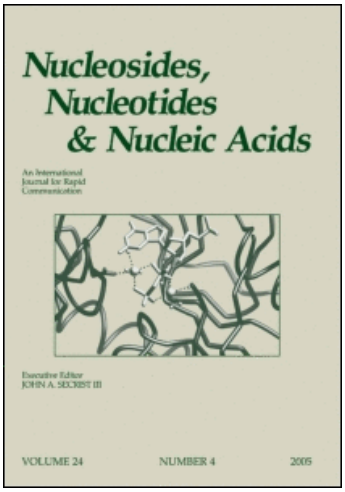

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X-Ray Crystallographic Studies of the A-Form of DNA

U. Heinemann[a]; H. Lauble[a]; R. Frank[b]; H. Blöcker[b]
[a] Abteilung Saenger, Institut für Kristallographie, Freie Universität Berlin, Berlin [b] GBF, Gesellschaft für Biotechnologische Forschung, Braunschweig, West Germany

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X-RAY CRYSTALLOGRAPHIC STUDIES OF THE A-FORM OF DNA

U. Heinemann*, H. Lauble, R. Frank§ and H. Blöcker§
Abteilung Saenger, Institut für Kristallographie, Freie Universität Berlin, Takustraße 6, D-1000 Berlin 33 and §GBF, Gesellschaft für Biotechnologische Forschung, Mascheroder Weg 1, D-3300 Braunschweig, West Germany

Abstract. The three-dimensional structure in the crystalline state of the self-complementary oligodeoxyribonucleotides d(GCCCGGGC) and d(GGGATCCC) is described and compared with other DNA fragments in the A-form.

We have determined the three-dimensional structures of the self-complementary DNA fragments d(GCCCGGGC) and d(GGGATCCC) by X-ray crystallography (ref. 1 and Lauble, Frank, Blöcker and Heinemann, in preparation). Both oligonucleotides adopt A-form DNA helices in the crystalline state (Fig. 1). To probe whether the data base on A-DNA structures accumulated so far permits generalizations concerning their sequence-dependent helical conformation we have compared the most important structural parameters of our oligonucleotides with those of other unmodified A-DNA octamers[2-6] for which coordinates or the relevant parameters are available. The parameters investigated are as defined by Dickerson and colleagues[7,8].

It is evident from Tab. 1 that the ten possible base-pair steps occur with very different frequency in our data base. There is a strong bias in favour of CC/GG steps, reflecting the tendency of poly(dG)·poly(dC)-like sequences to adopt the A-form of DNA[5], while the steps AA/TT, AG/CT and CA/TG are not represented at all. Recently, however, d(GTGTACAC) has been reported to adopt the A-form of DNA in

