The probability of an encounter of two Brownian particles before escape

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Abstract
We study the probability of meeting of two Brownian particles before one of them exits a finite interval. We obtain an explicit expression for the probability as a function of the initial distance between the two particles using the Weierstrass elliptic function. We also find the law of the meeting location. Brownian simulations show the accuracy of our analysis. Finally, we discuss some applications to the probability that a double-strand DNA break repairs in confined environments.

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Introduction
The problem of coalescence and clustering in an open space has been considered by Chandrasekar [1] (see also [6] for a review). Little work has been dedicated to the case of a competition between the coalescence of Brownian-independent particles and the possible escape at the boundary of a domain where the particles are absorbed. This situation is however reminiscent of many biophysical problems, for example, the probability of a correct repair of a broken DNA molecule inside the nucleus. One mode of repair is known as non-homologous end joining [5], which depends crucially on the initial distance between the two free DNA strands: either the branches meet or one of them can curl up before and then the probability of connecting is very low (almost zero). Here we consider the drastic simplification that the motion of the DNA molecule tip can be approximated as a one-dimensional Brownian motion (see the discussion).

We consider the motion of two independent Brownian particles $X_1(t)$ and $X_2(t)$ inside an interval $[a, b]$, with the following rules: when the two particles meet, they coalesce into a single one subjected to a Brownian motion. We compute the probability $P_M$ that the two particles meet before one of them hits the boundary of the interval and obtain an explicit
expression for the probability of the two particles clustering, as a function of the initial position. When the initial points are \( a < x_1 < x_2 < b \), we obtain that

\[
P_M(x_1, x_2) = \frac{-2}{\pi} \text{Im} \log \mathcal{P} \left( \frac{\omega(Z - a)}{L \sqrt{8}} \right),
\]

(1)

where \( \text{Im} \) is the imaginary part, \( \mathcal{P} \) is the Weierstrass elliptic function defined by equation (8), \( L = b - a \), \( Z = x_2 + \sqrt{-1}x_1 \) and

\[
\omega = \int_{1}^{+\infty} \frac{dx}{[x(x-1)]^{1/2}} = 5.244115106
\]

(2)

is a universal number defined by an elliptic integral. We further obtain the probability distribution of their meeting point. Finally, the analytical formulas are compared with Brownian simulations, where we gain the information about the variance. The role of the Weierstrass elliptic function is quite surprising here and really comes from the method of conformal mapping. We wonder if our result can be recovered from elementary probability arguments. A Brownian interpretation of an elliptic integral was given in [3].

**Formulation**

The dynamics of each particle is given for \( i = 1, 2 \) by

\[
dX_i = \sqrt{2D_f} \, dw_i,
\]

(3)

where \( D_f \) is the diffusion constant and \( w_1 \) and \( w_2 \) are two Brownian motions of unit variance. We are interested in the probability \( P_M \) that the two particles meet before one of them exits the interval \([a, b]\). If we consider the two random times

\[
\tau_1 = \inf\{t > 0 \mid X_1(t) = a \text{ or } X_2(t) = b, X_1(0) = x_1 \text{ and } X_2(0) = x_2, x_1 < x_2\}
\]

\[
\tau_2 = \inf\{t > 0 \mid X_1(t) = X_2(t), X_1(0) = x_1 \text{ and } X_2(0) = x_2, x_1 < x_2\}
\]

then for \( x = (x_1, x_2) \), the probability

\[
P_M(x) = Pr\{\tau_2 < \tau_1 | x\}
\]

(4)

satisfies the Laplace equation

\[
\Delta P_M(x) = 0 \quad \text{for} \quad x \in T
\]

\[
P_M(x) = 1 \quad \text{for} \quad x \in D
\]

(5)

\[
P_M(x) = 0 \quad \text{for} \quad x \in \partial T - D,
\]

where \( T \) is a right-angled triangle with vertices \( a, b \) and \( b + a \sqrt{-1} \). \( D \) is the side joining \( a \) to \( b + a \sqrt{-1} \). Indeed,

\[
P_M(x) = Pr(X(\tau) = y \in T | X(0) = x) = \int_T G(x, y) \, dS_y,
\]

