Biophysical Journal, Volume *114*

Supplemental Information

Chromatin Configuration Affects the Dynamics and Distribution of a Transiently Interacting Protein

Assaf Amitai

MODELING THE INTERACTION OF A PROTEIN WITH CHROMATIN

We study here the following dynamical process. A protein (point particle) starts from a distance a from monomer, part of a long polymer. The protein diffuses until encountering a monomer again. Upon encounter, it binds for a certain amount of time and finally disassociates and diffuses until encountering another monomer to which it can bind (main text Fig.1a,b).

Our goal is to estimate the overall protein dynamics and the time it takes for the protein to find a specific monomer. Chromatin is represented by flexible chain polymer [1], which describes a linear chain of beads (monomers) connected with the following potential:

$$\phi(\boldsymbol{R}) = \frac{\kappa}{2}\sum_{n=2}^{N}\left(\boldsymbol{R}_n - \boldsymbol{R}_{n-1}\right)^2, \tag{1}$$

where $\boldsymbol{R} = (\boldsymbol{R}_1, \boldsymbol{R}_2, ..., \boldsymbol{R}_N)$, the spring constant $\kappa = dk_BT/b^2$ is related to the standard-deviation b of the distance between adjacent monomers [1], with k_B is the Boltzmann coefficient, T the temperature and d the dimensionality (dim 3). Since a chromatin locus (monomer) moves 3 orders of magnitude slower than a protein, we shall assume that the particle is moving while the monomer positions are drawn from the polymer equilibrium distribution in a domain Ω, which we will take to be a sphere of radius A representing the nucleus.

1. The monomer site are traps of size ϵ

The protein starts at $t = 0$ at a distance a from monomer n, whose position is given by $\boldsymbol{R}_n$ (main text Fig.1b). The protein diffuses until being absorbed on another monomer. Absorption occurs at a distance ϵ from the monomer (main text Fig.1b). The pdf of the protein position ($p(\boldsymbol{x}, t)$) satisfies the Forward-Fokker-Planck equation with mixed boundary conditions

$$\begin{aligned}
\frac{1}{D}\frac{\partial p(\boldsymbol{x},t)}{\partial t} &= \Delta p(\boldsymbol{x},t),\ \boldsymbol{x} \in \tilde{\Omega}_{\epsilon,N}, \\
P(\boldsymbol{x},0) &= \delta(\boldsymbol{x} - (\boldsymbol{R}_n + \boldsymbol{a})), \\
\frac{\partial p}{\partial \boldsymbol{n}_i} &= 0 \text{ for } \boldsymbol{x} \in \partial\Omega, \\
p(\boldsymbol{x},t) &= 0 \text{ for } \boldsymbol{x} \in \partial\Omega_a = \cup_{i=1}^{N}\partial\Omega_{\epsilon_i},
\end{aligned} \tag{2}$$

where D is the diffusion coefficient of the particle, $\tilde{\Omega}_{\epsilon,N} = \Omega \setminus \Omega_a = \cup_{i=1}^{N} \Omega_{\epsilon_i}$, $\partial\Omega_{\epsilon_i}$ is the surface of a ball centered around monomer i

$$\Omega_{\epsilon_i} := B(\boldsymbol{R}_i(t), \epsilon). \tag{3}$$

Finding the MFPT $\tau(\boldsymbol{x})$ for the protein to find any of the traps (monomers), starting from position $\boldsymbol{x}$ is equivalent to solving the following boundary value problem (b.v.p) [2]

$$\begin{aligned} \Delta\tau(\boldsymbol{x}) &= -\frac{1}{D},\ \boldsymbol{x} \in \tilde{\Omega}_{\epsilon,N}, \\ \partial_n \tau &= 0 \text{ for } \boldsymbol{x} \in \partial\Omega, \\ \tau(\boldsymbol{x}) &= 0 \text{ for } \boldsymbol{x} \in \partial\Omega_a = \cup_{i=1}^{N} \partial\Omega_{\epsilon_i}. \end{aligned} \tag{4}$$

2. The transition probability depends on the Neumann Green's in the spherical domain with traps

We first find the probability that the protein finds monomer l before finding any other monomer, which we denote the *transition* probability. Finding this probability is equivalent to solving the following b.v.p [3]

$$\begin{aligned} \Delta u_l(\boldsymbol{x}) &= 0,\ \boldsymbol{x} \in \tilde{\Omega}_{\epsilon,N}, \\ \partial_n u_l &= 0 \text{ for } \boldsymbol{x} \in \partial\Omega, \\ u_l(\boldsymbol{x}) &= 0 \text{ for } \boldsymbol{x} \in \partial\Omega_a = \cup_{i=1, i\neq l}^{N} \partial\Omega_{\epsilon_i}, \\ u_l(\boldsymbol{x}) &= 1 \text{ for } \boldsymbol{x} \in \partial\Omega_{\epsilon_l}. \end{aligned} \tag{5}$$

Starting from position $\boldsymbol{x}$, the probability u_l to find monomer l is given by [3]

$$u_l(\boldsymbol{x}) = \frac{C_l}{N\bar{C}} + 4\pi\epsilon C_l \left[G(\boldsymbol{x}, \boldsymbol{R}_l) - \frac{1}{N\bar{C}} \left(\sum_{j=1}^{N} C_j G(\boldsymbol{x}, \boldsymbol{R}_j) \right) \right] + \epsilon\chi_l, \tag{6}$$

where C_l is the capacity of monomer l in units of ϵ and $\bar{C}$ is the average capacity. Indeed, the absorbing monomers can be thought of as capacitors with certain boundary condition on their surface. The higher their capacity is, the larger is the probability that the particle will be captured by them. If we were to take non-spherical traps, that would change the capacity by some numerical constant ($\mathcal{O}(1)$) and thus, the capture time and probability.

$G(\boldsymbol{x},\boldsymbol{y})$ is the Neumann Green's function of the Laplacian in a sphere of radius A, which is given by [3]

$$G(\boldsymbol{x},\boldsymbol{y}) = \frac{1}{4\pi|\boldsymbol{x}-\boldsymbol{y}|} + \frac{A}{4\pi|\boldsymbol{x}|\boldsymbol{r}'} + \frac{1}{4\pi A}\log\left[\frac{2A^2}{A^2 - |\boldsymbol{x}||\boldsymbol{y}|\cos\theta + \boldsymbol{x}\boldsymbol{r}'}\right] + \frac{1}{6|\Omega|}\left(\boldsymbol{x}^2+\boldsymbol{y}^2\right) - \frac{7}{10\pi A}, \tag{7}$$

where $\boldsymbol{r}' = |\boldsymbol{x}'-\boldsymbol{y}|$, $\boldsymbol{x}' = \frac{\boldsymbol{x}A^2}{|\boldsymbol{x}|^2}$, $|\Omega|$ is the volume of the domain and

$$\chi_l = -\frac{4\pi C_l}{N\bar{C}}\left[(\boldsymbol{G}\boldsymbol{C})_l - \frac{1}{N}\boldsymbol{C}^T\boldsymbol{G}\boldsymbol{C}\right], \tag{8}$$

where

$$\boldsymbol{G}_{i,j} = \begin{cases} Q_i & i=j, \\ G_{ij}, & i\neq j, \end{cases} \tag{9}$$

where $G_{i,j} = G(\boldsymbol{R}_i(t),\boldsymbol{R}_j(t))$ and $Q_i(\boldsymbol{R}_i(t))$ is the regular part of the Green's function (self interacting term). The monomers capacity vector is

$$\boldsymbol{C}^T = (C_1, C_2, ..., C_N) \tag{10}$$

We take the monomer traps to be spherical. For spherical traps (eq.3) we have $C_i = \epsilon$. Thus

$$\chi_l = -\frac{4\pi C_l}{N\bar{C}}\left[\sum_{i\neq l} C_i G_{li} + C_l Q_l - \frac{1}{N\bar{C}}\left(\sum_{ij,i\neq j} C_i C_j G_{ij} + \sum_i C_i^2 Q_i\right)\right]. \tag{11}$$

We shall take $C_i = C$ for $i = 1..N$, thus

$$\chi_l = -\frac{4\pi C}{N}\left[\sum_{i\neq l} G_{li} + Q_l - \frac{1}{N}\left(\sum_{ij,i\neq j} G_{ij} + \sum_i Q_i\right)\right]. \tag{12}$$

From now on will work with spherical traps for which $C = 1$.

