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Helix or coil? Fate of a melting heteropolymer

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Abstract – We study the probability that a partially melted heteropolymer at the melting temperature will either melt completely or return to a helix state. This system is equivalent to the splitting probability for a diffusing particle on a finite interval that moves according to the Sinai model. When the initial fraction of melted polymer is g, the melting probability fluctuates between different realizations of monomer arrangements on the chain. For a fixed value of g, the melting probability distribution changes from unimodal to a bimodal as the strength of the disorder is increased.

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Thermally-induced helix-coil transitions in heteropolymers exhibit intriguing thermodynamic and kinetic features [1–8] that stem from, among other mechanisms, different intrinsic melting temperatures of the monomeric constituents, say, A and B, and *quenched* random distributions of monomers along the chain. Due to this randomness, an arbitrarily long A-rich helix region with a high local melting temperature can act as a barrier to hinder the melting of the entire chain into a random coil. As the temperature is raised, the nucleation of multiple coils may occur at distinct points along the condensed helical chain. Nevertheless, as considered in ref. [3], the simplified situation in which there is a single coil portion starting at a free end of the chain (fig. 1) highlights the essential physical role of randomness on melting kinetics.

In this letter, we focus on the case of a single coil and study the probability that a partially melted heteropolymer returns to its native helical state (and the complementary probability that the chain denatures). Our analysis is based on making an analogy, established in ref. [3], between the motion of the boundary point in a partially melted heteropolymer and a particle diffusing in a random potential —the Sinai model [9].

Let $E_+(Y)$ be the probability for a heteropolymer of (contour) length L that contains a partially melted segment of length Y to ultimately melt completely, while $E_-(Y) = 1 - E_+(Y)$ is the probability that this heteropolymer condenses into a helix. This melting probability is equivalent to the *splitting probability* $E_+(Y)$ that the boundary point (fig. 1) starts at Y and reaches L without ever reaching 0 (and correspondingly for $E_-(Y)$).

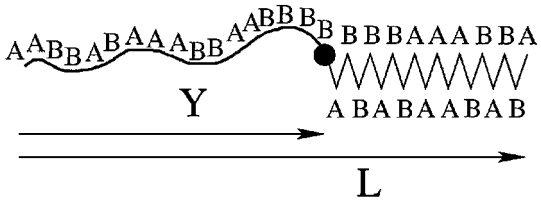

Fig. 1: Illustration of a partially melted heteropolymer with the interface between the melt (left) and helix (right) at Y.

For a random potential that corresponds to a heteropolymer, these splitting probabilities are different for each arrangement of monomers in the heteropolymer. One of our primary results is that these probabilities exhibit huge sample-specific fluctuations. Consequently, the average and the typical behaviors are completely different and neither is representative of the behavior of a single chain. Moreover, we show that the distribution of the splitting probabilities changes from a single peak centered around its most probable value for weak disorder, to double peaked, with most probable values close to 0 and 1 for sufficiently strong randomness. Thus much care is needed in the interpretation of experimental data of heteropolymer melting kinetics.

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Although the arrangement of monomers in a heteropolymer is typically correlated over a finite range, we make the simplifying assumption that such correlations are absent. The location of the equivalent boundary point between the coil and helix portions of the chain then diffuses in the interval $[0, L]$ in presence of a quenched and random position-dependent force $F(x)$, with

$$\begin{aligned} \langle F(x)\rangle &= f_0, \\ \langle F(x)F(x')\rangle - f_0^2 &= \sigma_F^2\,\delta(x-x'). \end{aligned} \tag{1}$$

The interpretation of f_0 and σ_F through the microscopic parameters has been presented in ref. [3]. Not going into details, which can be found in the original work [3], we just note that the mean force $f_0 > 0$ when the temperature T exceeds the melting heteropolymer temperature T_m (and $f_0 < 0$ for $T < T_m$), while σ_F is proportional to the difference in the melting temperatures for A and B homopolymers. We focus here on the case when temperature T is exactly equal to T_m, such that $f_0 = 0$ but σ_F remains finite.