(6)

where \( \tau \) is the first exit time and the Green’s function \( G \) is the solution of (see [7])

\[
\Delta G(x, y) = 0 \quad \text{for} \quad x \in T
\]

\[
G(x, y) = \delta y(x) \quad \text{for} \quad x \in D
\]

(7)

\[
G(x, y) = 0 \quad \text{for} \quad x \in \partial T - D.
\]

\( G(x, y) \) is the probability density function to exit in \( y \in D \) when the particle starts initially in \( x \) (see also [2, chapter 15, p 192] for another proof). We shall derive an explicit expression of the encounter probability \( P \). To solve the equation, we shall use the invert of a Schwarz–Christoffel mapping to map the triangle into the upper complex half-plane \( H \). By using the explicit, the solution of the Laplace equation in \( H \), we will find the solution of (5). It turns out that the Schwarz–Christoffel mapping of interest is a Weierstrass function.
Analytical derivation of the encounter probability

It will be convenient to do all our computations for the choice \( a = 0, b = \omega \), where \( \omega \) is defined in (2). Note that \( \omega \) and \( \sqrt{-1} \omega \) are a pair of fundamental periods for the Weierstrass \( \wp \) function with parameters \( g_2 = 1 \) and \( g_3 = 0 \) \( ^{[4]} \), defined by

\[
\wp' \wp^2 = 4 \wp^3 - g_2 \wp - g_3, \tag{8}
\]

a function we are going to use in the following. It is a matter of a dilation to deduce the results for the case of general \( a, b \) from our special case.

In the spaces \( H = \{ z \in \mathbb{C} | \text{Im} z > 0 \} \) and \( \overline{H} = \{ z \in \mathbb{C} | \text{Im} z \geq 0 \} \), we consider \( f : H \rightarrow \mathbb{C} \) to be the branch of \( z(z - 1)^{1/4} \) defined as follows: for \( z \in H \), we set

\[
z = r_0 \exp(\theta_0 \sqrt{-1}) \quad \text{and} \quad z - 1 = r_1 \exp(\theta_1 \sqrt{-1}), \tag{9}
\]

where \( r_0 = |z|, r_1 = |z - 1|, 0 \leq \theta_0, \theta_1 \leq \pi \). In that case,

\[
f(z) = (r_0 r_1)^{1/4} \exp \left( \frac{\theta_0 + \theta_1}{4} \right) \sqrt{-1} \right]. \tag{10}
\]

\( f \) has a continuous extension to \( \overline{H} \):

\[
f(x) = \begin{cases} 
[x(x - 1)]^{1/2} & \text{if } x \geq 1 \\
-\sqrt{-1} \left[|x(x - 1)| \right]^{1/2} & \text{if } x \leq 0 \\
-\left( \frac{1 + \sqrt{-1}}{2} \right) \left[|x(1 - x)| \right]^{1/2} & \text{if } 0 \leq x \leq 1.
\end{cases} \tag{11}
\]

We shall now define \( F : \overline{H} \rightarrow \mathbb{C} \) by

\[
F(\zeta) = \int_1^\zeta \frac{dz}{f(z)}. \tag{12}
\]

The Schwarz reflection lemma shows that \( F \) is a conformal mapping of \( \overline{H} \) onto the triangle \( T \) in \( \mathbb{C} \) having as vertices \( 0, \omega, \sqrt{-1} \omega \), where \( \omega = \int_1^{\infty} f(x) \, dx \) (see figure 1). \( F \) maps \( 1, \infty \) onto \( 0, \omega, \sqrt{-1} \omega \) respectively and the half-line \( [1, +\infty) \) onto the segment \( [0, \omega) \) of the real axis, the half line \( [-\infty, 0] \) onto \( \{ \omega + t\omega \sqrt{-1} | 0 \leq t \leq 1 \} \) and the segment \( [0, 1] \) of the real axis onto \( \{ \sqrt{-1}(1 - t)\omega | 0 \leq t \leq 1 \} \). Moreover, \( F \) is conformal on \( H \).

