

# Theoretical study of kinetics of zipping phenomena in biomimetic polymers

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In this work we use theory to obtain a mathematical expression for a time correlation function  $c(l, t)$  that provides insight into the zipping phenomena along a polymer going through a conformational transition. The polymer is modeled as an Ising-like chain with each segment being in one of two states: bound (+1) or unbound (−1). The time correlation function  $c(l, t)$  predicts the correlation between the state of the  $j$ th polymer segment at time 0 and the state of the  $(j \pm l)$ th polymer segment at time  $t$ . The expressions for  $c(0, t)$ ,  $c(1, t)$ , and  $c(2, t)$  obtained from our theory are dependent on the values of  $k_0$  and  $k_1$ , where  $2k_0$  is the rate coefficient for one segment changing from an unbound state to a bound state when both the neighboring segments are in an unbound state, and  $2k_1$  is the rate coefficient for one segment changing from an unbound state to a bound state when both the neighboring segments are in a bound state. The ratio  $k_1/k_0$  is an indication of the extent of cooperativity of binding adjacent segments on the polymer. We observe that  $c(0, t)$ ,  $c(1, t)$ , and  $c(2, t)$  decay to 0 (no correlation) more slowly and the maximum values of  $c(1, t)$  and  $c(2, t)$  are lower for low values of  $k_1/k_0$  as compared to high values of  $k_1/k_0$ . This is because at low values of  $k_1/k_0$  the consecutive binding of adjacent segments along the polymer occurs slowly, while at high values of  $k_1/k_0$  the cooperativity of binding adjacent segments is high and the segments along the polymer bind in a fast zipping mechanism.

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Conformational transitions in polymers can be described as zipping phenomena if a change in state of one segment along the polymer affects the states of the neighboring segments, and the cascade effect progresses along the polymer. For example, in the case of a conformational transition of the polymer from one rotational isomeric state to another, the rotation of one backbone bond along a polymer could cause the material on either side of the bond to go through a swinging motion [1]. If each of the segments along the polymer can be in one of two rotational states, we can treat the polymer chains as one-dimensional Ising-like chains. Such treatment can also be extended to conformational changes in biopolymers such as DNA and proteins. When a single-stranded DNA molecule binds specifically and hybridizes, as a consequence of the Watson-Crick base-pairing rules, to a complementary single-stranded DNA molecule, each base pair on the single-stranded DNA molecule goes from an unbound state (−1 state) to a bound state (+1 state). In addition, as each base pair gets bound to its complementary base pair, the neighboring base pairs are in closer proximity to their complementary base pairs, and thus the hybridization progresses along the DNA, zipping the two single-stranded molecules to form a double-stranded helix [2]. Another example is the helix-coil transition in proteins, where each residue along the protein can go from a random coil state (not bonded) to a helical state (hydrogen bonded to the third preceding residue); the helix-coil transition progresses from one residue to the neighboring residue in a zipping fashion [3]. To characterize the zipping kinetics of Ising-like chains, we calculate a time correlation function that predicts the correlation between the state of the  $j$ th segment at time 0 and the state of the  $(j \pm l)$ th segment along the chain at time  $t$ .

In this paper, we study the kinetics of binding of a “target” polymer to a complementary “probe” polymer. The target and probe polymers are each modeled as a chain of distinct segments. Each probe segment binds exclusively with

its unique complementary target segment with a single binding energy. Our aim is to study the kinetics of binding of the probe to the target by calculating the time correlation function  $\langle c(l, t) \rangle$  defined as

$$c(l, t) = \langle \mu_{j \pm l}(t) \mu_j(0) \rangle, \quad (1)$$

where  $\mu_{j \pm l}(t)$  is the state of the  $(j \pm l)$ th segment at time  $t$ ,  $\mu_j(0)$  is the state of the  $j$ th segment at time  $t=0$ ,  $j$  is the probe segment that starts (or nucleates) the binding at time  $t=0$ , and  $l$  is the  $l$ th neighbor of the  $j$ th probe segment. Therefore,  $c(l, t)$  predicts the correlation between the state of the  $(j \pm l)$ th probe segment at time  $t$  and the state of the  $j$ th probe segment at time 0.

