Kinetics of Helix–Coil Transition in All Sizes of Polypeptides

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ABSTRACT: The relaxation behavior of the helix–coil transition has been investigated for all sizes of polypeptides. Unlike previously reported results, regardless of the size of polypeptides, the first-order kinetics plays a principal role in the relaxation process when a helical state is relaxed to a half-coiled state [i.e., $s(\mathrm{f}) \simeq 1$, where $s(\mathrm{f})$ is the helix stability parameter at the final state]. On the other hand, when a helical state is relaxed to a coiled state [i.e., $s(\mathrm{f}) \ll 1$], the zeroth-order kinetics plays a major role. In addition, the range of the validity of a kinetic version of the zipper model has been investigated. We have found that when a helical state is relaxed to a state where $s(\mathrm{f}) \leq 1$, the zipper model is valid for polypeptides with chain length N satisfying the relation $N < 1/(\sigma\gamma_{\mathrm{C}})^{1/2}$ where σ is the cooperativity parameter and γ_{C} is the coil nucleation rate parameter.

In recent years, the kinetics of a zipper model has been widely used for the study of the unwinding behavior of polypeptides and polynucleotides.[3] It has been found that the unwinding behavior of the zipper model follows the equation[2a,3]

$$N\frac{\mathrm{d}\theta(t)}{\mathrm{d}t} = -2(k_{\mathrm{b}} - k_{\mathrm{f}}) - 2k_{\mathrm{f}}\sum_{n=1}^{N} C_n(1\cdots10\cdots0) + (2-\gamma)k_{\mathrm{b}}C_1(t) + (2k_{\mathrm{b}} - 2k_{\mathrm{f}} + \gamma N\sigma k_{\mathrm{f}})C_0(t) \quad (1)$$

and

$$s(\mathrm{f}) = k_{\mathrm{f}}/k_{\mathrm{b}}$$

where $\theta(t)$ is the fraction of helical residues at time t, N is the number of segments in a polypeptide, and k_{f} and k_{b} are respectively the forward and backward rates of forming a helix. In eq 1, C_n $(1\cdots10\cdots0)$ is the concentration of conformational species with the right ends open and the left ends closed, and $C_1(t)$ and $C_0(t)$ are respectively the total concentrations of conformational species with one and no helical residue. The σ is the nucleation parameter and γ is the helix nucleation rate parameter.

For a system which experiences a large perturbation [i.e., $s(0) \gg 1$ and $s(\mathrm{f}) \ll 1$ where $s(0)$ and $s(\mathrm{f})$ are the helix stability parameters for the initial and final states of the relaxation], eq 1 predicts that the unwinding proceeds linearly for a large portion of the unwinding time with its slope equal to $2k_{\mathrm{b}}[1 - s(\mathrm{f})]/N$. This is so because a few terms in the sum $\Sigma C_n(1\cdots10\cdots0)$ of eq 1 [e.g., $C_N(1\cdots1)$ and $C_{N-1}(1\cdots10)$] contribute only to the initial portion of the relaxation, while the rest of the terms in the sum are relatively small for all t. The last two terms in eq 1, $C_1(t)$ and $C_0(t)$, contribute only to the final state of the relaxation. Thus, in the case of a large perturbation, the zeroth-order kinetics plays a major role in the relaxation process. If the forward and reverse reactions are about equally favored [i.e., $s(\mathrm{f}) \simeq 1$], the first term is nearly zero for all t. The second term, on the other hand, decays exponentially with the relaxation time τ_0 (where τ_0 is the inverse of a slope of the exponential portion of the relaxation curve) having the form[3]

$$\tau_0 \sim (N + 1)^2 \quad (2)$$

when N is large and σ is small in such a way that $N\sigma$ is small.

In this paper, we intend to investigate whether or not these two predictions, i.e., the zeroth-order reaction when $s(\mathrm{f}) \ll 1$ and the first-order reaction when $s(\mathrm{f}) \simeq 1$, hold for all chain lengths of polypeptides. This will be achieved by using a kinetic version of the Zimm–Bragg theory.[4] (This theory allows the coil state within a chain and hence is applicable to all chain lengths.) In addition, we intend to find the ranges in which the zipper model predictions, i.e., the slopes being equal to $2[1 - s(\mathrm{f})]/N$ for $s(\mathrm{f}) \ll 1$ and $\sim(N + 1)^{-2}$ for $s(\mathrm{f}) \simeq 1$, are valid.

