	26.5596	19.7246	−6.83497
AA2	N1−(H)N6	26.5596	18.3196	−8.24002
	N6(H)−N7	25.8557	20.5186	−5.33711
GA2	N2(H)−N7	25.2565	19.7119	−5.54458
	N3−(H)N6	25.8557	20.0286	−5.82707
GG4	N2(H)−N3	25.2565	19.1273	−6.12914
	N3−(H)N2	25.2565	19.2668	−5.98971
AA3	N6(H)−N7	25.8557	21.2088	−4.64694
	N7−(H)N6	25.8557	20.594	−5.26168

isolated DNA bases and base pairs has been calculated. The results reported in Table 6 reveal that there is a decrease in atomic volume upon the formation of hydrogen bonding. The volume of hydrogen is reduced by 2 to 11.0 au. A similar phenomenon is seen in the case of a weak interaction of CH_4, $HCCl_3$. HCCH, HCN, HF, and $HCCl_3$ with benzene.[54] The result of $\rho(r_c)$, $(\nabla^2\rho(r_c))$ at HBCP and all of the integrated properties

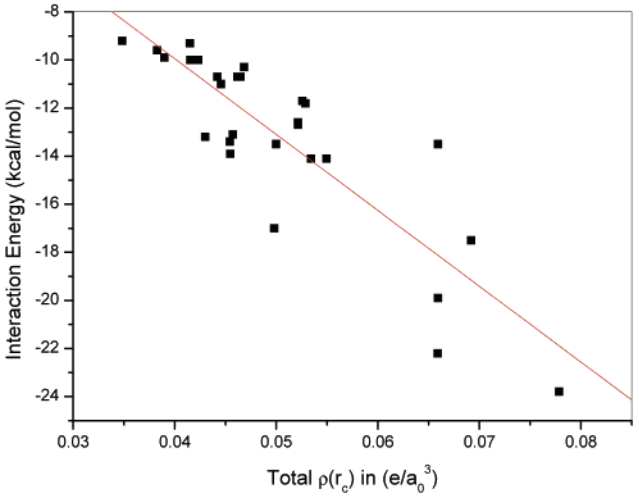


Figure 3. Relationship between the interaction energy and total $\rho(r_c)$ of the DNA base pairs.

derived from the electron density suggests that the criteria defining H-bond interaction on DNA base pairs are highly satisfied.

Relationship between Total Electron Density and H-Bonding Interaction Energy. The amplitude of electron density at each bond critical point has been summed over to get the total electron density for each H-bonded base pairs and has been used for further analysis. Regression analysis has been performed to establish the linear relationship between the total electron density at the HBCP and the interaction energy of various DNA base pairs. Figure 3 shows the variation of total electron density at the BCP versus the interaction energy of various base pairs of DNA. The linear relationship obtained is given below

$$\text{interaction energy} = -315.555\sum\rho(r_c)\text{ at HBCP} + 2.676 \quad (7)$$

The correlation coefficient for this fit is −0.859, which indicates the existence of a reasonable linear relationship between $\rho(r_c)$ and the interaction energy. The usefulness of $\rho(r_c)$ in explaining the hydrogen-bonding interaction between DNA bases is evident from the linear relation. Generally, these relationships have been developed for a series of homologous model systems, which have a good linear relationship between the interaction energy and electron density at the BCP. Although DNA base pairs do not constitute such a homologous system, $\rho(r_c)$ exhibits a reasonably good linear relation with the interaction energy.

It can be seen from Figure 3 that the H-bonded base pairs having their interaction energy in the range of −9 to −15 kcal/mol, show clustering in the density region between 0.030 and 0.055 e/a_0^3 and exhibit a good linear relationship with their interaction energy. The paring of GCWC and 2aminoAT is stabilized by three potential hydrogen bonds with the total electron density at the HBCPs being more than 0.05 e/a_0^3, and hence they do not fall in the linear region.

It is interesting to observe that the total density of base pairs CC and GG1 deviates from the linear fit when compared to that of other higher-energy base pairs. Base pairs CC and GG1 have a higher total electron density value and hence the corresponding deviation. Even though base pairs GG1 and GG3 form two hydrogen bonds with each other, there is the possibility of additional hydrogen bonding between the H atom of one guanine base and the O atom of the other guanine base as

