Phase diagram of force-induced DNA unzipping in exactly solvable models

D. Marenduzzo,[1,*] A. Trovato,[2] and A. Maritan[1,*]

[1]*International School for Advanced Studies (SISSA), and Istituto Nazionale di Fisica della Materia, Via Beirut 2-4, 34014 Trieste, Italy*
[2]*Niels Bohr Institutet, Blegdamsvej 17, 2100 København Ø, Denmark*

The mechanical separation of a double helical DNA structure induced by forces pulling apart the two DNA strands ("unzipping") has been the subject of recent experiments. Analytical results are obtained within various models of interacting pairs of directed walks in the $(1,1,\ldots,1)$ direction on the hypercubic lattice, and the phase diagram in the force-temperature plane is studied for a variety of cases. The scaling behavior is determined at both the unzipping and melting transitions. We confirm the existence of a cold denaturation transition recently observed in numerical simulations: for a finite range of forces, the system is unzipped by *decreasing* the temperature. The existence of this transition is rigorously established for generic lattice and continuum space models.

I. INTRODUCTION

In recent years, micromanipulation and nanomanipulation of single biological macromolecules have become feasible due to a dramatic improvement of experimental techniques. By using devices such as optical tweezers [1,2], soft microneedles [3], and atomic force microscopes [4], it is now possible to access physical and mechanical properties of fundamental biological objects, namely, proteins, nucleic acids, and molecular motors, on the scale of individual molecules. Special effort has been devoted to the measurement of force-elongation characteristics of double stranded DNA molecules (dsDNA), determining its response to external forces and torques in the absence of enzymes. The *mechanical unzipping* of dsDNA structure by a force pulling the end of one of the two strands, the end of the other strand being anchored to some physical support, was studied by Bockelmann and co-workers [5,6], who measured the average force along the opening of the two strands. Mechanical forces are in fact exerted on the DNA molecule by different enzymes during the process of DNA replication or transcription [7,8]. On the other hand, the double helical structure of dsDNA may be disrupted "in vitro" by changing pH, solvent conditions and/or temperature [9]. This transition is known as *melting denaturation*, and it has long been studied by theoretical physicists [10–12]. Only recently, DNA mechanical denaturation has been the subject of theoretical studies. Most of these studies considered a simple extension of the Poland-Sheraga model [11], in which the two DNA strands are homogeneous ideal polymer chains interacting with each other, introducing a constant force pulling apart the two strands by acting on one extremity of both strands. By using a mapping into a quantum-mechanical problem, it was shown [13–16] that the opening of the two strands occurs only if the pulling force is increased to a critical value. The unzipping transition turns out to be a first order phase transition, whereas the melting transition is second order, in the ideal case, in d

$=3$ [recently both simulations and exact results showed that the melting transition becomes first order, when considering mutually self-avoiding walks (SAW's) [17,18]]. The heterogeneous case was also studied with similar techniques [14]. Very recently, Monte Carlo simulations of interacting pairs of self avoiding walks on a cubic lattice and bead-and-string chains in the continuum space determined the whole phase diagram in the force-temperature plane, revealing the existence of a re-entrant zipping-unzipping transition by decreasing the temperature for a finite range of forces [19].

In this paper, we obtain exact analytical results for a class of simple lattice models of interacting pairs of homogeneous directed self-avoiding walks. We extend the model introduced in Ref. [19] in $D=1+1$ to the generic dimension case $D=d+1$, and analyze both the scaling behavior of the first order unzipping transition and the multicritical scaling laws at the melting transition in the force-temperature plane. We also consider different versions of the model, depending on whether the crossing of the two walks is allowed or not, or is simply penalized by an entropy cost. In all cases, we find that the critical pulling force *increases* with temperature at low T, thus implying the existence of a *cold* unzipping transition [19]. This seemingly paradoxical property is due to the competition between the energy gained by increasing the open portion of DNA and the entropy lost with the full stretching of the separated strands. Cold unzipping will be exactly proved for both ideal and self-avoiding chains in the lattice, and for a discrete chain with a constant distance between consecutive beads in the continuum space. We also discuss the role of denatured *bubbles* forming in the dsDNA opening, as opposed to the end opening of the strands induced by the pulling force. By comparing the phase diagram of the different models considered, we point out that the approximation of neglecting bubbles and considering only Y-shaped configurations shares many of the features of a mean-field type approximation, with an upper critical dimension $d_c=4$.

Our paper is organized as follows. In Sec. II we introduce the models of directed walks on the lattice in any dimension D, and compute their thermodynamical properties, deriving the phase diagram in the force-temperature plane. In Sec. III we analyze the scaling laws at both the thermal melting and

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*Also at The Abdus Salam International Center for Theoretical Physics, Strada Costiera 11, 34100 Trieste, Italy.

mechanical unzipping transitions, and we highlight the features that are physically more interesting in our exact results (namely, the existence of a reentrant cold unzipping transition, our main result, and the role of forbidding the mutual crossing of the two strands). In Sec. IV A we discuss the physical meaning of re-entrance in our (lattice) models, generalizing the proof of its occurrence to the more realistic case of SAW's. In Sec. IV B we also prove that a discrete chain in the continuum *space* undergoes cold unzipping, and then argue why such an effect was not observed in previous calculations [14–16], performed in the limit of a continuum *chain*. Eventually, we discuss some related models (with generic SAW's), and give some additional technical details in the Appendixes.

II. EXACT SOLUTION OF THE LATTICE MODELS

A. Introduction of the models and their behavior for thermal melting

We consider a simple class of models in a $D=(d+1)$-dimensional hypercubic lattice $\mathbf{Z^D}$. The two strands of a homogeneous DNA molecule with N base pairs are mimicked by two SAW's, directed along the $(1,\ldots,1)$ direction. The two chains have one end in common, while at the other end a force $\vec{g}$ is pulling in the $(1,-1,0,\ldots,0)$ direction. The walks gain a binding energy $-\epsilon$ ($\epsilon>0$) every time bases with the same monomer index (or same projection upon $(1,\ldots,1)$) interact, i.e., *wrong base pairing* is forbidden.

The canonical partition function for two N-step directed self avoiding walks (DSAW's) is

$$Z_N(\beta,\vec{g})=\sum_{\vec{x}\in\mathbf{Z^D}}p_N(\vec{x},\beta\epsilon)\exp(\beta\vec{g}\cdot\vec{x}),\qquad(1)$$

where $p_N(\vec{x},\beta\epsilon)$ is the canonical partition function of two directed interacting strands whose last base pairs are at relative distance $\vec{x}$. The following recursion relation holds for $p_N(\vec{x},\beta\epsilon)$:

$$p_{N+1}(\vec{x},\beta\epsilon)=\sum_{i,j=1}^{D}p_N(\vec{x}-\vec{e}_i+\vec{e}_j,\beta\epsilon)$$
$$\times\{1+[\exp(\beta\epsilon)-1]\delta_{\vec{x},\vec{0}}\},\qquad(2)$$

where $\vec{e}_i$, $i=1,\ldots,D$, are the canonical Euclidean versors of the D-dimensional space, and δ is the Kronecker delta.

These and similar equations have been intensively studied, at $\vec{g}=\vec{0}$, within simple models of DNA thermal melting [17,19], and, in $D=2$, within the context of random walk adsorption [20] and wetting problems [21]. Note that the choice of the $(1,\ldots,1)$ direction, along which the walks are directed, is crucial in allowing us to write local recursion relations. It is thus no surprise that the model belongs to the same universality class of random walks in $d=D-1$ dimensions [22].

It is well known (see Ref. [17] for a recent review), that, in the absence of a pulling force, within the model defined by

Eq. (2), dsDNA undergoes a phase transition between a low temperature double stranded phase and a high temperature denatured state only for $D>3$ ($d>2$): when $D=2$ and 3, dsDNA remains double stranded at all temperatures.

