23.3.2.5. *Syn/anti glycosyl bond geometry*

The glycosyl bond angle, χ, about the bond connecting a sugar ring to a base is a special case of torsion angle, and is defined by O4′—C1′—N1—C2 for pyrimidines and O4′—C1′—N9—C4 for purines. In A- and B-DNA, the normal range of χ is 160 to 300°. This is known as the *anti* conformation (right-hand side of Fig. 23.3.2.13) and swings the sugar ring out away from the minor groove edge of the base pair. In Z-DNA, pyrimidines also exhibit the *anti* glycosyl bond conformation, but purines adopt the *syn* geometry shown on the left-hand side of Fig. 23.3.2.13. Now the sugar ring is rotated so that it intrudes into the minor groove, and χ lies in the range 50 to 90°.

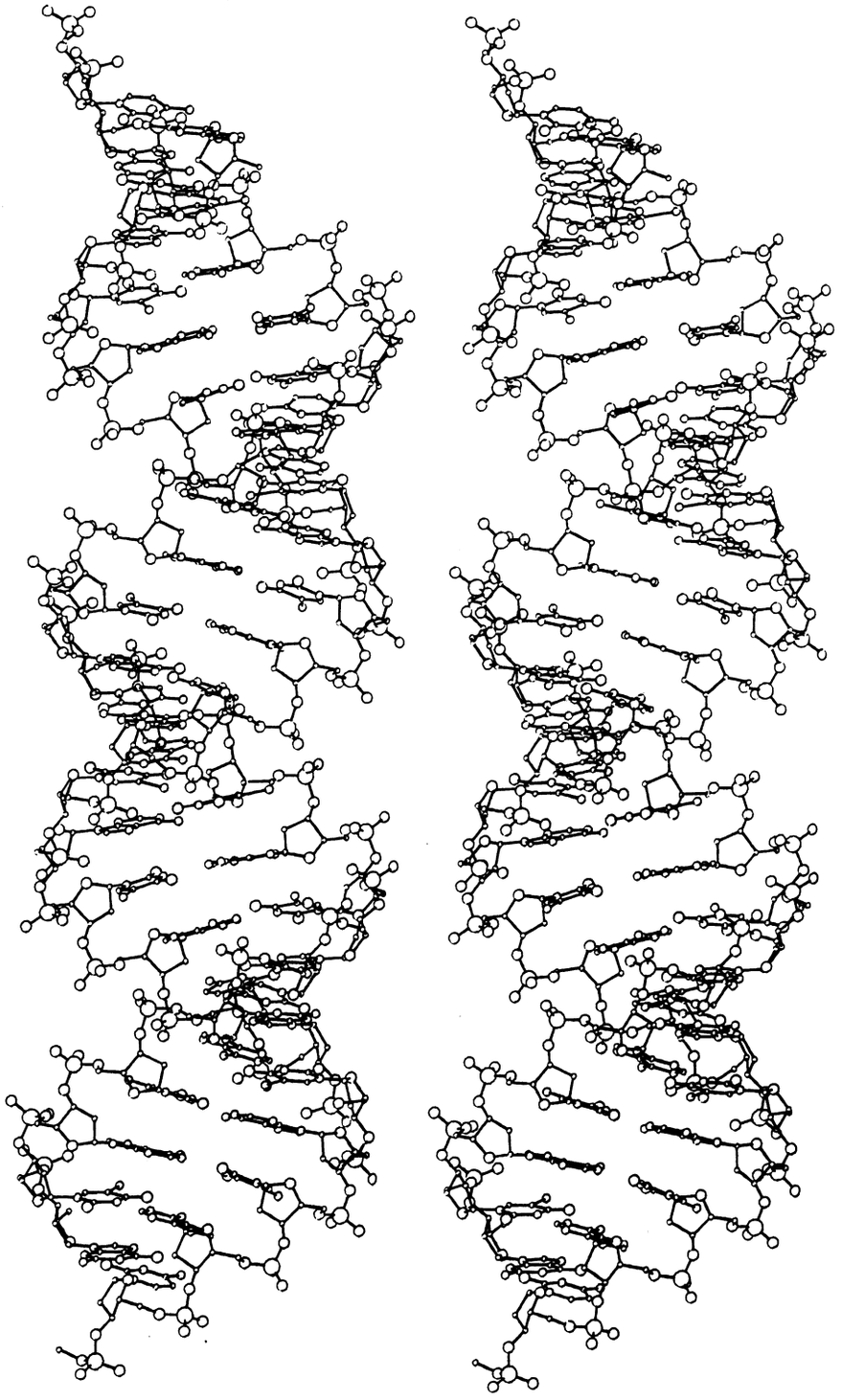

Fig. 23.3.3.1. The A-DNA stereo pair drawing from which Fig. 23.3.1.2 was derived, with repeating sequence -(G-T-A-T-A-C)$_n$-. The impression of the A helix as a ribbon wrapped around an imaginary core is even more strongly developed in this stereo. (From Dickerson, 1983.)

