

Handedness in nature

Poonam Tandon, V.D. Gupta, C. Mehrotra & D. C. Gupta

Department of Physics, University of Lucknow, Lucknow 226 007(India)

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Nature manifests handedness at various levels in the animal as well as vegetable world. It expresses itself in the genetic material, proteins and polypeptides. The predominant conformation in which the DNA molecule exists is the right handed form known as B-DNA. The A form is also right-handed. Since the discovery of left-handed Z form of DNA, several questions have been raised about its role in the evolutionary process and metabolism. It is now well established that whereas the right handed form can accommodate any sequence of nucleotides, the Z form is generally found in sequences having alternating purines and pyrimidines only, e.g. poly d (G-C).

In the present communication we report a study of the reversible transitions between B, Z and other condensed states (ψ (+), ψ (-)) of DNA. This is based on the one dimensional Ising model propounded for ferromagnetic transition and modified suitably by introducing singular interaction between 1 : 4 neighbours (hydrogen bond formation) for the helix \rightleftharpoons coil transition observed in several proteins and polypeptides. Results for B \rightleftharpoons Z \rightleftharpoons ψ (-) \rightleftharpoons coil transitions in poly (dG-dC) and poly(dG-me⁵ dC) have been obtained. Results are consistent with the change in the environmental conditions e.g. change in the cationic concentration of the solvent and methylation of the cytosine residue. The nucleation parameter is consistent with the stabilization/destabilization of the ordered state under these conditions. Possible reasons for the preponderance of right handed DNA over left-handed are discussed.

Key-words—Symmetry, DNA, conformation, transition.

INTRODUCTION

SYMMETRY is an integral part of nature and activity of man (Text-figs 1-6). Most of the natural macromolecules which constitute the vegetable world (polysaccharides, proteins, nucleic acids, etc.) have symmetry elements present in them. Man made molecules such as polyethylene, polypropylene, polytetrafluoroethylene, polypeptides, polyaminoacids, polynucleic acids etc. are also all symmetric. Whether it is a piece of architecture, painting or other creative activities, symmetry adds beauty, harmony and proportion to it. The crystals of snow flakes are an excellent example of the symmetry in nature (Text-fig. 1). However, symmetry conveys much more than these aesthetic attributes. It implies economy of design and underlines laws of conservation. The translational, rotational and mirror symmetry are manifestations of conservation of linear momentum, angular momentum and parity respectively. These conservation laws, in turn, depend on the nature of interactions. For example, if the frictional forces are present, momentum and energy are not conserved.

The abundance of symmetry in the vegetable world is evident in leaves, flowers, fruits and many a time even

in the expansion or growth of a plant. Handedness which could be right or left handed is only one of the symmetry elements. It is not merely an accident or coincidence that proteins, nucleic acids and enzymes are all right handed. It means that only the L-amino acids can combine to give a conformation which is biologically active. The way many creepers wind themselves around the support and the dangling tendrils all have a helical symmetry.

The symmetry of the organic world is entirely different from that of the inorganic world. In an aging process it is observed that left-handed residues enter in a sequence of right handed residues. Too many of such odd residues can result in death. Handedness is therefore characteristic of life. In fact, in some ways search for extraterrestrial life is based on the search for biomolecules which go into right-handed conformation. No such importance is attached to symmetry in inorganic molecules.

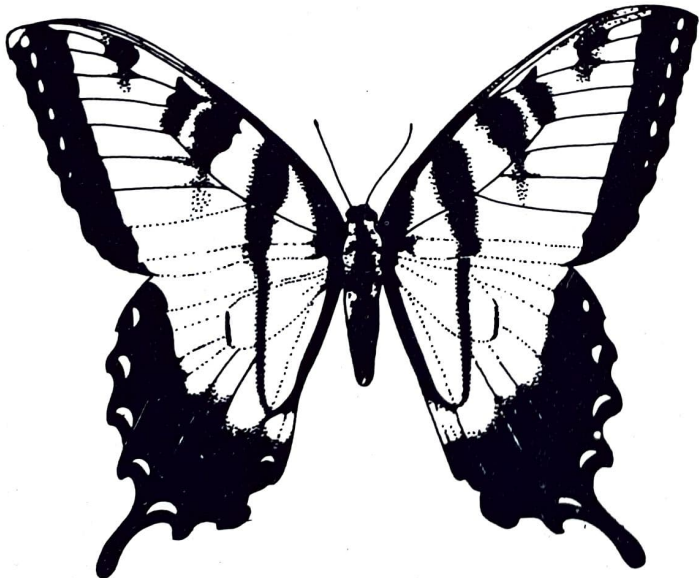
The preponderance of right-handed over left-handed DNA raises many important questions from the view point of natural laws of nature. What are the forces which are responsible for this? Some comments on this would be made towards the end of this paper.

