

# *A new vision of the DNA triple-helix: structural, spectroscopic and electronic parameters for hydrogen bonding for Watson-Crick and Hoogsteen pairing*

## *Uma nova visão da tripla hélice do DNA: parâmetros estruturais, espectroscópicos e eletrônicos de ligações de hidrogênio para os emparelhamentos de Watson-Crick e Hoogsteen*

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### Abstract

Through the B3LYP/6-31+G(d,p) calculations, the intermolecular structures of double and triple DNA helix formed by Thymine (T) Adenine (A) were fully optimized. Based on analysis of structural parameters, vibrational modes and infrared absorption intensities, specific hydrogen bonds on the scaffolds of the purine and pyrimidine were identified. On behalf of charge transfer criterion between the HOMO and LUMO frontier orbitals of the proton receptor and donor respectively, the application of the NBO and ChEIPG protocols have provided unsatisfactory results. Meanwhile, all hydrogen bonds were characterized through the QTAIM descriptors, by which new intermolecular profiles have been pointed out to both of double (TA) and (TAT) triple-DNA helix.

**Keywords:** DNA. Triple-helix. Hydrogen bond.

### Resumo

Através dos cálculos B3LYP/6-31+G(d,p), as estruturas intermoleculares da dupla e tripla hélices do DNA formadas por Timina (T) Adenina (A) foram totalmente otimizadas. Com base na análise de parâmetros estruturais, modos vibracionais e intensidades de absorção no espectro de infravermelho, foram identificadas ligações de hidrogênio entre as bases purina e pirimidina. Pela transferência de carga entre os orbitais de fronteira HOMO e LUMO respectivamente do receptor e doador de prótons, a aplicação dos protocolos NBO e ChEIPG proporcionaram resultados insatisfatórios. Todavia, todas as ligações de hidrogênio foram caracterizadas através de descritores QTAIM, pelos quais novos perfis intermoleculares foram obtidos tanto para a dupla (TA) quanto para a tripla (TAT) hélices do DNA.

**Palavras-chave:** DNA. Tripla hélice. Ligação de hidrogênio.

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## Introduction

The Deoxyribose Nucleic Acid molecule is a nucleotide polymer formed by phosphate and pentose. Within its structure, the purine and pyrimidines nitrogenous bases bound to pentose is also widely known. As benchmarks, the Adenine (A) and Guanine (G) constitute the purine bases whereas Cytosine (C) and Thymine (T), and as long as the uracil (U) for the Ribonucleic Acid (TRAVERS; MUSKHELISHVILI, 2015), all these last ones encompass the pyrimidine bases. The nucleotide sequence to form the DNA chain, wherein each one may interact with others in order to form the double antiparallel helix with right-handed orientation. As it is well known, the O<sup>⋯</sup>H and N<sup>⋯</sup>H hydrogen bond interactions formed by Adenine (A) and Thymine (T) constitute the driving force to the DNA interchain cross-links (KOOL, 2001). However, the DNA may assume another less known configuration in the form of triple-helix rather than that double one vastly established. In practice, the nucleotide chain binds to the double helix in parallel or antiparallel directions (GOÑI; DE LA CRUZ; OROZCO, 2004), or even like a DNA doubly curved, by which leads to an intramolecular triple helix. In other words, regardless if double or single chains, they are formed and coexist as per the hydrogen bond strength (SZATYŁOWICZ; SADLEJ-SOSNOWSKA, 2010).

Upon the formation of the triple helix, the addition of another chain causes changes in the capability of the DNA to recognize some proteins, and therefore, the mechanisms and functions of the own DNA are altered. Because the specificity of the oligonucleotides for binding with the double chain, the triple helix has been used as important tool to the sequencing of genetic materials, validating then, this ternary structure as an inhibitor for the proliferation of the tumor cells creating a chain formed by complementary bases to the genetic code of a certain type of cancer or pathogenesis (SINGHAL *et al.*, 2011).

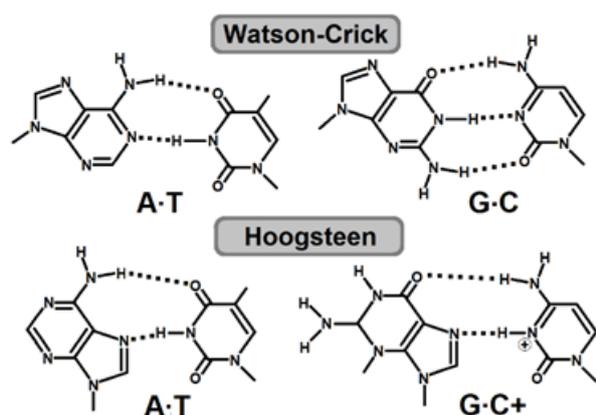
Historically, the discovery and advances in studies about the DNA triple helix occurred simultaneously to those of the famous double one. In 1871, however, Miescher has isolated a compounds formed by phosphorus atoms and aromatic derivatives, such as the purine and pyrimidines (DAHLM, 2005). As starting point, this substance was marked as the DNA that we know, even though, initially it has been called of “nuclein”. Decades later, in the XX century, precisely in 1929 Levene realized that the DNA was a polymer composed by a sequence of pentoses, phosphate groups and nitrogenous

bases (SCHMIDT; LEVENE, 1938), without yet, any concrete relationship with the genetic material. Years henceforth, in 1940, the first evidences which the DNA could be a powerful molecule able to bring the genetic information, Avery *et al.* (1994) have found that immune bacteria can be undergone to a virulence damage whether a DNA from another microorganism was inserted on it (AVERY; MACLEOD; MCCARTY, 1994). In this same year, the spectroscopy analysis has revealed that nucleotides were the responsible by the absorption UV radiation instead of proteins. In this time, the power of the UV radiation as causing vector of genetic mutation was already known.

