Kinetics of the helix-coil transition

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Abstract – Based on the Zimm-Bragg model we study cooperative helix-coil transition driven by a finite-speed change of temperature. There is an asymmetry between the coil $\rightarrow$ helix and helix $\rightarrow$ coil transition: the latter is displayed already for finite speeds, and takes shorter time than the former. This hysteresis effect has been observed experimentally, and it is explained here via quantifying system’s stability in the vicinity of the critical temperature. A finite-speed cooling induces a non-equilibrium helical phase with the correlation length larger than in equilibrium. In this phase the characteristic length of the coiled domain and the non-equilibrium specific heat can display an anomalous response to temperature changes. Several pertinent experimental results on the kinetics of helical biopolymers are discussed in detail.

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Biopolymers carry information which is embedded not only in the linear sequence of the monomers, but also in the conformational structures \([1]\). These structures are determined by the sequence, but they also adjust to environmental conditions. A pertinent example is the helix-coil transition (HCT), which denotes the disruption of the ordered conformation —e.g., the $\alpha$-helix of proteins or the triple-helix of collagen— to form a disordered coil \([1]\). This order-disorder transition occurs when the temperature is raised or a chemical denaturant is added.

The importance of helices in biopolymers motivated many studies on thermodynamic and kinetic aspects of HCT \([1–8]\). The basic model in this field was proposed by Zimm and Bragg (ZB) and successfully applied for describing the HCT both in \([1–5]\) and out \([6–12]\) of equilibrium. The virtue of the model is the simplicity of its ingredients: cooperativity and the free-energy preference to form a helix. Many studies devoted to the kinetics of the HCT concentrate on the relaxation from a non-equilibrium state, which is prepared experimentally via, \textit{e.g.}, laser-induced temperature jump \([8]\). This setup is adequate for small globular proteins whose relaxation time is short. The situation is different for HCT in collagen \([13–16]\), which has very long relaxation times to equilibrium (hours and days), so that the HCT has to be probed by necessarily finite-rate temperature changes, and the very description of the HCT has to be essentially kinetic \([16]\) (the equilibrium HCT still exists at unrealistically long times \([15]\)). Kinetic effects are also encountered in HCT for DNA \([17,18]\) and for crystals of globular proteins, where each site of the crystal contains one protein \([19]\). This ordered protein ensemble amplifies memory and hysteresis effects and allows their clear experimental identification \([19]\).

These experimental setups call for a unifying theoretical approach. Here we study the helix-coil kinetics of ZB model driven by finite-speed temperature changes. We reproduce and explain several basic experimental findings, and also predict new effects. Conceptually, there is an even deeper interest in the kinetics of the basic ZB model, since the stability of many proteins does have both kinetic and thermodynamic aspects \([20]\).

In the ZB model one assigns the spin variable $s_i = 1$ \((s_i = -1)\) for the $i$-th helix (coiled) region of the polymer, and assumes the following free energy for the spins \([1,2]\):

$$F[s] = -J \sum_{i=1}^{N-1} s_is_{i+1} - h(T) \sum_{i=1}^{N} s_i,$$  \hspace{1cm} (1)

where $s \equiv (s_1, \ldots, s_N)$, $N$ is the total number of regions, and $J > 0$ stands for the cooperative interaction\(^{1}\).

\(^{1}\)Note that the ZB model has several different appearances. All of them are equivalent to (1) for a long chain.
The mechanisms of cooperativity for the main biopolymers (α-helices, DNA, collagen, etc.) are reviewed in [1,2,14]. The term $h(T)$ in (1) is the free-energy difference of fast atomic variables in region $i$, calculated for a fixed value of the slow spin $s_i$ [21]. We thus assume time scale separation [7,8]: the joint probability $P(s,a)$ of fast (a) and slow (s) variables factorizes as $P(s|P_{eq}(a|s))$, where the conditional probability $P_{eq}(a|s)$ is always (also for kinetic processes) at equilibrium with the bath temperature $T$ [21]. The dynamics of the spins is then governed by the free energy (1), where $h(T)$ favors helix (coil) formation at low (high) $T$: $h(T_c) = 0$ at the equilibrium HCT temperature $T_c$, while $h(T) > 0$ ($h(T) < 0$) for $T < T_c$ ($T > T_c$). Experiments and ab initio calculations are consistent with a linear change of $h(T)$ in the vicinity of $T_c$ ($\alpha > 0$ is a constant and $k_B = 1$) [1–4]:

$$h(T) = \alpha(T_c - T).$$

The interaction strength in the model is characterized by $\sigma = e^{-4J/T}$ [2]. In the highly cooperative regime $\sigma \ll 1$ the equilibrium helix-coil transition resembles a real phase transition, which combines the features of first-order (jumping order parameter) and the second-order (large correlation length) phase transitions [1,2,22].

The ZB model was originally proposed for describing the α-helix–coil transition in polypeptides and proteins [1,2]. Later on the equilibrium ZB model was successfully applied to the duplex-coil transition in DNA [22] and to some aspects of the triplex-coil transition in collagen [14]. In the latter two cases the ZB model is regarded as a skeletal model producing important qualitative conclusions. The purpose of this letter is to understand the basic physics of hysteresis and memory effects during the helix-coil transition in terms of the ZB model.

Now the system described by (1) interacts with a bath at temperature $T$. We assume that the elementary bath-driven process amounts to local disruption (or creation) of a single helix: $s_j \rightarrow -s_j$ (spin-flipping), and that the dynamics is given by the following master equation [23]:

$$\hat{P}(s,t) = \sum_{j=1}^{N} [P(s_j,t)w(s|s_j) - P(s,t)w(s_j|s)],$$

where $s_j = (s_1,\ldots,s_{j-1},-s_j,s_{j+1},\ldots,s_N)$, $P(s,t)$ is the time-dependent probability of $s = (s_1,\ldots,s_N)$, $\hat{P} = \partial_t P$, and where the first (second) term in the RHS of (3) describes the in-flow (out-flow) of probability to the configuration $s$ due to spin-flipping. $w(s|s_j)$ is the transition rate $s_j \rightarrow s$ which is standardly taken in the Glauber form [23]: $w(s|s_j) = \frac{1}{2}[1 - s_j \tanh(\beta h_j)]$, where $\Gamma$ is the relaxation frequency, $\beta = 1/T$ and $\mu_1 \equiv h + J(s_{j-1} + s_{j+1})$ is the local field acting on $s_j$; see (1). Thus, the spin-flip is probable if it decreases $F$. This ensures relaxation to the equilibrium $P_{eq}(s) \propto e^{-\beta F(s)}$ for a constant $T$ [23].

Note that the spin-flipping can occur anywhere in the chain. Thus, the studied kinetics of the ZB model differs from the zipper kinetics [10–12,17], where the disruption of the helix can occur only at the end-points of the chain. The zipper kinetics is expected to be valid for relatively short chains, undergoing relaxation from the completely helical to the completely coiled chains [10]. Here we consider long chains.

Let us introduce the following averaged quantities:

$$m(t) \equiv \langle s_i \rangle_t, \quad \epsilon(t) \equiv \langle s_i s_{i+1} \rangle_t, \quad \epsilon_2(t) \equiv \langle s_i s_{i+2} \rangle_t,$$

where $\langle \ldots \rangle_t$ is the average over $P(s,t)$, while $\frac{1}{2}\sum_i \epsilon_i$ is the fraction of helical regions. For $N \gg 1$ (long chain) the boundary effects are neglected, all spins are equivalent, and (3), (4) imply

$$\Gamma^{-1} \dot{m} = -(1 - a_1)m + \frac{a_0}{2} + \frac{a_2}{2} \epsilon_2,$$

$$\Gamma^{-1} \dot{\epsilon} = -2\epsilon + a_1 + (a_0 + a_2)m + a_1 \epsilon_2,$$

$$a_1 = \kappa_+ - \kappa_-, \quad a_0,2 = \pm \tanh(\beta h) + \kappa_+ + \kappa_-, \quad \text{(7)}$$

where $\kappa_{\pm} = \frac{1}{2} \tanh(\beta h \pm 2\beta J)$. Equations (5), (6) are first two equations of the infinite hierarchy of moment equations. For $h = 0$ this hierarchy is exactly solvable [23]. For $h \neq 0$, there is no exact solution, and one has to rely on approximations [6,7].

