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We solve a two-dimensional model for polymer chain folding in the presence of mechanical pulling force (f) exactly using equilibrium statistical mechanics. Using analytically derived expression for the partition function we determine the phase diagram for the model in the f-temperature (T) plane. A square root singularity in the susceptibility indicates a second order phase transition from a folded to an unfolded state at a critical force (f_c) in the thermodynamic limit of infinitely long polymer chain. The temperature dependence of f_c shows a reentrant phase transition, which is reflected in an increase in f_c as T increases below a threshold value. As a result, for a range of f values, the unfolded state is stable at both low and high temperatures. The high temperature unfolded state is stabilized by entropy whereas the low temperature unfolded state is dominated by favorable energy. The exact calculation could serve as a benchmark for testing approximate theories that are used in analyzing single molecule pulling experiments. © *2013 American Institute of Physics.* [http://dx.doi.org/10.1063/1.4794154]

Since the pioneering experiments[1–3] demonstrating that titin, a large protein with multiple subunits, can be unfolded upon application of mechanical force, f, single molecule pulling experiments with increasing sophistication have been used to extract the folding landscapes of proteins[4,5] and RNA.[6,7] The experimentally accessible coordinate in these experiments is the molecular extension, R, which is conjugate to f and represents typically the distance between the ends of the molecule of interest. Parameters describing the folding landscape, such as the barrier to unfolding at $f = 0$, stability of the bound or folded states with respect to the unbound states, and location of the transition state are extracted from measurements (unbinding rates as a function of f for example) by assuming that a single reaction coordinate, R, suffices. Although such measurements and interpretations have provided insights into some aspects of the folding mechanisms the inability to confirm the accuracy of the extracted parameters by using independent measurements of the key quantities remains a major, but not widely discussed, problem. This situation is exacerbated by a paucity of exactly solvable models (however see Ref. 8), which can be used to test the accuracy of various commonly used approximate procedures to extract the folding landscape parameters from measured trajectories.

Motivated in part by the reasons stated above, in this work we obtain an exact solution on the effect of force on a remarkable model introduced over forty years ago by Zwanzig and Lauritzen (ZL)[9] in the context of polymer crystallization. In addition, there is growing interest in the collapse transition of self-attracting polymer chains, because of the potential relevance to protein folding,[10–12] and the ZL model captures the essential ingredients that describe polymer collapse. Of course, chain folding is also at the heart of self-assembly of proteins and RNA. Such transitions are caused by a competition between the self-attraction between segments of the poly-

mer (tending to collapse the chain) and the conformational entropy that favors expansion. Typically, at low temperatures the collapsed state is stable dominated by energy or enthalpy. Increase in T populates extended conformations that are stabilized by entropy. Since, the ZL model includes both these effects we suspect that certain generic aspects of chain folding can also emerge from a deeper study of this interesting model. Although the ZL model or the extension investigated here and elsewhere[13,14] may not be directly applicable to proteins the study of such models is interesting in its own right, and for clarifying unusual aspects of phase transitions in polymers.[15]

Although the ZL model may not be easily realized in experiments our work expands the range of exactly solvable models, which are always useful in providing insights in the study of more realistic but mathematically less tractable systems. The continuous ZL model of polymer crystallization by chain folding contains physically interesting interactions quite distinct from those of the Ising model while allowing the study of a second order phase transition and other thermodynamic properties by analytical methods.

For the ZL model we construct the equilibrium phases of the ZL model in the [f, T] variables where T is the temperature. Previously such phase diagrams have been obtained numerically using models introduced to understand protein folding[16,17] and also by theoretical methods for lattice homopolymer models.[18] The ZL model was introduced as a caricature of polymer crystallization, which in the absence of f exhibits a phase transition that can be treated exactly by equilibrium statistical mechanics. The ZL model leads to a novel second order-like phase transition from an extended state to a folded state in the thermodynamic limit of infinite chain length. The exact solution to the ZL model provided here shows folding-unfolding transition in the presence of mechanical force (f). In particular, we show that a second order phase

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transition also occurs from a folded state to an extended state at a critical force f_c at a fixed T. The exact calculation of the phase boundary separating the folded and extended states show a reentrant phase transition in which the extended state is stable at both high and low temperatures at finite f.