In our model each of the segments on the probe can adopt one of two states: bound (+1) and unbound (−1). There are  $2^N$  possible states for an  $N$ -segment-long probe. The types of transition between states of the probe are illustrated in Fig. 1.  $2k_0$  is the rate of one segment changing from an unbound state to a bound state when both the neighboring segments

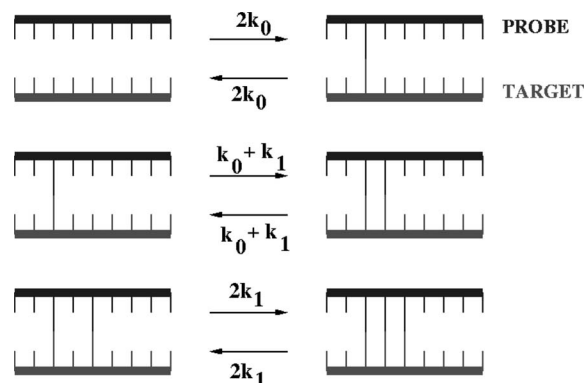
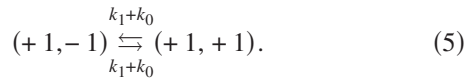
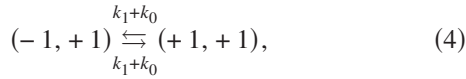
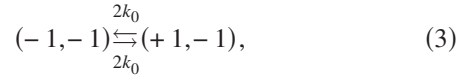
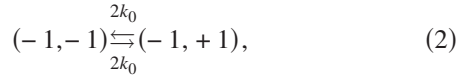


FIG. 1. Three possible cases of probe-target segment binding.

are in an unbound state.  $k_1+k_0$  is the rate of one segment changing from an unbound state to a bound state when only one of the neighboring segments is in a bound state.  $2k_1$  is the rate of one segment changing from an unbound state to a bound state when both the neighboring segments are in a bound state. We assume that the rate constants for the reverse and forward reactions are the same.

For a two-segment-long probe, there are four possible states:  $\mu=(-1,-1)$ ,  $(+1,-1)$ ,  $(-1,+1)$ , and  $(+1,+1)$ . The transitions between states for a two-segment-long probe are as follows:



The  $j$ th element of the state  $\mu$  is denoted by  $\mu_j$  [1]. For example, the first element of the state  $\mu=(+1,-1)$  is denoted by  $\mu_1=+1$  and the second element of the state is denoted by  $\mu_2=-1$ . We can represent each of the four states  $\mu$  in the form of a vector  $|\mu\rangle$ . The state  $(+1,+1)$  is represented by  $|\mu\rangle=(1,0,0,0)$ , state  $(+1,-1)$  is represented by  $|\mu\rangle=(0,1,0,0)$ , state  $(-1,+1)$  is represented by  $|\mu\rangle=(0,0,1,0)$ , and state  $(-1,-1)$  is represented by  $|\mu\rangle=(0,0,0,1)$ . (See [13] for a vector representation of the  $2^N$  states of an  $N$ -segment probe).

If  $f(\mu,t)$  is the probability of being in state  $\mu$  at time  $t$ , the master equation for a two-segment probe undergoing the reactions in Eqs. (2)–(5) in matrix form is

$$\begin{aligned} \frac{d}{dt} \begin{pmatrix} f(+1,+1,t) \\ f(+1,-1,t) \\ f(-1,+1,t) \\ f(-1,-1,t) \end{pmatrix} &= \begin{pmatrix} -2k_1-2k_0 & k_0+k_1 & k_0+k_1 & 0 \\ k_0+k_1 & -(k_1+3k_0) & 0 & 2k_0 \\ k_0+k_1 & 0 & -(k_1+3k_0) & 2k_0 \\ 0 & 2k_0 & 2k_0 & -4k_0 \end{pmatrix} \\ &\times \begin{pmatrix} f(+1,+1,t) \\ f(+1,-1,t) \\ f(-1,+1,t) \\ f(-1,-1,t) \end{pmatrix}. \end{aligned} \quad (6)$$

