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CONFORMATION AND FOURIER TRANSFORM OF AN EXACT SIDE-BY-SIDE MOLECULAR MODEL OF B-DNA

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Summary. An accurate side-by-side conformation with a good stereochemistry is proposed for the B-DNA. The structure does not present any super helical torsion and its right and left-handed sections, composed of three nucleotides per chain, are connected by two different bends each comprising two nucleotides. Atomic coordinates and a stereo view are given as well as dihedral angles. Diffracted intensities are calculated for this molecular conformation and compared to experimental values and to other DNA models.

Introduction. The DNA in its B-form is generally defined as a right-handed double helix with bases paired according to the WATSON-CRICK scheme. But many experimental facts question the unicity of this model with regard to the conformation of the sugar-phosphate chain. For example, right-handed helices close to the classical B-form have been proposed as models in X-Ray studies on crystals of short sequences of nucleotides (1). But the crystallization of sequences of alternating purines and pyrimidines allowed the determination of a left-handed double helix, the Z-DNA (2) (3), as a new model with a dinucleotide as unit. A polymorphism is also considered for the DNA models used for interpretations of X-Ray results on fibres (4) and left-handed helices were proposed as models for polynucleotides of alternating purines and pyrimidines (5) (6). Besides X-Ray studies, results obtained from solutions are also explained by using the Z-form of DNA (7) (8) or the simultaneous presence of right and left-handed helices (9) (10). In this last case, variations of the physico-chemical conditions induce transition between right and left-handed forms (11) (12) (13). Moreover, theoretical DNA models presenting succession of right and left sections have been proposed (14) (15) as alternatives to the right-handed double helix model of the B-DNA. These side-by-side models are also interesting because they are composed of junctions between helices of opposite screw sense, junctions which should

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be of some importance for the interpretation of experiments on transitions between different DNA conformations. However, most side-by-side conformations are defined with physical models and do not have a good precision in atomic coordinates. Moreover, they generally present a torsion giving to the model of the bicatenary DNA molecule a super helical conformation (15) (16). It is from these imperfect or distorted models that conclusions have been drawn on their relevance for the interpretation of X-Ray measurements on B-DNA fibres (17). In the present paper a precise side-by-side conformation of type II (15) is proposed. It is an improvement of a previous model of the B-DNA (18) which presents a better regularity in the spacing between bases and no super helical torsion. Its stereochemistry is good even for the nucleotides in the junctions between right and left-handed sections. Dihedral angles as well as coordinates of atoms are given and a comparison between calculated and experimental diffracted intensities is presented.

Methods. a) Geometrical conditions. A certain number of constraints are imposed for the realization of the side-by-side model in order to take into account the information deduced from X-Ray measurements. Therefore, the repeat unit must be of 34 Å length and one should have distances near to 3.4 Å between successive bases (ten nucleotide pairs in one unit). The side-by-side model is perfect if there is exactly 360° rotation between the 11th and the first nucleotide in the chain ; units are then exactly superposed along the main axis of the conformation. In the present model, the unit of ten nucleotides is composed of three nucleotides on a right-handed helix followed by two nucleotides for the transition to the left-handed section also constituded of three nucleotides. Then two nucleotides realize the transition to an other right-handed section. The main axis of the conformation is defined by the axis of the section in right-handed helix which is given dihedral angles close to those proposed by Arnott for the B-DNA (19). The model of the bicatenary DNA molecule is composed of two complementary and antiparallel chains, the pairing of bases is made as proposed by WATSON and CRICK. Consequently, the conformation must present a dyadic symmetry and, for the side-by-side model, a dyad axis must be present in each right or left-handed section, in the plan of its central bases. All these axes should have the same direction as no superhelical torsion is permitted. Sugar rings are C_2' endo but variations of their conformation are allowed (20) and do not exclude the C_3' endo form especially for the nucleotides in bends. Right and left sections present opposite orientations of the oxygen in the sugar rings ; up or down depending on the screw sense of the section in which they are included. Bases are always in position anti. The first condition a good conformation must satisfy is the stereochemistry and, therefore, constraints have been imposed in order for contacts between non-bonded atoms to agree with van der Waals radii commonly used for atoms (21) including hydrogen for the present calculations.

b) Model building and calculations. Model building and computation of atomic coordinates are performed according to the procedures used previously (18) (22). Hence a conformation verifying the geometrical constraints and presenting a good stereochemistry is obtained by working simultaneously on a kind of Kendrew molecular model and the computer. From this calculated model, the Fourier transform is computed using the cylindrical coordinates of atoms and values of the diffracted intensities are then obtained with relations and parameters previously used (22).

