POLYMER TRANSLOCATION THROUGH A NANOPORE

By

ABEL GEBREEGZIABHER GEBRESILASSIE

SUBMITTED IN PARTIAL FULFILLMENT OF THE
REQUIREMENTS FOR THE DEGREE OF
MASTER OF SCIENCE IN PHYSICS
AT
ADDIS ABABA UNIVERSITY
ADDIS ABABA, ETHIOPIA
JULY 2010

ADDIS ABABA UNIVERSITY
DEPARTMENT OF
PHYSICS

Supervisor: DR. TATEK YERGOU

Examiners: DR. MULUGETA BEKELE

DR. LEMI DEMEYU

ADDIS ABABA UNIVERSITY

Date: **JULY 2010**

Author: **ABEL GEBREEGZIABHER GEBRESILASSIE**

Title: **POLYMER TRANSLOCATION THROUGH A NANOPORE**

Department: **Physics**

Degree: **M.Sc.** Convocation: **JULY** Year: **2010**

Permission is herewith granted to Addis Ababa University to circulate and to have copied for non-commercial purposes, at its discretion, the above title upon the request of individuals or institutions.

Signature of Author

For my family and friends!

Table of Contents

List of Figures

Abstract

In this paper we investigate Monte Carlo simulation of polymer translocation through a nanopore. To this end we used the bond fluctuation method (BFM) to study the translocation process of a polymer chain of length N in two dimensions, in the absence of external force on the polymer (i.e. unbiased translocation). To overcome the entropic barrier we consider a polymer which is initially placed in the middle of the pore and study the average escape time τ needed for the polymer to completely exit the pore on either side of the end. Numerically we find that the escape time τ scales with the chain length N as $\tau \sim N^{1+2\nu}$, where ν is the Flory exponent as far as the pore is small enough. And this scaling agree with the translocation time of a polymer which passes through a nanopore in one direction only. In this work, we examine the interplay between the pore length L, width W and other parameters while simulating the translocation process. We also study the statistical properties of a polymer chain by calculating the average-squared end-to-end distance R^2 and the average-squared radius of gyration R_g^2 of a chain polymer; and the diffusion constant D for the dynamical properties.

Acknowledgements

I came up to this passing through many ups and downs, for this I would like to thank the almighty God.

Following, my deepest gratitude goes to my advisor Dr.Tatek Yergou for his limitless and invaluable effort in guiding and supervising me and of course for his friendly approach through out this work. With out him this thesis wouldn't come up to its end. I am also grateful to Dr. Mulugeta Bekele for his support and encouragement. It was a pleasure to meet such an excellent scientist and wonderful person.

Special thanks goes to T. Ala-Nissila for his important suggestions and discussions in this work.

I am also very much pleased to forward my unreserved affection and thank to my parents: my Mom Azeb M., my Dad G/Egziabher G. and the rest of the family.

What would be the years of study be like with out friends? I can surely say, not as joyful and fun as with you: Ashenafi, Brihanu, Fitsum, Mehari, Mesay, Seid, Simachew, Solomon N., Solomon W., Tekalign, Yibekal, and others.

Last but not least, a very special person whose contribution was limitless, my beloved Rahel T. I thank you so much for your understanding, tolerance and the patience you had with me and for the strength and love you gave me.

Chapter 1

Introduction to polymer physics

Although there are many definitions to the word polymer, simply defined, a polymer is a large molecule made up of many small simple chemical units, joined together by chemical reaction. For example a DNA molecule is an extremely long polymer made up of up to 10^7 nucleotides. Polymers are of two types regarding their nature. And these are natural polymers and synthetically produced polymers which are artificial ones. Most artificially produced polymers are a repetitive sequence of a particular atomic group, and take the form $(-A-A-A-A-A-A-A-)$. The basic unit of a polymer is called the structural unit or monomer unit. The monomers need not be identical molecular subunits. Polymers whose monomers are identical are termed as homopolymers while a polymer that has at least two different monomers is called a heteropolymer. And the number of units in a polymer is called the degree of polymerization. In general, polymeric materials are very flexible like rubber, and are easily formed into fibers, thin films, etc.

Generally polymer science has many branches among which one is polymer physics. And it is the field of physics associated to the study of polymers, their fluctuation, mechanical properties, as well as the kinetic of reactions involving degradation and polymerization of polymers and monomers respectively. While it focuses on an aspect of the study of condensed matter physics, the field of polymer physics has developed as a branch of statistical physics. Disordered polymers are too complex to be described using a deterministic method. However statistical approaches can yield results and are often pertinent since large polymers (that is to say, polymers that contain a large number of monomers) can be described efficiently as systems at thermodynamic limit.

The statistical approach of polymer physics is based on an analogy between a polymer and a Brownian motion, or some other type of random walk. Experimental approaches to polymer physics are also common to determine the chemical, physical, and material properties of polymers. These experimental approaches lead to more accuracy in theoretical model formulation and hence allow better understanding of polymer properties.

According to their shape polymers can be classified as linear, star and branched ones. We concentrate here on linear polymers constructed from individual monomeric units that may not be identical. The aim of this section is to introduce basic concepts in polymer physics. We first summarize static properties for ideal and real polymer chains.

1.1 Static properties of polymers

We now derive static properties of ideal polymers. Our calculations in this section are based on the freely-jointed chain model (fig. 1.1) which is the simplest model to describe a polymer. Here, a polymer is regarded as a random walk and interactions among individual monomers are neglected. In addition, the individual monomers are considered point-like, i.e. steric effects are not taken into account. Despite its simplicity, it is a useful tool to gain insight into polymer physics.

1.1.1 Ideal polymer chains

Consider a flexible polymer consisting of $N+1$ monomers. A conformation can be identified by the set of N position vectors $\vec{R}_i$ (i = 0,....,N), or by the set of bond vectors

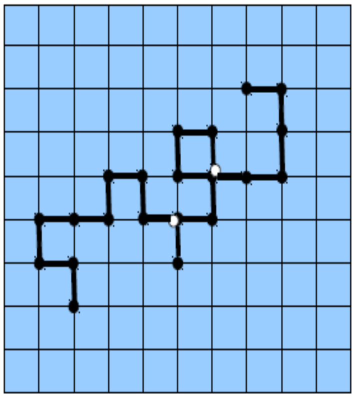

Figure 1.1: The random walk model of a polymer chain. The white and black dots are the segments and the thick lines are the bonds.

$\vec{r}_i = \vec{R}_i - \vec{R}_{i-1}$(i = 0,. ..,N). The latter set represents an ensemble of independent connection vectors.

There are two popular static properties by which the spatial size of a polymer is characterized. A first entity related to the size of a polymer is its end-to-end vector $\vec{R}$ that is defined as seen in (figure 1.2):

$$\vec{R} = \sum_{i=0}^{N} \vec{r}_i = \vec{R}_N - \vec{R}_0 \tag{1.1.1}$$

Since there is no preferred direction, the average value of the end-to-end vector vanishes: $< \vec{R} >= 0$. The simplest non-zero average is the mean-square end-to-end vector $< \vec{R}^2 >$.

$$< R^2 >= \sum_{i=1}^{N} \sum_{j=1}^{N} < \vec{r}_i . \vec{r}_j > \tag{1.1.2}$$

Assuming all bond vectors having the same length b, the last formula can be expressed as

$$< R^2 >= b^2 \sum_{i=1}^{N} \sum_{j=1}^{N} < \cos\theta_{ij} >= Nb^2 \tag{1.1.3}$$

where we take into account that directions between different bond vectors are uncorrelated. The last equation reveals that the mean-square end-to-end vector is directly

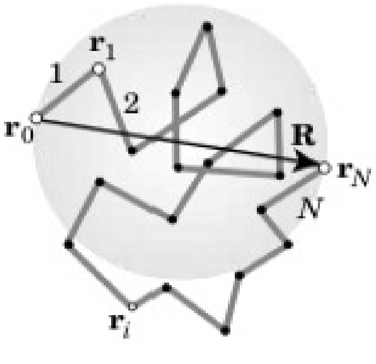

Figure 1.2: End-to-end vector $\vec{R}$ defined by $\vec{R}$=$\vec{r_N}$- $\vec{r_0}$.

proportional to the number of monomer bonds: $R^2 >\sim N$ [1]. However, this well-known formula exhibits a small taint which is the occurrence of values of $\vec{R}$ being larger than the maximal extended length Nb. A more realistic model is available in the literature [2]. The above mentioned similarity between polymer chains and random walks is applied frequently to illustrate the behavior of polymers and to solve problems in polymer science.