Following the analogy with splitting probabilities, the probability that a homopolymer (no random potential) ultimately melts when a length Y is initially in a random coil state is [10]

$$E_+(Y) = \frac{1-e^{-vY/D}}{1-e^{-vL/D}} = \frac{1-z}{1-z^{L/Y}}, \tag{2}$$

where, for later convenience, we define $z \equiv e^{-vY/D}$. Here D is the diffusion coefficient and the velocity $v > 0$ for $T > T_m$ and $v < 0$ for $T < T_m$. For $T = T_m$, corresponding to $v = 0$, these splitting probabilities simplify to $E_+(Y) = 1 - E_-(Y) = g = \frac{Y}{L}$, the classical result for unbiased diffusion [10]. We now focus on the corresponding behavior for a heteropolymer at the melting temperature where the boundary point moves in the random potential defined by eq. (1).

We first present an effective-medium approximation for $\mathcal{P}(E_+(Y))$, akin to the optimal fluctuation method of Lifshitz [11], to describe the statistical features of the ultimate fate of a single chain. The basis of this approximation is to replace each realization of the Sinai model by an effective environment whose mean bias matches that of the Sinai model (fig. 2). In the effective medium, the distribution of bias velocities in the continuum limit is

$$P(v) = \frac{1}{\sqrt{2\pi\sigma_v^2}}\,\exp\left(-\frac{v^2}{2\sigma_v^2}\right). \tag{3}$$

Since there is a one-to-one connection between the bias in the effective model and the splitting probability $E_+(Y)$, we may now convert the distribution of bias velocities to the distribution of splitting probabilities by

$$\mathcal{P}(E_+) = P(v)\,\frac{\mathrm{d}v}{\mathrm{d}E_+}. \tag{4}$$

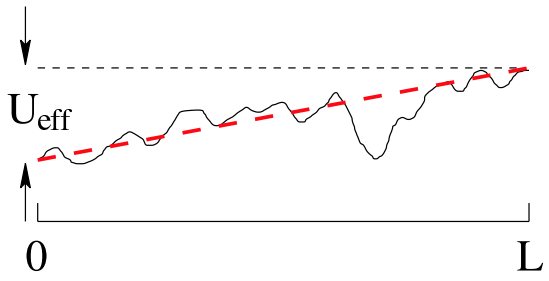

Fig. 2: (Color online) A typical realization of the potential in the continuum limit of the Sinai model (smooth curve) and the potential in the corresponding effective medium (thick dashed line).

To perform this transformation, we use eq. (2) to solve for v as a function of E_+ for fixed Y. This inversion is feasible only for $g = \frac{Y}{L} = \frac{1}{2}, \frac{1}{3}, \frac{1}{4}, \frac{1}{5}$, because solving a polynomial up to quartic order is involved. For the simplest case of a particle starting at the midpoint, $\frac{Y}{L} = \frac{1}{2}$, then eq. (2) becomes $E_+ = 1/(1+z)$. Inverting gives

$$\begin{aligned} v(E_+) &= \frac{2D}{L}\ln\left(\frac{E_+}{1-E_+}\right), \\ \frac{\mathrm{d}v}{\mathrm{d}E_+} &= \frac{2D}{LE_+(1-E_+)}. \end{aligned} \tag{5}$$

Substituting these results into eq. (3) and using eq. (4) gives,

$$\begin{aligned} \mathcal{P}(E_+) = &\frac{1}{\sqrt{2\pi\sigma_v^2}}\,\frac{2D}{LE_+(1-E_+)} \\ &\times \exp\left(-\frac{2D^2}{\sigma_v^2 L^2}\ln^2\left(\frac{E_+}{1-E_+}\right)\right). \end{aligned} \tag{6}$$