Kinetic Version of Zimm–Bragg Theory

The master equation corresponding to the helix–coil transition of the Zimm–Bragg theory[4] can be written as[5,6]

$$\frac{\mathrm{d}P(\sigma_1\sigma_2\ldots\sigma_N;t)}{\mathrm{d}t} = -\sum_{j=1}^{N} w_j(\sigma_j)P(\sigma_1\ldots\sigma_j\ldots\sigma_N;t) + \sum_{j=1}^{N} w_j(\sigma_j')P(\sigma_1\ldots\sigma_j'\ldots\sigma_N;t) \quad (3)$$

Here, $\sigma_j = 0$ or 1, σ_j' satisfies the relation $\sigma_j + \sigma_j' = 1$, and $P(\sigma_1\sigma_2\cdots\sigma_N;t)$ is the probability that a polypeptide chain is in a conformational state defined by a sequence $\sigma_1, \sigma_2, \ldots, \sigma_N$ at time t. The quantity $w_j(\sigma_j)$ is the kinetic constant corresponding to the transition from σ_j to σ_j' of the polypeptide group.

We further define the reduced probability function which furnishes the probability of the nth through $(m + n)$th bond to be in the state $\sigma_n, \sigma_{n+1}, \ldots, \sigma_{n+m}$, independent of the state of the remaining bonds:[6,7]

$$\gamma^{(n)}(\sigma_n\sigma_{n+1}\ldots\sigma_{n+m}) = \sum_{\sigma_1}\cdots\sum_{\sigma_{n-1}}\sum_{\sigma_{n+m+1}}\cdots\sum_{\sigma_N}P(\sigma_1\ldots\sigma_n\ldots\sigma_{n+m}\ldots\sigma_N;t) \quad (4)$$

The rate equation for the reduced probability function can be derived from eq 3 as

$$\begin{aligned}\frac{\mathrm{d}\gamma^{(n)}(\sigma_n\cdots\sigma_{n+m})}{\mathrm{d}t} = {} & -\sum_{j=n+1}^{n+m-1}[w_j(\sigma_j)\gamma^{(n)}(\sigma_n\ldots\sigma_j\ldots\sigma_{n+m}) - \\ & w_j(\sigma_j')\gamma^{(n)}(\sigma_n\ldots\sigma_{j-1}\sigma_j'\sigma_{j+1}\ldots\sigma_{n+m})] - \\ & \sum_{\sigma_{n-1}}[w_n(\sigma_n)\gamma^{(n-1)}(\sigma_{n-1}\sigma_n\ldots\sigma_{n+m}) - \\ & w_n(\sigma_n')\gamma^{(n-1)}(\sigma_{n-1}\sigma_n'\sigma_{n+1}\ldots\sigma_{n+m})] - \\ & \sum_{\sigma_{n+m+1}}[w_{n+m}(\sigma_{n+m})\gamma^{(n)}(\sigma_n\ldots\sigma_{n+m}\sigma_{n+m+1}) - \\ & w_{n+m}(\sigma_{n+m}')\gamma^{(n)}(\sigma_n\ldots\sigma_{n+m-1}\sigma_{n+m}'\sigma_{n+m+1})] \quad (5a)\end{aligned}$$

for $m \geq 2$

$$\begin{aligned}\frac{\mathrm{d}\gamma^{(n)}(\sigma_n\sigma_{n+1})}{\mathrm{d}t} = {} & -\sum_{\sigma_{n-1}}[w_n(\sigma_n)\gamma^{(n-1)}(\sigma_{n-1}\sigma_n\sigma_{n+1}) - \\ & w_n(\sigma_n')\gamma^{(n-1)}(\sigma_{n-1}\sigma_n'\sigma_{n+1})] - \\ & \sum_{\sigma_{n+1}}[w_{n+1}(\sigma_{n+1})\gamma^{(n)}(\sigma_n\sigma_{n+1}\sigma_{n+2}) - \\ & w_{n+1}(\sigma_{n+1}')\gamma^{(n)}(\sigma_n\sigma_{n+1}'\sigma_{n+2})] \quad (5b)\end{aligned}$$

and

$$\frac{d\gamma^{(n)}(\sigma_n)}{dt} = -\sum_{\sigma_{n-1}}\sum_{\sigma_{n+1}}[w_n(\sigma_n)\gamma^{(n-1)}(\sigma_{n-1}\sigma_n\sigma_{n+1}) - w_n(\sigma_n')\gamma^{(n-1)}(\sigma_{n-1}\sigma_n'\sigma_{n+1})] \quad (5c)$$

According to Schwarz,[8] the following rate parameters are assigned for the three elementary steps in the helix–coil transition:

I. Growth

$$001 \underset{k_b}{\overset{k_f}{\rightleftarrows}} 011 \qquad \text{where } k_f/k_b = s(\mathrm{f}) \quad (6a)$$

II. Helix nucleation

$$000 \underset{\gamma_H k_b}{\overset{\sigma\gamma_H k_f}{\rightleftarrows}} 010 \quad (6b)$$

III. Coil nucleation

$$101 \underset{\sigma\gamma_C k_b}{\overset{\gamma_C k_f}{\rightleftarrows}} 111 \quad (6c)$$

With these rate parameters, $w_n(\sigma_n)$ in eq 5 can be written explicitly as

$$w_j(\sigma_j) = \nu(\sigma_{j-1}\sigma_j\sigma_{j+1})[1 - (2\sigma_j - 1)(\sigma_{j+1} + \sigma_{j-1} - 1)\delta][1 + \epsilon(2\sigma_j - 1)] \quad (7)$$

where

$$\nu(000) = \nu(010) = \gamma_H k_b(1 + s)(1 + \sigma)$$
$$\nu(110) = \nu(100) = \nu(011) = \nu(001) = 2k_b(1 + s)$$
$$\nu(111) = \nu(101) = k_b\gamma_C(1 + s)(1 + \sigma)$$
$$\delta = (1 - \sigma)/(1 + \sigma)$$
$$\epsilon = -(s - 1)/(s + 1)$$

The differential rate equations of eq 5 are the coupled equations, in which the $(n + 1)$th order reduced probability function is needed to find the nth order reduced probability function. In order to truncate the coupled equation, Vol'kenstein et al.[9] have introduced a doublet closure relation, and Silberberg and Simha[10] have introduced the generalized closure relation of the form

$$\gamma^{(j)}(\sigma_j\ldots\sigma_k\ldots\sigma_m) = \frac{\gamma^{(j)}(\sigma_j\ldots\sigma_k\ldots\sigma_l)\gamma^{(k)}(\sigma_k\ldots\sigma_l\ldots\sigma_m)}{\gamma^{(k)}(\sigma_k\ldots\sigma_l)} \quad (8)$$

which is exact at equilibrium. Schwarz[11] has shown that eq 5 leads to the rate equation of Go if one introduces the triplet closure relation [i.e., $k = j + 1$, $l = j + 2$, and $m = j + 3$]. Rowlings and Schneider[12] pointed out that the matrix method of Craig and Crothers is equivalent to the first order Taylor expansion of eq 5a when one introduces the triplet closure relation.

Rowlings and Schneider[12] have also shown that for $N = \infty$ the doublet closure relation (i.e., the approximation of Vol'kenstein et al.) is very good for s(f) near unity and $\gamma_H = \gamma_C = 1$ and that the triplet closure relation is very good for $s(\mathrm{f}) \ll 1$ and $\gamma_H = \gamma_C = 1$. Our computation as shown in Tables I and II also indicates that the doublet closure is reasonable if $s(\mathrm{f}) = 0.2$ and is very good if $s(\mathrm{f}) \simeq 1$. The doublet closure, however, is very poor if γ_H and/or γ_C are much greater than unity as shown in Figure 1. We have found that the above conclusions also hold for finite N. This finding is very useful since one may compute the relaxation curve for finite chains within a reasonably short computing time. That is, when $s(\mathrm{f}) \simeq 1$, although it takes a very long time for a system to reach equilibrium, the entire relaxation curve can be calculated accurately and fast by using the doublet closure relation (which contains $2N$ independent equations and $4N$ dependent equations). On the other hand, when $s(\mathrm{f}) \ll 1$, since equilibrium is reached in a very short period of time, the relaxation curve may also be calculated accurately and fast by using the triplet closure relation (which contains $4N$ independent and $10N$ dependent equations; thus, one time cycle to generate a new set of distribution functions will take longer time, but fewer cycles are required to generate the entire relaxation curve).

