



# Looping dynamics of a flexible chain with internal friction at different degrees of compactness



Nairhita Samanta, Rajarshi Chakrabarti\*

Department of Chemistry, Indian Institute of Technology Bombay, Mumbai, Powai 400076, India

## HIGHLIGHTS

- Loop formation and reconfiguration dynamics of polymer chain.
- Internal friction and denaturant concentration.
- Compacted chain.

## ARTICLE INFO

### Article history:

Received 9 February 2015

Received in revised form 24 March 2015

Available online 12 May 2015

### Keywords:

Brownian motion  
Internal friction  
Polymer dynamics

## ABSTRACT

In recent times single molecule experiments have shown the importance of internal friction in biopolymer dynamics. Such studies also suggested that the internal friction although independent of solvent viscosity has a strong dependence on denaturant concentration. In addition, recent simulations showed that the weak interactions contribute to the internal friction in proteins. In this work we made an attempt to investigate how a single polymer chain with internal friction undergoes reconfiguration and looping dynamics in a confining potential that accounts for the presence of the denaturant, by using recently proposed “Compacted Rouse with internal friction”. We also incorporated the effect of hydrodynamics by extending this further to “Compacted Zimm with internal friction”. All the calculations are carried out within the Wilemski Fixman framework without invoking excluded-volume effect. By changing the strength of the confinement we mimicked chains with different degrees of compactness at different denaturant concentrations. While compared with experiments our results are found to be in good agreement.

© 2015 Elsevier B.V. All rights reserved.

## 1. Introduction

In recent past there have been efforts based on single molecule experiments to elucidate the role of internal friction in protein folding [1,2]. These single molecule experiments showed internal friction to play a significant role in folding especially when the protein starts with a more compact unfolded state. Among the different types of experiments carried out to study the dynamics of the unfolded proteins, the most common one is a combination of Förster resonance energy transfer (FRET) and nanosecond Fluorescence correlation spectroscopy (nsFCS), where two residues  $n$  and  $m$  of a protein are labelled with fluorescence probes and the fluctuation of the distance between them is observed from the efficiency of energy transfer. An auto-correlation function is then calculated from the distribution, which eventually gives a characteristic relaxation time, also called the reconfiguration time ( $\tau_{nm}$ ) [1]. In another type of fluorescence experiment, two different residues of a protein are again tagged with a fluorescence quencher and donor. The time required for the donor to be quenched which happens

\* Corresponding author.

E-mail address: [rajarshi@chem.iitb.ac.in](mailto:rajarshi@chem.iitb.ac.in) (R. Chakrabarti).