In 1950, the researching group headed by Chargaff has identified the purines and pyrimidines binding to nucleotides in a defined proportion (CHARGAFF, 1950). The adenine and thymine amounts were equivalent likewise to those for cytosine and guanine. These events gave support to qualify the DNA as being the responsible by the transmission of the genetic information, although little was known about its structure, mainly how a specific conformation or configuration would provide a transfer or carriage of genetic content. Nevertheless, in 1951, Franklin and Gosling (1953) have proposed the wide famous crystallographic DNA structure achieved from X-ray experiments (FRANKLIN; GOSLING, 1953). This was the historical discovery that opened new horizons for a real understanding of the DNA capability within the living organisms. Thus, in 1953 Watson and Crick exposed the DNA structure that we know so far (WATSON; CRICK, 1953), whose uniqueness highlighted the double helix stability due to the hydrogen bond formation. To this finding and recognized standing, Watson and Crick were awarded with the medicine Nobel Prize in 1962.

As an attempt to demonstrate the structure of the “nuclein”, also in 1953 Pauling and Corey presented a theoretical model for the DNA triple helix (PAULING; COREY, 1952). From this time on, Rich *et al.* (1961) examined this ternary structure, despite the “nuclein” was double backbone type (RICH *et al.*, 1961). However, it is worthy to note that Pauling and Corey (1952) made no mention concerning that the “nuclein” would has a triple helix form. In fact, the first certification of the DNA triple helix is signed to Felsenfeld and Rich (1957), which carried out a study involving the a single chain formed by purines and pyrimidines bases linked to a double DNA structure (FELSENFELD; RICH, 1957). In 1959, Hoogsteen presented a crystallographic structure of the DNA triple helix (HOOGSTEEN, 1959), suggesting, then, the formation of hydrogen bonds through the nitrogenous bases, Figure 1.

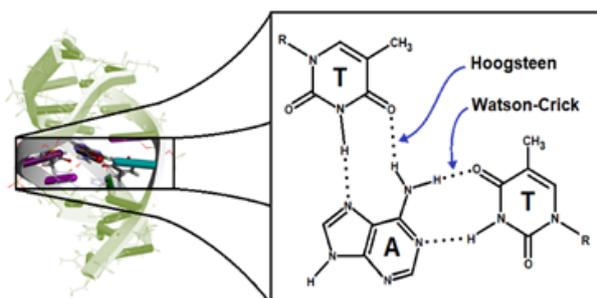
**Figure 1** – Watson-Crick and Hoogsteen pairing in the DNA triple helix, Nikolova *et al.* (2011).



Source: The authors.

In the year of 1968, Morgan and Wells reported a biological application of the triple helix through oligonucleotide action (MORGAN; WELLS, 1968), and thereby, the achieved result was the promotion of the DNA cleavage leading to an inhibition of its transition. In more recent dates, precisely the year of 1986, it was discovered that the third chain binds at the major pyrimidine groove of the double helix through the hydrogen bond formation. As aforementioned, Hoogsteen (1959) has already highlighted this hydrogen bond scenery (HOOGSTEEN, 1959). In agreement with the specialized literature, the DNA triple helix possesses a more rigid structure, although the weakening of the hydrogen bond upon the Hoogsteen understanding whether compared to that of Watson and Crick. At light of the thymine-adenine complex (TA), and by inserting another thymine unit in conformity with the Hoogsteen conception, the (TAT) structure can be found in several triple helix sequences, such as is presented in Figure 2 whose structure is deposited in the PDB source coded as “1R3X” (GOTFREDSEN; SCHULTZE; FEIGON, 1998).

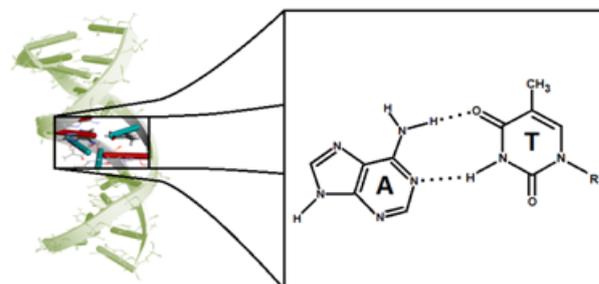
**Figure 2** – Localization of the (TAT) complex in the DNA triple helix (PDB code “1R3X”)



Source: Gotfredsen *et al.* (1998)

In dimer, Figure 3, the intermolecular structure (TA) can be easily found because the double helix embodies the A-T and C-G partners. Hereinafter, the location of the TA dimer is evidenced in a crystallographic structure of the double helix available in the PDB code “6CQ3” (DELGADO; VANCE; KERNS, 2018).

**Figure 3** – Localization of the TA dimer in the DNA double helix (PDB code “6CQ3”)



Source: Delgado *et al.* (2018).

The chemical knowledge concerning the  $C=O \cdots H-N$  and  $N \cdots H-N$  hydrogen bonds framed in conformity with the Hoogsteen and Watson and Crick moieties became vital for better understanding the formation of the DNA chains in double and triple helices. On the energetic point of view, other reported studies shown that the DNA triple helix is less stable rather than the double one (BACHURIN *et al.*, 2018). As it is widely established, the importance of the hydrogen bond properties to the understanding of a wide range of processes is considered unquestionable, not only those whose nature is essentially chemistry, but other ones framed in the biological areas highly essential for life, such as the DNA of our current interest and its functionality. In applicable terms, before the whole historical background of the hydrogen bonds, to get the properties of this interaction upon the formation of the double and triple helices of the DNA, beforehand the centenary chemical bonding model elaborated by Lewis (1916) is enough to some extent (LEWIS, 1916), wherein a hydrogen atom interacts non-covalently towards an electronegative center, which can be fluorine, oxygen, nitrogen or any other as long as if provides a high electronic density source. Nowadays, the universal hydrogen bond model is recognized by the IUPAC (ARUNAN *et al.*, 2011) as follows:



It can be observed that, once Y is bound to W, its main characteristic depends from the electronegativity. Meanwhile, the hydrogen, which is avid by electrons, is bound covalently to X, which quite similar to W, i.e., it must has

a compliant electronegativity to the intermolecular stability of this model (DESIRAJU, 2011). From the upfront theories elaborated in order to comprehend the hydrogen bond phenomenology, Pauling was a defender of the electronegativity (MURPH *et al.*, 2000). In 1954, Coulson and Danielson developed the first quantum calculations of systems formed through the hydrogen bond (COULSON; DANIELSON, 1954). With the improvement of the electronic structure approaches followed by the exponential increasing of the computational capability effort for processing data, the use of quantum chemical approaches have become ever more promising (PENG *et al.*, 2012), and consequently, the hydrogen bond studies more feasible from theoretical viewpoint.