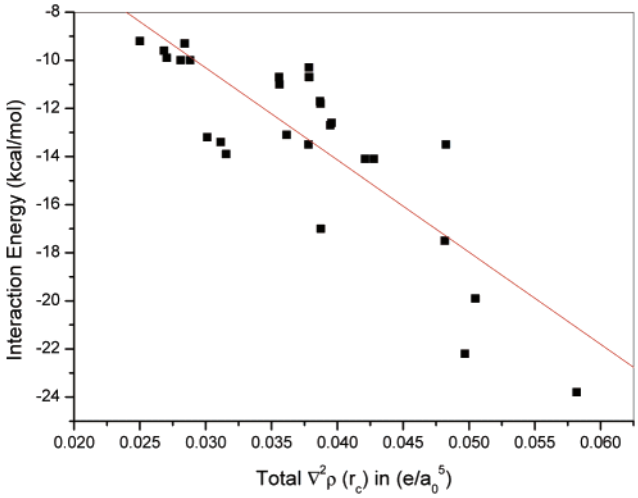


Figure 4. Relationship between the interaction energy and total $\nabla^2\rho(r_c)$ of the DNA base pairs.

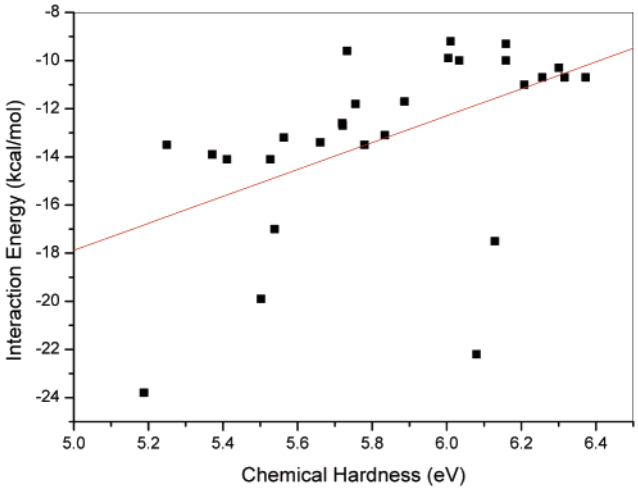


Figure 5. Relationship between the interaction energy and chemical hardness of all DNA base pairs.

described in the previous study.[18] The presence of an additional BCP is evident from Figure 2 in the case of GG3 between O6- - -H(C8). However, it is not possible to identify such additional BCPs in the case of GG1 with the help of electron density topography.

Relationship between Total Laplacian of Charge Density and H-Bonding Interaction Energy. Similarly, we have also used the sum of the Laplacian of electron density at the HBCPs to probe the strength of hydrogen bonding between DNA base pairs. To the best of our knowledge, such an analysis has not been made to unravel the strength of H bonding in DNA base pairs. The Laplacian of charge density at the HBCP is given in Table 1. The Laplacian indicates that there is charge depletion between the two base pairs and hence the weak interaction between the two systems. The variation of the total Laplacian of electron density at the HBCP with the interaction energy has also been fit to a linear equation. The results are shown in Figure 4. The linear fit is

$$\text{interaction energy} = -383.116\sum\nabla^2\rho(r_c)\ \text{at HBCP} + 1.182 \quad (8)$$

The correlation coefficient is −0.827. Similar to the electron density variation, the total Laplacian of electron density at HBCP exhibits a meaningful relationship depicting the greater depletion

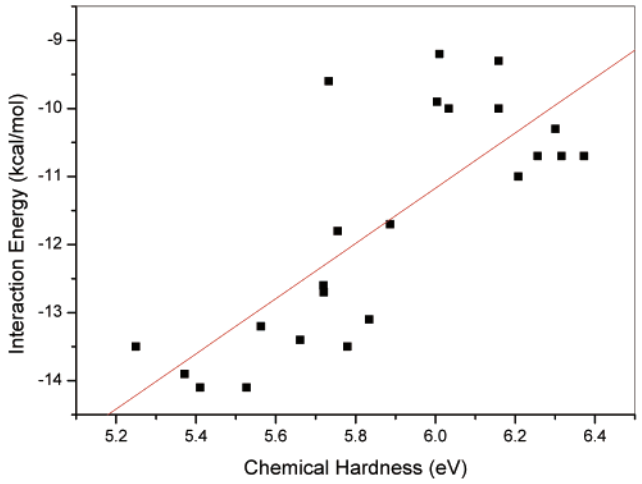


Figure 6. Relationship between the interaction energy and chemical hardness of the DNA base pairs excluding higher-binding-energy species.

