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ARTICLE

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A new D-DNA form of poly(dA-dT).poly(dA-dT): an A-DNA type structure with reversed Hoogsteen pairing

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Abstract The D-DNA double helix model of poly(dA-dT).poly(dA-dT) proposed in the literature is not in accordance with some notable experimental facts and physicochemical conditions to which it is related. Thus, the fibre X-ray diffraction pattern of D-DNA obtained at a relative humidity lower than that giving the A-DNA form is singularly not taken into account when one assumes that there is only one D structure of B-DNA type. We rather suggest that there are actually two different forms of D-DNA, namely D_A which partakes in the D-A-B transitions and D_B associated with the D-B change of conformation. Although these two DNA structures have the same helical parameters (pitch and number of residues per turn), in agreement with X-ray data, their detailed conformations are considerably different. Whereas D_B is indeed the structure generally defined as D-DNA, a critical analysis based on a comparison between different possible DNA double helices leads us to propose dihedral angles, a set of atomic coordinates and a stereo view of another new form of D-DNA, the D_A structural model. It is a right-handed double helix with a dinucleotide as the repeat unit. The furanose rings are of the A-DNA type (C3′ *endo*) and the bases are hydrogen bonded according to the reversed Hoogsteen pairing. Such a disposition renders the D_A model unsuitable for poly(dI-dC).poly(dI-dC), the other alternating polynucleotide observed in the D_B structure. The consistency of these two different D-DNA structures of poly(dA-dT).poly(dA-dT) with the general aspects of hydration and helix-helix transitions of DNA, as well as with the conformational variability of AT base sequences, is discussed.

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Introduction

The X-ray pattern of the D-DNA double helical structure is only obtained from the fibre diffraction of two polynucleotides with repetitive alternating base sequences, namely poly(dA-dT).poly(dA-dT) (Davies and Baldwin 1963; Arnott et al. 1974) and poly(dI-dC).poly(dI-dC) (Mitsui et al. 1970). These two polynucleotides can adopt the B conformation, depending on the amount of salt in the fibre and the relative humidity (Leslie et al. 1980). Moreover, the first one is also found in the A-DNA structure but it is important to note that when the A, B and D patterns are obtained from the same poly(dA-dT).poly(dA-dT) fibre, the D-form always corresponds to the lower relative humidity (r.h.). So, by increasing the r.h., one can observe the successive D-A-B conformational transitions (Mahendrasingam et al. 1983; Abouelkassimi et al. 1991).

The D double helix is highly overwound with respect to B-DNA; it has only about eight nucleotide pairs per turn and therefore a rotation of 45° between successive nucleotides in a strand while the axial rise per residue is near to 3 Å (the helix pitch height is 24 Å) (Arnott et al. 1974). The controversy over the D conformation has been the subject of many studies on DNA structures. A seven-fold left-handed double helix with Hoogsteen rather than Watson-Crick base pairing was also proposed (Drew and Dickerson 1982) by assuming that the seventh layer line is a meridional one. However, further analysis of the X-ray data as well as observation of the D-B reversible structural transition have clearly indicated that the D-DNA double helix is right-handed like A- and B-DNA (Mahendrasingam et al. 1986; Abouelkassimi et al. 1991). Thus, the D-DNA molecular model currently put forward in the literature (Arnott et al. 1974; Premilat and

Albiser 1986) for poly(dA-dT).poly(dA-dT), as well as for poly(dI-dC).poly(dI-dC), is of the B-DNA type in view of its C2′ *endo* sugar puckering and Watson-Crick base pairing. It is a widely accepted model despite the fact mentioned above that the D-form is also observed in fibres at a r.h. lower than A-DNA (before the transition from D to A) and in that case it should have a conformation related to the A-form rather than to B-DNA.