23.3.3. Comparison of A, B and Z helices

Figs. 23.3.3.1–23.3.3.3 show the original stereo pairs that were re-drawn by Irving Geis in preparing Figs. 23.3.1.2–23.3.1.4. These stereo pairs were constructed from X-ray structures of A-, B- and Z-DNA oligomers by deleting the outermost base pair from each end, eliminating the backbone as far as the first phosphate group, and then stacking these trimmed-down helices on top of one another, with phosphate groups overlapping, to create an infinite helix. They are improvements over the idealized infinite helices generated from fibre diffraction in that they display local variation in helix parameters that only single-crystal analyses can reveal. In the present context, they are good subjects for discussion of the differences between the three helix types.

23.3.3.1. *x displacement and groove depth*

A-DNA (Wahl & Sundaralingam, 1996, 1998), B-DNA (Berman, 1996; Dickerson, 1998*b*) and Z-DNA (Ho & Mooers, 1996; Basham *et al.*, 1998) have each been the subject of recent reviews, to which the reader is referred for details that cannot be covered here. The distinctive properties of the three helices are listed in Table 23.3.3.1. The most obvious distinction is handedness: A and B are right-handed helices, whereas Z is left-handed. Moreover, the position of each base pair relative to the helix axis is quite different. As noted in Fig. 23.3.2.13, the helix axis passes through base pairs in B-DNA, lies on the minor groove side of base pairs in Z-DNA, and on the major groove side in A-DNA. In terms of the helix parameters of Fig. 23.3.2.12, A-DNA has a typical *x* displacement of $d_x = +3$ to $+5$ Å, B-DNA has $d_x = -1$ to 0 Å, and Z-DNA has $d_x = -3$ to -4 Å. There is virtually no overlap between these three ranges; *x* displacement, d_x, in fact, is a better criterion for differentiating the three classes of helix than is sugar ring conformation.

A direct consequence of these *x* displacement values is great differences in depths of major and minor grooves. Both grooves are of equivalent depth in B-DNA because base pairs sit on the helix axis. In A-DNA, a base pair is pushed off-axis so

that its minor edge approaches the helix surface, making the minor groove very shallow and the major groove cavernously deep. In Z-DNA, it is the major edge of each base pair that is pushed toward the surface, so that the minor groove is deep and the major groove is so shallow as hardly to be characterized as a groove at all. It is sometimes stated that 'Z-DNA has no major groove', but space-filling stereos, such as Fig. 1 of reference Z6 or Fig. 3 of Z23 reveal the shallowest of major grooves running around the helix cylinder, flanked by very slightly higher phosphate backbones.