The elements of the  $4 \times 4$  matrix on the right-hand side are obtained by counting all possible ways to enter a state from every other state, and all possible ways to leave a state. For

an  $N$ -segment-long probe Eq. (6) can be written in general form as

$$\frac{d\mathbf{f}}{dt} = M\mathbf{f}, \quad (7)$$

where  $M$  is a  $2^N \times 2^N$  matrix and  $\mathbf{f}$  is a vector of length  $2^N$ . The solution to Eq. (7) is

$$\mathbf{f} = \exp(Mt)\mathbf{f}_0 \quad (8)$$

where  $\mathbf{f}_0$  is the initial state of  $\mathbf{f}$ .

To calculate  $\exp(Mt)$ , we first need to express  $M$  in a general form for an  $N$ -segment probe. We can rewrite  $M$  in terms of spin matrices and operators [1]. Here we use the operators  $\sigma_j^x$  and  $\sigma_j^z$ . When the operator  $\sigma_j^x$  acts on the vector  $|\mu\rangle$ , it produces a new vector  $|\mu'\rangle$  which is the same as vector  $|\mu\rangle$  except that the  $j$ th spin is changed. For example, if  $\mu_j=-1$  then  $\sigma_j^x|\mu\rangle=|\mu'\rangle$  where  $\mu'_j=+1$  and if  $\mu_j=+1$  then  $\sigma_j^x|\mu\rangle=|\mu'\rangle$  where  $\mu'_j=-1$ . When the operator  $\sigma_j^z$  (the diagonal operator) acts on  $|\mu\rangle$ , we get

$$\sigma_j^z|\mu\rangle = \mu_j|\mu\rangle. \quad (9)$$

In other words, the operator  $\sigma_j^z$  gives the value of the  $j$ th element of the state  $\mu$  (see [13] for the matrix forms of the operators  $\sigma_j^x$  and  $\sigma_j^z$  for the two-segment case).

The matrix  $M$  can be rewritten in terms of the operators  $\sigma_j^x$  and  $\sigma_j^z$  as

$$= -2k_0 \sum_j (I - \sigma_j^x) - \frac{1}{2}(k_1 - k_0) \sum_j (I - \sigma_j^z) \left( I + \frac{\sigma_{j-1}^z + \sigma_{j+1}^z}{2} \right) \quad (10)$$

where  $I$  is the identity matrix. Matrices  $I$ ,  $\sigma_j^x$  and  $\sigma_j^z$  are all  $2^N \times 2^N$  in size (see [13] for details on how to obtain this expression).

To obtain  $c(l,t)$  [Eq. (1)] in terms of  $M$ , we can express  $c(l,t)$  in terms of the conditional probability function [1]  $f(\mu,t|\nu,0)$  as

$$c(l,t) = \sum_{\mu,\nu} \mu_{j+l} \nu_j f(\mu,t|\nu,0) f_{eq}(\nu), \quad (11)$$

where  $f(\mu,t|\nu,0)$  is the probability of being in state  $\mu$  at time  $t$  given that the system was in state  $\nu$  at time zero, and  $f_{eq}$  is the equilibrium probability that the system is in state  $\nu$ , which is equal to  $1/2^N$ . The sum is carried out over all possible  $\mu$  and  $\nu$ , i.e., all possible states in the ensemble. From Eq. (8),  $f(\mu,t|\nu,0) = \langle \mu | \exp(Mt) | \nu \rangle$  since  $|\nu\rangle$  is the state at time 0. Substituting the expression for  $f_{eq}$  ( $=2^{-N}$ ) and  $f(\mu,t|\nu,0)$  in Eq. (11), we get

$$c(l,t) = \sum_{\mu,\nu} \mu_{j+l} \nu_j \langle \mu | \exp(Mt) | \nu \rangle 2^{-N}. \quad (12)$$