More explicitly, it can be noted that in DNA fibres at high r.h. the B double helix conformation exhibits two well-defined grooves, the minor and major ones, the widths of which are sufficient to allow a complete hydration of the phosphate groups of the two antiparallel sugar-phosphate chains. When the water activity is lowered in a DNA fibre, the less numerous water molecules are shared by the constitution of water bridges between the phosphate groups of the complementary chains. The double helix therefore undergoes a change of structure characterized by a pronounced reduction of the corresponding interatomic distances (Saenger et al. 1986).

The drawing closer of these phosphate groups from the B-DNA structure can be realized according to two possible different ways: either the major groove width or the minor groove one is strongly diminished. The first process corresponds to the B to A helix-helix transition with a change of the sugar puckering from C2′ *endo* to C3′ *endo*; the second one is related to the much less frequent B- to D-form transition (Lipanov et al. 1989). In this last case, observed in fibre X-ray diffraction studies of poly(dA-dT).poly(dA-dT) or poly(dI-dC).poly(dI-dC), the sugar pucker remains in its B-type C2′ *endo* mode. These two conformational transitions are reversible. Nevertheless, it must be noticed that when the B-D transition is performed (high salt content in the fibre), the A-DNA structure is never obtained, whereas when the transition B-A (low salt) is realized with a poly(dA-dT).poly(dA-dT) fibre, the D-form can also singularly be obtained, as already mentioned, at a r.h. much lower than that giving A. The hydration economy of D-DNA is then fulfilled by an important reduction of the minor groove and a complementary enlarging of the major groove. In addition, during the D-A transition that follows by increasing the r.h., the sugar puckering is supposed to change from the C2′ *endo* mode to C3′ *endo*. The very large major groove of the D-form is then deeply contracted to obtain the A structure while the diameter of the helix increases up to the large value of A-DNA. The very singular conclusion one should draw from these results is that the transition D-A involves a considerable change of the DNA helix conformation while the r.h. of the fibre remains at a very low value (about 55%) (Abouelkassimi et al. 1991). These modifications are even more important than those required for the A to B transition, which is achieved at a convenient high r.h. near to 90% (Lindsay et al. 1988; Harmouchi et al. 1990).

The other essential point to be emphasized is that the same D molecular structure of a long DNA chain can apparently be obtained under two very different physicochemical conditions; a unique paradoxical situation! It is more logical and coherent with experiment to suppose that the DNA form obtained at a lower r.h. than A is a double helix with the A-type sugar pucker (C3′ *endo*) and narrow major groove, rather than the D helix implying for the D to A change a considerable modification of the sugar pucker and a drastic reduction of the major groove width. So, this alternative hypothesis consists in assuming that the molecular structure obtained before A (let us name it $D_{A)}$ is different from the one partaking in the D-B transition. This last is the generally defined D-DNA; it should actually be named D_B since its dihedral angle values are near to those of B-DNA and its minor groove is contracted in continuity with the B form. Thus, two different physicochemical conditions applied to poly(dA-dT).poly(dA-dT) fibres induce in that polynucleotide respectively two different helical structures. However, experimental results show that the general parameters of these two helices are indeed the same whereas their detailed geometry can be widely divergent, as indicated below.

The purpose of the present study is to establish a molecular model for the D_A structure which actually overcomes the difficulties encountered in interpreting experimental data related to the D-DNA conformation. The consistent results we obtained from testing different possible models led us to the conclusion that an alternating right-handed double helix model with A-type sugar puckering and reversed Hoogsteen base pairing could be the most convenient D_A form of poly(dA-dT).poly(dA-dT) partaking in the D-A-B sequence of helix-helix transitions. This new DNA structure is described in detail; dihedral angles, atomic coordinates and a stereo representation are given. Consequences following from taking into account this new molecular model in the relation between hydration and conformational transitions of DNA are discussed.