Since the uncoiling of a DNA molecule (melting) is closely related to the translation and transcription of

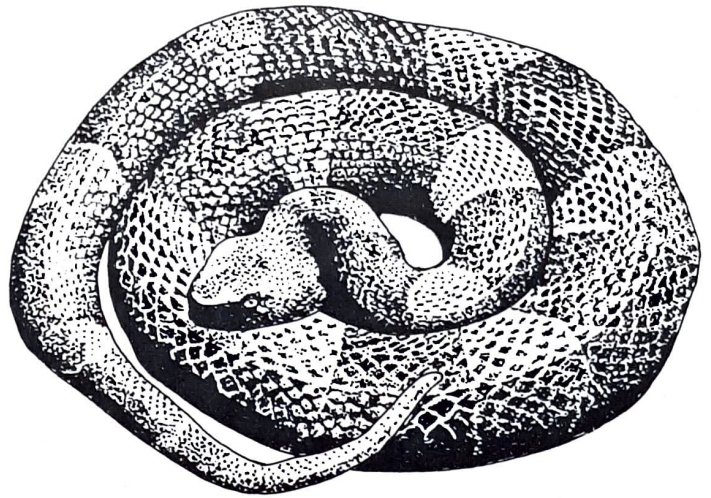


Text-figure 1. Crystalline forms of snow flakes. (Courtesy of the U.S. Weather Bureau; Photo by W.A. Bentley.)

genetic information, it has been the subject of extensive experimental and theoretical studies (Mc Campbell *et al.*, 1989; Ramsing *et al.*, 1989; Ya Azbel, 1980 a,b,c). This form of double stranded DNA is the right handed B-DNA which has a pitch of 34\AA and 10 base pairs/turn. However, with the discovery of Z-DNA by Rich *et al.*

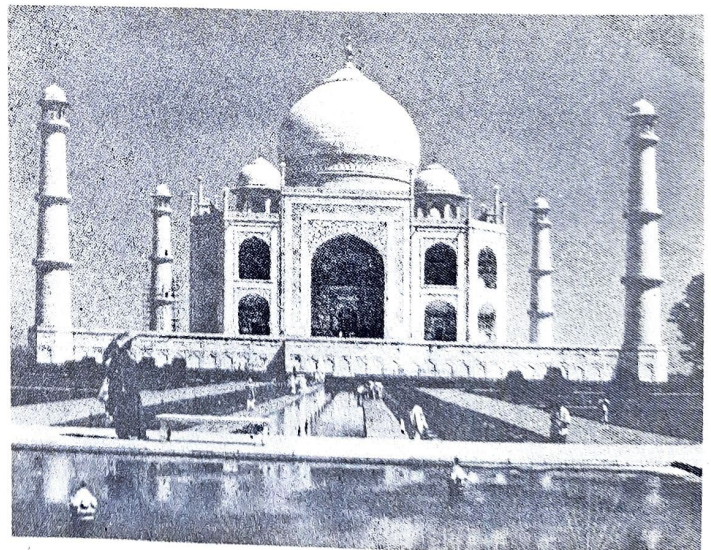


Text-figure 2. Tiger swallowtail butterfly. (Courtesy of the Field Museum of Natural History, Chicago, Illinois.)

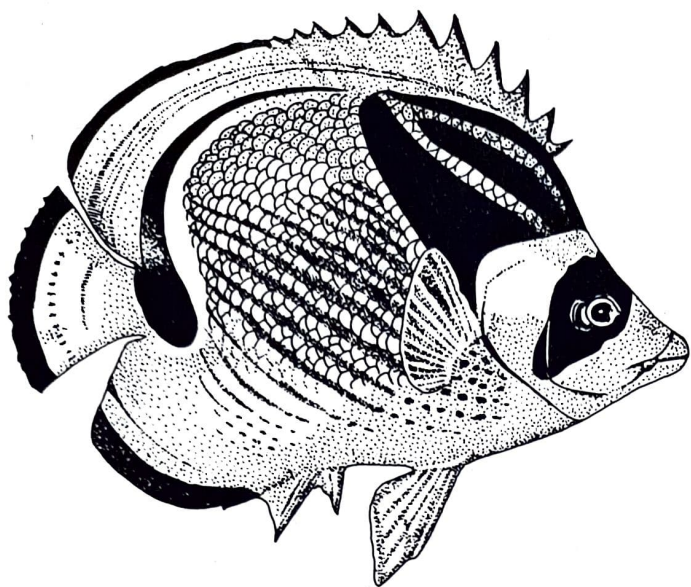


Text-figure 3. Broad-banded copperhead snake. (Courtesy of the Field Museum of Natural History, Chicago, Illinois.)

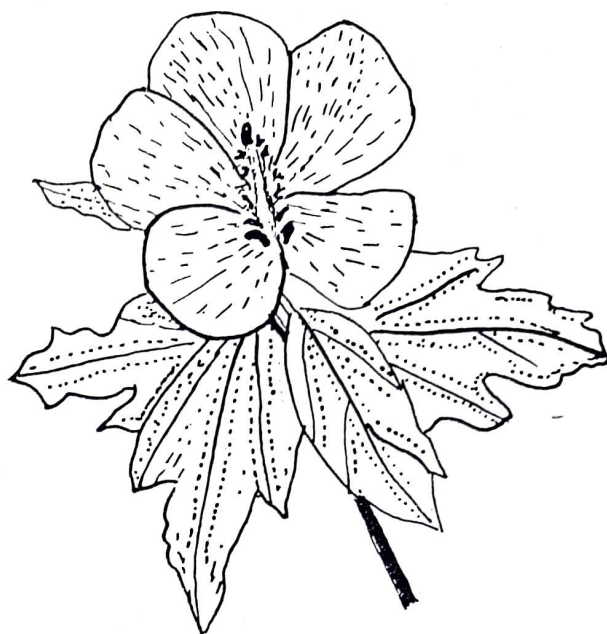
(1984) such studies have received an additional push. All spectroscopic (proton NMR, ORD, CD) and physicochemical studies such as X-ray diffraction, I.R., U.V. etc. (Behe & Felsenfeld 1985; Chaires & Sturtevant, 1986, 1988; Gulatto *et al.*, 1989; atha & Brahmchari 1985, 1986; Latha *et al.*, 1983; Narasimhan & Bryan 1984; Ramesh & Brahmchari, 1983; Souche *et al.* 1985; Feigon *et al.*, 1985; Zacharias *et al.*, 1982) indicate that Z-DNA is a left-handed structure. It has a pitch of 44.6\AA and 12 base pairs/turn. This conformation is chiefly observed in Poly (dG-dC) under proper environmental conditions. Although Poly (dA-dT) does not exist in the Z form, it is found that isolated A-T pairs can be accommodated in the sequence of C-G pairs (Latha & Brahmchari, 1986; Wang *et al.*, 1985; Rich *et al.*, 1984; Jovin *et al.*, 1987). It may however be added here that in a recent report Adam *et al.* (1986 in Jovin *et al.*, 1987) have reported existence of Z-conformation