To facilitate the calculation we estimate G_{ij} using the equilibrium distribution of the monomers positions.

$$P_{eq}(\boldsymbol{R}) = \left(\frac{2\pi}{\kappa}\right)^{3(N-1)/2}\exp\left[-\frac{\kappa}{2}\sum_{n=2}^{N}\left(\boldsymbol{R}_n - \boldsymbol{R}_{n-1}\right)^2\right], \tag{13}$$

where we used the harmonic bead potential (eq.1). This pdf is that of a flexible polymer in bulk (free domain). When the size of the domain is of the order of the polymer radius of gyration ($R_g = \sqrt{N}b/6$) [1], the polymer configurations are affected by the domain wall.

Thus, we consider the limit $A \gg R_g$ ($R_g = \sqrt{N}b/6$) where of P_{eq} is valid. Additionally, to simplify the calculations we shall anchor the first monomer $n = 1$ at the origin.

Next we compute the stationary Green's function

$$\tilde{G}_{ij} = \int_{\Omega_N} G(\boldsymbol{R}_i, \boldsymbol{R}_j) P_{eq}(\boldsymbol{R})\, d\boldsymbol{R}. \tag{14}$$

We now estimate the different terms for the average Green's function

$$I_1 = \int_{\Omega_N} \frac{1}{4\pi|\boldsymbol{R}_i - \boldsymbol{R}_j|} P_{eq}(\boldsymbol{R})\, d\boldsymbol{R} = \frac{1}{b^3}\left[\frac{3}{2\pi|i-j|}\right]^{3/2} \int \frac{1}{4\pi|\boldsymbol{r}|} e^{-\frac{3r^2}{2|i-j|b^2}}\, d\boldsymbol{r} \tag{15}$$

$$= \frac{1}{b^3}\left[\frac{3}{2\pi|i-j|}\right]^{3/2} \int_0^\infty r e^{-\frac{3r^2}{2|i-j|b^2}}\, dr, \tag{16}$$

where we use the marginal pdf

$$P(\boldsymbol{R}_i, \boldsymbol{R}_j) = \frac{1}{b^3}\left[\frac{3}{2\pi|i-j|}\right]^{3/2} e^{-\frac{3(\boldsymbol{R}_i - \boldsymbol{R}_j)^2}{2|i-j|b^2}}. \tag{17}$$

Solving the integral, we get

$$I_1 = \frac{3^{1/2}}{(2\pi)^{3/2}|i-j|^{1/2}b}. \tag{18}$$

We assumed here that ϵ is small with respect to the distance between monomers: $|R_i - R_j| = \sqrt{i-j}b \ll \epsilon$. When ϵ is larger, this assumption breaks and the expression for the distance between the initial release site and the surface of the capture ball on the target monomer is more complicated. We further assume that we are in the limit $A \gg R_g$ where

$$\left\langle \frac{A}{4\pi|\boldsymbol{x}|\boldsymbol{r'}} \right\rangle \approx \frac{1}{4\pi A}, \tag{19}$$

and

$$\frac{1}{4\pi A}\left\langle \log\left[\frac{2A^2}{A^2 - |\boldsymbol{x}||\boldsymbol{y}|\cos\theta + \boldsymbol{x}\boldsymbol{r'}}\right]\right\rangle \approx \frac{1}{4\pi A}\log(1) = 0. \tag{20}$$

Finally

$$\langle R_n^2 \rangle = nb^2. \tag{21}$$

Substituting all the terms we find the average Green's function

$$\tilde{G}_{ij} = \frac{3^{1/2}}{(2\pi)^{3/2}|i-j|^{1/2}b} + \frac{b^2}{6|\Omega|}(i+j) - \frac{3A^2}{5|\Omega|}. \tag{22}$$

The regular part of the Green's function is

$$\tilde{Q}_i = \frac{2b^2 i}{6|\Omega|} - \frac{3A^2}{5|\Omega|}. \tag{23}$$

3. Estimating χ_l

First, we will approximate the double series sum in eq.(12)

$$\sum_{i\neq j,i=1}^{N} \tilde{G}_{ij}. \tag{24}$$

We will calculate each term separately. First

$$S_j = \sum_{i\neq j,i=1}^{N} \frac{1}{|i-j|^{1/2}} = \sum_{i=1}^{j-1} \frac{1}{(j-i)^{1/2}} + \sum_{i=j+1}^{N} \frac{1}{(i-j)^{1/2}} = S_{j1} + S_{j2}. \tag{25}$$

We will approximate this series sum using the Euler-Maclaurin (EM) formula

$$\sum_{i=a}^{b} f(i,c) \approx \int_a^b f(i,c)di + \frac{f(a,c)+f(b,c)}{2} + \frac{1}{12}(f^{'}(b,c) - f^{'}(a,c)), \tag{26}$$

where

$$f(i,c) = \frac{1}{(c-i)^{1/2}}. \tag{27}$$

Taking $a = 1, b = c-1$, the boundary terms are

$$\frac{f(a,c)+f(b,c)}{2} = \frac{1}{2}\left(\frac{1}{|c-1|^{1/2}} + 1\right). \tag{28}$$

The first derivative of (27) is

$$f'(i,c) = \frac{1}{2}\frac{1}{(c-i)^{3/2}}. \tag{29}$$

Hence, the boundary derivative terms are

$$\frac{1}{12}(f^{'}(i,c) - f^{'}(i,c)) = \frac{1}{12}\left(\frac{1}{2} - \frac{1}{2|c-1|^{3/2}}\right) \tag{30}$$

and the integral

$$\int_1^{c-1} \frac{1}{(c-i)^{1/2}} di = -2(c-i)^{1/2}|_1^{c-1} = 2(c-1)^{1/2} - 2. \tag{31}$$

Combining all the terms:

$$\begin{aligned} S_{j1} = \sum_{i=1}^{j-1} \frac{1}{(j-i)^{1/2}} &= 2(j-1)^{1/2} - 2 + \frac{1}{2}\left(S_{j1} = \frac{1}{|j-1|^{1/2}} + 1\right) \\ &+ \frac{1}{12}\left(\frac{1}{2} - \frac{1}{2|j-1|^{3/2}}\right), \end{aligned} \tag{32}$$

while

$$S_{j2} = \sum_{i=j+1}^{N} \frac{1}{(i-j)^{1/2}} = 2(N-j)^{1/2} - 2 + \frac{1}{2}\left(\frac{1}{|N-j|^{1/2}} + 1\right) + \frac{1}{12}\left(\frac{1}{2} - \frac{1}{2|N-j|^{3/2}}\right). \tag{33}$$

