Abstract

Polymer translocation is relevant to various biological processes, like passage of mRNA from nucleus to cytoplasm through nuclear pores after transcription, horizontal gene transfer in bacterial conjugation, transport of proteins and viral injection of DNA into the host cells. Polymer translocation also finds application in gene therapy, controlled drug delivery, and rapid DNA sequencing. Due to these technological applications, polymer translocation has gained considerable attention in the last two decades both theoretically and experimentally. Experiments have demonstrated that single-stranded DNA and RNA molecules can be electrophoretically driven through biological and synthetic nanopores. By using *S. aureus* α-hemolysin to form a single channel across a lipid bilayer separating two buffer-filled compartments, it was found that the ionic current through pore depends strongly on the polynucleotide sequence passing through the pore and could be used for sequencing of DNA and RNA molecules. Currently, three types of nanopores are used for sequencing purpose: biological, synthetic and hybrid nanopores. However, developing such a sequencing devices is still a challenge mainly because of remarkably fast translocation rate of ssDNA molecule through the nanopore ($\sim$ 1 nucleotide/μs). Current research has been focused on to the slowing down translocation of DNA molecule inside the pore. One possible solution can be the introduction of pore-polymer interactions. Also, these biopolymers and proteins are semiflexible in nature. However, most theoretical studies on polymer translocation assume completely flexible polymers. In this thesis, we study theoretically the driven translocation of a *semiflexible* polymer through narrow pores. The goal of this thesis is to study the effect of varying pore-polymer interactions, pore geometry and hydrodynamics on the translocation time statistics of semiflexible polymer to gain a deeper understanding of their fundamental role in polymer translocation and devise better sequencing strategies.

In the first problem, we study the *sequencing of semiflexible polymers of varying bending rigidity using patterned pores*. We first establish interplay between bending rigidity and pore polymer interactions for the translocation of a homogeneously semiflexible polymer. We then consider a heteropolymer made up of alternate stiff and flexible segments. We find that statistical fluctuations in the translocation time could be utilised for efficient sequencing of heteropolymers with varying bending rigidity, by suitably engineering pore-polymer interactions and combining readouts from multiple pores.

In the second problem, we focus on the role of pore geometry in the translocation process. Experiments on translocation of a single stranded DNA through a protein channel MspA,

which has a nearly conical geometry, indicate that such a pore is a promising candidate for nanopore DNA sequencing and other nanosensor applications. Here, we consider the *driven translocation of a semiflexible polymer through an interacting conical pore*. We study the effect of (i) the apex angle of the pore, (ii) the rigidity of the polymer, (iii) the stickiness of the pore, and (iv) the driving force, on the translocation time. We show that the translocation time shows interesting non-monotonic behavior as the pore geometry is altered by changing the apex angle of the pore.

In the third problem, we study flow driven translocation of a polymer through a narrow channel. Experimental and theoretical studies have indicated the importance of hydrodynamic interactions for driven polymer translocation through pores. Specifically, flow driven translocation involve the crossing of a free energy barrier set by the competition of the hydrodynamic drag and the entropic pressure due to the confinement of the polymer inside the pore. Theoretical and numerical studies indicate that the critical flow rate to overcome this barrier is independent of the length of the polymer and the pore geometry. We study *fluid flow driven translocation of semiflexible polymer chain through nanopore*. To incorporate hydrodynamics, we implement hybrid molecular dynamics-multiparticle collision dynamics algorithm. We show that the critical flow rate shows a striking dependence on the bending rigidity of the polymer as well as on the width of the pore.

We believe that in future, these studies on the dynamics of semiflexible polymer, will be useful for designing nanopore based devices for sequencing purpose and also understanding the physical aspects of biomolecular transport in different pore geometries.