The mean-square end-to-end vector is a suitable measure for the size of a linear polymer. Unfortunately, branched or ring polymers can not appropriately be described by this quantity. A more convenient quantity is the radius of gyration (figure 1.3) $\vec{R_g}$ that measures the dimension of the polymer relative to its center of mass. It is given by:

$$R_g^2 = \frac{1}{N+1}\sum_{i=0}^{N}(\vec{r_i} - \vec{r_G})^2 \tag{1.1.4}$$

where

$$\vec{r_G} = \frac{1}{N+1}\sum_{i=0}^{N}\vec{r_i} \tag{1.1.5}$$

where we assume in equation 1.1.5 that all monomers having the same mass. As before, the square radius of gyration is usually averaged over the ensemble of allowed conformations resulting in the mean-square radius of gyration:

$$< R_g^2 >= \frac{1}{N+1}\sum_{i=0}^{N} < (\vec{r_i} - \vec{r_G})^2 > \tag{1.1.6}$$

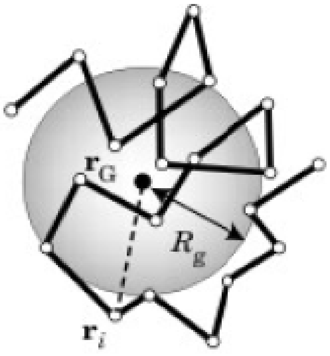

Figure 1.3: Center of mass $\vec{r_G}$ and the radius of gyration R_g in the bead-stick model.

For a linear, ideal polymer chain, the square radius of gyration can be easily calculated. The discrete sums are converted into integrals over the contour of the polymer. After a few lines of calculation one arrives at the following expression :

$$< R_g^2 >= \frac{b^2 N}{6} = \frac{1}{6} < R^2 > \tag{1.1.7}$$

Thus, the mean-square radius of gyration of an ideal, linear polymer obeys the same scaling behavior as its mean-square end-to-end vector.

1.1.2 Real polymer chains

In the previous section, conformations of ideal chains were discussed. We now take into account interactions between monomers that are separated by many bond lengths along the polymer chain. In particular, we discuss alterations in the statistical properties if steric interactions are considered, i.e. the polymer consists of monomers with a finite lateral dimension. To keep things simple we restrict our analysis to spherical monomers.

Excluded volume interaction

The ideal chain model assumes that the polymer segments can overlap with each other as if the chain were a phantom chain. One key result of the last section was that an ideal polymer can be interpreted as a random walk, i.e. every polymer segment is independent from all others. However, prohibiting a pair of monomers to occupy the same spatial location directly leads to correlations between the monomers. Thus in reality, two segments (monomers) can not occupy the same space at the same time. This interaction between segments is called ***Excluded Volume Interaction (Effect)***. Following this line, a real polymer chain can consequently be characterized as a self-avoiding random walk, i.e. a random walk that does not visit the same point more than once.

A detailed analysis of real polymer chains was carried out by Flory [2]. Flory calculated configurations of real polymers based on the idea that their size is governed by two competing interactions. On one hand, steric repulsion is responsible for polymer swelling. On the other hand, chain connectivity creates an attraction counteracting monomer departure. Flory combined both interactions and derived a single parameter, ν , which summarizes the net interaction between monomers. An important result from Flory′s theory for a polymer in good solvent is that it yields a universal power-law dependence of polymer size R on the number of monomers N, i.e.

$$R^2 \sim N^{2\nu} \tag{1.1.8}$$

where ν

$$\nu = \frac{3}{2+d} \tag{1.1.9}$$

where d is the dimension in which the polymer resides.

In contrast to ideal chains, the scaling behaviour of the polymer size now exhibits a dependence on the dimension of space d in which the polymer resides. Compared to ideal linear polymers where $\nu = 1/2$, Flory concluded the scaling exponent for real chains to be $\nu = 3/4$ and $\nu = 3/5$ in two and three dimensions respectively.

1.2 Dynamic properties of polymer chains

As studying either mean-squared end-to-end or the radius of gyration are the basic quantities to study the static properties of a polymer chain, the first quantity that we look for in studying the dynamic property is determining the diffusion coefficient D of the center of mass of a polymer chain. First we shall see a polymer model which is believed to be a real model of polymer chains, the Rouse model.

1.2.1 The Rouse model

In the Rouse Model [3] monomers connected by springs set up the polymer chain, shown in figure 1.4 below. The average distance between two consecutive monomers is taken to be b, i.e. the root-mean-square bond length. Interaction between monomers is exerted only by the connecting springs. Excluded volume and hydrodynamic interactions with the surrounding solvent are disregarded. The motion of a Rouse chain can be described by a Langevin equation which determines the time evolution of the individual monomer positions. Assuming a harmonic form of the interaction potential yields:

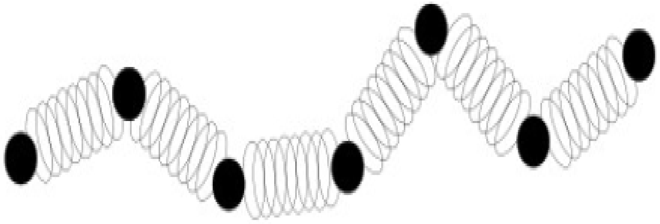

Figure 1.4: Bead-spring model with 7 beads and 6 springs.

$$\zeta \frac{d\vec{r}_i}{dt} = -k(2\vec{r}_i - \vec{r}_{i+1} - \vec{r}_{i-1}) + \vec{f}_i \tag{1.2.1}$$

$i = 2, 3, 4......., N - 1$

where ζ is the monomers friction coefficient, k the amplitude of the harmonic force and f_i a random force with Gaussian statistics. Care must be taken for the first and last monomer.

$$\zeta \frac{d\vec{r}_1}{dt} = -k(\vec{r}_1 - \vec{r}_2) + \vec{f}_1 \tag{1.2.2}$$

$$\zeta \frac{d\vec{r}_N}{dt} = -k(\vec{r}_{N-1} - \vec{r}_N) + \vec{f}_N \tag{1.2.3}$$

Two key quantities connected to the dynamical behavior are the diffusion coefficient of the polymers center of mass, D , and the relaxation time of the polymer chain, τ_R. These two parameters exhibit a distinct scaling dependence on the number of monomers N.

$$D \sim N^{-1} \tag{1.2.4}$$

$$\tau_R \sim N^{1+2\nu} \tag{1.2.5}$$

as it would be seen clearly below.

1.2.2 Polymer diffusion

To understand the diffusion of a polymer chain, we will focus on the diffusion of the center of mass which is analogous to a single particle diffusion. To this end we can see the diffusion equation of a single particle in one dimension which is given by the following relation:

$$\frac{\partial P(x,t)}{\partial t} = D \frac{\partial^2 P(x,t)}{\partial x^2} \tag{1.2.6}$$

where $P(x,t)$ is the probability of the particle being at a position x at a time t.