To express  $c(l,t)$  in terms of operators, we first define the state vector  $|0\rangle$  to represent the equilibrium state where all  $|\mu\rangle$  are equally likely, i.e., the states  $\mu_j=+1$  and  $\mu_j=-1$  are equally likely for all sites  $j$ . Since the forward rate and reverse rate are equal, every element in the  $|0\rangle$  vector has the value  $2^{-(1/2)^N}$ . Therefore, the vector  $|0\rangle$  can be expressed in terms of  $|\mu\rangle$  as

$$|0\rangle = 2^{-(1/2)N} \sum_{\mu} |\mu\rangle. \quad (13)$$

If we apply  $\sigma_j^z$  to the  $|0\rangle$  state, we effectively multiply each component of the  $|0\rangle$  state by the spin of the  $j$ th site. We call this an excitation of the  $j$ th site, and we define  $|1_j\rangle$  as a vector representing an excitation of the  $j$ th site. Mathematically,  $|1_j\rangle$  can be expressed as

$$|1_j\rangle = 2^{-(1/2)N} \sum_{\mu} \mu_j |\mu\rangle = \sigma_j^z |0\rangle. \quad (14)$$

Similarly, the vector  $|n_{i_1, i_2, \dots, i_n}\rangle$  represents an excitation of the  $i_n$ th site, followed by an excitation of an  $i_{n-1}$ th site, followed by an excitation of an  $i_{n-2}$ th site, and so on, where  $1 \leq n \leq N$ , and  $i_1, i_2, \dots, i_{n-1}$  and  $i_n$  are distinct, and their order of excitation is unimportant. The vector  $|n_{i_1, i_2, \dots, i_n}\rangle$  is defined mathematically as

$$|n_{i_1, i_2, \dots, i_n}\rangle = 2^{-(1/2)N} \sum_{\mu} \mu_{i_1} \cdots \mu_{i_n} |\mu\rangle = \sigma_{i_1}^z \cdots \sigma_{i_n}^z |0\rangle. \quad (15)$$

Since  $|1_{j+l}\rangle = 2^{-(1/2)N} \sum_{\mu} \mu_{j+l} |\mu\rangle$  and  $|1_j\rangle = 2^{-(1/2)N} \sum_{\mu} \mu_j |\mu\rangle$ , Eq. (12) reduces to

$$c(l, t) = \langle 1_{j+l} | \exp(Mt) | 1_j \rangle. \quad (16)$$

In obtaining a final expression for  $c(l, t)$  from Eq. (16), we will need to be able to calculate the action of  $M$  on  $|n_{i_1, i_2, \dots, i_n}\rangle$  [since later in the calculation of  $\exp(Mt)$  we will obtain states other than  $|1_i\rangle$ , such as  $|2_{i_1, i_2}\rangle$ ,  $|3_{i_1, i_2, i_3}\rangle$ ,  $|4_{i_1, i_2, i_3, i_4}\rangle$ , etc.]. To do this we break the matrix  $M$  in Eq. (10) into two parts,

$$M = H_0 + V, \quad (17)$$

where  $H_0$  is the first term  $[-2k_0 \sum_j (I - \sigma_j^x)]$  and  $V$  is the second term  $\{-1/2(k_1 - k_0) \sum_j (I - \sigma_j^x) [I + (\sigma_{j-1}^z + \sigma_{j+1}^z)/2]\}$ . This allows us to express the difference between  $k_1$  and  $k_0$  as a perturbation.

The action of  $M$  on  $|n_{i_1, i_2, \dots, i_n}\rangle$  is now obtained by adding the actions of  $H_0$  and  $V$  on  $|n_{i_1, \dots, i_n}\rangle$  together.  $H_0$  acting on  $|n_{i_1, \dots, i_n}\rangle$  gives (see [13])

$$H_0 |n_{i_1, \dots, i_n}\rangle = -4k_0 n |n_{i_1, \dots, i_n}\rangle. \quad (18)$$

