

Z-DNA

The formation of Z-DNA is extremely composition and base sequence dependent. In general, only alternating co-polymers can form Z-DNA (G-C)₂, the compositional isomer, dG:dC, does not form Z-DNA at all.

The formation of Z-DNA is solvent dependent. In oligonucleotides, it forms only in the presence of alcohol and either very high or very low salt. Moreover, as we shall see, the salt concentration affects the sugar puckering assumed.

The main characteristics of Z-DNA is that it is a left-handed double helix. (examine **FIGURE 32**). It contains ~12-13 base pairs/turn of helix so it is a relatively loosely wound helix. It is called Z-DNA because of the zig-zag pattern of the phosphate back bone. In fact, this zig-zag forms the repeating unit of the Z-form DNA- UNLIKE A AND B-DNA, THE REPEATING UNIT OF Z-DNA IS A DINUCLEOTIDE. We will illustrate why that is in a moment.

This zig zag pattern of the backbone is a result of an alternating χ angle configuration in the backbone and with the correlated differences in the sugar pucker. The pucker of the C, or **pyrimidine** is **C2'endo**, and the base is in the **anti** configuration. The G, or **purine** residue is in the **syn** configuration. The sugar attached to the G residue is in the **C3'endo** configuration.

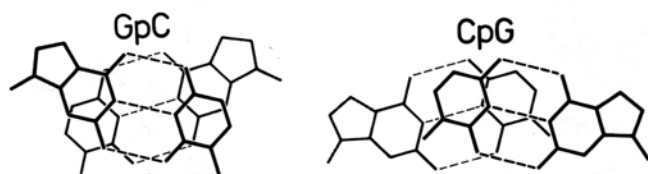


Figure 37 Stacking of adjacent bases in left-handed poly(dG-dC) poly (dG-dC) for sequences d(GpC), left, and d(CpG), right. Note that in d(GpC), intrastrand stacking between guanine and cytosine occurs and base-pairs are related by screw rotation. In contrast, in d(CpG) only interstrand stacking between cytosines is indicated and guanines interact with O_{4'} of adjacent deoxycytidine. Dots in minor groove represent location of helix axis. Drawn with Z₁-DNA coordinates given in (917).

As a consequence of this alternating backbone conformation, the base stacking patterns in Z-DNA are quite bizarre (**FIGURE 37**). In the GpC step, relatively normal intrastrand base stacking interactions occur, while in the CpG step, there is a very extensive INTERSTRAND stacking of the C residues. The G residues are not stacked with the bases at all, but are instead stacked over the O₄ of the furanose of the adjacent cytidines. This pattern repeats its way down the chain.

These things; the alternating sugar pucker and associated anti/syn conformation together and the alternating base stacking patterns serve to place the phosphates associated with the G and C bases in chemically non-equivalent environments. They in fact are different distances from the helix axis CpG=6.2 and GpC=7.6. Summing these factors together should convince you that the repeating unit of the Z-DNA is the dinucleotide.

The helical projections of Z-DNA are also unique. Z-DNA has only a minor groove; the G-C base pairs are not symmetrically related to the helix axis. Instead, they are shifted, with the C5 of the cytosine and the N7 and C8 atoms projecting into the major groove. This gives the Z-DNA helix its bizarre appearance, the major "groove" is convex as opposed to the normal concave. Because of this shift, the minor groove is extremely deep and very narrow, so the information content of this DNA structure is limited.

As I stated before, solvent has a remarkable affect on Z-DNA structure at the microscopic level. In low salt, the N2 of guanine is hydrogen bonded via a H₂O molecule to the PO₄ on the 3' side of the base. In this

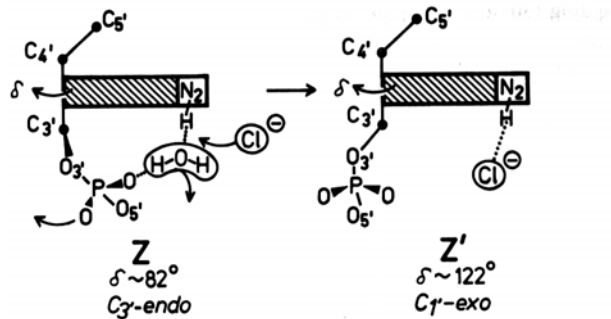


Figure 38 Solvent interactions in Z-DNA. Left: a water molecule mediates an intranucleotide hydrogen bond between N_2 and the phosphate group at the 3' end of *syn*-deoxyguanosine. Right: the water molecule is replaced by chloride which repels the phosphate. As a consequence, torsion angle δ changes from 82° (C_3' -endo sugar pucker) to 122° (C_1' -exo). Redrawn from (302).