We now relate the velocity variance σ_v^2 to the disorder in the Sinai model. For Sinai disorder, the mean-square potential difference between two points separated by a distance L is (fig. 2)

$$U_{\rm eff}^2 \equiv \int_0^L\int_0^L \langle F(x')F(x'')\rangle \mathrm{d}x'\mathrm{d}x'' = \sigma_F^2\,L. \tag{7}$$

Thus there is a net force $F_{\rm eff} \sim U_{\rm eff}/L \sim \sigma_F/\sqrt{L}$, from which we infer the velocity scale $\sigma_v \sim \sigma_F/(\gamma\sqrt{L})$, where γ is the viscosity coefficient. We then use the fluctuation-dissipation relation $D = kT/\gamma$ [12] to rewrite eq. (6) as

$$\mathcal{P}(E_+) = \frac{1}{\sqrt{\pi\alpha}}\,\frac{1}{E_+(1-E_+)}\,\exp\left(-\frac{1}{\alpha}\ln^2\left(\frac{E_+}{1-E_+}\right)\right), \tag{8}$$

with

$$\alpha = \sigma_F^2\,L/[2(kT)^2] \tag{9}$$

a dimensionless measure of the strength of the Sinai potential relative to thermal fluctuations. The important feature of the splitting probability distribution in eq. (8)

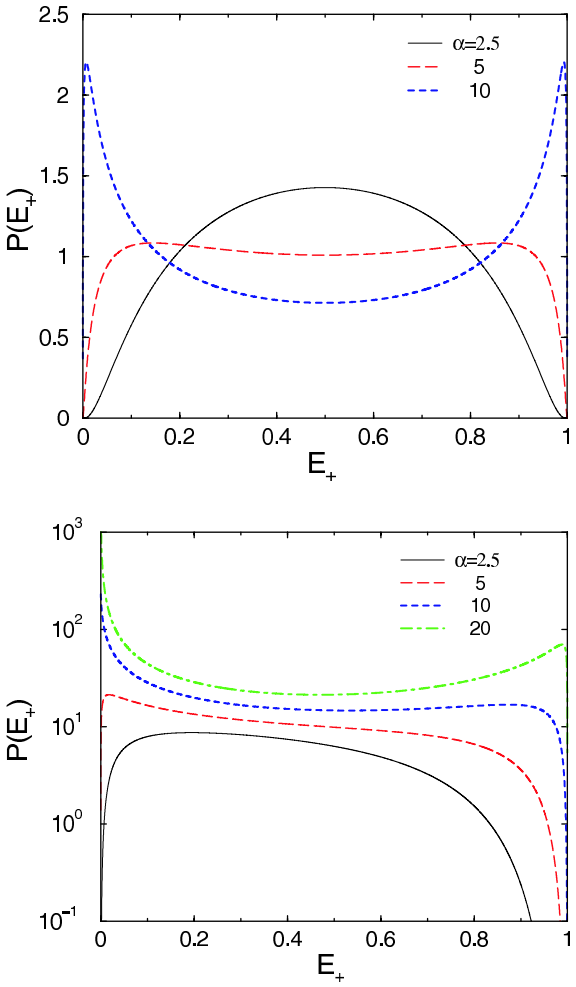

Fig. 3: (Color online) Effective-medium prediction for the splitting probability distribution for the Sinai chain when the particle starts at $Y = L/2$ (top) and $Y = L/3$ (bottom, logarithmic scale).

is its change from unimodal to bimodal as the disorder parameter α increases past $\alpha_c = 4$ (fig. 3).

In the critical case $\alpha = \alpha_c$ the maximum at $E_+ = 1/2$ is quartic and the distribution is close to uniform for $0.2 < E_+ < 0.8$. Thus any value of E_+ in this range is nearly equally probable. For α exceeding α_c, two maxima emerge continuously at $E_+ = \frac{1}{2}(1 \pm \sqrt{3(\alpha - \alpha_c)}/3)$. Curiously, although the disorder-average value $\langle E_+ \rangle = 1/2$ for $\alpha > \alpha_c$, the probability distribution has a minimum at $E_+ = 1/2$. In this strong disorder limit, the underlying mechanism for the bimodality of the distribution is that a typical realization of the environment has a net bias (see fig. 2) so that the splitting probability is either close to zero or to one.