Let us represent  $i_1, \dots, i_n$  by the set  $S_n$ . Thus  $|n_{i_1, \dots, i_n}\rangle$  can be denoted by  $|n_{S_n}\rangle$ . The operator  $V$  acting on  $|n_{S_n}\rangle$  gives

$$\begin{aligned} V |n_{S_n}\rangle &= -\frac{1}{2}(k_1 - k_0) \sum_j (I - \sigma_j^x) \left( I + \frac{\sigma_{j-1}^z + \sigma_{j+1}^z}{2} \right) |n_{S_n}\rangle \\ &= -\frac{1}{2}(k_1 - k_0) \left( 2n |n_{S_n}\rangle + \sum_{\substack{j \notin S_n \\ j \pm 1 \in S_n}} |(n+1)_{S_n \cup \{j\}}\rangle \right. \\ &\quad \left. + \sum_{\substack{j \in S_n \\ j \pm 1 \in S_n}} |(n-1)_{S_n \setminus \{j\}}\rangle \right), \end{aligned} \quad (19)$$

where the notation  $S_n \cup j$  represents a set  $\{i_1, \dots, i_n, j\}$  (when  $j \notin S_n$ ) and the notation  $S_n \setminus j$  represents a set  $\{i_1, \dots, i_n\}$  without element  $j$  (when  $j \in S_n$ ) (see [13]).

Adding the expressions for  $H_0 |n_{S_n}\rangle$  [Eq. (18)] and  $V |n_{S_n}\rangle$  [Eq. (19)], we get

$$\begin{aligned} M |n_{S_n}\rangle &= -(3k_0 + k_1)n |n_{S_n}\rangle - \frac{1}{2}(k_1 - k_0) \left( \sum_{\substack{j \notin S_n \\ j \pm 1 \in S_n}} |(n+1)_{S_n \cup \{j\}}\rangle \right. \\ &\quad \left. + \sum_{\substack{j \in S_n \\ j \pm 1 \in S_n}} |(n-1)_{S_n \setminus \{j\}}\rangle \right). \end{aligned} \quad (20)$$

Having established the action of  $M$  on  $|n_{S_n}\rangle$  we can obtain an expression for  $\exp(Mt)$  in Eq. (16). Using the Baker-Hausdorff expansion [4] (see [13] for the expansion) to calculate  $\exp(Mt)$ , the expression for  $c(l, t)$  [Eq. (16)] becomes

$$= \langle 1_{j+l} | \exp(M_D t) \exp(M_N t) \left( I - \frac{1}{2} [M_D, M_N] + \cdots \right) | 1_j \rangle, \quad (21)$$

where  $M_D$  is the diagonal part of the matrix  $M$ ,

$$M_D |n_{S_n}\rangle = -(3k_0 + k_1)n |n_{S_n}\rangle, \quad (22)$$

$M_N$  is the off-diagonal part of the matrix  $M$ ,

$$\begin{aligned} M_N |n_{S_n}\rangle &= -\frac{1}{2}(k_1 - k_0) \left( \sum_{\substack{j \notin S_n \\ j \pm 1 \in S_n}} |(n+1)_{S_n \cup \{j\}}\rangle \right. \\ &\quad \left. + \sum_{\substack{j \in S_n \\ j \pm 1 \in S_n}} |(n-1)_{S_n \setminus \{j\}}\rangle \right), \end{aligned} \quad (23)$$

and  $[M_D, M_N]$  is the commutator of  $M_D$  and  $M_N$ . Using Eq. (21), we get expressions for  $c(0, t)$ ,  $c(1, t)$ , and  $c(2, t)$  as shown in Eqs. (24)–(26). We can get expressions for  $c(3, t)$ ,  $c(4, t)$ ,  $c(5, t)$ , etc., using higher-order terms in the Baker-Hausdorff expansion and the Taylor series expansion for the term  $\exp(M_N t)$  (see [13] for details)

$$\begin{aligned} c(0, t) &= \exp(-(3k_0 + k_1)t) \left[ 1 + \frac{t^2}{4}(k_1 - k_0)^2 - \frac{t^3}{12}(k_1 - k_0)^2 \right. \\ &\quad \times (3k_0 + k_1) + \frac{t^4}{16}(k_1 - k_0)^2 \left( \frac{(k_1 - k_0)}{2} + \frac{(3k_0 + k_1)}{3} \right) \\ &\quad \left. + \cdots \right], \end{aligned} \quad (24)$$

$$\begin{aligned} c(1, t) &= 2t^2 \exp(-(3k_0 + k_1)t) \left[ \frac{1}{8}(k_1 - k_0)^2 - \frac{t}{24}(k_1 - k_0)^2 \right. \\ &\quad \times (3k_0 + k_1) + \frac{t^2}{48}(k_1 - k_0)^2 \left( (k_1 - k_0)^2 + \frac{(3k_0 + k_1)^2}{2} \right) \\ &\quad \left. + \cdots \right], \end{aligned} \quad (25)$$

$$c(2, t) = \frac{1}{96} t^4 (k_1 - k_0)^4 \exp(-(3k_0 + k_1)t) + \cdots \quad (26)$$