However, we note that in Eq. (2) the two strands are allowed to cross each other, without any restriction. This seems rather unphysical, since every real chain has a finite "hard core" distance. Thus one should also consider the case in which crossing between different strands is forbidden (recent studies of both homogeneous [23] and heterogeneous [24] DNA melting transition have indeed considered the $d=1$ case with forbidden crossing). Let us focus for the moment on the $D=2$ case, with no pulling force, where the effect of forbidding crossing is most dramatic. Here the direction $(1/\sqrt{2},1/\sqrt{2})$ can be identified as "time," and its normal $(1/\sqrt{2},-1/\sqrt{2})$ as "space" (x). The model with crossing (w.c.) implies no restriction on the relative distance x, whereas the one without crossing (w.o.c.) implies that x cannot change sign, e.g., $x\geq0$. The model w.o.c. is equivalent to surface adsorption models previously considered [20]. While the thermal melting of the two strands w.c. takes place at $T_c=\infty$, in the model w.o.c. $T_c=\epsilon/\log(4/3)$, as can be deduced from Ref. [20]. To elucidate this point further, we have tackled an intermediate model, where we do not forbid crossing but we make it disadvantageous, by assigning a cost $V>0$ each time the strands pass through one another. With calculations similar to those reported below, we find that melting takes place at the critical temperature (as a function of V):

$$T_c(V)=\epsilon\left[\log\left(\frac{4e^V}{3e^V+1}\right)\right]^{-1}.\qquad(3)$$

As expected, as $V\to\infty$, Eq. (3) yields $T_c\to\epsilon/\log(4/3)$, whereas $T_c\sim\epsilon/V$ as $V\to0$.

To implement the noncrossing constraint in the model in a generic dimension, we require that, if the DSAW's join, one coming from direction $\vec{e}_i$ and the other from direction $\vec{e}_j$ (with $i\neq j$), when they divide again, they cannot both proceed along their previous direction; i.e., we forbid that the first walk goes along direction $\vec{e}_i$ *and* the second one along $\vec{e}_j$. This excludes one configuration out of $D(D-1)$ at the splitting point (the remaining D possibilities would lead to a zipping of the two strands). As regards the $D=3$ thermal melting, again the model w.c. has $T_c=\infty$; however, if crossing is forbidden as described above, the critical temperature is $T_c=\epsilon/\log(9/8)$. This result was also found in a similar calculation by Rubin [25]. For $D>3$, models with and without crossing both undergo a denaturation transition at a finite, though different, critical temperature, so that the effect of forbidding crossing here is less important (the critical temperatures are the same at the leading order $1/D$ in the $D\to\infty$ expansion, as expected).

B. Behavior of the models at nonzero force

Let us now turn to models with a pulling force $\vec{g}$ in a generic dimension D, with $\vec{g}=(g,-g,0,\ldots,0)$. We can find

the asymptotic value of the canonical partition function [Eq. (1)] by locating [17,19,26] the singularity closest to the origin of its generating function:

$$Z(z,\beta\epsilon,\beta g) = \sum_{N=0}^{\infty} z^N \sum_{\vec{x}} p_N(\vec{x},\beta\epsilon) \exp(\beta\vec{g}\cdot\vec{x}), \quad (4)$$

which we will also refer to as the grand partition function. We stress that $p_N(\vec{x},\beta\epsilon)$ is a generic partition function: its detailed form will depend on whether or not we allow crossing.

To proceed, it is useful to partition the DNA molecule in ds helices (with the strands attached to each other) and *bubbles*, sequences in which the two chains share just the first and last base pairs; we also single out the contribution of the unzipped end of the two DSAW's, i.e., the part from the last contact to the end. In this way, the grand partition sum (4) can be expressed as

$$Z(z,\beta\epsilon,\beta g) = \frac{1}{1-Dz\exp(\beta\epsilon)} \frac{\exp(\beta\epsilon)}{1-\dfrac{\exp(\beta\epsilon)}{1-Dz\exp(\beta\epsilon)}B(z)}$$

$$\times S(z,\beta g), \quad (5)$$

where we have defined

$$B(z) = \sum_{N=2}^{\infty} z^N b_N,$$

$$S(z,\beta g) = 1 + \sum_{N=1}^{\infty} z^N \sum_{\vec{x}} [c_{N-1}(\vec{x}) - c_{N-1}(\vec{0})\delta_{\vec{x},\vec{0}}]$$

$$\times \exp(\beta\vec{g}\cdot\vec{x}). \quad (6)$$

In Eq. (6), b_N is the number of $2N$-step bubbles, and $c_N(\vec{x})$ the partition function of two N-step DSAW's never touching each other and having their last sites at a mutual distance $\vec{x}$ and their initial sites at a relative distance $\vec{e}_{i_0} - \vec{e}_{j_0}$ for some $i_0 \neq j_0$. By summing over all possibilities for initial conditions [see Eq. (8) below], $b_N = \sum_{i\neq j;i,j=1}^{D} c_{N-2}(\vec{e}_i - \vec{e}_j)$, so that we need to find an explicit expression for the c_N's. The equations they obey are

$$c_{N+1}(\vec{x}) = \sum_{i,j=1}^{D} c_N(\vec{x}-\vec{e}_i+\vec{e}_j) - c_N(\vec{0}) \sum_{i\neq j;i,j=1}^{D} \delta_{\vec{x},\vec{e}_i-\vec{e}_j}. \quad (7)$$

Note that, in Eq. (7), $\vec{0}$ acts as a sink or absorbing state, i.e., once the two walks join, they never leave. In this way, $c_N(\vec{x})$ with $\vec{x}\neq\vec{0}$ counts the number of pairs of walks that never touch each other (and with the last monomers at a relative distance $\vec{x}$), while $c_N(\vec{0})$ counts the number of remaining pairs of walks that at some point come into contact and then remain stuck together. This last quantity plays the role of an arbitrary constant and has to be subtracted from the final

counting as in Eq. (6) (see Ref. [25] for another example in which this prescription was used in a $D=3$ example).

In order to simplify the presentation, from now on we restrict our calculations on models w.o.c. (detailed calculations for this case and the outline of calculations for the simpler models w.c. are deferred to Appendix A). The initial conditions for such models are

$$c_0(\vec{x}) = \left(\sum_{i\neq j;i,j=1}^{D} \delta_{\vec{x},\vec{e}_i-\vec{e}_j}\right) - \delta_{\vec{x},\vec{e}_{i_0}-\vec{e}_{j_0}}, \quad (8)$$

where $\vec{e}_{i_0}$ and $\vec{e}_{j_0}$ are the directions forbidden as described in Sec. II A.

By performing a Fourier and a discrete Laplace transform on Eq. (7), and by using the relation between b_N and c_N given above, we can derive an explicit expression for the bubble generating function $B(z)$ [see Eq. (A6)]. The singularities of the second denominator of the grand partition function [Eq. (5)] are necessary to find the melting temperature. We find that the equations locating these two singularities are

$$z_1 = \frac{1}{D^2}, \quad (9)$$

$$\exp(-\beta\epsilon) - Dz_2 = B(z_2). \quad (10)$$

The first singularity z_1 leads to typical random walk behavior in the absence of any interaction. The second singularity $z_2(\beta\epsilon)$ is a function of the strength of the attractive interaction between the two strands, thus determining the behavior in the native zipped phase. At $g=0$, the critical temperature for thermal melting is obtained when the two singularities above coincide ($z_1=z_2$). Unlike the models w.c., which have $T_c=\infty$ in $D\leq3$, those w.o.c. have a finite critical temperature in any $D\geq2$ (see Appendix A for further details).