Thus

$$S_j = \sum_{i\neq j, i=1}^{N} \frac{1}{|i-j|^{1/2}} = 2((N-j)^{1/2} + (j-1)^{1/2}) + \frac{1}{2}\left(\frac{1}{|N-j|^{1/2}} + \frac{1}{|j-1|^{1/2}}\right) - \frac{1}{12}\left(\frac{1}{2|N-j|^{3/2}} + \frac{1}{2|j-1|^{3/2}}\right) - \frac{35}{12}, \quad \text{for } j = 2..N-1, \tag{34}$$

while

$$S_N = \sum_{i=1}^{N-1} \frac{1}{|N-i|^{1/2}} = 2(N-1)^{1/2} + \frac{1}{2}\frac{1}{|N-1|^{1/2}} - \frac{1}{24}\frac{1}{|N-1|^{3/2}} - \frac{35}{24}. \tag{35}$$

and

$$S_1 = \sum_{i=2}^{N} \frac{1}{(i-j)^{1/2}} = 2(N-1)^{1/2} + \frac{1}{2}\frac{1}{|N-1|^{1/2}} - \frac{1}{24}\frac{1}{|N-1|^{3/2}} - \frac{35}{24}. \tag{36}$$

We now sum S_j over all the monomers:

$$S = S_1 + S_N + \sum_{j=2}^{N-1} S_j = 2\left(\sum_{j=1}^{N-1}(N-j)^{1/2} + \sum_{j=2}^{N}(j-1)^{1/2}\right) + \frac{1}{2}\left(\sum_{j=1}^{N-1}\frac{1}{|N-j|^{1/2}} + \sum_{j=2}^{N}\frac{1}{|j-1|^{1/2}}\right) - \frac{1}{12}\left(\sum_{j=1}^{N-1}\frac{1}{2|N-j|^{3/2}} + \sum_{j=2}^{N}\frac{1}{2|j-1|^{3/2}}\right) - \frac{35}{12} - \sum_{j=2}^{N-1}\left(\frac{35}{12}\right). \tag{37}$$

Again, we use EM formula to estimate the series terms in S (eq.37)

$$s_1 = \sum_{j=1}^{N-1}(N-j)^{1/2} \approx \frac{2}{3}(N-1)^{3/2} + \frac{1}{2}\left((N-1)^{1/2}+1\right) + \frac{1}{24}\left((N-1)^{-1/2}-1\right), \tag{38}$$

$$s_2 = \sum_{j=2}^{N}(j-1)^{1/2} \approx \frac{2}{3}(N-1)^{3/2} + \frac{1}{2}\left((N-1)^{1/2}+1\right) + \frac{1}{24}\left((N-1)^{-1/2}-1\right), \tag{39}$$

$$s_3 \approx \sum_{j=1}^{N-1}\frac{1}{(N-j)^{1/2}} \approx 2 - 2(N-1)^{1/2}, \tag{40}$$

$$s_4 \approx \sum_{j=2}^{N}\frac{1}{(j-1)^{1/2}} \approx 2(N-1)^{1/2} - 2, \tag{41}$$

$$s_5 \approx \sum_{j=1}^{N-1} \frac{1}{(N-j)^{3/2}} \approx -2(N-1)^{-1/2} + 2, \tag{42}$$

$$s_6 \approx \sum_{j=1}^{N-1} \frac{1}{(N-j)^{3/2}} \approx -2(N-1)^{-1/2} + 2, \tag{43}$$

Introducing back into eq.(37)

$$\begin{aligned} S &= 2(s_1+s_2) + \frac{1}{2}(s_3+s_4) - \frac{1}{24}(s_5+s_6) - \frac{35(N-1)}{12} \\ &= \frac{8}{3}(N-1)^{3/2} + 2(N-1)^{1/2} + \frac{1}{3}(N-1)^{-1/2} - \frac{55}{12} - \frac{35N}{12}. \end{aligned} \tag{44}$$

For large N, we take only terms of $\mathcal{O}(1)$ or higher in S:

$$S \approx \frac{8}{3}(N-1)^{3/2} - \frac{35N}{12} + 2(N-1)^{1/2} - \frac{55}{12}. \tag{45}$$

Now we use

$$\sum_{1}^{N} i = \frac{N(N+1)}{2}. \tag{46}$$

Thus, the N^{-2} term in χ_l (eq.12), when substituting eqs.23, 45 and 46

$$\begin{aligned} \sum_{ij;j\neq i} G_{ij} + \sum_i Q_i = \frac{3^{1/2}}{(2\pi)^{3/2}b}\left(\frac{8}{3}(N-1)^{3/2} - \frac{35N}{12} + 2(N-1)^{1/2} - \frac{55}{12}\right) \\ + \frac{b^2N^2(N+1)}{6|\Omega|} - \frac{3A^2N^2}{5|\Omega|}. \end{aligned} \tag{47}$$

To estimate the N^{-1} term in χ_l (eq.12) we introduce eq.(34), taking only terms of $\mathcal{O}(1)$ or higher. For $2 < l < N$, we find

$$\begin{aligned} \sum_{i\neq l} G_{li} + Q_l = \frac{3^{1/2}}{(2\pi)^{3/2}b}\left(2\left((N-l)^{1/2} + (l-1)^{1/2}\right) - \frac{35}{12}\right) \\ + \frac{N}{|\Omega|}\left[\frac{b^2(N+1+2l)}{12} - \frac{3A^2}{5}\right], \end{aligned} \tag{48}$$

while

$$\sum_{i\neq 1} G_{1i} + R_1 = \frac{3^{1/2}}{(2\pi)^{3/2}b}\left(2(N-1)^{1/2} - \frac{35}{24}\right) + \frac{N}{|\Omega|}\left[\frac{b^2(N+3)}{12} - \frac{3A^2}{5}\right], \tag{49}$$

and

$$\sum_{i\neq N} G_{Ni} + R_N = \frac{3^{1/2}}{(2\pi)^{3/2}b}\left(2(N-1)^{1/2} - \frac{35}{24}\right) + \frac{N}{|\Omega|}\left[\frac{b^2(3N+1)}{12} - \frac{3A^2}{5}\right]. \tag{50}$$

Introducing (48), (49), (50) and (47) into (12):

$$\chi_l = -\frac{4\pi}{N}\left[\frac{3^{1/2}}{(2\pi)^{3/2}b}\left(2(N-l)^{1/2}+2(l-1)^{1/2}-\frac{8}{3}\frac{(N-1)^{3/2}}{N}-\frac{2(N-1)^{1/2}}{N}+\frac{55}{12N}\right)\right.$$
$$\left.+\frac{Nb^2(2l-(N+1))}{12|\Omega|}\right] \approx -\frac{4\pi}{N}\left[\frac{3^{1/2}}{(2\pi)^{3/2}b}\left(2(N-l)^{1/2}+2(l-1)^{1/2}-\frac{8(N-1)^{3/2}}{3N}\right)\right.$$
$$\left.+\frac{Nb^2(2l-(N+1))}{12|\Omega|}\right]. \tag{51}$$

We we took terms of order $\mathcal{O}\left(N^{1/2}\right)$ or higher

$$\chi_1 = -\frac{4\pi}{N}\left[\frac{3^{1/2}}{(2\pi)^{3/2}b}\left(2(N-1)^{1/2}-\frac{8}{3}\frac{(N-1)^{3/2}}{N}-\frac{2(N-1)^{1/2}}{N}+\frac{35}{24}+\frac{55}{12N}\right)-\frac{Nb^2(N+1)}{12|\Omega|}\right]$$
$$\approx -\frac{4\pi}{N}\left[\frac{3^{1/2}}{(2\pi)^{3/2}b}\left(2(N-1)^{1/2}-\frac{8(N-1)^{3/2}}{3N}\right)-\frac{Nb^2(N+1)}{12|\Omega|}\right] \tag{52}$$

