Kafri, Mukamel, and Peliti Reply: The Comment of Hanke and Metzler [1] questions the validity of the analysis presented in [2] to DNA chains of finite length as used in experiments. Their argument is that for the analysis to be valid "each of the three segments going out of a vertex must be much longer than the persistence length ℓ_p of this segment." By using the persistence lengths $\ell_p(L) \sim 40$ Å for a single strand and $\ell_p(H) \sim 500$ Å for a double helix (bound segment) they arrive at the conclusion that in order to observe the asymptotic behavior found in [2] one needs chains which are far longer than those studied experimentally.

This assertion is a consequence of a misinterpretation of the analysis given in [2]. In this analysis one considers a loop interacting with *the rest of the chain* and not just with the vicinal double helices. Thus, in [2] each of the two lines attached to the loop is, in fact, composed of an alternating sequence of bound segments and denaturated loops. It may be viewed as a stick-and-joint structure, whereby adjacent double helices are loosely attached to each other via an open loop. The "rest of the chain" as considered in Ref. [2] is, in fact, a jointed rod structure with a persistence length which is given by $\ell_p(H)$ when the distance between loops, ξ, is larger than $\ell_p(H)$ and is given by ξ when $\xi < \ell_p(H)$.

In the Comment the authors claim that the analysis of [2] is valid only when the helical segment is flexible and thus much larger than the persistence length $\ell_p(H)$, where it could be described by a self-avoiding walk. This claim is incorrect. The analysis is valid as long as the chain contains a sufficient number of loops to allow considering the stick-and-joint structure as a self-avoiding walk. Thus, even short chains of length of the orderof 5000 base pairs could allow for about 20 joints which is large enough to make the analysis of [2] valid. This is clearly evident from experimental melting curves [3,4] of chains of such lengths. These curves exhibit over 10 individual subtransitions corresponding to the existence of a large number of loops (since some of the peaks correspond to more than one loop). Thus, the claim made in [1] that the Fisher exponent $c = 1.766$ should be employed when the bound segment is a rigid rod is not valid. Moreover, many experiments were carried out on chains of a length of the order of 10^6 base pairs [5] where the asymptotic regime considered in [2] is easily accessible.

Our observation [2] that the effective loop entropy parameter c is, in fact, larger than 2 affects other parameters which have been applied in modeling DNA. One such example is the cooperativity parameter σ_0, which affects the melting curve rather drastically. Within the Poland-Scheraga (PS) approach the average distance between loops near the transition is given by $\xi \approx 1/\sigma_0$ for $c > 1$. This parameter has been estimated in various studies to be very small, of the order of 10^{-3} to 10^{-5} [3–7]. We point out that this small numerical value is obtained by fitting experimentally sharp melting curves to a theory which yields a *continuous transition* [6,7] (namely, the PS model with $1 < c < 2$), or sometimes *no transition at all* [5] ($c = 0$). Small σ_0 makes a continuous transition look sharp, yielding a good fit with experiment. In particular, σ_0 is usually estimated by considering the maximal value of the temperature derivative of the order parameter θ near the transition. For $c < 2$ one has [8] $\Psi \equiv -(\partial\theta/\partial T)_{\max} \propto \sigma_0^{-1/(2-c)}$. The large observed Ψ yields a very small σ_0 when fit with, for example, $c = 1.5$, 1.766 [6,7], or $c = 0$ [5]. However, since the effective c is larger than 2, the transition is expected to be *first order* where Ψ is infinite, irrespective of σ_0. The large but finite Ψ values found in experiment could be attributed to *finite size* rounding effects of a *first order* transition rather than to a very small σ_0.

We believe that the vast amount of melting curves data existing in the literature should be reevaluated using the correct exponent c in order to obtain a realistic estimate for the cooperativity parameter. Certainly this should result in a larger cooperativity parameter σ_0 which would in turn be reflected in an even smaller persistence length of the stick-and-joint structure of the molecule. It would also be very interesting to measure σ_0 directly from single molecule experiments using, for example, fluorescence correlation spectroscopy.

We thank H. A. Scheraga and E. Yeramian for helpful discussions.

Y. Kafri and D. Mukamel
Department of Physics of Complex Systems
The Weizmann Institute of Science
Rehovot 76100, Israel

L. Peliti
Dipartimento di Scienze Fisiche and Unità INFM
Università "Federico II"
Complesso Monte S. Angelo
I-80126 Napoli, Italy

Received 27 December 2001; published 18 April 2003
DOI: 10.1103/PhysRevLett.90.159802
PACS numbers: 87.14.Gg, 05.70.Fh, 63.70.+h, 64.10.+h

[1] A. Hanke and R. Metzler, preceding Comment, Phys. Rev. Lett. **90**, 159801 (2003).
[2] Y. Kafri, D. Mukamel, and L. Peliti, Phys. Rev. Lett. **85**, 4988 (2000); Eur. Phys. J. B **27**, 132 (2002).
[3] R. D. Blake *et al.*, Bioinformatics **15**, 370 (1999), and references therein; J.W. Bizzaro, K. A. Marx, and R. D. Blake, Mater. Res. Soc. Symp. Proc. **489**, 73 (1998).
[4] R. M. Wartell and A. S. Benight, Phys. Rep. **126**, 67 (1985).
[5] R. D. Blake, Biopolymers **26**, 1063 (1987).
[6] B. R. Amirikyan, A.V. Vologodski, and Yu. L. Lyubchenko, Nucleic Acids Res. **9**, 5469 (1981).
[7] D. M. Crothers and B. H. Zimm, J. Mol. Biol. **9**, 1 (1964).
[8] D. Poland and H. A. Scheraga, *Theory of Helix-Coil Transitions in Biopolymers* (Academic, New York, 1970).