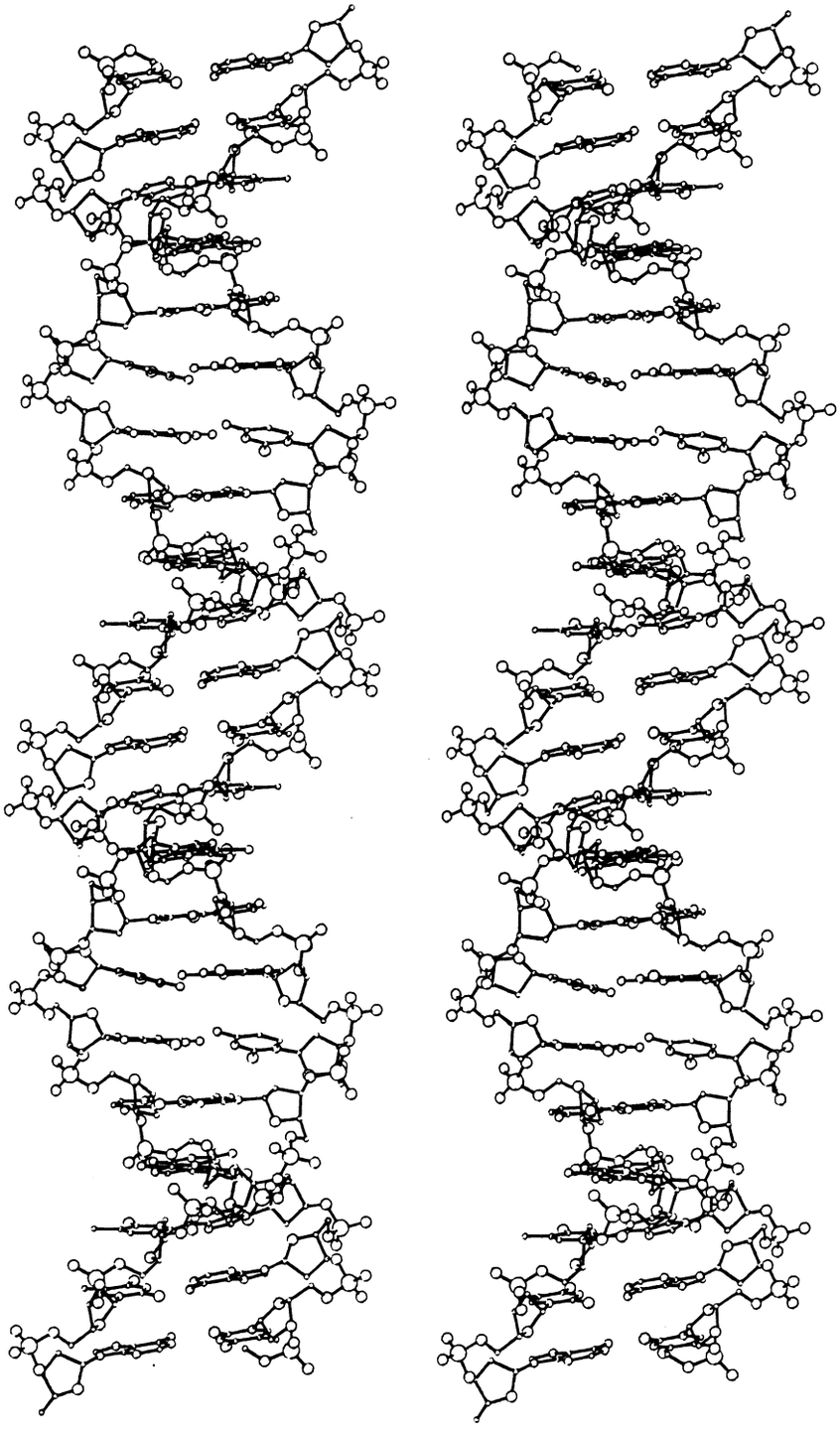

Fig. 23.3.3.2. The B-DNA stereo pair drawing from which Fig. 23.3.1.3 was derived, with repeating sequence -(G-C-G-A-A-T-T-C-G-C)$_n$-. The variation of minor groove widths on the front and back sides of the helix is striking. (From Dickerson, 1983.)

23.3.3.2. *Glycosyl bond geometry*

In both A- and B-DNA, all glycosydic bonds are *anti*, with sugar rings swung to either side away from the minor groove, as in Fig. 23.3.3.4(*a*). As mentioned earlier, when viewed into the minor groove, the backbone chains describe a clockwise rotation, with the chain on the right running downward, and that on the left upward, as in Fig. 23.3.2.1. In Z-DNA, both chains run in the *opposite* direction, leading to a counterclockwise rotation sense viewed into the minor groove. But Z-DNA has yet another striking (and defining) feature. Purines and pyrimidines alternate along each chain. G and C are most strongly favoured by far, but A and T can substitute intermittently at a price in stability. Breaking the strict alternation of purines and pyrimidines is even more unfavourable and is rarely encountered in crystal structures (Table A23.3.1.3). At each purine base, the glycosyl bond is rotated into the minor groove to the *syn* position, as in Fig. 23.3.3.4(*c*). This causes the local backbone directions, defined by sugar ring atoms C4′ and C3′, to be parallel in the two strands. Z-DNA avoids becoming a parallel-chain helix by performing a local chain reversal at each pyrimidine. In Fig. 23.3.3.4(*c*), although the local C4′–C3′ chain direction at the cytosine sugar is downward, the double loop in backbone chain gives it a net upward orientation. In stereo Fig. 23.3.3.3, the ascending backbone chain rises smoothly past each guanine, with a chain path parallel to the helix axis. However, the chain bends abruptly at right angles when passing a cytosine, in a direction tangential to the helix cylinder. Guanine sugar rings point their O4′ oxygen atoms in the backward chain direction (as is also true for all bases in A- and B-DNA), but cytosine sugars point their oxygens in the forward direction. This 'up at G, across at C' pathway and inversion of sugar rings is what produces the zigzag backbone pathway that leads to the name Z-DNA. The O4′ atom of each cytosine sugar is stacked on top of the guanine ring of the subsequent nucleotide, and this stacking of a polar O (or N) on top of a polarizable aromatic ring contributes to the stability of the Z helix, as it does to many other base–base interactions to be discussed later (Bugg *et al.*, 1971; Thomas *et al.*, 1982; B32).

23.3.3.3. *Sugar ring conformations*

Sugar ring conformations in A- and B-DNA have a logical structural basis. The B-DNA backbone is more extended than the A-DNA backbone, with P–P distances of *ca* 6.6 Å along one chain, compared with *ca* 5.5 Å in A-DNA. In turn, C2′-*endo* is a more extended ring conformation than C3′-endo, demonstrable in Fig. 23.3.2.4 by a greater distance between C5′ and O3′ atoms. Hence, it is logical that

references