If we solve this differential equation we have the following results.

$$< x >= 0 \tag{1.2.7}$$

$$< x^2 >= 2Dt \tag{1.2.8}$$

where D is the diffusion constant. For $d \geq 1$ (d dimension) we shall have the expression for equation 1.2.8

$$< r^2(t) >= 2dDt \tag{1.2.9}$$

If we rearrange equation 1.2.9, we can write the expression for the diffusion constant D as

$$D = \frac{< r^2(t) >}{2dt} \tag{1.2.10}$$

Thus D is the diffusion constant that expresses the diffusion of a single particle's CM motion. But in actual case, the diffusion constant for a polymer is different from the one we presented above. And it was the Rouse Model which discussed above first treats polymer dynamics to a good approximation. The Rouse model described above was developed to describe the dynamics of a polymer molecule in solution. The Rouse model predicts that the mean square displacement $r^2(t)$ of the molecule's CM is:

$$< r^2(t) >= 2d\frac{k_B T}{N\zeta}t \tag{1.2.11}$$

where k_B is Boltzmanns constant, T is the temperature, ζ is the friction coefficient of one monomer and N is the number of monomers. Comparing with equation 1.2.10 above we have for the free solution diffusion constant D as:

$$D = \frac{k_B T}{N\zeta} \tag{1.2.12}$$

As we can see the relationship between the diffusion constant D and the polymer length N is inversely proportional:

$$D \sim N^{-1} \tag{1.2.13}$$

Though the Rouse model considers neither hydrodynamic interactions nor the excluded volume effect, it is still the basis for polymer dynamics and is considered as a real polymer model.

1.3 Introduction to polymer translocation

In this section we discuss the process of a polymer translocation through a small pore. Molecular transport through cell membranes is an essential mechanism in living organisms. Such events occur frequently in living cells. Often, the molecules are too long, and the pores in the membranes too narrow, to allow the large molecules to pass through as a single unit. In such circumstances, these molecules have to deform themselves to squeeze -i.e- translocate- themselves through the pores. Thus the translocation of biopolymer through nanometer-scale pores is one of the most crucial process in biology. Such as DNA and RNA translocation across nuclear pores, protein transport through membrane channels, and virus injection [4-6]. Moreover, translocation processes might eventually prove useful in various technological applications, such as rapid DNA sequencing [7-8], gene therapy and controlled drug delivery, etc [9]. In addition to its biological relevance, the translocation process through nanometer-sized pores is of fundamental interest for physicists and chemists. Because the diameter of these channels is not much larger than the polymers passing through them, as a result the translocation dynamics in these small constrictions is a result of multiple steric, hydrodynamic, and electrostatic interactions [10]. During the past years, an increasing number of elaborate experimental [11-18], theoretical [19-32] and numerical [33-40] approaches have been applied to elucidate the physics of the translocation process under various conditions.

The translocation of a polymer through a nanopore faces a large entopic barrier due to the loss of a great number of available configurations. In order to overcome the barrier and to speed up the translocation, an external field or interaction is often introduced. The possible driving mechanisms include an external electric field, a chemical potential difference, or selective adsorption on one side of the membrane. For example, in 1996, Kasianowicz et al. [10] reported that an electric field can drive single-stranded DNA and RNA molecules through the $\alpha - hemolysin$ channel of inside diameter 2 nm and that the passage of each molecule is signaled by the blockade in the channel current.

Inspired by the experiments [10], a number of recent theories [19-32] have been developed for the dynamics of polymer translocation. Even without an external driving force, polymer translocation remains a challenging problem. To this end, Park and Sung [19] and Muthukumar [22] considered equilibrium entropy of the polymer as a function of the position of the polymer through the nanopore. The geometric restriction leads to an entopic barrier. Standard Kramer analysis of diffusion through this entopic barrier yields a scaling prediction of the translocation time $\tau{\sim}N^2$ for long chains. However, as Chuang et al. [25] noted, this quadratic scaling behavior is at best only marginal for phantom polymers and cannot be correct for a self-avoiding polymer. The reason is that the equilibration time; $\tau_{equil}{\sim}N^2$ for a phantom polymer and $\tau_{equi}{\sim}N^{1+2\nu}$ for a self-avoiding polymer, where ν is the Flory exponent ($\nu = 3/4$ and $3/5$ in 2D and 3D, respectively). Thus the exponent for τ_{equil} is larger than two for self-avoiding polymers, implying that the translocation time is shorter than the equilibration time of a long chain, thus rendering the concept of equilibrium entropy and the ensuing entropic barrier inappropriate for the study of translocation dynamics. Chuang *et al.*[25] performed numerical simulations with Rouse dynamics for a 2D lattice model to study the translocation for both phantom and self-avoiding polymers. They decoupled the translocation dynamics from the diffusion dynamics outside the pore by imposing the artificial restriction that the first monomer, which is initially placed in the pore, is never allowed to cross back out of the pore. We will refer to the translocation time obtained this way as τ_{tran}. Their results show that for large N, translocation time τ_{tran} scales approximately in the same manner as equilibration time, but with a larger prefactor.

Of the three main translocation processes of a polymer chain studied to date either theoretically or by computer simulation, namely :

I. Unbiased translocation,wherein the polymer translocates purely due to thermal fluctuations

II. Field-driven translocation, wherein translocation is driven by a potential difference across the pore or an electric field applied, and

III. Pulled translocation, wherein translocation is facilitated by a pulling force at the head of polymer;

In this thesis we focus on the unbiased polymer translocation through a small pore.

From the statistical physics perspectives, the translocation problem can be seen as a kind of tunneling process over an entropic barrier. This entropic barrier arises because the number of states available to the polymer is significantly decreased by the presence of the membrane.

For a polymer of length N which holds a SAW, the partition sum $Z_b(N)$ in the bulk scales as:

$$Z_b(N) \approx A\mu^N N^{\gamma-1} \tag{1.3.1}$$

The last factor, $N^{\gamma-1}$ is called the enhancement factor, with a universal exponent γ, $\gamma = 49/32$ and $\gamma \approx 1.16$ in two and three dimensions respectively- while A and μ are not universal, where μ is the connectivity constant. The corresponding number of states for the same polymer but whose end is tethered to the membrane is approximated as:

$$Z_w(N) \approx A_1\mu^N N^{\gamma_1-1} \tag{1.3.2}$$

in which μ is not affected by the introduction of the membrane, γ_1 is a different universal exponent $\gamma_1 = 61/64$ and $\gamma_1 \simeq 0.68$ in two and three dimensions respectively, while A_1 is again not universal.

Consider a translocating polymer, for which there are n monomers on one side and the rest $(N-n)$ monomers on the other side of the pore. Since this situation can be seen as two strands of polymers with one end (of each strand) tethered on the membrane, the number of states for the polymer is given by $Z_w(n)Z_w(N-n)$ which attains a minimum value when $n = \frac{N}{2}$.

Thus the effective entropic barrier faced by the translocating polymer is $\triangle S$, where

$$\triangle S = S_b - S_w \tag{1.3.3}$$

where S_b and S_w are the bulk entropy and the entropy after the introduction of the membrane respectively. And we know that:

$$S = k_B lnZ \tag{1.3.4}$$

where k_B is the Boltzmann factor, and here we assume $k_B = 1$. Thus;

$$\Delta S = lnZ_b - lnZ_w \tag{1.3.5}$$

and,

$$Z_w = Z_w(n)Z_w(N-n) \tag{1.3.6}$$

at $n = \frac{N}{2}$

$$Z_w = [Z_w(\frac{N}{2})]^2 \tag{1.3.7}$$

As a result we find the total entropy expression for the whole system as follows:

$$\Delta S = rln(N) + t \tag{1.3.8}$$

where r and t are given as follows:

$$r = \gamma - 2\gamma_1 + 1 \tag{1.3.9}$$

and

$$t = lnA - 2lnA_1 + 2(\gamma_1 - 1)ln2 \tag{1.3.10}$$

Thus since we are studying unbiased polymer translocation, to overcome the entropic barrier we put the middle monomer tethered mid-way in the hole. We shall discuss this in detail later in chapter two.

Generally, we investigate the unbiased translocation dynamics in a 2D lattice model by focusing on different parameters. In particular, we investigate the effect of varying the pore length and width, the effect of polymer-wall interaction on the polymer translocation on the escape time. We also see that the dependence of the stiffness of the polymer on the translocation dynamics.

Chapter 2

Models and Methods

Although there are many methods and techniques to simulate any kind of simulation work, Monte Carlo (MC) and Molecular Dynamics (MD) are by far the most popular ones. As a result one has to make a decision to use one of these according to the problem in hand. If one chooses to use MC, then one has a further choice, namely whether to do the simulation on a lattice or in the continuum. It is also important to decide how detailed a microscopic model to use. For the long time, large-distance phenomena which are of interest here, a realistic, microscopic model for the polymer would require too much computer time. Instead, for simulating our problem; polymer translocation, we use simple coarse grained models, which incorporate the essential physics such as the non crossability of the chains and thus we used a lattice MC method.