configuration, the sugar is in the C_3' endo configuration. In high salt, this water is replaced by a Cl^- ion. The H-bond is no longer made and the negative Cl^- repels the PO_4 and pushes the sugar into the C_1' -exo conformation (Figure 38).

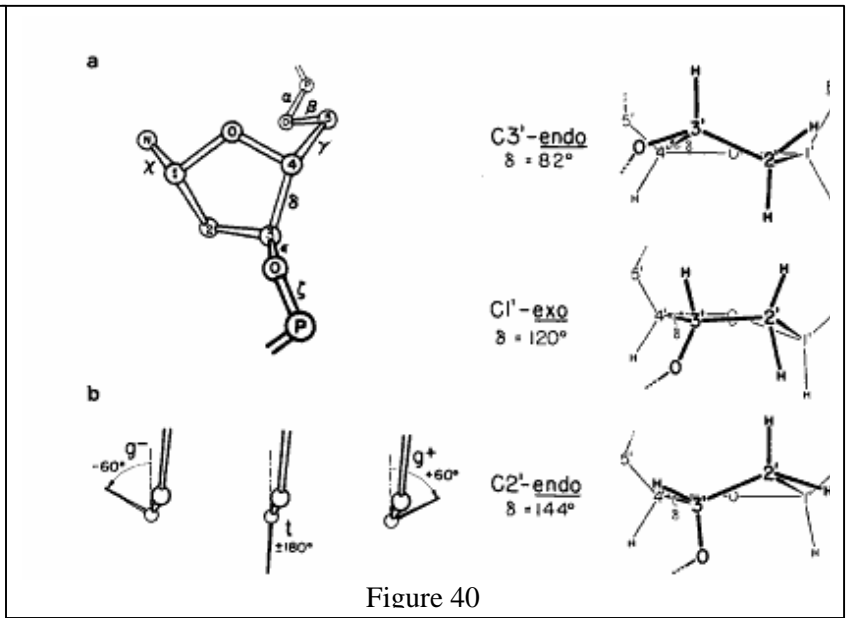
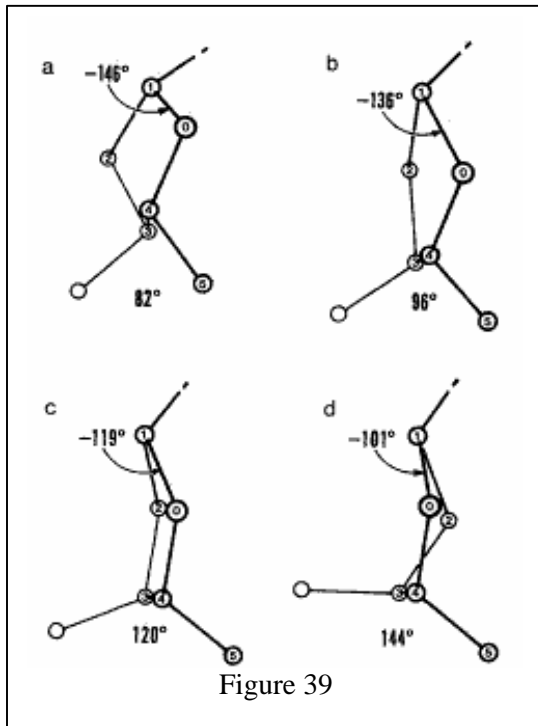
Polymorphism of B-DNA

The fine structure of B-form DNA is very polymorphic—assuming different values for the structural parameters we have discussed; sugar pucker varies, χ varies, propeller twist can be large or small as can be base pair twist or roll. In B-DNA, these parameters and the variations in them are SEQUENCE DEPENDENT!!! This sequence dependence can be understood from the viewpoint that the base pairs wish to maximize their stacking interactions while avoiding steric clashes.