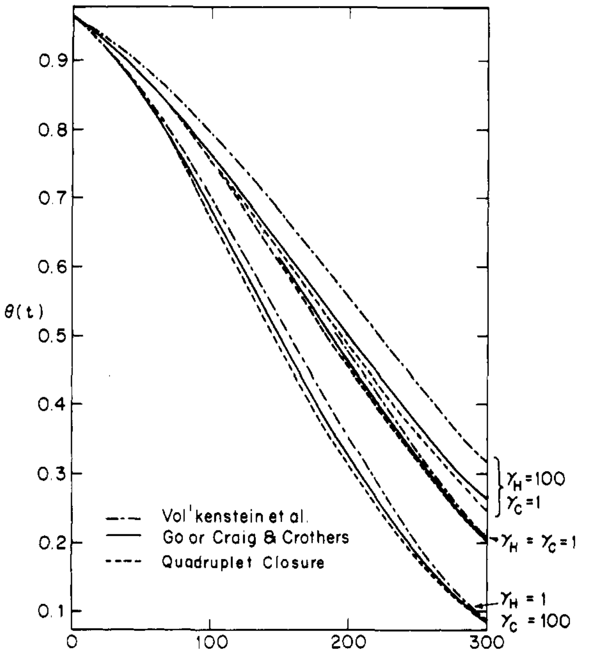

Figure 1. Dependence of the kinetic curve on γ_H and γ_C when $N = \infty$ for the three closure relations. Here, Vol'kenstein et al. and Go or Craig and Crothers imply the doublet and triplet closures, respectively. The equilibrium parameters used are $\sigma = 10^{-4}$, $s(0) = 1.0506$ [$\theta(0) = 0.9634$], and $s(\mathrm{f}) = 0.7$ [$\theta(\infty) = 0.0348$].

Table I
Fraction of Helical Contents vs. Time *t* for $\sigma = 10^{-2}$, $\gamma_H = \gamma_C = 1$, and $s(\mathrm{f}) = 0.2$

k_bt	Doublet closure	Triplet closure	Quadruplet closure
0	0.9999	0.9999	0.9999
2	0.9500	0.9501	0.9501
4	0.8536	0.8542	0.8542
6	0.7260	0.7285	0.7288
8	0.5821	0.5898	0.5910
10	0.4369	0.4533	0.4562
12	0.3031	0.3304	0.3356
14	0.1911	0.2280	0.2356
16	0.1067	0.1486	0.1581
18	0.0515	0.0912	0.1015
20	0.0217	0.0525	0.0626
∞	0.0031	0.0031	0.0031

Results and Discussions

If a completely helical state [i.e., $s(0) \gg 1$] is relaxed to a completely coiled state [i.e., $s(\mathrm{f}) \ll 1$], the Zimm-Bragg model becomes the zipper model as $\sigma\gamma_C \rightarrow 0$. This can be seen from eq 6; the helix nucleation step eq 6b does not occur in this case since $\gamma^{(n)}(010)$ is initially close to zero, and the coil nucleation step eq 6b also does not occur because of a small magnitude of $\gamma_C\sigma$. Furthermore, $\gamma^{(n)}(011)$

Table II
Fraction of Helical Contents with $\sigma = 10^{-4}$, $\gamma_H = \gamma_C = 1$, $s(0) = 1.0$, and $s(f) = 0.995$

k_bt	Doublet closure	Triplet closure	Quadruplet closure
400	0.4817	0.4817	0.4818
800	0.4661	0.4662	0.4662
1200	0.4528	0.4529	0.4530
1600	0.4415	0.4416	0.4417
2000	0.4319	0.4320	0.4321
2400	0.4237	0.4238	0.4239
2800	0.4168	0.4169	0.4170
3200	0.4109	0.4110	0.4111
3600	0.4059	0.4060	0.4061
4000	0.4017	0.4018	0.4019
4400	0.3981	0.3982	0.3983
4800	0.3951	0.3952	0.3953
5200	0.3925	0.3926	0.3927
5600	0.3904	0.3904	0.3905
6000	0.3885	0.3886	0.3886

Table III[a]

		γ_C =		
k_bt	Zipper	0	0.01	0.1
0	1.000	1.000	1.000	1.000
5	0.901	0.900	0.897	0.874
10	0.803	0.800	0.792	0.720
15	0.705	0.701	0.685	0.557
20	0.607	0.603	0.579	0.403
25	0.509	0.504	0.474	0.271
30	0.411	0.406	0.372	0.167
35	0.313	0.309	0.274	0.093
40	0.215	0.212	0.182	0.045
45	0.119	0.120	0.099	0.018
50	0.042	0.048	0.038	0.005

[a] This table shows the dependence of γ_C on $H(t)$ when $N = 100$. The parameters used are $\sigma = 10^{-2}$, $\gamma_H = 1$, $s(0) = 50$, and $s(f) = 0.02$. The data on the second column were obtained by using the zipper model, and those on the third to fifth columns were obtained by using the triplet closure relation.