In MC method the subsequent configurations of the polymer is generated stochastically (randomly). The collective motion of a chain is modeled by the acceptance of an attempted new configuration. Under certain circumstances one can use such an approach not only for static properties but also for the investigation of the dynamics of the system. In order to use MC methods for the simulation of the dynamical properties of polymers, one needs a method which is based on local stochastic moves. For a non reversal random walk (RW) or self-avoiding walk (SAW), that is a random walk with excluded volume for nearest and next-nearest neighbors along the chain only, it can be shown that this method reproduces the Rouse model (the more realistic model of polymers). In such a case the local configurations and the attempted moves are the same as in the case in which one includes the excluded volume interaction between all monomers. In order to fulfill this requirement, it is necessary to structure the algorithm which will be discussed later.

2.1 Lattice models

2.1.1 Standard lattice algorithm

MC simulations for lattice polymers in which a flexible polymer chain is modeled by a self-avoiding random walk (SAW) on a periodic lattice have been widely used to study the properties of linear and ring polymers, both for dilute chains as well as for entangled chains at moderate density.

The advantages of working on a lattice are clear. Since one is dealing with a discretized system, one can use integer arithmetic instead of floating point. This means that determining the distance between two monomers can be done very quickly leading to a very fast update procedure. For large enough memory, as is standard for modern computers, one can store the entire lattice and check the excluded volume constraint simply by checking the occupation of the lattice sites. Another advantage of this lattice algorithm is that it can be used in all spatial spaces and is ergodic.

2.1.2 Bond Fluctuation Method

In order to circumvent some of the difficulties of the standard lattice MC methods, particularly at high density, one might try to construct a chain of small spheres and allow the bond angle and even the bond length to vary. Off-lattice simulations in which the bond angle but not the length is allowed to vary, the pearl necklace model, as well as models in which both the bond angle and length are allowed to fluctuate, the bead-spring model, have become very popular recently, particular for studying dense melts and tethered chain systems. However, what is needed for our simulation is a dynamic algorithm which moves a polymeric object by local jumps of monomers, which is useful for investigating dynamic as well as static properties of polymers. Consequently we use the BFM first introduced by I. Carmensin and K. Kremer [41] in 1988.

Definition of the Bond Fluctuation Method

Consider a polymer chain that consists of N monomers (bonds). Although we can use different types of lattice models, here we used a square lattice with lattice constant one unit. Each monomer occupies four lattice sites of a unit cell. This model can be named as a four-site model in 2D. To satisfy the SAW condition, each lattice site can only be part of a single monomer. And the bond length between two adjacent monomers fluctuates in the range of 2 which is the minimum distance which guarantees the excluded volume effect and $\sqrt{13}$ lattice units which is the upper limit, which guarantees that bonds will never get cut and that there is no bond crossing. Figure 2.1 shows all the possible positions of a monomer that could be bonded with the monomer positioned at 0. As the bond length is in the range of $2 \leq l \leq \sqrt{13}$ lattice units, lattices with the same color represent equal bond lengths. As an example the four blue colors show the possible positions of a monomer that can be bonded with the center monomer positioned at 0 with a bond length of 2 lattice units. All together there are 36 bond vectors and the lattices numbered from 1 to 36 represent these possible positions between two bonded monomers.

In short the steps that we follow to implement the BFM are:

Bond fluctuation Monte Carlo method

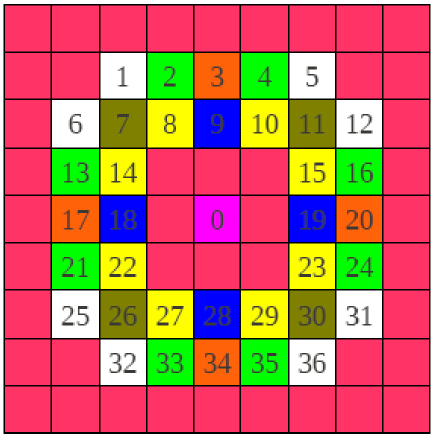

Figure 2.1: A figure showing the restriction of the bond length or segment length $2 \leq l \leq \sqrt{13}$ for the two-dimensional case. Assuming monomer or bead 0 on the plaquette in the center, the bead connecting bead 0 can occupy 1 of the 36 allowed plaquettes, which are labeled by numbers 1 to 36.

(1) Choose an initial state of the polymer

(2) Randomly choose a monomer

(3) Randomly choose a plaquette (direction) (from among the allowed possibilities) to which a move will be attempted

(4) Check the excluded volume and bond length restrictions; if these are violated return to step (2)

Optional conditions:

If the move leads to an energetic difference $\triangle E$ for example due to an electric field or an adsorbing force to the walls. In this case a Metropolis algorithm is implemented which is defined as:

(5) Calculate the energy change ΔE between the new and the old configurations of the system, and if $\Delta E < 0$ the move is accepted, otherwise

(6) Generate a random number r such that 0 < r < 1

(7) If $r < e^{-\frac{\triangle E}{k_\beta T}}$, accept the move , otherwise

(8) Go to step 2. N elementary moves define one MC time step.

2.2 Simulation procedure

Since we use a lattice for our simulation purpose, the first thing that we do is preparing the lattice itself. Thus a 5000 X 5000 square lattice was formed. Then by putting the center of mass of polymer at the center of the lattice, we tried to see how the chain diffuses through time by the bond fluctuation Monte Carlo method explained above. We see how the CM of the polymer diffuses from the initial position for different times, and we computed the diffusion constant D.

To study the effect of self-avoidance on translocation in the coiled state, higher dimensional simulations (d > 1) are necessary. Two dimensional polymers are ideally suited to this purpose for dual reasons that excluded volume effects are more apparent, while computation times are shorter than three dimensional case.

In our simulation the membrane (wall) with the hole (pore) is constructed from a row of immobile monomers arranged in a straight line, with L lattice constant gap or length representing the pore. The length L and width W of the pore are free parameters which have influence on the translocation dynamics. For example a pore of $L = 3$ and $W = 2$ lattice units is small enough to allow only a single monomer to pass through. Since we are investigating a non-equilibrium process, the initial condition may play an important role. According to our setup, a polymer of size N is initially placed in a state in which the number of monomers n on each side of the pore is equal. The free energy F in this state can be expressed as [42]

$$F = A_1 ln(n) + A_2 ln(N - n) + n\Delta\mu \tag{2.2.1}$$

The factors $A_{1,2}$ depend on conformational statistics on each side, $\Delta\mu$ is the difference in chemical potential between the two reservoirs. In case of an undriven (unbiased) system, i.e. no difference in solvent on both sides, $A_1 = A_2$ and $\Delta\mu = 0$. Thus, F exhibits a free energy barrier symmetric in n/N. This symmetry means that a translocation of the polymer to the left or to the right is equally likely.

Thus in the present work we consider a polymer which is initially placed symmetrically in the middle of the pore to overcome the entropic barrier, i.e, the initial configuration is constructed by fixing the middle monomer $\frac{N}{2}$ in the hole, and equilibrating the remaining monomers for more than the relaxation or equilibration time $\tau_{equil} \sim N^{2.50}$ in two dimension. After this equilibration is finished, at $t = 0$, the fixed middle monomer is allowed to move freely. Thus the simulation ends at a time $t = t' > 0$ when the entire polymer is on either side of the membrane. We call this t' the escape time. This procedure is repeated for a large number of times for each polymer length N, and take the escape time τ which happened most. Numerically, τ can be sampled much more efficiently than τ_{tran}, where τ_{tran} is defined as the time that the polymer needs to translocate through a pore by putting the first monomer at the gate of the pore under a restriction that it never gets back, and the whole translocation process ends when the last monomer is on the other side of the pore. We will show numerically that the escape time τ scales as $\tau^{1+2\nu}$ in agreement with our result [43]. Wolterrink *et al.* [30] have studied the translocation dynamics scaling for a 3D lattice model of a polymer. They have also found that τ scales as $\tau^{1+2\nu}$, in agreement with our work.