For $Y = \frac{L}{3}$, a similar calculation gives the splitting probability distribution shown in fig. 3. For weak disorder, the splitting probability is peaked at a point close to the value $\frac{1}{3}$ that arises in the case of no disorder. When α is sufficiently large, the splitting probability has peaks near 0 and 1, corresponding to strong disorder where a typical configuration has an overall net bias. The intermediate regime of α gives the strange situation in which there is a peak at one extremum but not the other.

For a general starting point, the inversion $v = v(E_+)$ and thus the form of $\mathcal{P}(E_+)$ can be determined asymptotically in the limits $|vL/D| \to \infty$. For $vL/D \to -\infty$, $z \to +\infty$, and eq. (2) becomes $E_+ \sim z^{-(L-Y)/Y}$. Solving for $v(E_+)$ and $\frac{dv}{dE_+}$ and using these results in eq. (4), the splitting probability distribution starting from $Y \equiv gL$ is

$$\mathcal{P}(E_+) = \frac{1}{\sqrt{4\pi\alpha}} \frac{1}{(1-g)E_+} \exp\left(-\frac{\ln^2 E_+}{4\alpha(1-g)^2}\right). \quad (10)$$

As α is varied, this distribution changes from having a peak at the most probable value of E_+ to a peak at $E_+ = 0$. In the complementary limit $vL/D \to +\infty$, corresponding to $z \to 0$ and $E_+ \to 1$, the distribution is again eq. (10), but with $g \to 1 - g$ and $E_+ \to 1 - E_+$.

We now give an exact solution for the splitting probabilities that qualitatively substantiates the heuristic results given above. Consider the Fokker-Planck for the probability distribution for a particle that moves in the Sinai potential,

$$\frac{\partial}{\partial t} P = D\left[\frac{\partial^2}{\partial x^2} P - \beta \frac{\partial}{\partial x}(F(x)P)\right], \quad (11)$$

where $\beta = 1/kT$ and $P(x,t)\,dx$ is the probability that the particle is in the range $[x, x + dx]$ at time t and $F(x)$ is the force at x.

Suppose that particles are injected at a constant rate at Y to maintain a fixed concentration $P(Y) = 1$ when absorbing boundary conditions at $x = 0$ and $x = L$ are imposed. Then the stationary solution to the Fokker-Planck equation is

$$P(x) = e^{\beta \mathcal{F}_Y(x)} \left[1 - \frac{\int_Y^x \exp[-\beta \mathcal{F}_Y(x)]\,dx}{\int_Y^L \exp[-\beta \mathcal{F}_Y(x)]\,dx}\right], \quad (12)$$

for $x \geqslant Y$, while for $x \leqslant Y$ one has

$$P(x) = e^{\beta \mathcal{F}_Y(x)} \left[1 - \frac{\int_Y^x \exp[-\beta \mathcal{F}_Y(x)]dx}{\int_Y^0 \exp[-\beta \mathcal{F}_Y(x)]\,dx}\right], \quad (13)$$

where $\mathcal{F}_Y(x) \equiv \int_Y^x dx' F(x')$.

