2003

Comment on "Why is the DNA Denaturation Transition First Order?"

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Recently, Kafri, Mukamel, and Peliti [1] extended the classical Poland-Scheraga (PS) model for the denaturation transition of DNA [2]. According to PS, the energetic binding of bases in the double helix competes with the entropic contribution of denatured loops, implying that the nature of the transition depends on the exponent c in the statistical weight $\Omega(2k) \sim s^k k^{-c}$ for a closed loop of length $2k$: for $1 < c \leq 2$ it is of second order, while for $c > 2$ it is of first order [1,2]. Fisher, taking the effects of self-avoidance within a denatured loop into account, found $c = d\nu \approx 1.766$ in $d = 3$, i.e., a second order transition [3]. In Ref. [1] it was obtained that the exponent c is modified if additional effects of self-avoidance between a denatured loop and the vicinal double helices are included. For a single loop within two strands of double helix, it was found that [1]

$$c = d\nu - 2\sigma_3 \approx 2.115, \qquad d = 3, \tag{1}$$

i.e., a first order transition, where σ_3 is a topological exponent related to a 3-vertex of a polymer network [4].

This conclusion is valid in the asymptotic scaling limit for long flexible, self-avoiding chains; i.e., each of the three segments going out from a vertex must be much longer than the persistence length ℓ_p of this segment (even though individual values of the ℓ_p may be different). If this condition is fulfilled, the analysis for the PS-inspired model in Ref. [1] is consistent [5,6]. However, we point out in this Comment that it does not apply to the chains typically used in experiments [7]: the DNA double helix being quite rigid, we expect the transition in such systems to be of second order.

The typical length of DNA used in experiments varies from about 100 to 5000 base pairs (bp), the latter corresponding to a whole viral DNA [7]. In such DNA, a chain "monomer" m, which corresponds to a bead in a freely jointed chain, represents one persistence length ℓ_p. For the single strand in a denatured loop, typically $\ell_p(L) \sim$ 40 Å (roughly eight bases), whereas for the double helix $\ell_p(H) \sim 500$ Å (100 bp) [8]. Even if one assumes that a segment of ten monomers $m(H)$ of the double helix is already long enough to be sufficiently close to the asymptotic scaling limit for long chains (which is hopelessly optimistic [9], and also much less than taken in the simulations [5]), one can *at best* place five loops even on the longest chains such that the flexibility condition is not violated. However, with a maximum number of only five loops, the system is governed by finite size effects, and the analysis in Ref. [1] is no longer valid.

Conversely, only 80 bases (40 bp) are needed to form ten monomers $m(L)$ such that a denatured loop can be considered as sufficiently flexible. The longer chains in the experiments can thus exhibit a fairly large number of such loops, if the segments of the double-stranded helix between them are allowed to be of the order of $\ell_p(H)$ (see below). It is therefore justified to neglect the entropy of the double-stranded helix [2]. Following this picture, a vertex with three outgoing legs would not tie together three flexible chains, but rather two flexible chains (belonging to the loop) and one *rigid rod* (the double helix). However, a rigid rod represents an irrelevant object for flexible, self-avoiding chains in the scaling limit for $d = 3$ [10], which implies for the present case that σ_3 in Eq. (1) is replaced by zero. This, in fact, reproduces the original value $c \approx 1.766$ [3], i.e., a second order transition.

Finally, we note that at the denaturation transition of real DNA the average length ξ of bound helical segments between loops is of the order of a few hundred bp, thus comparable with $\ell_p(H)$ and much larger than $\ell_p(L)$ [see, e.g., Eq. (9.129) in Ref. [2]]. This large value of ξ reflects the fact that the denaturation transition of real DNA is *highly cooperative;* in the PS model, this is generally modeled by the (nonuniversal) cooperativity parameter $\sigma_0 \ll 1$ [2,7,11] which enters the statistical weight of loops in the partition function, leading to $\xi \sim 1/\sigma_0 \gg 1$ [see Eqs. (9.1), (9.129), and (9.115a) in Ref. [2]].

We thank M. Kardar and H. Scheraga for comments. This work was supported by the DFG and by NSF Grant No. DMR-01-18213.

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Received 9 October 2001; published 18 April 2003
DOI: 10.1103/PhysRevLett.90.159801
PACS numbers: 87.14.Gg, 05.70.Fh, 63.70.+h, 64.10.+h

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