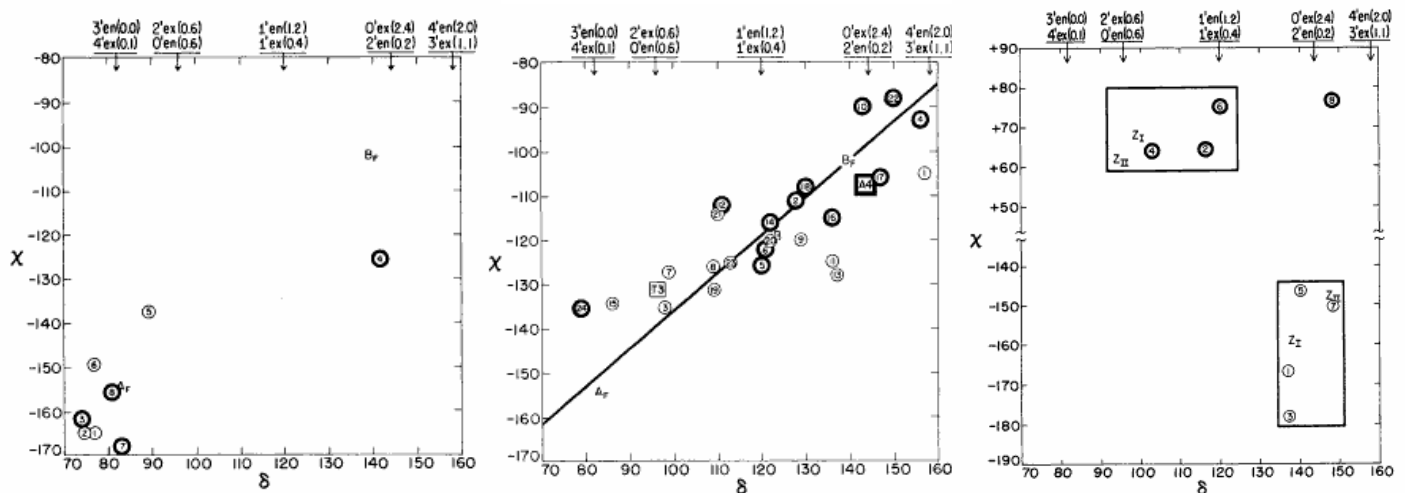
The purpose of propeller twisting is to maximize stacking interactions. The degree of propeller twist is somewhat correlated with helical twist. At values close to 36° , propeller twists are near to zero because satisfactory stacking interaction can occur. Deviations from this ideal result in decreased stacking compensated for by propeller twists. Propeller twists, however, can cause steric clashes in alternating py-pu sequences. These clashes occur between G O6 and A N6 in the major groove for pu3'-py5' sequences and in the minor groove between G N3 and N2 or A N3 atoms for py3'-py5' sequences. The potential for overlap is about twice as severe in the minor groove as compared with that in the major groove. All these clashes can be relieved by the use of one or all of the following strategies.

1. reduce propeller twist
2. open roll angle
3. shift base pair along helical stack so that the purine is pulled out of the helical stack.
4. Decrease the local twist angle

Just like the Ramachandran plots for amino acids which show that particular types of secondary structure have particular values of χ and ϕ angles. Particular pattern variations in sugar torsion angle χ with ϕ are characteristic of a type of DNA. Consider first a C_1' endo configuration of the sugar. Viewed down the C_4' - C_3' bond, there is an 82° ϕ torsion angle between the C_5' and O_3' and the χ angle is 146° . As one opens-up the ϕ by "pushing-up" (anthropomorphically speaking) on O_3' , this move the C_2' carbon leftward, closing down χ (See Figures 39 & 40).



So the kinematic plots for the three different types of DNA double helices are (Figure 41):



A-DNA δ never varies so χ is set

Z-DNA two ranges, one for each base C and G

χ for syn is already restricted on steric constraints

χ for anti adopts a broad value range

δ for G causes it to slip out into groove an unrestricted movement

δ for C changes move it into and away from the helix axis and its

partner so changes in it have dramatic consequences, therefore a narrow range (Figure 42).

