METAMORPHOSES OF A DOUBLE HELIX

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The X-ray analysis of single crystals of short DNA fragments shows very different conformations of double helical DNA depending on the base sequence (1-3). We have previously found that a DNA with a particular sequence - poly(dG-dC)·poly(dG-dC) - adopts different double helical conformations in solution, depending on the solvent composition (4-6).

The R-L transition of poly(dG-dC) in solution (4) involves the cooperative change from a right-handed B-DNA to a left-handed Z-DNA upon increasing the salt concentration as indicated by circular dichroism, Raman- and NMR-spectroscopy. A detailed study of the thermodynamics and kinetics of this transition was made by using oligo(dG-dC) of different chain lengths. (Varying the number of base pairs provides a very convenient variable for quantitative measurements of such cooperative phenomena in linear macromolecules.) Fig. 1 depicts the results obtained for the equilibrium between the R- and the L-form of oligo(dG-dC) as function of the chain length and the salt concentration.

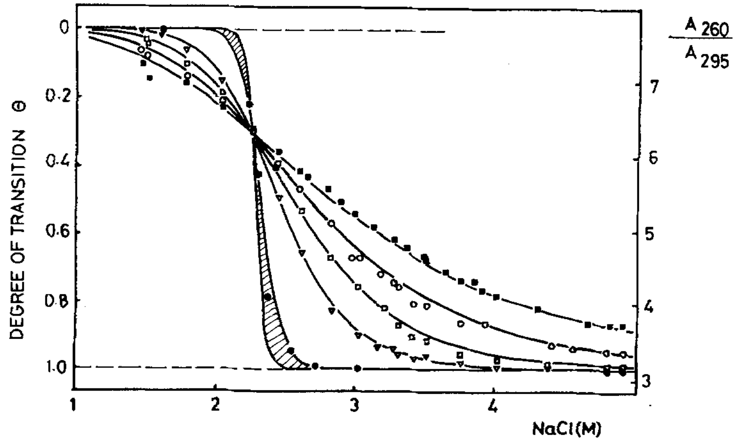

Fig. 1: Equilibrium between the R-form at low salt and the L-form of oligo(dG-dC) at high salt as a function of the sodium chloride concentration for molecules with different numbers of base pairs : six (■), eight (o), eleven (□), sixteen (∇) and about hundred (●).

Keeping the salt concentration constant but varying the water concentrations by adding glycerol, ethylene glycol etc. to the solutions indicates that the B-form of DNA may be preferentially stabilized by an additional cooperative interaction with water molecules as compared to the Z-form.

Experiments with ethidium bromide show that the preferred interaction of these molecules with the R-form shifts the equilibrium in a cooperative way at low concentrations of this intercalating dye.

Kinetic studies allow a detailed mechanism to be proposed which involves for the nucleation reaction about six base pairs.

The quantitative evaluation of the thermodynamics and kinetics of this order-order transition, together with the structural information available, allows for the first time a detailed understanding of such a conformational change of double helical DNA.

The conformations of biological macromolecules are important for their function. It is therefore easy to visualize various regulatory mechanisms for the biological role of natural DNA, based on such conformational changes, although it may be inadvisable at present to extrapolate from the simple model system described above to the complexity of natural DNA in the cell. Further studies will decide whether the structure of natural DNA may be somewhat more complex and variable than originally proposed (7).

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