In this context, the study of biomolecular systems formed by hydrogen bond interactions, such as the DNA, for instance, intrinsic results derived from the geometry, spectroscopy and energy, all of them are available (KOOL, 2001). Regarding the  $C=O \cdots H-N$  and  $N \cdots H-N$  hydrogen bonds existing in the (T) and (A) bases with the formation of the double or triple DNA helices, the hydrogen bond theory is quite useful in this regard, in particular whether the electronegativity ranges of the nitrogen and oxygen atoms are taken into account. In other words, a theoretical study of all hydrogen bonds in the (TA) and (TAT) complexes must be worthwhile, mainly if the charge transfer is quantified (LUO; LIU; YANG, 2017), the infrared vibrational modes are identified, and in an overview, if the intermolecular profile can be undergone to a quantum-chemical characterization.

### Computational procedure and details

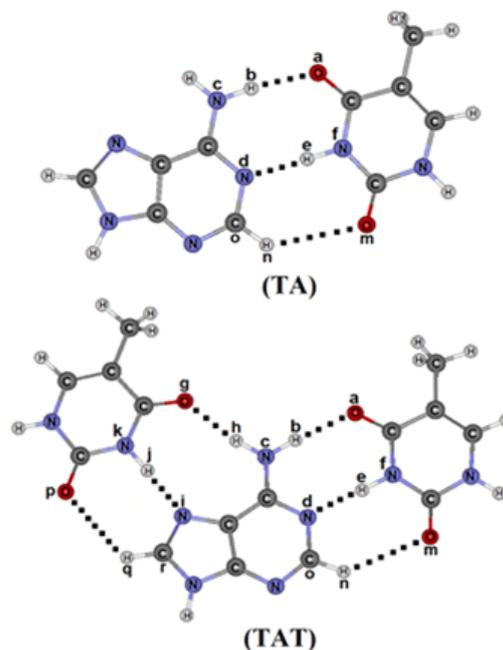
The geometries of the (TA) and (TAT) complexes were fully optimized in minima of the potential energy surface at the B3LYP/6-31+G(d,p) (OLIVEIRA *et al.*, 2009) level of theory with all calculations performed by the GAUSSIAN quantum software program (FRISCH *et al.*, 2004). As results, the structural parameters and infrared vibrational modes were obtained, and of course, the analysis of the Natural Bond Orbital (NBO) theory and Charges from Electrostatic Potentials using a Grid based method (ChEIPG) were used to estimate the atomic charges (MAO, 2014; WIBERG; RABLEN, 2018), and therefore the charge transfer amounts were determined. For the topological integrations, the descriptors of the Quantum Theory of Atoms in Molecules (QTAIM) (BADER, 1991) were obtained through the AIM2000 software (SOFTWARE..., 2001).

## Results and discussion

### Structural analysis

The optimized geometries of the (TA) and (TAT) complexes computed through the B3LYP/6-31+G(d,p) level of theory are presented in Figure 4. With respect to the hydrogen bonds framed by the Watson-Crick statement as well as those ones from Hoogsteen, the distance values are listed in Table 1.

**Figure 4** – Optimized geometries of the (TA) dimer and (TAT) trimer obtained from the B3LYP/6-31+G(d,p) calculations.



Source: The authors.

Furthermore, the Table 1 also lists the bond length variations when the structures of (TA) and (TAT) are compared one each other. In the dimer structure, the  $(N^d \cdots H^e - N^f)$  and  $(O^a \cdots H^b - N^c)$ , hydrogen bonds are formed, which are in line with the canonic forms of the (TA) base, wherein, by means of the proton transfer, either  $H^e$  or  $H^b$ , the tautomerism on  $(N^d - H^e \cdots N^f)$  and  $(O^a - H^b \cdots N^c)$  hydrogen bonds arises (GODBEER; AL-KHALILI; STEVENSON, 2015).

Recent theoretical studies reveal fairly satisfactory results for hydrogen bond distances, wherein, if compared with our current values of 1.8303 and 1.9237 Å, we can cite 1.889 Å for  $(N^d \cdots H^e - N^f)$  and 1.7990 Å for  $(O^a \cdots H^b - N^c)$  obtained by Richardson *et al.* (2003) as well as 1.808 Å published by Nosenko *et al.* (2013) Despite these results have been computed via DFT and MBPT approaches, in addition the B3LYP/DZP++ and

**Table 1** – Values of the hydrogen bond distances ( $R_{Y\cdots H}$ ) and bond lengths of the H-X subunit ( $r_{H-X}$ ) computed at the B3LYP/6-31+G(d,p) calculations.

