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ATOMIC COORDINATES AND CALCULATED INTENSITIES FOR A SIDE BY SIDE D.N.A. MODEL.

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Summary. A precise conformation of the side-by-side type is proposed for the B-D.N.A. form. In this model the antiparallel chains are related by a dyadic symmetry and binding between complementary bases is realized using Watson-Crick pairing. The elementary unit, comprising 10 nucleotides for one chain, is composed of one segment in a right handed helix, a second segment rotated to the left and two bends. Cylindrical atomic coordinates are given for atoms in the elementary unit and the square of the Fourier transform is calculated for this conformation and compared to the well known double helix and to experimental data.

Introduction.X-ray measurement on crystalized fragments of D.N.A. allowed to propose a new conformation for the D.N.A. double strand. This conformation is very different from the Crick-Watson B-D.N.A. form as it takes the form of a left handed helix (1). Left handed helices seem to be also possible in synthetic D.N.A. fibres (2). These facts increase the interest for D.N.A.conformations presenting simultaneously right and left handed helices e.a side-by-side models. For the two different proposed models (3) (4) the segments of right and left handed helix are each composed by five base pairs which are associated as in Watson Crick model. What differentiates these two conformations is essentially that for type I, sugar rings are C(3) endo for nucleotides in left handed helical segments and C(3) exo for right handed ones, but they are always C(3)exo for the type II. As a consequence in the type I the oxygen atoms of the sugar rings have the same orientation and in type II they are alternatively up and down. Side-by-side models are proposed in very general forms ; no precise atomic coordinates are given and thus comparisons with experimental data as well as with the double helix model can only treat overal features. Moreover the two methods used (3) (5) for calculations of diffracted intensities give results which do not agree. In the present paper a completely defined side-by-side model for D.N.A. is given which allows precise calculations of diffracted intensities.

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As we encountered difficulty when trying to build the type I structure (essentially for nucleotides in helix rotating to the left) we propose atomic coordinates for a D.N.A. conformation similar to the type II. Cylindrical coordinates as well as Fourier transforms are determined for a stereochemically possible conformation of the bicatenary molecule. Curves of the diffracted intensities are therefore calculated and compared to experimental data and to values associated with the double helix model in its B form.

Method. a) Geometrical conditions. In order to define with precision a D.N.A. conformation similar to the type II it is necessary to impose some detailed characteristics of the structure. Firstly, the two antiparallel sugar-phosphate chains and the stacking of the complementary bases must present a good stereochemistry. Sugar rings are put in their C(3) exo conformation which is the admitted one for the B-D.N.A. form (6) but, as sugar rings present great flexibility (7) perturbations of their conformations are allowed during the process of improvement of the chain conformation. The 3.4 Å distance along the axis is a characteristic parameter for the B-D.N.A. revealed by X-ray diffraction. In the proposed conformation the 3.4 Å distance should be found essentially in the interval between successive base-pairs which will be maintened perpendicular to the axis of the structure. Another important feature observed on X-ray patterns is the regular interval between layer lines corresponding to an axial distance of 34 Å. In the double helix model this distance corresponds to the height of 10 pairs of nucleotides. Therefore in the new conformation, the repetitive unit will be constituted by 10 nucleotides per chain. Indeed this conformation will present alternation of three nucleotides on a right handed helix and three nucleotides on a left handed one. These segments will be separated by two types of bends corresponding respectively to the right handed to left handed helix transition and vice-versa. Each bend will be composed of two nucleotides. The 10 nucleotides unit on a chain must be associated with a complementary unit on the antiparallel chain. This condition imposes the existence of a dyad axis perpendicular to the axis of the structure ; moreover, in order for obtaining units of ten nucleotide pairs which exactling repeat through a translation of 34 Å along the main axis, the dyad axis in the right and left segments must have the same direction. For the beginning of the chain, one imposes the geometrical parameter of the B-D.N.A. double helix form (6) to nucleotides in right handed helix. Moreover the axis of the structure must also be the axis for the right handed segments of the chain. Nevertheless, if one retains the dihedral angles of the B-D.N.A. form for the left handed segments of the chain, these latter will present axes with directions very far from the axis of the structure. It will thus be almost impossible to superpose the axes of the successive right handed helical segments. As a consequence, the dihedral angles of nucleotides in left handed segment will be modified taking into account the imposed geometrical conditions.