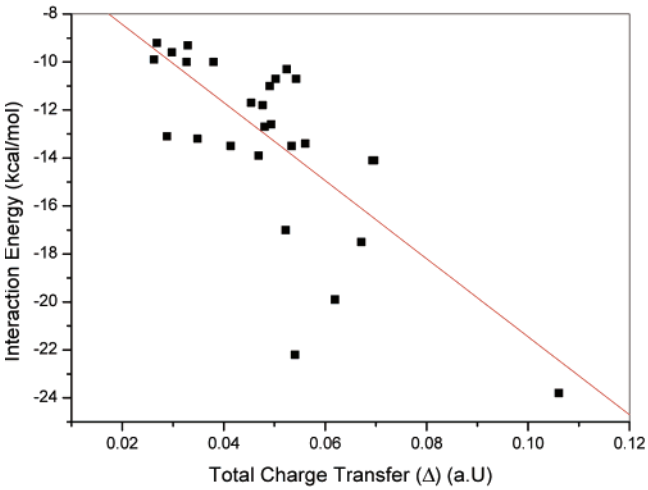


Figure 7. Relationship between the total charge transfer of hydrogen atoms in H bonding and the interaction energy of the DNA base pairs.

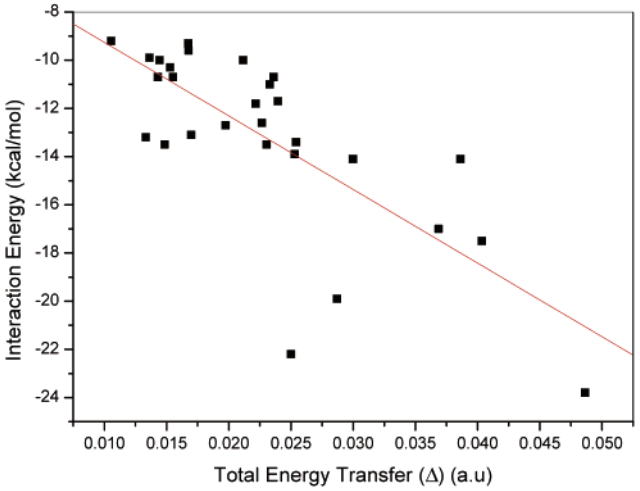


Figure 8. Relationship between the total energy transfer of hydrogen atoms in H bonding and the interaction energy of the DNA base pairs.

of electron density in the hydrogen-bonded region of the base pairs with numerically more interaction energy. This clearly reassures us of the presence of the closed-shell type of interaction between the two DNA base pairs.

TABLE 7: Calculated Charge Transfer for the Formation of DNA Base Pairs Using Parr's Equation

DNA base	adenine	guanine	thymine	cytosine
adenine	0	0.019	−0.035	−0.025
thymine	0.035	0.053	0	0.01
guanine	−0.019	0	−0.053	−0.044
cytosine	0.025	0.044	−0.01	0

Relationship between Chemical Hardness and H-Bonding Interaction. Chemical hardness has been used on several occasions to understand the stability of the chemical species along with the electronic structure principles.[38−46] Using the calculated values of the ionization potential and electron affinity, we have calculated the chemical hardness and chemical potential. The fractional electrons transfer in the formation of the DNA base pair have also been computed from the chemical hardness and chemical potential of the isolated DNA bases. The calculated global reactivity descriptors such as chemical hardness and chemical potential for various DNA bases and base pairs are listed in Table 2. It is evident form the reactivity descriptors that thymine is the hardest species among the four DNA bases considered here. The hardness of the bases varies as T > C > G > A. It is a well-known fact that the both the ionization potential and electron affinity obtained from Koopman's theorem do not include an electron relaxation term upon ionization and electron reorganization energy after electron capture. Therefore, these values have to be carefully analyzed. It is evident from chemical hardness values that G and A are soft species when compared to T and C. Because of the inverse relationship between the hardness and stability, guanine and adenine are the reactive species when compared to T and C.

The calculated global reactivity descriptors for DNA base pairs show that TT3 is the hardest base pair whereas GCWC is the softest base pair and hence their corresponding reactivities. A linear regression analysis between the interaction energy and chemical hardness for various DNA base pairs have been carried out. The linear regression analysis yields

$$\text{interaction energy} = 5.587\ \text{chemical hardness} - 45.815, \quad R = 0.501 \quad (9)$$

It can be seen from the regression analysis that there is not good correlation between the interaction energy and chemical hardness. The removal of higher-binding-energy data points marginally improves the correlation between interaction energy and chemical hardness.

$$\text{interaction energy} = 4.056\ \text{chemical hardness} - 35.51, \quad R = 0.780 \quad (10)$$

A similar feature is also evident from the electron density analysis at the bond critical points with interaction energy.