is very small except at the two ends (i.e., when $n = 1$ and $n = N - 2$). This means that the unwinding starts mainly from the two ends of the chain. Tables III and IV show the normalized helical fraction $H(t)$ versus time for large perturbations. As shown in these tables, the zipper model agrees with the Zimm–Bragg model as $\gamma_C \rightarrow 0$ (see Table III) and $\sigma \rightarrow 0$ (see Table IV). Note that $H(t)$'s given in

$$H(t) = (\theta(t) - \theta(\infty))/(\theta(0) - \theta(\infty)) \tag{9}$$

columns 2 and 3 of the two tables are linearly proportional to t with their increments equal to $2[1 - s(\mathrm{f})]/N = 0.02$. Also note that the data on each column of Table III match closely with those on the corresponding column of Table IV. This is because the product $\sigma\gamma_C$ in each column of Table III is set equal to that in the corresponding column of Table IV. Thus, these two tables show that when a completely helical state is relaxed to a completely coiled state, the relaxation behavior is governed by the product $\sigma\gamma_C$. Our computation indicates that coil nucleations from the middle of the chain vanish when

$$N\sqrt{\sigma\gamma_C} < 1 \tag{10}$$

Table IV[a]

	Zipper, σ =	Zimm–Bragg, σ =		
k_bt	10^{-6}	10^{-6}	10^{-4}	10^{-3}
0	1.000	1.000	1.000	1.000
5	0.901	0.901	0.899	0.876
10	0.803	0.803	0.795	0.723
15	0.705	0.704	0.689	0.561
20	0.607	0.605	0.584	0.407
25	0.509	0.506	0.479	0.275
30	0.411	0.408	0.377	0.171
35	0.313	0.310	0.278	0.096
40	0.215	0.212	0.185	0.047
45	0.119	0.119	0.101	0.019
50	0.042	0.045	0.039	0.005

[a] The dependence of σ on $H(t)$ when $N = 100$. The parameters used are $\gamma_C = 1$, $\gamma_H = 1$, $s(0) = 50$, and $s(f) = 0.02$. The data on the second column were obtained by using the zipper model, and the data on the third to fifth columns were obtained by using the triplet closure relation.

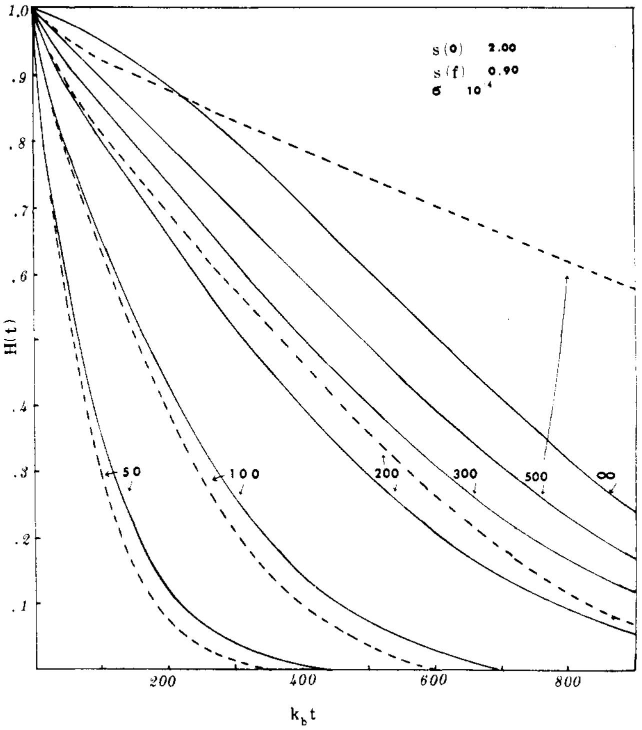

Figure 2. Kinetic curves showing the dependence of the unwinding on chain lengths (ranging from 50 to ∞) for a large perturbation. The parameters used are $s(0) = 2.0$, $s(\mathrm{f}) = 0.9$, $\sigma = 10^{-4}$, and $\gamma_H = \gamma_C = 1$. The dotted lines are obtained by using the zipper model of Appendix B.

If $s(\mathrm{f})$ is not much less than unity [say $s(\mathrm{f}) = 0.9$], the sum $\Sigma C_n(1 \ldots 10 \ldots 0)$ in eq 1 does not approach zero fast enough, so that the relaxation does not proceed quite linearly with time. This is also true for the Zimm–Bragg model as shown in Figure 2. Here, the dotted lines in Figure 2 are obtained by using the zipper model (see Appendix B for the computational procedure). For $N \lesssim 100$ the relaxation of the zipper model proceeds slightly faster than that of the Zimm–Bragg model. This is because a kinetic version of the zipper model contains the assumption that all species in $C_n(t)$ are present in equal amounts. This assumption apparently becomes somewhat erroneous unless $s(\mathrm{f})$ is much less than unity. From Figure 2, one also notes that for $N \gtrsim 200$ the relaxation of the Zimm–Bragg model