Results. For the best conformation presently obtained, the numbering of nucleotides starts with nucleotides 0,1,2 which are on a right-handed helix. The first bend is realized with nucleotides 3 and 4 then, 5, 6 and 7 are on a pseudo left-handed helix. The second bend is formed with nucleotides 8 and 9. Finally, the 10th nucleotide is in the conformation of the B-DNA right-handed helix. As for the preceding model (18) the sugar rings of nucleotides 3 and 8 are in C_3' endo in order to change the direction of rotation of the chain. In the left-handed section, the dihedral angles about $C_4'-C_5'$ in sugars are diminished of some hundred degrees compared to the right-handed section e.a. a transition g-g to t-g. The dihedral angles of nucleotides 5, 6, 7 are somewhat different ; these nucleotides are not exactly on a left-handed helix. The side-by-side conformation presents dyad axes in the base plans of nucleotides 1, 6 and 11... ; these axes are parallel and allow an easy calculation of the coordinates of atoms on the antiparallel and complementary chain. Note that for the determination of the conformation of the nucleotides 7, 8 and 9, one has taken into account the fact they must be paired with nucleotides symmetrical (dyad axis) of 3, 4 and 5. Irregularities in spacing between nucleotides 7, 8, 9 and 10 are mainly due to the constraints of getting the 10th nucleotide in, exactly, the right-handed helix conformation and also of having only a 34 Å translation between this nucleotide and the 0th (no rotation about the main axis). Small tilts and twists have been introduced in view to improve the stacking of the corresponding bases. Dihedral angles corresponding to the best conformation obtained are given in table I ; progression along the chain is 5'-3' and values are expressed with Arnott's conventions (23). Cylindrical coordinates of atoms in the unit are listed in table II and a stereo view is given in figure I. Curves of the square of the Fourier transform corresponding to this side-by-side DNA model are presented in figure II and compared to experimental values and curves associated to the double helix model.

Discussion. The present conformation proposed for the B-DNA is a precise side-by-side model ; each chain is constituted of right and left-handed sections with equal numbers of nucleotides. The length of the repeat unit is 33.7 Å in accordance with experimental values and successive units are just translated along the main axis e.a. the structure is not a super double helix. One can see in table I that changes in the direction of the sugar-phosphate chain is obtained

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	37.4	154	154.5	- 93	- 48	146
2	- 146.5	37.4	154	153.5	- 90	- 65	146
3 $1^{\underline{st}}$ bend	- 146	34.4	83	- 150	11	- 172	125
4	- 171.5	20	158	- 58	116	- 37	102
5 left-handed segment	165	- 80	153	174	- 132	32	58
6	162	- 60	149	- 168	- 131	33	53
7	161	- 73	158	- 59	123	- 39	58
8 $2^{\underline{nd}}$ bend	115	- 60.5	100	47	15	- 166	71.5
9	134	167	158	163	- 87	- 61	123
10 right-handed helix	- 146.5	42	154	154.5	- 93	- 48	137

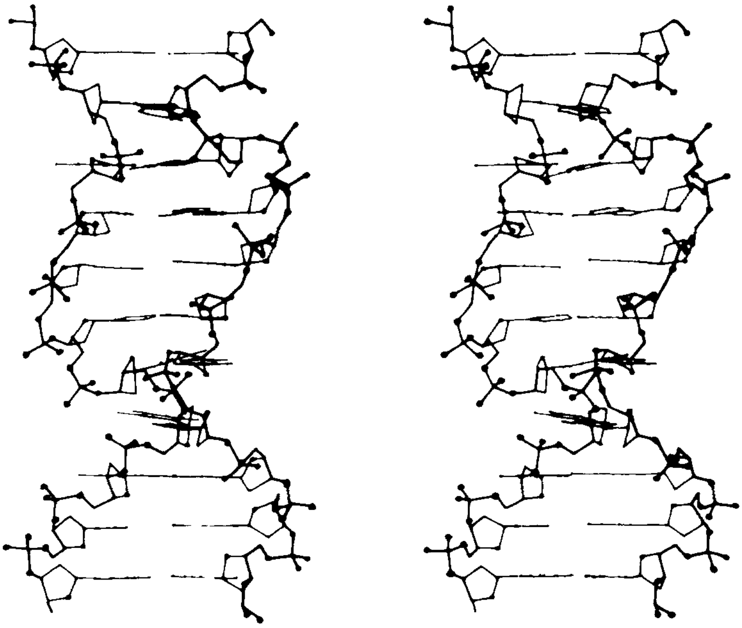

Figure I. Stereoscopic view of 11 pairs of nucleotides of the side-by-side DNA model. (One can see there is no superhelical torsion).