I. ZWANZIG-LAURITZEN MODEL

The ZL model considers a long polymer molecule whose conformations are restricted to a plane. At $f = 0$ the chain molecule folds into lamellar structures at low temperatures reminiscent of conformations adopted by crystallizing polymers. A conformation of the ZL chain, displayed in Fig. 1, shows that it can fold upon itself by paying a pending penalty, which is compensated by attraction between the chain segments. Consequently, at $f = 0$ the chain molecule folds into lamellar structures at low temperatures. The molecule folds into N segments ranging from one to infinity,

$$1 \leq N < \infty. \tag{1}$$

The folds are uniform occupying a length q (Fig. 1). Let the length of ith segment be x_i, with values in the range,

$$0 \leq x_i < \infty, \tag{2}$$

with the constraint that the total length L,

$$\sum_{i=1}^{N} x_i + (N-1)q = L \tag{3}$$

be fixed.

We apply a mechanical force, $\vec{f}$, to one end of the molecule with the other end fixed (Fig. 1). The total energy of a conformation consists of (1) a bending energy u for

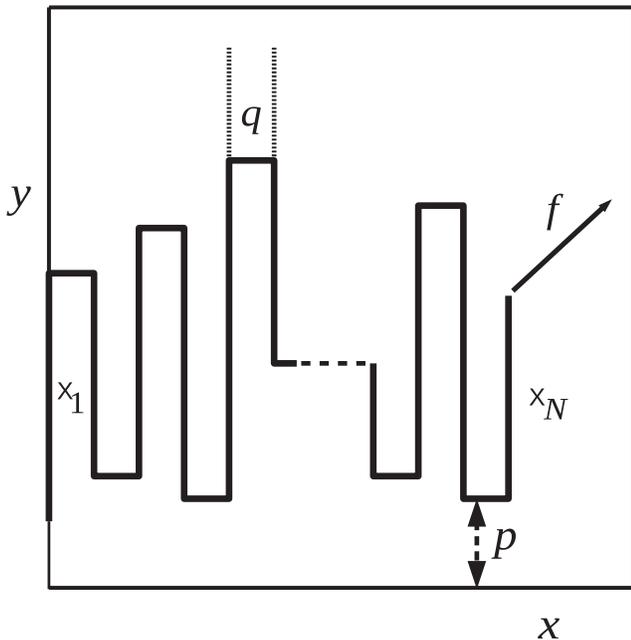

FIG. 1. Conformation of a polymer chain in the ZL model. Two contiguous vertical lines define a fold. There is a energy gain per each fold that is achieved by paying a bending penalty. The length of each fold is q. A force f is applied to one end of the chain. The calculations are done by assuming that the force is along the x axis.

each fold (Fig. 1), (2) the interaction energy between any pair of neighboring segments of length x_i and x_{i+1}, and (3) the stretching energy due the applied mechanical force at one end. Two neighboring segments interact with short-ranged van der Waals forces. ZL assumed that the attractive energy of interaction between ith and $(i + 1)$th segments is $-J \min(x_i, x_{i+1})$, where $\min(a, b)$ stands for the smaller of the length of the two segments. The proportionality constant J is taken to be positive. The stretching energy due to the applied force $\vec{f}$ is taken to be,

$$-\vec{f} \cdot (\vec{R}), \tag{4}$$

where, $\vec{R}$ is the end-to-end distance of the molecule. In the present calculations we assume that the force is applied only along the x direction. The total energy of a given conformation of the chain molecule is

$$E(x_1, ...x_n) = (N-1)u - J \sum_{i=1}^{N-1} \min(x_i, x_{i+1})$$
$$-f_x(N-1)q - f_y(x_N + p), \tag{5}$$

where $(N-1)q$ is the end-to-end distance along the x direction and $x_N + p$ is the end-to-end distance along y direction with arbitrary p, as shown in Fig. 1.

At first glance the ZL model resembles a one-dimensional model with short range interactions, which cannot exhibit a phase transition. However, ZL pointed out that this model is analogous to the familiar one-dimensional Ising model with N possible states for each of the N sites. A two-dimensional Ising model can be thought of as a one-dimensional Ising system in which each site has 2^N sites. Thus, apparently the ZL model has enough of the two-dimensional features to exhibit an interesting second order transition from an extended to folded states even in the absence of force.