Materials and methods

Molecular models of poly(dA-dT).poly(dA-dT) double helices were determined by following the procedure previously used to compute atomic coordinates of nucleotides in a double helical conformation (Premilat and Albiser 1983, 1997, 1999). Bond lengths and bond angles are taken from the listing given by Seeman et al. (1976). They can be very slightly varied but they are always maintained in intervals of values determined by X-ray studies on single crystals (Gelbin et al. 1996). The geometry of the sugar-phosphate backbone is thus completely defined by the set of values given to its dihedral angles. These angles can be modified starting from values corresponding to DNA double helical structures determined previously (Premilat and Albiser 1983, 1986). Variations of the sugar ring conformations are possible during the process of improvement of the helical conformation. However, their angle values remain in the intervals characterizing respectively the A or B sugar puckers.

The other torsional angles of the phosphate chain are subject to much larger variations in order for the molecular model to agree with the experimental data. Base pairs are maintained almost perpendicular to the helix axis unless atomic overlaps do impose the introduction of a slight tilt or twist.

The two antiparallel and complementary sugar-phosphate chains and bases are associated according to the Watson-Crick or Hoogsteen pairing modes. So, the calculated conformation must present a dyadic symmetry and good hydrogen bonds between bases. The stereochemistry of the molecular models is tested and possible too short interatomic distances are eliminated by very small variations of the dihedral angles. When a chain is built in a proper helical form, the antiparallel and complementary one is adjusted, by rotation around the common helical axis, to a position that realizes a good fit for hydrogen bonds between base pairs. The cylindrical coordinates of the atoms are then calculated in a reference frame that uses a dyad axis and the screw axis. The dyadic symmetry of the system is used so that the cylindrical coordinates (R, ϕ, z) of a given atom of the main sugar-phosphate chain and the bases on one helix correspond to the coordinates $(R, -\phi, -z)$ for the homologous atom on the complementary helix. Fibre X-ray patterns and experimental data presently used are those already given in a previous detailed study on poly(dA-dT).poly(dA-dT) (Abouelkassimi et al. 1991).

Results

Diffraction patterns of the D structure obtained from the D-B or D-A-B transitions reveal distinct Bragg spots and important intensities on the equatorial and the two higher lines, the upper one being meridional. The observed Bragg reflections correspond to a tetragonal lattice which can be indexed (Abouelkassimi et al. 1991) with the unit cell dimensions $a = b = 17.1$–18.2 Å and $c = 24$–25.1 Å, depending on the r.h. This spacing is actually closely related to the DNA helix diameter, which should therefore not be larger than about 18.5 Å. Thus, the D-form of poly(dA-dT).poly(dA-dT) or poly(dI-dC).poly(dI-dC) is a double helix of about eight nucleotide pairs per turn, a pitch near to 24 Å and a translation along the helix axis of 3 Å between successive homologous atoms (Arnott et al. 1974). However, the repetitive alternating base sequences presented by these two polynucleotides lead us to consider the D structure as a four-fold helix with a dinucleotide as the repeating unit and thus 6 Å for the rise per residue.

According to the preceding observations, we impose, for the search of a structural model of D_A, that beside the necessary good stereochemistry and agreement with fibre X-ray data, the diameter of the double helix must be near to 18.5 Å. It must have a narrow major groove and an A-type sugar puckering. Since the experimentally determined number of nucleotide pairs in a helix pitch varies from 8.07 to 8.40 (4.03 to 4.20 residues) (Abouelkassimi et al. 1991), the rotation per residue can then be fixed at a value between 89.2° and 85.7°. Moreover, this large rotation, combined with the slight 6 Å rise per residue and with the small diameter of the double helix, imposes the bases to be nearly parallel and equidistant in order to avoid inter-chain atomic clashes, mainly between adenine bases. In the present case, such geometrical conditions can only be fulfilled if the base pairs are practically perpendicular to the helix axis, while they can be highly inclined in the much larger cylinder formed by the A-DNA structure.

