Cyclization of a Polymer: A First Passage Problem for a Non-Markovian Process

I.M. Sokolov

Institut für Physik, Humboldt-Universität zu Berlin, Invalidenstr. 110, D-10115 Berlin, Germany

(Dated: March 22, 2002)

We discuss a problem of cyclization of a polymer molecule, which is an important example of reaction in a system showing strongly non-Markovian behavior on the timescales of interest. We show that the knowledge of the joint three-time probability distribution of the end-to-end distance is sufficient for the full description of the cyclization kinetics, so that the survival probability follows rigorously as a solution of the Volterra integral equation. The corresponding kinetics can easily be evaluated numerically. We moreover discuss how do some well-known approximations appear from this exact scheme due to decoupling.

Kinetics of reactions involving polymers (especially the luminescent energy transfer) has attracted much theoretical attention in the last decade (see e.g. [2,3,4,5,6,7,8]), due to experimental relevance and to a plenitude of applications. Cyclization of a polymer, or luminescence quenching in a system of a donor and acceptor attached to the ends of the polymer molecule belongs to the most complex problems in the field: It is a case of a diffusion-controlled reaction in a system exhibiting considerably non-Markovian behavior on the timescales of interest [2,3,4,5,6,7,8]. This non-Markovian behavior mirrors the essentially many-particle nature of the system. Even for the simplest situation, in which the polymer is modelled by a Rouse chain, i.e. the excluded volume effects and the hydrodynamical interactions between the monomers (“beads”) are neglected, the existing theoretical approaches fail to give an exact description of the situation and make additional physical assumptions. Thus, their domain of applicability is inevitably restricted. In what follows we give an exact solution for a special situation when the reaction takes place on a contact, and show that it only depends on three-time joint probability density of the end-to-end distance. We also discuss how do some standard approximations emerge.

The theoretical approaches typically start from the Langevin equation for the whole chain of \( N \gg 1 \) monomers, and try to reduce the overall dynamics to the manageable effective one. The simplest approach consists in describing the evolution of the end-to-end distance as an effective diffusion [5]. A more accurate Wilemski-Fixman theory (WF) [6] and its equivalents [4,8] express the reaction rates through the effective sink-sink correlation function and assume local equilibration. The comparison of theoretical results with the results of numerical simulations of the underlying dynamics [9] for the case when the reaction takes place with probability 1 whenever the ends of the chain (the monomers 0 and \( N \) ) approach each other at the distance \( a \), shows that the WF approach leads to systematic overestimate of the mean first contact time of the ends of the polymer, while neglecting the effective diffusion assumption leads to underestimates. The simulations in [8] started from the equilibrium (Boltzmann) initial distribution of the end-to-end distance \( r_0 \), with \( r_0 > a \). Another approach [8] is based on the reduction of the full equation of motion to the equation of motion of the end-to-end distance using the projection operator formalism. The corresponding equation is again approximate. We note that the methods of Refs. [3,4,6,8] are based on the Smoluchowski approach in the theory of diffusion-controlled reactions, in which the reaction probability follows from the solution of the full or reduced diffusion equation.

In the case of the reaction taking place with probability 1 on contact, as discussed in Ref. [7], introducing a sink term in the exact or reduced Fokker-Planck equation (like in the WF theory or in Ref. [8]) is equivalent to posing an absorbing boundary condition \( P(r-a) = 0 \) (a ”black sphere”). Such problem can be reformulated as the first passage problem from the initial distance \( r = r_0 \) between the ends to \( r = a \) [3,8,7]. In the Markovian case, such first passage problem can be solved using an alternative approach [10] based on the renewal property; the idea stemming from Montroll and Weiss [10]. This approach can be generalized to the non-Markovian situation.

In what follows we concentrate on the solution of the initial-condition problem, not averaged over the initial positions. The reason is two-fold: First, the recent success of micromanipulation of polymers makes the situation experimentally relevant, while no theoretical predictions for the kinetic curves are available. Second, the initial condition problem renders clear the geometrical nature of standard approximations [3,4,8]. The results for the equilibrium initial condition can be obtained by additional numerical averaging.