To compute the function \( F \) given by (12), or more precisely its inverse, we introduce the following transformation: \( z \in H \rightarrow p = \varphi(z) \in \mathbb{C} \),

\[
\varphi(z) = \sqrt{\frac{z}{4(z - 1)^{1/4}}}. \tag{13}
\]
where the square root is the one such that $\text{Re } p \geq 0$. With the above notations, $p = \frac{1}{2} \sqrt{\frac{|\alpha|}{2} + \sqrt{\alpha^2 - 1}}$. $\phi$ is a homeomorphism of $\mathcal{H}$ onto the quadrant $Q = \{ p \in \mathbb{C} | \text{Re } p \geq 0, \text{Im } p \leq 0 \}$ and $\phi$ is conformal on $Q = \{ p \in \mathbb{C} | \text{Re } p > 0, \text{Im } p < 0 \}$. On the space $\mathcal{H}$,

$$f(z) \, dz = \phi^*(g(p) \, dp), \quad (14)$$

where

$$g(p) = \frac{\sqrt{8}}{\sqrt{4p^3 - p}}$$

and $\sqrt{4p^3 - p}$ is the branch in $Q$ which is real positive on $\left[ \frac{1}{2}, \infty \right]$. $\phi$ maps $\left[ 1, \infty \right]$ onto $\left[ \frac{1}{2}, 0 \right]$, $\left[ 0, 1 \right]$ onto $\left[ -\sqrt{-1}, 0, \infty \right]$ and $\left[ -\infty, 0 \right]$ onto $\left[ \frac{1}{2}, 0 \right]$. Relation (14) in (12) implies that

$$F(\zeta) = \int_{\phi(\zeta)}^{+\infty} g(p) \, dp = \sqrt{8} \int_{\phi(\zeta)}^{+\infty} \frac{1}{\sqrt{4p^3 - p}} \, dp. \quad (15)$$

We recall that the Weierstrass elliptic function $\wp$ with $g_2 = 1, g_3 = 0$, is defined as $\zeta = \wp(\xi)$ such that

$$\xi = \int_{\zeta}^{+\infty} \frac{1}{\sqrt{4p^3 - p}} \, dp. \quad (16)$$

Relation (15) implies that

$$\phi(\zeta) = \wp \left( \frac{F(\zeta)}{\sqrt{8}} \right). \quad (17)$$

Equivalently, (17) implies that

$$\zeta = \frac{(4\wp \left( \frac{F(\zeta)}{\sqrt{8}} \right))^2}{(4\wp \left( \frac{F(\zeta)}{\sqrt{8}} \right))^2 - 1}.$$  

Hence, for $Z \in T$, we have

$$F^{-1}(Z) = \frac{(4\wp \left( \frac{Z}{\sqrt{8}} \right))^2}{(4\wp \left( \frac{Z}{\sqrt{8}} \right))^2 - 1}. \quad (18)$$

To compute (5), we shall find a harmonic function $u$ with the boundary condition

$$u|0, \omega| \cup [\omega + \{ t\omega + \sqrt{-1} | 0 \leq t < 1 \}] = 0$$

$$u|\{(1 + \sqrt{-1})t\omega| - 1 < t < 0 \} = 1.$$  

This harmonic function can be expressed using the harmonic function $v$ in $\mathcal{H}$ with the boundary conditions

$$v = \begin{cases} 0 & \text{on } [-\infty, 0[ \cup [1, +\infty) \cr 1 & \text{on } [0, 1]. \quad (19) \end{cases}$$

For $Z \in T$, it is given by

$$u(Z) = v(F^{-1}(Z)) = v \left( \frac{(4\wp \left( \frac{Z}{\sqrt{8}} \right))^2}{(4\wp \left( \frac{Z}{\sqrt{8}} \right))^2 - 1} \right).$$
Actually, the function $v$ for $z \in H$ is given by

$$v(z) = \frac{1}{\pi} \text{Im} \log \left( \frac{z - 1}{z} \right),$$

(19)

where $\log \frac{z - 1}{z}$ is the branch on $\overline{H} - \{0,1\}$ that is real for $z \in ]1, +\infty[$, i.e.

$$\log \frac{z - 1}{z} = \log \frac{r_0}{r_1} + \sqrt{-1}(\theta_1 - \theta_0).$$

(20)

Finally, we obtain for $Z \in T$ the expression

$$u(Z) = -\frac{2}{\pi} \text{Im} \log \mathfrak{P} \left( \frac{Z}{\sqrt{8}} \right),$$

(21)

where $\log$ is the branch on $H - \{0\}$ which is real on $]0, +\infty[$. This result can be seen as a generalization of Spitzer’s law concerning the winding of a two-dimensional Brownian motion [8].