For the last monomer:

$$\chi_N = -\frac{4\pi}{N}\left[\frac{3^{1/2}}{(2\pi)^{3/2}b}\left(2(N-1)^{1/2}-\frac{8}{3}\frac{(N-1)^{3/2}}{N}-\frac{2(N-1)^{1/2}}{N}+\frac{35}{24}+\frac{55}{12N}\right)+\frac{Nb^2(N+1)}{12|\Omega|}\right]$$
$$\approx -\frac{4\pi}{N}\left[\frac{3^{1/2}}{(2\pi)^{3/2}b}\left(2(N-1)^{1/2}-\frac{8(N-1)^{3/2}}{3N}\right)+\frac{Nb^2(N+1)}{12|\Omega|}\right]. \tag{53}$$

4. Computing the transition probability $u_l(n)$

We continue to estimate the site-to-site transition probability $u_l(n)$ by averaging over eq.6. We assume that the particle started at a distance $a \ll b$ from monomer $\boldsymbol{R}_n$. We thus need to estimate

$$S_{\boldsymbol{x},l} = \sum_{j=1}^{N} G(\boldsymbol{x}, \boldsymbol{R}_j), \tag{54}$$

that we write as

$$S_{\boldsymbol{x},l} = G(\boldsymbol{x}, \boldsymbol{R}_n) + \sum_{j=1, j\neq n}^{N} G(\boldsymbol{x}, \boldsymbol{R}_j). \tag{55}$$

Since we take $|\boldsymbol{x} - \boldsymbol{R}_n(t)| = a$, we estimate the sum over the Green's function as

$$\sum_{j=1, j\neq n}^{N} G(\boldsymbol{x}, \boldsymbol{R}_j) \approx \sum_{j=1, j\neq n}^{N} G(\boldsymbol{R}_n, \boldsymbol{R}_j). \tag{56}$$

We replace again the Green's function $G(\boldsymbol{R}_n, \boldsymbol{R}_j)$ by $\tilde{G}_{nj}$:

$$S_{\boldsymbol{x},n} \approx \langle G(\boldsymbol{x}, \boldsymbol{R}_n)\rangle + \sum_{j=1, j\neq n}^{N} \tilde{G}_{nj}. \tag{57}$$

Introducing expression 48 to eq.(57)

$$\begin{aligned} S_{\boldsymbol{x},n} \approx & \frac{1}{4\pi a} + \frac{3^{1/2}}{(2\pi)^{3/2} b}\left(2\left((N-n)^{1/2} + (n-1)^{1/2}\right) - \frac{35}{12}\right) \\ & + \frac{N}{|\Omega|}\left[\frac{b^2(N+1+2n)}{12} - \frac{3A^2}{5}\right], \end{aligned} \tag{58}$$

where we used that

$$\left\langle \frac{1}{4\pi|\boldsymbol{r}|} \right\rangle = \int \frac{1}{4\pi|\boldsymbol{r}|} P(\boldsymbol{r}, a) r^2 \sin(\theta) dr d\theta d\phi = \frac{1}{4\pi a}, \tag{59}$$

with $\boldsymbol{r} = \boldsymbol{x} - \boldsymbol{R}_n$ and the probability distribution of the particle is

$$P(\boldsymbol{r}, a) = \frac{\delta(\boldsymbol{r} - a)}{4\pi \boldsymbol{r}^2}. \tag{60}$$

Substituting eqs. (22), (23), (58), (51) all the elements to eq.6, we find that for $2 < n < N$

$$\begin{aligned} u_l(n) &= \frac{1}{N} + 4\pi\epsilon\left[G(\boldsymbol{x}, \boldsymbol{R}_l) - \frac{1}{N}\left(\sum_{j=1}^{N} G(\boldsymbol{x}, \boldsymbol{R}_j)\right)\right] + \epsilon\chi_l \\ &= \frac{1}{N} + 4\pi\epsilon\left[\frac{3^{1/2}}{(2\pi)^{3/2} b}\left(|n-l|^{-1/2} - \frac{2}{N}\Big((N-l)^{1/2} + (l-1)^{1/2} + (N-n)^{1/2}\right.\right. \\ &\quad \left.\left. + (n-1)^{1/2} - \frac{4(N-1)^{3/2}}{3N} - \frac{35}{24}\Big)\right) - \frac{1}{4\pi a N}\right], \text{ for } 2 < l < N \text{ , } l \neq n \end{aligned} \tag{61}$$

$$\begin{aligned} u_1(n) = \frac{1}{N} + 4\pi\epsilon\Bigg[\frac{3^{1/2}}{(2\pi)^{3/2} b}\Bigg(|n-1|^{-1/2} - \frac{2}{N}\Big(2(N-1)^{1/2} + (N-n)^{1/2} + (n-1)^{1/2} \\ - \frac{4(N-1)^{3/2}}{3N} - \frac{35}{24}\Big)\Bigg) - \frac{1}{4\pi a N} + \frac{b^2}{6|\Omega|}\Bigg]. \end{aligned} \tag{62}$$

$$\begin{aligned} u_N(n) = \frac{1}{N} + 4\pi\epsilon\Bigg[\frac{3^{1/2}}{(2\pi)^{3/2} b}\Bigg(|N-n|^{-1/2} - \frac{2}{N}\Big(2(N-1)^{1/2} + (N-n)^{1/2} + (n-1)^{1/2} \\ - \frac{4(N-1)^{3/2}}{3N} - \frac{35}{24}\Big)\Bigg) - \frac{1}{4\pi a N} - \frac{b^2}{6|\Omega|}\Bigg]. \end{aligned} \tag{63}$$

$$u_n(n) = \frac{1}{N} + 4\pi\epsilon\Bigg[\frac{3^{1/2}}{(2\pi)^{3/2}b}\Bigg(- \frac{4}{N}\Big((N-n)^{1/2} + (n-1)^{1/2} - \frac{2(N-1)^{3/2}}{3N} - \frac{35}{48}\Big)\Bigg) + \frac{1}{4\pi a}\left(1 - \frac{1}{N}\right)\Bigg]. \tag{64}$$

For the end monomer $(n = 1)$

$$u_1(1) = \frac{1}{N} + 4\pi\epsilon\Bigg[\frac{3^{1/2}}{(2\pi)^{3/2}b}\Bigg(- \frac{4}{N}\Big((N-1)^{1/2} - \frac{2(N-1)^{3/2}}{3N} - \frac{35}{96}\Big)\Bigg) + \frac{1}{4\pi a}\left(1 - \frac{1}{N}\right) + \frac{b^2}{6|\Omega|}\Bigg]. \tag{65}$$

For $2 < l < N$

$$u_l(1) = \frac{1}{N} + 4\pi\epsilon\Bigg[\frac{3^{1/2}}{(2\pi)^{3/2}b}\Bigg((l-1)^{-1/2} - \frac{2}{N}\Big((N-l)^{1/2} + (l-1)^{1/2} + (N-1)^{1/2} - \frac{4(N-1)^{3/2}}{3N} - \frac{35}{48}\Big)\Bigg) - \frac{1}{4\pi aN}\Bigg], \tag{66}$$

and for $l = N$

$$u_N(1) = \frac{1}{N} + 4\pi\epsilon\Bigg[\frac{3^{1/2}}{(2\pi)^{3/2}b}\Bigg((N-1)^{-1/2} - \frac{4}{N}\Big((N-1)^{1/2} - \frac{2(N-1)^{3/2}}{3N} - \frac{35}{96}\Big)\Bigg) - \frac{1}{4\pi Na} - \frac{b^2}{6|\Omega|}\Bigg]. \tag{67}$$