Text-figure 4. Taj Mahal, Agra, India. (Courtesy of the Government of India Tourist Office, 201 N. Michigan Ave., Chicago, Illinois.)



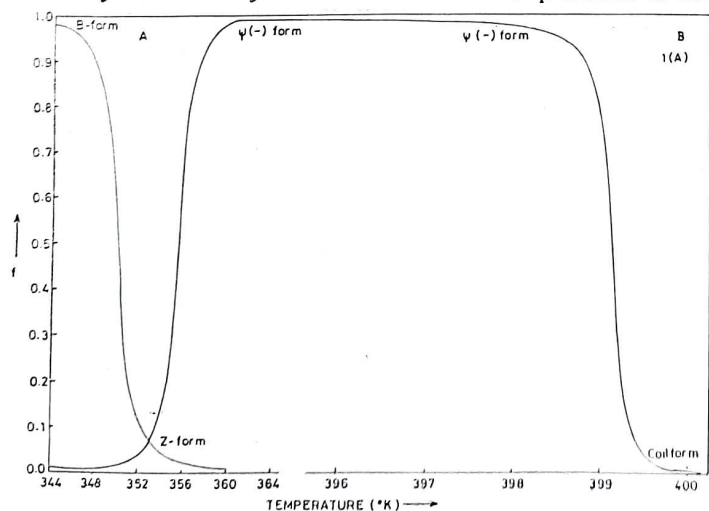
Text-figure 5. Banded butterfly fish (Courtesy of the Field Museum of Natural History, Chicago.)



Text-figure 6. Flower symmetry

in Poly (dA-dT) films containing Ni^{++} and low water activity. Z-DNA has also been detected in fibres and films of DNA, poly- and oligo-mers, in supercoiled plasmids, and in chromosomes and cells. Z structure is unique in many ways. It is considered as variant of sugar modification and has been observed in double stranded RNA as well (Cruz *et al.*, 1986 in Jovin *et al.*, 1987). Further, it is observed that d(C-G)_n oligomers (n=2,3 and 4) crystallize in the left handed Z conformation but the corresponding d(G-C)_n oligomers are not found to do so (Jovin *et al.*, 1987). Thus the two sequence isomers must have different energetics.

Methylation of the cytosine residue at the C5 position is found to bring about changes in the biological activity of the molecule, e.g., it is prevalent in eukaryotic and prokaryotic genome of viral DNA (Souche *et al.*, 1985). Methylation of cytosine residue at C5 position is also

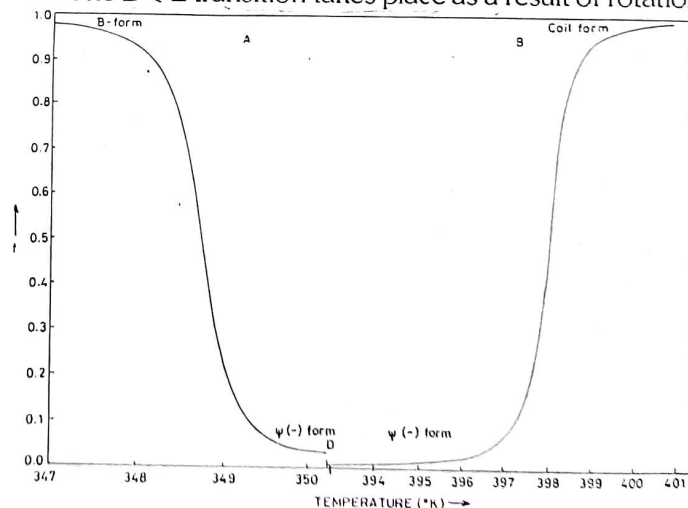


Text-figure 7. Theoretical transition-curves for poly (dG-dC) :
(A) $B \rightleftharpoons Z$ and $Z \rightleftharpoons \Psi$
(B) $\Psi(-) \rightleftharpoons \text{coil}$

responsible for the destabilization of B structure (Latha & Brahmchari, 1986; Souche *et al.*, 1985; ehe & Felsenfeld, 1985; Narsimhan & Bryan, 1984; Chaires & Sturtevant, 1986, 1988). This is mainly due to unfavourable interactions between the hydrophobic methyl group and water molecule. This destabilization of B helix would in turn, lead t the stabilization of Z conformation.

The study of Z-DNA is of both physicochemical and biological interest. The conformation is considered to be important in regulating gene activity, and it is an important intermediate in genetic recombination in a simple eukaryote, the yeast like fungus called *Ustilago* (Marx, 1985). It is quite possible that the preponderance of the right-handed over the left-handed DNA is related to the biological evolution process of the universe.

