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Long-range interaction and heterogeneity yield a different kind of critical phenomenon

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DNA denaturation, wetting in two dimensions, depinning of a flux line, and other problems are known to map onto a phase transition with effective long-range interaction. In a disordered system the latter yields a giant, nonuniversal, temperature-dependent critical index, and macroscopic fluctuations at a finite distance from the critical temperature. In the vicinity of the critical region the Gibbs distribution is invalid, and thermodynamics must be calculated from first principles. There are no fluctuations above the critical temperature.

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I. PHYSICS OF DNA MELTING

Thermal unbinding (melting, coiling, denaturation) of a double-stranded DNA molecule has been biologically important, physically unique, and extensively studied for nearly four decades [1–7]. A quenched DNA molecule is an extraordinary long one-dimensional (1D) system—the total length of a single mammalian DNA is 1.8 m; it consists of ~ 5 billion nucleotide base pairs. Their sequence is related to genetic information, yet at a long range it is random [8]. The fraction of unbound base pairs as a function of temperature (“the DNA melting curve”) is proportional to DNA light absorption at about 260 nm and may be directly measured. DNA nucleotide base pairs [adenine-thymine (AT), guanine-cytosine (GC)] are large (“mesoscopic”) organic molecules. Their unbinding releases a few thousand degrees of freedom. The corresponding entropy is $s \sim 10$ per site [1,2]. (Here and on the Boltzmann constant is 1). Thus, the well known Poland-Scheraga model [1,2] of DNA melting introduces AT and GC binding energies $E_1 = -sT_1$ and $E_2 = -sT_2$ correspondingly. The “fusible” T_1 and “refractory” T_2 are close: $T_1 \simeq T_2 \sim 300$ K, $\Delta T = T_2 - T_1 \sim 30$ K. The boundary energy $J \sim 3000$ K per bound segment accounts for an incomplete unbinding at the boundaries. The loop entropy is $-c \ln L$ per unbound segment (L is the total number of nucleotide pairs there). The value of the constant c increases from 1.5 (for random walks which form a closed loop [1,2]) to slightly higher than 2 (when one accounts for strand self-avoidance [6], excluded volume, loop interactions [5,6] between, and stiffness [7] of various DNA segments). The resulting Poland-Scheraga effective Hamiltonian H, calculated from the energy $(-sT)$ per site, for an infinite circular DNA equals [1–3]

$$H = \Sigma E(l_n, \Delta x_n; L_n),$$

$$E(l_n, \Delta x_n; L_n) = s l_n(\delta T - \Delta T \Delta x_n) + (J + cT \ln L_n), \quad (1)$$

$$\delta T = T - \overline{T}, \quad \overline{T} = T_1 \overline{x} + T_2(1 - \overline{x}), \quad \Delta x_n = \overline{x} - x_n. \quad (2)$$

Here $\overline{x}$ is the AT concentration for the entire DNA. Equation (1) reduces the Hamiltonian to the energy of successive bounded segments (l_n and x_n are the number of base pairs and the AT concentration at the nth such segment) and to their effective long-range repulsion ($J + cT \ln L_n$) at the distance L_n. Consistent with the Landau-Peierls theorem, $c > 1$ in Eq. (1) yields a critical point in a one-dimensional (1D) system [1–6,9].

Transport in a disordered low-dimensional system with long-range interaction yielded new concepts of localization, metal-insulator transition, giant fluctuations, and representative and ensemble averages. I demonstrate that a similar situation in thermodynamics also calls for new concepts and implies a new kind of critical phenomena. Not by chance, previous theories of DNA unbinding varied from the essential [3] to the Kosterlitz-Thouless [4] singularity to the first and second order transitions [5]. New results are not restricted to DNA. DNA denaturation maps onto a variety of other problems: the binding transition of a polymer onto another polymer, a membrane, or an interface [10]; wetting in two dimensions [11]; depinning of a flux line from a columnar defect in type-II superconductors [12]; and localization of a copolymer at a two-fluid interface [13].