The spin-temperature anzatz amounts to assuming that the probability $P(s,t)$ has a locally Gibbsonian form with two time-dependent parameters $\beta_1$ and $\beta_2$ [24,25]:

$$P(s,t) \propto \exp \left[ \beta_1(t) \sum_i s_i s_{i+1} + \beta_2(t) \sum_i s_i \right].$$

This amounts to expressing the term $\epsilon_2$ in (5), (6) via $\epsilon$ and $m$ by means of equilibrium formulas [25]

$$\epsilon_k = m^2 + (1 - m^2)^{1-k}(\epsilon - m^2)^k, \quad k = 2,3,\ldots$$

Thus we assume that the higher-order moments $\epsilon_k > 2$ relax to the local equilibrium (9), before $m(t)$ and $\epsilon(t)$ relax to equilibrium [9,24,25]. Equations (5), (6) with $\epsilon_2$ given by (9) are now a closed pair of equations that reproduces exactly the equilibrium limit. Equations (5)–(7), (9) are consistent with the above-mentioned exact solution for $h = 0$, since they correctly predict the diverging relaxation time for $\beta J \gg 1$, as well as the transition from the exponential to a power law decay [25]. The reliability of the spin-temperature anzatz is confirmed by its applications in NMR/ESR physics [24,25]. For the derivations of (8) via the projection-operator method see [26].

The equilibrium $m$ is obtained from putting to zero the LHS of (5), (6) with $\epsilon_2$ given by (9): $m_{eq} = \sinh(\beta h_i)[\sinh^2(\beta h) + e^{-4\beta J}]^{-1/2}$. In the cooperative regime $\sigma = e^{-4\beta J} \ll 1$, $m_{eq}$ shows a sharp transition from $m_{eq} = -1$ (coil) to $m_{eq} = 1$ (helix) [1]; see fig. 1.

Note that for $h = 0$ (right at $T = T_c$) (5), (7) predict that the relaxation time of $m(t)$ is $\frac{1}{\Gamma(1 - a_1)} = \frac{1 + \sigma}{2\Gamma}$. This agrees with the known result [6] and shows that
of each normal curve refers to cooling from $v_t$ and then holding $T$; $v_t$ changes to heating at $v_t$. The equilibrium $T_c$ is crossed for $v_t = 0.2$ and $t = 0.6$. Thick curve: equilibrium $m_{eq}$, which changes between $m_{eq} = -1$ (coil) and $m_{eq} = 1$ (helix). Thick dashed curve: $v_t/T = 2 \times 10^{-6}$. Normal curves (from bottom to top): $v_t/T = 5 \times 10^{-5}, 2 \times 10^{-5}, 10^{-5}$. The dashed counterpart of each normal curve refers to cooling from $v_t = 0$ till $v_t = 0.4$, and then holding $T$ constant.

The relaxation time is larger for more cooperative transitions and for lower temperatures. These aspects were numerically confirmed in simulations [12].

Now assume that the bath temperature $T(t)/T_c = \zeta_0 - vt$ decreases with speed $v$ from a higher temperature $T_c$, $\zeta_0 > T_c$ (at which the system was equilibrated) to a lower temperature $T_c$, $\zeta_0 < T_c$. Then $T(t)$ increases back to $T_c$ with the same speed (reheating): $T(t)/T_c = \zeta_0 + vt$. For identification of asymmetries in the system response, the reheating temperature profile is taken to be the mirror reflection of the cooling profile.