The $B \rightleftharpoons Z$ transition takes place as a result of rotation



Text-figure 8. Theoretical transition-curves for poly (dG-dC) :
(A) $B \rightleftharpoons \Psi(-)$
(B) $\Psi(-) \rightleftharpoons \text{coil}$

around the glycosidic bond resulting in syn-conformation and C3' endo sugar pucker of purines. This combined with the rotation of cytidine residue in the anti-conformation gives rise to the characteristic zig-zag of the sugar phosphate backbone (Jovin *et al.*, 1987; Rich *et al.*, 1984; Wang *et al.*, 1979).

The exact mechanism of $B \rightleftharpoons Z$ transition is not yet fully understood. However, it is definitely related to the lowering of water activity in presence of reagents like salts, alcohols, increasing temperature and in particular, presence of cations like Na^+ and Mg^{++} . The cations play an important role in masking the phosphate repulsions. These stabilizing forces are further reinforced by modification of water structure around the DNA molecule in the presence of salts. The stability/destability of the B helix is inherent in the sugar phosphate backbone conformation.

Various theories have been advanced for explaining the $B \rightleftharpoons Z$ and $Z \rightleftharpoons$ coil transitions. The later transition, in certain cases is preceded by another transition called $Z \rightleftharpoons \psi$ (-) transition (Chaires & Sturtevant, 1986, 1988). The ψ (-) is the condensed state of the DNA with left-handed conformation and the geometry of B form. The ψ (-) form is found in solution containing polyethylene glycol and a critical NaCl concentration (Chaires & Sturtevant, 1988). The counter ψ (+) form is also reported to occur in sodium acetate solution or in the presence of Hexamine cobalt. It has a right-handed conformation but different geometry.

In the present communication we have made efforts to explain order \rightleftharpoons order and order \rightleftharpoons disorder transitions in a variety of conformationally permissible polynucleotide system. We have also tried to explain the specific heat measurements in the neighbourhood of transition. In brief, the theoretical approach is a modification and development of the Zimm and Bragg (1959) theory of helix \rightleftharpoons coil transition. In fact all theories which have been framed to explain phase transition in biomolecules are based on a two phase cooperative model first enunciated by Ising for a chain of linear spins to explain ferromagnetism (Agnihotri *et al.*, 1981).

THEORY

The present theory is a variant of the Zimm and Bragg (1959) formalism enunciated for helix \rightleftharpoons coil transition. This has been earlier used to explain order \rightleftharpoons order transition in case of Poly-L-Proline I \rightleftharpoons Poly-L-Proline II (right handed to left handed) transition (Agnihotri *et al.*, 1981). In Brief if we assume σ_1 and σ_2 to be the nucleation parameters and s_1 and s_2 are the growth parameters in the states h_1 and h_2 which represent the right-handed and left-handed helices in order \rightleftharpoons order transition, e.g., $B \rightleftharpoons Z$ transition then the transition matrix can

be written down as :

$$M = \begin{matrix} & h_1 & h_2 \\ \begin{matrix} h_1 \\ h_2 \end{matrix} & \begin{bmatrix} s_1 & \sigma_2 s_2 \\ \sigma_1 s_1 & s_2 \end{bmatrix} \end{matrix} \quad (1)$$

Going through the matrix evaluation formalism outlined by Zimm and Bragg (1959), we obtain expression for the fraction of segments in the form I (say from B in $B \rightleftharpoons Z$ transition):

$$f_1 = \frac{1}{N} \frac{\ln Z}{\ln s_1} = \frac{\frac{s_1}{\lambda_1} \frac{\delta \lambda_1}{\delta s_1} + B \frac{s_1}{\lambda_2} \frac{\delta \lambda_2}{\delta s_1} + \frac{1}{N} \left(\frac{s_1}{A_1} \frac{\delta A_1}{\delta s_1} + B \frac{s_1}{A_2} \frac{\delta A_2}{\delta s_1} \right)}{(1+B)} \quad (2)$$

where Z is the partition function of N segment chain, λ_1 and λ_2 are eigen values of M .

$$B = \left(\frac{X_2}{X} \right)^{sub} \left(\frac{A_2}{A_1} \right) \quad (3)$$

with $X_1 = s_1 \lambda_1$ and $X_2 = s_1 \lambda_2$

$$A_1 = \frac{s_1 + s_2 x - b \lambda_2}{\lambda_1 - \lambda_2} \quad (4a)$$

$$A_2 = \frac{s_1 + s_2 x - b \lambda_1}{\lambda_2 - \lambda_1} \quad (4b)$$

$$b = \frac{1 + x - \sigma_2 - \sigma_1 x}{1 - \sigma_1 \sigma_2} \quad (5)$$

and $x = \sigma'' / \sigma'$

Where σ' and σ'' are the parameters giving the interaction of end segments with the solvent when they are in states h_1 and h_2 respectively.