As regards the force-dependent third factor in Eq. (5), it reads

$$S(z,\beta g) = zS_{sing}(z,\beta g) + 1 - zc(z,\vec{0}). \quad (11)$$

A third new singularity, depending on the external force, and fundamental in our calculations arises when computing

$$S_{sing}(z,\beta g) \equiv \int_{[-\pi,\pi]^D} \frac{d^D\vec{q}}{(2\pi)^D} \tilde{c}(z,\vec{q}) \sum_{\vec{x}} \exp[(\beta\vec{g}-i\vec{q})\cdot\vec{x}], \quad (12)$$

where $\tilde{c}(z,\vec{q})$ and $c(z,\vec{0})$ are given in Eqs. (A4) and (A5). Note that in Eq. (12) one can immediately compute the integrals on $dq_3 \ldots dq_D$, by using the well known identity $2\pi\delta(q) = \sum_x \exp(-iqx)$, so that one is left with the double integral
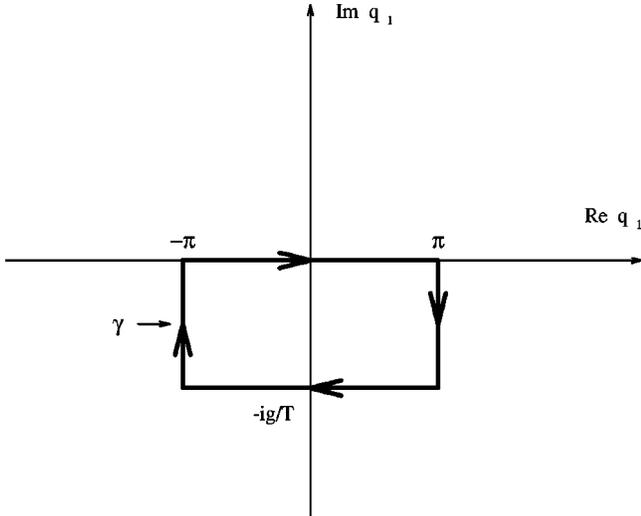
FIG. 1. Contour of integration γ in the complex plane used for the evaluation of the integrals in Eq. (14).

$$\int_{-\pi}^{\pi} \frac{dq_2}{(2\pi)} \int_{-\pi}^{\pi} \frac{dq_1}{(2\pi)} \tilde{c}(z, q_1, q_2, 0, \ldots, 0)$$

$$\times \sum_{x_1, x_2} \exp[(\beta g - i q_1) x_1 + (-\beta g - i q_2) x_2].$$

(13)

We now give details of the evaluation of the inner integral only, the outer one being equivalent. Defining $h(q_1, q_2) \equiv [\tilde{c}(z, q_1, q_2, 0, \ldots, 0)]^{-1}$, we aim at proving that the complex translation $q_1 \to q_1 - i\beta g$ can be performed in the integral

$$\int_{-\pi}^{\pi} \frac{dq_1}{2\pi} \frac{\exp(-i q_1 x_1)}{h(q_1, q_2)}.$$

Note that h is a periodic function of q_1. We extend q_1 to complex numbers, and consider the contour γ as shown in Fig. 1. By the residue theorem, one can write

$$\int_{-\pi}^{\pi} \frac{dq_1}{2\pi} \frac{\exp(-i q_1 x_1)}{h(q_1, q_2)} + \int_0^{-\beta g} \frac{i \, dy}{2\pi} \frac{\exp(-i \pi x_1 + x_1 y)}{h(\pi + iy, q_2)}$$

$$- \int_{-\pi}^{\pi} \frac{dq_1}{2\pi} \frac{\exp(-i q_1 x_1 - \beta g x_1)}{h(q_1 - i\beta g, q_2)}$$

$$+ \int_{-\beta g}^0 \frac{i \, dy}{2\pi} \frac{\exp(i \pi x_1 + x_1 y)}{h(-\pi + iy, q_2)} = \sum_{q_0} \text{Res}(\mathcal{H}, q_0), \quad (14)$$

where the sum runs over all poles q_0 of

$$\mathcal{H} \equiv \frac{\exp(-i q_1 x_1)}{h(q_1, q_2)}$$

(at fixed q_2) inside the contour γ, and $\text{Res}(\mathcal{H}, q_0)$ is the

residue of $\mathcal{H}$ at q_0. Note that due to the periodicity of h, the second and fourth terms in the previous equation cancel, and thus the complex translation can be performed provided that no pole of $\mathcal{H}$ can be found inside the contour γ. An equivalent conclusion can be reached for the outer integral on dq_2. The condition of having no poles inside the contours of integration is satisfied as long as $z < z_3(\beta g)$, where

$$z_3(\beta g) = \frac{1}{(D-2)^2 + 2 + 2\cosh(2\beta g) + 4(D-2)\cosh(\beta g)}$$

(15)

is found by solving $h(-i\beta g, i\beta g) \propto (1 - z f(-i\vec{\beta g})) = 0$, with $f(\vec{q})$ defined in Eq. (A2). In this case, we find consistently that $z_3(\beta g)$ is just the singularity in the resulting expression $S(z, \beta g) = 1 + z[\tilde{c}(z, -i\vec{\beta g}) - c(z, \vec{0})]$.

As z_3 is always smaller than z_1 (for $g \neq 0$), the singularity closest to the origin has to be determined between z_2, controlled by the attractive energy ϵ, and z_3, controlled by the pulling force g. If $z_2 < z_3$, the DNA molecule is zipped; otherwise it is unzipped. The free energy per monomer f and the average distance between the two ends (projected onto $\hat{g} \equiv [1, -1, 0, \ldots, 0]$), $\langle x_g \rangle$, are defined as

$$f \equiv \lim_{N \to \infty} -T \frac{\log\left[\sum_{\vec{x}} p_N(\vec{x}, \beta \epsilon) \exp(\beta \vec{g} \cdot \vec{x})\right]}{N}, \quad (16)$$

$$\langle x_g \rangle \equiv \lim_{N \to \infty} \langle \hat{g} \cdot \vec{x} \rangle = -\frac{\partial f}{\partial g} N. \quad (17)$$

These quantities read in the thermodynamic limit,

$$f = T \log z_2(\beta \epsilon), \quad \frac{\langle x_g \rangle}{N} = 0, \quad g < g_c(T, \epsilon), \quad (18)$$

$$f = T \log z_3(\beta g);$$

$$\frac{\langle x_g \rangle}{N} = z_3(\beta g)[4 \sinh(2\beta g) + 4(D-2)\sinh(\beta g)],$$

$$g > g_c(T, \epsilon), \quad (19)$$

where the critical force $g_c(T, \epsilon)$ is found by imposing $z_2(\beta \epsilon) = z_3(\beta g)$, as given in Eqs. (10) and (15). The above equations show the existence of a first order transition at $g = g_c(T, \epsilon)$, if $g_c(T, \epsilon) > 0$. The phase diagram for the models w.c. can be found exactly in the same way (see Appendix A for some details on this). It is interesting to note that the singularity $z_3(\beta g)$ does not depend on whether or not we allow crossing, whereas z_2 in the case w.c. is different from the case w.o.c. This is enough to make the whole phase diagram different for the two kinds of models, as will be discussed in Sec. III.

Here we stress that the main interest in using directed walks is that they are a subclass of SAW's in the same di-

mension. However, qualitatively similar results can also be obtained with simple random walks (RW's) [28], but in this case it would not be physically meaningful to forbid crossing as done above. Experimentally, however, it should not be hard to set up an experiment closely related to the calculation we have performed, by stretching the ds molecule in one given direction before applying the external force.

$$g_c(T,\epsilon) = \frac{T}{2} \cosh^{-1}\left[\frac{1}{2} \frac{1}{\sqrt{1-\exp(-\beta\epsilon)} - [1-\exp(-\beta\epsilon)]} - 1\right]. \tag{20}$$

The model exhibits a first-order "unzipping" transition if we move at a fixed value of $T < \epsilon/\log(4/3)$, as shown in Eq. (18). As shown in Fig. 2, $\lim_{T\to 0} g_c(T,\epsilon) = \epsilon/2$, and $g_c(T,\epsilon)$ attains its maximum at $T = T_M \simeq 0.9\epsilon$, where $g_c(T_M) \simeq 0.68\epsilon > \epsilon/2$. The transition is second order at $g=0$; as in Ref. [17], we find that, close to the melting point,

$$\langle n \rangle \equiv \frac{\partial}{\partial(\beta\epsilon)} \log Z_N \sim \tau^{-1} f(\tau N^{\phi_t}), \tag{21}$$

where $\langle n \rangle$ is the mean number of native contacts, with $\tau = (T-T_c)/T_c$, and $\phi_t = 1/2$ for the crossover exponent at thermal melting in the $D=2$ case. The scaling function $f(x)$ behaves as usual,

$$f(x) \to 0 \quad \text{as} \quad x \to +\infty,$$

$$f(x) \sim x \quad \text{for} \quad |x| \ll 1, \tag{22}$$

$$f(x) \sim -|x|^{1/\phi_t} \quad \text{for} \quad x \to -\infty,$$

such that $\langle n \rangle \sim N^{\phi_t}$ at the transition.
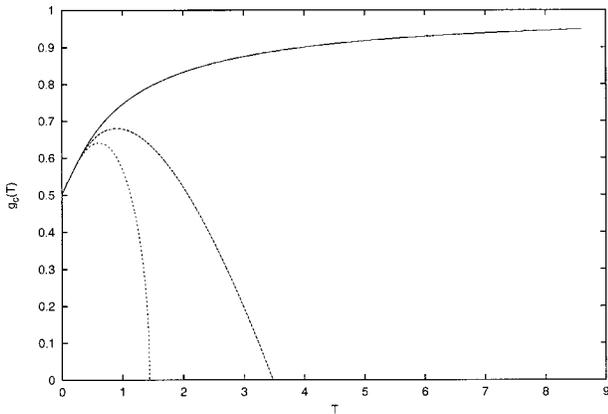
FIG. 2. Phase diagram for the two-dimensional models of DSAW's ($\epsilon = 1$ in the figure). The solid curve refers to the model with crossing, the long-dashed curve to the model without crossing, and the dashed curve to the model which considers only Y-shaped configurations.

