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Biophysical Chemistry of Protein and DNA

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ABSTRACT

In the process of binding to DNA, protein molecules attach to certain patterns in the base sequence of the double helix. These patterns are responsible for determining the functions of the DNA in the cell. In order to offer an overview of the principles of DNA polymer physics, protein-DNA interactions and their research in single-DNA experiments, and a few sections of chromosomal structure at the large scale, the objective of these notes is to provide an overview of these topics. In addition, we will discuss the many ways in which chromosomal topology may be regulated.

Keywords: DNA, DNA-protein interactions, chromosome structure

INTRODUCTION

As a consequence of their chemical complementarity and the fact that they are made up of two long polymer chains that are wrapped around one other, DNA molecules in cells take on the appearance of a double helix. Cytosine, adenine, thymine, and guanine are the chemical groups that make up the sequence that the double helix employs to encode genetic information. These chemical groups are represented by the letters A, T, G, and C. According to the rules of complementary base pairing, which indicate that A=T and G≡C, bases that are complimentary to one another bind to one other in a double helix. This is because the bases are complementary to one another. These principles are determined by the chemical structures of the bases, which permit the creation of two hydrogen bonds between A and T (=), but three hydrogen bonds between G and C (≱). Approximately 600 Daltons (Da) is the estimated molecular weight of a pair of base pairs.

Information that is duplicated genetically is kept in the two copies that are located along the two polynucleotide chains that make up the double helix pattern. Using each chain as a template to construct a new chain that is complementary to the previous chain is what makes DNA replication feasible.

OBJECTIVE

1. Research biophysical chemistry of protein and DNA.
2. Protein structures: primary, secondary, tertiary, and quaternary.

Basic physical properties of the DNA double helix

The structure of DNA is responsible for the development of a great deal of fascinating physical properties.

Inflexibility On the other hand, the double helix of DNA is a semiflexible polymer that is moderately rigid and has a persistence length of around 50 nanometers. Approximately 0.34 nanometers separate each pair of base pairs along the double helix, which has a total of 150 base pairs, also known as bp. Due to the fact that the thickness of a double helix is around 2 nanometers, the DNA persistence length of a double helix is both long and thin. The length DNA molecules that are double-helixed are often very long polymers that are found in living organisms. As an example, the chromosome of the λ bacteriophage is roughly 16 microns in length, which is equivalent to 48502 base pairs. The bacterial chromosome of E. coli is about 1.5 millimeters in length, with a length of 4.6 megabase pairs, which is equivalent to 4.6 base pairs. Small "plasmid" DNA molecules from E. coli are typically between 2 and 10 kilobases, or between 0.7 and 3 microns in length, when it comes to genetic engineering. Last but not least, the bigger chromosomal DNAs that are present in the nucleus of human cells are around 200 megabase pairs long, which is equivalent to a few centimeters.

Differences that might occur The DNA molecules in the ionized phosphate on the backbone

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carry one electron charge per base pair, which is about 6 electrons per nanometer. This results in the formation of an environment inside the cell that is mostly aqueous and is characterized by DNA molecules that are infused with ions. Because of the high electric charge density along the double helix, it is a potent polyelectrolyte that has strong electrostatic interactions with other molecules that are electrically charged. A Debye length of less than one nanometer (λD) is about 0.3 nanometers per micrometer (√M), where M is the concentration of 1:1 salt in milliliters per liter (mol/liter). owing to the fact that cells contain a concentration of univalent salts that ranges from 100 to 200 millimolar (mM). As a consequence of this, electrostatic interactions with DNA, despite their intense nature, are essentially limited in their range. Electrostatic repulsions in double-stranded DNA are responsible for producing an effective hard-core diameter of around 3.5 nanometers when the salt concentration is at physiological values.

Proteins and DNA

As objects for biophysical investigation, DNA molecules are intriguing enough to be considered fascinating in and of themselves. Despite the fact that DNA is capable of performing a number of in vivo functions, the actualization of these activities requires a wide variety of protein molecules. Proteins, which are polymers which are composed of amino acids, are the workhorses of the cell. They are folded into specific shapes via the complex interactions that occur between amino acids. The length of folded proteins may vary anywhere from a few tens of nanometers to hundreds of nanometers, and the majority of proteins are found in the range of 100 to 1000 amino acids. Folded proteins can be found in a variety of sizes. This occurs due to the fact that the mass of each amino acid is around 104 to 105 Da on average, and the space that each amino acid occupies is approximately one cubic nanometer.