b) Model building. Computations of atomic coordinates are performed with a procedure previously used (8) ; bond lengths and valence angles used are those listed by Arnott (9). Dihedral angles corresponding to nucleotides in the left handed segments and in the bends are to be determined but one should note that the number of constraints on the system does not allow an easy computation of these angles. This is why a kind of Kendrew molecular model was built in order to evaluate the unkown dihedral angles. Buth such a model does not permit precise measurements and, moreover as atomic space filling is not materialized it hardly gives a good idea about the stereochemistry of a conformation. Nevertheless this model give approximate values of the dihedral angles which can be used as starting data for computations of the cylindrical coordinates of atoms. With the computed coordinates one can test the conformation as regards the different constraints : if the stereochemistry is good, one has to verify whether the binding of complementary bases is possible. In fact a conformation verifying the imposed constraints and presenting an acceptable stereochemistry, is progressively obtained by going back and forth between the model and the computer and vice-versa.

c) Fourier transform. The computation of the theoretical values of intensities diffracted by the new D.N.A. conformation is performed using the same expressions as for the double helix model (10) (8). Thus, due to the dyadic symmetry between complementary chains, the following simplified expression can be used for the structure factors on the layer line ℓ (11) :

$$F(\ell,\xi) = \sum_n \sum_j f_j \, J_n(2\pi R_j \xi) \cos\left(\frac{2\pi \ell z_j}{c} - n\Phi_j\right) = \sum_n A_n(\ell,\xi)$$

where ξ is the radial coordinate in reciprocal space and R_j, Φ_j, z_j the cylindrical coordinates of the atoms in the ten nucleotides unit. Order n of Bessel functions J_n are defined according to the rule : $\ell = n t + m u$ with m a positive, negative or null integer. For the present computations n is taken from -13 to $+13$ for all values of ℓ because here $\ell = n + m$. Atomic scattering factors f_j are those given by Fraser (12). The diffracted intensities averaged over the orientation angle in reciprocal space is calculated as (8) : $I(\ell,\xi) = \sum_n A_n^2(\ell,\xi)$.

Results. In the best conformation obtained sugar rings in nucleotides 1 and 2 are in the B-D.N.A. double helix form. The first bond is realized between the sugar rings of nucleotides 3 and 4. The nucleotides 5, 6 and 7 are on a pseudo left handed helix. The second bend is formed between the sugar rings of nucleotides 8 and 9. Finally the sugar ring of nucleotide 10 takes the conformation of the B-D.N.A. double helix. It was necessary to modify the conformations of the sugars in the bends in order to maintain the imposed geometry. Hence, the conformations of sugar rings of nucleotides 3 and 8 remain very near to C(3) endo. They correspond respectively to base interval of 3.58 Å for the first bend and 3 Å for the second one ; this last value is due to constraints for association between complementary bases in the two antiparallele strands ; bases complementary to bases of the second bend must be in the conformation of the bases in the first bend (dyadic symmetry). The chain of ten nucleotides constituting a unit present a distance of 34.4 Å along the main axis. Successive units are obtained only by a 34.4 Å translation along this axis and

Table I. Chain dihedral angles for the nucleotides of the unit.