III. SCALING LAWS FOR THERMAL MELTING AND UNZIPPING

Let us focus, for concreteness, on the result for the model in $D=2$ w.o.c., in order to analyze the scaling laws of the system. The phase diagram, as also found also in Ref. [19], explicitly reads (see Fig. 2)

The exact expressions for $\langle n \rangle$ and $\langle x_g \rangle$ can be found by inverse Laplace transforms of the quantities $Z(z,\beta g,\beta\epsilon)$, $[\partial/\partial(\beta\epsilon)]Z(z,\beta g,\beta\epsilon)$ and $[\partial/\partial(\beta g)]Z(z,\beta g,\beta\epsilon)$. However, if we only need scaling relations in the thermodynamic limit, we can use the discrete Tauberian theorem (see Ref. [27] and Appendix B), which relates the critical behavior of a series to the asymptotic behavior of its coefficients. By using this method, we find, in the vicinity of the unzipping mechanical transition,

$$\langle n \rangle \sim \frac{h_1[N^{\phi_1}(A_1\gamma + A_2\tau)]}{A_1\gamma + A_2\tau}, \tag{23}$$

$$\langle x_g \rangle \sim -\frac{h_2[-N^{\phi_2}(A_1\gamma + A_2\tau)]}{A_1\gamma + A_2\tau}, \tag{24}$$

where $A_1(T_c,g_c), A_2(T_c,g_c)$ are determined in such a way that $dg_c(T,\epsilon)/dT = -(A_2/A_1)(g_c/T_c)$, $\gamma = (g-g_c)/g_c$, $\tau = (T-T_c)/T_c$, and $\phi_1 = \phi_2 = 1$ for the two crossover exponents, consistently with the fact that the unzipping transition is first order [the explicit forms of $A_1(T_c,g_c)$ and $A_2(T_c,g_c)$ are worked out in Appendix B]. Note that $A_1 > 0$, whereas A_2 is negative in the re-entrant part of the transition curve. The scaling functions $h_{1,2}(x)$ behave in a similar way to $f(x)$, and thus we obtain that $\langle n \rangle \sim N^{\phi_1}$ and $\langle x_g \rangle \sim N^{\phi_2}$ are both extensive at the transition point. The physical interpretation is that a macroscopic portion of the chain is still in the double stranded state, but the rest of the chain is unzipped; these are just the two phases coexisting at the first order transition. This result will be used later to justify the use of Y-shaped configurations.

It is instructive to compare this phase diagram with that of the same $D=2$ case when we allow crossing. The transition line (plotted in Fig. 2), obtained from $z_2 = z_3$ (see Appendix A) is

$$g_c(T,\epsilon) = T \tanh^{-1}[1-\exp(-\beta\epsilon)]$$

$$= \frac{\epsilon}{2} + \frac{1}{2\beta}\log[2-\exp(-\beta\epsilon)]. \tag{25}$$

Both models behave similarly near $T=0$; they yield a transition to the *cold denatured* state described in Ref. [19].
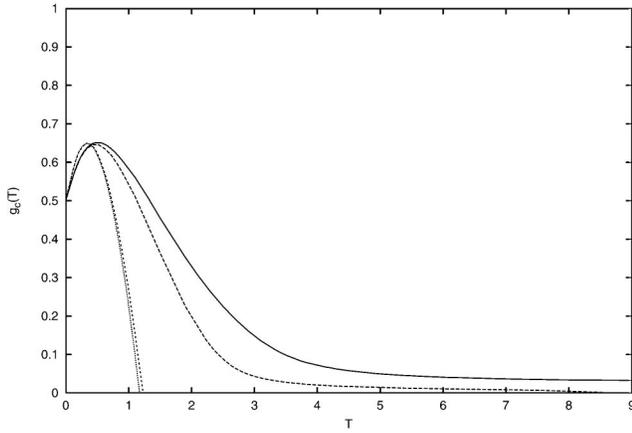
FIG. 3. Phase diagrams in $D=3$ and 4 dimensions for models with and without crossing ($\epsilon=1$ in the figure). It can be seen that the difference between the four-dimensional models is negligible. In $D=3$ (model without crossing), $T_c \simeq 8.49\epsilon$. Solid line: model $D=3$ with crossing. Long-dashed line: model $D=3$ without crossing. Dashed line: model $D=4$ with crossing. Dotted line: model $D=4$ without crossing.

When we move at a constant force g such that $g_c(0)<g$ $<\text{Max}_T[g_c(T,\epsilon)]$, at low enough temperatures, the molecule is unzipped, and it zips by increasing T. This feature of the phase diagrams seems paradoxical at first sight, since one would expect the critical force to decrease monotonically as the temperature is increased. The physical explanation of this result will be given below. In the model w.c., moreover, g_c always increases, approaching ϵ as $T\rightarrow\infty$, and the two strands remain zipped for every temperature when $g<\epsilon$. In the model w.o.c., instead, the two strands again unzip by further increasing the temperature. As regards scaling, on the other hand, the two models are identical, so that we can say

FIG. 4. (a) An example of a Y-shaped configuration for the DNA molecule: in this approximation bubbles are neglected. (b) A completely stretched configuration for directed walks, which is dominant for $T\rightarrow 0$.

that the effect of forbidding crossing is irrelevant in the renormalization group sense, but has a dramatic effect on the form of the critical line.

Let us now discuss the results that we have obtained in higher dimensions (the critical lines for three- and four-dimensional models are shown in Fig. 3). Common to all models is the cold unzipping transition found in the $D=2$ case. Moreover, the scaling laws at the unzipping transition do not depend on dimensionality in the crossover exponents. On the other hand, the thermal melting has dimensionality-dependent critical exponents (see Refs. [11,17]). Consequently, the behavior of the critical line $g_c(T,\epsilon)$ near the end point $T=T_c$ also depends on D. As $T\rightarrow T_c^-$ the result that we find in generic dimension is

$$\frac{g_c(T,\epsilon)}{T} \sim \begin{cases} \epsilon/T - \epsilon/T_c(D), & D=2,4 \\ \exp\left[-\dfrac{a}{[\epsilon/T - \epsilon/T_c(D)]}\right], & D=3 \\ [\epsilon/T - \epsilon/T_c(D)]^{1/2}\{\log[\epsilon/T - \epsilon/T_c(D)]\}^{-1/2}, & D=5 \\ [\epsilon/T - \epsilon/T_c(D)]^{1/2}, & D>5, \end{cases} \tag{26}$$

where a is a constant, and $T_c=\infty$ when $D=2$ and 3 for models w.c.

