Conclusions and Following Research Work

In this thesis, using a theoretical model, we attempt to understand the behaviour of short as well as long DNA molecules in different confined environments. A brief summary of our findings are listed below :

- As a first problem, we considered DNA in a concentrated solution and varied the value of salt present in the solution. We considered a relatively larger range of the salt concentration from 0.1 - 5.0 M and studied the thermal as well as mechanical stability of DNA in the concentrated solution. Motivated by the experiments performed by Khimji *et al* [2], we proposed a theoretical description of the behaviour of DNA molecule at higher concentration. For our study we modified the standard PBD model and have shown that the model has sufficient features to explain the behaviour of DNA at lower as well as at higher concentrations. Through the numerical calculation of canonical partition function we found that the variation in the melting temperature of the system with the value of salt concentration. Our findings shown that there is a critical value below which the cations shield the repulsion between the two negative strands of DNA. Once this value is crossed, the repulsion between the cations destabilize the double stranded DNA. Our results are found in good agreement with the experimental findings of Khimji *et al* [2]. Due to unavailability of the experimental results for infinite chains we could not compare our results for force induced unzipping of DNA molecule at high concentration.

- In the next problem we considered a phage-λ DNA molecule sequence of different base pair length that is confined in conical as well as cylindrical geometry. We considered the thermal stability of confined DNA molecule using the PBD model. Through the numerical calculation of various thermodynamics

quantities of interest, we have shown that not only the confinement but also the geometry of the confinement plays a crucial role in the stability as well the overall activity of the DNA molecule. When the confining wall is closer, the configuration space for the DNA molecule is restricted which suppresses the entropy of the chain. Since the geometry of a cylinder and a cone differs, the effect of confinement in these two case are also different. Hence the melting temperature of the system in cylindrical geometry is more than the melting temperature of the DNA that is confined in conical geometry upto a certain extent. In the case of conical confinement, we varied the angular separation (θ) as well as the pore diameter (δ). In the case of cylindrical confinement, we varied the cylinder diameter (r). With the increase in the values of these variables, the melting temperature (T_m) of DNA molecule decreases in both the geometries, however, the nature or the decrease in the values are not same in both the geometries. While in the case of cylindrical confinement, the complete chain feel the presence of confining wall, in the case of conical confinement, there is a segment of the chain which might not be seeing the confining wall due to the angular separation of the walls. There is another interesting feature in this study we have observed. The behaviour of long and short DNA molecules in both the geometries. When there is a short DNA molecule is confined in either conical or cylindrical geometry, the molecule is very stable, however, as the length of the molecules increases, the stability in conical confinement decreases after certain length. For the case, when the molecule is confined in cylindrical confinement there is no change or substaintial decrease in the stability of the molecule with increasing length. This is due to the angular confinement in conical geometry. In case of cylindrical confinement, the complete chain is restricted while in the case of conical confinement, there is a segment of the chain which might not be seeing the confining wall as the separation is angular. Through the simulation of the short DNA molecule that is confined in a cylindrical as well as in spherical geometry, Huaping*et al.* [188] has found that the melting temperature of the system decreases with the increasing diameter of the cylinder/sphere. Our findings were found to be in close agreement with the simulation results of [188]. The theoretical findings of this work may attract experimentalists to design the shells of different geometries and investigate the effect of the geometry of the shell on the stability of encapsulated DNA.

- The next problem which we have studied was motivated by the translocation

process in the cell. We have studied the thermal denaturation of a DNA molecule that is passing through a pore. Through the numerical calculations in a thermal ensemble, we have calculated the average separation of the base pairs of a DNA molecule. We have considered a DNA molecule that is confined in conical and cylindrical shaped pores. Due to the geometry of each wall, the denaturation of the DNA molecule has been found different in each geometry. Not only, the denaturation but also the melting profile of the DNA molecule passing through these geometries differ significantly. The geometry of a cone is such that the distance between the molecule and the wall increases from vertex to end. Hence, the base pairs at the vertex of the cone are restricted while the base pairs at the end have a greater entropic contribution in the opening. The same argument is not valid when DNA is confined in a cylindrically shaped core. The parallel walls of a cylinder restrict the space uniformly, due to which there is suppression of the entropy to the opening of the DNA molecule. We also considered different-length DNA molecules in these two geometries. We have found that for DNA confined in a conically shaped pore; the transition temperature is higher for the shorter molecule [180]. For DNA confined in a cylindrical pore, we have found that the transition temperature increases with the length of the molecule. We have also studied the effect of pore width on the thermal stability of the molecule passing through these two pores. We have also considered a random sequence of DNA molecules that is confined in a cylinder and have studied the melting profile of it. Our findings show that the stability of the DNA molecule passing through a pore heavily depends on the geometry of the pore. We have also studied the sequence effect on the denaturation profile of a DNA molecule confined in a cylindrical geometry. We have shown how the denaturation profile of a heterogeneous DNA molecule differs from that of a homogeneous DNA molecule. In many interesting experiments, researchers have shown how the transport properties of the dsDNA encapsulated in a carbon nanotube change with the change in the diameter of the tube [92, 93]. To have a fair understanding of the stability of DNA inside the nanotube, experimentally one can explore the effect of pore geometry on the stability of a DNA molecule during translocation process. The role of entropy from the two regions (constrained and unconstrained) would be exciting to explore. The primary source of entropy is the open pairs and strand fluctuations. The theoretical model considered here underestimate the entropy due to the

strand fluctuation. These two sources of entropy play crucial roles in the opening of dsDNA depending on the size of the pore. How the entropy of dsDNA affect the translocation process will be subject for future interest.

■ Future Scope: Following Research Work

After theoretical studies of DNA confinement effect through the statistical model, we want to simulate the DNA in confinement too. We study the simulation results of DNA and have gotten some significant results, but the results are till now not conclusive. It demands some more study than maybe we will be able to conclude any things. That is why we do not put this work as a chapter rather, we prefer to put as a future following work.