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Short Communication

Relationes

The Molecular Electrostatic Potentials of the Complementary Base Pairs of DNA

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The perturbations in the molecular electrostatic potentials of the bases of the nucleic acids, brought about by hydrogen-bonding into complementary pairs are evaluated by a superposition procedure.

Key words: DNA, complementary base pairs of ~

The molecular electrostatic potential [1] created in the surrounding space by the electron density distribution and the set of nuclear charges of a molecule has proven a very useful tool for discussing the possible sites of electrophilic attacks on large heterocycles [2]. In previous papers [3, 4, 5] we have given and discussed from this point of view the molecular potentials of the bases of the nucleic acids: adenine, guanine, cytosine, thymine and uracil computed from *ab initio* wave functions. In the present work we investigate the modifications in the molecular potentials of the individual bases brought about by their pairing through hydrogen bonding in the Watson–Crick complementary scheme of DNA: adenine–thymine and guanine–cytosine.

The computation of the molecular potential of the base pairs has been performed by a simple superposition, in the regions considered, of the individual potentials of the two molecules placed in the appropriate relative orientations. Such a procedure has been shown, in a detailed study of small hydrogen-bonded systems [6], to reproduce very satisfactorily all the qualitative features of the modifications of the potential of the two partners upon hydrogen bonding.

The most interesting regions to consider are the ones surrounding the minima of the potentials of the isolated bases in the most attractive regions, which are situated in the molecular plane in the neighbourhood of N_1, N_3 and N_7 of adenine, N_7,

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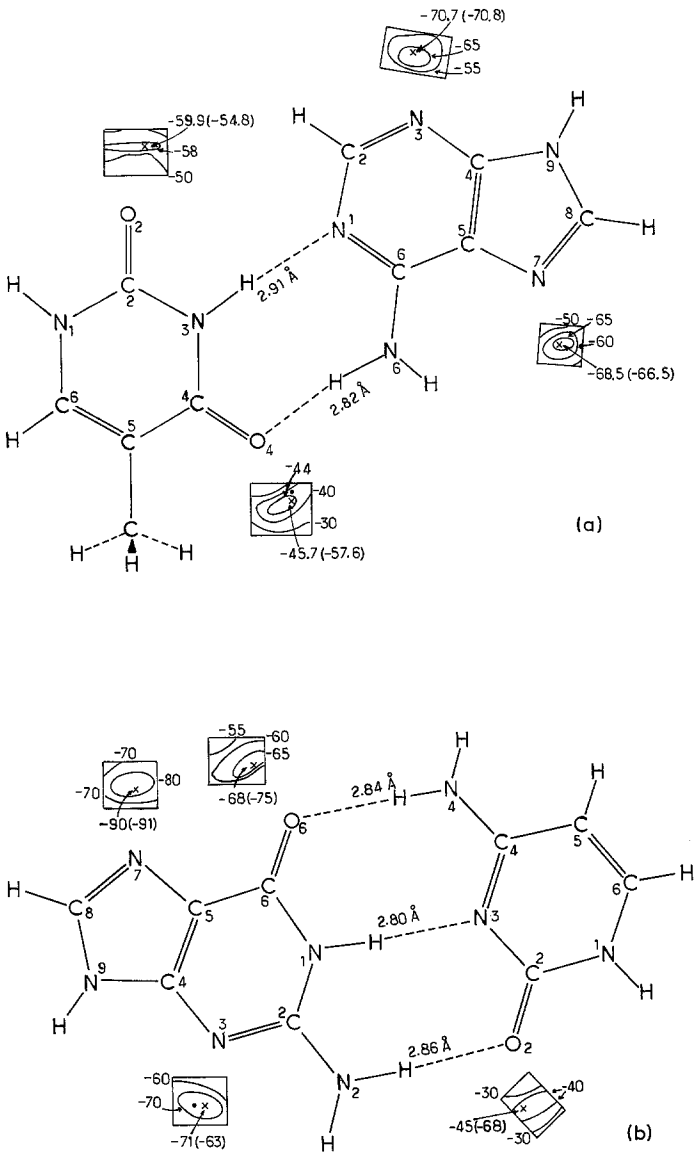

Fig. 1. The molecular potential in the most attractive in-plane regions of the complementary base pairs of DNA (a) adenine–thymine; (b) guanine–cytosine.