II. EVALUATION OF THE PARTITION FUNCTION IN THE PRESENCE OF FORCE

We take the continuum limit of the model. In this limit, the canonical partition function $Z(L)$, which is the sum of the Boltzmann factors $e^{-\beta E_N}$ of all configurations of a polymer molecule subject to the constraint of fixed total length L, is

$$Z(L) = \sum_{N=1}^{\infty} \int_0^\infty \cdots \int_0^\infty dx_1 \cdots dx_N$$
$$\times \delta \left(\sum_{i=1}^{N} x_i + (N-1)q - L \right) e^{-\beta E_N}, \tag{6}$$

with $\beta = \frac{1}{k_B T}$, and k_B is Boltzmann's constant. As we sketch below, the partition function $Z(L)$ can be evaluated analytically following the strategy developed by ZL. We start with Eq. (6) and perform a Laplace transform of the partition function with respect to length L to eliminate the delta function on the right-hand side of Eq. (6). Then we invert the transform to obtain $Z(L)$. Using the following relation,

$$\min(a, b) = \frac{1}{2}(a+b) - \frac{1}{2}|a-b|, \tag{7}$$

we can write the potential energy in the following form

$$E_N = (N-1)u - \frac{1}{2}J\sum_1^{N-1}(x_i + x_{i+1})$$

$$+ \frac{1}{2}J\sum_1^{N-1}|x_i - x_{i+1}|) - f_x(N-1)q - f_y(x_N + p).$$

(8)

We write Eq. (8) as

$$E_N = (N-1)u - J\sum_1^N x_i$$

$$+ \frac{1}{2}J\left(x_1 + x_N + \sum_1^{N-1}|x_i - x_{i+1}|\right)$$

$$- f_x(N-1)q - f_y(x_N + p).$$

(9)

The sum $\sum_1^N x_i$ in Eq. (9) can be replaced by $L - (N-1)q$, leading to

$$E_N = (N-1)(u + Jq) - JL$$

$$+ \frac{1}{2}J\left(x_1 + x_N + \sum_1^{N-1}|x_i - x_{i+1}|\right)$$

$$- f_x(N-1)q - f_y(x_N + p).$$

(10)

By substituting Eq. (10) into Eq. (6) we obtain,

$$Z(L) = \sum_{N=1}^\infty [e^{-\beta(u+Jq-f_xq)}]^{N-1}e^{\beta JL}$$

$$\times \int_0^\infty \cdots \int_0^\infty dx_1 \cdots dx_N$$

$$\times \delta\left(\sum_{i=1}^N x_i + (N-1)q - L\right)$$

$$\times \exp\left[-\frac{1}{2}\beta J(x_1 + x_N) + \frac{1}{2}J\sum_1^{N-1}|x_i - x_{i+1}|)\right]$$

$$\times e^{\beta f_y(x_N+p)}.$$

(11)

Taking the Laplace transform on both sides to eliminate the delta function on the right-hand side of Eq. (11), we obtain,

$$\int_0^\infty dL e^{-(\eta+\beta J)L}Z(L) = \sum_{N=1}^\infty [e^{-\beta(u+Jq-f_xq)}]^{N-1}$$

$$\times e^{-\eta(N-1)q}\int_0^\infty \cdots \int_0^\infty dx_1 \cdots dx_N e^{-\eta\sum_1^N x_i}$$

$$\times \exp\left[-\frac{1}{2}\beta J(x_1 + x_N) + \frac{1}{2}J\sum_1^{N-1}|x_i - x_{i+1}|)\right]$$

$$\times e^{\beta f_y(x_N+p)}.$$

(12)

The integrals in Eq. (12) are evaluated using the following method. We define a partial generating function with the

initial point fixed at the origin. Let us define a recursion relation of the partial generating function with fixed $x_N = x$.

$$g(z,x) = te^{-\gamma|x-z|}e^{-\eta x}\left[\int_0^\infty g(x,y) + e^{-\gamma x}\right],$$

(13)

where $t = e^{-\beta(u+Jq-f_xq)}$ and $\gamma = \frac{1}{2}\beta J$. The needed generating function is

$$G(t,\eta) = \int_0^\infty e^{\beta f_y x}g(z=0,x).$$

(14)

The term $\int_0^\infty g(x,y)$ in Eq. (13) is the generating function in the absence of mechanical force, which is explicitly calculated in Ref. 9 by solving the differential equation given by

$$\int_0^\infty dy g(x,y) = -e^{-\gamma x} + \frac{\eta\alpha}{2t}\frac{J_\nu(\alpha e^{-\eta x/2})}{J_{\nu-1}(\alpha)},$$