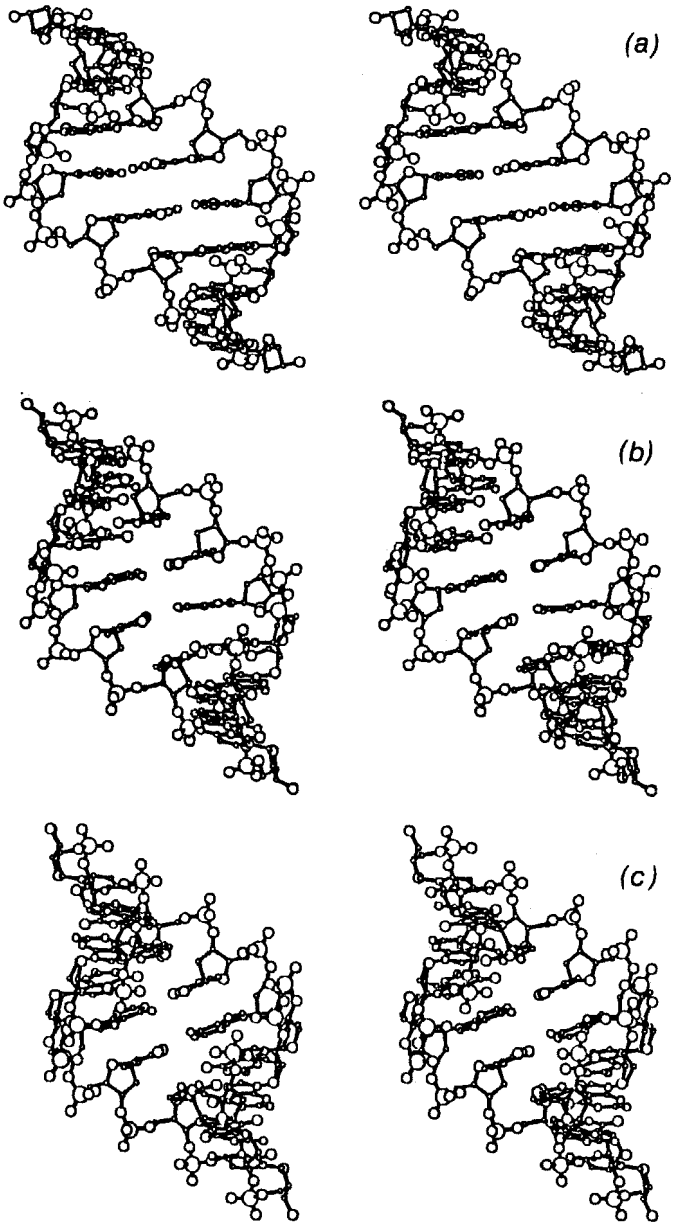

FIG. 1 (next page). Stereographic drawings of crystalline d(GCCCGGGC) (a) and d(GGGATCCC) (b) as well as a model of d(GGGATCCC) based on idealized coordinates derived from fiber diffraction studies of random-sequence DNA (c, Arnott and Chandrasekaran, personal communication), looking into the major groove. Note the narrowing of the groove and the increasing base-pair tilt going from (a) to (c). Also, compare the stacking arrangement at the central base-pair step between (a) and (b): In d(GCCCGGGC) the CG (pyrimidine-purine) step is characterized by extensive cross-strand guanine-guanine stacking while in d(GGGATCCC) the central AT step shows perfect intra-strand purine-pyrimidine stacking.

TABLE 1. Base pair steps in A-DNA helices

	AA/TT	AC/GT AG/CT	AT CA/TG	CC/GG CG	GA/TC GC	TA
d(CCCCGGGG)*				3 1		
d(GCCCGGGC)*				2 1	1	
d(GGCCGGCC)*				2 1	1	
d(GGGCGCCC)*				2 1	1	
d(GGGGCCCC)				6	1	
d(GGGATCCC)			1	4	2	
d(GGTATACC)		2	1	2		2
Twist** (°)		32(0)	30(3)	33(4) 22(4)	34(2) 31(3)	30(0)
Roll (°)		1(0)	2(1)	6(3) 4(5)	10(1) 6(3)	15(2)
Slide (Å)		1.2(0)	1.0(1)	1.7(4) 2.2(1)	1.8(4) 1.2(4)	1.5(2)
Propellor Twist (°)		14(3)	9(2)	10(4) 6(2)	8(2) 10(4)	12(3)

*These oligonucleotides display perfect dyad symmetry in the crystal, hence identical base pair geometry is present at both ends of the helix. **Parameters as described by Dickerson and colleagues (refs. 7,8), see text for description. Numbers in parentheses give the standard deviation of the sample and refer to the last digit.

the crystal[9] demonstrating that runs of G are not a prerequisite for A-DNA.

The CG base-pair step clearly displays unique properties. It shows significantly reduced helical Twist and increased Slide over all other steps. These parameters indicate that the cross-strand overlap between guanine bases observed in the structure of d(GCCCGGGC) is a general feature of CG steps in A-DNA helices. The rather small Propellor Twist of the base pairs involved in CG steps further enhances the inter-strand stacking interaction. The unique conformation of A-DNA at the CG step is accompanied by an unusual conformation of the sugar-phosphate backbone which pulls apart the flanking phosphate groups by about 1Å farther than at normal base-pair steps[1,2,4]. Theoretical considerations[10] have predicted the behaviour of CG steps seen in crystalline A-DNA. By comparison, the CC/GG steps representing more than half of our sample are characterized by intermediate Twist, Roll, Slide and Propellor Twist.

The presently available data base on the structure of A-DNA does already allow generalizations about the helical fine structure. Accurate predictions of three-dimensional structure based on nucleotide sequence information must await more structures to be determined.

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