Comparison with simulations

When the initial positions of the Brownian particles are $0 \leq x_1 < x_2 \leq 1$, the scaled meeting probability is given by

$$P_M(x_1, x_2) = -\frac{2}{\pi} \text{Im} \log \mathfrak{P} \left( \frac{x_2 + \sqrt{-1}x_1}{\sqrt{8}} \right),$$

(22)

where $\mathfrak{P}$ is defined in equation (2). In figure 2, we present the graph of the probability $P_M$ of forming a cluster, plotted as a function of the initial position $x_1$ with the restriction that $x_1 < x_2$. We present two simulations: in the first one, we fix the point $x_2$ at the middle of the interval ($x_2 = 0.5$) and the other graph is obtained for a point $x_2$ chosen very close to the boundary ($x_2 = 0.99$). As can be observed, the shape of the encounter probability changes drastically. In figure 2, we have superimposed the Brownian simulations (mean and variance) with the analytical solution.

We remark that the probability of meeting does not depend on the diffusion constant.

The position of encounter

To satisfy our last curiosity, we finish with the computation of the probability $p(Z; E)$, $Z = x_2 + \sqrt{-1}x_1$ for the two particles, starting at positions $(x_1, x_2)$, $0 \leq x_1, x_2 \leq \omega'$ to coalesce in a measurable subset $E$ of $[0, \omega]$. Given $E \in [0, \omega]$, the function $Z \in T \rightarrow p(Z; E) \in [0, 1]$ is harmonic in the interior of $T$ and

$$p(Z; E) = \begin{cases} 0 & \text{if } z \in [0, \omega] - E \\ 1 & \text{if } z \in E. \end{cases}$$

(23)

Using the conformal transformation $T \rightarrow \overline{H}$,

$$Z \rightarrow z = \psi(Z) = \frac{4\mathfrak{P}(\frac{Z}{\sqrt{8}})^2}{4\mathfrak{P}(\frac{Z}{\sqrt{8}})^2 - 1},$$

(24)

it is sufficient to compute for any measurable subset $M$ of $[0, 1]$, the function $z \in \overline{H} \rightarrow P(z; M) \in [0, 1]$ having the properties as follows.

(i) $P$ is harmonic in $H$. 

5
Figure 2. Probability $P_M$ for two Brownian particles of meeting before one of them escapes the interval $[0,1]$. We compare the analytical solution equation (5) with Brownian simulations. For each position, we averaged 2000 realizations. The variance is presented as error bars. Right: we start at a middle point of the interval ($x_2 = 0.5$) and plot the probability as a function of $x_1$ (with $x_1 < x_2$ for the second point. Left: we chose for $x_2$ a point very close to the boundary ($x_2 = 0.99$). The effect of the boundary layer appears clearly for ($x_2 = 0.99$).

(ii)

$$P(z; M) = \begin{cases} 0 & \text{if } z \in [0,1] - M \\ 1 & \text{if } z \in M. \end{cases} \quad (25)$$

(iii) For any $z \in H, M \in \mathcal{M}([0,1]) \rightarrow P(z; M)$ is a measure on the $\sigma$-algebra $\mathcal{M}([0,1])$ of the measurable subsets of $[0,1]$. Then,

$$p(Z; A) = P(\psi(Z), \psi(A)).$$

We shall remark that condition (3) above shows that to determine $P$, it is sufficient to compute $P(z, \cdot)$ for $M$, a closed interval $[\alpha, \beta]$ of $[0,1]$. This is similar to the determination of the function $v$ above. Hence,

$$P(z; [\alpha, \beta]) = \frac{1}{\pi} \text{Im} \log \frac{z - \beta}{z - \alpha}.$$  \quad (26)

This expression shows that for $z \in H, M \in \mathcal{M}([0,1]) \rightarrow P(z; M)$ has a density $D(z; \alpha)$, $z \in H, \alpha \in [0,1]$, with respect to the Lebesgue measure on $[0,1]:$

$$D(z; \alpha) = \frac{\partial P}{\partial \alpha}(z; [\alpha, \beta]) = -\frac{1}{\pi} \text{Im} \frac{1}{z - \alpha}.$$  \quad (27)