only within a certain distance, gives an estimation of loop formation time ( $\tau_{nm,loop}$ ) in a protein [3]. Both the time scales,  $\tau_{nm}$  and  $\tau_{nm,loop}$  seem to have a nonzero intercept when plotted against the solvent viscosity. This residual reconfiguration or looping time has been attributed to “internal friction” which is present within the protein and assumed to be independent of the solvent around. Unfortunately a molecular picture of this internal friction is still lacking, but it is believed that dihedral rotations, hydrogen bonding and other weak interactions contribute to internal friction. Recent simulations on proteins support such propositions as well [4–7]. This also tells why internal friction is more when the protein is in more compact unfolded state. Though the notion of “internal friction” is not very old in the chemical physics community [8,9], it has always been a topic of research among polymer rheologists [10–12]. For example Rabin and Öttinger looked at the origin of internal viscosity in a Gaussian chain [10,11]. Following an idea of de Gennes [13] they derived an expression for the relaxation time,  $\tau_{rel}$  associated with internal viscosity as  $\tau_{rel} = R^3/k_B T(\eta_s + \eta_i)$  where,  $R = aN^\nu$  and  $a, N$  are the monomer size and chain length respectively,  $\nu$  is the Flory exponent [14–16]. Therefore in the limit solvent viscosity  $\eta_s \rightarrow 0$ , it has a non-zero intercept proportional to the internal viscosity  $\eta_i$ . This is in the same spirit as that of Khatri and McLeish [17], where a modified Rouse model gives a mode relaxation time which is dependent on internal friction,  $\tau_p^{RIF} = \tau^R/p^2 + \tau_{int}$ . Such a model gives a reconfiguration time between any two monomers  $n$  and  $m$  as  $\tau_{nm} \simeq 0.82\tau^R + \tau_{int}$  [18], where  $\tau^R$  is the rouse time, proportional to the solvent viscosity. Although such a model qualitatively can predict the trend of the variation of reconfiguration time as a function of solvent viscosity and produce a non-zero intercept but cannot account for the changes in “internal friction” at different degrees of compactness encountered in experiments [19,20]. It is expected that the protein experiences different level of “internal friction” at different concentrations of the denaturant as the compactness of it changes. This can be seen from the plots of the reconfiguration time [2] against the solvent viscosity at different denaturant concentrations where the intercepts give the time scale due to “internal friction”. The higher the denaturant concentration the smaller the intercept. In the present study we extend recently proposed models [18,21] to include the effect of the compactness of the polymer chain to internal friction by introducing a confining harmonic potential to each monomer of the chain which accounts for the change in chain conformation due to denaturant. At a lower denaturant concentration chain is more compact so the confining potential is steeper, but as the denaturant concentration increases the confining potential becomes shallower. With this model, the looping dynamics is studied within Wilemski Fixman (WF) framework [22] assuming the polymer chain to be Gaussian. Loop formation between any two parts of a bio-polymer is supposedly the primary step of protein folding, DNA cyclization [23–25]. It is worth mentioning that WF formalism seems to work fine here and has been used to calculate the same in presence of hydrodynamic interactions by Chakrabarti [26] and the effect of viscoelastic solvent [27,28]. The method has also been used in the past extensively [29–34] to investigate other aspects of the polymer looping problems. We would also like to point out that the effects of excluded-volume interaction are not accounted for in our calculations and so the influence of compactness does not include slowing down due to entanglement effects.

The paper is arranged as follows. The details of the polymer models are given in Section 2. Section 3 deals with the methods. Results and discussions are represented in Section 4. Section 5 is the conclusion.

## 2. Polymer model

In the Rouse model, a polymer chain is imagined as a series of Brownian particles connected by harmonic springs with no hydrodynamic interactions and excluded volume effect [35,36]. If  $R_n(t)$  is the position of the  $n$ th monomer at time  $t$ , where  $n$  can be varied from 0 to  $N$ , then the dynamics of the Rouse chain with  $(N + 1)$  monomers is described by the following equation of motion

$$\zeta \frac{\partial R_n(t)}{\partial t} = k \frac{\partial^2 R_n(t)}{\partial n^2} + f(n, t) \quad (1)$$

where  $\zeta$  is the friction coefficient and  $k = \frac{3k_B T}{b^2}$  is the spring constant with Kuhn length  $b$ .  $f(n, t)$  is the random force with moments

$$\langle f(n, t) \rangle = 0, \langle f_\alpha(n, t_1) f_\beta(m, t_2) \rangle = 2\zeta k_B T \delta_{\alpha\beta} \delta(n - m) \delta(t_1 - t_2). \quad (2)$$

A standard procedure to treat such a system is to describe the dynamics in the form of normal modes ( $X_p$ )

$$\zeta_p^R \frac{dX_p(t)}{dt} = -k_p^R X_p(t) + f_p(t). \quad (3)$$

Here,  $\zeta_p^R = 2N\zeta$  for  $p > 0$  and  $\zeta_0^R = N\zeta$ . The relaxation time of  $p$ th mode is  $\tau_p^R = \frac{\zeta_p^R}{k_p^R} = \frac{\tau^R}{p^2}$  and  $k_p^R = \frac{6\pi^2 k_B T p^2}{Nb^2}$ . The slowest relaxation time  $\tau^R = \frac{N^2 \zeta b^2}{3\pi^2 k_B T}$  is called Rouse time.

Rouse model does not take into account the effects of hydrodynamic interactions. The simplest possible model which takes care of it, is due to Zimm [35,36]. It is possible to show that in  $\theta$  condition under pre-averaged hydrodynamic interaction, the Zimm chain can be described by the same Eq. (3) but with a different scaling of friction co-efficient including

Download English Version:

<https://daneshyari.com/en/article/974101>

Download Persian Version:

<https://daneshyari.com/article/974101>

[Daneshyari.com](https://daneshyari.com)