For concreteness the numerical solutions of (5), (6) are displayed for the dimensionless parameters (see (2)):

$$\zeta_0 = 1.2, \quad \zeta_1 = 0.8, \quad \alpha = 0.75, \quad \sigma = 3.34 \times 10^{-4},$$

and various values of the dimensionless cooling-heating speed $v_t/T$. The values of $\alpha$ and $\sigma$ correspond to the helix-coil transition in poly-$\gamma$-benzyl-glutamate [3]. They are typical for other cooperative helix-coil transitions [4].

The order parameter $m$ defines the helicity fraction $\frac{1+ m}{2}$. Figure 1 displays the non-equilibrium $m$ vs. the dimensionless time $vt$, as obtained from solving numerically (5), (6), (9) with the time-dependent temperature $T(t)$. Figure 1 shows that for a small (but finite) speed $v_t/T$ the transition helix $\rightarrow$ coil during the reheating is more visible and takes shorter time than the reverse transition coil $\rightarrow$ helix during the cooling. The same conclusion (not displayed) holds when doing heating and then cooling. The symmetry between helix $\rightarrow$ coil and coil $\rightarrow$ helix is recovered in the equilibrium limit $\frac{1+m}{2} \approx 1$. The asymmetry also disappears in the weakly cooperative case $\sigma \approx 1$. This asymmetry is an example of hysteresis and it was observed experimentally for highly cooperative HCT in collagen [13–16], crystalline proteins [19] and DNA [18].

To gain a deeper understanding of the hysteresis, let us study in more detail the system's memory. Compare the cooling-heating behavior of $m(t)$ with the situation, where the temperature decreases till the lowest point and is then held constant; see fig. 1. This cooling-holding scenario produces curves which are almost identical to the cooling-heating curves, except at the vicinity of the equilibrium reheating transition, i.e., $m(t)$ does not react on the reheating before the sign of $h$ changes. Let us quantify the memory via susceptibility

$$\chi(t, t') = \lim_{\varepsilon \to 0} [m(t) - \tilde{m}(t)]/\varepsilon. \quad (11)$$

Here $\tilde{m}(t)$ is obtained under the same cooling-heating temperature setup, but $\varepsilon$-perturbed at $t'$.

$$\tilde{T}(t)/T_c = \zeta_0 - vt + \varepsilon(\bar{t} - t)\delta - vt' \delta - vt) \theta[vt' + \delta - vt]. \quad (12)$$

where $\theta[t]$ is the step function, and where the perturbation duration $2\delta$ is small but finite; see fig. 2. The perturbation is designed such that at equilibrium, where $m(t)$ is a function of the time-dependent temperature $T(t)$, $\chi(t, t')$ is non-zero only for $|v(t) - t'| < \delta$. In the regime where the above asymmetry is present, there are basically three scenarios for the behavior of $\chi(t, t')$; see fig. 2. i) A perturbation introduced during the cooling in the vicinity of $T_c$ is memoryzed and amplified. This memory need not be monotonic: itrevives once $T(t)$ crosses $T_c$ during the reheating; see fig. 2. ii) The same perturbation introduced during the reheating in the vicinity of $T_c$ creates a stronger immediate response, but a weaker memory, as compared to the previous case. iii) Outside of the vicinity of $T_c$ the response resembles that in equilibrium: $\chi(t, t')$ is maximal for $t \approx t'$ and quickly decays for $|t - t'| > \delta$; see fig. 2. We thus see how the hysteresis emerges from the unstabilities at $T(t) \approx T_c$ during the cooling and reheating.