| (TA)                                     |                 |                        |
|--|-----------------|------------------------|
| Hydrogen bonds                           | $R_{Y\cdots H}$ | $\Delta R_{Y\cdots H}$ |
| $(N^d\cdots H^e - N^f)$                  | 1.8303          | –                      |
| $(O^a\cdots H^b - N^c)$                  | 1.9237          | –                      |
| $(O^m\cdots H^n - C^o)$                  | 2.8672          | –                      |
| Bonds H–X                                | $r_{H-X}$       | $\Delta r_{H-X}$       |
| $(N^e - H^f)_{(T)-(Watson-Crick)}$       | 1.0473          | 0.0335                 |
| $(N^c - H^b)_{(A)-(Watson-Crick)}$       | 1.0218          | 0.0010                 |
| $(C=O^a)_{(T)-(Watson-Crick)}$           | 1.2375          | 0.0129                 |
| $(C^o - H^n)_{(A)-(Watson-Crick)}$       | 1.0871          | 0.0052                 |
| (TAT)                                    |                 |                        |
| Hydrogen bonds                           | $R_{Y\cdots H}$ | $\Delta R_{Y\cdots H}$ |
| $(N^d\cdots H^e - N^f)_{(Watson-Crick)}$ | 1.8262          | -0.0041                |
| $(O^a\cdots H^b - N^c)_{(Watson-Crick)}$ | 1.9749          | 0.0512                 |
| $(O^m\cdots H^n - C^o)_{(Watson-Crick)}$ | 2.7965          | -0.0707                |
| $(N^k\cdots H^j - N^i)_{(Hoogsteen)}$    | 1.8060          | 0.0041                 |
| $(O^g\cdots H^h - N^c)_{(Hoogsteen)}$    | 1.9959          | 0.0326                 |
| $(O^p\cdots H^q - C^r)_{(Hoogsteen)}$    | 2.8025          | -0.0647                |
| Bonds H–X                                | $r_{H-X}$       | $\Delta r_{H-X}$       |
| $(N^e - H^f)_{(T)-(Watson-Crick)}$       | 1.0475          | 0.0335                 |
| $(N^c - H^b)_{(A)-(Watson-Crick)}$       | 1.0207          | 0.0000                 |
| $(C=O^a)_{(T)-(Watson-Crick)}$           | 1.2358          | 0.0112                 |
| $(C^o - H^n)_{(A)-(Watson-Crick)}$       | 1.0874          | 0.0003                 |
| $(N^k - H^j)_{(T)-(Hoogsteen)}$          | 1.0441          | 0.0300                 |
| $(N^c - H^h)_{(A)-(Hoogsteen)}$          | 1.0185          | 0.0000                 |
| $(C=O^g)_{(T)-(Hoogsteen)}$              | 1.2346          | 0.0099                 |
| $(C^q - H^r)_{(A)-(Hoogsteen)}$          | 1.0819          | 0.0000                 |

All values in Å. Variations of hydrogen bond distances and bond lengths are expressed by  $R_{Y\cdots H}$  and  $\Delta R_{Y\cdots H}$ , respectively.

**Source:** The authors.

MP2/aug-cc-pVDZ combinations of levels of theory were used. Still in agreement with Nosenko *et al* (2013), which have used the B3LYP/6-31+G(d) theoretical level for modeling of the (TA) system, the results of 1.852 and 1.9749 Å are in better concordance with the values of 1.8303 and 1.9237 Å, respectively. Analyzing directly the values of the hydrogen bond distances presented, Table 1, it can be perceived a meaningful difference between the results of 1.8262 and 1.8060 Å for the  $(N^d\cdots H^e - N^f)_{(Watson-Crick)}$  and  $(N^k\cdots H^j - N^i)_{(Hoogsteen)}$  interac-

tions, and truly, this same systematic tendency is not verified in  $(O^a\cdots H^b - N^c)_{(Watson-Crick)}$  and  $(O^g\cdots H^h - N^c)_{(Hoogsteen)}$ , whose values are 1.9749 and 1.9959 Å, respectively.

In opposition to the best of knowledge about the intermolecular interaction strength by taking into account the bond length, the hydrogen bonds formed in the Hoogsteen moiety might be the weaker. It should be noticed that the interpretation of the intermolecular distances can be ruled by atomic requirements because the results must be shorter than the sum of the van der Waals tabulated radii, in these cases, for oxygen, nitrogen and hydrogen, whose values are 1.52, 1.55 and 1.20 Å, respectively (ROWLAND; TAYLOR, 1996). Comparing the (TA) and (TAT) structures, the distances of the  $(N^d\cdots H^e - N^f)_{(Watson-Crick)}$  and  $(N^k\cdots H^j - N^i)_{(Hoogsteen)}$  hydrogen bond in the triple helix are often shorter, and thereby, a substantial contribution to the intermolecular stability is assumed. At light of the foregoing values, for the van der Waals radius, wherein, for oxygen and hydrogen the sum is 2.72 Å, the (TA) dimer is stabilized through the  $(N^d\cdots H^e - N^f)$  and  $(O^a\cdots H^b - N^c)$  hydrogen bonds, being, then, an additional interaction between  $O^m$  and  $H^n$  shall not be expected. Through the result of 2.8672 Å for the  $(O^m\cdots H^n - C^o)$  hydrogen bond distance, this contact is not supported by the van der Waals radii and therefore might be discarded on the structural point of view. Due to the formation of the (TAT) trimer, even the shortening of the  $(O^m\cdots H^n - C^o)$  and  $(O^p\cdots H^q - C^r)$  hydrogen bond distances, whose values are -0.0707 and -0.0647 Å, at the first sight, similarly to the (TA) dimer, the (TAT) trimer should be a stable structure not only by means of the two Watson-Crick hydrogen bonds like  $(N^d\cdots H^e - N^f)$  and  $(O^a\cdots H^b - N^c)$ .