Nucleotide number	DIHEDRAL ANGLES(about atomic bond)						
	$\theta^{(o)}$ (O_4-C_5)	$\xi^{(o)}$ (C_5-C_4)	$\sigma^{(o)}$ (C_4-C_3)	$\omega^{(o)}$ (C_3-O_1)	$\phi^{(o)}$ (O_1-P)	$\psi^{(o)}$ $(P-O_4)$	$\chi^{(o)}$ (C_1-N)
1 right handed helix	-146.5	36.4	156.5	154.7	-95.6	- 46.1	150.5
2	-146.5	36.4	156.5	155.7	-93.6	- 70	150.5
3 $1^{\underline{st}}$ bend	-144	34.4	83	- 174	15	-168	124.6
4	-160	36.4	145	96	-87	- 80	112.6
5 left handed segment	-130	45	149	133	-96	- 84.5	72.2
6	-122	33.4	154.5	140	-100	- 89	71.6
7	-124	32	153.5	140	-111	5	75.5
8 $2^{\underline{nd}}$ bend	170	- 24.6	107	58.5	-12	-175	16
9	-172	157.5	149.5	169	-77.6	- 67	121
10 right handed helix	-146.5	37.4	156.5	154.7	-95.6	- 46.1	138.9

thus dyadic axis in right and left handed segments have the same orientation. The complementary chain is easily obtained with a Watson-Crick bases association. Pairs of bases are almost perpendicular to the main axis. Dihedral angles along the sugar phosphate chain are given in table I. Progression is done in the 5-3 direction and values correspond to Arnott conventions (9). Cylindrical coordinates for atoms in the unit are given in table II. It can be noted that the mean interval between bases is of the order of 3.4 Å with limiting values of 3 Å and 4.3 Å. In fig. 1 are given curves of the square of the Fourier transform corresponding to this D.N.A. conformation.

Discussion. The proposed conformation has been difficult to realize, it still presents irregularities, mainly in spaces between bases. The total height of 34.4 Å for one unit is very near to the experimental value. The Watson-Crick type of bases association is maintained and dyad axes in same direction for right and left handed segments allow an easy determination of the complementary chain and avoid a superhelical distorsion of the conformation. Interatomic distances are as satisfactory as in the B-double helix model ; one should note that one sugar ring in each bend has to be C(3) endo in order to avoid bad interatomic contacts. Residues 4 and 8 exhibit unusual values for the ω angles (table I). These values are necessary for the bending of the sugar-phosphate chain and are therefore inherent to the present model. Moreover a similar value for ω has

Table II. Cylindrical coordinates for nine nucleotides of an unit. (the coordinates of first nucleotide can be obtained by removing 3.38 Å from z_j and 36 Å from Φ_j of nucleotide 2).

