Theory of the helix-coil transition of DNA based on the correlated walk model

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Abstract. The helix-coil transition of DNA is treated in terms of a model in which the hydrogen-bonding (and stacking) energy $-K$ is attained only if the segments carrying bases (A,T,G.C.) of each strand make four correct turns to generate a half-helix. This model is equivalent to a modified Ising chain with up to fourth nearest neighbor interactions and highly biased statistical weights. The average degree of helicity computed for the model can be fitted well with the observed light-absorption data with an optimum choice of the ratio $t \equiv p/q$ of the correct turn probability p to the incorrect turn probability q. The value of t is 0.0238 for several DNA which show among the sharpest melting transions, leading to the fact that the turn probability p depends mainly on the common backbone configuration carrying the bases. A relation is obtained among the melting temperature T_m, the ratio t and the bond energy K : $T_m = (-\ln t)^{-1} K/k_B$, which indicates that (a) the melting temperature T_m varies linearly with the average bond energy K and therefore the $G - C$ pair content, and (b) the actual melting temperature $T_M(357K)$ is reduced by the factor $-\ln t = 3.74$ from the bond temperature $T_b \equiv K/k_B(\sim 1335K)$. This relation also predicts the rise of the melting temperature T_m with increasing salt concentration, which tends to make the helical DNA more stable (higher K) *and* make the strands more flexible (higher t).

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1. Introducción

In the mid-fifties, Doty and his associates [1,2] and others [3], demonstrated experimentally that a single polypeptide (and also a DNA) in solution undergoes a helix-coil transition. Polypeptides and DNA are quite different in molecular configuration, and their (single and double) helical conformations are very different from each other [3,4]. The melting curves —the average degree of helicity against temperature— are similar, however; only the temperature range of transition is a little narrower for DNA than for polypeptides (of large molecular weights). These fascinating experimental discoveries were followed by a great number of theories [3,5,6].

In particular, Zimm and Bragg (Z-B) [6] developed a theory of the helix-coil transition for polypeptides in terms of the solutions of a strongly-biased Ising chain. This theory describes the qualitative features of the melting curve very well; the narrow temperature range of transition is accounted for by the smallness of the so-called nucleation parameter, σ, which roughly represents the degree of difficulty with which a polypeptide arranges itself into a first helical turn (to gain a hydrogen bonding). Recently, we proposed a new theory based on the correlated walk model which incorporates both the physical shape (helix or coil) and the hydrogen bonding [7]. The statistical mechanical calculations reproduce the essential features of the $Z-B$ theory, and relate the nucleation parameter σ with the probability p of the model polymer making a correct turn: $\sigma \sim t^3 \equiv [p(1-p)^{-1}]^3$. We will, in the present paper, extend our theory to the cases of DNA, which are far more complicated in structure than the polypeptides but which nonetheless exhibit similar helix-coil transitions.

The basic model and the principal results of the calculations are as follows:

In a double-helical state of DNA, each segment of the strand carrying one of the bases (A,T,G,C) follows the preceding segment in a well oriented manner; ten segments, if oriented properly, complete a helix of well defined pitch (34Å) and diameter (20Å). Only with this conformation, the base pair A-T or G-C, one base from each strand, can attain a hydrogen bonding. Based on these observations, we set up a model in which a hydrogen bonding is attained it a segment and its three predecessors counting from one end of the strand all make the *correct turns* with the probability p. This model is equivalent to the linear correlated walk with biased step probabilities $(p, q \equiv 1 - p)$ and the dynamical correlation extending over the four previous steps [8]. Also, the model is equivalent to the linear Ising model with biased weights and up to four nearest neighbor interactions [8]. The partition function for the model can be formulated by means of the transfer matrix, and the free energy per segment can be expressed simply in terms of the maximum eigenvalue of the transfer matrix, (Eq. (2-6)). The average degree of helicity calculated for the model can be fitted with the measured relative absorbance data [2,9] for DNA with the choice of the parameter p. The present theory establishes a relation among the melting temperature T_m, the correct turn probability p and the bond energy K:

