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Short Communications

The Molecular Electrostatic Potential of the B-DNA Helix

II. The Region of the Adenine-Thymine Base Pair

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The electrostatic molecular potential minima around the adenine-thymine base pair within a B-DNA helix are computed, taking into account the contributions of the sugar-phosphate backbone and of the adjacent base-pairs. The deepest potential in the pair is associated with N_3 of adenine. It is less deep than that associated with the guanine moiety in a G-C pair, as studied in paper I of the series. The potential in the vicinity of the NH_2 group of adenine is falling between those around the NH_2 groups of guanine and cytosine in the G-C pair. The order of affinity towards electrophilic agents of the NH_2 groups of guanine, adenine and cytosine incorporated in complementary base pairs into the B-DNA helix correlates with the reactivity of these bases in DNA towards the triol carbonium ion of benzo[a]pyrene, considered as the ultimate metabolic carcinogen derived from that hydrocarbon.

Key words: Electrostatic potential – Adenine-thymine pair – Carcinogenic metabolites

In the first paper of this series [1] we have computed the electrostatic molecular potential minima around the guanine-cytosine base pair within a B-DNA mini-helix, taking into account the contributions of the sugar phosphate backbone and of the adjacent base-pairs. In the present note this work is extended to the adenine-thymine pair placed in similar conditions (Fig. 1). The procedure adopted is strictly the same as in Ref. [1] and we describe therefore directly the results obtained.

Table 1 presents the effect of the two sugar-phosphate backbones of the helix upon the potential of the central A-T pair. In this approximation the effect of the adjacent base pairs is neglected. The table indicates the regions of the minima of the electrostatic potentials, compared to the minima found previously for the separate A and T bases [2] and the isolated A-T pair [3]. The most striking effect associated

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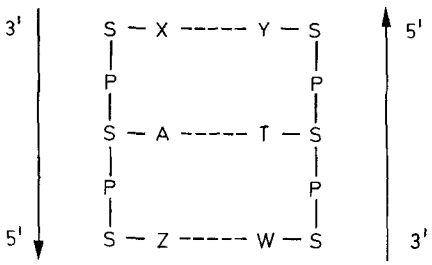

Fig. 1. Model compound considered in the computations. S and P stand for deoxyribose and phosphate respectively; X, Y, Z and W could be either adenine, thymine, guanine or cytosine

Table 1. Electrostatic potential minimum (in kcal/mole) at different sites of the central A-T pair in the mini B-DNA of Fig. 1 taking into account the sugar-phosphate backbone. The stars point out the positions of deepest minima. The numbering of the sites corresponds to standard notations of nucleic acids, the letters within parentheses refer to the nature of the base. The minima are in the plane of the bases and base pairs except for those corresponding to the NH_2 group of adenine; for this group the numbers 3' or 5' indicate the side at which they are located (see Fig. 1). The effect of the adjacent base pairs is not included here.

Sites	Single bases	Paired bases	Paired bases within B-DNA
N7(A)	−67.5	−70.5	−218.7
N3(A)	−71.8*	−72.7*	−238.5*
04(T)	−58.7	−47.7	−179.5
02(T)	−55.9	−61.9	−228.3
N6(A)3'	−15.6	−21.1	−158.2
N6(A)5'	−15.6	−21.1	−157.9

with the incorporation of the base pair into the helix is undoubtedly, as it was the case for the G-C pair, the very strong increase in the absolute values of the potential minima, reflecting the parallel increase of the affinity of the bases towards electrophilic agents. The situation obviously corresponds to the penetration of the strong potential of the phosphates [4] into the vicinity of the bases and its superposition upon the potential inherent to the bases themselves. Because of the disappearance in the base pair of the potential minimum close to the N_1 atom of adenine in the free base it is not astonishing to find the deepest minimum to be in the vicinity of N_3 of adenine. This global minimum is somewhat less deep than that associated with the guanine base in the G-C base pair [1] and this correlates satisfactorily with the usual greatest reactivity of guanine towards electrophilic agents in nucleic acids [5]. Worth noting is the inversion in the ordering of the two minima around O_4 and O_2 of thymine between the free base and the base paired with adenine [3]: the deeper minimum is associated with O_4 in the former case and with O_2 in the latter. The situation may be related to the binding of a Na^+ ion between two O_2 atoms from neighbouring uracil residues (on two strands) observed in the double stranded crystal structure of ApU [6].

