

CHAPTER 19

DNA NANOMECHANICS

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Introduction

The field of DNA (deoxyribonucleic acid) nanomechanics is a young and fascinating one. Molecular biology and associated biochemical structures are primarily concerned with the fundamental length scale, which is expressed in nanometers ($1 \text{ nm} = 10^{-9} \text{ m}$). Therefore, the study of mechanical properties at such a length scale of a system is referred to as nanomechanics. The genetic substance responsible for the development, growth, and reproduction of all living things is DNA, which is also the most advanced material that can be used in nanotechnology. The DNA of a eukaryotic cell is arranged into chromosomes within living organisms. Chromatin makes up each chromosome. The nucleosome, a DNA segment that encircles a histone protein a little less than twice, is the basic building block of chromatin. Long DNA is therefore rolled up, sealed into nucleosomes, and arranged into beads on a string structure. To thoroughly comprehend how DNA is arranged and processed throughout numerous active biological processes, such as DNA transcription, DNA replication, recombination, and repair inside the cell, one must be aware of the mechanical properties of DNA.¹ The structural and mechanical characteristics of DNA molecules have been better understood because to technical advancements in singlemolecule force spectroscopy investigations throughout the past 25 years. The enormous effort of improving our understanding of DNA nanomechanics has been accomplished by several theoretical and numerical investigations. Therefore, studies in this area are critical to comprehending biological processes and offer fresh perspectives on the rapidly developing subject of DNA nanotechnology.

Structural properties of the DNA

One of the most important areas of macromolecular science is comprehending the structure and functional characteristics of biological macromolecules. Nucleic acids, lipids, proteins, and carbohydrates are the four main types of biological macromolecules. Among these, nucleic acids are the genetic component that is necessary for all living things to exist, and a change in their sequence can have an impact on how an organism functions normally. There are two different kinds of nucleic acids: ribonucleic acid (RNA) and DNA. Both may function as genetic material, depending on the organism. The interesting heteropolymer macromolecule found in living cells is called DNA. It creates a double helix with two antiparallel strands. Nucleotides make up its composition. Pentose sugar, nitrogenous bases, and a phosphate backbone make up each nucleotide. There are two kinds of nitrogenous bases: purines and pyrimidines. Purines (guanine and adenine) have two aromatic rings, whereas pyrimidines (cytosine and thymine) have a tiny, five-atom aromatic

single ring. A (adenine), T (thymine), C (cytosine), and G (guanine) are the abbreviations for the four bases mentioned above. As a result, DNA includes a message written in this alphabet of four letters, which is made up of the nucleic acids (A, T, C, and G).

Overview of mechanical properties of DNA

Six primary helical parameters must be investigated in order to comprehend the structural characteristics of DNA, which is a double helix. Three angles—twist, roll, and tilt—and three distances—shift, slide, and rise—can be related to subsequent base-pair planes. In addition, a few more geometries that are thought to accurately specify the position and orientation of the base pair in space with respect to its predecessor along the helical axis are shear, stretch, stagger, buckle, propeller, opening, x-displacement, y-displacement, inclination, tip, and pitch.

DNA under the force

DNA's stretchy characteristics have long piqued my interest. Researchers examined the force versus extension behaviour of individual ds-DNA using magnetic tweezers. It also demonstrates that the FJC model can describe the behaviour of ds-DNA at low forces but not at intermediate forces. Conversely, the WLC model provides a good explanation of the force-extension behaviour of DNA at low and moderate forces. It suggests that some local curvatures in DNA are the cause of the departure of the FJC model. Additionally, it has been noted that DNA undergoes an overstretching transition at stresses greater than 65 pN, at which point the WLC model breaks down. The ds-DNA force-extension curve is thus divided into three regions: the overstretching transition zone (c), the enthalpic region (b), and the entropic region (a). DNA remains in the entropic region below 10 pN pressures. Semiflexible DNA extends under the control of entropic spring. Enthalpic area refers to the intermediate force region, which is above 10 pN but below 65 pN. Here, the force increases suddenly because of the flexible DNA's elongation. The overstretching transition zone (over 65 pN) is characterised by a small force fluctuation, nearly doubled DNA length, a B to S transition, and force-induced DNA melting. Therefore, significant force applications should result in severe deformations of the double helix structure, including unzipping, unwinding, overstretching, and acute bending. Another review provides a more detailed explanation of how force affects DNA behaviour.