In the D_B form (Premilat and Albiser 1986) the minor groove is indeed strongly reduced, but the B-type sugar pucker avoids bad atomic contacts between bases and the sugar-phosphate chains since the bases are mainly in the large major groove, as they are in the B-DNA helix. The A-DNA double helix has a very small rise per residue, but its important diameter allows the bases to be located in the large minor groove and unsatisfactory atomic contacts are therefore avoided. When the helix turn is increased up to 90° per dinucleotide while the sugar pucker is maintained in its A-type mode, the bases bonded according to the Watson-Crick pairing are then displaced towards the narrow major groove and the small helix diameter makes it impossible to avoid atomic clashes. Consequently, the Watson-Crick base-pairing mode must be rejected for the D_A structure. Besides, double helices of poly(dA-dT).poly(dA-dT) built with the Hoogsteen pairing could not be accepted either because they present a strong overlapping of the sugar-phosphate chains. That unfavourable situation is due to the relative disposition of the glycosidic bonds and, in that case, to a particularly short C1′-C1′ distance. Nevertheless, by keeping the sugar pucker in the A-type mode and using the reversed Hoogsteen pairing mode, the bases in D_A remain located in the large minor groove. Atomic contacts between bases and atoms of the tight major groove are then avoided, and the stereochemistry of the compact D_A conformation becomes acceptable.

In the Hoogsteen pairing, one base plan must be rotated by 180° from its position in the Watson-Crick pairing (Saenger 1984) in order to have correct hydrogen bonds for the paired bases. This is unnecessary for the reversed Hoogsteen pairing mode. In that case, however, the two associated nucleotides present different conformations because their respective glycosidic bonds are antiparallel (see Fig. 2) and therefore no longer in the helical symmetry. The repeating unit of the resulting double helix is a dinucleotide and dyadic axes are located between consecutive base plans.

Figure 1 shows a stereo drawing of the optimized model of the D_A duplex structure of poly(dA-dT).poly(dA-dT). It is a right-handed double helix with 8.2 base pairs (4.1 residues) per pitch and a rotation per residue of 87.8°. The furanose puckering of the two nucleotides, which constitute the structural repeating unit, are different but both are in the C3′ *endo* mode. The proposed structure presents no atomic overlap between the two antiparallel sugar-phosphate strands. Base plans are parallel and thymine bases are in the vicinity of the helix axis while the adenine ones are more remote. This also contributes to make the structure free of too short contacts between non-bonded atoms and to have bases paired according to the reversed Hoogsteen mode (Fig. 2) with hydrogen bonds of generally admitted lengths (Fuller 1959; Taylor and Kennard 1982;

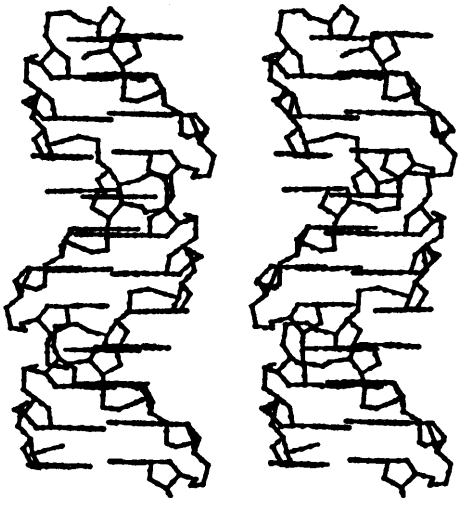

Fig. 1 A stereo drawing of the D_A right-handed double helical structure

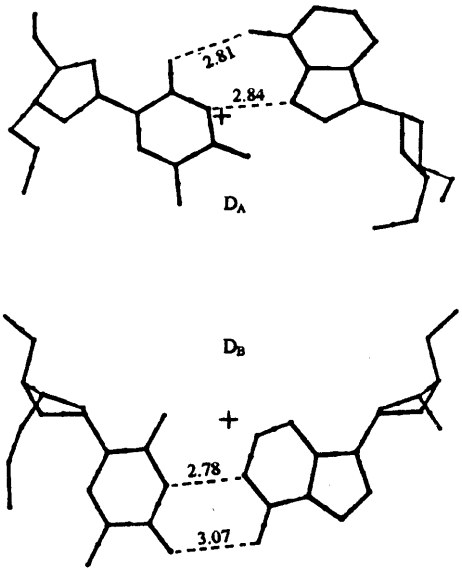

Fig. 2 Drawing showing the hydrogen bonding between adenine and thymine bases of poly(dA-dT).poly(dA-dT). D_A: reversed Hoogsteen pairing; D_B: Watson-Crick pairing. The *numbers* indicate the hydrogen bond distances in angstroms; + indicates the helix axis