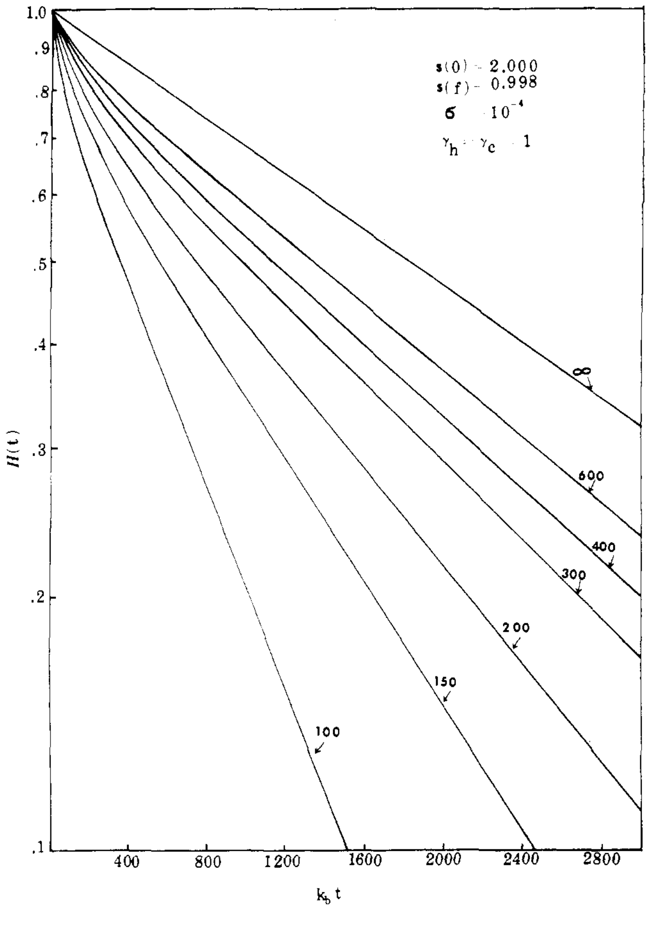

Figure 3. Kinetic curve showing the dependence of the unwinding on chain lengths (ranging from 100 to ∞) for a small perturbation. The parameters used are $s(0) = 2.0$, $s(\mathrm{f}) = 0.998$. $\sigma = 10^{-4}$, and $\gamma_{\mathrm{H}} = \gamma_{\mathrm{C}} = 1$.

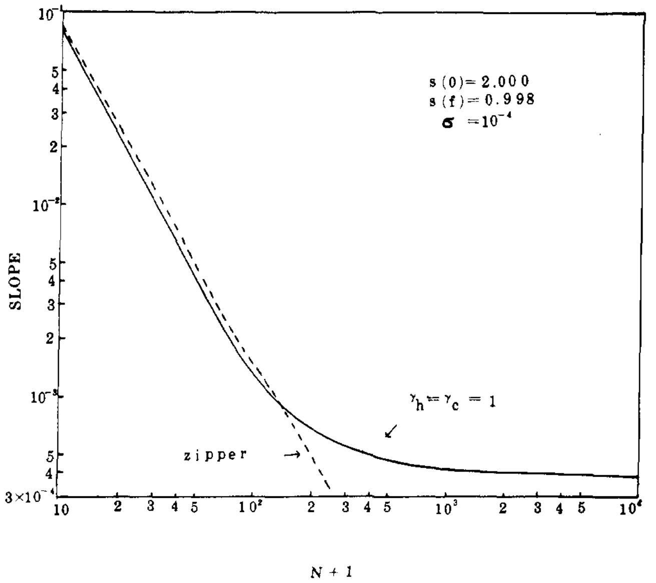

Figure 4. Slopes of Figure 3 (which is inversely proportional to the relaxation time τ_0) versus chain lengths. The dotted line is obtained by using the zipper model.