$$k_B T_m = \left[- \ln \left(\frac{p}{q} \right) \right]^{-1} K, \qquad (1.1)$$

where k_B is the Boltzmann constant. Several remarkable properties can be derived from this relation. In particular, it is experimentally known [10] that the salt (NaCl) content in the solvent (water) greatly effects the melting temperature T_m, changing T_m as much as 40°C. When the salt concentration is raised, the strands of DNA become less ionized, which tends to make the helical molecule more stable (higher K) *and* to make the strands more flexible (higher t). According to (1.1), these two effects raise the melting temperature.

The model and its solution are described in detail in section 2. Physical interpretations of the results are given in section 3.

2. The model and its solution

Let us take a DNA in a double-helical state. In this state, each segment of the strand carrying one of the four bases (A,T,G,C) follows the preceding segment in a well-oriented manner (along a hypothetical helix of a pitch of 34 Åand a diameter of 20 Å). Only with this conformation, the base pair A-T or G-C, one base from each strand, can attain a hydrogen bonding. Based on these observations the partition function for the DNA will be calculated by the following rules:

We look at segments of each strand successively from one end.

(a) If a segment follows the preceding segment in the *correct direction*, the statistical factor p is given; otherwise the factor $q \equiv 1 - p$ is assigned. The same rule applies to both strands of equal length.

(b) The Boltzmann factor $\exp(K/k_B T)$, where K represents the *bond energy* assumed equal for both A-T and G-C pairs, is given if the $j, (j-1), (j-2), \ldots$, and $(j-k)$-th segments of both strands all make correct turns; otherwise unity is assigned.

The statistical factor p represents the probability that the segment takes a suitable conformation generating part of a helix. This factor p will be very small compared with unity because the unsuitable conformation corresponds to a far greater phase-space volume. In order that a base pair may attain the hydrogen bonding, backbone segments carrying the bases must be making correct turns and correctly positioned. If the several preceding segments did not make correct turns, the pair in question may be out of a regular position and cannot achieve bonding even if they make correct turns. This feature is incorporated in the rule (b). The number $k+1$ of segments whose correlated conformation is needed for the attainment of the bonding, should be five or a greater number since the five base pairs can form the minimum helical conformation in which the five successive bases from each strand arranges themselves into a half-helix of the specified pitch 34 Åand diameter 20 Å. Of course the higher the k-value, the harder become the calculations of the thermodynamic properties.

The partition function Z for the model DNA may be calculated by use of the Ising languages as follows. We assign $+1$ or -1 to the state μ_j of each segment. The statistical weight of a system-state μ_j for the chain of n bases is given by the following factors:

(a) The correct (incorrect) turn factor $p(q)$ if $\mu_j = -\mu_{j-1}(+\mu_{j-1})$

(b) The Boltzmann factor $\exp(K/k_B T) \equiv exp(\beta K)$ if $\mu_j = -\mu_{j-1} = \mu_{j-2} = \ldots = (-1)^k \mu_{j-k}$, and unity otherwise.

The total bond energy can be represented by the hamiltonian

$$H = -K \sum_{j=1}^{n} f(\mu_{j-k}, \ldots, \mu_{j-2}, \mu_{j-1}, \mu_j), \qquad (2.1)$$

where

$$f(\mu_1, \mu_2, ..., \mu_k, \mu_{k+1}) = \begin{cases} 1 & \text{if } \mu_1 = -\mu_2 = ... = (-1)^k \mu_{k+1} \\ 0 & \text{otherwise} \end{cases} \qquad (2.2)$$

Notice that this hamiltonian corresponds to that of the Ising chain with first to k-th nearest neighbor interactions.