For $n = N$

$$u_N(N) = \frac{1}{N} + 4\pi\epsilon\Bigg[\frac{3^{1/2}}{(2\pi)^{3/2}b}\Bigg(- \frac{4}{N}\Big((N-1)^{1/2} - \frac{2(N-1)^{3/2}}{3N} - \frac{35}{96}\Big)\Bigg) + \frac{1}{4\pi a}\left(1 - \frac{1}{N}\right) - \frac{b^2}{6|\Omega|}\Bigg]. \tag{68}$$

For $2 < l < N$

$$u_l(N) = \frac{1}{N} + 4\pi\epsilon\Bigg[\frac{3^{1/2}}{(2\pi)^{3/2}b}\Bigg((N-l)^{-1/2} - \frac{2}{N}\Big((N-l)^{1/2} + (l-1)^{1/2} + (N-1)^{1/2} - \frac{4(N-1)^{3/2}}{3N} - \frac{35}{48}\Big)\Bigg) - \frac{1}{4\pi aN}\Bigg], \tag{69}$$

and finally

$$u_1(N) = \frac{1}{N} + 4\pi\epsilon\Bigg[\frac{3^{1/2}}{(2\pi)^{3/2}b}\Bigg((N-1)^{-1/2} - \frac{4}{N}\Big((N-1)^{1/2} - \frac{2(N-1)^{3/2}}{3N} - \frac{35}{96}\Big)\Bigg) - \frac{1}{4\pi Na} + \frac{b^2}{6|\Omega|}\Bigg]. \tag{70}$$

5. Computing the conditional MFPT $\tau_l(n)$ to monomer l starting from monomer n

We next compute the conditional mean first passage time (MFPT) $\tau_l(\boldsymbol{x})$ of the particle to a specific monomer site l before encountering any of the other monomers, given it started at position $\boldsymbol{x}$. The conditional dynamics of the particle obeys the Langevin equation [4]

$$d\boldsymbol{x} = \boldsymbol{a}(\boldsymbol{x})dt + \sqrt{2D}d\boldsymbol{\omega}, \tag{71}$$

where

$$\boldsymbol{a}(\boldsymbol{x}) = 2D\frac{\nabla u_l(\boldsymbol{x})}{u_l(\boldsymbol{x})}, \tag{72}$$

with $u_l(\boldsymbol{x})$ the transition probability (eq.5). Moving according to this Langevin equation, the particle experiences a drift pushing it away from all monomers except for its final destination l. The MFPT to find l is the solution of

$$\begin{aligned}
\Delta\tau_l(\boldsymbol{x}) + 2\frac{\nabla u_l(\vec{x})}{u_l(\vec{x})}\cdot\nabla\tau_l(\boldsymbol{x}) &= -\frac{1}{D},\ \boldsymbol{x}\in\tilde{\Omega}_{\epsilon,N}, \\
P(\boldsymbol{x},0) &= \delta(\boldsymbol{x}-(\boldsymbol{R}_n+\boldsymbol{a})), \\
\partial_n\tau_l &= 0 \text{ for } \boldsymbol{x}\in\partial\Omega, \\
\tau_l(\boldsymbol{x}) &= 0 \text{ for } \boldsymbol{x}\in\partial\Omega_a = \Omega_{\epsilon_l}.
\end{aligned} \tag{73}$$

To estimate $\tau_l(\boldsymbol{x})$, we define the variable $v_l = \tau_l(\boldsymbol{x})u_l(\boldsymbol{x})$. Hence, $v_l(\boldsymbol{x})$ is the solution of the b.v.p

$$\begin{aligned}
D\Delta v_l(\boldsymbol{x}) &= -u_l(\boldsymbol{x}),\ \boldsymbol{x}\in\tilde{\Omega}_{\epsilon,N}, \\
\partial_n v_l &= 0 \text{ for } \boldsymbol{x}\in\partial\Omega, \\
v_l(\boldsymbol{x}) &= 0 \text{ for } \boldsymbol{x}\in\partial\Omega_a = \cup_{i=1}^{N}\partial\Omega_{\epsilon_i}.
\end{aligned} \tag{74}$$

The solution $v_l(\boldsymbol{x})$ can be written as the eigenfunctions expansion

$$v_l(\boldsymbol{x}) = \sum_{i=0}^{\infty} a_i w_{i,\epsilon}(\boldsymbol{x}), \tag{75}$$

where $w_{i,\epsilon}(\boldsymbol{x})$ are the eigenfunctions of the Laplacian in the perturbed domain $\tilde{\Omega}_{\epsilon,N}$ [5], obeying the equation

$$\Delta w_{i,\epsilon}(\boldsymbol{x}) + \lambda_{i,\epsilon} w_{i,\epsilon}(\boldsymbol{x}) = 0, \tag{76}$$

with $\lambda_{i,\epsilon}(\boldsymbol{x})$ the corresponding eigenvalues of the homogeneous.

Introducing the expansion to eq.(74), we get

$$D\sum_{i=0}^{\infty} a_i \lambda_{i,\epsilon} w_{i,\epsilon}(\boldsymbol{x}) = u_l(\boldsymbol{x}), \tag{77}$$

To find the coefficients a_i we multiply by $w_{j,\epsilon}(\boldsymbol{x})$ and integrate over the whole domain. Using the orthonormality of the eigenfunctions

$$Da_j\lambda_{j,\epsilon} = \int_{\tilde{\Omega}_{\epsilon,N}} w_{j,\epsilon}(\boldsymbol{x}) u_l(\boldsymbol{x}) dV, \tag{78}$$

giving

$$a_j = \frac{\langle w_{j,\epsilon}(\boldsymbol{x}) u_l(\boldsymbol{x})\rangle}{D\lambda_{j,\epsilon}}. \tag{79}$$

Introducing back to eq.(75)

$$v_l(\boldsymbol{x}) = \sum_{i=0}^{\infty} \frac{\langle w_{j,\epsilon}(\boldsymbol{x}) u_l(\boldsymbol{x})\rangle w_{i,\epsilon}(\boldsymbol{x})}{D\lambda_{j,\epsilon}}. \tag{80}$$

We shall approximate $v_l(\boldsymbol{x})$ with the first term

$$v_l(\boldsymbol{x}) \approx \frac{\langle w_{0,\epsilon}(\boldsymbol{x}) u_l(\boldsymbol{x})\rangle w_{0,\epsilon}(\boldsymbol{x})}{D\lambda_{0,\epsilon}}. \tag{81}$$

The perturbed zero order eigenfunction is given by

$$w_{0,\epsilon}(\boldsymbol{x}) = \frac{1}{|\tilde{\Omega}_{\epsilon,N}|^{1/2}} - \frac{4\pi\epsilon}{|\tilde{\Omega}_{\epsilon,N}|^{1/2}} \sum_{j=1}^{N} G(\boldsymbol{x}, \boldsymbol{R}_j) + \mathcal{O}(\epsilon^2). \tag{82}$$