Hence $p(Z; E)$ has a density with respect to the arc length on the segment $[(1 + \sqrt{-1})(1 - t)\omega | 0 \leq t \leq 1]$, which for $A \in [(1 + \sqrt{-1})(1 - t)\omega | 0 \leq t \leq 1]$ is equal to

$$d(Z; A) = D(\psi(Z), \psi(A)) \left| \frac{d\psi}{dZ} (A) \right|. \quad (27)$$

Recall that $\psi$ maps the segment $[(1 + \sqrt{-1})(1 - t)\omega | 0 \leq t \leq 1]$ diffeomorphically onto the interval $[0,1]:$

$$\frac{1}{\psi(Z) - \psi(A)} = \frac{(\psi(\frac{Z}{\sqrt{8}})\psi(\frac{A}{\sqrt{8}}))^2}{(\psi(\frac{Z}{\sqrt{8}})\psi(\frac{A}{\sqrt{8}}))^2 - (\psi(\frac{Z}{\sqrt{8}})\psi(\frac{A}{\sqrt{8}}))^2}.$$  \quad (28)
where

\[ \Psi'(w) = \frac{d\Psi}{dw}(w) \]  

and using the different equation satisfied by \( \Psi \), we obtain that

\[ \frac{d\psi}{dZ} = -\sqrt{8} \left( \frac{\Psi'(\frac{Z}{\sqrt{8}})}{\Psi(\frac{Z}{\sqrt{8}})} \right)^3. \]  

Finally, the meeting density function (27) is given explicitly by

\[ d(Z; A) = \frac{\sqrt{8}}{\pi} \left| \frac{\Psi'(\frac{1}{\sqrt{8}})}{\Psi(\frac{1}{\sqrt{8}})} \right|^3 \Im \frac{(\Psi'(\frac{1}{\sqrt{8}})\Psi'(\frac{1}{\sqrt{8}}))}{(\Psi'(\frac{1}{\sqrt{8}})\Psi'(\frac{1}{\sqrt{8}}))^2 - (\Psi(\frac{1}{\sqrt{8}}))^2}. \]  

where \( Z \in T \) and \( A \in [\omega(1-t)(1+\sqrt{-1})|0 \leq t \leq 1] \). If \( E \) is a measurable subset of the state space \([0, \omega]\), then the probability for two particles starting at position \( Z \) of meeting at \( E \) is given by

\[ p(Z; E) = \sqrt{2} \int_E d(Z; (a + a\sqrt{-1})) da, \]

which concludes this part. To finish, we extend our formula for an initial segment \([a, b]\). In this case, the probability of meeting before the escape scales into

\[ P(Z) = \frac{\omega^2}{\pi} \Im \log \frac{\Psi(\omega(Z - a))}{L\sqrt{8}}, \]

where \( Z \in T' \) is the triangle in \( \mathbb{C} \) with vertices \( a, b, b + (b - a)\sqrt{-1} \). In the limit of large \( L \), using the double-pole expansion of \( \Psi \) at 0, for \( Z \) in a neighborhood of 0, we have

\[ \Psi(Z) = \frac{1}{Z^2} + O(\tilde{Z}). \]

Thus for large \( L \), for \( \tilde{Z} = \frac{\omega(Z - a)}{L\sqrt{8}} \), equation (33) becomes

\[ P(Z) \rightarrow_{L \to \infty} \frac{4}{\pi} \Im \log \tilde{Z} = \frac{4}{\pi} \arctan \left( \frac{x_1}{x_2} \right). \]

We shall remark that this law is twice the one of the Cauchy variables at time 1, that is \( \text{Prob} \{ |C_1| < \frac{\alpha}{\sqrt{2}} \} \). This suggests that this asymptotic result might be recovered by elementary considerations on the Brownian motion. Finally, the meeting probability density function at point \( A \) is now given by

\[ d(Z; A) = \frac{\omega\sqrt{8}}{\pi L} \left| \frac{\Psi(\frac{\omega(A - a)}{L\sqrt{8}})}{\Psi(\frac{\omega(A - a)}{L\sqrt{8}})^3} \right|^3 \times \Im \frac{(\Psi(\frac{\omega(Z - a)}{L\sqrt{8}})\Psi(\frac{\omega(A - a)}{L\sqrt{8}}))}{(\Psi(\frac{\omega(Z - a)}{L\sqrt{8}})\Psi(\frac{\omega(A - a)}{L\sqrt{8}}))^2 - (\Psi(\frac{\omega(A - a)}{L\sqrt{8}}))^2}. \]