Ionic effects on DNA elasticity

The genetic code of a living organism is linked to its entire biological processes. Therefore, the process of decoding DNA must follow a regular protocol and proceed at a consistent pace. However, changes in the environment around DNA could impact how normally it functions. DNA mutations can be caused by even these differences. Therefore, in order to assess various anomalous corporal behaviours, it is imperative to examine DNA mechanics under a variety of physiological situations. Living cells include a variety of ions (Na^+ , K^+ , Ca^{2+} , Mn^{2+} , Mg^{2+} , H^+ , and Fe^{2+})

that are important for respiration, electric communication, muscle contraction, DNA packaging, chromatin remodelling, and DNA bending. This functioning can be inappropriately varied by differences in ion concentration

Protein-binding effects on DNA elasticity

Macromolecules known as proteins are composed of one or more extended chains of residues from amino acids. The twenty conventional amino acids can be arranged in a plethora of ways, and each one is associated with a specific protein that serves a particular purpose. Thus, proteins perform a wide range of functions, including DNA packing, gene regulation, immunology, reaction to stimuli, transport of other molecules, catalysis, and DNA sequence processing. The process by which proteins bind to DNA and interact with it is not easily understood because: (i) each protein has unique mechanical and electrostatic properties, which can be either repulsive or attractive; (ii) protein binding can be sequence-dependent (for sequence-specific proteins like CENP-B) or independent (for nonsequence-specific proteins like HMGB1, HU, and H-NS); and (iii) for nonsequence-specific proteins, the bending stiffness varies according to the different sequences. Binary chemical reaction kinetics can be used to represent DNA-protein interactions. However, a number of variables, including binding sites, protein content, and salt concentration, affect how well proteins bind to DNA. Long DNA is packed into bacteriophage capsids, where it is compressed to a significant length and fits into a little space. Histone protein helps DNA flex in the nucleosome. DNA is constantly under tension during chromatin remodelling, which may cause structural distortions. The required torques and local forces at the distorted DNA in the base pairs are covered in another article. Replication, transcription, and DNA repair are just a few of the ongoing biological activities that depend on the distortion of DNA structure brought about by protein interactions. During genetic regulation, DNA interacts with several proteins to generate loops that are either shorter than or equal to its persistence length. It is noteworthy that the bending fluctuations of free DNA in solutions differ from those of DNA bound to the protein.

In a study conducted in Maryland, scientists discovered that when positively charged dendrimers connect to DNA, electrostatic repulsion on the DNA backbone is reduced, increasing the bending flexibility of DNA. They did not find any appreciable alteration in DNA's stretch modulus, though. DNA-binding structural proteins known as high mobility group B (HMGB) are essential for chromatin structure maintenance, transcription, replication, and DNA repair. They interact with the DNA locally, causing it to bend. Through the use of single-molecule pulling studies, Scientists have shown that the HMGB protein greatly enhances the flexibility of DNA. Human TRF1 protein binding to telomeric DNA results in its stiffness being higher than that of non-binding, according to a recent study by Garai and colleagues (unpublished data). Drugs can interact with DNA and change its mechanical properties, much like proteins do. Researchers in Maryland discovered the mechanical characteristics of DNA in the presence of intercalators. When intercalators are present, the DNA's stretch modulus rises noticeably in comparison

to naked ds-DNA; nevertheless, the persistence length and bending modulus fall.

Conclusion

A semiflexible, negatively charged polymer is double-stranded DNA. Many active biological processes depend on conformational dynamics and the structural flexibility of DNA. Furthermore, different ionic circumstances have a direct effect on biomolecular processes as DNA packaging, replication, and repair. DNA's stiffness is determined by its persistence length, which is 50 nm. It does, however, vary based on the DNA's surrounding surroundings and size sequences. As the quantity of ionic salts increases, the persistence length of the naked DNA decreases.

References

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