The coefficient is

$$\begin{aligned}
\langle w_{0,\epsilon}(\boldsymbol{x}) u_l(\boldsymbol{x})\rangle \approx \int_{\tilde{\Omega}_{\epsilon,N}} \Bigg[& \frac{1}{|\tilde{\Omega}_{\epsilon,N}|^{1/2}} \times \frac{1}{N} + \frac{1}{|\tilde{\Omega}_{\epsilon,N}|^{1/2}} \times 4\pi\epsilon \Bigg[G(\boldsymbol{x}, \boldsymbol{R}_l) \\
& - \frac{1}{N}\left(\sum_{j=1}^{N} G(\boldsymbol{x}, \boldsymbol{R}_j)\right) \Bigg] - \frac{4\pi\epsilon}{|\tilde{\Omega}_{\epsilon,N}|^{1/2}} \sum_{i=1}^{N} G(\boldsymbol{x}, \boldsymbol{R}_j) \times \frac{1}{N} + \frac{1}{|\tilde{\Omega}_{\epsilon,N}|^{1/2}} \epsilon\chi_l \Bigg] \\
= & \frac{|\tilde{\Omega}_{\epsilon,N}|^{1/2}}{N} + |\tilde{\Omega}_{\epsilon,N}|^{1/2}\epsilon\chi_l + \mathcal{O}(\epsilon^2),
\end{aligned} \tag{83}$$

where we used the definition of $u_l(\boldsymbol{x})$ (eq.6) and took only order $\mathcal{O}(\epsilon)$ terms. We also used

$$\int_{\tilde{\Omega}_{\epsilon,N}} G(\boldsymbol{x}, \boldsymbol{R}_j) = 0. \tag{84}$$

The corresponding eigenvalue is

$$\lambda_{0,\epsilon} = \frac{4\pi\epsilon N}{|\Omega|} - \frac{(4\pi\epsilon)^2}{|\Omega|}\left(\sum_{i,j;i\neq j} G_{ij} + \sum_i Q_i\right) + \mathcal{O}(\epsilon^2). \tag{85}$$

We recall that

$$\sum_{ij;j\neq i} G_{ij} + \sum_i Q_i = \frac{3^{1/2}}{(2\pi)^{3/2}b}\left(\frac{8}{3}(N-1)^{3/2} - \frac{35N}{12} + 2(N-1)^{1/2} - \frac{55}{12}\right) + \frac{b^2N^2(N+1)}{6|\Omega|} - \frac{3A^2N^2}{5|\Omega|}. \tag{86}$$

Thus

$$\lambda_{0,\epsilon} = \frac{4\pi C\epsilon N}{|\Omega|} - \frac{(4\pi C\epsilon)^2}{|\Omega|}\left(\frac{3^{1/2}}{(2\pi)^{3/2}b}\left(\frac{8}{3}(N-1)^{3/2} - \frac{35N}{12} + 2(N-1)^{1/2} - \frac{55}{12}\right) + \frac{b^2N^2(N+1)}{6|\Omega|} - \frac{3A^2N^2}{5|\Omega|}\right) + \mathcal{O}(\epsilon^2). \tag{87}$$

We recall that $\tau_l = v_l/u_l$

$$\tau_l(\boldsymbol{x}) \approx \frac{\langle w_{0,\epsilon}(\boldsymbol{x})u_l(\boldsymbol{x})\rangle w_{0,\epsilon}(\boldsymbol{x})}{D\lambda_{0,\epsilon}u_l(\boldsymbol{x})} = \frac{1}{D\lambda_{0,\epsilon}}\left(\frac{1}{N} + \epsilon\chi_l\right)\left[\frac{1}{u_l(\boldsymbol{x})} - 4\pi C\epsilon\sum_{j=1}^{N}\frac{G(\boldsymbol{x},\boldsymbol{R}_j)}{u_l(\boldsymbol{x})}\right]. \tag{88}$$

The particle starts its motion from the a neighborhood of monomer n. We shall use again the pre-averaging approximation

$$\int\int_{\Omega_N}\frac{1}{u_l(\boldsymbol{x})}P_{eq}\left(\boldsymbol{R}\right)\delta(|\boldsymbol{x}-\boldsymbol{R}_n| = a)d\boldsymbol{x}d\boldsymbol{R} \approx \frac{1}{u_l(n)}, \tag{89}$$

where $\boldsymbol{x} \in B(\boldsymbol{R}_n(t), a)$. For $n = l$

$$\begin{aligned}&\int\int_{\Omega_N}\frac{G(\boldsymbol{x},\boldsymbol{R}_j)}{u_l(\boldsymbol{x})}P_{eq}\left(\boldsymbol{R}\right)\delta(|\boldsymbol{x}-\boldsymbol{R}_l| = a)d\boldsymbol{x}d\boldsymbol{R}\\ &\approx \frac{1}{u_l(l)}\int_{\Omega_N}G(\boldsymbol{x},\boldsymbol{R}_j)P_{eq}\left(\boldsymbol{R}\right)d\boldsymbol{R} \approx \frac{\tilde{G}_{nj}}{u_n(n)},\end{aligned} \tag{90}$$

and

$$\tau_n(n) \approx \frac{1}{D\lambda_{0,\epsilon}}\left(\frac{1}{N} + \epsilon\chi_n\right)\left[\frac{1}{u_n(n)} - \frac{4\pi C\epsilon}{u_n(n)}\sum_{j=1}^{N}\tilde{G}_{nj}\right]. \tag{91}$$

When $n \neq l$, we use the Taylor approximation to expand the encounter probability $u_l(\boldsymbol{x})$ for small ϵ

$$\begin{aligned}&\sum_j\int\int_{\Omega_N}\frac{G(\boldsymbol{x},\boldsymbol{R}_j)}{u_l(\boldsymbol{x})}P_{eq}\left(\boldsymbol{R}\right)\delta(|\boldsymbol{x}-\boldsymbol{R}_n| = a)d\boldsymbol{x}d\boldsymbol{R} \approx \sum_j\int\int_{\Omega_N}G(\boldsymbol{x},\boldsymbol{R}_j)\Bigg[N\\ &-4\pi\epsilon N^2\left(G(\boldsymbol{x},\boldsymbol{R}_l) - \frac{1}{N}\sum_{i=1}^{N}G(\boldsymbol{x},\boldsymbol{R}_i) + \chi_l\right)\Bigg]P_{eq}\left(\boldsymbol{R}\right)\delta(|\boldsymbol{x}-\boldsymbol{R}_n| = a)d\boldsymbol{x}d\boldsymbol{R}\\ &\approx \int\int_{\Omega_N}G(\boldsymbol{x},\boldsymbol{R}_n)\left[N - 4\pi\epsilon N^2\left(G(\boldsymbol{x},\boldsymbol{R}_l) - \frac{1}{N}\sum_{i=1}^{N}G(\boldsymbol{x},\boldsymbol{R}_i) + \chi_l\right)\right]\\ &P_{eq}\left(\boldsymbol{R}\right)\delta(|\boldsymbol{x}-\boldsymbol{R}_n| = a)d\boldsymbol{x}d\boldsymbol{R} = N\sum_j\tilde{G}_{nj} - 4\pi\epsilon N^2\tilde{G}_{nn}\left[\tilde{G}_{nl} + \chi_l - \frac{1}{N}\sum_j\tilde{G}_{nj}\right]\end{aligned} \tag{92}$$

where, assuming that $a \ll b$, we only take one element in the sum over all monomer, where the singular term scales as a^{-1}. This happens for $j = n$. Finally, substituting expression (92) to eq.(88), we find an approximation for the MFPT

$$\tau_l(n) \approx \frac{N^{-1} + \epsilon\chi_l}{D\lambda_{0,\epsilon}} \left[\frac{1}{u_l(n)} - 4\pi\epsilon N \left(\sum_j \tilde{G}_{nj} - 4\pi\epsilon N \tilde{G}_{nn} \left[\tilde{G}_{nl} + \chi_l - \frac{1}{N} \sum_j \tilde{G}_{nj} \right] \right) \right] \quad (93)$$

We estimated here the MFPT using the first eigenvalue of the Laplacian and the long time asymptotic of the heat kernel [6]. Since the particle starts close to its target, higher eigenvalues will contribute to the MFPT [7], and our expression for the MFPT can be extended to include them by estimate the contribution of higher term eigenvalues.