Besides the distances, the hydrogen bond strength can be also estimated by analyzing the H–X subunit. For stronger hydrogen bond and due to the charge transfer, the H–X bond length is more largely enhanced. The values of the H–X bond distances involved in the formation of the TAT complexes are listed in Table 1. In an overview, the bond lengths increase after the complexations. In (TA), the greatest  $\Delta r_{H-X}$  variation of 0.0335 Å in the  $(H^e - N^f)$  bond length agrees with the shortest hydrogen bond distances, i.e.,  $(N^d\cdots H^e - N^f)$ , and the same profile in the (TAT) trimer is also confirmed. Regarding to one of the promising hydrogen bonds,  $(O^m\cdots H^n - C^o)$ , it is likewise important to focus in the analysis of the  $(C^o - H^n)_{(T)-(Watson-Crick)}$  bond as a center for proton donating. In trimer, the value of 0.0003 Å albeit is a slight variation, surely this manifestation on proton donor bond upon the hydrogen bond

formation might be questionable. Not only  $(O^{m\cdots}H^n-C^o)$  but, the trimers also exhibit the  $(O^{p\cdots}H^q-C^r)$ -<sub>(Hoogsteen)</sub> hydrogen bond, in whose proton donors, the  $H^h-N^c$  and  $H^q-N^r$  bonds, the invariabilities of their lengths suggest that this intermolecular contact is missing, validating then the characteristic of four hydrogen bonds formed in the TAT structure.

*Infrared modes*

The values of the stretch frequencies and absorption intensities for the dimer and trimer are organized in Table 2.

**Table 2** – Values of the stretch frequencies ( $\nu^{Str}$ ), shifting frequencies ( $\Delta\nu^{Str}$ ) and absorption intensities ( $I^{Str}$ ) of the H-X and hydrogen bonds.

| (TA)                                   |             |                   |           |
|--|-------------|-------------------|-----------|
| Bonds H–X                              | $\nu^{Str}$ | $\Delta\nu^{Str}$ | $I^{Str}$ |
| $(N^c-H^b)_{(A)-(Watson-Crick)}$       | 3.413       | -68.38            | 1.083     |
| $(N^e-H^f)_{(T)-(Watson-Crick)}$       | 2.985       | -622.41           | 2.183     |
| $(C^o-H^n)_{(A)-(Watson-Crick)}$       | 3.265       | 5.12              | 5.41      |
| Hydrogen bonds                         |             |                   |           |
| $(N^d\cdots H^e)$                      | 57.04       | –                 | 3.95      |
| $(O^a\cdots H^b)$                      | 101.4       | –                 | 0.05      |
| $(O^m\cdots H^n)$                      | 57.04       | –                 | 3.95      |
| (TAT)                                  |             |                   |           |
| Bonds H–X                              | $\nu^{Str}$ | $\Delta\nu^{Str}$ | $I^{Str}$ |
| $(N^c-H^b)_{(A)-sim}$                  | 3.412       | -68.97            | 641.8     |
| $(N^c-H^b)_{(A)-assim}$                | 3.540       | -69.19            | 1.162     |
| $(N^e-H^f)_{(T)-(Watson-Crick)}$       | 2.978       | -628.61           | 2.465     |
| $(N^k-H^j)_{(T)-(Hoogsteen)}$          | 3.038       | -569.35           | 1.764     |
| $(C^o-H^n)_{(A)-(Watson-Crick)}$       | 3.193       | -3.05             | 2.58      |
| $(C^r-H^q)_{(A)-(Hoogsteen)}$          | 3.265       | 0.35              | 6.78      |
| Hydrogen bonds                         |             |                   |           |
| $(N^i\cdots H^j-N^k)_{(Hoogsteen)}$    | 66.43       | –                 | 3.25      |
| $(O^g\cdots H^h-H^c)_{(Hoogsteen)}$    | 107.8       | –                 | 0.45      |
| $(N^d\cdots H^e-N^f)_{(Watson-Crick)}$ | 66.43       | –                 | 3.25      |
| $(O^m\cdots H^n-C^o)_{(Watson-Crick)}$ | 66.43       | –                 | 3.25      |
| $(O^p\cdots H^q-C^r)_{(Hoogsteen)}$    | 66.43       | –                 | 3.25      |

Values of  $\nu$  and  $I$  are given in  $cm^{-1}$  and  $km.mol^{-1}$ , respectively.

**Source:** The authors.

With respect to the frequencies of the H–X bonds, all of them present red-shift effects in (TA) and (TAT) helices, what is in line with the variation values of the bond

lengths debated early. Important factor occurs in the  $\Delta\nu^{Str}$  red-shift of  $-622.41\text{ cm}^{-1}$  in the  $(N^e-H^f)_{(T)-(Watson-Crick)}$  oscillator, wherein its bond length was more drastically enhanced due to the shorter hydrogen bond distance, i.e.,  $(N^d\cdots H^e)_{(Watson-Crick)}$ . It seems of a weakening of the proton donor bond caused by the stronger hydrogen bonds. In the (TAT) system, the largest red-shift values of  $-628.61$  and  $-569.35\text{ cm}^{-1}$  are manifested in the  $(N^e-H^f)_{(T)-(Watson-Crick)}$  and  $(N^k-H^j)_{(T)-(Hoogsteen)}$  bonds in the pentagonal pyrimidine rings. For the oscillators of the  $(C^o-H^n)_{(A)-(Watson-Crick)}$  proton donor, the result of  $-3.05\text{ cm}^{-1}$  is the smaller red-shift. In fact, these bonds vary softly due to the complexations, wherein the blue-shifting stretching frequencies were observed (GRABOWSKI, 2011), whose values are  $5.12$  and  $0.35\text{ cm}^{-1}$ . One important event concerns to the absorption intensities, in this case, the hydrogen bond stretch frequencies often named of new vibrational modes. According to the values, there is not any systematic tendency to the interaction strength profile already discussed, in special, it must to cite the value of  $66.43\text{ cm}^{-1}$  for  $(N^d\cdots H^e)_{(Watson-Crick)}$ ,  $(O^m\cdots H^n)_{(Watson-Crick)}$  and  $(O^p\cdots H^q)_{(Hoogsteen)}$ .