Let us first note that the reaction process depends only on the single variable \( r \) so that the problem is essentially one-dimensional. Moreover, the trajectories of our process are continuous and nowhere differentiable, just like the trajectories of the usual Wiener process are (vide infra). Let us consider the relation between the distribution of the first passage time to a sphere of the radius \( r = a \) around the origin of the coordinates \( F(a, t \mid r_0, 0) \) and the conditional probability for the ends to be found at distance \( r \); If the trajectory starts at point \( r_0 \), and is found at \( r \) at time \( t \), it may have already visited \( r \) before, at some time \( t' < t \). Thus, the conditional probability to
be at \( r \) at time \( t \), provided the particle started at \( r_0 \) at 
\( t = 0 \), \( G(r,t \mid r_0, t_0) \), is given by the following equation:
\[
G(r,t\mid r_0,0) = \delta(r - r_0)\delta(t) 
+ \int_0^t F(r,t'\mid r_0,0)G(r,t\mid r,t';r_0,0)dt',
\]
where \( G(r,t \mid r,t';r_0,0) \) is the conditional probability to
be at \( r \) at time \( t \), provided \( r \) was visited earlier at time \( t' \)
and that the particle started at \( r_0 \) at \( t = 0 \). This equa-
tion is essentially the definition of the first passage time
distribution and holds for all processes with continuous
trajectories, whether Markovian or not. For a Marko-
vinian process the conditional probability \( G(r,t \mid r_0,0) \)
is a Green’s function, and \( G(r,t \mid r,t';r_0,0) \) depends only
on the latest the arguments to the right of the line, so
that \( G(r,t \mid r,t';r_0,0) \equiv G(r,t \mid r,t') \). In this case, our
Eq. [1] reduces to a well-known renewal equation for the
first-passage time \( [1] \). If the particle definitely does not
start at \( r_0 = r \), the \( \delta \)-functional term can be omitted.

According to the Bayes formula, \( G(r,t \mid r_0,0) = 
P(r,t \mid r,t';r_0,0)/P(r_0,0) \) and \( G(r,t \mid r,t';r_0,0) = 
P(r_0,0)/P(r_0,0) \) (where \( P(r_0,0), P(r,t \mid r,t';r_0,0) \)
and \( P(r_0,0) \) are the one-, two-and three-time joint probability
distributions. The corresponding one-dimensional distributions as functions
of \( r \) can be expressed as integrals of the overall joint
probabilities over the surface of the sphere of radius
\( r \), so that \( P(r,t \mid r_0,t_0) = \int_{S} dsP(r,t; r_0,t_0) \) and
\( P(r,t \mid r,t';r_0,0) = \int_{S} \int_{S} dsds'P(r,t; r,t';r_0,0) \), so that
the overall equation reads
\[
\int_{S} dsP(r,t; r_0,0) = 
\int_{0}^{t} F(r,t' \mid r_0,0)\int_{S} \int_{S} dsds'P(r,t; r,t';r_0,0)
\int_{S} \int_{S} dsds'P(r,t; r,t';r_0,0)dt',
\]
where \( |r_0| > r \). It is reasonable to rewrite this equation in
the following form:
\[
\int_{0}^{t} F(r,t' \mid r_0,0)Q(t,t',r_0,0)dt' = 1,
\]
with the kernel
\[
Q(t,t',r_0) = \frac{\int_{S} \int_{S} dsds'P(r,t; r,t';r_0,0)P(r_0,0)
\int_{S} \int_{S} dsds'P(r,t; r,t';r_0,0)}{
[\int_{S} \int_{S} dsds'P(r,t; r,t';r_0,0)][\int_{S} \int_{S} dsds'P(r,t; r,r_0,0)].
\]
This is an exact equation expressing the pdf of first pas-
sage time through the three-time joint probability distribu-
tion of the end-to-end distance. As stated, we concen-
trate on the initial value problem and discuss the distribu-
tion of the first passage times as depending on \( r_0 \).