To finish, we shall provide the asymptotic for \( d(Z; A) \) for large \( L \). Using the meromorphic property of \( \Psi \), we obtain the following expansion of its derivative at the origin:

\[ \Psi'(Z) = -\frac{2}{Z^3} + O(1), \]

\[ \left| \frac{\Psi(\frac{\omega(A - a)}{L\sqrt{8}})}{\Psi(\frac{\omega(A - a)}{L\sqrt{8}})^3} \right| \approx \left| \frac{\omega A}{2L\sqrt{8}} \right|^3 \]
\[
\left( \frac{\partial}{\partial \omega} \left( \frac{\omega (Z - a)}{L \sqrt{8}} \right) \right)^2 \approx \frac{4(L \sqrt{8})^{12}}{(\omega^2 A Z)^6} \tag{38}
\]

\[
\left( \frac{\partial}{\partial \omega} \left( \frac{\omega (Z - a)}{L \sqrt{8}} \right) \right)^2 \approx 2 \left( \frac{L \sqrt{8}}{\omega Z} \right)^2 \left( \frac{L \sqrt{8}}{\omega A} \right)^6 \tag{39}
\]

\[
\left( \frac{\partial}{\partial \omega} \left( \frac{\omega (Z - a)}{L \sqrt{8}} \right) \right)^2 \approx 2 \left( \frac{L \sqrt{8}}{\omega A} \right)^2 \left( \frac{L \sqrt{8}}{\omega Z} \right)^6. \tag{40}
\]

Thus,

\[
d(Z; A) \approx \frac{\omega \sqrt{8}}{\pi L} \frac{\omega A}{2L \sqrt{8}} \left( \frac{4(L \sqrt{8})^{12}}{(\omega^2 A Z)^6} \right) \frac{1}{2\left( \frac{L \sqrt{8}}{\omega} \right)^8} \text{Im} \left( \frac{(AZ)^{-6}}{Z^{-2} A^{-6} - Z^{-6} A^{-2}} \right)
\approx \frac{16|A|^3}{\pi} \text{Im} \left( \frac{1}{Z^{-2} A^{-6} - Z^{-6} A^{-2}} \right)
\approx \frac{16|A|^3}{\pi} \text{Im} \left( \frac{1}{Z^4 - A^4} \right). \tag{41}
\]

**The mean conditional time for a collision before exit**

We shall continue here with the expression for the mean conditional time \( \tau_m(x) \) to meet before one of the particles escape. The conditional time \( \tau_m(x) \) to hit the diagonal of the triangle before the other sides is associated with the conditional process \( X^* \) solution of the stochastic differential equation [2]:

\[
dX^*(t) = 2D \nabla p(X^*(t)) dt + \sqrt{2D} dW,
\]

where \( p \) is the probability (33). \( \tau_m(x) \) satisfies Dynkin’s equation [7]:

\[
D \Delta \tau_m + 2D \nabla \tau_m \cdot \nabla p = -p \quad \text{in} \ T,
\]

\[
\tau_m = 0 \quad \text{on} \ D,
\]

where \( D \) is the diagonal (there are no conditions on the other side). Thus, \( w = pt_m \) satisfies

\[
D \Delta w = -p \quad \text{in} \ T,
\]

\[
w = 0 \quad \text{on} \ \partial T. \tag{43}
\]

We recall that the solution of the Dirichlet problem

\[
\Delta u = k \quad \text{in} \ H,
\]

\[
u = 0 \quad \text{on} \ \partial H, \tag{44}
\]

is

\[
u(y) = \int_H G(y, z_1)k(z_1) \, dz_1, \tag{45}
\]

where the Green’s function \( G \) is given by

\[
G(y, z_1) = \frac{1}{2\pi} \ln \frac{|y - z_1|}{|y - \bar{z}_1|}. \tag{46}
\]

Using now that for any conformal transformation \( \phi \),

\[
\Delta(\phi(y)) = |\phi'(z)|^2 \Delta u(\phi(z)) = -|\phi'(z)|^2 p(\phi(z)). \tag{47}
\]
we obtain

\[(uo\phi)(z) = -\frac{1}{D} \int_H |\phi'(z_1)|^2 p(\phi(z_1)) G(z - z_1) \, dz_1 \]  