$$\frac{s_1}{\lambda_1} \frac{\delta \lambda_1}{\delta s_1} = \frac{X_1 - 1}{X_1 - X_2} \quad (6a)$$

$$\frac{s_1}{\lambda_2} \frac{\delta \lambda_2}{\delta s_1} = \frac{X_2 - 1}{X_2 - X_1} \quad (6b)$$

$$\frac{s_1}{A_1} \frac{\delta A_1}{\delta s_1} = \frac{s^2 (2\sigma - 1 + b - x - b\sigma) + s (1 + x - b + b\sigma - 2\sigma x)}{[(1-s)^2 + 4\sigma x] (s + x - bX_1)} \quad (7a)$$

$$\frac{s_1}{A_2} \frac{\delta A_2}{\delta s_1} = \frac{s^2 (2\sigma - 1 + b - x - b\sigma) + s (1 + x - b + b\sigma - 2\sigma x)}{[(1-s)^2 + 4\sigma x] (s + x - bX_2)} \quad (7b)$$

where $\sigma = \sigma_1 \sigma_2$ and $s = s_1 / s_2$

The extension of this formalism for specific heat is straightforward. The specific heat is related to the molar enthalpy and entropy changes in the transition from state I to state II. From well known thermodynamic relation free energy F is given by

$$F = -KT \ln Z \quad (8)$$

and the internal energy U is given by

$$U = -T^2 \frac{\delta}{\delta T} \left(\frac{F}{T} \right) \quad (9)$$

Differentiating the above equation with respect to temperature and making use of

$$s = \exp \left[\frac{\Delta H}{R} \left(\frac{1}{T} - \frac{1}{T_f} \right) \right] \quad (10)$$

where ΔH is the molar change in enthalpy about the transition point and T_f is the transition temperature.

We get specific heat C_v as

$$C_v = \left(\frac{\delta U}{\delta T} \right)_V = Nk \left(\frac{\Delta H}{RT} \right)^2 \left(s \frac{\delta f_1}{\delta s} \right) \quad (11)$$

where

$$\begin{aligned} \frac{\delta f_1}{\delta s} = & -\frac{f_1}{1+B} \frac{\delta B}{\delta s} + \frac{1}{(1+B)} \left[\frac{\delta}{\delta s} \left(\frac{s_1}{\lambda_1} \frac{\delta \lambda_1}{\delta s_1} \right) + \frac{1}{N} \frac{\delta}{\delta s} \left(\frac{s_1}{A_1} \frac{\delta A_1}{\delta s_1} \right) \right. \\ & + \frac{\delta B}{\delta s} \left(\frac{s_1}{\lambda_2} \frac{d \ln \lambda_2}{\delta s_1} + \frac{1}{N} \frac{s_1}{A_2} \frac{\delta A_2}{\delta s_1} \right) + B \left\{ \frac{\delta}{\delta s} \left(\frac{s_1}{\lambda_2} \frac{\delta \lambda_2}{\delta s_1} \right) \right. \\ & \left. \left. + \frac{1}{N} \frac{\delta}{\delta s} \left(\frac{s_1}{A_2} \frac{\delta A_2}{\delta s_1} \right) \right\} \right] \quad (12) \end{aligned}$$

with

$$\frac{\delta B}{\delta s} = NB \left[\frac{1}{X_2} \frac{\delta X_2}{\delta s} - \frac{1}{X_1} \frac{\delta X_1}{\delta s} \right]$$

$$+ B \left[\frac{1-b}{(s+x-bX_1)} \frac{\delta X_1}{\delta s} - \frac{1-b}{(s+x-bX_2)} \frac{\delta X_2}{\delta s} \right] \quad (13)$$

$$\frac{\delta X_1}{\delta s} = \frac{1}{2} + \frac{[(s-1)+2\sigma]}{2[(s-1)^2 + 4\sigma s]^{1/2}} \quad (14a)$$

$$\frac{\delta X_2}{\delta s} = \frac{1}{2} - \frac{[(s-1)+2\sigma]}{2[(s-1)^2 + 4\sigma s]^{1/2}} \quad (14b)$$

$$\frac{\delta}{\delta s} \left(\frac{s_1}{\lambda_1} \frac{\delta \lambda_1}{\delta s_1} \right) = \frac{\sigma(s+1)}{[(s-1)^2 + 4\sigma s]^{3/2}} \quad (15a)$$

$$\frac{\delta}{\delta s} \left(\frac{s_1}{\lambda_2} \frac{\delta \lambda_2}{\delta s_1} \right) = -\frac{\sigma(s+1)}{[(s-1)^2 + 4\sigma s]^{3/2}} \quad (15b)$$

Now in case of helix coil transition, in the present notation the fraction of ordered segments

$$f_h = \frac{1}{N} \frac{\ln Z}{\ln s} = \frac{[1-C_1(1-B)] - (\alpha N) [1-C_1(1+B)]}{1+B} \quad (16)$$

where

$$B = \left(\frac{X_2}{X_1} \right)^N \left(\frac{C_2}{C_1} \right) \quad (17)$$

$$C_1 = \frac{X_1-s}{X_1-X_2}; \quad C_2 = \frac{X_2-s}{X_2-X_1}$$

with $\alpha = x/y$; $x = X_1 + X_2$ and $y = X_1 - X_2$

For $N \rightarrow \infty$ if the roots are not degenerate and $X_1 > X_2$

$$f_h = \left[1 - C_1 \left(\frac{1-B}{1+B} \right) \right] \quad (18)$$

The specific heat C_v is given as

$$C_v = Nk \left(\frac{\Delta H}{RT} \right)^2 s \frac{\delta f_h}{\delta s} \quad (19)$$

$$s \frac{\delta f_h}{\delta s} = \frac{1}{(1+B)} \left[\left(s \frac{\delta B}{\delta s} \right) (C_1 - f_h + C_1 \alpha N) + \alpha C_1 (C_1 - 1) \right]$$

$$[(1-B) - \alpha(1+B)N] - (1/N) [1 - (1+B)C_1] (1-X_2) (\alpha^2 - 1)] \quad (20)$$