The transfer matrix T for k=2 is [11]

$$T = \begin{pmatrix} q & p & 0 & 0 \\ 0 & 0 & pe^{\beta K} & q \\ q & pe^{\beta K} & 0 & 0 \\ 0 & 0 & p & q \end{pmatrix} \equiv q\widehat{T}, \qquad (2.3)$$

which can be obtained by looking at the succession of two-base states from (μ_{j-2}, μ_{j-1}) to (μ_{j-1}, μ_j). The corresponding characteristic equation

$$|\widehat{T} - \lambda| = 0, \qquad (2.4)$$

has all non-negative roots λ's. In the limit of large n, the partition function is dominated by λ_0^n:

$$\text{tr}\left\{e^{-\beta H}\right\} \sim \lambda_0^n, \qquad (2.5)$$

where λ_0 denotes the maximum root. The *average degree of helicity* defined by

$$\langle f \rangle = \lim_{n \to \infty} \frac{\text{tr}\left\{\frac{1}{n} f e^{-\beta H}\right\}}{\text{tr}\left\{e^{-\beta H}\right\}}, \qquad (2.6)$$

is then given by

$$\langle f \rangle = \beta^{-1} \frac{\partial \ln \lambda_0}{\partial K}. \qquad (2.7)$$

The process of finding the maximum root λ_0 of the characteristic Eq.(2.4) can be simplified in the following manner. Instead of looking at the succession of k-segment states, which is required for obtaining the transfer matrix T, we examine the succession of turns (correct or incorrect) and construct a *succession-of-turn* (or *turn*) *matrix*. Thus, for $k = 2$ we look at the succession of turns from $\mu_{j-2}\mu_{j-1}$ [$= +1(-1)$ for incorrect (correct) turn] to $\mu_{j-1}\mu_j$, and obtain

$$U \equiv \begin{pmatrix} u_{ii} & u_{ic} \\ u_{ci} & u_{cc} \end{pmatrix} = \begin{pmatrix} q & p \\ q & pe^{\beta K} \end{pmatrix} \equiv q\widehat{U}. \tag{2.8}$$

The reduced succession-of-turn matrix $\widehat{U}$ has also non-negative eigenvalues, and its maximum eigenvalues is identical to that of the corresponding reduced transfer matrix $\widehat{T}$. The last property is not unexpected because the attainments of the hydrogen bonding formulated in terms of either the transfer matrix or the turn matrix have the same physical content. Since the size of the turn matrix is smaller for the same model, we will hereafter use this matrix.

As stated earlier, for the treatment of the helix-coil transition for DNA, we have to look at the model with $k = 4$ or greater. For $k = 4$, the succession-of-turn matrix is given by

$$U = \begin{pmatrix} q & p & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & q & p & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & q & p & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & q & p \\ q & p & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & q & p & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & q & p & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & q & pe^{\beta K} \end{pmatrix} \equiv q\widehat{U}. \tag{2.9}$$

The corresponding characteristic equation of the form (2.4) can be transformed to

$$\lambda^4[\lambda^4 - (s+1)\lambda^3 + (s-t)\lambda^2 + t(s-t)\lambda + t^2(s-t)] = 0, \tag{2.10}$$

where

$$t \equiv \frac{p}{q}, \qquad s \equiv t\exp(\beta K). \tag{2.11}$$

The maximum root λ_0 depends on the two variables (s, t). Since for constant $t\,ds = te^{\beta K}d(\beta K) = \beta s dK$, we obtain from (2.7)

$$\langle f \rangle = s\frac{\partial \ln \lambda_0}{\partial s}. \tag{2.12}$$

Using the explicit form of the quartic equation:

$$\lambda^4 - (s+1)\lambda^3 + (s-t)\lambda^2 + t(s-t)\lambda + t^2(s-t) = 0, \tag{2.13}$$

we then obtain

$$\langle f \rangle = \frac{s}{\lambda_0} \frac{\lambda_0^3 - \lambda_0^2 - \lambda_0 t - t^2}{4\lambda_0^3 - 3(s+1)\lambda_0^2 + 2(s-t)\lambda_0 + t(s-t)} \tag{2.14}$$