Nelson et al. 1987). The chain dihedral angles and the geometrical parameters characterizing this new helical conformation are presented in Tables 1 and 2. In these tables, data corresponding to the A, B and D_B conformations are also given for comparison. The atomic coordinates of an optimized model of the D_A right-handed double helical structure are given in Table 3. Note that the larger atomic distance to the helix axis (R value) is 8.52 Å; it corresponds to an oxygen of a phosphate group. So, in agreement with X-ray data, the diameter of the double helix is less than 18.5 Å. Results showing the very good agreement between experimental data and calculations performed with the D_B structural model have been presented in a previous work (Premilat and Albiser 1986).

Discussion

The different DNA double helical structures at present determined can essentially be distributed among two families, the A- and B-DNA, and a few intermediate forms like the Z (Wang et al. 1979) or S (Premilat and Albiser 1999) conformations adopted by regular or alternating base sequences. The extended and eccentric E-DNA structure recently proposed (Vargason et al. 2000) is another possible intermediate form. Computer modeling including solvent (Olson and Zhurkin 2000) describes deformations of DNA during the B-A transition. Nevertheless, beside important differences in terms of their overall conformation (rise per residue, number of base pair per helix pitch, etc.), the furanose puckering modes, which differ in the A- and B-DNA helices (C3′ *endo* for A and C2′ *endo* for B), constitute a fundamental distinction between these two structural families. The reversible helix-helix transitions between these two DNA groups are well known. They are observed by changing the salt content of a DNA fibre and by varying the relative humidity of its environment. It is now well established that the B-type forms are observed at high relative humidity whereas the A structure appears when both humidity and salt content are relatively low. Thus, when the water activity is reduced, only the oxygen atoms of the phosphate groups of the antiparallel strands remain hydrated and, consequently, the major groove of

Table 1 Dihedral angles for the D_A right-handed double helix of poly(dA-dT).poly(dA-dT). Angle values for A, B and D_B (Premilat and Albiser 1983, 1986) are also indicated; χ is the angle about the glycosidic bond

DNA structure	D_A		A-DNA	B-DNA	D_B
Dihedral angles (°)	Adenine	Thymine			
α (O3′-P-O5′-C5′)	–68.0	–50.5	–59.63	–30.93	–34.00
β (P-O5′-C5′-C4′)	154.0	154.0	163.55	148.71	144.00
γ (O5′-C5′-C4′-C3′)	57.0	58.0	51.20	37.02	43.46
δ (C5′-C4′-C3′-O3′)	81.0	90.0	81.00	132.32	153.77
ϵ (C4′-C3′-O3′-P)	–135.0	–137.2	–136.26	–156.80	–157.04
ξ (C3′-O3′-P-O5′)	–56.5	–101.2	–87.11	–133.62	–154.70
χ	–179.0	–176.5	–165.00	–123.00	–106.00 (adenine), –102.00 (thymine)

Table 2 Geometrical parameters for the right-handed D_A, A, B and D_B (Premilat and Albiser 1983, 1986) double helices of poly(dA-dT).poly(dA-dT). The residue is a dinucleotide (dA-dT) of one strand

DNA structure	D_A	A-DNA	B-DNA	D_B
Rotation per residue (°)	87.80	65.45	72.00	89.98
Rise per residue (Å)	6.02	5.12	6.78	6.06
Helix pitch (Å)	24.08	28.16	33.90	24.24
Hydrogen bond (Å)				
N6···O2	2.81	–	–	–
N7···N3	2.84	–	–	–
N1···N3	–	2.99	2.94	2.78
N6···O4	–	2.92	2.96	3.07
P-P distance (Å)[a]				
Major groove	3.81	8.94	17.03	14.42
Minor groove	17.32	16.32	12.10	8.02
Sugar pucker	C3′ *endo*	C3′ *endo*	C2′ *endo*	C2′ *endo*