IV. PHYSICAL EXPLANATION OF REENTRANCE

A. Reentrance in lattice models

To obtain some physical insight into our analytical results, we compute the free energy of a Y-shaped molecule of DNA with a force pulling at the extremities (see Fig. 4). In this way, we neglect all the configurations with *bubbles*. Such an

approximation is valid at low T, and yields the exact result in the limit $T\rightarrow 0$. Since the configurations of the unzipped part are weighted by $\exp(\beta\vec{g}\cdot\vec{x})$, in this limit only the completely stretched configuration will contribute to the free energy for the unzipped part of the Y. In the limit of low temperature, the free energy is then

$$F(m,N) \sim -(N-m)(\epsilon + T\log\mu) - 2gm, \tag{27}$$

where m is the number of monomers in the unzipped part, N is the total number of bases, and μ is the connective constant

of a single walk. Note that Eq. (27) [with $\vec{g} = g(1,0, \ldots ,0)$] is also valid in the case of two self-avoiding walks, since the connective constant of SAW's constrained to avoid the fully stretched unzipped part, is the same as for ordinary SAW's [27,29] (for a more detailed discussion on SAW's we refer to Appendix C). By minimizing with respect to m, we find the critical force $g_c(T,\epsilon)$, such that Eq. (27) is minimum for $m=0$ when $g<g_c(T,\epsilon)$, and for $m=N$ when $g>g_c(T,\epsilon)$:

$$g_c(T,\epsilon) \overset{T\to 0}{\sim} \frac{1}{2}(\epsilon + T \log \mu). \qquad (28)$$

This is indeed what we have found in our calculations, and confirms that reentrance is a robust feature of lattice models, not depending on dimensionality or self-avoidance. In other words, Eq. (28) means that, at low T, it is more difficult to open a dsDNA helix as T is increased, because the energy gain obtained through the unzipping is more than compensated for by the entropy loss, since there is only one possible completely stretched configuration versus μ^{N-m} possibilities for the double stranded portion of the chain (we will see in Sec. IV B that the entropy loss in the continuum space exhibits a power law correction). For high enough T, on the other hand, other configurations will also contribute to the open portion, increasing its entropy, and the energy gain will eventually favor the unzipped state, except that in $D=2$ w.c., where the presence of bubble enhances the entropy of the native portion at any T, as explained below.

We have also calculated the phase diagram obtained by considering only the Y configuration: this amounts to putting the generating function for bubbles $B(z)=0$ in Eq. (5). As expected, the Y approximation gives the exact behavior [Eq. (28)] in the limit $T\to 0$, whereas it becomes more and more wrong as T is increased (see Fig. 2, where we plot the two-dimensional case explicitly given by $g_c(T,\epsilon) = (T/2)\cosh^{-1}[\exp(\beta\epsilon)-1]$. For the critical line near the melting point, this approximation yields $g_c(T,\epsilon) \sim (T_c - T)^{1/2}$ for all D, which from Eq. (26) is correct only for $D>5$ ($d>4$). This is because such an approach neglects bubbles, which are expected to be more and more relevant as d decreases (for $d>d_c=4$, once the two walks have split away, they basically never meet again) and T increases. In this view, it is clear that the puzzling behavior found in the $D=2$ model with crossing, where g_c increases for all T, is due to the growing presence of bubbles: before DNA can be unzipped, we have to disentangle all the bubbles that are forming, which is harder and harder as $T\to\infty$.

B. Reentrance in the continuum

We now prove that discrete chains in continuum space also undergo a cold denaturation for $T\to 0$. Let us consider two N-monomer chains in $\mathbf{R^d}$ with no constraint on the directedness, with a force $\vec{g}$ pulling at the extremities, and with a constant unitary distance between consecutive monomers. As $\beta\to\infty$, bubbles can be neglected and only Y-shaped configurations contribute to the partition sum. The partition function for a Y configuration then reads:

$$Z_N(\beta\epsilon,\beta g) = \sum_{m=0}^{N-1} Z_{N-m}^z(\beta\epsilon) Z_{2m}^u(\beta g), \qquad (29)$$

where $Z_{N-m}^z(\beta\epsilon) = \int_{\mathbf{R}^d} d^d\vec{x}_1 \ldots d^d\vec{x}_{N-m-1} \delta(|\vec{x}_1| -1) \ldots \delta(|\vec{x}_{N-m-1}|-1) \exp[(N-m)\beta\epsilon]$ is the partition function of the zipped portion of the strands, and $Z_{2m}^u(\beta g) = \int_{\mathbf{R}^d} d^d\vec{y}_1 \ldots d^d\vec{y}_{2m} \delta(|\vec{y}_1|-1) \ldots \delta(|\vec{y}_{2m}| -1) \exp(\beta\vec{g}\cdot\Sigma_{i=1}^{2m}\vec{y}_i)$ is that of the unzipped end. Chain discreteness is crucial in ensuring the validity of Eq. (29) for $\beta\to\infty$, since when one bubble has formed, the length of the stretched portion of the chain can be at most $\Sigma_{i=1}^{2m-1}\vec{y}_i = 2(m-1)(\vec{g}/|\vec{g}|)$. The integrals in Eq. (29) can be performed in any dimensions, and the evaluation of $Z_{2m}^u(\beta g)$ involves the modified Bessel function of the first kind of order $(d-2)/2$. In particular,

$$Z_{2m}^u(\beta g) \overset{\beta\to\infty}{\sim} (2\pi/\beta g)^{m(d-1)} \exp(2m\beta g),$$

and there is a power law correction with respect to the lattice result. We find that

$$Z_N(\beta\epsilon,\beta g) \overset{\beta\to\infty}{\sim} \sum_{m=0}^{N-1} \Omega_d^{N-m-1} \exp[(N-m)\epsilon] Z_{2m}^u(\beta g),$$

where Ω_d is the surface area of the unit sphere in d dimensions. From this, the critical force is easily found,

$$g_c(T,\epsilon) \overset{T\to 0}{\sim} \frac{\epsilon}{2} - \frac{d-1}{2} T \log\frac{T}{\epsilon} - \frac{T}{2}\log\left[2^{2d-3} \pi^{(d/2)-1} \Gamma\left(\frac{d}{2}\right)\right], \qquad (30)$$

where Γ is the Euler gamma function. The critical line $g_c(T,\epsilon)$ increases at low T, and re-entrance is also present in the continuum, even enhanced with respect to the lattice case. The leading term $T \log T$ in Eq. (30) [due to the power law correction in $Z_{2m}^u(\beta g)$] is indeed not present in the $d=1$ case, when one correctly recovers Eq. (28) for a lattice random walk with $\mu=2$.

We finally wish to discuss the relation of the present treatment with previous work [13–16] done on the unzipping of homo-DNA in the limit of a continuum chain. The ds molecule with the pulling force was described by means of an effective Hamiltonian, which, apart from an irrelevant center of mass term, reads

$$H = \int_0^N dn\left[\frac{Td}{b^2}\left(\frac{d\vec{r}}{dn}\right)^2 + V(\vec{r}(n)) - \vec{g}\cdot\frac{d\vec{r}}{dn}\right], \qquad (31)$$

where $\vec{r}$ is the relative separation between the strands, b is the effective Kuhn length of single-stranded DNA, and V is a realistic short range attractive potential, namely a δ function or a potential well [the two cases should be equivalent according to the standard quantum theory as long as $\int d\vec{r}V(\vec{r})$ is the same]. The system described by Eq. (31) is equivalently represented by a quantum system with a non-
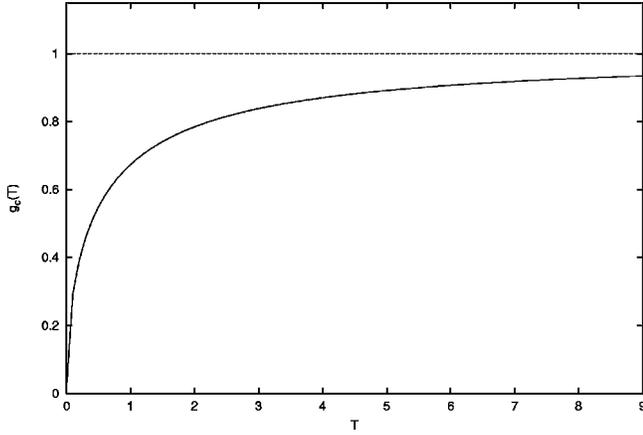
FIG. 5. Critical force in $d=1$, found with quantum mapping. The solid line is the result with a symmetric square well, the dashed line the result with a δ function. The parameters are chosen so that the integral of the potentials over space is the same.

Hermitian Hamiltonian. One finds [14,15] that there is a first order unzipping transition when the force reaches the critical value

$$g_c(T,\epsilon) = \sqrt{-\frac{4\epsilon_0(T)Td}{b^2}}, \quad (32)$$

where $\epsilon_0(T)$ is the ground state energy of the quantum Hamiltonian obtained from Eq. (31) when $\vec{g}=\vec{0}$. In the quantum-mechanical system, for $g<g_c(T,\epsilon)$ the ground state is a bound state, while for $g>g_c(T,\epsilon)$ the spectrum of Eq. (31) is continuous.

