DNA transitions as observed by fibre diffraction

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This presentation focuses on x-ray and neutron fibre diffraction studies of structural polymorphism observed in polymeric DNA either of natural origin or synthetically produced to allow the study of a number of well-defined repetitive sequences. Particular emphasis is placed on the reproducibility observed in changes of the conformation and organization of molecules of DNA in fibres in response to changes in hydration. This reproducibility implies a high degree of specificity in the interaction of water with DNA and provides a powerful stimulus for characterizing in as much detail as possible the changes in DNA conformation induced by changes in hydration and the location of water with respect to the DNA in the various conformations.

The resolution of fibre diffraction data from DNA is rarely better than 2 Å *i.e.* comparable to the length of the hydrogen bonds through which water molecules interact with each other and with hydrogen bond donor and acceptor groups in macromolecules such as DNA. Despite the more limited resolution and the complexities involved in data extraction and analysis, fibre diffraction has made critical contributions in characterising the various conformations assumed by DNA molecules and in identifying the factors important in stabilising these conformations and inducing transitions between them. In contrast to the situation for single crystal oligonucleotide work which provides extremely detailed high-resolution information on local sequence dependent variation in structure, fibre diffraction offers information that relates strongly to the regularity and cooperativity of the continuous polymer. The fibrous state, with its typical mix of highly ordered and amorphous regions, can accommodate changes in molecular conformation and packing much more readily than can single crystals, and it is possible for example to study transitions between conformations and changes in molecular arrangement. Since changes in the water content of a fibre can be controlled by varying the relative humidity of the fibre environment, studies of fibres offer the possibility of time-resolved studies of stereochemical pathways followed in structural transitions. While x-ray fibre diffraction methods are not well suited to the study of the location of water in these systems, neutron diffraction, through the isotopic replacement of H_2O by D_2O, can highlight the distribution of water around the DNA polymer. Furthermore, selective deuteration of specific DNA residues is now being employed to address other structural issues in DNA polymorphism.