Specific heat is a well-known indicator of the helix-coil transitions, which are observed via calorimetric methods [1]. Recalling the discussion before (2) and definitions (7), one can see that the energy of the spins is $Nu(t) [21], with

$$u(t) = -Jc(t) - \partial_{\beta}[\beta h(T)] m(t). \quad (13)$$
The origin of this formula should be clear from (1), (4). Note that the term \(-\delta_3[\beta h(T)]\) is similar to the known equilibrium formula \(E = -\delta_3[\beta F]\) relating energy \(E\) to the free energy \(F\). The specific heat \(c(t)\) is the response of \(u(t)\) to the temperature change \([T \equiv dT/dt]\)

\[
c(t) \equiv \dot{u}(t)/T(t) = -[\dot{J} + \alpha T_c \dot{m}]/\dot{T}.
\] (14)

The equilibrium specific heat \(c_{eq}\) is always positive and shows two sharp and symmetric peaks at \(T = T_c\); see fig. 3. For the non-equilibrium specific heat \(c\) we see again the asymmetry between helix \(\rightarrow\) coil and coil \(\rightarrow\) helix transitions: the peak of \(c\) during cooling is either absent or less visible than the one during the reheating. Now \(c(t)\) can be negative, i.e., the internal energy can decrease upon reheating; see fig. 3. This is partially related to the response of \(m(t)\): fig. 1 shows that when cooling changes to reheating, \(m(t)\) continues to increase due to its memory. In contrast, \(m_{eq}\) decreases under reheating. The negative part of \(c\) is most pronounced for a finite cooling-reheating speed \(v\); see fig. 3. Note that a negative specific heat is met in glasses, within a different scenario that is also related to large relaxation times [27].

The kinetic transition temperature \(T_c\) can be related to the peak of the specific heat [15,16]; see fig. 3. For not very small \(v\), \(T_c\) is approximately a linear function of \(x \equiv \ln \left[\frac{T_c}{T_c'}\right]\); thus \(T_c\) is not susceptible to moderate changes in the cooling-reheating speed \(v\). The same scaling of the kinetic transition temperature was seen experimentally for the helix-coil transition of collagen [15]. For the parameters of fig. 3 we obtained \((T_{G,R} - T_c)/T_c = a_{C,R} x + b_{C,R}\) for \(x \in [-2, -3.5]\). Here the lower indices \(C\) and \(R\) refer to the cooling and reheating, respectively, while \(a_R = 0.09, a_C = -0.12, b_R = 0.32\), and \(b_C = -0.41\). We see that \(T_R > T_c > T_C\).

The correlation function \(g(k,t) = \langle s_i s_{i+k}\rangle_t - \langle s_i\rangle_t\langle s_{i+k}\rangle_t\) describes the spatial structure of fluctuations. Equation (9) implies \(g(k,t) = [1 - m^2(t)]e^{-k/t(t)}\), where

\[
\xi(t) = \left(\ln \left[\frac{1 - m^2(t)}{\epsilon(t) - m^2(t)}\right]\right)^{-1},
\] (15)

is the correlation length, or the cooperative unit length, which plays an important role in describing the cooperativity of the polymer structure [1]. The equilibrium \(\xi_{eq}\), obtained from (15) by \(m(t) \rightarrow m_{eq}\) and \(\epsilon(t) \rightarrow \epsilon_{eq}\), displays two sharp peaks at \(T = T_c\); see fig. 4. It directly relates to the cooperativity parameter: \(\xi_{eq}(T = T_c) = 1/k\) [1]. \(\xi_{eq}\) is small both below and above \(T_c\), since there are no much equilibrium fluctuations there.

The non-equilibrium behavior of \(\xi(t)\) is different: for finite speeds \(\xi(t)\) increases during cooling, and its maximum is reached for the lowest \(T\); see fig. 4. \(\xi(t)\) is maximal at a certain finite speed of the cooling-reheating. Around its maximum it is larger than \(\xi_{eq}(T = T_c)\). Thus, the equilibrium relation between step-like change of the order parameter \(m\) and the correlation length is broken in kinetics: now \(m(t)\) does not show transition during cooling, but \(\xi(t)\) is large. The reason for a large \(\xi(t)\) is that the spin-spin interaction energy \(\epsilon(t)\) is close to 1 for both \(T < T_c\) and \(T > T_c\), while \(m(t)\) is far from \(+1\); see (15) and fig. 1. Thus, there are many helical and coiled domains, whose total spin should sum to zero implying long correlations. Yet another interpretation of a large \(\xi(t)\) is that due to memory the system does not see the sign change of \(h(T)\), but it sees the lowering of \(T(t)\), which naturally increases its correlation length \(\xi(t)\). Thus, the finite-rate cooling plays a selective role suppressing one mechanism and activating another. In the non-cooperative case \(\sigma 