(15)

with, $\alpha = \left(\frac{8\gamma t}{\eta^2}\right)^{1/2}$ and $\nu = 2\gamma/\eta$ and u is replaced by $u + Jq - f_xq$. Using Eqs. (13)–(15), we can evaluate the generating function in presence of mechanical force exactly. We obtain

$$G(t,\eta) = \frac{\Gamma\left(1 - \frac{a}{2} + \nu\right)}{\Gamma\left(2 - \frac{a}{2} + \nu\right)}$$

$$\times \frac{\eta\alpha^{\nu+1} {}_pF_q\left[\left\{1 - \frac{a}{2} + \nu\right\}; \left\{1 + \nu, 2 - \frac{a}{2} + \nu\right\}; -\frac{\alpha^2}{4}\right]}{J_{\nu-1}(\alpha)\Gamma(\nu+1)},$$

(16)

with $a = \frac{2\beta f_y}{\eta}$ and $\eta > \beta f_y - 2\gamma$. Hence we get,

$$\int_0^\infty dL e^{-(\eta+\beta J)L}Z(L) = e^{\beta(u+Jq-f_xq)}e^{\eta q}G(t,\eta).$$

(17)

The partition function $Z(L)$ can be found by taking the inverse Laplace transform,

$$Z(L) = e^{\beta(u+Jq-f_xq)}\frac{1}{(2\pi i)}\int_{c-i\infty}^{c+i\infty} d\eta e^{\eta L + \eta q + \beta JL}G(t,\eta).$$

(18)

The contour of integration is a straight line, parallel to the imaginary axis, to the right of all singularities of the integrand.

We now analyze the analytic properties of $G(t,\eta)$ in the complex η plane. Originally, the function $G(\eta)$ is calculated for real η with the imposed condition $\eta - \beta f_y + 2\gamma > 0$. Now, we wish to analytically continue $G(\eta)$ off the real η axis. The Bessel function has branch points at the origin, and the usual cut along the negative real axis, but the related function,

$$\Lambda_{\nu-1}(z) = \Gamma(\nu)\left(\frac{z}{2}\right)^{-\nu+1}J_{\nu-1}(z)$$

(19)

is an entire function of z and a meromorphic function of order $\nu - 1$. We start with real positive η and hence real positive ν, where the function G is well defined, and can be written as

$$G(t,\eta) = \frac{\Gamma(\nu)\Gamma\left(1 - \frac{a}{2} + \nu\right)}{\Gamma(\nu+1)\Gamma\left(2 - \frac{a}{2} + \nu\right)}$$

$$\times \frac{\eta\alpha^2 {}_pF_q\left[\left\{1 - \frac{a}{2} + \nu\right\}; \left\{1 + \nu, 2 - \frac{a}{2}\right\}; \frac{-\alpha^2}{4}\right]}{(2)^{1-\nu}\Lambda_{\nu-1}(\alpha)}.$$

(20)

For simplicity, we assume that the pulling force is along x direction (Fig. 1). The function $_pF_q[\{1 - \frac{a}{2} + \nu\}, \{1 + \nu, 2 - \frac{a}{2}\}, \frac{-\alpha^2}{4}]$ reduces to Λ_ν. Both Λ_ν and $\Lambda_{\nu-1}$ are analytic functions of complex ν everywhere except at singularities of the gamma function. At these points, which are negative integers, they have simple poles. However, in the ratio, the singularities cancel out exactly at these points. This implies that the singularities of G in the complex plane are determined solely by the zeros of the denominator, which are now poles. This accomplishes the desired analytic continuation of the ratio of the positive real axis into the entire complex plane.

Let us define,

$$\sigma = \frac{2}{(\beta J)^{1/2}} \exp\left[-\frac{\beta}{2}(u + Jq - f_x q)\right], \qquad (21)$$

so that,

$$\alpha = \sigma \nu. \qquad (22)$$

In order to evaluate the contour integral in Eq. (18), we need to find the zeros of the denominator, which are the zeros of the Bessel function equation,

$$J_{\nu-1}(\sigma \nu) = 0. \qquad (23)$$

Each of the zeros will be a function of σ as well as the external force. To each zero, there corresponds to a particular value of η, which are all real. The sequence of all zeros of $J_{\nu-1}(\sigma \nu)$, corresponds to the sequence of all real $\eta's$, which is given by

$$\eta_1 > \eta_2 > \eta_3 > \cdots, \qquad (24)$$

indicating the largest one is η_1. Let R_i denote the residue at each pole of $G(\eta)$ corresponding to each η_i. We obtain,

$$Z(L) = \exp(\beta(u + JL + Jq - f_x q)) \sum_i R_i \exp(L\eta_i). \qquad (25)$$