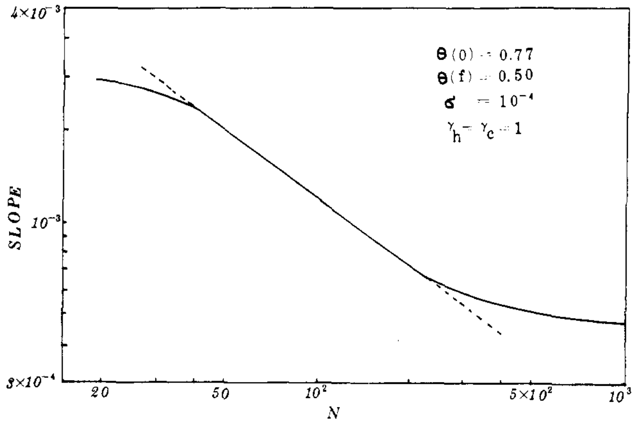

Figure 5. Dependence of the relaxation time on chain lengths, when a polypeptide with length N is relaxed from $\theta(0) = 0.77$ to $\theta(\infty) = 0.5$. The parameters used are $\sigma = 10^{-4}$ and $\gamma_{\mathrm{H}} = \gamma_{\mathrm{C}} = 1$.

proceeds faster than that of the zipper model and that the deviation between the two models becomes large as N increases. This is so because the coil nucleation from the middle of the chain becomes quite significant when the chain length, N, is longer than the cooperative length, $1/(\sigma)^{1/2}$. In the case of equilibrium, it has been found that the zipper model becomes valid for $N(\sigma)^{1/2} < 1$.[8,13-15] In the case of kinetics, however, γ_{C} apparently plays the role of determining the range of the validity of the zipper model. For example, when $N = 500$, $\sigma = 10^{-4}$, and $\gamma_{\mathrm{H}} = 1$, the slope of the linear portion of the relaxation curve of the Zimm–Bragg model yields 0.001 when $\gamma_{\mathrm{C}} = 1$ and 0.0008 when $\gamma_{\mathrm{C}} = 0.1$, while the zipper model yields 0.0004. As $\gamma_{\mathrm{C}} \rightarrow 0$ the slope of the zipper model approaches that of the Zimm–Bragg model. Our computation for this case [i.e., $s(\mathrm{f}) = 0.9$] confirms the inequality given by eq 10.

As shown in Figure 3, when the relaxation of a system takes place from $s(0) = 2.0$ to $s(\mathrm{f}) = 0.998$, the relaxation curve of the Zimm–Bragg model, like the zipper model, decays exponentially for all chain sizes. The slopes of the exponential portion of Figure 3 are shown in Figure 4. Here, the dotted line is obtained from the zipper model (see Appendix B for the computational procedure). From this figure, one finds that the relaxation time τ_0 is proportional to $(N + 1)^2$ when $N \lesssim 100$. This is in agreement with the result of the zipper model. Small discrepancy between the two models in this region (i.e., $N \lesssim 100$) is due to the fact that the zipper model contains an approximation as discussed. When $N > 100$, the relaxation time of the zipper model deviates considerably from that of the Zimm–Bragg model. This is because the Zimm–Bragg model allows coil nucleations in the middle of the chain. Our computation for this case [i.e., $s(\mathrm{f}) \simeq 1$] also indicates the emperical relation given in eq 10 is valid.

Figure 5 shows the effect of the chain lengths on the relaxation time when the relaxation of a system takes place from $\theta(0) = 0.77$ to $\theta(\infty) = 0.50$. We find that the relaxation time τ_0 (the straight line drawn in Figure 5) varies as

$$\tau_0 \sim N^{3/4} \qquad (11)$$

Experiments on DNA show that τ_0 depends approximately linearly on N.[16] This discrepancy probably occurs because DNA unwinding is governed by hydrodynamic forces which are not readily described by an Ising model.

Appendix A

The numerical calculations of a kinetic version of the Zimm–Bragg model with the triplet closure relation have been carried out as follows: First, the initial equilibrium distributions of $\gamma^{(n)}(1)$, $\gamma^{(n)}(11)$, $\gamma^{(n)}(111)$, and $\gamma^{(n)}(000)$ are obtained from the Zimm–Bragg formulation:

$$\gamma^{(n)}(1) = \frac{(\lambda_0 - 1)(1 - \lambda_1)}{(\lambda_0 - \lambda_1)^2 \Xi}(\lambda_0^{N-n+1} - \lambda_1^{N-n+1})(\lambda_0^n - \lambda_1^n)$$

$$n = 1, \ldots, N$$

$$\gamma^{(n)}(11) = s\frac{(\lambda_0 - 1)(1 - \lambda_1)}{(\lambda_0 - \lambda_1)^2 \Xi}(\lambda_0^{N-n} - \lambda_1^{N-n})(\lambda_0^n - \lambda_1^n)$$

$$n = 1, \ldots, N - 1$$

$$\gamma^{(n)}(111) = s^2\frac{(\lambda_0 - 1)(1 - \lambda_1)}{(\lambda_0 - \lambda_1)^2 \Xi}(\lambda_0^{N-n-1} - \lambda_1^{N-n-1})(\lambda_0^n - \lambda_1^n)$$