with

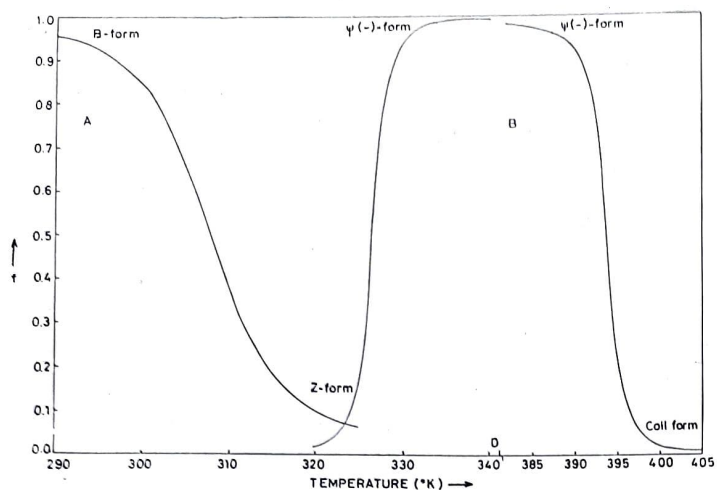
$$s \frac{\delta B}{\delta s} = B [N(2C_1 - 1) + \alpha] \quad (21)$$

RESULTS AND DISCUSSION

All the input parameters, i.e. enthalpy change around the transition point for a given chain length, transition temperatures and nucleation parameters are given below (Table 1-3). The data in table 1 and table 2 correspond to Poly(dG-dC) ($N=2150$) and Poly(dG-dC) ($N=800$) respectively and the data in table 3 corresponds to Poly(dG-me⁵dC) ($N=500$). These data have been obtained from the work of Chaires and Sturtevant (1986, 1988) and Behe and Felsenfeld (1985).

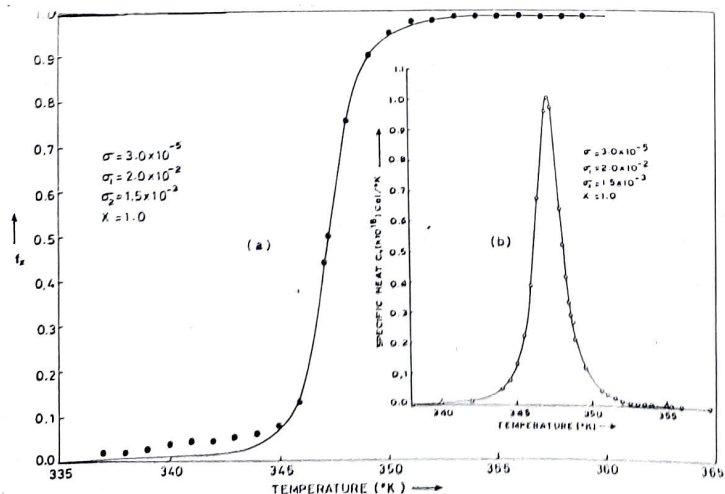
ORDER \rightleftharpoons ORDER TRANSITION

Theoretical transition curves for $B \rightleftharpoons Z$, $Z \rightleftharpoons \psi(-)$, $Z \rightleftharpoons B$ and $B \rightleftharpoons \psi(-)$ transitions have been obtained from equation (2). These transition curves are shown in text figures 7(A), 8(A), 9(A), 10(a) and 11(a). Apparent discontinuity at a point D in figures is due to the jump in the temperature scale. Various transition parameters which provide the best fit to the experimental data are given in

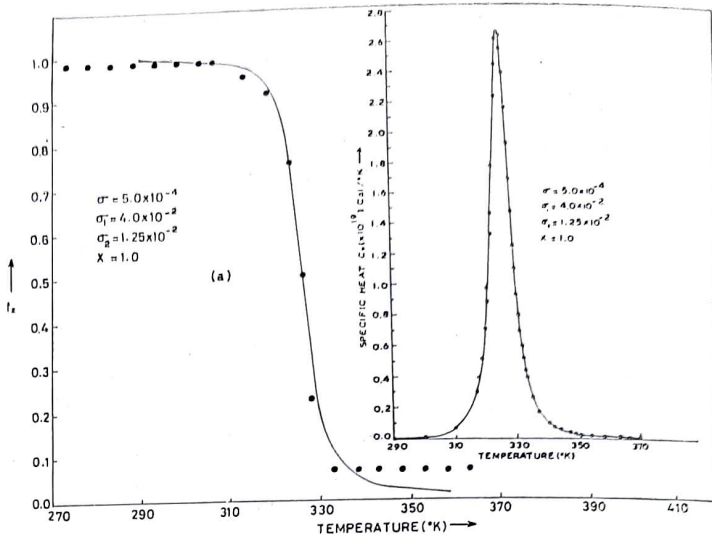


Text-figure 9. Theoretical transition-curves for poly (dG-me5 dC) :
(A) $B \rightleftharpoons Z$ and $Z \rightleftharpoons \psi(-)$ (B) $\psi(-) \rightleftharpoons \text{coil}$

table 1,2, and 3. The end effect parameter x has been chosen to be equal to unity because end effects are negligible for a very long chain. The conversion of Poly (dG-dC) and its methylated analogue from a right-handed to a left-handed helix has been ascribed to the salt related electrostatic interactions of polynucleotide and to the alteration of the water structure around the guanine amino group. From text-figures 7(A) and 10(a) it is clear that the sharpness of $B \rightleftharpoons Z$ transition increases with increase in Mg^{++} concentration which results in the smaller value of σ at the higher Mg^{++} concentration. This is unlike $\psi(-)$ to coil transition where the transition is sharper at lower Mg^{++} concentration. In general the B form is favoured at low temperatures. However, as the concentration is raised (say at 2.35 M NaCl) the Z form is favoured. Now if the temperature is raised polynucleotide conformation shifts towards the B form (Text-fig 11 a). Higher salt concentration favours the Z form by masking the phosphate repulsions. From text-figure 7(A) and 9 (A) it is obvious that $B \rightleftharpoons Z$ transition is sharper in the case