III. PHASE TRANSITION

We are interested in the thermodynamic limit, corresponding to the length of the polymer molecule going to infinity. In the large L limit, the largest η_1 will dominate the sum. Consequently, the partition function becomes,

$$\lim_{L\to\infty}[L^{-1} \log Z(L)] = \beta J + \eta_1(\sigma, \beta, f_x). \qquad (26)$$

We have neglected terms that vanish in the large L limit. Thus, the evaluation of $Z(L)$ as well as the free energy reduces to the computation of a particular zero in Eq. (23) that gives the largest η_1.

The behavior of α for the largest order is known to be

$$\alpha = \nu - 1 + a_1(\nu - 1)^{1/3}, \qquad (27)$$

for large ν, and

$$\alpha = \sigma \nu. \qquad (28)$$

Comparing these equations, we conclude that for $\sigma < 1$, there is no solution for positive ν. There is an asymptotic solution $\nu = \infty$, and for $\sigma > 1$, there is a unique solution $0 < \nu < \infty$.

We assume here that the fold energy u is positive, σ is monotonically increasing function of both temperature and force. Thus, σ is unity at the transition point determined by either

$$\frac{2}{(\beta_c J)^{\frac{1}{2}}} \exp\left[-\frac{\beta_c}{2}(u + Jq - f_x q)\right] = 1, \qquad (29)$$

for fixed f_x, or

$$\frac{2}{(\beta J)^{\frac{1}{2}}} \exp\left[-\frac{\beta}{2}(u + Jq - f_c q)\right] = 1, \qquad (30)$$

for arbitrary β. Equation (30) represents the exact form of the critical force for arbitrary β.

In the limit $\beta \to \beta_c$ from above or $f_x \to f_c$ from above at a constant β, ν approaches ∞, so that,

$$\sigma \nu = \nu + a\nu^{1/3}. \qquad (31)$$

It follows that

$$\nu = a^{3/2}(\sigma - 1)^{-3/2}, \qquad (32)$$

if $T \sim T_c^+$ or $f_x \sim f_c^+$, or equivalently,

$$\nu^{-1} = a^{-3/2}(\sigma - 1)^{3/2}. \qquad (33)$$

IV. THERMODYNAMICS

We discuss the thermodynamic properties of the model in the long chain limit. In the thermodynamic limit, the Helmholtz, A, free energy per unit length is given by

$$\lim_{L\to\infty}\left(\frac{A}{L}\right) = -J - \beta^{-1}\eta_1. \qquad (34)$$

By defining the reduced temperature $T' = \frac{1}{\beta J}$, we obtain the reduced free energy,

$$A' = \lim_{L\to\infty}\left(\frac{A}{LJ}\right) = -1 - T'\eta_1. \qquad (35)$$

The reduced mean energy is given by

$$E' = \lim_{L\to\infty}\left(\frac{E}{LJ}\right) = -T'^2\frac{\partial A'/T'}{\partial T'}. \qquad (36)$$

The average end-to-end distance in the direction of f_x is $\langle(N-1)q\rangle$ can be found by differentiating the partition function with respect to f_x,

$$\langle(N-1)q\rangle = \beta^{-1}\frac{\partial \ln Z}{\partial f_x}|_{T'}. \qquad (37)$$

In the thermodynamic limit, the average end-to-end distance per unit length, l, along the x direction is,

$$l = \lim_{L\to\infty}\left(\frac{1}{L}\langle(N-1)q\rangle\right) = -J\left(\frac{\partial A'}{\partial f}\right)_{T'}. \qquad (38)$$

We are interested in the vicinity of the transition point, which is in the neighborhood of $\sigma = 1$. Suppose, $\sigma = 1$, when $T' = T_c(\gamma)$ and f_x is fixed, then Taylor series expansion of σ is given by

$$\sigma(T') = 1 + \left[\frac{1}{2T_c} + \frac{u/J + q}{2T_c^2} - \frac{f_x q}{2T_c^2 J}\right](T' - T_c) + \cdots \qquad (39)$$

