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A NOVEL Z-STRUCTURE FOR POLY d(GC).POLY d(GC)

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Summary

A novel zig-zag (Z) structure is proposed for poly d(GC).poly d(GC). The proposed model closely resembles the crystal structure of $d(CG)_3$.

Introduction

Recently a structure was proposed for poly d(GC).poly d(GC) (1) at high salt. The structure is a six-fold helix (n = 6) with height per residue, h = 7.25 Å similar to the crystal structure (2) of $d(CG)_3$ (n = 6, h = 7.40 Å). Asymmetric unit in both the cases is a dinucleotide. The structure of poly d(GC).poly d(GC) was reported to be very similar to that of $d(CG)_3$. However, the proposed polymer structure (1), on inspection differs from the structure of $d(CG)_3$ in two major aspects: (i) progression of the sugar-phosphate backbone and separation between two neighbouring chains and (ii) stacking arrangement of the bases. In this communication, we present a novel left handed Z-DNA model for poly d(GC).poly d(GC). We also show that the present model is very similar to the structure of $d(CG)_3$ in most aspects including the two mentioned above.

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A Novel Z-Structure

The conformational parameters of the model of poly d(GC). poly d(GC) are given in Table 1. It is seen that GpC fragment has (C3'-endo, g^+g^+ - C2'-endo) conformation while CpG fragment has (C2'-endo, g^+g^+ - C3'-endo) conformation (3). C3'-endo sugars have gt conformation around C4'-C5' bond and C2'-endo sugars have gg conformation around the same bond. The purines are attached to C3'-endo sugars and have syn conformation while the pyrimidines are connected to C2'-endo sugars and have anti conformation. Both in GpC and CpG fragments the phosphate groups have g^+g^+ conformation (3,4). However, two neighbouring phosphorus atoms do not have the same radius: in GpC R_p = 7.30 Å

Table 1 [a,b]

Conformational Parameters of Z-Structure for poly d(GC).poly d(CG).

Conformational parameters	CpG	GpC
α(C3' - O3')	260	193
β(O3' - P)	75	93
γ(P - O5')	77	110
δ (O5' - C5')	165	143
ϵ (C5' - C4')	155	85
ζ (C4' - C3')	94	156
χ (C1' - N9G)	235	-
χ (C1' - N1C)	-	30

[a] Alphabetical nomenclature of the torsion angles adopted from Seeman et al (5).

[b] Molecular models were generated for n = 6, h = 7.5 Å using modified LALS procedure with dinucleotide as the asymmetric unit. Bond lengths and bond angles were maintained at standard values.

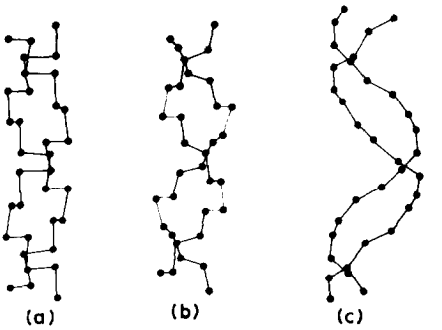

Fig. 1 : Progression of the phosphorus atoms (dark circles) along the helix axis (a) the present model, (b) crystal structure of $d(CG)_3$, missing phosphorus atoms are also indicated and joined by thin lines and (c) the model proposed by Arnott et al (1).

and in CpG, R_p = 6.25 Å. Two phosphorus atoms in pGp are vertically separated along the helix-axis with d(P---P) = 7.24 Å and in pCp they are horizontally away from each other with d(P---P) = 7.21 Å. The nonidentical radii and dissimilar spatial disposition of two neighbouring phosphorus atoms around the helix-axis bring about the zig-zag progression of the sugar phosphate backbone. This is illustrated in Fig.1a which shows the positions of the phosphorus atoms (dark circles) along the helix-axis. It is seen from Fig.1a that minor and major grooves are equally deep. One more important feature of the structure is that the oxygen atoms of two neighbouring sugar residues in the same chain point in opposite directions while the oxygen atoms of the sugars in the antiparallel chains across the base-pair point in the same direction. The imidazole part of the G residues lies on the outer surface of the helix along with the phosphates in GpC. Thus, C8, N7 and O6 of G are exposed to the environment. Cytosine residues are buried inside with O2 atoms close to the helix centre.