II. REPRESENTATIVE HAMILTONIAN AND EXACTLY SOLVABLE MODEL

The physics of DNA unbinding is related to its generic small parameters in Eq. (1). The DNA melting temperature ~ 300 K is low compared to $J \sim 3000$ K. Thus, DNA melts in the vicinity of its ground state. [Indeed, the relative difference between the melting temperature of an AT or GC homopolymer and of its ground state is [1–3] $\sim 0.1 \exp(-J/T) \sim 10^{-5}$.] At any temperature above T_1 and below the DNA melting temperature, the ground state consists of bounded and unbounded domains, which are related to the DNA nucleotide sequence and were accurately calculated [3]. The temperatures T_1 and T_2 are close. So, by Eq. (1), when $T > \overline{T}$, to compensate for the strong repulsion ($J + cT \ln L$) of the ground state bounded domains they must be sufficiently large and enriched in the refractory component. Successive melting of such domains yields a characteristic stepwise DNA melting curve [1,2], which provides certain

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information about the DNA nucleotide sequence [3]. The closer to the DNA melting temperature T_c, the larger the ground state melted domains are, the stronger the repulsion of bounded domains is in Eq. (1), thus the larger and the more refractory they must be. When $T \to T_c$, their $l_n \propto \ln L_n$, and $L_n \to \infty$ [3]. Thus, sufficiently close to the melting temperature, L_n and l_n exceed any finite correlation length, correlations in and between ground state bounded domains vanish, and the probability $w_n \equiv w(l_n, \Delta x_n)$ of a quenched bounded domain with a given Δx_n at l_n is Gaussian,

$$w_n \equiv w(l_n, \Delta x_n) = (l_n / 2\pi D^2)^{1/2} \exp(-l_n \Delta x_n^2 / 2D^2),$$
$$D^2 = \bar{x}(1-\bar{x}). \qquad (3)$$

We derive the representative (i.e., dominant in the calculation of the free energy) Hamiltonian in a sufficiently close vicinity of the melting temperature. When $l_n \to \infty$, the most probable quenched values of l_n and x_n are close, and their mean deviations $\delta l = \overline{|l_n - \bar{l}|}$, $\delta x = \overline{|x_n - \bar{x}|}$ (from here on a bar denotes the average) are relatively small: $\delta l \ll \bar{l}$, $\delta x \ll \Delta \bar{x}$. When $L_n \to \infty$, the effective repulsion energy $(J + cT \ln L_n) \to \infty$ implies relatively small thermal fluctuations of the ground state l_n and Δx_n, while $\delta L = \overline{|L_n - \bar{L}|}$ is $\sim L_n$ (all these statements are accurately verified later). Bounded domains of the length $l_n \simeq \bar{l}$, separated by large distances $L_n \sim \bar{L} \gg \bar{l}$, imply that their $w(l_n, \Delta x_n; L_n) \sim w(\bar{l}, \Delta\bar{x}; \bar{L})$ is approximately the probability of a bounded domain, thus approximately the relative number of bounded sites $\bar{l}/(\bar{l} + \bar{L}) \simeq \bar{l}/\bar{L}$, which is $\sim l_n / L_n$. The resulting relation $w(l_n; \Delta x_n; L_n) \sim l_n / L_n$ reduces the representative Δx_n at l_n to l_n and L_n only: $\Delta x_n \simeq D\sqrt{(1/l_n)\ln(L_n/l_n)}$ (where the relative contribution to Δx_n of the factor in L_n / l_n is $\sim 1/l_n \to 0$). Substituting such Δx_n into Eq. (1), one replaces H with the representative Hamiltonian H_r,

$$H_r = \Sigma E_r(l_n, L_n),$$
$$E_r(l_n, L_n) = (s l_n \delta T - s D \Delta T \sqrt{2 l_n \ln L_n}) + (J + cT \ln L_n). \qquad (4)$$