From the steady current

$$J = -D\left[\frac{\partial}{\partial x} P - \beta(F(x)P)\right], \quad (14)$$

the splitting probabilities $E_\pm(Y)$ are simply

$$E_-(Y) = \frac{\tau_+}{\tau_- + \tau_+}, \qquad E_+(Y) = \frac{\tau_-}{\tau_- + \tau_+}, \quad (15)$$

where $\tau_\pm = 1/J_\pm$, with $J_\pm$ being the flux to the boundaries at 0 and L, respectively. Thus $\tau_\pm$ define the "resistance" of a finite interval with respect to passage across the two boundaries and are given explicitly by

$$\begin{aligned} \tau_- &= \int_0^Y e^{-\beta \mathcal{F}_0(x)}\, \mathrm{d}x, \\ \tau_+ &= \int_Y^L e^{-\beta \mathcal{F}_Y(x)}\, \mathrm{d}x. \end{aligned} \tag{16}$$

We emphasize that the force integrals $\mathcal{F}$ are *independent* variables in each integrand so that τ_- and τ_+ are also *independent* random variables.

The quantities defined in eq. (16) are the continuous-space counterparts of Kesten variables [13] that play an important role in many stochastic processes. For example, negative moments of τ describe the positive moments of a steady diffusive current in a finite Sinai chain [14–18]. A surprising feature is that the disorder-average currents $J_\pm$ scale with system length L as $L^{-1/2}$ and are much larger than Fickian which scale as L^{-1} in homogeneous environments. Thus Sinai chains have an anomalously high conductance, despite the fact that diffusion is logarithmically confined [9], and positive moments of τ grow as $e^{\sqrt{L}}$ [14–18].

Let $\Psi_-(\tau_-)$ and $\Psi_+(\tau_+)$ denote the distribution functions of the random variables τ_- and τ_+, respectively. Then the moment generating function of the splitting probability $E_+(Y)$ can be written as

$$\langle e^{-\lambda E_+}\rangle = \int_0^\infty\!\!\int_0^\infty \Psi_-(\tau_-)\Psi_+(\tau_+)\, e^{-\lambda \tau_-/(\tau_-+\tau_+)}\, \mathrm{d}\tau_-\mathrm{d}\tau_+. \tag{17}$$

Integrating over $\mathrm{d}\tau_+$, we formally change the integration variable from τ_+ to E_+ to give

$$\langle e^{-\lambda E_+}\rangle = \int_0^1 \frac{\mathrm{d}E_+}{E_+^2} e^{-\lambda E_+} \int_0^\infty \tau\, \mathrm{d}\tau\, \Psi_-(\tau)\, \Psi_+(r\tau), \tag{18}$$

where $r = E_-/E_+$. From this expression we may read off the following form for the probability density $\mathcal{P}(E_+)$ of the splitting probability $E_+(Y)$:

$$\mathcal{P}(E_+) = \frac{1}{E_+^2} \int_0^\infty \tau\, \mathrm{d}\tau\, \Psi_-(\tau)\, \Psi_+(r\tau). \tag{19}$$

For a random potential without a net bias, $f_0 = 0$, the distribution $\Psi_-(\tau)$ is given by (see, *e.g.*, ref. [18]):

$$\begin{aligned} \Psi_-(\tau) = \frac{\sqrt{2}}{\pi\beta\sigma_F} \frac{1}{\alpha_-^{1/2}\tau^{3/2}} \int_{-\infty}^\infty \mathrm{d}u\, \mathrm{ch}\, u\, \cos\left(\frac{\pi u}{\alpha_-}\right) \\ \times \exp\left(\frac{\pi^2}{4\alpha_-} - \frac{u^2}{\alpha_-} - \frac{2\mathrm{ch}^2 u}{\beta^2\sigma_F^2\tau}\right), \end{aligned} \tag{20}$$

where $\alpha_- = \beta^2\sigma_F^2 Y/2$ and $\mathrm{ch}\, u$ denotes the hyperbolic cosine. Then $\Psi_+(\tau)$ is obtained from eq. (20) by replacing $\alpha_- \to \alpha_+ = \beta^2\sigma_F^2(L-Y)/2$.