After solving eq. (2.13) numerically by computers and identifying the maximum root λ_0, we calculated the average degree of helicity, $\langle f \rangle$, as a function of s for selected values of t. The resulting curve (1-$\langle f \rangle$ *versus* ln s) is shown in solid line in Fig. 1. The average degree of helicity, $\langle f \rangle$ increases monotonically to unity as $s \equiv t \exp(\beta K)$ is raised to ∞ (zero temperature). The smaller the value of the parameter $t \equiv p/q \sim p$, the more abrupt the transition occurring around $s = 1$. Experimentally, the average degree of helicity can be observed directly by measuring the relative absorbance at wavelength $= 260 \mu$m [9], the fitting between theory and experiment for Pneumococcus (0.15 M sodium chloride and 0.015 M sodium citrate) is obtained by choosing the melting temperature T_m (=85.2°C) such that

$$s_m = t \exp\left(\frac{K}{k_B T_m}\right) = 1, \tag{2.15}$$

and adjusting the parameter $t(= 0.0238)$. As we see in Fig. 1, the fitting is very good. We will discuss physical significances of our theory in the following section.

3. Discussions

In the preceding section, we calculated the average degree of helicity, $\langle f \rangle$ for our simple model and obtained good fits with the experimental data. From this calculation, we can draw several conclusions, which will be enumerated below.

(a) *The melting temperature and the bond energy*

The melting temperature T_m and the bond energy K are related by eq. (2.15). By solving this equation for T_m, we obtain

$$T_m = (-\ln t)^{-1} \frac{K}{k_B}. \tag{3.1}$$

The optimum value of the parameter t is given by
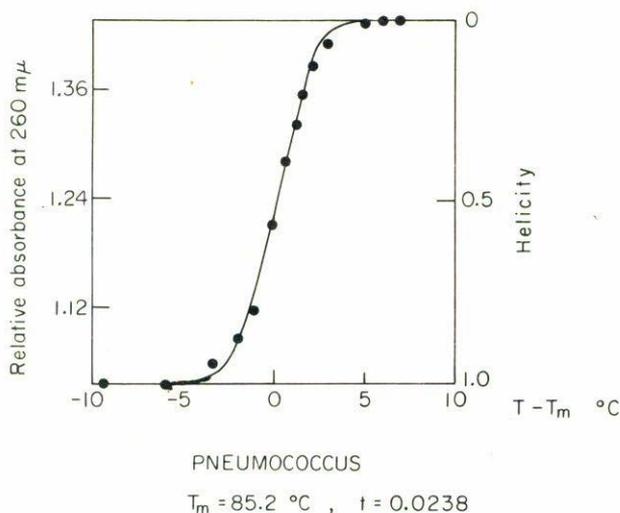
PNEUMOCOCCUS

$T_m = 85.2$ °C , $t = 0.0238$

FIGURA 1. The relative absorbance at 260 mμ for Pneumococcus measured by Marmur and Doty [9] is shown as a function of the temperature T. The theoretical (solid) curve is obtained from (2.13) and (2.14) by choosing $T_m = 85.2°C$ and t=0.0238.

$$t = 0.0238. \tag{3.2}$$

The actual melting temperature T_m is *reduced* by the factor $- \ln t = 3.74$ from the *equivalent bond temperature* corresponding to the bond energy,

$$T_b \equiv \frac{K}{k_B}. \tag{3.3}$$

In fact, the relation (3.1) yields an estimate of the bond energy K if the melting temperature T_m is given. For the present case, we obtain

$$T_b = 1335K. \tag{3.4}$$

The reduction of the actual melting temperature to the range in which water exists in the liquid phase, is very important from the biological point of view since biological actions generally occur in the aqueous environment.