Here we choose L=7 and W=3 just for simplicity as they both are free parameters. Figure 2.2 represents a polymer tethered mid way on the pore ready to escape either side of the membrane after relaxation.

Figure 2.3 shows that a schematic representation of a polymer of length N=51 after it translocated or escaped to the right side of the membrane.

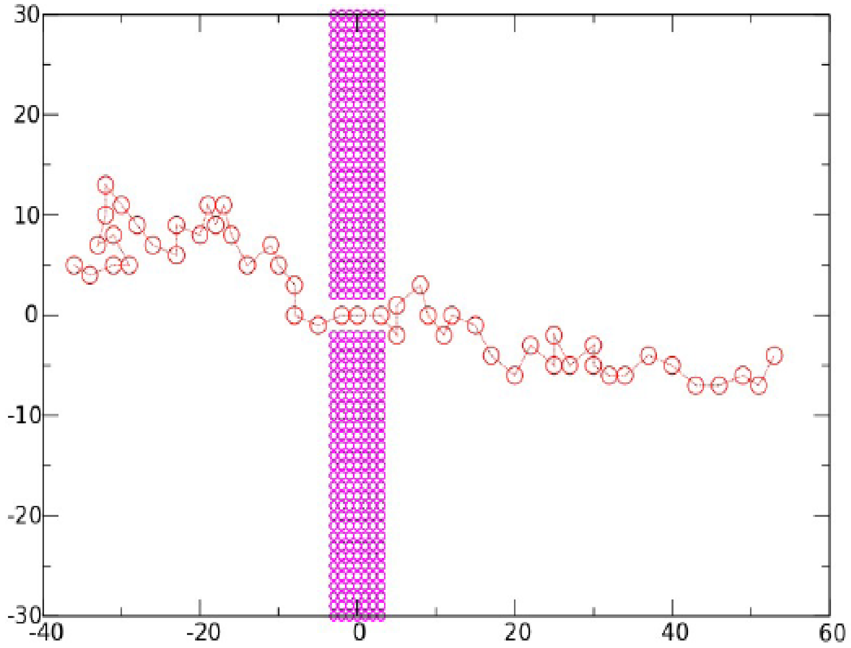

Figure 2.2: Schematic representation of a polymer of length N=51 after relaxation. The middle of a polymer is initially placed in the center of the pore. The pore has a length of $L = 7$ and width of $W = 3$.

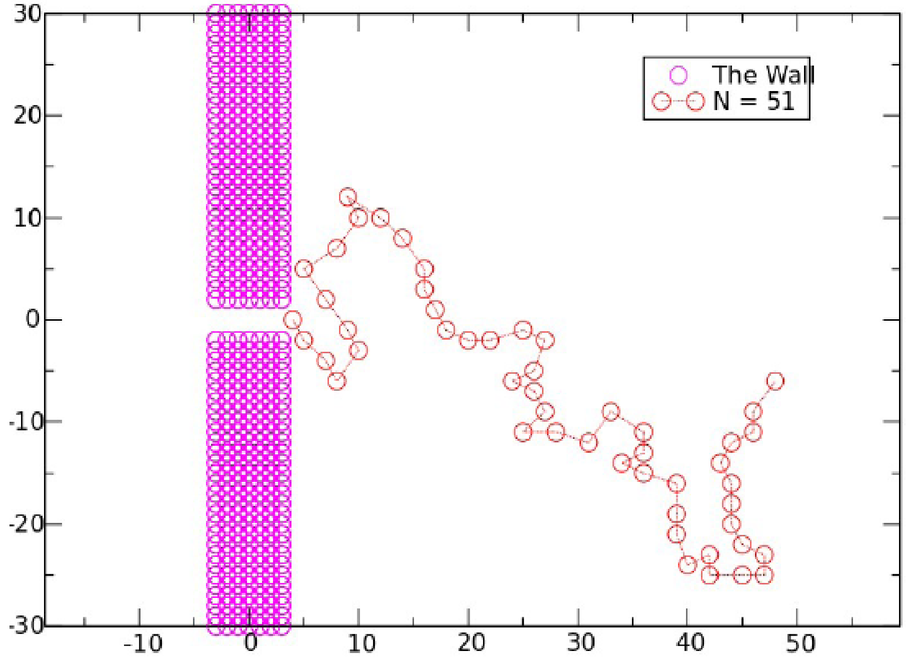

Figure 2.3: Schematic representation of a polymer of length $N = 51$ after translocated through a pore of length L=7 and width W=3.

Chapter 3

Results and Discussion

The organization of this chapter is as follows. In the first section we discuss the results of the diffusion of a polymer chain in a random media with the bond fluctuating model combined with the single-segment Monte Carlo moves which we discussed previously. In this section we see both the static and dynamic behaviors of a polymer chain. In the next section, results from polymer translocation through a nanopore are discussed.

3.1 Results from polymer diffusion

In this section, before we directly go to the dynamical properties, we first control the static ones. Thus during our simulation we calculated the average-squared end-to-end distance and the average-squared radius of gyration of a polymer chain as a function of polymer length N. As discussed in the first chapter, from Flory's theory, a polymer in a good solvent yields a universal power-law dependence of the number of monomers N on the size of the polymer. As a result, for a self avoiding (SA) polymer chain the Flory exponent 3/4 for the two dimensional case is clearly exhibited. The log-log plot of $< R^2 >$ versus N (fig 3.1) and log-log plot of $< R_g^2 >$ versus N (fig 3.2) have slopes of 1.513 and 1.51 respectively which agree with Flory's theory [3] of being 1.5 in two dimensional. Thus both average-squared end-to-end distance and the average-squared radius of gyration have a scaling power of $N^{2\nu}$, where ν is the Flory exponent.

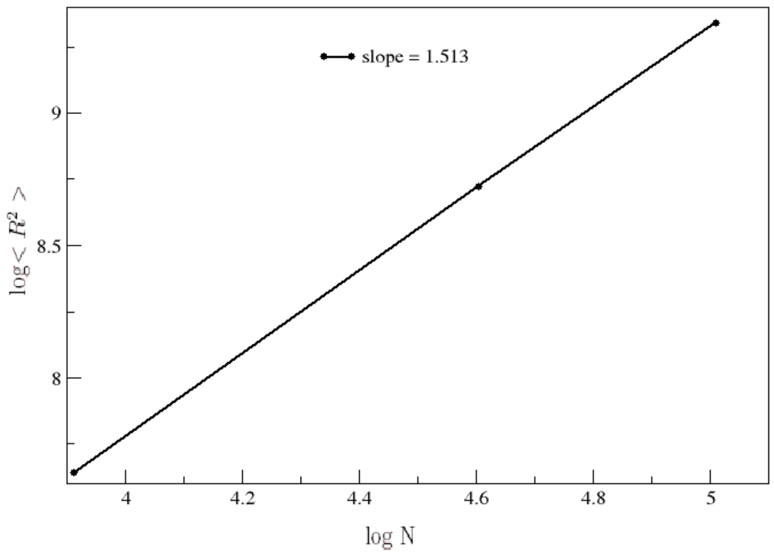

Figure 3.1: Plot of log$< R^2 >$ versus log N for a SAW done with the four-site model.

When we come to the dynamical properties we monitored the diffusion of the center of mass of the chain by using our dynamic Monte Carlo method described in the previous sections. The time dependent mean square displacement of the center of mass CM of the chain is $r^2(t)$ and is given by:

$$r^2(t) =< [\vec{r}_{cm}(t) - \vec{r}_{cm}(0)]^2 > \tag{3.1.1}$$

$r^2(t)$ describes the diffusion of the over all system.