The Hamiltonian (4) describes an ideal gas of domain pairs in different "states" (l_n, L_n). When $\Delta T = 0$, then H_r reduces to the exact Hamiltonian (1) of a homopolymer. In the general case H_r presents an exactly solvable model of the DNA melting, which relates the DNA free energy $f = \phi T$ per site to the normalization condition for the Gibbs probability $p(l, L)$ of given l and L,

$$p(l,L) = \exp[-(l+L)\phi - E_r(l,L)/T], \qquad \sum_{l,L}^{\infty} p(l,L) = 1. \qquad (5)$$

The exact solution of Eq. (5) for ϕ is straightforward, but it is more explicit in a physically transparent form. When $T > \bar{T}$, the first term in E_r in Eq. (4) is the energy increase for the average $\bar{x}$. The second term describes the energy decrease at a refractory domain. When $l_n \gg 1$, their competition yields a sharp minimum in E_r / T and (nonuniversally) renormalizes the loop entropy constant c,

$$E_r(l,L)/T = (J/T) + (c - \gamma)\ln L + (s \Delta T / 4T)(l - l_{\mathrm{m}})^2 / l_{\mathrm{m}}, \qquad (6)$$

$$l_{\mathrm{m}} = 0.5(D \Delta T / \delta T)^2 \ln L, \quad \gamma = s(D\Delta T)^2 / 2T\delta T. \qquad (7)$$

When $\phi l \ll 1$ and $\ln L \gg 1$, then $\phi l \propto \phi \ln L$ may be neglected compared to ϕL, and Eqs. (5)–(7) yield

$$P(L) = \sum_{l=1}^{\infty} p(l,L) = M^{-1} (\ln L)^{1/2} (1/L^{1+\xi}) \exp(-L\phi),$$
$$\int_1^{\infty} P(L)\,dL, \quad \bar{G} = \int_1^{\infty} GP\,dL = 1, \qquad (8)$$

$$\xi = c - 1 - \gamma, \quad M = (s\delta T / 2\pi T)^{1/2} (\delta T / D \Delta T) \exp(J/T), \qquad (9)$$

where $\bar{G}$ is the thermodynamic average of any $G(L)$.

III. VERIFICATION AND SOLUTION

Equation (8) provides an exact implicit formula for the dimensionless free energy ϕ as a function of two parameters M and ξ (rather than of five parameters J/T, $\Delta T/T$, $T/\bar{T}$, $\bar{x}$, and c, which determine ϕ in a nonrenormalized case). By Eqs. (9) and (7), temperature dependent ξ is the renormalized c. When temperature increases, ξ also *increases*, and c moves away from its critical Landau-Peierls value 1 below which there can be no singularity.

By Eq. (8), $\phi \geq 0$. It reaches $\phi = 0$ at the critical temperature T_c where

$$\xi_c \equiv \xi(T_c) = \pi^{1/3} [2M(T_c)]^{-2/3} \ll 1. \qquad (10)$$

There are no unbounded fluctuations at $T > T_c$.

When $\phi \to 0$, then, by Eq. (8), $\bar{L} \to \infty$, $\delta L = \overline{|L - \bar{L}|} \sim \bar{L}$. By Eq. (6), $|l - l_{\mathrm{m}}| \propto \sqrt{l_{\mathrm{m}}} \ll l_{\mathrm{m}}$, since, by Eq. (7), $l_{\mathrm{m}} \propto \ln L \to \infty$. This verifies the derivation of H_r in the previous section. The relative error in the transformation from Eq. (1) to Eqs. (4) and (6) is $\sim 1/\ln L$. Since $L \sim \bar{L}$, the error $\to 0$ when $\bar{L} \to \infty$. The absolute inaccuracy in the critical term $\xi \ln L$ is $\sim \xi_c \ll 1$.

Consider the vicinity of the critical point. Equations (7), (9), and (10) yield two different asymptotics of $\int P\,dL$ in Eq. (8),

$$(\phi^{\xi}/\xi) |\ln \phi|^{1/2} \simeq 0.5 \sqrt{\pi} \xi^{-1.5} - M \quad \text{when} \quad \xi \ln(1/\phi) \gg 1, \qquad (11a)$$

$$(2/3) |\ln \phi|^{23} = M \quad \text{when} \quad \xi \ln(1/\phi) \ll 1. \qquad (11b)$$

Correspondingly,

$$\phi \sim (\tau / \sqrt{|\ln \tau|})^{1/\xi},$$

$$\tau \simeq (0.75\sqrt{\pi})\xi^{-3/2}(\xi_c - \xi) \quad \text{if} \quad \xi_c - \xi \ll \xi_c^{3/2}, \tag{12a}$$

$$\phi \sim \exp[-(1.5M)^{2/3}] \quad \text{if} \quad \xi \ll M^{-3/2}. \tag{12b}$$

The width of the interval (12a) is

$$(T_c - T) \sim \delta T_c^* \sim T_c - T^* \sim (T_c - \overline{T})\xi_c^{-3/2}. \tag{13}$$

In the interval (12b)

$$l_{\mathrm{m}} \sim \overline{T}/(s\xi_c \delta T). \tag{14}$$

When l_{m} becomes less than the correlation length r_c (r_c is in the number of base pairs), i.e., when $\delta T < 0.3K/r_c$, the presented approach is inapplicable. Then successive melting of ground state domains proceeds according to Ref. [3] and allows for a certain DNA sequencing.

All calculations are based on statistics. Thus, they assume $N \gg \overline{L}$, i.e.,

$$N \gg 1/\phi. \tag{15}$$

DNA is not completely melted in the entire interval (13) if

$$\ln N > 1/\xi_c. \tag{16}$$

IV. SPECIFICITY OF THE DNA CRITICAL POINT

DNA critical indexes are dominated by the nonuniversal decrease in the renormalized long-range interaction ‘‘charge’’ c with temperature. At T_c it is higher than the critical Landau-Peierls $c=1$ by $\xi_c \ll 1$. In DNA $J/T \sim \overline{T}/\Delta T \sim 10$, $D \sim 0.5$ [1,2], and $c \simeq 2$ [9–12]. So, by Eqs. (7), (9), and (10),

$$\xi_c \sim 0.01, \quad (T_c - \overline{T})/\overline{T} \simeq (s/2c_1)(D\Delta T/\overline{T})^2 \sim 0.01. \tag{17}$$

Such close proximity to $c=1$ yields crucial implications. The critical exponents in Eqs. (12a) and (12b) are giant,

$$1/\xi \sim (1/\xi_c) + (\xi_c - \xi)/\xi_c^2, \quad M^{2/3} \sim (1/\xi_c)(T - \overline{T})/(T_c - \overline{T}),$$

$$1/\xi_c \sim 100, \quad (\xi_c - \xi)/\xi_c^2 \lesssim 10^{-3}(T_c - T)/(T_c - \overline{T}) \lesssim 10. \tag{18}$$

Equation (8) in the cases (11a) and (11b) yields correspondingly

$$\overline{L} \sim \delta\overline{L} \sim \tau/\phi, \quad \Delta L \simeq \tau^{1/2}/\phi \gg 1, \tag{19a}$$

$$\overline{L} \sim \delta L \sim \Delta L \sim 1/\phi, \tag{19b}$$

where $\Delta L = \sqrt{\overline{L^2} - \overline{L}^2}$. This implies giant fluctuations when $\overline{L} \to \infty$.