Comparison of the two proposed models with the crystal structure of $d(CG)_3$

Z-DNA fragment of $d(CG)_3$ has the following important features (2): (i) zig-zag progression of the sugar-phosphate backbone (Fig.1b) and both major and minor grooves are deep; (ii) R_p (8.0 Å) in GpC is higher than R_p (6.9 Å) in CpG; (iii) imidazole part of G residues (i.e. C8, N7 and O6 atoms) is located on the outer surface of the helix along with the phosphate groups in CpC fragments and (iv) there is intra strand stacking overlap between G and C in GpC while there exists interstrand stacking overlap between C and C in CpG (Fig.2b). Let us now examine how the two proposed structures compare with the single crystal structure of $d(CG)_3$, in relation to the features mentioned above.

On comparison, Fig.1a and 1b show striking similarity. In both the structures, the sugar-phosphate backbone has zig-zag progression and the minor and major grooves are equally deep. But the model of Arnott et al. (shown in Fig.1c) is quite different (1); neither the phosphate groups have zig-zag progression nor the minor and major grooves are equally deep. In Fig.1c the two antiparallel chains are too close to each other as compared to the structure of $d(CG)_3$.

In our model R_p in dGpC is 7.30 Å and R_p in dCpG is 6.25 Å; similar to those found in $d(CG)_3$. In the model of Arnott et al., R_p in dGpC is 8.5 Å and R_p in dCpG is 9.5 Å, quite in contrast to the structure of $d(CG)_3$ where R_p (in dCpG) $<$ R_p (in dG_pC). On the contrary, one finds close similarities between our model and the structure of $d(CG)_3$. In both the cases, imidazole of G residues occur at the outer surface of the

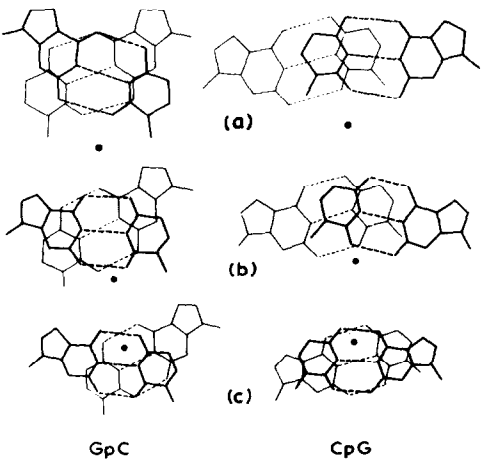

Fig. 2 : Stacking arrangements for GpC and CpG sequences (a) the present model, (b) the crystal structure of $d(CG)_3$ and (c) the model proposed by Arnott et al (1).

helix along with the phosphates in GpC which have larger radii than those in CpG. Even though in the model of Arnott et al. G's have higher radii than C's, the former are always about 3 Å inside the helix surface (see Fig.3 of reference 1).

Stacking patterns as found in our model (Fig.2a) and as observed in $d(CG)_3$ (Fig.2b) are almost identical. In GpC, there is physical overlap between intrastrand G and C in both the cases while in CpG there exists interstrand stacking overlap between C and C (Fig.2a and 2b). In the model of Arnott et al. stacking overlap in GpC (Fig.2c) is very similar to that found in $d(CG)_3$ (Fig.2b). However, in CpG stacking overlap is between intrastrand C and G and not between interstrand C and C.

Thus, it is our model which closely resembles the crystal structure of $d(CG)_3$ and not the one proposed by Arnott et al (1). It is indeed surprising that Arnott et al. (1) have claimed that the model of poly d(GC).poly d(GC) as proposed by

them is very similar to Z-DNA found in the crystal. In view of the fact that Arnott et al. admitted that the model given by them is not necessarily the only one solution to the fibre data of poly d(CG).poly d(GC) at high salt, the present model merits refinement against fibre diffraction data of poly d(GC).poly d(GC).

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