Some proteins have the ability to enclose DNA inside cells, whereas others link with specific base-pair sequences that are very short (less than 20 base pairs) and less discriminating, that is, they associate with DNA of almost any sequence. As a result of the positively charged patches that are present on their surfaces, many of the proteins that bind DNA have a net positive charge in solution. This helps them stick to the double helix structure. Hydrophobic amino acids are found in a significant number of DNA-binding proteins. These amino acids either bridge the gap between bases or establish hydrogen bonds with the bases themselves.

There are a large variety of functions that may be performed by proteins that bind the double helix in cells (Fig. 1). HU and Fis from Escherichia coli are two examples of proteins that fold the double helix in order to fit inside the cell. Histones from humans and other eukaryotic cells are other examples of proteins that fold within the cell. In order to make it easier for other proteins to do their more complex jobs, some proteins mark certain sections. For instance, transcription factors are responsible for initiating the process of converting DNA to RNA, which is the first step in the process of breaking down a gene. In addition to the proteins that have just been stated, there are additional proteins that catalyze the breakage and resealing of the DNA backbone, which enables topological and cut-and-paste alterations to be made to DNA molecules. Burning chemical fuels like as ATP, NTP, and dNTP allows a more advanced "protein machine" to duplicate, transcribe, and repair the double helix. This is accomplished via the metabolic process. Proteins are responsible for the transformation of a molecule of DNA from its unmodified state into a chromosome. Proteins do this by imparting DNA with its biological activity and personality.

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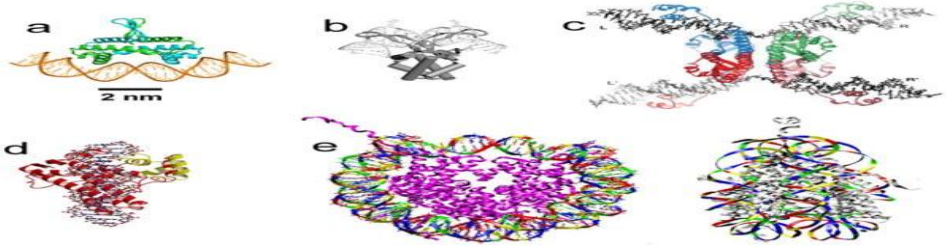

Proteins that are capable of catalytic actions are referred to as enzymes. The ability of certain of these enzymes to cut DNA at particular base-pair sequences, DNA ligases to reseal damaged covalent backbones along DNA molecules, and topoisomerases to modify DNA topology are all examples of enzymes that are constrained to specific situations. The manipulation of DNA structure is accomplished "in vitro," or in the test tube, with the help of these instruments. The use of these enzyme tools makes it feasible to cut and paste disparate segments of DNA together. Furthermore, when paired with DNA base-pairing, it enables the "hybridization" of independent DNA molecules that have complementary overhangs. In genetic engineering, the technique of reintroducing synthetic DNA sequences into cells is the fundamental premise that underpins the field. In order to selectively and controllably end-attach DNA molecules to surfaces and particles, you may apply the same fundamental principles. Alternatively, you can use these ways to assemble DNA molecules into nanoscale assemblies that you design.

The double helix is often altered and twisted by DNA-binding proteins; thus, it is essential to have a solid grasp of the mechanics of DNA in order to explain its actions. An further repercussion is that the study of protein-DNA interactions may be accomplished via the use of DNA mechanics. Over the course of the last fifteen years, this has been used extensively for the purpose of conducting single-molecule DNA tugging and twisting investigations in order to investigate proteins that act along DNA. These notes aim to give a brief overview of DNA statistical mechanics, talk about models that can be helpful when thinking about protein-DNA interactions through the lens of single-DNA micromechanics experiments, and describe some of the biophysical issues that come up when dealing with whole chromosomes.