(b) *The physical meaning of the parameter t*

The parameter $t \equiv p/q$ represents the ratio of the correct turn probability p to the incorrect turn probability q. Physically, it is the ratio of the correct phase-space volume to the incorrect phase-space volume. The value $t = 0.0238$ is typical of those DNA which show among the sharpest melting curves and which have homogeneous base composition along the strands. In fact, the melting curves for bacteriophage $T_4r(T_m = 84°C)$, $T6r^+(T_m = 86°C, T2(T_m = 85°C)$, Mycoplasma Gallisepticum $(T_m = 86°C)$, and synthetic A-T (adenine-thymine) DNA $(T_m = 65°C)$ can all be fitted with the same t-value. This means that the turn probability p depends mainly on the (common) backbone configuration which carries the bases (A,T,G,C). The latter is consistent with the fact that all DNA, despite of a variety of possible base compositions, generate an almost universal helical state of the same pitch and diameter.

In our model the double strands get a hydrogen bonding only after each strand completes *four successive correct turns*. Using the above t-value, we obtain

$$t^4 \equiv \left(\frac{p}{q}\right)^4 = (0.0238)^4 = 3.21 \times 10^{-7}, \tag{3.5}$$

which means that the favorable phase-space volume for generating half a helix is very small compared with that for a random coil.

The melting curves can be altered significantly by the salt content in the solvent. The data quoted so far are at the standardized salt content: 0.15 M sodium chloride and 0.015 M sodium citrate. The effect of the salt concentration will be discussed separately in subsection (d).

(c) *The melting temperature and the G-C pair content*

Experiments show that the melting temperature T_m varies linearly with the content of G-C base pairs [9]. This can be understood simply as follows. The average bond energy K is a linear function of the G-C pair content (as the unit bond energy is a little greater for the G-C pair than for the A-T pair) Eq. 3.1 then dictates the linear relation between the melting temperature T_m and the G-C pair content for the same t.

(d) *The melting temperature and the salt concentration*

The effect of the salt concentration on the melting transition in the synthetic DNA dI: dBC (I = inosine, BC = 5-bromocystosine) reported by Inman and Baldwing [10] is shown in Fig. 2. For this DNA, the melting temperature T_m changes almost 40°C as the salt concentration is raised from 0.0025M-Na$^+$(A) to 0.0105 M-Na$^+$ (B), and to 0.212M-Na$^+$(C). This behavior can be interpreted as follows (See Fig. 2).
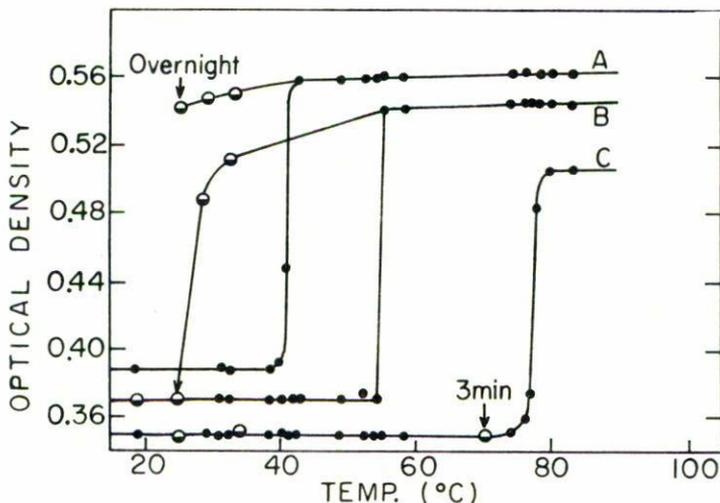
FIGURA 2. Effect of salt concentration on the melting transition in dI:dBC observed by Inman and Baldwin [10]. The cooling curves with half filled circles are non-equilibrium values. Curve A, 0.0025 M-Na$^+$; curve B, 0.0105 M-Na$^+$; curve C, 0.212 M-Na$^+$.