Let us focus on the $d=1$ case, corresponding to our two-dimensional models without crossing constraints. It is well known that, at $g=0$, both a symmetric square well and a δ function always have at least one bound state, meaning that DNA remains ds at all T. In Fig. 5 we show the critical force for the two potentials [obtained simply from Eq. (32)]. It can be seen from the figure that, at high T, both potentials saturate toward the same limit, as in our calculation for the model w.c. This is expected since the δ potential case can be recovered from our equation (2) in the limit of both continuum space and time (see Fig. 4). At low T, however, $g_c(T,\epsilon) \sim (T/\Delta)^{1/2}$ for a square well of width Δ, and is constant for the δ potential, so that re-entrance is present only in the former case, but with a behavior different from that found in the lattice. This already signals that the low temperature behavior of the solution obtained through the quantum mapping is rather unphysical. This is due to the fact that in the limit of a continuum chain the chain constraint is modeled in a "soft" way, by using a harmonic potential between consecutive beads along the chain. This interaction is usually assumed to be entropic [as in Eq. (31)], and thus effectively vanishes at $T=0$. In this limit Eq. (31) describes a set of N "free" particles moving in an effective potential determined by V and g. Consequently, the quantum mapping is expected to describe the system well except in the low-temperature limit. Indeed, the re-entrance found for the

square well potential is due to the unboundedness of the potential "felt" by the "free particles" as soon as $g \neq 0$. As $T \to 0$, fluctuations are not important, and the particles stay close to the minimum of such potential, which is $-\infty$ for a force that is small but finite. This is enough to unzip the strands [30].

As Zhou observed in Ref. [16], one can improve this model by placing a hard core either inside the potential well or at a finite distance from the δ (this is analogous in spirit to introducing the crossing constraint in our lattice models). Once again, one finds that for T near T_c, which is now finite, both potentials predict

$$g_c(T,\epsilon) \overset{T \to T_c}{\sim} (T_c - T)$$

as in the lattice model [see Eq. (26)], whereas for low T the δ shows no re-entrance and the potential well displays a $T^{1/2}$ behavior. We note, once again, that the low temperature behavior of such "quantum" models is an artifact, when considered as polymer chain models, due to the "soft" enforcing of the chain constraint. In this respect, discrete chain models in the continuum space are more realistic, either with constant bond length or with harmonic springs between consecutive beads. In the first case we have indeed proved [see Eq. (30)] the existence of cold mechanical denaturation. In the second case it was shown to occur by means of numerical simulations [19].

V. CONCLUSIONS

To conclude, we have studied simple models for DNA mechanical unzipping induced by a pulling force. By using analytical techniques, the relevance of forbidding the crossing of the two strands and the role played by bubble formation in the denaturation process were discussed throughout the whole force-temperature plane. The scaling properties of the system along the transition line were also determined. The existence of a *cold mechanical denaturation* for a finite range of forces at low enough temperatures was proved exactly in a general case for both lattice and continuum space models. The fundamental role of chain discreteness was emphasized in comparison with related models studied by means of quantum mapping techniques. Even if we neglected many important effects, such as base pairs heterogeneity, intrinsic helicity, wrong base pairing, and different stacking energy for the natured and denatured states, it would be interesting to experimentally test this prediction stemming from such a simple model. Furthermore, on the basis of preliminary results (analytical and numerical) we anticipate that even in the presence of *quenched* randomness in the contact potential our models display a re-entrant transition, so in this sense it is really a "universal" feature.

APPENDIX A: COMPUTATION OF $B(z)$ IN MODELS OF DSAW'S WITHOUT CROSSING AND OF THE PHASE DIAGRAM FOR MODELS WITH CROSSING

We here first work out the details to obtain an explicit expression for $B(z)$, defined in Eq. (6). Starting from Eqs. (7), we can perform Fourier and discrete Laplace transforms to obtain

$$\tilde{c}(z,\vec{q}) \equiv \sum_{N=0}^{\infty} z^N \sum_{\vec{x}} \exp(i\vec{q}\cdot\vec{x}) c_N(\vec{x})$$

$$= \frac{1}{1-zf(\vec{q})} [\tilde{c}_0(\vec{q}) - zf_0(\vec{q})c(z,\vec{0})], \quad (A1)$$

where we have made the following definitions:

$$f_0(\vec{q}) \equiv 2\sum_{i<j;i,j=1}^{D} \cos(q_i - q_j), \quad f(\vec{q}) \equiv D + f_0(\vec{q}), \quad (A2)$$

$$c(z,\vec{x}) \equiv \sum_{N=0}^{\infty} z^N c_N(\vec{x}), \quad \tilde{c}_0(\vec{q}) \equiv \sum_{\vec{x}} \exp(i\vec{q}\cdot\vec{x}) c_0(\vec{x}). \quad (A3)$$

Using $c(z,\vec{0}) = \int_{[-\pi,\pi]^D} [d^D\vec{q}/(2\pi)^D] \tilde{c}(z,\vec{q})$, Eq. (A1) is easily solved since, by permuting variables inside the resulting integrals, it is possible to see that they do not depend on the particular step which we forbid. We obtain

$$\tilde{c}(z,\vec{q}) = \frac{1}{1-zf(\vec{q})} \frac{\tilde{c}_0(\vec{q}) - zW_1(z)[A(D)f_0(\vec{q}) - \tilde{c}_0(\vec{q})]}{1 + zW_1(z)}, \quad (A4)$$

$$c(z,\vec{0}) = A(D) \frac{W_1(z)}{1 + zW_1(z)}, \quad (A5)$$

where $A(D) = 1 - [1/D(D-1)]$ is the reduction factor due to the crossing constraint. As a result, using $B(z) = z^2 \Sigma_{i\neq j;i,j=1}^{D} c(z,\vec{e}_i - \vec{e}_j)$, we obtain

$$B(z) = A(D) \frac{z^2 W_2(z)}{1 + z_2 W_1(z)}, \quad (A6)$$

where

$$W_1(z) = \int_{[-\pi,\pi]^D} \frac{d^D\vec{q}}{(2\pi)^D} \frac{f_0(\vec{q})}{1 - zf(\vec{q})},$$

$$W_2(z) = \int_{[-\pi,\pi]^D} \frac{d^D\vec{q}}{(2\pi)^D} \frac{f_0^2(\vec{q})}{1 - zf(\vec{q})}. \quad (A7)$$

The singularity $z_1 = 1/D^2$, leading to the usual random walk behavior, comes in when evaluating the above integrals; their denominator becomes negative as $\vec{q} \to 0$ for $z > z_1$.

Here we also give a brief outline of the calculation necessary to find the phase diagram for the models of Sec. II of

DSAW's when crossing is allowed. These models are simpler to solve than the corresponding models w.o.c., since it is not necessary to partition the molecule of DNA as done in the text in Eq. (5), which allows us to write a more explicit formula for the grand partition function. Indeed we can simply start from recursion relations (2), and, after Fourier and Laplace transform, find the expression

$$\tilde{p}(z,\vec{q},\beta\epsilon) = \frac{1}{1-zf(\vec{q})} \frac{1}{1-[1-\exp(-\beta\epsilon)]W_0(z)}, \quad (A8)$$

for the quantity $\tilde{p}(z,\vec{q},\beta\epsilon)$, defined as

$$\tilde{p}(z,\vec{q},\beta\epsilon) = \sum_{N=0}^{\infty} z^N \sum_{\vec{x}} \exp(i\vec{q}\cdot\vec{x}) p_N(\vec{x},\beta\epsilon) \quad (A9)$$

with $p_N(\vec{x},\beta\epsilon)$ defined as in Eq. (1) and

$$W_0 = \int_{[-\pi,\pi]^D} \frac{d^D\vec{q}}{(2\pi)^D} \frac{1}{1-zf(\vec{q})}. \quad (A10)$$

The final form of the grand partition function, for DSAW's w.c. in the presence of a pulling force, is

$$Z(z,\beta\epsilon,\beta g) = \frac{1}{1-z/z_3(\beta g)} \frac{1}{1-[1-\exp(-\beta\epsilon)]W_0(z)}, \quad (A11)$$

with $z_3(\beta g)$ defined as in Eq. (15). Alternatively, one can proceed exactly as in Sec. II, but with initial conditions

$$c_0(\vec{x}) = \sum_{i\neq j;i,j=1}^{D} \delta_{\vec{x},\vec{e}_i - \vec{e}_j}. \quad (A12)$$

The only resulting difference would be to have $A(D) = 1$ in Eqs. (A4) and (A6); after a bit of algebra, one can convince oneself that the partition function found by recollecting the different factors in Eq. (5) is the same as that found in Eq. (A11). In doing this, one needs to compute the relations between the integrals $W_0(z)$, $W_1(z)$, and $W_2(z)$, which may be done as, e.g., in Ref. [25]. For example, the bubble generating function for both kind of models could also be simply expressed as

$$B(z) = A(D)[1 - Dz - 1/W_0(z)]. \quad (A13)$$

Changing the dimension dependent factor $A(D)$ from $A(D) = 1$, when crossing is allowed, to $A(D) = 1 - [1/D(D-1)]$, when crossing is forbidden, is enough for the melting transition temperature to become finite for $D \leq 3$.