Table II. Cylindrical coordinates for nine nucleotides of an unit. Cartesian coordinates x, y, z, with the x axis along the dyadic direction can be calculated with $x_j = R_j \cos \Phi_j$; $y_j = R_j \sin \Phi_j$; $z_j = Z_j$. (The coordinates of atoms of nucleotide 1 can be obtained by removing 3.36 Å from Z_j and 36° 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	7.63	-55.00	-14.79	7.56	- 18.84	-11.44	8.39	- 13.81	-7.83
C'_5	7.61	-46.71	-15.72	7.72	- 9.41	-12.12	8.59	- 19.24	-6.67
C'_4	7.48	-36.69	-14.99	7.41	- 0.35	-11.25	7.90	- 28.56	-6.74
O'_5	6.12	-32.59	-14.84	6.07	4.19	-11.45	6.69	- 28.97	-5.93
C'_3	8.08	-36.70	-13.59	7.58	- 2.00	- 9.75	7.52	- 32.27	-8.13
C'_2	6.88	-40.36	-12.77	6.80	7.61	- 9.21	6.13	- 26.95	-8.27
C'_1	5.68	-34.20	-13.50	5.55	8.40	-10.20	5.55	- 29.08	-6.77
N	4.50	-44.41	-13.52	4.26	- 0.05	- 9.99	4.99	- 14.15	-6.58
O'_1	8.66	-28.17	-13.22	8.94	- 1.30	- 9.35	7.69	- 42.92	-8.20
P	8.80	-25.76	-11.67	9.48	- 6.46	- 8.10	9.18	- 46.00	-7.84
O'_2	10.10	-21.65	-11.45	9.72	- 0.97	- 6.96	10.05	- 39.05	-7.57
O'_3	8.88	-33.81	-10.87	10.80	- 9.71	- 8.45	9.80	- 50.30	-8.98
	NUCLEOTIDE 5			NUCLEOTIDE 6			NUCLEOTIDE 7		
O'_4	9.00	-51.82	- 6.55	8.18	- 91.91	- 3.56	8.15	-128.83	0.23
C'_5	7.94	-49.96	- 5.61	7.50	- 87.48	- 2.44	7.15	-126.16	1.21
C'_4	7.82	-58.60	- 4.69	7.44	- 94.99	- 1.30	7.11	-134.78	2.27
O'_5	7.08	-55.79	- 3.49	6.72	- 90.15	- 0.19	6.30	-131.07	3.38
C'_3	7.38	-68.59	- 5.25	6.95	-106.33	- 1.59	6.77	-146.58	1.84
C'_2	5.80	-68.52	- 4.89	5.48	-106.50	- 1.16	5.25	-147.88	2.00
C'_1	5.80	-61.19	- 3.53	5.43	- 95.68	- 0.09	5.08	-138.55	3.38
N	4.84	-48.90	- 3.44	4.49	- 82.25	- 0.16	3.99	-125.65	3.35
O'_1	8.07	-76.21	- 4.65	7.81	-112.89	- 0.83	7.54	-153.44	2.67
P	8.02	-87.32	- 5.01	8.13	-123.85	- 1.20	9.11	-151.31	2.79
O'_2	9.21	-88.77	- 5.87	9.48	-123.60	- 1.82	9.53	-144.05	2.00
O'_3	6.81	-90.85	- 5.73	7.19	-128.57	- 2.16	9.92	-158.05	2.26

Table II (cont'd.)

	NUCLEOTIDE 8			NUCLEOTIDE 9			NUCLEOTIDE 10		
O'_4	9.28	-150.05	4.36	7.76	-164.54	7.96	7.73	-129.29	12.65
C'_5	8.31	-144.96	5.09	8.23	-162.24	9.29	7.85	-121.74	11.65
C'_4	7.58	-151.34	6.07	8.06	-151.92	9.62	7.59	-111.48	12.20
O'_5	6.62	-144.86	6.80	6.78	-147.44	9.26	6.20	-108.05	12.20
C'_3	6.98	-161.33	5.46	8.29	-149.44	11.08	8.09	-110.07	13.63
C'_2	5.75	-163.86	6.33	6.88	-150.87	11.63	6.84	-113.24	14.41
C'_1	5.29	-148.25	6.43	6.03	-144.85	10.43	5.68	-108.29	13.52
N	4.61	-132.83	6.37	4.74	-152.83	10.32	4.54	-119.08	13.52
O'_1	8.02	-168.69	5.57	8.89	-140.89	11.24	8.62	-101.16	13.87
P	8.79	-169.55	6.97	8.95	-136.43	12.68	8.70	- 97.46	15.37
O'_2	10.10	-165.43	6.89	10.25	-132.33	12.80	10.02	- 93.51	15.56
O'_3	9.15	-178.52	7.27	8.94	-143.11	13.73	8.67	-104.93	16.32