Domain lengths: Generally, the state of the studied linear polymer is inhomogeneous and consists of helical and coiled domains. To characterize the domain lengths, we consider the probability \(P_{\pm}(k) = \left[\prod_{j=1}^{k}1e^{-k/\xi}\right]_{\pm}\) of having a helical (\(P_+\)) or coiled (\(P_-\)) domain of length \(k\). The transfer matrix treatment of (8) leads to \(P_{\pm}(k) = \gamma_\pm e^{-k/\eta_\pm}\), where \(\gamma_\pm\) and \(\eta_\pm\) do not depend on \(k\). Thus, \(e^{-1/\eta_\pm} = P_{\pm}(2)/P_{\pm}(1)\), or

\[
\eta_\pm(t) = \left(\ln \left[\frac{2 \pm 2m(t)}{1 + \epsilon(t) \pm 2m(t)}\right]\right)^{-1},
\] (16)

where \(\eta_+\) and \(\eta_-\) are, respectively, the characteristics length of the helical and coiled domains. Naturally, the equilibrium \(\eta_{-eq}\) is large in the coiled phase and decreases under cooling becoming small in the helical phase; see fig. 5. Likewise, \(\eta_{+eq}\) is large (small) in the helical (coiled)

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Fig. 3: Specific heat \(c\) vs. \(vt\) under cooling-reheating with parameters (10). Normal curve: \(v/T = 5 \times 10^{-3}\). Dashed curve: \(v/T = 5 \times 10^{-3}\). Dashed-thick curve: \(v/T = 10^{-3}\). Thick curve: equilibrium \(c_{eq}\).

Fig. 4: Correlation length \(\xi\) vs. \(vt\) under cooling-reheating with parameters (10). Normal curve: \(v/T = 5 \times 10^{-3}\). Dashed curve: \(v/T = 5 \times 10^{-3}\). Dashed-thick curve: \(v/T = 10^{-3}\). Thick curve: equilibrium \(\xi_{eq}\).
phase. Note that $\eta_{eq}(t) = \eta_{-eq}(T_c)$. In contrast to the equilibrium $\eta_{-eq}$, we see in fig. 5 that $\eta_-(t)$ can increase in time, if the cooling is not very slow. It decreases once the reheating starts. Thus $\eta_-$ reacts stronger on the decrease of temperature, than on changing the sign of $h$. Since during the cooling the order parameter $m$ increases, we see that the number of helical segments increases, but the typical coiled domain gets larger. Figure 5 also shows that $\eta_-$ can behave non-monotonically with time. For very small speeds, $\eta_-$ reproduces (with a delay) the shape of $\eta_{-eq}$; see fig. 5. The behavior of $\eta_+(t)$ under cooling-reheating is less interesting; it follows, in a delayed and weakened form, the shape of $\eta_{+eq}$; see fig. 6. (The same conclusion holds for $\eta_+$ during the heating from $T < T_c$ and then recoiling.) Note that for finite speeds we can have $\eta_- > \eta_+$ at low temperatures; see figs. 5, 6.

**Relations with experiments:** We now discuss several experimental results on helical biopolymers that demonstrate clear signs of irreversibility and hysteresis.

Admittedly, many experiments in polypeptides and proteins do not show visible signs of memory and hysteresis (unless caused by irreversible aggregation), mainly because the experimental temperature changes are too slow compared to relevant relaxation times [20].