APPENDIX B: TAUBERIAN THEOREM AND ITS APPLICATIONS

The discrete Tauberian theorem (see Ref. [27]) states that the relations

$$c(z) \equiv \sum_{N=0}^{\infty} c_N z^N \overset{z \to z^{*-}}{\sim} \left(\frac{1}{1 - z/z^*} \right)^{\rho} L\left(\frac{1}{1 - z/z^*} \right) \quad \text{(B1)}$$

and

$$c_N \overset{N \to \infty}{\sim} \frac{N^{\rho - 1}}{(z^*)^N \Gamma(\rho)} L(N) \quad \text{(B2)}$$

are equivalent, provided that $\rho > 0$, $\{c_N\}$ is a positive monotonic sequence, and L is "slowly varying" in the sense specified in Ref. [27].

We apply this theorem here first to find the scaling laws of the unzipping transition to give an example of how the relations reported in Sec. III can be recovered. When approaching the critical line at $g = g_c$ from the unzipped phase, the smallest singularity is $z_3(\beta g)$, as defined in Eq. (15). The leading behavior, as $z \to z_3^-$, is

$$Z(z, \beta \epsilon, \beta g) \overset{z \to z_3^-}{\sim} \frac{1}{\exp(-\beta \epsilon) - D z_3 - B(z_3)} \frac{1}{1 - z/z_3}, \quad \text{(B3)}$$

$$\frac{\partial Z(z, \beta \epsilon, \beta g)}{\partial (\beta g)} \overset{z \to z_3^-}{\sim} - \frac{1}{\exp(-\beta \epsilon) - D z_3 - B(z_3)} \frac{1}{(1 - z/z_3)^2}$$
$$\times \frac{\partial z_3 / \partial (\beta g)}{z_3(\beta g)}, \quad \text{(B4)}$$

$$\frac{\partial Z(z, \beta \epsilon, \beta g)}{\partial (\beta \epsilon)} \overset{z \to z_3^-}{\sim} \frac{\exp(-\beta \epsilon)}{[\exp(-\beta \epsilon) - D z_3 - B(z_3)]^2} \frac{1}{1 - z/z_3}, \quad \text{(B5)}$$

where we have neglected inessential factors when $g \sim g_c$. Consequently, the application of the Tauberian theorem yields

$$Z_N(\beta \epsilon, \beta g) \overset{N \to \infty}{\sim} \frac{1}{\exp(-\beta \epsilon) - D z_3 - B(z_3)} z_3^{-N}, \quad \text{(B6)}$$

$$\frac{\partial Z_N(\beta \epsilon, \beta g)}{\partial (\beta g)} \overset{N \to \infty}{\sim} - \frac{N}{\exp(-\beta \epsilon) - D z_3 - B(z_3)}$$
$$\times z_3^{-N} \frac{\partial z_3 / \partial (\beta g)}{z_3(\beta g)}, \quad \text{(B7)}$$

$$\frac{\partial Z_N(\beta \epsilon, \beta g)}{\partial (\beta \epsilon)} \overset{N \to \infty}{\sim} \frac{\exp(-\beta \epsilon)}{[\exp(-\beta \epsilon) - D z_3 - B(z_3)]^2} z_3^{-N}. \quad \text{(B8)}$$

The canonical partition function Z_N can be expressed in terms of previously defined quantities as $Z_N(\beta \epsilon, \beta g) = \sum_{\vec{x}} p_N(\vec{x}, \beta \epsilon) \exp(\beta \vec{g} \cdot \vec{x})$ [see Eqs. (1) and (4)].

Note that at the critical line $z_2(\beta \epsilon) = z_3(\beta g_c)$, implying that the ϵ-dependent denominator in the above equations

vanishes, as the critical line is approached [that is, $\gamma \equiv (g - g_c)/g_c \ll 1$ and $\tau \equiv (T - T_c)/T_c \ll 1$]. In this limit the order parameters obey

$$\langle n \rangle \equiv \frac{\partial Z_N / \partial (\beta \epsilon)}{Z_N} \overset{N \to \infty}{\sim} \frac{\exp(-\beta \epsilon)}{A_1 \gamma + A_2 \tau}, \quad \text{(B9)}$$

$$\langle x_g \rangle \equiv - \frac{\partial Z_N / \partial (\beta g)}{Z_N} \overset{N \to \infty}{\sim} \frac{\partial z_3 / \partial (\beta g)}{z_3(\beta g_c)} N. \quad \text{(B10)}$$

The coefficients $A_1(T_c, g_c)$ and $A_2(T_c, g_c)$ determine the normal direction in the $[\log(T), \log(g)]$ plane, and are reported below:

$$A_1(T_c, g_c) = \beta_c g_c \left(D + \frac{\partial B(z_3(\beta_c g_c))}{\partial z_3} \right) z_3^2(\beta_c g_c)$$
$$\times [4 \sinh(2 \beta_c g_c) + 4(D - 2) \sinh(\beta_c g_c)], \quad \text{(B11)}$$

$$A_2(T_c, g_c) = - \beta_c g_c \left(D + \frac{\partial B(z_3(\beta_c g_c))}{\partial z_3} \right) z_3^2(\beta_c g_c)$$
$$\times [4 \sinh(2 \beta_c g_c) + 4(D - 2) \sinh(\beta_c g_c)]$$
$$+ \beta_c \epsilon \exp(-\beta_c \epsilon). \quad \text{(B12)}$$

As expected, it may be easily checked that, whatever direction we choose to approach the critical curve, physical quantities such as Eq. (B9) only depend on the projection of this direction on the normal to the critical line. To show this, one first needs to observe that criticality is achieved through the vanishing of the denominator in Eq. (B9), and then to apply the implicit function theorem to this denominator.

Recently, some authors [13,14] suggested, as an alternative order parameter for the unzipping transition, the number m of monomers from the last contact to the end. By using the same tools as before, we can find some quantities of interest such as the probability distribution of having m monomers "liberated" (in the equations below, we suppose $1 \ll m \ll N$). In general,

$$P(m) = \frac{\sum_W \delta_{n_{u.z.}, m} p_W}{\sum_W p_W}, \quad \text{(B13)}$$

where W are pairs of directed walks, p_W is their Boltzmann weight, and $n_{u.z.}$ is the number of "liberated" monomers of the configuration. The possible enforcing of the crossing constraint does not affect the following equations, simply shifting the critical melting temperature T_c.

At zero force and $T < T_c$, in the native state,

$$P(m) \propto \exp[-m \log(z_1/z_2)] m^{\alpha(d)}, \quad \text{(B14)}$$

where $m^{\alpha(d)} = m^{-1/2}$ in $d = 1$, $[\log(m)]^{-1}$ in $d = 2$, and constant for $d > 2$. We recall that $z_1 = 1/D^2$, with $D = d + 1$. At criticality,

$$P(m) \propto (N-m)^{\phi_t - 1} m^{\alpha(d)}, \qquad (B15)$$

where in the first factor there are logarithmic corrections in $d=2$ and 4 to the power-law behavior controlled by the crossover thermal exponent ϕ_t [17]. Above T_c, we have

$$P(m) \propto (N-m)^{\beta(d)} m^{\alpha(d)}, \qquad (B16)$$

with $\beta(d) = -|1-d/2| - 1$ if $d \neq 2$, in $d=2$ $m^{\beta(d)} = 1/[N \log^2(N)]$. At force different from zero, in the zipped phase, we obtain

$$P(m) \propto \exp[-m \log(z_3/z_2)], \qquad (B17)$$

while, in the unzipped phase,

$$P(m) \propto \exp[-(N-m)\log(z_2/z_3)] \qquad (B18)$$

if $T < T_c$, and

$$P(m) \propto \exp[-(N-m)\log(z_1/z_3)] \qquad (B19)$$

if $T > T_c$. Just at criticality, the probability distribution is flat.