Clearly, the expressions for  $c(0, t)$ ,  $c(1, t)$ ,  $c(2, t)$  [Eqs.

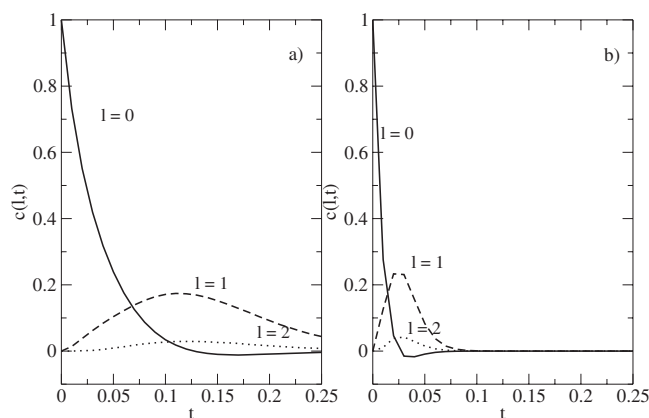


FIG. 2. A plot of  $c(l, t)$  vs  $t$  for  $l=0$  (solid),  $l=1$  (dashed), and  $l=2$  (dotted) at (a)  $k_1/k_0=30$  (b)  $k_1/k_0=150$ .

(24)–(26)] are dependent on the values of  $k_0$  and  $k_1$ . The ratio  $k_1/k_0$  is an indication of the extent of cooperativity of binding adjacent segments to their complementary target segments. To study the effect of varying values of  $k_1/k_0$  on  $c(l, t)$  we plot  $c(0, t)$  (solid line),  $c(1, t)$  (dashed line), and  $c(2, t)$  (dotted line) [Eqs. (24)–(26)] in Fig. 2 for  $k_1/k_0=30$  and  $k_1/k_0=150$ . A value of 1 for  $c(l, t)$  indicates strong correlation and a value of 0 indicates no correlation. The  $c(0, t)$ ,  $c(1, t)$ , and  $c(2, t)$  in Fig. 2(a) decay to 0 much slower than those in Fig. 2(b). In addition, the maximum values of  $c(1, t)$  and  $c(2, t)$  are lower in Fig. 2(a) than in Fig. 2(b). This is because when  $k_1/k_0$  is high, the cooperativity of binding adjacent segments to their complementary target segments is high and the probe binds to the target in a fast zipping mechanism. The fast zipping mechanism causes the correlation functions for the neighboring segments ( $l=1, 2, \dots$ ) to have a sharp increase to a maximum at short times followed by a sharp decay to zero as seen for  $k_1/k_0=150$  in Fig. 2(a). Instead at  $k_1/k_0=30$  the consecutive binding of adjacent probe segments along the probe molecule occurs slowly. The expressions for  $c(0, t)$ ,  $c(1, t)$ , and  $c(2, t)$  [Eqs. (24)–(26)] can be used to fit the time correlation results from stochastic or deterministic simulations. Such a fit would allow us to obtain values of  $k_1/k_0$  and hence provide a better understanding of how neighboring segments cooperate while binding to their complementary target segments. This in turn will help us better explain the mechanism of probe-target binding.