Text-figure 10. (a) Experimental (•) and theoretical (-) transition-curves for $B \rightleftharpoons Z$ in poly (dG-dC) (b) Theoretical Specific heat-curve for $B \rightleftharpoons Z$ in poly (dG-dC)

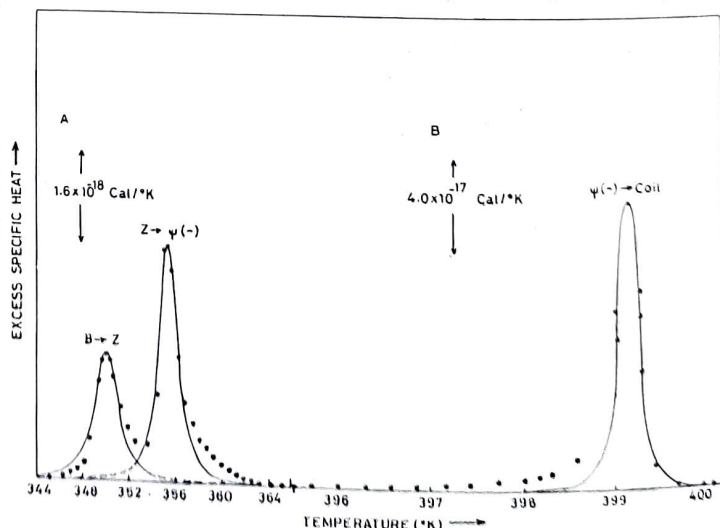


Text-figure 11. (a) Experimental (•) and theoretical (-) transition-curves for $Z \rightleftharpoons B$ in poly (dG-dC) (b) Theoretical specific heat-curve for $Z \rightleftharpoons B$ in poly (dG-dC)

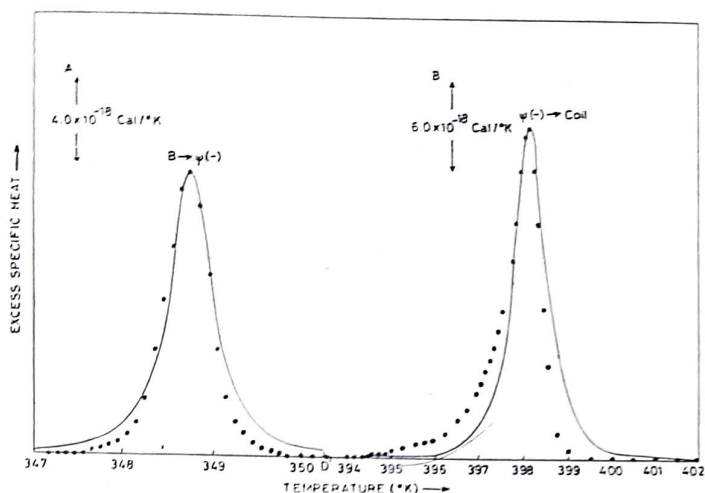
of Poly (dG-dC) as compared to its methylated analogue but in case of $Z \rightleftharpoons \psi(-)$ transition situation is otherwise. Methylation leads to the stabilization of the Z form. The B form is stabilized by the spine of water in the minor groove. The methylation of cytosine at C5 position destabilizes the B form due to unfavourable interaction between the hydrophobic methyl group and the water-molecule. It stabilizes the Z form due to favourable interactions of the methyl group with the imidazole ring of guanine and the carbon atom of sugar. In addition to the $B \rightleftharpoons Z$ transition Poly(dG-dC) also shows a right handed to left handed ($B \rightleftharpoons \psi(-)$) transition with a geometry different from that of Z (Text - fig. 13 A).

HELIX COIL TRANSITION

The helix coil transition ($\psi(-) = \text{coil}$) profiles obtained from expression(16) in case of Poly(dG-dC) and Poly(dG-



Text-figure 12. Experimental (•) and theoretical (-) specific heat-curves for poly (dG-dC);
(A) $B \rightleftharpoons Z$ and $Z \rightleftharpoons \psi(-)$ (B) $\psi(-) \rightleftharpoons \text{coil}$



Text figure 13. Experimental (•) and theoretical (-) specific heat-curves for poly (dG-dC):
(A) $B \rightleftharpoons \Psi (-)$ (B) $\Psi (-) \rightleftharpoons \text{coil}$

$\text{me}^5 \text{dC}$) at different Mg^{++} concentrations are shown in text-figure 7(B), 8(B) and 9(B). From the text-figures, it is obvious that the transition is sharper at lower Mg^{++} concentration. This is also evident from the smaller value of the nucleation parameter and the larger concomitant change in enthalpy. As stated earlier, methylation leads to stabilization of the Z helix. This stabilization will also manifest itself in a smaller value of nucleation parameter while going from the left handed Z to the left handed $\psi(-)$ but not necessarily in going from $\psi(-)$ to coil form because the degree of stabilization is different in the two forms. The experimental data also supports this. The higher value of α is indicative of the fact that methylation leads to a perturbed and destabilized $\psi(-)$ helix. As expected ΔH is also small.