Note that for the Rouse chain and many other so-called
generalized Gaussian structures \( [1] \) the random process
describing temporal changes of the distance between each
two beads is Gaussian, since it is a weighted sum of many
Gaussian random variables describing the uncorrelated
displacements of beads. Thus, for example, the three-
time joint probability distribution is
\[
P(r,t \mid r,t';r_0,0) = \frac{(2\pi)^{-n/2}}{\sqrt{\det A}} \exp \left(-\frac{1}{2}R\hat{A}^{-1}R\right),
\]
where the vector \( R \) is a \( n \)-component vector
\((x,y,z,x',y',z',x_0,y_0,z_0)\) and the covariance matrix
\( \hat{A} = [(R_0 R_0)] \) consists of \( n \) diagonal blocks:
\[
\hat{A} = 
\begin{pmatrix}
D(0) & D(t-t') & D(t) \\
D(t-t') & D(0) & D(t') \\
D(t) & D(t') & D(0)
\end{pmatrix}
\]
(6)
where \( \hat{D}(t) \) is a diagonal matrix \( \hat{D}(t) = \hat{I}\phi(t) \) (\( \hat{I} \) is a unit matrix).
The function \( \phi(t) \) is a relaxation function of the
structure, \( \phi(t) = \langle x(t)x(0) \rangle \). The corresponding
two-point distributions read
\[
P(r,t \mid r_0,0) = \frac{(2\pi)^{-3}}{\sqrt{\det B}} \exp \left(-\frac{1}{2}R\hat{B}^{-1}R\right)
\]
(7)
with  
\[
\hat{B} = 
\begin{pmatrix}
D(0) & D(t) & D(t) \\
D(t) & D(0) & D(t) \\
D(t) & D(t) & D(0)
\end{pmatrix}
\]
(8)
and the one-point density reads \( P(r_0,0) = 
[2\pi\phi(0)]^{-3/2} \exp \left[-\left(r_0^2/2\phi(0)\right)\right] \).

The integrals over the two-point functions, say
\( \int_{S} \int_{S} dsds'P(r,t; r_0,0) \), can be evaluated analytically. Taking the
z-axis to follow the direction of \( r_0 \) one gets (r=a):
\[
\int_{S} \int_{S} dsds'P(r,t; r_0,0) = 
\frac{2a^2}{\pi} \frac{\sin[\frac{a\phi(t)}{\phi(0) - \phi(0)}]}{\phi(0) - \phi(0)}.
\]
(9)
Let us now consider the three-time pdf
\( \int_{S} \int_{S} \int_{S} dsdsds'P(r,t; r,t';r_0,0) \). Taking the point \( r_0 \)
to lay on the z-axis and the end-point \( r \) to have a zero
y-coordinate, the integrals over the azimuthal angles
can be performed analytically, so that the corresponding
distribution reduces to
\[
P(r,t \mid r,t';r_0,0) = \frac{a^4}{(2\pi)^5/2A^{3/2}\phi(\phi) \times}
\times \exp \left[-\frac{a^2(2\phi_0 - \phi_2 - \phi_3 + r_0^2\phi_0^2 - \phi_1^2)}{2A\phi(\phi)}\right] \times
\times \int_{0}^{\pi} \int_{0}^{\pi} \int_{0}^{\pi} I_0 \left[a^2\sin\psi\sin\theta(\phi(\phi_0 - \phi_2\phi_3)\right] A(\phi) \times
\times \exp [f(a,r_0,\{\phi\})/A(\psi)] A(\psi)\sin\sin\theta d\phi d\theta d\psi,
\]
where \( \theta \) and \( \psi \) are the corresponding polar angles. Here
\( A(\phi) = \phi_0^3 + 2\phi_1\phi_2\phi_3 - \phi_0(\phi_2^2 + \phi_2^2 + \phi_3^2) \), \( I_0 \) is the modified
Bessel function, and
\[
f(a,r_0,\{\phi\}) = a^2\cos\psi\cos\theta(\phi_2\phi_3 - \phi_0\phi_1) + 
+ ar_0 [(\phi_1\phi_2 - \phi_0\phi_3) \cos \theta + (\phi_1\phi_3 - \phi_0\phi_2) \sin \theta].
\]
where $\phi_0 = \phi(0)$, $\phi_1 = \phi(t-t')$, $\phi_2 = \phi(t)$ and $\phi_3 = \phi(t')$. These forms are universal and apply to any Gaussian model, whether linear or branched chain, or a network.

Let us now turn to a special case of the Rouse chain. For long enough chain the time correlation function $\phi(t)$ can be approximated through

$$\phi(t) = \langle L^2 \rangle \frac{8}{\pi^2} \sum_{p} p^{-2} \exp(-\lambda_p t)$$

(12)

where for a Rouse chain the summation runs over the odd integers $p$ and $\lambda_p = p^2/\tau_R$ \cite{2}. In what follows we use the rms size of the chain $\langle L^2 \rangle^{1/2}$ and the Rouse time $\tau_R$ as length and time units, so that $r$ and $t$ are nondimensional. In these units we get $\phi(t) = \frac{8}{\pi^2} \sum_{n=0}^{\infty} (2n+1) \exp(-2(2n+1)^2t)$. This function is continuous in zero, so that $\langle [x(t) - x(0)]^2 \rangle = 2(1 - \phi(t))$ tends to zero for small $t$, which fact verifies the continuity of the trajectories necessary for our consideration. The Volterra equation can be then solved numerically by approximating the integral in Eq.(1) by a finite sum. This solution and the evaluation of the double integral, Eq.(11) in the kernel is performed using MATHCAD. The corresponding first-passage time distributions for different initial conditions are shown in Fig.1 for the initial distances $r_0 = 1, 2, 4$ and $8$ and for $a = 0.1$. The numerical accuracy of the results is around one per cent. We note that with decreasing the distance, the typical mean first passage time decreases very fast; the maximum of the curve corresponding to $r_0 = 1$ is at $t_{\text{max}} \sim 0.01$, and is not resolved on the scales of Fig.1. This effect is due to the small-scale motion corresponding to higher modes \cite{4,8} and mirrors the compact exploration of space by the chain’s end. On the other hand, the large-scale relaxation is mostly connected with the lowest mode, which is slow.

Let us now discuss the emergence of the Wilemski-Fixmann approximation. To do this we return to Eq.(2), now reading

$$\int_{S} ds P(r,t; r_0,0) \frac{\int_{S} ds' P(r',t'; r_0,0)}{P(r_0,0)} = \int_{0}^{t} F(r,t' | r_0,0) \int_{S} ds' P(r',t'; r_0,0) \int_{S} ds P(r,t; r_0,0) dt'$$

(14)

and average both sides over the equilibrium distribution of $r_0, P(r_0,0)$. We note that the function multiplying $F$ under the integral in the r.h.s. does not depend on $r_0$, so that only $F$ is averaged, giving rise to the averaged first-passage distribution $\bar{F}$, and that the average in the l.h.s. is a one-time marginal distribution, i.e. $\int_{S} ds P(r,t)$. Thus, the equation for $\bar{F}$ reads:

$$\int_{0}^{t} \bar{F} (r,t' | r_0,0) \frac{\int_{S} ds' P(r',t; r_0,0)}{\int_{S} ds P(r,t)} \int_{S} ds P(r',t') dt' = 1.$$  

(15)

Note that the process $r(t)$ is stationary we denote

$$\bar{F}(r,t) = F(r,t)$$

FIG. 1: The first passage time pdf’s for $a = 0.1$ and $r_0 = 1, 2, 4$ and $8$ (from left to right). The solid curves correspond to the solution of equation, Eq.(11) with the exact kernel, Eq.(8). The dotted lines (shown for $r_0 = 1, 2, 4$) correspond to the Wilemski-Fixmann approximation, Eq.(13), see text for details. The inset shows the case $a = 0.5$ and $r_0 = 2$, for which the WF-approximation ceases to perform reasonably.

\begin{align*}
\text{where } \phi_0 = \phi(0), \phi_1 = \phi(t-t'), \phi_2 = \phi(t) \text{ and } \phi_3 = \phi(t'). \text{ These forms are universal and apply to any Gaussian model, whether linear or branched chain, or a network.}
\end{align*}
\[ \int_S \int_S d\mathbf{s} ds' P(\mathbf{r}, t; \mathbf{r}', t') = C(t - t'). \]

Due to correlation decoupling at long time, \( \int_S d\mathbf{s} P(\mathbf{r}, t) \int_S d\mathbf{s}' P(\mathbf{r}', t') \) is exactly \( C(\infty) = C_\infty \), if the corresponding limit does not vanish. Thus, we can write

\[ \int_0^t \bar{F}(r, t' \mid x_0, 0) \frac{C(t - t')}{C(\infty)} dt' = 1. \quad (16) \]

Applying the Laplace transform to both sides of the equation, we get \( 1/u = \bar{F}(u)/\bar{C}(u) \), so that

\[ \bar{F}(u) = C_\infty / [uC(u)]. \quad (17) \]

Moreover, since \( C_\infty = \lim_{t \to \infty} C(t) \), for \( u \) small one has \( C(u) = C_\infty/u + A + ... \), with \( A = \lim_{u \to 0} (C(u) - C_\infty/u) \). Noting that the mean first passage time \( \bar{\tau} = \int_0^\infty tF(t)dt = -\frac{d}{du} \bar{F}(u)|_{u=0} \), one arrives at

\[ \bar{\tau} = C_\infty \left( \frac{1}{u^2} \frac{1}{C(u)} + \frac{1}{u} \frac{\bar{C}'(u)}{C^2(u)} \right)|_{u=0} = \frac{A}{C_\infty} = \int_0^\infty \left( \frac{C(t)}{C_\infty} - 1 \right) dt, \quad (18) \]

which is exactly Eq. (12) of Ref. [6]. The approach of Ref. [6] is an approximation of the same nature: It assumes that the random process \( r(t) \) is an Ornstein-Uhlenbeck process (the only one Gaussian Markovian process, the one with \( \phi(t) \simeq \exp(-\alpha t) \), with \( \alpha = 2/\tau_R \) [6]), for which Eq. (14) is exact. Compared to the WF-theory it contains an additional assumption, namely one of the effectively exponential relaxation of \( \phi \) and has typically a lower accuracy.

Compared to the general case, our solution applies to a rather special sink function ("black sphere", or a \( \delta \)-sink), but our derivation here is rigorous and much less technical than the original WF approximation, and can apply to a variety of cases where the approximation fails. Let us say a few words on the general sink function. In general, in the WF theory one has \( C(t - t') = \int_{c_1} \int_{c_2} d\mathbf{x} d\mathbf{x}' S(\mathbf{x})S(\mathbf{x}')P(\mathbf{r}, t; \mathbf{r}', t') \), where \( S(\mathbf{x}) \) characterizes the sink strength. Although such expressions have no immediate counterparts within the first passage time formalism, they can be obtained as mean-field approximations when one associates \( S(\mathbf{x}) \) with the density of absorbing regions in a problem where the absorbing boundary is corrugated or even not singly-connected. In this case, the corresponding surface integrals Eq. (13) are changed for the volume integrals weighted with the sink function.

The same approximation can be done, of course, also in a general non-Markovian form, Eqs. (14). The corresponding forms may be no more exact, but still take into account mode details of the process than WF ones do.

Let us summarize our findings. The cyclization of a polymer is an example of a diffusion-controlled reaction in a system exhibiting strongly non-Markovian behavior on the timescales of interest. Considering the reaction as a first-passage process, one is able to provide an exact equation governing the reaction probability. This equation can be readily solved numerically, giving the kinetic curves. We also discuss how the popular Wilemski-Fixman approximation emerges from the exact scheme as a pseudo-Markovian decoupling.

The partial financial support by the Fonds der Chemischen Industrie is gratefully acknowledged.

[1] S.F. Burlatsky, G.S. Oshanin, and A.V. Mogutov, Phys. Rev. Lett. 65, 3205 (1990); G. Oshanin, A. Blumen, M. Moreau, and S.F. Burlatsky, J. Chem. Phys. 103, 9864 (1995); T. Pálszegi, I.M. Sokolov and H. Kaufmann, Macromolecules 31, 2521 (1998); I.M. Sokolov, J. Mai and A. Blumen, J. Lumin., 76-77, 377 (1998); E.N. Bodunov, M.N. Berberan-Santos, J.M.G. Martinho, Chem. Phys. 274, 243 (2001)

[2] G. Srinivas, A. Yethiraj, and B. Bagchi, J. Chem. Phys. 114, 9170 (2001); J. Sung and S. Lee, J. Chem. Phys. 115, 9050 (2001); G. Srinivas, K.L. Sebastian, and B. Bagchi, J. Chem. Phys. 116, 7276 (2002); E.N. Bodunov, M.N. Berberan-Santos, J.M.G. Martinho, J. Lumin. 96, 269 (2002)

[3] G. Wilemski and M. Fixman, J. Chem. Phys. 60, 866 (1974); ibid. 878 (1974)

[4] M. Doi, Chem. Phys. 9, 455 (1975)

[5] A. Szabo, K. Schulten, and Z. Schulten, J. Chem. Phys. 74, 4350 (1980)

[6] P.G. de Gennes, J. Chem. Phys. 76, 3316 (1982)

[7] R.W. Pastor, R. Zwanzig, and A. Szabo, J. Chem. Phys. 105, 3878 (1996)

[8] T. Bandyopadhyay and S.K. Ghosh, J. Chem. Phys. 116, 4366 (2002)

[9] S. Redner, A Guide to First-Passage Processes, Cambridge Univ. Press, Cambridge, 2001

[10] E. Montroll and G.H. Weiss, J. Math. Phys. 6, 167 (1965)

[11] J.-U. Sommer and A. Blumen, J. Phys. A 28, 6699 (1995); H. Schiessel, Phys. Rev. E 57, 5775 (1998)

[12] M. Doi, S. F. Edwards, The Theory of Polymer Dynamics, Oxford Science Publ., Oxford, 1997.