and

$$\gamma^{(n)}(000) = \frac{1}{(\lambda_1 - \lambda_0)^2}[(\lambda_1 - 1)\lambda_0^{N-n-1} + (1 - \lambda_0)\lambda_1^{N-n-1}] \times [\lambda_0^n(\lambda_1 - 1) + \lambda_1^n(1 - \lambda_0)]$$

where

$$\begin{Bmatrix}\lambda_0\\ \lambda_1\end{Bmatrix} = \frac{1}{2}\{1 + s \pm \sqrt{(1 - s)^2 + 4\sigma s}\}$$

and

$$\Xi = \frac{\lambda_0^{N+1}(\lambda_0 - s) + \lambda_1^{N+1}(s - \lambda_1)}{\lambda_0 - \lambda_1}$$

Other dependent functions are obtained from the following relations:

$$\begin{aligned}
\gamma^{(n)}(0) &= 1 - \gamma^{(n)}(1)\\
\gamma^{(n)}(10) &= \gamma^{(n)}(1) - \gamma^{(n)}(11)\\
\gamma^{(n)}(01) &= \gamma^{(n+1)}(1) - \gamma^{(n)}(11)\\
\gamma^{(n)}(00) &= 1 - \gamma^{(n)}(1) - \gamma^{(n+1)}(1) + \gamma^{(n)}(11)\\
\gamma^{(n)}(110) &= \gamma^{(n)}(11) - \gamma^{(n)}(111)\\
\gamma^{(n)}(011) &= \gamma^{(n+1)}(11) - \gamma^{(n)}(111)\\
\gamma^{(n)}(100) &= 1 - \gamma^{(n+1)}(1) + \gamma^{(n+1)}(11) - \gamma^{(n)}(000) - \gamma^{(n+2)}(1)\\
\gamma^{(n)}(001) &= \gamma^{(n)}(00) - \gamma^{(n)}(000)\\
\gamma^{(n)}(101) &= \gamma^{(n)}(10) - \gamma^{(n)}(100)\\
\gamma^{(n)}(010) &= \gamma^{(n+1)}(1) - \gamma^{(n+1)}(11) - \gamma^{(n)}(11) + \gamma^{(n)}(111)
\end{aligned}$$

Thus, the $14N$ initial distribution functions are obtained from the above equations for given $s(0)$, σ, and N.

Next, the time dependent part of the distribution functions are obtained with the use of the relation

$$f(t + \Delta t) = f(t) + \Delta t(\mathrm{d}f/\mathrm{d}t)$$

where f represents either $\gamma^{(n)}(1)$, $\gamma^{(n)}(11)$, $\gamma^{(n)}(111)$, or $\gamma^{(n)}(000)$, and $\mathrm{d}f/\mathrm{d}t$ is given by eq 5 where the quadruplet distribution is truncated by eq 8. Thus, the entire relaxation curve is obtained by an iteration procedure starting from the initial distribution functions.

Appendix B

We have used the following simplified version of the zipper model. In order to save a computation time, we assume that all the species in $C_n(t)$ are equal in concentrations. This leads to the following differential equations[3]

$$k_b^{-1}\frac{\mathrm{d}C_N(t)}{\mathrm{d}t} = -2C_N(t) + d_{N-1}sC_{N-1}(t)$$

$$k_b^{-1}\frac{\mathrm{d}C_i(t)}{\mathrm{d}t} = -(\mathrm{d}_i s + 2)C_i(t) + 2C_{i+i}(t) + \mathrm{d}_{i-1}sC_{i-1}(t)$$

$$i = N - 1, \ldots, 2$$

$$k_b^{-1}\frac{\mathrm{d}C_1(t)}{\mathrm{d}t} = -(\mathrm{d}_1 s + \gamma)C_1(t) + 2C_2(t) + \gamma\sigma NsC_0(t)$$

$$k_b^{-1}\frac{\mathrm{d}C_0(t)}{\mathrm{d}t} = -\gamma\sigma NsC_0(t) + \gamma C_1(t)$$

where $d_i = 2(N - i)/(N - i + 1)$ for $i = 1, \ldots, N - 1$.

The entire relaxation curve is generated by an iteration procedure from the above equation with the following initial distributions

$$C_0 = 1/Q$$

$$C_n = \sigma(N - n + 1)s^n/Q$$

$$n = 1, \ldots, N$$

where

$$Q = 1 + \frac{\sigma s}{(1 - s)^2}[N - (N + 1)s + s^{N+1}]$$

References and Notes

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