The width of the transition (13) is small, yet macroscopic. By Eq. (17), $(T_c - T^*)/T_c \sim 10^{-4}$, i.e., $T_c - T^* \sim 0.003$ K; by Eqs. (9) and (12), at the crossover $\overline{L} \sim 10^{40}$. Thus, even in a solution with $\sim 10^{22}$ DNA nucleotide base pairs, all DNA molecules completely unbind in the interval (12b). At a macroscopic distance from T_c, the effective long-range interaction exceeds any macroscopic size of the system. The system can no more be divided into weakly interacting subsystems. Thus, the Gibbs distribution is invalid, and thermodynamics must be calculated from the first principles. The temperature T_N of complete melting of a finite DNA of the length N is determined by $L \sim N$, i.e., by

$$\theta_N = (T_c - T_N)/T_c \sim 1/\ln N. \tag{20}$$

Similar to $\delta L \sim \overline{L}$, the mean fluctuation $\Delta\theta_N$ of θ_N may be estimated from $\overline{L}(\theta_N + \Delta\theta_N) - \overline{L}(\theta_N) \sim \overline{L}(\theta_N)$, which yields

$$\Delta\theta_N/\theta_N \sim 1/\ln N. \tag{21}$$

Such fluctuation is macroscopic and observable. The approach presented suggests that this unusual critical behavior may be characteristic of any sufficiently strong and heterogeneous long-range interaction.

In a general case there are three distinctly different temperature intervals: $T_c - T^* \sim 0.003$ K, $T_c - \overline{T} \sim 3$ K, and $\Delta T \sim 40$ K. A giant nonuniversal temperature dependent critical exponent (12a) may be observed, by Eq. (16), when $\overline{x}(1 - \overline{x}) < 0.03(\ln N)^{3/4}$. Only in such heteropolymers, the nonuniversality of the giant critical index in Eq. (12a) may be studied (e.g., via its dependence on ΔT, which changes together with the solvent concentration in DNA solutions [2]).

The presented theory may be numerically tested. Once the ground state is accurately determined analytically [3], computer simulations enable the study of its fluctuations.

V. OUTSTANDING PROBLEMS AND SUMMARY

The crossover from Eq. (12b) to Eq. (12a) manifests the divergence of $l_n = \ln\overline{L}$ from $\overline{l} = \overline{\ln L}$. By Eq. (19a) the former $\to\infty$ when $T \to T_c$, while the latter, by Eqs. (8), (12a), and (12b), in both cases equals

$$\overline{l} \simeq 0.3(D\Delta T/\delta T_c)^2[\xi_c + 1/|\ln\phi|]^{-1}. \tag{22}$$

When $T \to T_c$, then $\overline{l} \simeq 0.3(D\Delta T/\delta T_c)^2(1/\xi_c)$. In DNA such $\overline{l}$ is ~ 3000, i.e., large, but finite. In the interval (12b), the exactly solvable model [Eqs. (4) and (5)] implies $l \sim l_{\mathrm{m}} \sim \ln\overline{L} \sim \overline{\ln L}$, which is independent of the way of averaging. The singularity emerges in the interval (12a), where $\ln\overline{L} \to \infty$ vs $\overline{\ln L} \sim 100$ calls for further theoretical study of the model, and for experimental study of heteropolymers with very low AT or GC concentration.

DNA heterogeneity implies low probability of the accidental complementarity of DNA nucleotide strands, and thus of their accidental binding in a loop, as well as slow formation and relaxation of knots. This may further increase c.

The presented calculation accounts for loop interaction in the value of c only. It should be complemented with a study similar to Refs. [5,6]. However, when $\overline{L} \to \infty$, the impact of any loop correlations vanishes, and may be disregarded.

Some systems [4,5] map onto the melting of directed polymers. Then Eq. (3), and the above approach, should be correspondingly amended. The approach should also be adjusted to and complemented with the specifics of the approach to other relevant problems in Refs. [10–13].

SUMMARY

An exactly solvable model of DNA melting is presented. It predicts a giant (>100) critical index. The latter may be observed when the AT or GC concentration is below $0.03(\ln N)^{0.75}$, where N is the total number of nucleotide pairs. In the vicinity of complete melting, the Gibbs distribution is invalid, and thermodynamics must be calculated from the first principles. The approach may be applied to other problems, and thus calls for further verification and generalization.

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