Similarly, for arbitrary T', Taylor series expansion of σ around the critical force f_c is given by

$$\sigma = 1 + \left[\frac{q}{2T'J}\right](f_x - f_c) + \cdots. \tag{40}$$

First consider the case with $f_x = 0$. The expansion in (39) shows that ν^{-1} is proportional to three halves power of the temperature deviation from T_c. Now, for $T' < T_c$, σ is less than unity and $\eta_1 = 0$. When T' becomes T_c^+, σ becomes greater than unity. The free energy is given by

$$A' = -1 - a_1^{-3/2}\left[\frac{1}{2T_c} + \frac{u/J + q}{2T_c^2}\right]^{3/2}(T' - T_c)^{3/2} \tag{41}$$

if $T' > T_c$, and,

$$A' = -1 \tag{42}$$

if $T' < T_c$.

Similarly, for specific heat,

$$\left(\frac{\partial E}{\partial T'}\right)_\gamma = 0 \tag{43}$$

if $T' < T_c$, and

$$\left(\frac{\partial E}{\partial T'}\right)_\gamma = \frac{3}{4}[T_c]\left[\frac{1}{2T_c} + \frac{u/J + q}{2T_c^2}\right]^{3/2}(T' - T_c)^{-1/2} \tag{44}$$

if $T' > T_c$. Specific heat shows inverse square singularity at the transition temperature. The discontinuity in specific heat shows a second order phase transition at $T' = T_c$ for fixed $f_x = 0$.[9]

It can be easily seen that in the absence of force, and for negative value of the bending energy u, in the interval $-\frac{J}{4e} - Jq < u < -Jq$, σ is infinite for both $T' = 0$ and $T' = \infty$, with a single minimum below unity at a finite temperature. It follows that σ will intersect unity at two temperatures and hence there are two phase transitions. At low enough temperatures, with negative bending energy, increasing the number of folds will minimize the total energy. This leads to the stabilization of the stable folded state. Such a possibility is not realized for positive fold energy.

Now, we fix T and vary the applied mechanical force. The expansion in (40) shows that ν^{-1} is proportional to the three halves power of the force deviation from f_c. For $f_x < f_c$, σ is less than unity and $\eta_1 = 0$. As $f_x \to f_c^+$, σ becomes greater than unity. The free energy is given by

$$A' = -1 \tag{45}$$

if $f_x < f_c$, and

$$A' = -1 - \left[\frac{q}{2a_1T'J}\right]^{3/2}(f_x - f_c)^{3/2} \tag{46}$$

if $f_x > f_c$.

The average end-to-end distance l per unit length in the thermodynamic limit is found in (38). If $\sigma < 1$, then we have $\eta_1 = 0$ and the mean distance per unit length is zero. In the thermodynamic limit, any finite end-to-end distance corresponds to $l = 0$. The average end-to-end distance per unit length vanishes when $f_x < f_c$ corresponding to the folded

state, and increases with the square root of the force difference above f_c for arbitrary T' representing the unfolded state as follows,

$$l = 0 \quad f_x < f_c \tag{47}$$

and

$$l = \frac{3}{2}\left[\frac{q}{2a_1T'J}\right]^{3/2}(f_x - f_c)^{1/2}, \tag{48}$$

if, $f_x > f_c$. Thus, the folded-unfolded transition in this model is second order even in the presence of force. Our calculations further reveal that the susceptibility $\chi = \frac{\partial l}{\partial f_x}$ of the polymer diverges as

$$\chi \propto (f_x - f_c)^{-1/2} \tag{49}$$

as f_x approaches the transition point from above. The divergence in susceptibility at the transition point, with the characteristic critical exponent 1/2 further establishes that the transition is second order.

V. PHASE DIAGRAM IN THE [*f*, *T*] PLANE

In Fig. 2, we show the regions of $f - T$ plane, where the chain is extended (white) and where it is chain folded (shaded) for this model. Remarkably, the phase diagram exhibits a reentrant behavior. The boundary separating the two phases occurs when

$$2T'^{1/2}e^{-\frac{\frac{u}{J}+q}{2T'}}e^{\frac{f_cq}{2JT'}} = 1. \tag{50}$$

This is an exact form for the temperature dependence of the critical force, f_c. The transition curve separates the region of extended chain and chain folded configurations. Upon crossing the phase boundary from below the folded chain undergoes a transition to the extended state via second order transition. From Eq. (50), we can write

$$\frac{f_c}{J}q = \left(\frac{u}{J} + q\right) - T'\log(4) - T'\log(T'). \tag{51}$$