The backbone of DNA contains recurring phosphate groups ($3'$, $5'$-internucleotide phosphodiester bridges) which are strongly acidic. These groups, located on the outer periphery of the double helix and exposed to water, are negatively ionized at any pH above 4. They attract cations like Na$^+$ and Ca^{++} if present in water. The binding of cations in the strands of DNA makes the molecule more energetically stable *and* it also makes the strands more flexible. As we can see from Eq. (3.1), both effects, that is, grater bond energies (stability) and greater t-value (flexibility) contribute to the rise in the melting temperature T_m. More specifically, the stabilization and the saturation of the hydrogen bonding and stacking energy should occur at lower salt concentration, say, up to 0.1 M NaCl; further addition of salt raises T_m mainly through the variation of t.

The rise in the melting temperature with increasing salt concentration can also be argued on the thermodynamic basis as follows. The Helmholtz free energy F is defined by

$$F = E - TS. \tag{3.6}$$

Aside from the kinetic energy which will omit the present consideration, the internal energy E arises from the hydrogen bonding and stacking energies for the helical DNA; this energy is a negative constant $-nK$ for the helical conformation and zero for the random-coil conformation.

For the helical state which is quite stable nearly up to the actual melting temperature, the entropy defined by

$$S \equiv k_B \ln \Omega, \tag{3.7}$$

where Ω represents the phase-space volume divided by $(2\pi\hbar)^3$, grows very slowly with temperature (since the dimension of the helical structure nearly remains the same). The free energy F for this state therefore decreases very slowly from the initial value $-nK$ as temperature is raised. This behavior is represented by the curve A in Fig. 3. For the random coil state, the entropy is much higher, and therefore, the free energy decreases much more rapidly from the initial value 0. This behavior is represented by the curve C. The intercept of the curves A and C determines the melting temperature T_m (below which the helical state has a low free energy and therefore this state is realized).

Let us now consider the effect of the salt concentration. With the addition of salt, the backbone-strands become less ionized. This tends to increase the bond energy $nK'(>nK)$ because of lesser Coulomb repulsion and makes the strands more flexible. The latter means higher phase-space volume and therefore higher entropy of the helical state. The free energy for this state then should start with the lower energy nK' and decrease more rapidly as represented by the curve B. The intercept of this curve with the coil-state curve C moves toward the high temperature side and therefore the melting temperature T_m is raised.

(e) *The refinement of the model*

We have discussed the helix-coil transition of DNA in terms of the model in which each strand gets a hydrogen bonding upon completing *four* correct turns. If both of the strands make four successive correct turns, they can form a (double) half-helix at optimum condition. To make sure the complete double-helical conformation, we may examine a model in which the hydrogen bonding is attained only upon completing *five* correct turns.

The succession-of-turn matrix for this case has the size 16×16. The maximum root λ_0 of the determinant equation is found to arise from the algebraic equation of fifth order:

$$\lambda^5 - (s+1)\lambda^4 + (s-t)\lambda^3 + t(s-t)\lambda^2 + t^2(s-t)\lambda + t^3(s-t) = 0 \tag{3.8}$$

The average degree of helicity computed in terms of the new λ_0 turns out to yield nearly the same curves for the same set of t-values. See (h) for further discussions.