For the Y-shaped configuration, at force different from zero, we obtain

$$P(m) \propto \exp[-(N-m)\log(z_y/z_3)] \quad \text{in the u.z. phase,} \qquad (B20)$$

$$P(m) \propto \exp[-m \log(z_3/z_y)] \quad \text{in the z. phase,} \qquad (B21)$$

$$P(m) \propto \text{const} \quad \text{at criticality,} \qquad (B22)$$

where $z_y = \exp(-\beta\epsilon)/\mu$ is the singularity controlling the free energy per monomer in the Y-zipped phase, and $\mu = D$ the connective constant of a single directed walk. At zero force, we obtain

$$P(m) \propto \exp[(-(N-m)\log(z_y/z_1)] m^{\alpha(d)} \quad \text{denatured phase,} \qquad (B23)$$

$$P(m) \propto \exp[-m, \log(z_1/z_y)] m^{\alpha(d)} \quad \text{native phase,} \qquad (B24)$$

$$P(m) \propto m^{\alpha(d)} \quad \text{at criticality.} \qquad (B25)$$

Let us give the details in a simple case, to obtain, e.g., Eqs. (B20), (B21) and (B22). One has

$$P(m) = \frac{Z_{N-m}^{PS} Z_m^{free}}{Z_N}, \qquad (B26)$$

where Z_{N-m}^{PS} is the partition function of two $(N-m)$ monomer chains with the end points in common (this is the original Poland-Sheraga model), Z_m^{free} is the partition of two m-monomer chains with no base pair in contact, and Z_N is given by Eq. (1). We have, for Y at nonzero force, $Z_{N-m}^{PS} = z_y^{-(N-m)}$, $Z_m^{free} \sim z_3^{-m}$, and

$$Z_N \sim z_y^{-N} \quad \text{native phase,} \qquad (B27)$$

$$Z_N \sim z_3^{-N} \quad \text{above criticality.} \qquad (B28)$$

APPENDIX C: Y CONFIGURATIONS WITH SAW'S

In this appendix we extend the analysis of Sec. IV to a Y configuration where the two chains are generic SAW's and not directed walks. Here we take $\vec{g} = g(1,0,\dots,0)$.

Let us call $c_N(\vec{0},\vec{x})$ the number of N-step SAW's ending in $\vec{x}$ and starting in $\vec{0}$, and $c_{N,\vec{g}} = \sum_{\vec{x}} c_N(\vec{0},\vec{x})\exp(\beta\vec{g}\cdot\vec{x})$ (so that $c_N \equiv c_{N,\vec{g}=\vec{0}}$). As a first step, we need to prove the existence of a connective constant $\mu_{\vec{g}}$ for a single SAW in the presence of a pulling force, i.e., $c_{N,\vec{g}} \sim \mu_{\vec{g}}^N$ for large N. The existence of a connective constant then follows [27] from the inequality

$$\sum_{\vec{x}} c_N(\vec{0},\vec{x})\exp(\beta\vec{g}\cdot\vec{x}) \leq \sum_{\vec{x},\vec{x}_1} c_{N_1}(\vec{0},\vec{x}_1)c_{N-N_1}(\vec{x}_1,\vec{x})$$
$$\times \exp(\beta\vec{g}\cdot\vec{x}_1)\exp[\beta\vec{g}\cdot(\vec{x}-\vec{x}_1)], \qquad (C1)$$

which implies the subadditivity of c_N [27]. From the connective constants of RW's and DSAW's, we can establish the following bounds [recall that here $\vec{g} = g(1,0,\dots,0)$] for the connective constant of a SAW in d dimensions:

$$d-1+\exp(\beta|\vec{g}|) \leq \mu_{\vec{g}} \leq 2(d-1)+2\cosh(\beta|\vec{g}|). \qquad (C2)$$

Let us now introduce the canonical partition function. It reads

$$Z_N = \sum_{m=0}^{N-1} \exp(\beta(N-m)\epsilon)c_{N-m-1}\sum_{\vec{x}_1,\vec{x}_2} c'_{2m}(\vec{x}_1,\vec{x}_2)$$
$$\times \exp[\beta\vec{g}\cdot(\vec{x}_2-\vec{x}_1)], \qquad (C3)$$

where $c'_{2m}(\vec{x}_1,\vec{x}_2)$ counts the SAW's which do not cross the first $N-m$ attached monomers of the Y, and $\vec{x}_1$ and $\vec{x}_2$ are the end points of the strands.

An upper bound is found if we allow the opened part of the Y to cross the first $N-m$ zipped monomers:

$$Z_N^{upper} = \sum_{m=0}^{N-1} \exp(\beta(N-m)\epsilon)c_{N-m-1}\sum_{\vec{x}_1,\vec{x}_2} c_{2m}(\vec{x}_1,\vec{x}_2)$$
$$\times \exp[\beta\vec{g}\cdot(\vec{x}_2-\vec{x}_1)]. \qquad (C4)$$

The grand canonical partition function defined from Eq. (C4) displays singularities in $z \equiv z_1 = 1/\mu_{\vec{g}}^2$ and in $z \equiv z_2 = 1/\mu \exp(\beta\epsilon)$, where μ is the connective constant of a standard SAW in d-dimensional space, i.e., $\mu = \mu_{\vec{g}=\vec{0}}$.

To find a lower bound for Z_N, we restrict the Y configurations to those with the joined part of the Y constrained to lay in the half-space $\{\vec{x}|\vec{x}\cdot\vec{e}_1 > 0, \vec{e}_1\cdot\vec{g}/|\vec{g}| = 0\}$ (the origin is in the bifurcation point), and the unzipped part forced to stay in the other half-space,

$$Z_N^{lower} = \sum_{m=0}^{N-1} \exp(\beta(N-m)\epsilon) c_{N-m-1}^{left} \sum_{\vec{x}_1, \vec{x}_2} c_{2m}^{right}(\vec{x}_1, \vec{x}_2)$$

$$\times \exp[\beta \vec{g} \cdot (\vec{x}_2 - \vec{x}_1)], \tag{C5}$$

where with $c_n^{left(right)}$ we have indicated the number of n-step SAW's constrained to stay in the left(right) half space. As the connective constants can be rigorously proved to be the same even for walks constrained in such a way (see Refs. [27,29] for details, it is important here that walks generated from a reflection through the hyperplane $\{\vec{x} | \vec{x} \cdot \vec{e}_1 > 0, \vec{e}_1 \cdot \vec{g}/|\vec{g}| = 0\}$ leave the scalar product $\vec{g} \cdot \vec{x}$ unchanged), the singularities of the grand partition function obtained from Eq. (C5) are the *same* as those of $\Sigma_{N=0}^{\infty} Z_N^{upper} z^N$. Thus the

grand partition function singularities associated to Z_N in Eq. (C3) are $z = z_1, z_2$ given above.

In summary, we have proved that a mechanical unzipping transition takes place when $\mu_{\vec{g}}^2 = \mu \exp(\beta\epsilon)$, similarly to the directed walk case. We suggest that a standard computation of $\mu_{\vec{g}}$ (for instance, through exact enumeration) could give an accurate phase diagram for the "Y approximation" with SAW's.

The bounds in Eq. (C2) immediately give two bounds within which the transition line $g_c(T, \epsilon)$ lies. In the $T \to 0$ limit, Eq. (28) follows, since both bounds give the same asymptotic transition line. This should be the same also for generic SAW's, since in the $T \to 0$ limit it is sufficient to consider only Y-shaped configurations. This demonstrates the existence of cold unzipping at sufficiently low temperature for the generic self-avoiding case.

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$$\frac{1}{2[d-1+\cosh(\beta g)]}.$$

The value of z_2 can be found as in Ref. [17].

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