However, there are susceptible experiments on crystals of globular proteins, which do see memory effects during various conformational changes [19]. Here each site of the crystalline structure contains one protein. Memory effects are amplified by this ordered structure and are visible in experiments [19]. Along these lines, we present here several new experimental results. Note that irreversibilities and hysteresis effects here are not associated with the crystalline structure per se [19]; they are related to helix-coil features proteins, while the crystalline structure only serves for amplifying these effects.

Figure 7 shows the denaturation process for the crystalline protein alcohol dehydrogenase. The process is monitored via the change of Young’s modulus with temperature. Recall that Young’s modulus is defined as the ratio of the applied stress (pressure) over the induced strain. Young’s modulus serves as an indicator of structural transitions [28,29], since in the denatured state it is smaller than in the native state. Young’s modulus of an alcohol dehydrogenase sample was measured via analyzing the electrically excited transverse resonance vibrations of the sample, which is cantilevered from one edge (another edge is free) [28,29]. The denaturation temperature of alcohol dehydrogenase ($\approx 45.5 ^\circ C$) is identified via the sudden jump of the Young modulus; see fig. 7. This agrees with the denaturation temperature obtained via calorimetric methods [30].

Figure 7 shows that once the heating is substituted by re-cooling in the vicinity of the critical temperature, the system follows a different path (hysteresis), although the heating-recooling speed was rather small. Moreover, even though the heating has been changed to re-cooling, the Young modulus keeps on decreasing till 40 °C due to the memory on the previous heating stage; see fig. 7. These effects agree qualitatively with the theoretical results found above via ZB model.

In contrast to polypeptides and proteins, there are established experimental results concerning the hysteresis and memory effects for DNA [17,18] and collagen [13–16]. In both these biopolymers the helical state (duplex for DNA and triplex for collagen) is stabilized by intermolecular (i.e., inter-strand) interactions.

Figure 8 displays the experimental denaturation of an amorphous DNA film. The same effects of hysteresis and
memory are present here. For other experimental indications of memory and hysteresis effects during DNA denaturations see refs. [18]. Reference [22] critically assesses the applicability of the Zimm-Bragg model to the helix-coil transition in DNA, and finds that many experimental aspects of this complex phenomenon are adequately reflected in the equilibrium Zimm-Bragg model.

Reference [14] investigates the equilibrium Zimm-Bragg model in the context of the helix-coil transition in collagen III. For this biopolymer the end-points of the three strands are held together by disulfide bonds, which precludes mismatches during the renaturation and makes possible the application of the Zimm-Bragg model. Indeed, it was found that although experimentally the helix-coil transition in collagen III (as well as in collagen I) is always kinetic — the proper equilibrium regime is hardly reached within the experimental observation time — some important aspects of the phenomenon can be described within the equilibrium Zimm-Bragg model in quantitative agreement with experiments [14]. We thus expect that the kinetics of the Zimm-Bragg model can describe the qualitative aspects of memory and hysteresis.

In sum, based on the Zimm-Bragg model we studied kinetics of the helix-coil transition driven by a finite-speed temperature change. We reproduced well-known experimental results on the hysteresis during the kinetic transition and explained it by quantifying the process memory. We also predicted new scenarios of kinetic helix-coil transition related to i) negative non-equilibrium specific heat accompanying the hysteresis; ii) correlation length becoming larger than in equilibrium.

There is an increasing evidence that the characteristics of many important biopolymers is controlled by both kinetic and thermodynamic factors [20]. For instance, the helix-coil transitions in collagen are normally kinetic, because the equilibrium is not reached within reasonable times. Moreover, the kinetic helix-coil transition temperature of collagen for various organisms is close to their physiological temperature [15], since this kinetic transition plays a role in achieving the flexibility of the collagen fiber [15]. Since our results indicate on new scenarios of kinetic helix-coil transitions in the basic Zimm-Bragg model, they can be relevant for understanding the interplay between the kinetics and thermodynamics in biopolymers.

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