ATOM	NUCLEOTIDE 2			NUCLEOTIDE 3			NUCLEOTIDE 4		
	R_j (Å)	Φ_j (o)	z_j (Å)	R_J (Å)	Φ_j (o)	z_j (Å)	R_j (Å)	Φ_j (o)	z_j (Å)
O_4	7.72	-52.95	2.08	7.70	-17.36	5.48	8.21	-10.60	9.70
C_5	7.68	-44.83	1.14	7.93	- 7.77	4.92	8.35	-16.15	10.89
C_4	7.57	-34.87	1.86	7.64	0.51	5.89	7.60	-25.57	10.82
O_5	6.22	-30.63	2.02	6.33	5.49	5.69	6.23	-24.72	11.28
C_3	8.19	-34.88	3.26	7.75	- 2.11	7.37	7.58	-36.47	9.44
C_2	7.02	-38.40	4.13	6.86	6.26	8.01	6.15	-28.36	8.97
C_1	5.79	-32.06	3.36	5.67	6.91	6.94	5.34	-26.58	10.18
N	4.58	-41.71	3.36	4.46	- 3.07	6.88	4.58	-11.75	10.11
O_1	8.74	-26.36	3.64	9.10	- 1.81	7.81	7.99	-40.49	9.51
P	8.92	-24.25	5.19	9.46	- 4.71	9.30	7.09	-50.55	9.52
O_2	10.23	-20.35	5.40	9.74	2.33	10.15	8.02	-58.12	8.95
O_3	9.0	-32.33	5.96	10.72	- 9.05	9.28	5.86	-49.41	8.70
	NUCLEOTIDE 5			NUCLEOTIDE 6			NUCLEOTIDE 7		
O_4	6.80	-52.13	11.08	6.93	- 93.49	14.43	7.29	-131.44	18.1
C_5	7.88	-55.52	11.93	7.96	- 94.04	15.44	8.23	-132.28	19.18
C_4	7.56	-64.54	12.77	7.80	-102.71	16.35	8.01	-141.01	20.02
O_5	6.62	-61.90	13.83	6.86	-100.48	17.42	7.02	-139.28	21.04
C_3	7.10	-74.40	12.03	7.47	-112.81	15.70	7.70	-150.48	19.27
C_2	5.60	-75.42	12.25	5.96	-114.60	15.83	6.19	-152.13	19.34
C_1	5.36	-67.38	13.53	5.67	-107.26	17.20	5.84	-145.74	20.71
N	4.41	-53.75	13.55	4.56	- 96.05	17.19	4.67	-134.35	20.74
O_1	7.89	-82.65	12.60	8.22	-120.01	16.40	8.43	-157.85	19.91
P	7.34	-93.93	12.89	7.83	-131.02	16.59	8.03	-168.64	19.99
O_2	8.57	-99.53	12.63	9.14	-135.53	16.41	9.26	-173.08	19.50
O_3	6.25	-97.86	12.00	6.87	-135.01	15.59	6.88	-171.59	19.14
	NUCLEOTIDE 8			NUCLEOTIDE 9			NUCLEOTIDE 10		
O_4	7.76	-170.15	21.55	7.44	-169.23	26.14	7.68	-128.95	30.24
C_5	7.75	-161.58	22.40	7.96	-165.04	27.36	7.78	-121.43	29.22
C_4	7.21	-164.21	23.77	7.74	-154.14	27.48	7.57	-111.06	29.78
O_5	6.57	-154.32	24.3	6.48	-150.09	26.97	6.21	-106.89	29.73
C_3	6.38	-175.05	23.83	7.89	-150.02	28.89	8.04	-109.87	31.23
C_2	5.14	-171.45	24.64	6.45	-149.74	29.39	6.77	-112.60	32.01
C_1	5.39	-157.08	25.03	5.61	-147.05	28.04	5.65	-106.76	31.04
N	4.62	-142.41	24.95	4.53	-158.68	28.00	4.43	-116.53	30.99
O_1	7.27	-182.97	24.41	8.67	-141.80	28.90	8.57	-100.96	31.50
P	7.79	-180.85	25.90	8.88	-136.30	30.24	8.61	- 97.38	33.01
O_2	9.26	-181.68	25.94	10.20	-132.31	30.16	9.95	- 93.78	33.26
O_3	7.25	-188.65	26.82	8.94	-142.25	31.40	8.49	-105.03	33.94