*Charge transfer*

The interactions between the Y and HX species upon the hydrogen bond formation can be interpreted by the quantification of the charge transfer ( $\delta q$ ) involving the frontier molecular orbitals and assumed as flowing from the HOMO toward the LUMO. For a punctual atomic charge balance

$$\delta q_Y = q_{Y, complex} - q_{Y, monomer} \quad (2)$$

and

$$\delta q_H = q_{H, complex} - q_{H, monomer}, \quad (3)$$

the values are listed in Table 3.

The charge transfer between the frontier molecular orbitals can be useful to predict the interaction strength, in spite of some discrepancies appeared when the DNA structure has been undergone for an analysis of charge transfer mechanism (SCHUSTER, 2004). In double helix, it is notably remarkable the existence of contradictory results between NBO and ChEIPG, although for the hydrogen bond formed between  $H^e$  and  $N^d$ ,  $(N^d\cdots H^e)_{(Watson-Crick)}$ , for instance, while a variation of  $0.013\text{ e.u.}$  for the NBO charge was computed for the hydrogen, the corresponding value obtained from ChEIPG is  $-0.024\text{ e.u.}$

About the nitrogen, Table 3, however, this atom presents a negative variation of -0.009 e.u. computed from the NBO calculations whereas an equivalent positive result of 0.009 e.u. achieved from ChEIPG approach.

**Table 3** – Values of the NBO ( $q^{\text{NBO}}$ ) and ChEIPG ( $q^{\text{ChelpG}}$ ) atomic charges and the charge transfer amounts ( $\delta q^{\text{NBO}}$ ) and ( $\delta q^{\text{ChelpG}}$ ).

| (TA)  |                  |                     |                         |                            |
|-------|------------------|---------------------|-------------------------|----------------------------|
| Atoms | $q^{\text{NBO}}$ | $q^{\text{ChelpG}}$ | $\delta q^{\text{NBO}}$ | $\delta q^{\text{ChelpG}}$ |
| $N^f$ | -0.599           | -0.039              | -0.640                  | 0.159                      |
| $N^c$ | -0.829           | 0.006               | -0.863                  | 0.008                      |
| $H^b$ | 0.461            | 0.018               | 0.456                   | 0.061                      |
| $N^d$ | -0.685           | -0.009              | -0.627                  | 0.009                      |
| $H^e$ | 0.477            | 0.013               | 0.335                   | -0.024                     |
| $O^m$ | -0.639           | -0.007              | -0.631                  | -0.014                     |
| $H^n$ | 0.243            | 0.015               | 0.089                   | 0.063                      |
| $C^o$ | -0.653           | -0.050              | -0.633                  | -0.053                     |
| (TAT) |                  |                     |                         |                            |
| Atoms | $q^{\text{NBO}}$ | $q^{\text{ChelpG}}$ | $\delta q^{\text{NBO}}$ | $\delta q^{\text{ChelpG}}$ |
| $N^k$ | -0.683           | -0.007              | -0.546                  | 0.090                      |
| $H^i$ | 0.479            | 0.015               | 0.202                   | -0.157                     |
| $O^s$ | -0.645           | -0.042              | -0.627                  | -0.047                     |
| $N^i$ | -0.531           | -0.040              | -0.232                  | 0.357                      |
| $N^c$ | -0.821           | 0.014               | -1.191                  | -0.320                     |
| $N^f$ | -0.601           | -0.041              | -0.748                  | 0.051                      |
| $H^h$ | 0.460            | 0.011               | 0.555                   | 0.169                      |
| $H^b$ | 0.457            | 0.014               | 0.560                   | 0.165                      |
| $N^d$ | -0.685           | -0.009              | -0.638                  | -0.002                     |
| $H^e$ | 0.477            | 0.013               | 0.352                   | -0.007                     |
| $O^a$ | -0.646           | -0.043              | -0.638                  | -0.058                     |

All values in electronic units (e.u.)

**Source:** The authors.

In general, it can be noted that the ChEIPG charge dispenses little more feasible charge transfer results. The same behavior can be observed in the ( $O^a \cdots H^b$ ) hydrogen bond in the trimer, in which, the oxygen presents an increasing of charge (-0.043 e.u.) whereas in the hydrogen a positive variation of 0.014 e.u. is revealed, both of these values were collected from NBO calculations. On the other hand, the ChEIPG values agree with the last NBO results. Divergent values of NBO and ChEIPG were obtained for (TAT), such as the  $H^e$  which presents positive and negative varia-

tions determined by NBO and ChEIPG, respectively. Contradictory results were also found in  $N^f$ ,  $N^c$ ,  $N^i$ ,  $N^k$  and  $H^j$ . By comparing the charge transfer values of the Watson-Crick hydrogen bonds of the (TA) and (TAT) helices, slight variations were perceived, e.g., the values of 0.006 and 0.0014 e.u. for  $N^c$  in double and triple helices, respectively. For the  $N^f$  atom, this variation was -0.039 e.u. in (TA) while -0.041 e.u. in triple one, what would indicate indirectly a charge transfer, although the positive variations on the hydrogen annul the existence of the intermolecular charge flux.

#### QTAIM topography

Table 4 lists the values of the QTAIM parameters: electronic density ( $\rho$ ) and Laplacian ( $\nabla^2\rho$ ) for dimer (TA) and trimer (TAT). These parameters are obtained based on spatial integrations over a region called of Bond Critical Point (BCP), wherein the Bond Paths (BP) are generated. The Figure 5 illustrates the whole set of BCPs and BPs localized on the structures of the (TA) and (TAT) complexes. While it has been contemplated, but no certification based on structural parameters for hydrogen bond distances has been valued, regardless BCPs were located for characterization of the ( $O^m \cdots H^n - C^o$ )<sub>(Watson-Crick)</sub> and ( $O^p \cdots H^q - C^r$ )<sub>(Hoogsteen)</sub> hydrogen bonds, herein in both (TA) as well as in (TAT). Through the electronic density values of 0.005 and 0.004 e.a $\text{o}^{-3}$  followed by the Laplacian results of 0.018 and 0.019 e.a $\text{o}^{-5}$ , the electronic structure of the (TAT) trimer is formed by six hydrogen bonds. Surely, the ( $O^m \cdots H^n - C^o$ )<sub>(Watson-Crick)</sub> hydrogen bond on dimer was also identified with the electronic density values of 0.004 e.a $\text{o}^{-3}$ , and not only this, the Laplacian presents a positive value. For these hydrogen bonds, the positive values of the Laplacian are used to characterize the interactions as formed by closed-shell centers, which is considered an electronic intermolecular criterion for validating the intermolecular contact (OLIVEIRA, 2013).