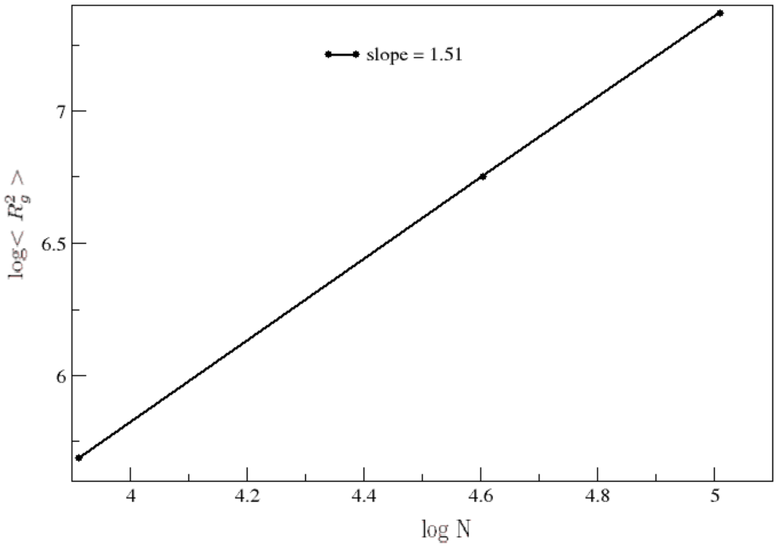

Figure 3.2: Plot of log$< R_g^2 >$ versus log N , the slope of the graph is 1.51 as mentioned on the onset which is close to $< R_g^2 > = < N^{2\nu} > = N^{1.5}$.

Following the Rouse Model one expects;

$$r^2(t) \sim t \tag{3.1.2}$$

In Rouse model the diffusion constant D is given by:

$$D = \frac{kT}{\zeta N} \tag{3.1.3}$$

with

$$4D = \lim_{t->\infty} \frac{r^2(t)}{t} \tag{3.1.4}$$

The diffusion constant D for a chain of 100 monomers is about $4.629X10^{-3}$ in square lattice units per Monte Carlo time step (fig. 3.3). From this we can conclude that the Rouse model defined for a random walk are not defined well for a two dimensional self avoiding walk as there is the effect of the excluded volume interaction in a self avoiding walk.

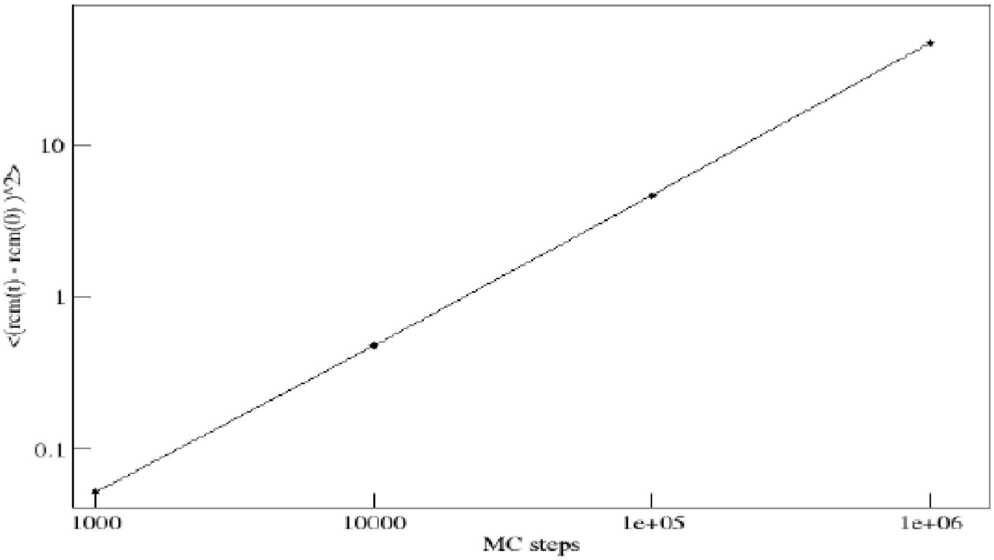

Figure 3.3: Plot of diffusion of center of mass $r^2(t) =< [\vec{r}_{cm}(t) - \vec{r}_{cm}(0)]^2 >$ for a SA polymer of chain length 100.

3.2 Translocation of a polymer

In this section we shall see the dependence of the translocation time or escape time in our case on different parameters such as polymer length N, pore length L and width W, the stiffness of the polymer chain, and polymer-wall interaction.

3.2.1 Escape time distribution for polymer translocation

We study the passage (translocation) of a self-avoiding polymer through a membrane pore in two dimensions. To do this we tried to see the distribution of the escape times of a polymer through a pore. We numerically measure the distribution $P_N(t)$ of the escape time t. Figure 3.4 shows the probability distribution function for $P_N(t)$ $N = 17, N = 37$

and $N = 67$. From the figure (3.4) we exhibit that the histogram of the escape time is a long tailed distribution in a good agreement with [46] as the probability distribution function decays for large values of escape times.

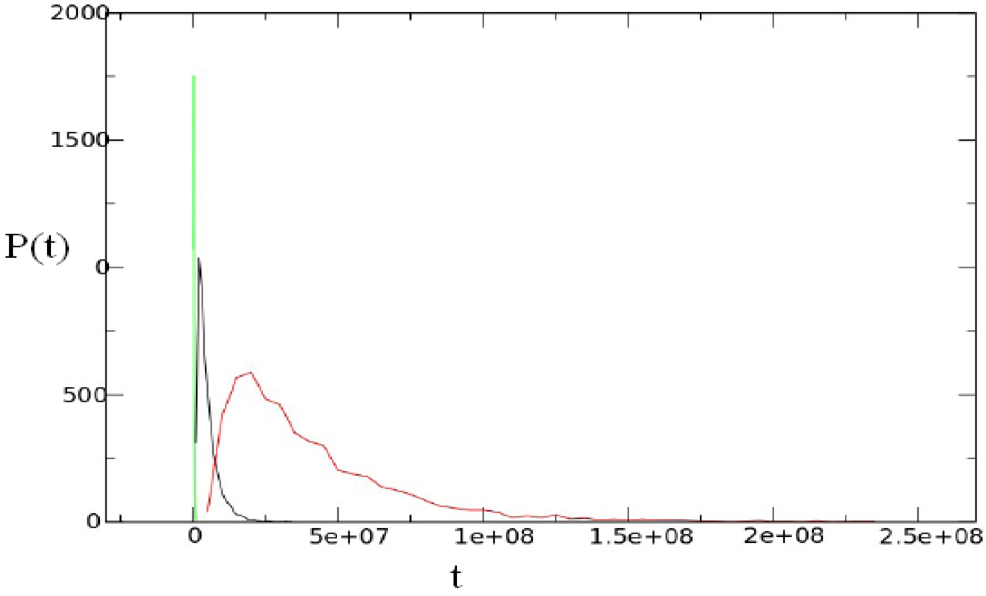

Figure 3.4: Escape time distribution of polymer translocation for $N = 17, N = 37$ and $N = 67$ left to right, obtained from 5000 runs each.

3.2.2 Polymer translocation through a short pore

As discussed in our simulation setup, the middle monomer is placed at the center of the pore; as a result the polymer can escape the pore from either side in a time defined as escape time τ. We simulated the escape time for short polymer chains for the scale of τ and took the escape time value which happened most. Interestingly the Flory exponent ν has been seen to influence the scaling of the escape time. The log-log plot of the escape time τ versus N is shown in figure 3.5 that shows $\tau \sim N^{\alpha}$, where we found α to be $\alpha = 2.58 \pm 0.01$ in agreement with $1 + 2\nu$.

Thus the scaling of $\tau \sim N^{1+2\nu}$ implies that τ scales in the same manner as the chain equilibration time τ_R in the Rouse theory which is defined as the time a polymer chain needs to move a distance equal to its radius of gyration R_g, $\tau_R \sim \frac{R_g^2}{D}$, $D \sim 1/N$ being the diffusion constant with a big prefactor.