6. Site-to-site transition rates as a CTMC

The particle can be either bound to one of the N monomers in the domain or diffuse between dis-association and capture events. We denote the unbound state as *in-transit* from one monomer site to the another. We assume that at site n, the particle remains bound for a characteristic time T_n, and leaves with a Poissonian rate. We define the process as a continuous time Markov chain (CTMC) (Fig.3a), where the release rate from site n is

$$q_{n,Tr_{nl}} = T_n^{-1} u_l(n), \text{ for } n = 1...N. \quad (94)$$

When the destination site l is far, the transition time is well described by a single exponent (eq.90 and [5]). We assume that the in-transit time until reattachment is Poisson-distributed. Thereby, the transition rate from the in-transit state Tr_{nl} to monomer site l has probability 1 and a rate

$$q_{Tr_{nl},l} = \tau_l(n)^{-1}. \quad (95)$$

When the particle is captured rapidly, multiple exponent contribute to the the transition time, that can be taken into account by defining multiple in-transit states. The $N(N+1) \times N(N+1)$ rate matrix Q whose entries are the rates $q_{n,Tr_{nl}}$ and $q_{Tr_{nl},l}$ describes the transitions between all states and can be used to find the time-dependent probability distribution function $P(\boldsymbol{S}, t)$, with the state vector $\boldsymbol{S} = (s_{b1}, s_{b2}, ..., s_{bN}, s_{it11}, s_{it12}, ..., s_{itNN})$, where the first N states are bound state and the next N^2, are in-transit states. The probability distribution function of the particle is given by

$$p(\boldsymbol{S}, t) = e^{Qt} p(\boldsymbol{S}, 0), \quad (96)$$

where $p(\boldsymbol{S}, 0)$ is the initial distribution of the particle in the different states.

THE REATTACHMENT PROBABILITY DEPENDS ON THE LOCAL DENSITY

To clarify the effect of monomer density on the reattachment probability, we estimated the local density around different monomers along the chain. For a given monomer m, the probability to find the n-th monomer at 3d distance between r and $r + dr$ is

$$p(r, n, m) = \left(\frac{1}{\sqrt{2\pi |m-n| \sigma^2}} \right)^3 e^{-\frac{r^2}{2|m-n|\sigma^2}}, \tag{97}$$

where $\sigma^2 = \frac{b^2}{3}$. The distribution $p(r, n)$ is normalized such that $4\pi \int_0^\infty p(r, n) r^2 dr = 1$.

The probability to find monomer n within a ball of radius h around m is ($\sigma_{m,n} = \sqrt{|n-m|}\sigma$)

$$\begin{aligned} P(h, n, m) &= 4\pi \int_0^h p(r, n) r^2 dr = \frac{2}{\sqrt{2\pi}} \int_0^{\frac{h}{\sigma_{n,m}}} e^{-\frac{x^2}{2}} x^2 dx = \frac{4}{\sqrt{\pi}} \int_0^{\frac{h}{\sqrt{2}\sigma_{n,m}}} e^{-x^2} x^2 dx \\ &= \mathrm{Erf}(y) - \frac{2}{\sqrt{\pi}} y e^{-y^2}, \end{aligned} \tag{98}$$

with $y = \frac{h}{\sqrt{2}\sigma_{n,m}}$.

The total monomer density around monomer m given that it is part of a polymer of length N is

$$\rho_m = \sum_{i=1}^{m-1} P(h, n, m) + \sum_{i=m+1}^{N} P(h, n, m). \tag{99}$$

In SM Fig.1 we plot the reattachment probability $u_n(n)$ as a function of ρ_m computed for different monomers along the chain. Since the middle monomer is closest to the center of mass of the polymer, the local density there is highest. Thus, the released particle is easily lost to other monomer and $u_n(n)$ is minimal. When the ball surrounding the release monomer m is larger, the average number of monomer within it will be larger (Fig.1a vs. b)

SELF AVOIDING POLYMER

We simulated the particle release and capture process for a self-avoiding polymer. For the purpose of the simulations, self-avoiding interactions were introduced by adding the

Lennard-Jones potential [8]

$$\phi_{LJ}(\boldsymbol{R}_1, ..\boldsymbol{R}_N) = \sum_{i,j,i\neq j} \phi^{i,j}_{\rm LJ}(\boldsymbol{r}_{i,j}), \tag{100}$$

with $\boldsymbol{r}_{i,j} = \boldsymbol{R}_i - \boldsymbol{R}_j$ and

$$\phi^{i,j}_{\rm LJ}(\boldsymbol{r}_{i,j}) = \begin{cases} 4\left[\left(\frac{\sigma}{\boldsymbol{r}_{i,j}}\right)^{12} - 2\left(\frac{\sigma}{\boldsymbol{r}_{i,j}}\right)^{6} + \frac{1}{4}\right] & \text{for } |\boldsymbol{r}_{i,j}| \geq 2^{1/6}\sigma \\ 0 & \text{for } |\boldsymbol{r}_{i,j}| < 2^{1/6}\sigma. \end{cases} \tag{101}$$

[1] M. Doi and S. F. Edwards, *The Theory of Polymer Dynamics* (Oxford: Clarendon Press, 1986).

[2] Z. Schuss, *Diffusion and Stochastic Processes. An Analytical Approach* (Springer-Verlag, New York, NY, 2009).

[3] A. F. Cheviakov and M. J. Ward, Math. Comput. Modelling **53**, 1394 (2011).

[4] S. Karlin and H. Taylor, *A Second Course in Stochastic Processes* (Academic Press, 1981).

[5] A. Amitai, I. Kupka, and D. Holcman, Phys. Rev. Lett **109**, 108302 (2012).

[6] D. S. Grebenkov and B.-T. Nguyen, SIAM Review **55**, 601 (2013).

[7] S. A. Isaacson and J. Newby, Phys. Rev. E **88**, 012820 (2013).

[8] J. E. Lennard-Jones, Proc. R. Soc. Lond. A **106**, 463477 (1924).

SUPPLEMENTARY FIGURES

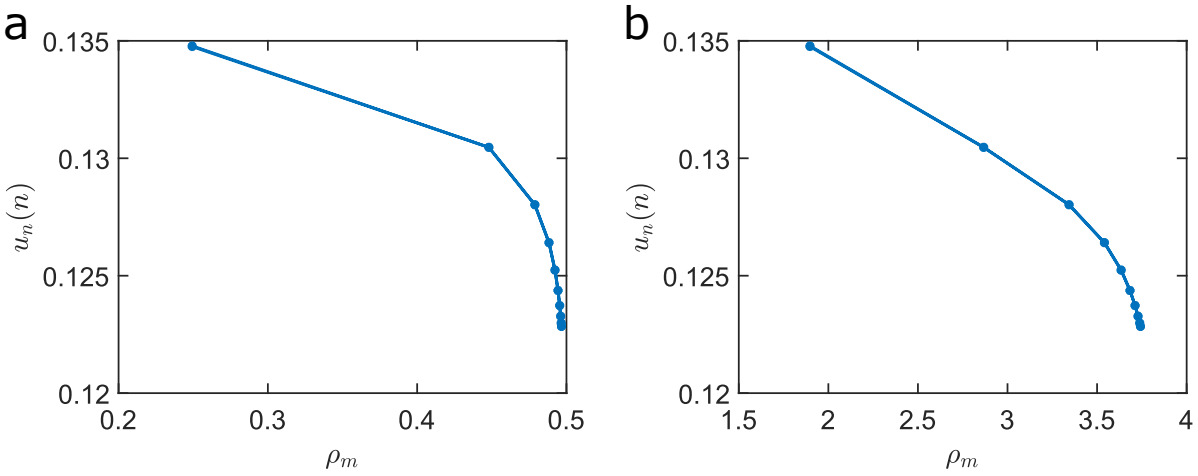

FIG. 1. **The reattachment probability depends on local monomer density.** The reattachment probability $u_n(n)$ as a function of the average local monomer density ρ_m estimated using different monomers along the chain (eq.99). The left most point corresponds to the chain extremities where the density is lowest, while the rightmost point corresponds to the middle monomer of the chain where the density is highest. The polymer has 20 monomer sites ($N = 20$), $a = 0.3b$, $\epsilon = 0.03b$, $A = 10b$. The surrounding ball (eq.98) is of radius $h = 1b$ (a) or $h = 3b$ (b).