The transition line in Fig. 2 increases at low temperatures due to the leading term $T'\log T'$ in Eq. (51). In the interval $u + Jq < f_cq < u + Jq + \frac{J}{4e}$, the folding transition
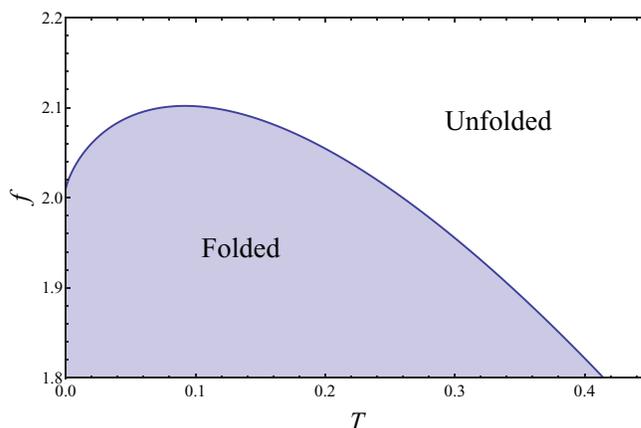

FIG. 2. Phase diagram in the $f - T$ plane with $q = 2$ and $u/J = 0.01$. At low temperatures the critical force increases as T increases reflecting the observed reentrant behavior.

occurs at a critical force over a range of temperatures. However, upon further lowering the temperature the chain becomes extended a process that is reminiscent of "cold denaturation." Hence, the extended state is stable at both high and low temperatures, implying that there is reentrant phase transition. At low enough temperatures, for the case of $f_c q > u + J q$, large end-to-end distance minimizes the total energy corresponding to a stable extended state. In particular, Fig. 2 shows the unusual behavior that at low enough temperatures the critical force required to unfold the chain is less that at a higher temperature. For example, f_c at $T = 0.05$ is less than f_c at $T = 0.1$.

VI. CONCLUSIONS

The exact solution of the ZL model for polymer chain folding in the presence of force shows a second order transition from a folded to an unfolded state provided the values of force are less than a critical value, $f_c(T)$. This prediction is not in accord with mean field theory, which suggests that the unfolding transition in the presence of external mechanical force is likely to be first order in all dimensions.[19] Indeed, molecular simulations of forced-unfolding of proteins exhibit a first order phase transition in three dimensions[16,17] in support of the predictions of the mean field. However in two dimensions, extensive Monte Carlo simulations performed on a self-avoiding walk model in a poor solvent[20] suggests that the folded to unfolded transition could have the hall marks of a second order, in accord with the present calculations. Furthermore, scaling analysis shows a second order phase transition at a critical force f_c.[21,22] Renormalization group analysis of polymer unfolding in special lattices also reveals a change in the nature of the phase transition as the spatial dimension exceeds two.[23] Thus, the upper critical dimension for force-induced unfolding of self-attracting polymers, and hence proteins are likely to be three.

Interestingly, for a range of $f < f_c(T)$ the ZL model exhibits a reentrant phase transition in which the disordered state is stable at low and high temperatures. As a consequence, $f_c(T)$ increases as T increases in the low T regime. Force-induced reentrant behavior may be a common feature in other model polymeric systems as well.[21,24,25] A recent simulation study in the constant force ensemble[25] showed that the phase boundary separating the adsorbed and desorbed states of two-dimensional self-avoiding polymer in the [f, T] plane is very similar in shape to the curve plotted in Fig. 2. The generality of reentrant phase transitions induced by force, which is similar to cold denaturation in proteins, remains to established. The generality of reentrant phase transitions induced by force, which is similar to cold denaturation in proteins has been found previously.[17,26,27] It would be of particular interest to characterize such transitions in proteins. This, of course, would require performing pulling experiments as a function of temperature and force.

Disorder-order-disorder transition has been studied in other models either exactly[28,29] or using mean-field theories[26,27,30] (for both lattice and continuous space) for DNA mechanical unzipping induced by pulling force. These models exhibit cold mechanical denaturation (reentrant behavior) for a finite range of forces at low enough temperatures even in the presence of quenched randomness. The instability of a low-temperature disordered state increase with temperature, and eventually at a critical temperature the low-lying excited or metastable state becomes stable, undergoing an inverse phase transition. This unusual and counterintuitive phenomenon does not violate the laws of thermodynamic, since the absolute measure for order and disorder is the entropy of the (isolated) system, which always increase (or at least does not decrease) with temperature. The reentrant transition for various models as well as the model presented here for polymeric systems suggest that they are universally present. We speculate that intrinsically disordered proteins might represent a reentrant phase of polypeptide chains.