About the remaining covalent bonds,  $\sigma$  or  $\pi$ , the values of electronic density are overestimated presenting also, negative results for the Laplacian, and being then, recognized as shared contacts. According to mathematical definition for the QTAIM, the electronic profile known as shared reflects values in range of  $\nabla^2\rho < 0$  as those ones belonging to high electronic concentrations regions along the BCP axis. Besides the BCPs and BPs, in Figures 5 are also listed the Ring Critical Points (RCP), which consist into a convergent representation of the elec-

**Table 4** – Values of the electronic density ( $\rho$ ) and Laplacian ( $\nabla^2\rho$ ) of the hydrogen bonds and H–X bonds.

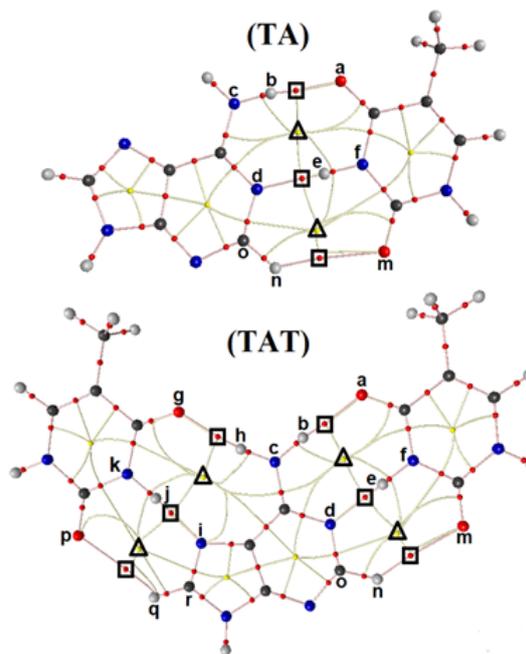
| TA   |        |                |
|--|--------|----------------|
| Hydrogen bonds   | $\rho$ | $\nabla^2\rho$ |
| (N <sup>d</sup> ...H <sup>e</sup> –N <sup>f</sup> )-(Watson-Crick) | 0.039  | 0.089          |
| (O <sup>a</sup> ...H <sup>b</sup> –N <sup>c</sup> )-(Watson-Crick) | 0.026  | 0.076          |
| (O <sup>m</sup> ...H <sup>n</sup> –C <sup>o</sup> )-(Watson-Crick) | 0.004  | 0.016          |
| Bonds H–X  | $\rho$ | $\nabla^2\rho$ |
| (N <sup>f</sup> –H <sup>e</sup> ) <sub>(T)</sub>                   | 0.308  | -1.6379        |
| (N <sup>c</sup> –H <sup>b</sup> ) <sub>(A)</sub>                   | 0.328  | -1.773         |
| (C=O <sup>a</sup> ) <sub>(T)</sub>                                 | 0.393  | -0.146         |
| (C=O <sup>m</sup> ) <sub>(T)</sub>                                 | 0.410  | -0.190         |
| (C–H <sup>n</sup> ) <sub>(A)</sub>                                 | 0.295  | -1.147         |
| TAT  |        |                |
| Hydrogen bonds   | $\rho$ | $\nabla^2\rho$ |
| (N <sup>d</sup> ...H <sup>e</sup> –N <sup>f</sup> )-(Watson-Crick) | 0.040  | 0.089          |
| (O <sup>a</sup> ...H <sup>b</sup> –N <sup>c</sup> )-(Watson-Crick) | 0.023  | 0.066          |
| (N <sup>k</sup> ...H <sup>j</sup> –N <sup>i</sup> )-(Hoogsteen)    | 0.040  | 0.096          |
| (O <sup>g</sup> ...H <sup>h</sup> –N <sup>c</sup> )-(Hoogsteen)    | 0.022  | 0.064          |
| (O <sup>m</sup> ...H <sup>n</sup> –C <sup>o</sup> )-(Watson-Crick) | 0.005  | 0.018          |
| (O <sup>p</sup> ...H <sup>q</sup> –C <sup>r</sup> )-(Hoogsteen)    | 0.004  | 0.019          |
| Bonds H–X  | $\rho$ | $\nabla^2\rho$ |
| (N <sup>e</sup> –H <sup>f</sup> ) <sub>(T)</sub> -(Watson-Crick)   | 0.307  | -1.635         |
| (N <sup>c</sup> –H <sup>b</sup> ) <sub>(A)</sub> -(Watson-Crick)   | 0.330  | -1.786         |
| (C=O <sup>a</sup> ) <sub>(T)</sub> -(Watson-Crick)                 | 0.394  | -0.138         |
| (N <sup>k</sup> –H <sup>j</sup> ) <sub>(T)</sub> -(Hoogsteen)      | 0.310  | -1.656         |
| (N <sup>c</sup> –H <sup>h</sup> ) <sub>(A)</sub> -(Hoogsteen)      | 0.332  | -1.797         |
| (C=O <sup>g</sup> ) <sub>(T)</sub> -(Hoogsteen)                    | 0.395  | -0.128         |
| (C=O <sup>p</sup> ) <sub>(T)</sub> -(Hoogsteen)                    | 0.407  | -0.213         |
| (C–H <sup>q</sup> ) <sub>(A)</sub> -(Hoogsteen)                    | 0.293  | -1.150         |

Values of  $\rho$  and  $\nabla^2\rho$  are given in e.a $\text{\AA}^{-3}$  and e.a $\text{\AA}^{-5}$ , respectively.

