Abstract

The stability and dynamics of the dsDNA (double-stranded deoxyribo nucleic acid) molecule depend on the cell environment. In this thesis, we investigate the statistical mechanics of DNA in thermal as well as force ensembles. The natural form of DNA is a double helix. The process of disintegration of DNA helix in two strands due to thermal fluctuations is known as *thermal melting* of DNA. The first problem which we study is the denaturation of DNA in a concentrated solution. Intracellular positive ions neutralize negative charges on the phosphates of a DNA strand, conferring greater strength to the hydrogen bonds that connect complementary strands and hence, to the overall stability of the double helix DNA. The dissociation of salt like *NaCl, MgCl, KCl* present in the cell, generate the positive ions. The amount of salt or the cations governs several activities of DNA inside the cell. The cations present in the cell act as the shielding agents, which neutralize the repulsion between the two negatively charged strands of the DNA molecule. We consider a wide range of salt concentrations ($0.1 - 5.0$ mM) and study the stability of the DNA using a statistical model known as Peyard-Bishop-Dauxois Model (PBD model). Through numerical calculations, we attempt to explain the different behaviour exhibited by DNA molecules in the range as mentioned above of salt. Our results show that while at the range 0.1-1.0 M, the cations present in the solution make DNA more stable; at higher values of salt concentrations, the stability of the double-strand DNA decreases. We also compare our results with the experimental findings of Khimji *et al.* and find a close agreement with the experimental results.

In the next problem, we consider dsDNA in confined geometry. In DNA encapsulation, the ability to preserve the DNA and efficiently release it, are the processes which are inversely related. The objective of good DNA encapsulation is to find an optimal balance between these two issues. There are several parameters, like the medium and topology of the carrier, that affect the DNA encapsulation technique. *In vivo*, the DNA molecule is confined in a limited space such as the cell chamber or a channel and is in highly dense solvent conditions. This confinement

restricts the conformational properties of DNA molecules inside the cell. The thermodynamic properties of DNA molecules highly depend on the nature of the confined space. In most of the studies, researchers have considered either cylindrical or spherical geometries of the confinement. In our studies, we consider DNA confined in cylindrical as well as in conical geometries and investigate the thermal stability of the molecule. Using the PBD model, we evaluate the melting profile of DNA of different lengths in these geometries. Our results show that not only the confinement but also the geometry of the confined space plays a prominent role in the stability and conformational properties of the molecule.

The conventional *DNA mapping* scheme, which uses enzyme-based labeling, is quite expensive and exhaustive. Recently, a new concept of *denaturation mapping* appeared. This new technique is more affordable and straightforward than the earlier techniques. The method of *denaturation mapping* works on the fact that the GC rich region requires a higher amount of energy than the AT rich region to melt. Several research groups use this technique to predict the sequence of a DNA molecule through the *optical mapping* of the denaturating DNA that is confined in a rectangular nanochannel. We study the thermal melting of DNA that is fully or partially confined in different geometries. By varying the fraction of base pairs (φ) that is confined in these two different geometries (conical and cylindrical), we calculate the denaturation profile of the DNA molecule. For the conically shaped confinement, we study the effect of the cone angle (θ) and the pore width (δ) on the melting profile of homogeneous DNA molecules. Similarly, for the cylindrically shaped confinement, we investigate the effect of cylinder diameter on the melting profile of homogeneous and heterogeneous DNA molecules.

In the last part of the thesis, we discuss the time evolution of the DNA molecule confined in cylindrical geometry. We have used the GROMACS to evaluate the root mean square displacement (RMSD) values, inter and intra base-pair parameters of DNA confined in cylindrical geometry. Our preliminary results show that confinement affects the conformational properties of the DNA molecule.