In addition to adding to the collection of exactly solvable polymer models exhibiting phase transitions, the present work could be used to test approximate theories used to obtain folding thermodynamics of proteins using single molecule pulling experiments, which assume that extension is an excellent parameter.

[1]M. Rief, H. Gautel, F. Oesterhelt, J. M. Fernandez, and H. E. Gaub, Science **276**, 1109 (1997).
[2]M. Z. Kellermeyer, S. B. Smith, H. L. Granzier, and C. Bustamante, Science **276**, 1112 (1997).
[3]L. Tskhovrebova, J. Trinick, J. Sleep, and R. Simmons, Nature (London) **387**, 308 (1997).
[4]J. Stigler, F. Ziegler, A. Gieseke, J. Gebhardt, and M. Rief, Science **334**, 512 (2011).
[5]A. Borgia, P. Williams, and J. Clarke, Annu. Rev. Biochem. **77**, 101 (2008).
[6]M. T. Woodside, C. Garcia-Garcia, and S. M. Block, Curr. Opin. Chem. Biol. **12**, 640 (2008).
[7]C. Hyeon and D. Thirumalai, Proc. Natl. Acad. Sci. U.S.A. **102**, 6789 (2005).
[8]V. Barsegov, G. Morrison, and D. Thirumalai, Phys. Rev. Lett. **100**, 248102 (2008).
[9]R. Zwanzig and J. I. Lauritzen, J. Chem. Phys. **48**, 3351 (1968).
[10]C. J. Camacho and D. Thirumalai, Proc. Natl. Acad. Sci. U.S.A. **90**, 6369 (1993).
[11]C. J. Camacho and D. Thirumalai, Phys. Rev. Lett. **71**, 2505 (1993).
[12]B. Schuler and W. A. Eaton, Curr. Opin. Struct. Biol. **18**, 16 (2008).
[13]A. Caliri, H. Bohr, and P. Wolynes, Phys. Lett. A **183**, 327 (1993).
[14]J. Lauritzen and R. Zwanzig, J. Chem. Phys. **52**, 3740 (1970).
[15]L. I. Klushin and A. M. Skvortsov, J. Phys. A: Math. Theor. **44**, 473001 (2011).
[16]D. K. Klimov and D. Thirumalai, Proc. Natl. Acad. Sci. U.S.A. **96**, 6166 (1999).
[17]D. K. Klimov and D. Thirumalai, Proc. Natl. Acad. Sci. U.S.A. **97**, 7254 (2000).
[18]R. Brak, P. Dyke, J. Lee, A. L. Owczarek, T. Prellberg, A. Rechnitzer, and S. G. Whittington, J. Phys. A: Math. Theor. **42**, 085001 (2009).
[19]A. Halperin and E. Zhulina, Europhys. Lett. **15**, 417 (1991).
[20]P. Grassberger and H. Hsu, Phys. Rev. E **65**, 031807 (2002).
[21]D. Marenduzzo, A. Maritan, A. Rosa, and F. Seno, Phys. Rev. Lett. **90**, 088301 (2003).
[22]A. Rosa, D. Marenduzzo, A. Maritan, and F. Seno, Phys. Rev. E **67**, 041802 (2003).

[23]I. Vidanovic, S. Arsenijevic, and S. Elezovic-Hadzic, Eur. Phys. J. B **81**, 291–302 (2011).
[24]J. Osborn and T. Prellberg, J. Stat. Mech. **2010**, P09018 (2010).
[25]A. M. Skvortsov, L. I. Klushin, A. A. Polotsky, and K. Binder, Phys. Rev. E **85**, 031803 (2012).
[26]P. L. Geissler and E. I. Shakhnovich, Phys. Rev. E **65**, 056110 (2002).
[27]P. L. Geissler and E. I. Shakhnovich, Macromolecules **35**, 4429 (2002).
[28]T. R. Einert, H. Orland, and R. R. Netz, Eur. Phys. J. E **34**, 55 (2011).
[29]D. Marenduzzo, A. Trovato, and A. Maritan, Phys. Rev. E **64**, 031901 (2001).
[30]E. A. Mukamel and E. I. Shakhnovich, Phys. Rev. E **66**, 032901 (2002).