Source: The authors.

tronic density in cyclic electronic structures assisted by resonance.

The values of electronic density and Laplacian on RCPs are listed in Table 5. In a direct and single comparison between dimer and trimer, lower values on RCPs show that, in spite of this descriptor confirms the existence of hydrogen bonds in the cyclic structure, the most intense charge density concentrations are found on shared and closed-shell designations (BUENO; OLIVEIRA, 2014; SANTOS; REGO; OLIVEIRA, 2014).

**Figure 5** – BCPs (small black squares) and RCPs (small black triangles) in the electronic structures of the dimer.


Source: The authors.

**Table 5** – Values of the electronic density ( $\rho$ ) and Laplacian ( $\nabla^2\rho$ ) of the RCPs.

| TAT  |        |                |
|--|--------|----------------|
| RCPs   | $\rho$ | $\nabla^2\rho$ |
| O <sup>a</sup> –H <sup>b</sup> –N <sup>c</sup> –C–N <sup>d</sup> –H <sup>e</sup> –N <sup>f</sup> | 0.005  | 0.021          |
| N <sup>d</sup> –H <sup>e</sup> –N <sup>f</sup> –O <sup>m</sup> –H <sup>n</sup> –C <sup>o</sup>   | 0.003  | 0.015          |
| O <sup>p</sup> –H <sup>q</sup> –C <sup>r</sup> –N <sup>i</sup> –H <sup>j</sup> –N <sup>k</sup>   | 0.003  | 0.015          |
| N <sup>c</sup> –H <sup>h</sup> –O <sup>g</sup> –N <sup>k</sup> –H <sup>j</sup> –N <sup>i</sup>   | 0.003  | 0.013          |
| (A) <sub>imidazolic</sub>  | 0.052  | 0.412          |
| (A) <sub>pirimidinic</sub>   | 0.025  | 0.182          |
| (T) <sub>Watson-Crick</sub>  | 0.019  | 0.151          |
| (T) <sub>Hoogsteen</sub>   | 0.019  | 0.151          |
| TA   |        |                |
| RCPs   | $\rho$ | $\nabla^2\rho$ |
| O <sup>a</sup> –H <sup>b</sup> –N <sup>c</sup> –C–N <sup>d</sup> –H <sup>e</sup> –N <sup>f</sup> | 0.003  | 70.013         |
| N <sup>d</sup> –H <sup>e</sup> –N <sup>f</sup> –O <sup>m</sup> –H <sup>n</sup> –C <sup>o</sup>   | 0.005  | 0.021          |
| (A) <sub>imidazolic</sub>  | 0.053  | 0.411          |
| (A) <sub>pirimidinic</sub>   | 0.025  | 0.182          |
| (T) <sub>pirimidinic</sub>   | 0.020  | 0.151          |

Values of  $\rho$  and  $\nabla^2\rho$  are given in e.a $\text{\AA}^{-3}$  and e.a $\text{\AA}^{-5}$ , respectively.

Source: The authors.

### Interaction energy

In Table 6 are listed the values of the interaction energies in the dimers (TA) and (TAT) trimers.

**Table 6** – Values of the electronic density ( $\rho$ ) and Laplacian ( $\nabla^2\rho$ ) of the RCPs.

| Systems                        | Energies |        |              |
|--------------------------------|----------|--------|--------------|
|                                | BSSE     | ZPE    | $\Delta ZPE$ |
| (A)                            | –        | 294.67 | –            |
| (T)                            | –        | 300.97 | –            |
| (AT) <sub>(Watson-Crick)</sub> | 2.65     | 599.77 | 4.11         |
| (TAT)                          | -74.93   | 904.54 | 7.91         |

| Systems                        | Energies  |            |              |
|--------------------------------|-----------|------------|--------------|
|                                | E         | $\Delta E$ | $\Delta E^C$ |
| (A)                            | -467.35   | –          | –            |
| (T)                            | -454.17   | –          | –            |
| (AT) <sub>(Watson-Crick)</sub> | -921.54   | -56.95     | -50.18       |
| (TAT)                          | -1,375.73 | -108.59    | -175.61      |

Values of BSSE, ZPE,  $\Delta ZPE$ ,  $\Delta E$  and  $\Delta E^C$  are given in  $\text{KJ.mol}^{-1}$ . Values of E are given in Hartree.

**Source:** The authors.

The unusual discrepant BSSE amount of  $-74.93 \text{ KJ.mol}^{-1}$  was obtained in the trimer (TAT) (SHERRILL, 2017). In the (TA) dimer, the BSSE value of  $2.65 \text{ KJ.mo}^{-1}$  is much more acceptable. Through the corrected values of the hydrogen bond energies, the ternary structure (TAT) presents an overestimated electronic stability in comparison to that in dimer (TA). Regardless the BSSE result, this scenery is quite similar to the uncorrected interaction energy values (AVIÑÓ *et al.*, 2002), or even if the correction is performed only by means of the ZPE results.

### Conclusion

Through the analysis of the structural parameters useful for characterizing the double and triple DNA helices, the last one is the most stable structure. Even though is widely known that two hydrogen bonds stabilize the dimer backbone, and notwithstanding the results of interaction distances are in line with this statement, QTAIM calculations characterized one additional hydrogen bond. Regarding the triple helix, two new hydrogen bonds were identified, being, both formed in conformity with the Hoog-

steen proposition. The analysis of this current work also revealed come inconsistencies, in particular relating the NBO and ChEIPG methods for atomic charge calculation carried in order to unveiling the intermolecular charge transfer. At light of spectroscopy infrared analysis, the hydrogen bond stretch frequencies were identified and examined, and mainly, the rising of red- and blue-shift effects on the proton donor subunits of the (TA) and (TAT) complexes.

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