1D Diffusion of a Protein on DNA

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May 17, 2007

Abstract

The binding of proteins on a specific site of DNA is a central process for many cellular function. One of the proposed mechanism is a process involve 1D sliding along DNA. Details of the 1D sliding depend on the specific form of the binding energy distribution. We will examinate different forms of this distribution.

Introduction

The mechanism for a fast and reliable locating process has long been investigated. In 1970, Riggs et al. gave the rate as high as $10^10 M^{-1}s^{-1}$, while the calculating maximum rate from Elowitz et al. was $10^8 M^{-1}s^{-1}$. One explanation for such a disagreement between experimental and theoretical result by Ritcher and Eigen was that while protein searching for its target on DNA, it go through both 3D and 1D diffusion repeatedly. The sliding of protein along DNA depends on the specific binding energy configuration. Recently, Slutsky and Mirny have consider the case of normal distribution for the binding energy. In this work, we will consider some other possible distribution: Delta Dirac distribution, uniform distribution, and exponential distribution.

General formulation

At every point on DNA, the protein can move forward or backward with some probability. So, it can be considered as a 1D random walk. We first calculate the mean first passage time (MFPT) from site 0 to L, the mean number of steps the particle has to make to reach the site L from 0 for the first time. In what follows, p_i denotes the probability to jump from site i to site $i+1$ (the right jump) and q_i denote the probability to jump from i to $i-1$ (the left jump). In general, $p_i + q_i \leq 1$ and $1 - p_i - q_i$ is the probability for particle to stay at i. Also, for convenience, we define $\alpha_i = p_i/q_i$. Murthy and Kehr gave the following expression for the MFPT

$$\bar{t}_{0,L} = L + \sum_{k=0}^{L-1} \alpha_k + \sum_{k=0}^{L-2} \sum_{i=k+1}^{L-1} (1+\alpha_k) \prod_{j=k+1}^{i} \alpha_j \tag{1}$$

It is the relation of MFPT to the probability configuration $\{p_i, q_i\}$. These probabilities depend on the specific binding energies and propotional to the transition rates $\omega_{i,i\pm1}$, where:

$$\omega_{i,i\pm1} = \nu \times \begin{cases} e^{-\beta(U_{i\pm1}-U_i} & \text{if} \quad U_{i\pm1} > U_i \\ 1.0 & \text{otherwise} \end{cases} \tag{2}$$

From (1), Slutsky and Mirny gave

$$\bar{t}_{0,L} = L^2 \langle e^{\beta(U_i - U_j)} \rangle = L^2 \int dU_i dU_j f(U_i) f(U_j) e^{\beta(U_i - U_j)} \tag{3}$$

We will use this equation for our later discussions. The other compontent need to carried out is the state life time, which is the inverse of the escaping rate. For any site i, particle can escapes to one of the two neighboring sites $i \pm 1$, so

$$\tau_i = \frac{1}{r_i} = \frac{1}{\omega_{i,i+1} + \omega_{i,i-1}} \tag{4}$$

Because we are considering the process with very large number of step, 10^6 - 10^9 possible sites, it is safe to use the average number

$$\langle \tau \rangle = 2\tau_0 \int dU_i dU_{i+1} dU_{i-1} \frac{f(U_i) f(U_{i+1}) f(U_{i-1})}{e^{-\beta(U_{i+1}-U_i)} + e^{-\beta(U_{i-1}-U_i)}} \tag{5}$$

where $\tau_0 = 1/(2\nu)$

Specific distributions

We are now ready to consider the model for different form of the biding energy distribution. Slutsky and Mirny obtained the expression for the normal distribution. In the following subsection, we will give the expression for Delta Dirac distribution, uniform distribution, and exponential distribtion.

Delta Dirac distribution

This is the simplest case, where the energy distribution function has the form,

$$f(U) = \delta(U - U_0) \tag{6}$$

i.e. the biding energy has a specific energy In this simple case, we have

$$\bar{t}_{0,L} = L^2 \tag{7}$$

$$\langle \tau \rangle = \tau_0 \tag{8}$$

and the diffusion coefficient

$$D_{1d} = \frac{1}{2\tau_0} \tag{9}$$

There is not much to say about this simple case.

Uniform distribution

First, consider the uniform energy distribution with range from $U_{\min}$ to $U_{\max}$

$$f(U_i) = \begin{cases} \frac{1}{U_{max}-U_{min}} & \text{for} \quad U_{\min} < U < U_{\max} \\ 0 & \text{for} \quad \text{otherwise} \end{cases} \tag{10}$$

In this case

$$\bar{t}_{0,L} \approx \frac{L^2}{\beta^2(U_{\max}-U_{\min})^2} e^{\beta(U_{\max}-U_{\min})} \tag{11}$$

and

$$\langle\tau\rangle = \frac{2\tau_0 \log 4}{\beta^3(U_{\max}-U_{\min})^3} e^{\beta(U_{\max}-U_{\min})} \tag{12}$$

So, the diffusion coefficeint for the uniform energy distribution is

$$D_{1d}(\Delta U) = \frac{\beta^5 \Delta U^5}{\tau_0 4 \log 4} e^{-2\beta\Delta U} \tag{13}$$

With this form of the diffusion coefficient, the rapid diffusion can only happen for a very specific range of the variable $\Delta U \sim 2.5 k_B T$ and decay rapidly as it moves away from this value.

Exponential distribution

The next energy distribution we consider in this section is the exponential distribution

$$f(U) = a e^{-aU} \tag{14}$$

with the condition $a > \beta$. The MFPT for exponential distribution is

$$\bar{t}_{0,L} = \frac{a^2 L^2}{a^2 - \beta^2} \tag{15}$$

and

$$\langle\tau\rangle = \frac{a^3 \tau_0}{(2a-\beta)(a+\beta)\beta} \left[-\pi \cot\left(\frac{a\pi}{2\beta}\right) - 2\psi\left(\frac{a}{2\beta}\right) + \psi\left(\frac{\beta-a}{2\beta}\right) + \psi\left(\frac{\beta+a}{2\beta}\right) \right] \tag{16}$$

where

$$\psi(x) = \frac{\Gamma'(x)}{\Gamma(x)} \tag{17}$$

The diffusion coefficient for the exponential distribution is

$$D_{1d}(a) = \frac{(a^2-\beta^2)(2a-\beta)(a+\beta)\beta}{\tau_0 a^5 \left[-\pi \cot\left(\frac{a\pi}{2\beta}\right) - 2\psi\left(\frac{a}{2\beta}\right) + \psi\left(\frac{\beta-a}{2\beta}\right) + \psi\left(\frac{\beta+a}{2\beta}\right) \right]} \tag{18}$$

This form of the diffusion coefficient oscilate with the value of a/β.

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