Substituting $\Psi_-(\tau)$ and $\Psi_+(\tau)$ into eq. (19) and integrating over $\mathrm{d}\tau$, we find

$$\begin{aligned} \mathcal{P}(E_+) = \frac{1}{\pi^2\sqrt{\alpha_-\alpha_+E_+E_-}} \int_{-\infty}^\infty\!\!\int_{-\infty}^\infty \mathrm{d}u_1\, \mathrm{d}u_2 \\ \times \frac{\mathrm{ch}\, u_1\, \mathrm{ch}\, u_2}{E_-\mathrm{ch}^2 u_1 + E_+\mathrm{ch}^2 u_2} \cos\left(\frac{\pi u_1}{\alpha_-}\right) \cos\left(\frac{\pi u_2}{\alpha_+}\right) \\ \times \exp\left(\frac{\pi^2}{4\alpha_-} + \frac{\pi^2}{4\alpha_+} - \frac{u_1^2}{\alpha_-} - \frac{u_2^2}{\alpha_+}\right). \end{aligned} \tag{21}$$

After cumbersome but straightforward manipulations, one of the integrals can be performed to recast the splitting probability distribution as

$$\begin{aligned} \mathcal{P}(E_+) = \frac{1}{\pi\sqrt{\alpha_-\alpha_+E_+E_-}} \frac{1}{E_-} \int_{-\infty}^\infty \mathrm{d}u\, \frac{\mathrm{ch}\, u}{\mathrm{ch}\, \eta} \\ \times \cos\left(\frac{\pi u}{\alpha_+}\right) \exp\left(\frac{\pi^2}{4\alpha_+} - \frac{u^2}{\alpha_+} - \frac{\eta^2}{\alpha_-}\right), \end{aligned} \tag{22}$$

where

$$\eta = \mathrm{sh}^{-1}\left(\frac{\mathrm{ch}\, u}{\sqrt{r}}\right). \tag{23}$$

To extract the asymptotic behavior of $\mathcal{P}(E_+)$ in the limits $E_+ \to 1$ and $E_+ \to 0$ note that because the integrand in eq. (22) contains an oscillating cosine term, only the behavior near $u = 0$ should matter. Thus assuming $\mathrm{ch}\, u \approx 1$ and expanding η^2 in a Taylor series in u up to second order,

$$\eta^2 = \ln^2 z_+ + \sqrt{E_+}\ln z_+\, u^2 + O\left(u^3\right), \tag{24}$$

we find the following asymptotic representation for $E_+ \to 1$:

$$\begin{aligned} \mathcal{P}(E_+) \sim \frac{\left(\alpha_- + \alpha_+\sqrt{E_+}\ln z_+\right)^{-1/2}}{\sqrt{\pi E_+}\; E_-} \\ \times \exp\left(-\frac{\ln^2 z_+}{\alpha_-} + \frac{\pi^2\sqrt{E_+}\ln z_+}{4\left(\alpha_- + \alpha_+\sqrt{E_+}\ln z_+\right)}\right), \end{aligned} \tag{25}$$

where $z_+ = (1+\sqrt{E_+})/\sqrt{E_-}$. This asymptotic form agrees quite well with the exact result in eq. (22), not only when $E_+ \to 1$, but also for moderate values of E_+ (fig. 4). Similarly, we obtain the asymptotics of $\mathcal{P}(E_+)$ for $E_+ \to 0$ merely by interchanging all subscripts $\pm$ to $\mp$ in eq. (25), and z_- is obtained from z_+ by interchanging the subscripts $\pm$ to $\mp$ in the latter.

When $E_+ \ll 1$ or $1 - E_+ \ll 1$, respectively, eq. (25) reduces to

$$\mathcal{P}(E_+) \sim \sqrt{\frac{2}{\pi\alpha_\pm \ln\left(4/E_\mp\right)}} \frac{1}{E_\mp} \exp\left(-\frac{\ln^2\left(4/E_\mp\right)}{4\alpha_\mp}\right). \tag{26}$$

Our effective-medium result in eq. (8) resembles the above exact asymptotic form apart from logarithmic and numerical factors.