Having an expression for  $c(l, t)$  has some major implications. Time correlation functions have proven useful in explaining the dynamics in physical systems, such as the relaxation of polymer chains in melts [5], segmental dynamics as a function of position along polymer chains [6], local rotational and vibrational movement of residues in proteins [7], domain growth in liquid crystals [8], and propagation of damage in elastic-plastic structures [9]. An analytical expression for the time correlation function, like the one we have obtained in this work, could be compared to the segmental dynamics data obtained by NMR, neutron spin echo spectroscopy, or time-resolved spectroscopy. Furthermore, since the model we have used (chain of spins) is simple and general, our time correlation function  $c(l, t)$  could be used to study not just conformational changes in polymers but the

dynamics of any system that can be represented as an Ising-like chain, for example, bistable magnetic nanowires. Bistable magnetic nanowires are one-dimensional Ising-like chains containing finite-size segments that have one of two spins. The magnetization of the nanowires can be completely reversed, starting from a saturated configuration where all the segments are of the same spin to a final state where the spins of all the segments are flipped. This can happen through either a sequence of single spin flips or a collective flipping of multiple segments. Vindigni *et al.* [10] have found that the magnetic nanowires can present a faster switching if there is a collective reversal of the nanowire segments. This collective reversal can be related to our model when cooperativity between segments is high, i.e.,  $k_1/k_0$  is high. Our results show that at high values of  $k_1/k_0$  all the segments along the polymer flip from the unbound state to the bound state in a rapid zipping fashion.

While this work captures the basic physics of the zipping phenomena in Ising-like chains, this can also serve as the first step toward developing a more comprehensive theory capable of accurately describing DNA hybridization. It is essential to point out the limitations of our simple deterministic model for studying DNA hybridization. A major assumption in our model is that the rate constants for the reverse and forward reactions are equal. The reasoning behind this is to ensure that the probe can access all states with equal probability at equilibrium, and also to ensure that the matrix  $M$  is Hermitian. In the case of DNA hybridization, the rate constants for binding and unbinding would be equal only at temperatures close to the melting temperature. An experimental study pertaining to the kinetics of DNA hybridization [11] suggests that, at the beginning of a DNA double helix formation, the reaction starts with two or three nucleotides on a single strand binding and unbinding to their complementary nucleotides on another strand in rapid equilibrium. The critical intermediate having two or three bound nucleotides on the double strand would rapidly unbind to form separate single strands, rather than react to form a complete DNA double-stranded helix. The equal forward and reverse rate constants in our work could represent this early kinetics of DNA helix formation. The experimental work further states that, when the critical intermediate adds another pair of bound nucleotides, it forms a helix nucleus which then zips up to form a complete double-stranded helix. The rate coefficients of forward (binding) and reverse (unbinding) reactions during the DNA zipping process have been determined experimentally by Craig *et al.* [11]. When the temperature is below the melting temperature of the DNA, the rate of binding of a nucleotide ( $k_{bind} \approx 10^7 \text{ mol}^{-1} \text{ s}^{-1}$ ) is 5–10 times faster than the rate of unbinding ( $k_{unbind} \approx 10^6 \text{ mol}^{-1} \text{ s}^{-1}$ ). Craig *et al.* found that with increasing temperature  $k_{bind}$  decreases and  $k_{unbind}$  increases. This suggests that our assumption of forward and reverse rate constants being equal would be valid at high temperatures such as the melting temperature of double-stranded DNA.

In our effort to move to a more complicated model for DNA hybridization, we plan to include some nontrivial equilibrium statistics, such as an energetic penalty for segments in the middle of the probe to get unbound when their neighboring segments stay bound. It is important to point out that



the current model is valid for zipping segments that are either on two separate polymers or rather distant on the same polymer. To include situations such as RNA or DNA hairpin loop formation, we will have to include additional conditions in our rate equations, such as the binding and unbinding of a segment where one of the neighboring segments is part of a hairpin loop. The rate constants for this transition would include  $k_c$  and  $k_o$ , the rate coefficients of hairpin closing and opening [12]. Information on these rate coefficients and their dependence on temperature is provided by Kuznetsov *et al.* [12], who have conducted rigorous kinetics measurements of the unwinding of a DNA hairpin. Another limitation of our work is the lack of experimental evidence to corroborate our results. This is because it is difficult to relate short-length

time correlation functions in such Ising-like chains to observable quantities. We are currently working on a mesoscale simulation model for kinetics of DNA hybridization, and we plan to use this simulation data in the future to establish a connection between experimentally measurable information and the parameters in the more complex theory.

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