The potential in the vicinity of the NH_2 group of adenine (above and below that group) deserves a special mention. Considered as a secondary site for electrophilic attacks, this group is in fact associated with a relatively very weak potential in the isolated base, although stronger than that of the NH_2 groups of isolated guanine

Table 2. Total electrostatic potential (in kcal/mole) at the electrophilic sites of the central A-T pair, due to the contributions of the phosphate-sugar backbone and of the three base pairs. The horizontal bar symbolizes the central A-T pair. The arrows indicate the 3′ to 5′ directions of the double helix. The stars point to the global minima

Sites	G-C ↑ / ↓ G-C	G-C ↑ / ↓ C-G	C-G ↑ / ↓ G-C	C-G ↑ / ↓ C-G	A-T ↑ / ↓ A-T	A-T ↑ / ↓ T-A	T-A ↑ / ↓ A-T	T-A ↑ / ↓ T-A
N7(A)	−237.4	−227.7	−225.0	−215.3	−224.1	−224.1	−222.0	−222.0
N3(A)	−247.7*	−235.6*	−247.6*	−235.5	−245.2*	−243.5*	−245.5*	−243.8*
O4(T)	−188.3	−201.7	−185.4	−198.8	−186.6	−190.1	−186.1	−189.6
O2(T)	−225.6	−225.9	−237.4	−237.7*	−233.7	−233.7	−235.0	−235.0
N6(A)3′	−181.3	−182.0	−177.7	−178.4	−173.3	−174.3	−172.6	−173.6
N6(A)5′	−175.9	−175.7	−170.9	−170.7	−168.1	−168.1	−165.6	−165.6

Sites	G-C ↑ / ↓ A-T	G-C ↑ / ↓ T-A	C-G ↑ / ↓ A-T	C-G ↑ / ↓ T-A	A-T ↑ / ↓ G-C	A-T ↑ / ↓ C-G	T-A ↑ / ↓ G-C	T-A ↑ / ↓ C-G
N7(A)	−230.5	−230.5	−218.1	−218.1	−231.0	−221.3	−228.9	−212.6
N3(A)	−241.6*	−239.9*	−241.5*	−239.8	−251.3*	−239.2*	−251.6*	−239.5*
O4(T)	−190.4	−193.9	−187.5	−191.0	−184.5	−197.9	−184.0	−197.4
O2(T)	−229.1	−229.1	−240.9	−240.9*	−230.2	−230.5	−231.5	−231.8
N6(A)3′	−175.9	−176.9	−172.3	−173.3	−178.7	−179.4	−178.0	−178.7
N6(A)5′	−174.2	−174.2	−169.2	−169.2	−169.8	−169.6	−167.3	−167.1

(which is even repulsive) and cytosine ($\simeq -7$ kcal/mole [1]). In the isolated complementary base pairs A-T and G-C, the potential in the vicinity of the NH_2 group of adenine (−21.1 kcal/mole) remains deeper than that of guanine (−19.4 kcal/mole) and of cytosine (−13.8 kcal/mole) [1]. However, when the base pairs are incorporated into the model nucleic acid helices the situation changes and the potential in the vicinity of the NH_2 group of adenine ($\simeq -158$ kcal/mole) is now intermediate between that of guanine ($\simeq -171$ kcal/mole) and that of cytosine ($\simeq -150$ kcal/mole). The importance of this situation is linked with the recent interesting findings that the metabolites of carcinogenic polycyclic aromatic hydrocarbons, such as the 7,8-dihydrodiol-9,10-oxide of benzo[a]pyrene and the triol carbonium cation derived from it by the opening of the epoxide ring, considered by many as the probable ultimate carcinogenic forms of this hydrocarbon, interact *in vitro* and *in vivo* with the NH_2 groups of DNA in decreasing order guanine > adenine > cytosine [7–10]. This order correlates with the affinity for electrophiles of these groups when incorporated with the model mini-DNA helices studied here and in conjunction with results on the steric aspects of the interaction between the metabolite and the model helices [11] suggests that the electronic factors put into evidence here could possibly be responsible for the observed ordering of the interaction.

As it was the case with the G-C pair the effect of the adjacent base-pairs is minor and the addition of its contribution (Table 2) does not change the general aspects of the results described above.

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