[a]The minimum inter-strand phosphate-phosphate distance

A-DNA becomes deep and narrow. This is clearly confirmed by the positions of water molecules determined from high-resolution crystal structures (Schneider et al. 1998), as well as by molecular dynamics simulations (Auffinger and Westhof 1998). Only oxygen atoms of the phosphate groups of the poly(dA-dT).poly(dA-dT) structure observed at a r.h. lower than that of A-DNA should also remain hydrated. The distinctive features of the A-DNA conformation should therefore logically be found and even reinforced in that double helix. The D_A model here proposed is in complete accordance with these views. It is a very compact helical structure of DNA with the tightest major groove, since phosphate groups of the complementary chains are actually in contact.

The successive D-A-B helix-helix transconformations of poly(dA-dT).poly(dA-dT) are achieved by increasing the r.h. of the polynucleotide fibre from 40% to 92%. Thus the D to A form transition clearly occurs at very low r.h. and if, in that situation, the D-DNA conformation had actually a B-type sugar pucker, the transition from D to A, observed when the r.h. is raised, should follow a route contrary to what is generally observed (a C3′ *endo* puckering for DNA sugar rings at low r.h. and a C2′ *endo* one at a higher r.h.). The A-B transition of that alternating polynucleotide is perfectly reversible. However, the A to D change is not possible (Mahendrasingam et al. 1983) unless an external tension is applied to the fibre (Abouelkassimi et al. 1991). Note that this is in agreement with the generally verified fact that a DNA helix-helix transition produced by a decrease of the r.h. cannot give a final helix with a rise per residue p larger than that of the original helix (Premilat and Albiser 1999). Since for consecutive nucleotides $p_D = 3$ Å and $p_A = 2.56$ Å, we cannot turn A into D with a decrease of the r.h. As soon as the transition from D to A is completed in a poly(dA-dT).poly(dA-dT) fibre free of tension, variations of the r.h. let only the reversible A-B transition appear and D is no longer obtained. When the salt content in the fibre is higher than for the D-A-B transitions, the reversible D-B transition can be observed by varying the r.h. Thus, the alternating sequence of poly(dA-dT).poly(dA-dT) allows this DNA to follow, depending on the external conditions, the two possible

Table 3 Cylindrical coordinates of the D_A right-handed molecular helix. The atomic coordinates corresponding to the complementary chain are simply obtained by changing the sign of ϕ and z. The following AT unit in the double helix is obtained by replacing ϕ by $(\phi + 87.80)$ and z by $(z + 6.02)$

	R (Å)	ϕ (°)	z(Å)		R (Å)	ϕ (°)	z (Å)
Phosphate				Adenine			
O3′	6.46	–149.59	–1.86	N9	4.58	–93.64	–1.65
P	6.47	–148.95	–0.26	C8	3.40	–103.63	–1.69
O1	7.85	–150.63	0.22	N7	2.37	–87.35	–1.70
O2	5.66	–159.46	0.31	C5	3.35	–67.03	–1.66
O5′	6.12	–134.87	0.01	C4	4.55	–76.33	–1.63
Deoxyribose				N3	5.76	–69.77	–1.58
C5′	7.26	–127.90	–0.36	C2	5.88	–56.61	–1.57
C4′	7.06	–116.11	–0.63	N1	5.15	–45.13	–1.60
C3′	6.59	–108.36	0.51	C6	3.81	–44.64	–1.64
C2′	6.56	–96.97	–0.27	N6	3.44	–24.34	–1.66
C1′	5.93	–99.94	–1.63				
O1′	6.13	–113.60	–1.69				
Phosphate				Thymine			
O3′	7.62	–107.37	1.48	N1	2.83	–72.16	1.31
P	7.26	–107.83	3.04	C6	2.88	–99.93	1.31
O1	8.52	–106.23	3.80	C5	2.20	–126.46	1.29
O2	6.85	–118.98	3.40	C7	3.37	–146.31	1.29
O5′	6.31	–97.08	3.19	C4	0.88	–150.40	1.26
Deoxyribose				O4	1.55	157.08	1.24
C5′	6.97	–86.93	2.65	N3	0.73	–32.09	1.26
C4′	6.15	–76.22	2.31	C2	2.08	–44.91	1.28
C3′	5.46	–68.85	2.47	O2	2.99	–26.26	1.28
C2′	4.59	–57.75	2.69				
C1′	4.24	–65.30	1.33				
O1′	5.20	–78.62	1.28				