Charge Transfer in the Formation of H-Bonded Bases Pairs. When two systems are brought together as in a reaction, they must form a single system with a constant value of μ. Therefore, there is a transfer of electrons from the less electronegative system to the other.[38] Using the first approximation, the fractional number of electrons transferred, ΔN, has been quantified using Parr's equation.[38] The charge transfers between the two DNA bases in the formation of DNA base pairs are shown in Table 7. It can be noted from Table 1 and Figure 2 that there are several possible canonical and noncanonical base pairs that can be formed between four DNA bases. In the formation of GC pairs, electrons flow from guanine to cytosine. Similarly in the formation of AT pairs, electrons flow from adenine to thymine. In CT pairs, electrons flow from T to C. Charge transfer takes place from G to A in the GA pairs. In AC pairs, electron transfer takes place from A to C. In GT pairs, electrons flow from G to T. Although it is not possible to estimate the flow of charge in each pair, a qualitative understanding of electron flow from one base to another can be estimated. It is evident from Parr's equation that charge transfer in different arrangements cannot be estimated. To gain more information about the charge transfer in each DNA base pairs, the integrated atomic charge on the hydrogen atoms involved in hydrogen bonding has been used to obtain the relationship between interaction energies.

The AIM-derived charges on the hydrogen atoms have been used as the criteria for charge transfer in each DNA pair as suggested by Popelier.[23,37] Because of the definition of AIM theory, atoms can be treated as quantum-mechanically distinct systems, and their properties may be computed by integrating over these atomic basins. Hence, charges derived from AIM theory are well defined, and this approach contrasts with traditional methods for population analysis in the sense that the charges derived from AIM theory are independent of the method and basis set. The net charge transfer has been calculated for each DNA base pair by adding the charges of hydrogen donor atoms. The total net charge transfer also correlated with the strength of stabilization, and attempts should be made to find other correlations. Thus, this total net charge has been used to obtain a linear relation with the corresponding interaction energy. The linear fit is

$$\text{interaction energy} = -162.706\ \text{total net charge of the H atoms in H bonds} - 5.179, \quad R = -0.716 \quad (11)$$

This fit makes it clear that the interaction energy of the base pairs involves more than an electrostatic contribution. Popelier et al. have also considered the role of primary and secondary interactions in the naturally occurring DNA base pairs. They have pointed out that simple rules to rationalize the pattern of energetic stabilization of DNA base pairs in terms of subsets of atoms remain elusive.[53] To probe how hydrogen atoms contribute to the stabilization of H bonding, the energetic destabilization of hydrogen atoms involved in hydrogen bonding has been used to obtain a linear relationship with the interaction energy of various DNA base pairs. The linear regression analysis revealed that the correlation coefficient is on the order of −0.744.

$$\text{interaction energy} = -305.427\ \text{total atomic energy of H atoms in H bonds} - 5.179 \quad (12)$$

It is evident from the linear fits presented in eqs 11 and 12 that simple correlation of changes in the properties of hydrogen atoms involved in base pairing are not sufficient to obtain complete information. It can noted from the previous study that the stabilization of H-bonded DNA base pairs originating in the HF contribution is mainly due to electrostatic interactions.[18] But in weakly bonded base pairs, the correlation interaction energy amounts to as much as 30−40% of the stabilization, and for some strong base pairs, the correlation interaction energy is repulsive.[18] Hence, in addition to the electrostatic interaction other interactions are also responsible for the stabilization of DNA. This may be due to the fact that the hydrogen-bonding interaction involves electrostatics (acid/base), polarization (hard/soft), van der Waals interactions (dispersion/repulsion or intermolecular correlation), and covalency (charge transfer).[55] Hence, a simple correlation of the interaction energy with charge

transfer on hydrogen atoms involved in the hydrogen bonding is inadequate to provide conclusive information on DNA base paring.

Conclusions

The hydrogen bonds present in the base pairs of DNA have been characterized in terms of Bader's AIM theory, $\rho(r_c)$ and $\nabla^2\rho(r_c)$ at HBCP, and various criteria proposed by Popelier for hydrogen bonding. The results confirmed that the hydrogen atom involved in H bonding exhibits similar topological features to the electron density and similar variations in the integrated atomic properties. The electron density topography analysis has also confirmed the presence of secondary interactions in various DNA base pairs. The interaction energy and electron density at HBCP exhibited a linear relation. Similarly, the interaction energy of various DNA base pairs versus hardness shows a linear relationship, thus ensuring the hardness−stability relationship. Using Parr's formula, the flow of electron transfer occurring between the various base pairs has been qualitatively assessed. Because of limitations of Parr's formula, it is not appropriate to describe charge transfer in all conformationally different DNA base pairs. The charge transfers in each case have been quantified with the help of AIM-derived charges on hydrogen atoms involved in hydrogen bonding. Because the H-bonding interaction involves various contributions from other interactions, it is not sufficient to relate the AIM-derived charges of the hydrogen atoms involved in base pairing to the interaction energy. However, both $\rho(r_c)$ and $\nabla^2\rho(r_c)$ could successfully explain the stability of various H-bonded canonical and non-canonical DNA base pairs.

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