(f) *The sharpness of the transition*

In our model, the favorable conformation of $k+1$ segments generates a hydrogen
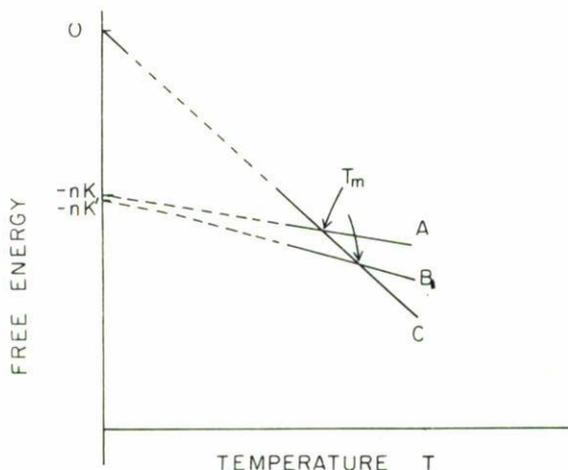
FIGURA 3. The Helmholtz free energy $F = E - TS$ *versus* the temperature T. For the helical
conformation the free energy decreases from $-nK$ very slowly as temperature is raised
(A), and for the random coil state the free energy decreases from 0 more rapidly (B).
The intercept defines the melting temperature T_m. Addition of salt raises the bond
energy K and the entropy associated with the helical state, generating a greater slope
in C than in A. The contribution of the kinetic energy assumed to be the same for all
cases is omitted from consideration.

bonding. This model is equivalent to a modified Ising Chain with $first-to-k-th$
nearest-neighbor interactions and biased statistical weights ($p \ll q$). As long as
the range of the interaction is finite, the transition is sharp but continuous for any
values of $t \equiv p/q$. However, if the range extends to infinity, the transition will
become discontinuous. Let us investigate this behavior in this subsection.

Examination of Eqs (2.13) and (3.8) indicates that the maximum eigenvalue λ_0
of the turn matrix for the model with the $k+1$ segment interaction can be obtained
from

$$\lambda^k - (s+1)\lambda^{k-1} + (s-t)\lambda^{k-2} + t(s-t)\lambda^{k-3} + \cdots + t^{k-3}(s-t)\lambda + t^{k-2}(s-t) = 0. \quad (3.9)$$

In the limit $k \to \infty$, the equation is reduced to

$$\lambda - (s+1) + \frac{s-t}{\lambda-t} = 0$$

or

$$(\lambda - t)(\lambda - s - 1) + s - t = 0, \tag{3.10}$$

yielding the desired solution

$$\lambda_0 = \max(1 + t, s). \tag{3.11}$$

By changing temperature, we observe that

$$\lambda_0 = \left\{ \begin{array}{ll} s & \text{if } T < T_c \\ 1 + t & \text{if } T \geq T_c \end{array} \right. \tag{3.12}$$

where the *critical temperature* T_c is determined by

$$1 + t = te^{K/k_B T_c}$$

or

$$k_B T_c = K \left\{ -\ln \left[\frac{t}{(1+t)} \right] \right\}^{-1} = K[-\ln p]^{-1}. \tag{3.13}$$

using (2.12) and (3.13), we then find that

$$\langle f \rangle = \left\{ \begin{array}{ll} 1 & \text{if } T < T_c \\ 0 & \text{if } T \geq T_c \end{array} \right., \tag{3.14}$$

which indicates a true thermodynamic phase transition at the critical temperature T_c.

This is an exact result in the thermodynamic limit in which the great-number-of-segment limit is taken before the range of the interaction is extended to infinity. According to the theorem due to Takahashi and Van Hove [12] no one-dimensional system with a finite-range interaction can undergo a thermodynamic phase transition. Linear systems with infinite ranges of interaction however are, in the thermodynamic limit, equivalent to two-dimensional systems with finite ranges of interaction, and can undergo an abrupt phase transition [8].

(g) *Comparison with the theory of Zimm and Bragg*

Zimm and Bragg, in their classic paper [6], examined the hydrogen bonding state

of a polypeptide in solution, and formulated the partition function of the model polymer in terms of matrices similar to the reduced succession -of-turn matrices.