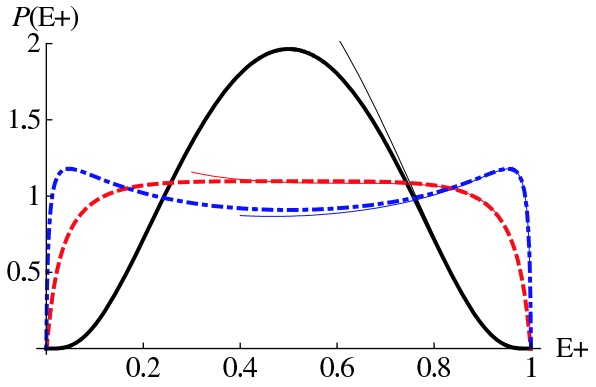

Fig. 4: (Color online) Exact distribution $\mathcal{P}(E_+)$, eq. (22), for $\alpha_- = \alpha_+ = 0.5$ (solid curve), $\alpha_\pm = 1.63$ (dashed curve), and $\alpha_\pm = 2.4$ (dash-dotted curve). Thin lines are the corresponding asymptotic results of eq. (25).

In summary, by making an analogy to first passage on a Sinai chain, we find that the evolution of a partially melted random heteropolymer at the melting temperature is controlled by the arrangement of monomers along the chain. Each heteropolymer realization has a unique kinetics and unique final fate that is not representative of the average behavior of an ensemble of such polymers. A related lack of self-averaging was recently found in anomalous diffusion [19,20].

* * *

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REFERENCES

[1] Wartell R. M. and Montroll E. W., *Adv. Chem. Phys.*, **22** (1972) 129.
[2] Poland D. and Scheraga H. R., *Theory of Helix Coil Transition in Biopolymers* (Academic, New York) 1970.
[3] de Gennes P. G., *J. Stat. Phys.*, **12** (1975) 463.
[4] Azbel M. Ya., *Phys. Rev. A*, **20** (1979) 1671.
[5] Scheraga H. A., Vila J. A. and Ripoll D. R., *Biophys. Chem.*, **101-102** (2002) 255.
[6] Krueger A., Protozanova E. and Frank-Kamenetzkii M. D., *Biophys. J.*, **90** (2006) 3091.
[7] Hwa T., Marinari E., Sneppen K. and Tang L. H., *Proc. Natl. Acad. Sci. U.S.A.*, **100** (2003) 4411.
[8] Ambjornsson T., Banik S. K., Krichevsky O. and Metzler R., *Phys. Rev. Lett.*, **97** (2006) 128105.
[9] Sinai Ya. G., *Theor. Probab. Appl.*, **27** (1982) 256.
[10] Redner S., *A Guide to First-Passage Processes* (Cambridge University Press, New York) 2001.
[11] Lifshitz I. M., Gredescul S. A. and Pastur L. A., *An Introduction to the Theory of Disordered Systems* (Wiley, New York) 1988.
[12] Gardiner C. W., *Handbook of Stochastic Methods* (Springer, New York) 2004.
[13] Kesten H., *Acta Math.*, **131** (1973) 207.
[14] Burlatsky S. F., Oshanin G., Mogutov M. and Moreau M., *Phys. Rev. A*, **45** (1992) 6955.
[15] Oshanin G., Mogutov M. and Moreau M., *J. Stat. Phys.*, **73** (1993) 379.
[16] Oshanin G., Burlatsky S. F., Moreau M. and Gaveau B., *Chem. Phys.*, **177** (1993) 803.
[17] Monthus C. and Comtet A., *J. Phys. I*, **4** (1994) 635.
[18] Monthus C., Comtet A. and Yor M., *J. Appl. Probab.*, **35** (1998) 255.
[19] Lubelski A., Sokolov I. M. and Klafter J., *Phys. Rev. Lett.*, **100** (2008) 250602.
[20] He Y., Burov S., Metzler R. and Barkai E., *Phys. Rev. Lett.*, **101** (2008) 058101.