Physical scales relevant to protein-DNA interactions

The length

When it comes to molecular biology, the basic unit of measurement that is relevant is the nanometer, which is equal to 10−9 meters. The size of almost all of the essential molecular units that are used by living organisms is around one nanometer. These molecular units include DNA bases, amino acids, simple sugars, and molecules that transmit energy such as ATP. Therefore, the nanometer is a measurement that may be used to determine both the granularity of information and the modularity of chemical configuration. It is important to keep in mind that a bacterial cell or a piece of a eukaryotic cell is about 10−6 m (μm) in length, which is equivalent to 1000 nm.

The primary concentration

The concentration of one molecule per cubic millimeter is another measurement that should be taken into consideration. This concentration is equal to 1015 molecules per liter, which is about 1.6 × 10−9 mol/liter, which is equal to 1.6 nM. The molecular mass is approximately 6 × 10^4. The quantity of transcription factor protein that might be present in a cell of a bacteria or a eukaryotic creature is about the same as this.

Sources of power,

We are going to concentrate on two basic energy scales. Given that the thermal energy per degree of freedom, denoted as kBT, is around 4 × 10−21 J at the ambient temperature (T =

300 K), we will estimate kBT to be essentially constant for biological systems. Binding energies of noncovalent bindings that stabilize biological molecules in their folded forms (such as folded proteins and the DNA double helix) are commonly measured in kBT units under normal physiological solution conditions. These binding energies are responsible for the stability of the folded forms of biological molecules. An example of this would be the fact that the base-pair binding energies throughout the DNA double helix vary from around 1 to 4 kBT per base pair at any given point.

In this particular setting, the second significant energy scale is that of a covalent chemical bond, which is much larger and roughly equivalent to 1 electron volt equals 40 kilonewtons. Because of the amount of energy that is responsible for maintaining the polymer backbones of protein and nucleic acid chains, biological molecules are able to endure changes to their secondary form, which is folded, without compromising their basic structure, which is the backbone.

The force

According to molecular biology, the force scale that is important is around $4 \times 10{-}12$ Newtons, which is equivalent to 4 piconewtons (pN). Due to the fact that the pN force scale corresponds to the stretching of noncovalent bonds that have a binding energy of a few kBT, it seems to be the usual force scale that is related with the conformational change of biomolecules.

To break a covalent bond, if one were to assume a force of around eV/Å, which is approximately 10−9 N, or 1 nN, it would be far larger than the force scale of a few pN.

In order to deconstruct a dimeric protein complex or remove a protein from DNA, it is feasible to quickly determine an estimate of the force scale that is necessary to accomplish this process. This should be done by exerting a few kBT of effort over a reaction distance of about one nanometer (the size of the binding site), which suggests a rupture force of around ten piconewtons. This is in accordance with the results of the experiments.

A protein that binds two sites that are ℓ away from one another requires a lower initial force in order to prevent DNA from being looped. This force is lower on the force scale. When anything like this takes place, the quantity of work that is done in opposition to the force that is being applied is roughly equivalent to $f\ell$. When $f\ell$ is more than 10kBT or when f is greater than $10kBT/\ell$, the rate of loop formation will be greatly lowered in comparison to the scenario when there is no force at all. Refer to the references for more in-depth calculations, which must take into account the effects of DNA bending. In addition to contributing to the force-extension free energy, it is essential to keep in mind that the elastic energy of DNA bending is responsible for controlling the pace of loop creation under zero tension conditions.

As an example, when the value of f is more than 0.1kBT/nm, which is about 0.4 pN, we see a significant suppression of loop formation for ℓ = 100 nm, which is a distance of 300 base pairs, which is often used for loop construction by site-specific DNA-looping proteins, as shown in gene regulation. Under these particular circumstances, we estimate a decrease in the loop formation rate of around $e{-}10 < 10{-}4$ when compared to the case where there is no force of any kind. The suppression of DNA looping by piconewton pressures has been a substantial finding that has been confirmed.