In the simplest version, their 2×2 matrix is given by

$$\hat{U}_{Z-B} = \begin{pmatrix} 1 & \sigma^s \\ 1 & s \end{pmatrix}, \tag{3.15}$$

where σ is a nucleation parameter. The corresponding matrix $\hat{U}$ in our theory is defined in Eqs. (2.8), and it is given by

$$\hat{U} = \begin{pmatrix} 1 & t \\ 1 & s \end{pmatrix}. \tag{3.16}$$

Note that if the relation

$$\sigma^s = t \tag{3.17}$$

is assumed, both matrices are equal to each other. As pointed out in our earlier work [7], the average degrees of helicity computed in terms of $\hat{U}_{Z-B}$ and $\hat{U}$, are mutually indistinguishable if the parameters $t \equiv p/q$ and σ take the same small value 10^{12} or less. This means that the nucleation parameter q which roughly represents the degree of difficulty of forming an initial helix can be related to the correct turn probability p. There exists however a significant difference between the two theories. In the present work, we look at the hydrogen bonding *and* physical conformation of the polymer, and characterize them in terms of two independent parameters K and p. We then obtained the relation (2.15) among the melting temperature T_m and the parameters (K, p), the relation which is basic to all of our discussions in (a) and (j). This important relation cannot be derived to the $Z - B$ model in which the hydrogen bonding states are accounted for directly but the associated physical shapes (helix or coil) are only implied.

(h) *Comparison with other theories*

In the present work, we looked at DNA of infinite molecular weights $(n \to \infty)$. Zimm [13] and Crothers *et al.* [14] studied the molecular-weight dependence of the melting curves, and showed that the melting transition becomes less and less sharp and moves toward the low temperature side as the molecular weight is reduced. This behavior is common to DNA and polypeptides. The case for the latter was demonstrated first by Zimm and Bragg [6] and it was reestablished in our earlier work [7].

The general qualitative features of the helix-coil transition for polypeptides and DNA can be derived in a variety of ways as evidence by a great number of publications

on the subject [3,5,6,13,14]. Generally speaking, a parameter (like the nucleation parameter σ and the correct turn probability p) which controls the sharpness of the transition should be introduced in a theory. When this is done properly, even a crudest model as characterized by a 2×2 matrix like (2.8) and (3.15) can generate the melting curve within experimental errors by an optimum choice of the parameter. In the present work the correct turn probability p is introduced in a more realistic manner, leading to a more complicated mathematical problem. The value obtained for p is meaningful, however, and this value may be compared with the results of future molecular theoretical calculations similar to those carried out for the polypeptides by Scheraga and his group [15].

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Resumen. Se estudia la transición hélice-hilo de la molécula DNA, en un modelo en el cual la energía $-K$ de los enlaces de hidrógeno solamente se obtiene si las bases (A,T,G,C) en cada hilo ejecutan cuatro desviaciones en la dirección correcta, de forma tal que generen una

media hélice. Este modelo es equivalente a uno de Ising con interacciones hasta el cuarto vecino próximo y pesos estadísticos con tendencia alta. El grado medio de helicidad calculada para este modelo ajusta bien con los datos de absorción de luz si se da un valor óptimo al cociente $t = p/q$ de la probabilidad de ejecutar una dirección correcta p a una incorrecta q. Para varias moléculas de DNA, el valor de $t = 0.0238$ es el que muestra la transición más abrupta, deduciéndose que la probabilidad p depende principalmente de la configuración de la estructura que soporta las bases. Se obtiene una relación entre la temperatura de fundido T_m, el parámetro t y la energía del enlace K. El resultado indica que: a) la temperatura de fundido T_m varía linealmente con K y consecuentemente con el contenido de pares $G - C$ y b) la verdadera temperatura de fundido $(T_m = 357°K)$ se reduce por el factor $-\ln t = 3.74$ de la temperatura de enlace $T_b = K/k_B \sim 1335°K$. Esta relación predice la elevación del punto de fusión T_m al incrementar la concentración de sal, la cual tiende a producir una hélice más estable (mayor K) y hacer los hilos más flexibles (mayor t).