with C'_3 endo forms of the sugar rings which are C'_2 endo elsewhere. Such a simultaneous presence of sugars in C'_2 and C'_3 endo forms on the same chain has already been proposed for an alternating B-DNA structure in right-handed helix (24). Bases are almost perpendicular to the main axis of the conformation, well oriented and positionned for the WATSON-CRICK pairing of antiparallel and complementary chains. They are in position anti or high anti and the stacking is as good in the left section as in the right one. One can note that bases are at larger distances from the main axis in the left-handed section and that the stacking is less good for the nucleotides in the bends. The larger default in regularity is the 4 Å distance between bases in the second bend which realizes the transition from the left to the right-handed section. It seems to be very difficult to improve the conformation in this region unless some constraints are withdrawn ; one could allow nucleotides of the right-handed section to be on a pseudo helix like those in the left one or accept a super helical torsion or even admit different numbers of nucleotides for the right and the left-handed parts. Such realistic modifications of the present model would render its realization much easier ; the present point was to demonstrate that the most constraint side-by-side conformation is also possible. Junctions between right and left-handed parts present a good stereochemistry. There is no bad atomic

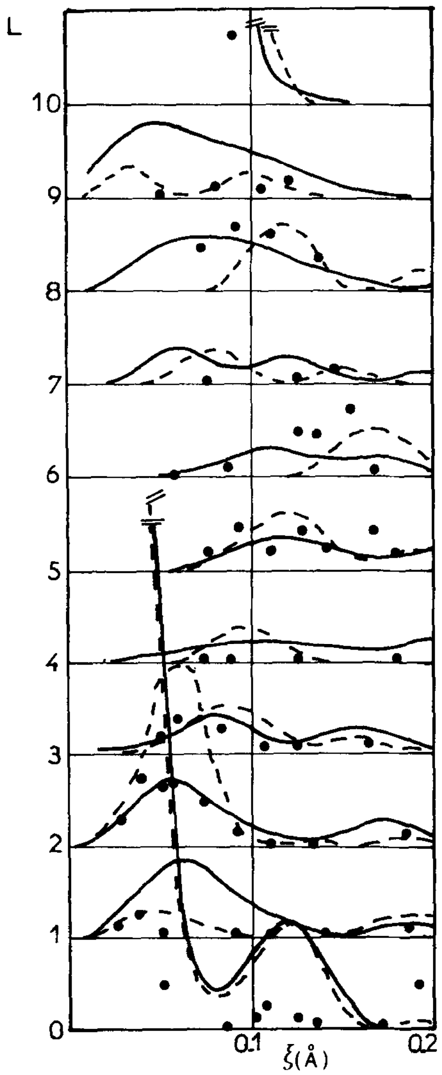

Figure II. Curves of the square of Fourier transform associated with the present model (——) ; curves for the B-DNA double helix (---) ; observed intensities (●).

contact, even between hydrogens, in the nucleotides of the two bends (contacts introduce in the first bend by the dihedral angle (O_1' P) close to the eclipse conformation do increase the van der Waals energy by less than 0.8 KCal/mole). This is also the case for the rest of the conformation and the total van der Waals energy (a 6-12 potential is used) of the present DNA model is as good as that associated to the refined right-handed double helix (19). Calculated diffracted intensities are in a much better agreement with experimental results than values previously obtained with side-by-side models (17) (18). The regular spacing of bases makes the meridian intensities to disappear except on layer lines 0 and 10. In figure II, one can see that the comparison with calculated intensities obtained with the double helix does not allow a choice between one or the other model. Besides its importance as an eventual alternative to the B-DNA double helix, the present side-by-side conformation is mainly interesting because of its junctions between right and left-handed helices. These stereochemically acceptable parts of the conformation may be relevant in many other conditions in which the DNA appears to be composed of sections in different forms as it seems to be the case in some experiments on solutions and fibers (25).

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