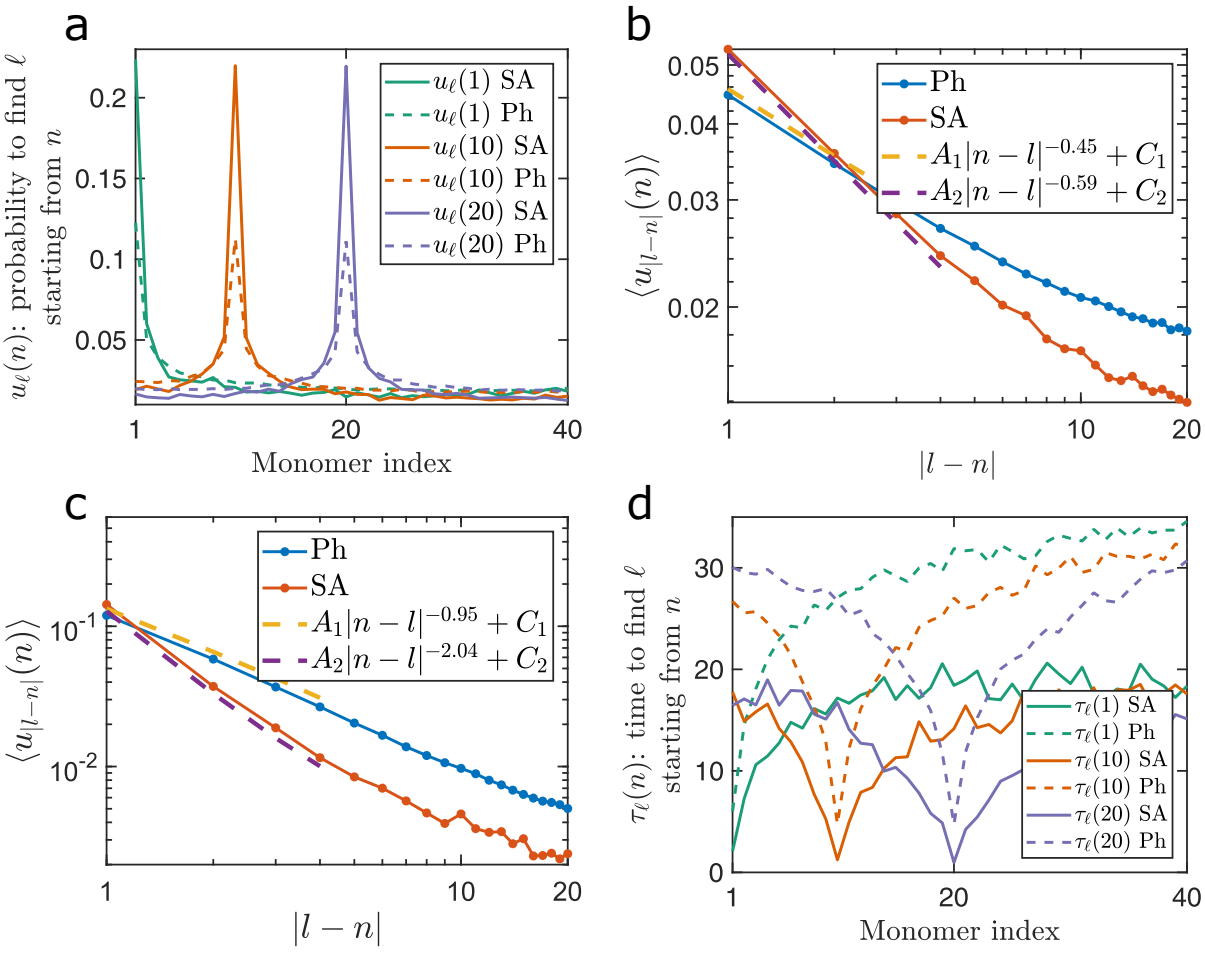

FIG. 2. **Transition between monomer sites.** (**a**) The transition probability $u_l(n)$ starting from site 1 (turquoise), 10 (orange) or 20 (purple). The polymer has 40 monomer sites ($N = 40$), $a = 0.3b$, $\epsilon = 0.07b$, $A = 10b$. The full lines are the result of Brownian simulations for a self avoiding polymer, where the LJ distance was taken to be $\sigma = 1b$ (eq.101). The dashed lines are the simulation results for a phantom polymer (without the LJ potential- see main text). (**b**) The transition probability averaged over all monomers $\langle u_{|l-n|}(n)\rangle$ for a phantom polymer (blue full curve) and a self avoiding polymer (red full curve). Also shown is the result of fitting a function of the form $A|l-n|^{-\alpha}+C$ to the two curves. (**c**) $u_l(n)$ was estimated from simulations with $\epsilon = 0.5b$ and $a = 0.7b$. The same analysis as in b was performed. (**d**) The mean first transition time $\tau_l(n)$ from site n to site l without interacting with any other site along the way. The full line lines are the result of BS for a self avoiding polymer and the dashed line is are the result for a phantom polymer. The results shown are for the case simulated in a,b.

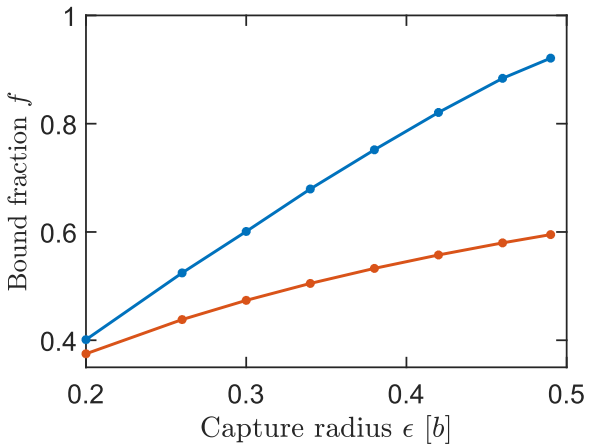

FIG. 3. **The bound fraction of particles to monomer site.** The fraction of bound particles f at monomer sites as a function of the capture radius ϵ. f was estimated from the long time behavior of the probability distribution function $p(\boldsymbol{S}, t)$, by solving the corresponding CTMC (described in the main text) (blue curve). In the Brownian simulations: $N = 100$, $a = 0.5b$, $A = 10b$. The time units are $10b^2/D$, with D the diffusion coefficient of the particle. Also shown is the bulk bound fraction estimate (red curve) given by $f_{bulk} = \frac{k_{on}}{k_{on}+k_{off}}$, with $k_{on} = \frac{4\pi\epsilon ND}{|\Omega|}$. This estimated assumes that the recapture probability and rate are uniform to all sites independent where the particle was released.