The potential minimum in the pair is indicated by a cross. The values in parentheses are the corresponding minima in the isolated bases. (The positions are the same except where indicated by a dark dot.) The wave functions utilized for computing the potential values are those of Ref. [8], that of cytosine was recomputed with the same basis using the experimental geometry [9]. The distances adopted between the end atoms in each hydrogen bond are as indicated

O_6, N_3 of guanine, N_1, O_2 of cytosine and O_4, O_2 of thymine (in the order indicated for each base).

When the two bases of the pairs, adenine–thymine or guanine–cytosine, are placed in the appropriate orientation, a supplementary potential due to the partner appears in each zone and modifies the global distribution. The resulting potentials obtained for the two base pairs are given in Fig. 1. Only the regions surrounding the minima situated outside the regions of the hydrogen bond are given because there are the zones where the most negative potential wells remain. In the regions situated along the hydrogen bonds themselves (N_3 of cytosine, N_1 of adenine; O_6 of guanine, O_4 of thymine) the negative potential of the isolated base is essentially cancelled (or nearly so) by the strong repulsive potential of the partner (see Ref. [6] for a detailed study of this phenomenon) and the remaining attractive character – if any – is much smaller than in the other regions so that it presents little interest in the present study.

The results indicate that

1) the positions of the potential minima are very little modified with respect to those in the isolated molecules.
2) the order of the most attractive positions is

$$N_7(G) > N_3(G) \simeq O_6(G) > O_2(C) \quad \text{in the G–C pair}$$
$$N_3(A) > N_7(A) > O_2(T) > O_4(T) \quad \text{in the A–T pair,}$$

with N_7 of guanine remaining the most attractive of all the positions. In more detail, it is observed that the molecular potential of adenine in the N_3 and N_7 regions is relatively little modified by the pairing with its partner. The same is true of the potential minimum close to N_7 of guanine whereas the region close to O_6 sees its attractive character decreased by the proximity of the repulsive NH_2 region of cytosine. Conversely, the attractive potential in the N_3 region of guanine is increased by the influence of the strong attractive character of cytosine. It is interesting that in spite of a very analogous relative disposition of O_2 of thymine and N_3 of adenine, no similar enhancement of the potential in the N_3 region of adenine is seen, due to the less attractive character of thymine in this area.

On the two pyrimidines, the oxygen atom involved in hydrogen bonding undergoes a decrease of its attractive character (stronger for cytosine). Moreover, in thymine, the oxygen which does not take part in the pairing undergoes an increase of its attractive character with respect to the situation in the isolated base, to the extent that this oxygen is, in the A–T pair, the most attractive of the two oxygens of thymine (the situation was inverse in the isolated base).

This 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 crystal structure of ApU [7].

References

1. Bonaccorsi, R., Scrocco, E., Tomasi, J.: J. Chem. Phys. **52**, 5270 (1970)
2. Pullman, A., in: Chemical and biochemical reactivity, Proc. of the VI'th Jerusalem Symposium, E. D. Bergmann and B. Pullman Eds., p. 402. New York: Academic Press 1974

3. Bonaccorsi, R., Pullman, A., Scrocco, E., Tomasi, J.: Theoret. Chim. Acta (Berl.) **24**, 51 (1972)
4. Bonaccorsi, R., Scrocco, E., Tomasi, J., Pullman, A.: Theoret. Chim. Acta (Berl.) **36**, 339 (1975)
5. Perahia, D., Pullman, A., Pullman, B.: Theoret. Chim. Acta (Berl.) **42**, 23 (1976)
6. Pullman, A., Berthod, H.: Theoret. Chim. Acta (Berl.), in press
7. Rosenberg, J. M., Seeman, N. C., Kim, J. J. P., Suddath, F. L., Nicolas, H. B., Rich, A.: Nature **243**, 150 (1973)
8. Clementi, E., André, J. M., André, M. Cl., Klint, D., Hahn, D.: Acta Phys. Acad. Sci. Hung. **27**, 493 (1969)
9. Barker, D. L., Marsh, R. E.: Acta Cryst. **17**, 1581 (1964)

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