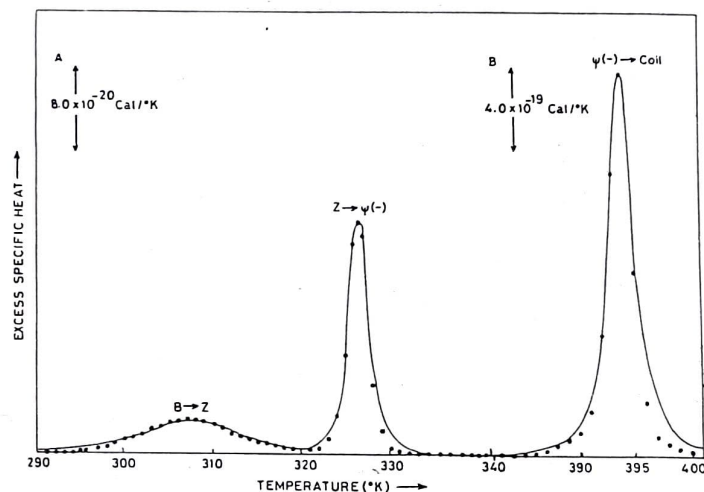
SPECIFIC HEAT

Specific heat is an important thermodynamic quantity which characterizes the conformational and dynamical state of a biopolymeric system. Recently measurements of specific heat have been reported by Chaires and Sturtevant (1986, 1988). Specific heat is the second derivative of Gibbs free energy and theoretical details leading to the expressions (11) and (19) have been given earlier in this communication. The theoretical specific heat curves for various polynucleotides under different environmental conditions and varying chain lengths are given in text-figures 10(b), 11(b), 12(A), 13(A) and 14(A). Experimental results are shown by circles. These results are in the neighbourhood of the transition points for Poly (dG-dC) ($N=2150$ and $N=800$) and Poly (dG-me⁵dC) ($N=500$). The former undergoes $B \rightleftharpoons Z \rightleftharpoons \psi(-) \rightleftharpoons \text{coil}$ and $B \rightleftharpoons \psi(-) \rightleftharpoons \text{coil}$ transitions under appropriate environmental conditions whereas in case of latter the transitions observed are $B \rightleftharpoons Z \rightleftharpoons (-) \rightleftharpoons \text{coil}$. All these specific heat curves

have a lambda point anomaly and would tend towards Delta function singularity in case of infinitely long system with large enthalpy changes. Sharpness of transition can be characterized by their half-widths (ΔT) given in table 1, 2 and 3. The closeness of the experimental and theoretical values of ΔT is a measure of the goodness of the agreement with the experimental measurements. In addition to half-width of transition the lambda curves also have a certain degree of asymmetry in the region of half-width measurement and much more so in the tail-end regions. These are most probably due to the presence of more than two phases in the system in the neighbourhood of the transition. A multiphase component theory is therefore necessary.

In case of helix to coil transition, the specific heat in general has a higher magnitude as compared with order \rightleftharpoons order transition. This is mainly due to large enthalpy changes involved. This could also be due to large enthalpy changes involved. This could also be due to the existence of a large number of short ordered segments in the disordered state, which play an important role in detailed balance of vibrational energy.

The preponderance of right handed over all other forms of DNA can be understood from the heat of transition given in table 1. The heat of transition from B to Z and Z to $\psi(-)$ is $(2.02+2.9)$ KCal/mole bp whereas directly from B to $\psi(-)$ is 2.82 KCal/mole bp. The former takes place under 1.0 mM Mg^{++} concentration and the later at 5.0 mM Mg^{++} concentration. Since the physiological conditions are nearer the first one, the transitions from B to Z and Z to $\psi(-)$, which are reversible, maintain the equilibrium concentration of right handed DNA whereas the other transitions from B to $\psi(-)$ even though being somewhat easier (lesser heat of transition) results in the loss of right handed form. But there is also a significant probability of $\psi(-)$ reverting back to the right



Text figure 14. Experimental (•) and theoretical (-) specific heat-curves for poly (dG-me⁵dC):
(A) $B \rightleftharpoons Z$ and $Z \rightleftharpoons \Psi (-)$ (B) $\Psi (-) \rightleftharpoons \text{coil}$

handed DNA via left handed Z form. Thus the right handed form tries to maintain higher concentration even after some loss in the left handed form. The same is also supported by the relative values of the nucleation parameter.

The more important question arises regarding the very synthesis of the left-handed form from the premodial matter. General opinion is that the preponderance of right-handed over left-handed biomolecules is related to the nonconservation of parity. The nonconservation of parity gives rise to larger emission of electrons with left handedness over those with right handedness. This in turn would imply that electromagnetic radiation related to left handed electrons will give rise to right handed polarisation and vice versa. Thus the electromagnetic radiation with right handed polarization will prevail over the left handed one. Since all chemical reactions result from an interaction of electromagnetic radiation with the reacting species, it would produce a larger number of right handed products over left handed. Further the energy difference between a right handed and left handed molecule has been worked out to be very small, i.e. roughly of the order of 10^{-7} . This difference is extremely small in itself. But it becomes large over a period of millions of years and as such results in the dominance of right handed species over left handed. Nature is thus basically asymmetric even though it loves order. The universe heading towards the state of maximum entropy is closely related to the asymmetric nature of the universe.

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