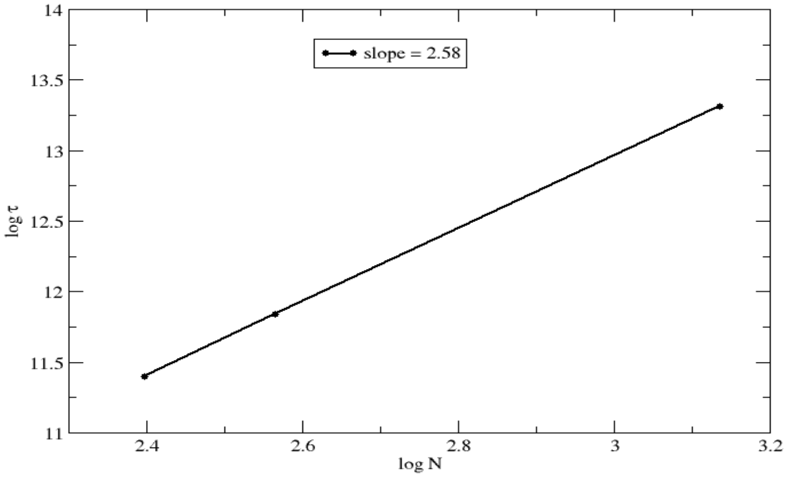

Figure 3.5: Log-log plot of escape τ as a function of polymer chain length N.

3.2.3 Dependence of polymer translocation on the stiffness of the chain

The stiffness of the polymer chain is controlled by an angle dependent potential energy given by [43]:

$$\frac{E}{k_\beta T} = \frac{-J}{k_\beta T} \sum_{i=1}^{N_{FB}-2} \cos\theta_i \tag{3.2.1}$$

where in the above expression, J is the interaction strength, N_{FB} is the number of segments in the chain, θ the angle between two adjacent bonds, k_β is the Boltzmann constant and T is the absolute temperature of the system. In this case we introduced dynamics by Metropolis moves of a single segment, with a probability of acceptance $\min[e^{\frac{-\Delta E}{k_\beta T}}, 1]$, where ΔE is the energy difference between the new and the old states. As to an elementary MC move which we discussed previously, we randomly select a monomer and attempt to move it onto an adjacent lattice site (in a randomly selected direction) and see if the new position does not violate the excluded-volume effect or maximal bond-length restrictions. But in this case, since there is an energy difference between the new and the old configurations of the polymer due to the stiffness of the polymer, we accept or reject the move according to Metropolis criterion.

In our simulation we set $k_\beta T = 1$ and $\frac{J}{k_\beta T} = 5$, and examined τ as a function of polymer length N. We find that $\tau \sim N^{2.51 \pm 0.01}$ and this confirms that the stiffness of the polymer does not affect the scaling behavior of τ. Figure 3.6 below illustrates the above discussion.

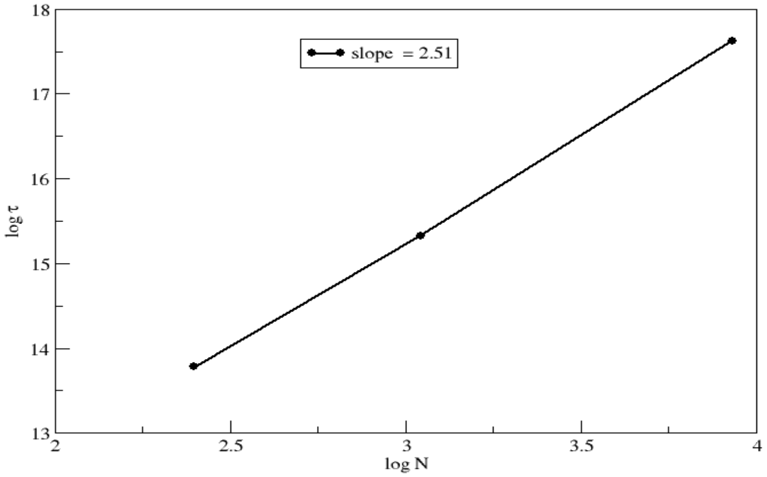

Figure 3.6: Log-log plot of escape τ as a function of polymer chain length N for a stiff polymer.

3.2.4 Dependence of polymer-pore interaction on polymer translocation

Polymer-pore interaction influences the translocation of a polymer chain through a pore. In recent experiments striking differences were found for the translocation time distribution of polydeoxyadenylic acid (poly(dA)100) and polydeoxycytidylic acid (poly(dC)100) DNA molecules [44,45]. The origin of the different behavior was attributed to stronger attractive interaction of poly(dA) with the pore. Thus during our simulation we have tried to see the dependence of a weak polymer-pore interaction on the translocation time. And from our result we observed an increase in the escape time with the polymer length N slowly as compared to the absence of polymer-wall interaction. Figure 3.7 shows that for short polymers, we plotted the log-log plot of the average escape time τ as a function of the polymer length, and we found a slope of 3.54, which when compared to the free one which is 2.5, there is a slight change. Thus for relatively weak interaction we see a linear dependence with the average escape time.

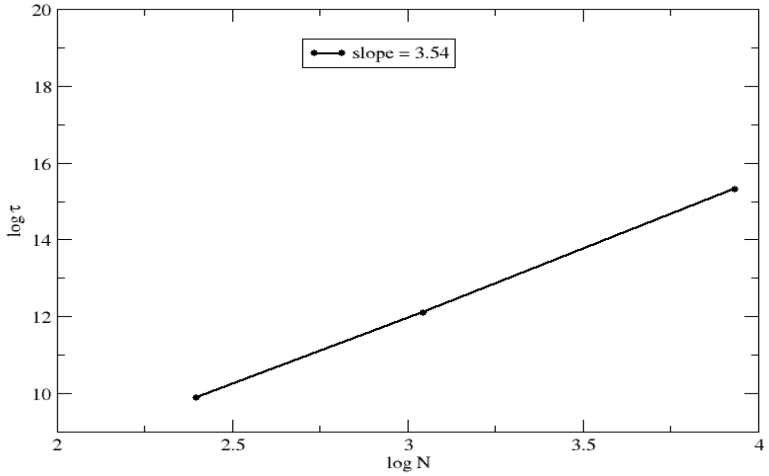

Figure 3.7: Log-log plot of average scape τ as a function of polymer chain length N for a polymer-pore interaction. Here $\varepsilon = -2.0$ which express the polymer-pore interaction

3.2.5 Polymer translocation through a wide pore

Here we present and discuss the result from our simulation, for the dependence of the average escape time as a function of polymer chain N for different pore widths. Figure 3.8 below illustrates the translocation of a polymer chain through pore widths having value, $W = 3, 4, 5, 6, 7, 8$. As it can be seen, when the pore's width increase the time needed for the same size of a polymer chain to escape from the pore is less as it can access many places within the pore.

Thus we can see an inverse relation between the average escape time and the pore width. From (Fig. 3.8) as the pore's width increases from $W = 3$ to $W = 8$ lattice units, we clearly see that the average escape time for a polymer chain of length N decreases.

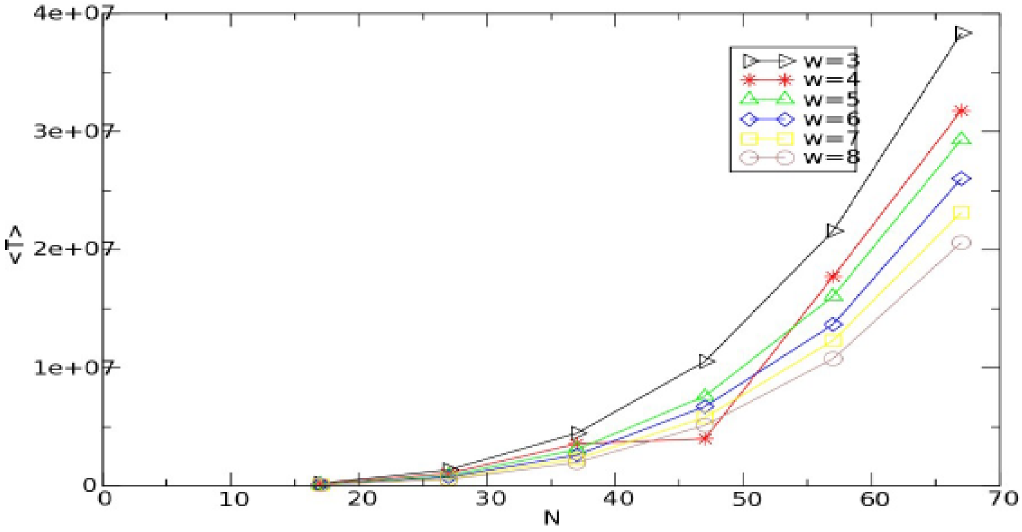

Figure 3.8: Average scape time τ versus the chain length for polymer translocation through a wide pore.