(48)

with \(Z = \phi(z) = F(z),\)

\[u(Z) = -\frac{1}{D} \int_T |F'(z_1)|^2 p(F(z_1)) G(F^{-1}(Z), z_1) \, dz_1 \]  

(49)

\[= -\frac{1}{D} \int_T |F'|^2 (F^{-1}(Z_1)) p(Z_1) G(F^{-1}(Z), F^{-1}(Z_1)) \frac{dz_1}{F' o F^{-1}(Z_1)}. \]  

(50)

Discussion

The dynamics of a double-strand DNA (dsDNA) break is a fundamental step of the repair process. There are no direct experimental measurements yet of the dynamics of dsDNA ends (telomere) in the confined nucleus environment, thus giving a fundamental role of the theory in understanding the physics of motion, leaving aside the molecular machinery involved in the repair process. Since the general picture of telomere motions is not clear, we have presented here a very coarse analysis based on the Brownian motion, which can be seen however as a drastic simplification of polymer motion in a confined environment, restricted by the nuclear crowding, including histones, the remaining DNA organization, nucleoli and many other nuclear components. When the microdomain surrounding the dsDNA break is sufficiently narrow (a long strip of length \(l\)), using the Rouse model for the polymer, with a persistence length \(l_0\), we can distinguish two cases: \(l < l_0\) or \(l > l_0\). The polymer is modeled as an ordered string of beads, each being connected to its next neighbors by a spring of elasticity constant \(k\). The mean length between the beads is \(l_0\). The motion of a string is governed by a multi-dimensional Langevin equation, the potential of which is due to the elastic forces.

For a bead at position \(x_i\), the motion is described by the Smoluchowski limit of the Langevin equation (\(i = 1, \ldots, N\)):

\[\dot{x}_i + \nabla U(x_i, x_{i+1}, x_{i-1}) = \sqrt{2D} \delta_i, \]  

(51)

where \(D\) is the diffusion constant, \(\delta_i\) are the \(\delta\)-correlated Brownian motion of variance 1, and the potential \(U\) is

\[U(x_{i-1}, x_i, x_{i+1}) = \begin{cases} 
U(x_i, x_{i-1}) + U(x_i, x_{i+1}) & \text{if } i = 2, \ldots, N - 1, \\
U(x_j, x_{j+1}) & \text{if } j = 1 \text{ or } j = N - 1 
\end{cases} \]  

(52)

and

\[U(x_i, x_{i+1}) = k \left( \frac{1}{2} |x_{i+1} - x_i|^2 - l_0 |x_{i+1} - x_i| \right). \]  

(53)

When \(l < l_0\), the polymer cannot collapse and the DNA ends may be approximated by the one-dimensional motion of the polymer chain. This approximation is so restrictive that the polymer relaxes to its equilibrium and the two ends meet with the probability one. When \(l > l_0\), there are two final possibilities: starting at an initial position, either the two branches touch or curl up and then they will not be able to be repaired in a reasonable time. We have restricted our analysis to a one-dimensional Brownian motion. A full analysis of this phenomenon is difficult and we shall now discuss some ideas to address it. First, our analysis is relevant for short DNA fragments between two neighboring nucleosomes where we assimilate the break location to the center of mass of the polymer, whose motion is Brownian. However,
the computation we presented here of the probability of binding before the escape cannot be
generalized easily to dimensions 2 or 3 because it depends heavily on conformal mappings.
To generalize our result, it is possible to use the Rouse model for a polymer and estimate
the probability that the two ends of the dsDNA break meet for the first time before one of
them collapses. Similarly, estimating the probability that the two ends meet before a given
time would also be relevant. These questions are much more difficult to address compared
to our analysis. However, a first step using simulations would be to estimate the mean first
passage time of one of the polymer ends to reach a small hole. This is already a nontrivial
generalization of the small hole theory, because the small hole is no longer small. We hope
that our analysis will help to understand better the mechanisms of repair processes occurring
in the extremophilic bacterium Radiodurans, where radiations are known to produce a nuclear
phase transition, leading to a restriction of the space and thus increasing the probability of
DNA repair [5].

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