modes of transition from the B-DNA structure to a helical form, with either a very narrow major groove (A and D_A) or a very narrow minor groove (D_B). We have here an example of the intrinsic structural variability of an alternative AT sequence of DNA (Klug et al. 1979; Klug 1993). The biological interest of that conformational adaptability of AT sequences has been demonstrated in studies on the TATA box, showing that alternating T and A bases in DNA are necessary for the realization of a protein/DNA complex initiating the process of transcription of diverse RNA. The fundamental importance of an A-type wide minor groove for the interaction with the protein was established by X-ray measurements (Kim et al. 1993a, 1993b; Burley 1996; Juo et al. 1996). Eight base pairs seem to be involved in the interaction. However, in that case, the DNA helix is unwound compared to A-DNA (Guzikevich-Guerstein and Shakked 1996) rather than overwound as in the D structures.

The D_A helix of poly(dA-dT).poly(dA-dT), here proposed as the D form which partakes in the D-A-B transitions, is actually a member of the A-DNA structural family. A dinucleotide constitutes the structural repeat unit of this right-handed double helix which has its sugar rings in the C3′ *endo* puckering mode, as in A-DNA. Consequently, values of the dihedral angles of the present D_A molecular model diverge by less than 10° from the A-DNA conformation except for the rotation axis about O3′-P bonds. Such structural features render easy to understand why the D to A transconformation of poly(dA-dT).poly(dA-dT) in fibre can actually be realized at very low r.h. (between 40% and 60%). Moreover, since poly(dA-dT).poly(dA-dT) can adopt the A, D_A or D_B form at low r.h., this polynucleotide will hardly be observed in the otherwise acceptable S structure which is an intermediate form between A and B presented by poly(dG-dC).poly(dG-dC) at low r.h. (Premilat and Albiser 1999). Conversely, since the G-C base pair cannot be hydrogen bonded in the reversed Hoogsteen base-pairing mode, the D_A conformation is not observed with this last alternating polynucleotide, although it can adopt the A-DNA structure.

Let us underline that the main difference between the presently proposed D_A structure and the other known DNA conformations occurs in the base pairing mode: a Watson-Crick type for all the known DNA double helices and a reversed Hoogsteen pairing for the D_A form of poly(dA-dT).poly(dA-dT). In that double helix the associated bases have glycosidic bonds oriented antiparallel to each other. The two consecutive nucleotides constituting the repeating unit have therefore very different conformations except for their sugar puckering, which are both in the A-DNA mode. In long polynucleotide chains, such structural constraints can only be fulfilled by alternating polymers. However, the alternating poly(dI-dC).poly(dI-dC) has never been obtained, as far as we know, in the A form but it is found in the D structure (Mitsui et al. 1970; Leslie et al. 1980) So, according to the present views, that structure is in all likelihood D_B since to obtain access to the D_A form this polynucleotide should also be able to turn into the A form with a reduced major groove. Moreover, note that the here-proposed D_A structure with its reversed Hoogsteen base pairing is not adapted at all to poly(dI-dC).poly(dI-dC), since it only allows the constitution of one hydrogen bond (at pH 8) between inosine and cytosine whereas two bonds are possible for the Watson-Crick base pairing in B and D_B.

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