Chapter 4

Conclusion

In this paper we presented and tested a Monte Carlo algorithm for both static and dynamical simulations of polymers. Due to the concept of fluctuating bond lengths, it has the advantage of giving realistic (Rouse) dynamics in all spatial dimensions and allowing for simulations of branched structures.

We presented polymer diffusion and polymer translocation through a nanoscopic pore in the absence of any external driving force. We addressed the translocation problem numerically. Our numerical results show that accurate estimates for the scaling exponents of the static behaviors of a polymer chain, namely the average squared end-to-end distance and the average squared radius of gyration as a function of the polymer length N are obtained. For a SA polymer our simulation results show that $< R^2 > \sim < R_g^2 > \sim N^{2\nu}$ which agree with a theoretical values predicted by Flory.

We have also studied the dynamical behaviors of a polymer chain. We saw the diffusion of a linear polymer chain and calculated the diffusion constant D. The diffusion process plays a major role in the translocation process. In the translocation process we investigated the the relationship between the escape time with different parameters that influences the process. Some of these parameters are the polymer length N, the width of the pore through which the polymer translocates, the stiffness of the chain and other parameters. As the presence of the wall produces an entropic barrier between the cis and trans side of the pore, we overcome this entropic barrier by initially placing the middle monomer of the polymer at the center of the pore in a symmetric position. This symmetry means that a translocation of the polymer to the left or to the right is equally likely. Indeed, we observe for unbiased translocation that on average 50 percent of the polymers migrate to the left and the other half are finally found in the right reservoir. Thus we studied the unbiased polymer translocation dynamics mainly by seeing the escape time that the chain leaves the pore either to the right or to the left of the pore instead of putting a restriction that the first monomer which is initially at the gate of the pore is never allowed to cross back out of the pore.

To this end our numerical results show that accurate estimates for the scaling exponents of the escape time as a function of N are obtained, which is $\tau \sim N^{1+2\nu}$.

Bibliography

[1] Doi M and Edwards S. The Theory of Polymer Dynamics.Oxford University Press, 2001.

[2] Flory P. Statistical Mechanics of Chain Molecules. Inter science New York, 1969

[3] Rouse P. A theory of the linear viscoelastic properties of dilute solutions of coiling polymers. J Chem Phys, 21, p. 1271, 1953

[4] R. V. Miller, Sci. Amer. 278, 66 (1998).

[5] J. Han, S. W. Turner, and H. G. Craighead, Phys. Rev. Lett. 83, 1688 (1999).

[6] S. W. P. Turner, M. Calodi, and H. G. Craighead, Phys. Rev. Lett. 88, 128103 (2002).

[7] D.-C. Chang, Guide to Electroporation and Electrofusion (Academic, New York, 1992).

[8] Bezrukov S M 2000 J. Membr. Biol. 174 113.

[9] J. J. Kasianowicz, E. Brandin, D. Branton, and D. W. Deaner, Proc. Natl. Acad. Sci. U.S.A. 93, 13770 (1996).

[10] M. Aktson, D. Branton, J. J. Kasianowicz, E. Brandin, and D. W. Deaner, Biophys. J. 77, 3227 (1999).

[11] A. Meller, L. Nivon, E. Brandin, J. A. Golovchenko, and D. Branton, Proc. Natl. Acad. Sci. U.S.A. 97, 1079 (2000).

[12] S. E. Henrickson, M. Misakian, B. Robertson, and J. J. Kasianowicz, Phys. Rev. Lett. 85, 3057 (2000).

[13]A. Meller, L. Nivon, and D. Branton, Phys. Rev. Lett. 86, 3435 (2001).

[14] A. F. Sauer-Budge, J. A. Nyamwanda, D. K. Lubensky, and D. Branton, Phys.Rev. Lett. 90, 238101 (2003).

[15] A. Meller, J. Phys.: Condens. Matter 15, R581 (2003).

[16] A. J. Storm, C. Storm, J. Chen, H. Zandbergen, J.-F. Joanny, C. Dekker, Nano Lett., 5, 1193 (2005).

[17] S. M. Simon, C. S. Reskin, and G. F. Oster, Proc. Natl. Acad. Sci. U.S.A. 89, 3770 (1992).

[18]W. Sung and P. J. Park, Phys. Rev. Lett. 77, 783 (1996).

[19] P. J. Park and W. Sung, J. Chem. Phys. 108, 3013 (1998).

[20]E. A. diMarzio and A. L. Mandell, J. Chem. Phys. 107, 5510 (1997).

[21]M. Muthukumar, J. Chem. Phys. 111, 10371 (1999).

[22]M. Muthukumar, J. Chem. Phys. 118, 5174 (2003).

[23]D. K. Lubensky and D. R. Nelson, Biophys. J. 77, 1824 (1999).

[24]E. Slonkina and A. B. Kolomeisky, J. Chem. Phys. 118, 7112 (2003)

[25]J. Chuang, Y. Kantor, and M. Kardar, Phys. Rev. E 65, 011802 (2002).

[26]Y. Kantor and M. Kardar, Phys. Rev. E 69, 021806 (2004).

[27] T. Ambjrnsson, S. P. Apell, Z. Konkoli, E. A. DiMarzio, and J. J. Kasianowicz, J. Chem. Phys. 117, 4063 (2002).

[28] U. Gerland, R. Bundschuh, and T. Hwa, Phys. Biol. 1, 19 (2004).

[29] A. Baumgrtner and J. Skolnick, Phys. Rev. Lett. 74, 2142 (1995).

[30]J. K. Wolterink, G. T. Barkema, and D. Panja, $http://arxiv.org/pdf/cond-mat/0509577$.

[31] S.-S. Chern, A. E. Cardenas, and R. D. Coalson, J. Chem. Phys. 115, 7772 (2001).

[32] H. C. Loebl, R. Randel, S. P. Goodwin, and C. C. Matthai, Phys. Rev. E 67, 041913 (2003).

[33]R. Randel, H. C. Loebl, and C. C. Matthai, Macromol. Theory Simul. 13, 387 (2004).

[34] Y. Lansac, P. K. Maiti, and M. A. Glaser, Polymer 45, 3099 (2004).

[35] C. Y. Kong and M. Muthukumar, Electrophoresis 23, 2697 (2002).

[36] Z. Farkas, I. Derenyi, and T. Vicsek, J. Phys.: Condens. Matter 15, S1767 (2003).

[37] P. Tian and G. D. Smith, J. Chem. Phys. 119, 11475 (2003).

[38] R. Zandi, D. Reguera, J. Rudnick, and W. M. Gelbart, Proc. Natl. Acad. Sci. U.S.A.

100, 8649 (2003).

[39] We note that in Ref. (28), the escape time discussed here is defined as the unthreading time for a polymer in the pore

[40] T. Ala-Nissila, S. Herminghaus, T. Hjelt, and P. Leiderer, Phys. Rev. Lett. 76, 4003 (1996).

[41] Macromolecules 1988,21,2819-2823.

[42] Muthukumar M. Polymer translocation through a hole. J Chem Phys, 111, p. 10371, 1999.

[43]Kaifu Luo, T. Ala-Nissila, See-Chen Ying, J. Chem. Phys. 124, 034714 (2006).

[44] A. Meller, L. Nivon, E. Brandin, J. A. Golovchenko, and D. Branton, Proc. Natl. Acad. Sci. U.S.A. 97, 1079 (2000).

[45]A. Meller and D. Branton, Electrophoresis 23, 2583 (2002).

[46]C. Chatelain, Y. Kantor and M. Kardar1, Phys. Rev. E 78, 021129 (2008).

Declaration

This thesis is my original work, has not been presented for a degree in any other University and that all the sources of material used for the thesis have been dully acknowledged.

Name: Abel Gebreegziabher

Signature:

Place and time of submission: Addis Ababa University, July 2010

This thesis has been submitted for examination with my approval as University advisor.
Name:Dr. Tatek Yergou

Signature: