sequence: TCGCGAATTCGCG
GCGCTTAAGCGCT

That sequence contains the recognition sequence for *Eco*RI, GAATTC, and is closely related to the dodecamer studied by Dickerson and colleagues[17]. Frederick *et al.* find that the protein-bound DNA has several unusual features, including three kinks. One kink (the 'neo-1' kink) is in the centre of the DNA molecule, on the dyad symmetry axis, and represents a torsional dislocation between two segments of B-form DNA. One can think of this kink as being generated in two steps: first, the DNA is unwound by 25° between the base pairs to either side of the kink, then the DNA is bent 12° into the minor groove. This is the mechanism of kinking postulated by Crick and Klug[7] in their kinked-helix model, but the present neo-1 kink differs from the Crick–Klug kink by restricting itself to a modest 12° bend, rather than taking advantage of the full 100° bend that model-building suggests is available. In the complex with *Eco*RI, the neo-1 kink is required to widen the major groove, facilitating access to the bases and allowing an extensive complementary interface with the protein dimer.

The other two kinks ('neo-2 kinks') differ from the neo-1 kink, but are identical to each other because they occupy equivalent positions about the complex's dyad axis. The neo-2 kinks separate the terminal (T)CGC blocks from the central GAA blocks and are produced in a different way from the neo-1 kink. They lack noticeable unwinding; a base-roll[17] into the minor groove produces a bend of 23°. While the central GAA blocks appear to be B-like, the terminal (T)CGC blocks appear to be A-like. Frederick *et al.* suggest that the neo-2 kink may arise from the joining of these two different DNA conformational blocks. It should be noted that in a previous model-building study, Selsing *et al.*[18] found that they could not build a stereochemically acceptable A–B junction of the sort proposed here. Selsing *et al.* found it necessary to have at least one intervening base pair separating orthodox A-and B-form regions. A better understanding of the neo-2 kink must await determination of the atomic positions of the base pairs involved.

A final striking feature of the *Eco*RI–DNA complex concerns the effects of DNA sequences flanking the enzyme's recognition sequence, GAATTC. Different flanking sequences are known to influence the hydrolysis rate by an order of magnitude[19]. Surprisingly, therefore, Frederick *et al.* see no contacts between *Eco*RI and DNA bases outside the recognition sequence; only the backbone appears to be contacted. They conclude that the flanking sequences may affect enzyme activity by changing the conformational free energy of the neo-2 kink or of the GCC terminal blocks. An alternative possibility is that different flanking sequences may give rise to different local DNA backbone conformations, for which the enzyme may have different affinities.

One must be aware that *Eco*RI is a hydrolytic enzyme, whose function is to cut the DNA chain between the bases G and A in the sequence GAATTC. The site of cleavage is only 1 bp away from the neo-2 kink and 2 bp away from the neo-1 kink. Presumably the enzyme acts by stabilizing a transition state in which the G-A backbone has an increased lability to hydrolysis. It is feasible that either the neo-2 kink or the neo-1 kink may destabilize the G-A backbone bond, and indeed this may turn out to be the *raison d'être* of the neo-2 kink. This does not detract from the important conclusion that for both CAP and *Eco*RI, and probably many other proteins, dramatically altered DNA structures will be important features in the DNA–protein complexes.

Taken together, the new studies of K-DNA and of CAP–DNA and *Eco*RI–DNA complexes show that the structure and function of a DNA molecule can be affected in important and unexpected ways both by the DNA sequence itself and by the interaction of specific proteins with the DNA. These results suggest that altered DNA conformations are likely to play an important part in DNA packaging and in the sequence-specific recognition of DNA by proteins. □

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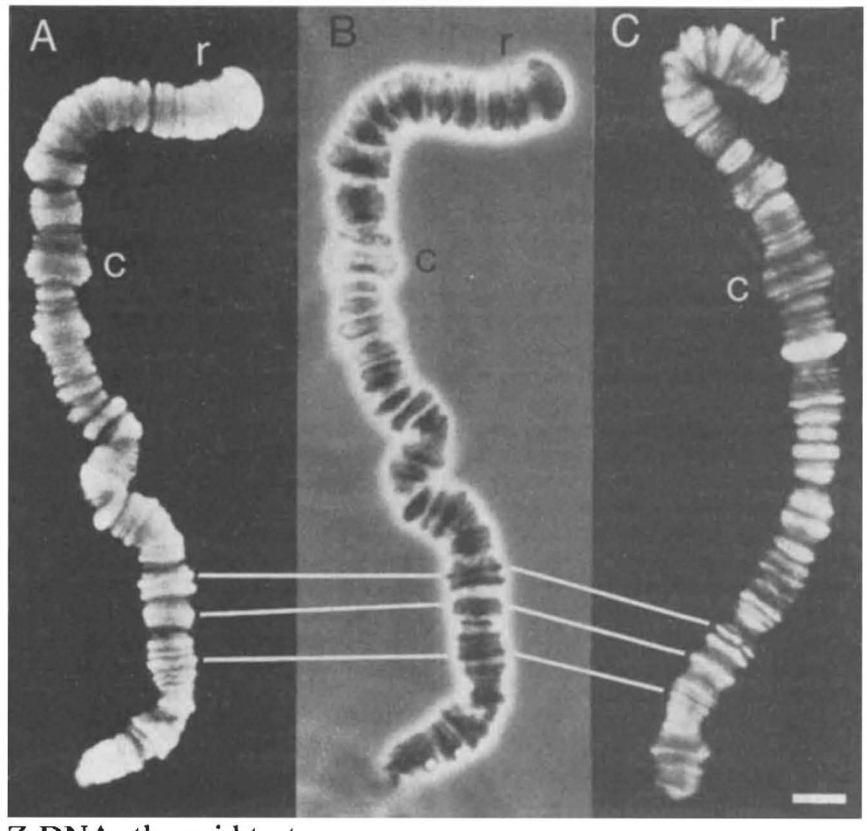

Z-DNA: the acid test

ACID treatment of polytene chromosomes of *Drosophila* before their exposure to an antibody against Z-DNA resulted in these striking immunofluorescent micrographs. A phase-contrast image of an isolated chromosome (B) allows its bands to be clearly identified and makes obvious that Z-DNA is associated with them, both in an acid-treated isolated chromosome (A) and in a 'squash preparation' of a chromosome prepared after acid fixation of the salivary gland (C). In less acid conditions, far less Z-DNA is apparent and it is confined to the periphery of the bands; acid treatment, by stripping proteins from the DNA and by protonating its bases, may both expose masked Z-DNA and induce the transition of B-DNA to Z-DNA. The lines connect bands, 'c' denotes centromere, 'r' the right-hand end of the chromosomes and the bar represents 10 μm. From Robert-Nicoud, M., *et al. EMBO J.* 3, 721 (1984).