A larger force is associated with the "stalling" of an energy-rich molecular machine, which is characterized by the conversion of 10 kBT into mechanical energy at each nm-dimensional step. In terms of scale, this stall force is about 10 kBT/nm, which is equivalent to 40 pN. This phenomenon is analogous to the stall forces that are seen in RNA and DNA polymerases.

a moment

Due to the fact that all dynamics at molecular scales are governed by thermal motion and are

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substantially overdamped, inertia is not a problem for things that are on the nanoscale or micrometer scale. The only thing that will be of importance to us is motion that is governed by diffusion constants, which may be represented as $D = kBT/(6\pi\eta R)$. R represents the scale size of the item, while η represents the viscosity of the fluid. The viscosity of water is around 10−3 Pa·s, whereas the viscosity of cytoplasm is approximately 5 × 10−3 Pa·s. It is observed that a self-diffusion time, denoted as τ, is formed, which is about 1 second for R = 1 μm and it is on the order of 10−9 seconds for R = 1 nm. As a result of its very high R dependence, the diffusion relaxation time shifts from molecular to human-observable timelines for items on the μm scale. This phenomenon is relevant to molecules that are as small as nm in size.

CONCLUSION

In order to characterize the polymer elasticity of DNA and other biological polymers, these lecturers have presented statistical-mechanical models. We have spoken about ways to include the impacts of DNA-binding proteins into these systems. There are still a lot of unanswered questions, especially on the kinetics of DNA-binding proteins. A typical DNA-binding protein forms an array of chemical interactions with its binding site, and this work has stressed the need of taking these multi-step kinetics into account. Additionally, a few of issues related to the structure of DNA molecules have been detailed. The most elementary one has to do with DNA supercoiling, or how one DNA molecule reacts when its internal connecting number is disturbed. The more complicated issue of DNA molecule (or chromosomal) entanglement has been addressed, mostly via the lens of the breadth of the catenation number distribution, ⟨Ca2⟩, a straightforward and practical measure for assessing entanglement in systems with several polymers.

REFERENCE

1. Rybenkov VV, Cozzarelli NR, Vologodskii AV. Proc Natl Acad Sci USA. 1993; 11:5307.
2. Goodsell DS. The machinery of life. Springer-Verlag; New York: 1992.
3. Swinger KK, Lemburg KM, Zhang Y, Rice PA. EMBO J. 2003; 22:3749.
4. Grindley NDF, Whiteson KL, Rice PA. Ann Rev Biochem. 2006; 75:567.
5. Taneja B, Patel A, Slesarev A, Mondragon A. EMBO J. 2006;25:398.
6. Luger K, Mader AW, Richmond RK, Sargent DF, Richmon TJ. Nature. 1997; 389:251.
7. Grandbois M, Beyer M, Rief M, Clausen-Schaumann H, Gaub HE. Science. 1999; 283:1727.
8. Krasnoslobodtsev AV, Shlyakhtenko LS, Lyubchenko YL. J Mol Biol. 2007; 365:1407
9. Marko JF, Siggia ED. Biophys J. 1997;73:2173.
10. Sankararaman S, Marko JF. Phys Rev E. 2005; 71:021911.
11. Blumberg S, Tkachenko AV, Meiners JC. Biophys J. 2005; 88:1692.
12. Yan J, Kawamura R, Marko JF. Phys Rev E. 2005; 71:061905.
13. Skoko D, Yan J, Johnson RC, Marko JF. Phys Rev Lett. 2005; 95:208101.
14. Gemmen GJ, Millin R, Smith DE. Proc Natl Acad USA. 2006; 103:11555.
15. Chen YF, Milstein JN, Meiners JC. Phys Rev Lett. 2010;104:048301.
16. Wang MD, Schnitzer MJ, Yin H, Landick R, Gelles J, Block SM. Science. 1998; 282:902.
17. Maier B, Bensimon D, Croquette V. Proc Natl Acad Sci USA. 2000; 97:12002
18. Hagerman PJ. Ann Rev Biophys Biophys Chem. 1988; 17:265.
19. Doi M, Edwards SF. Theory of Polymer Dynamics. Oxford University Press; New York: 1989. Sec. 8.8.
20. de Gennes PG. Scaling Concepts in Polymer Physics. Cornell University Press; Ithaca: 1979. Sec. I.4.1.