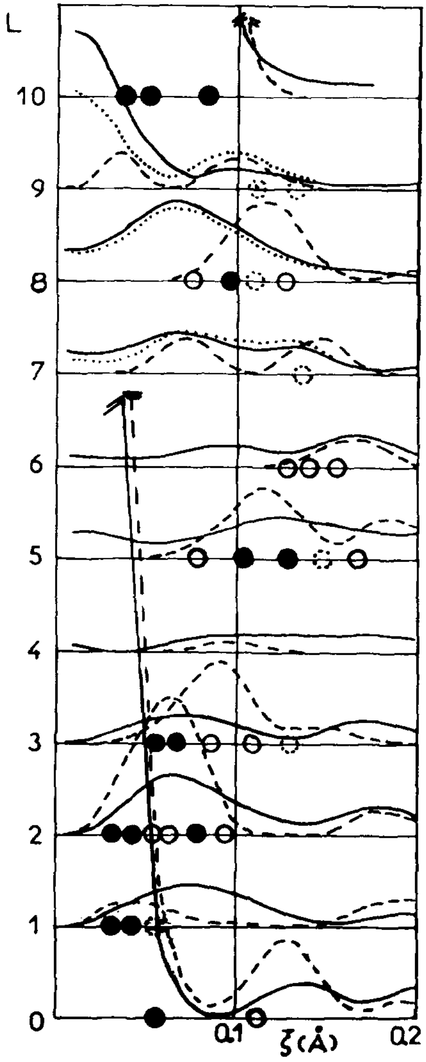

Figure 1. Curves of the square of Fourier transform associated with the new model (———) ; this model with bases perpendicular to the axis (....) ; curves for the B-D.N.A. Watson-Crick double helix (------). Spots indicate experimentally observed intensities. ● strong, O medium and ⁘ weak (11).

been found experimentaly (13). Improvements of this conformation could be obtained with refinement methods taking dihedral angles as variables. In that way left handed segments could be given a more regular conformation. Dihedral angles of the right handed segment (helix) could also be modified in order to decrease the interval between bases 7 and 8. Nevertheless it seems difficult to improve spaces between the bases near the bends as long as constraints are maintained on the geometry of the system. Note that the obtained conformation fits well to the orthorhombic lattice in the space group $P2_1 2_1 2_1$ e.a. the two molecules in the lattice have their dyad axis in the a direction and one is translated in the c direction with one third of the unit height (ten pairs of bases). Irregularities in the geometry, mainly in spaces between bases, introduce defects in the calculated intensities. Although layer lines 0 and 10 do agree with experiment as the double helix model, layer lines 1,2,6 and 8 presents wide maxima which could permit the existency of intensity spots (taking into account the lattice) which are not indeed observed. Moreover calculated curves present meridian values not equal to zero on layer lines 5,6,7,8 and 9 ; such intensities are not observed with B-D.N.A. These last results agree with conclusions presented recently (5) but the present completely defined side-by-side model furnishes a good starting point for an eventual refinement procedure. Atomic coordinates given for the proposed D.N.A. conformation allow precise calculations and shown that the side-by-side model is a realistic one as concerns the stereochemistry but the calculated intensity curves do not match as well to experimental data as for the double helix. Nevertheless, improvement are possible mainly by increasing the regularity of the present model ; one can already note that the Fourier curves of high order layer lines are improved when bases are maintained perpendicular to the axis of the system (Fig.1).

References

1. Wang,A.H.J., Quigley,G.J., Kolpak,F.J., Crawford, J.L., VanBoom, J.H., Van der Marel,G. & Rich,A.(1979),Nature 282, 680-686.
2. Arnott,S., Chandrasekaran, R., Birdsall, D.L., Leslie, A.G.W. & Ratliff, R.L. (1980), Nature 283, 743-745.
3. Bates, R.H.T., Levitt, R.M., Rowe, C.H., Doy,J.P. & Rodley, G.A. (1977), J.Royal Soc.(New Zeland) 7, 3, 273-301.
4. Sasisekharan, V. & Pattabiraman, N.(1976), Current Sci.,45; 779-783.
5. Greenall, R.J., Pigram,W.J. & Fuller, W.(1979), Nature 282,20-27.
6. Arnott, S. & Hukins, D.W.L. (1972), Biochem.Biophys.Res.Commun., 47, 1504-1509.
7. Levitt, M. & Warshal, A.(1978), J.Amer.Chem.Soc.,100, 2607-2613.
8. Premilat, S. & Albiser, G.(1975), J.Mol.Biol.,99, 27-36.
9. Arnott, S.(1970), In Progress in Biophys.& Mol.Biol.,21,265-319.
10. Cochran, N., Crick, F.M.C.& Vand,V.(1952), Acta Cryst., 5,581-586.
11. Langridge, R., Wilson, H.R., Hooper, G.W. & Wilkins, M.H.F., (1960), J.Mol.Biol., 2, 19-64.
12. Fraser, R.D.B., MacRae, T.P. & Suzuki, E.(1978), J.Appl.Cryst., 11, 693-694.
13. Sundaralingam, M.(1969), Biopolymers 7, 821-860.