How DNA Makes Us

* 1. What is DNA?

Have you ever wondered why no two people have the same fingerprint? Are you ever curious why you and your friend look so different? The answer to these questions lies in the chemical molecule that is found in the cells of all living organisms. This molecule is called **deoxyribose nucleic acid**, or **DNA**. DNA is responsible for all the functions inside our bodies. It makes you appear unique from anyone else you know. DNA is why you are the way you are.

To understand DNA better, we must examine it at a molecular level. Like other molecules in our bodies, DNA has a characteristic shape. This shape resembles a winding, circular staircase or ladder and is referred to as a **double helix**. Each DNA molecule is composed of two strands of DNA, held together by chemical bonds. Chemical bonds are also responsible for maintaining the double helical shape of DNA. Employing both **covalent** and **hydrogen bonds**, the structure of DNA is very strong and not easily disrupted. In fact, special enzymes in our bodies are required for unwinding DNA. Although DNA is a strong, solid molecule, it is also flexible. This allows it to bend and fold in many different ways to fit inside the nucleus of each of your cells. Now, let’s dive deeper into the specifics of a DNA molecule.

* 1. Vocabulary
* DNA
* Double helix
* Covalent bond
* Hydrogen bond
* Sugar-phosphate backbone
* Antiparallel
* 3’ end
* 5’ end
* Adenine
* Guanine
* Cytosine
* Thymine
* Complimentary base pairing

In the ladder model of DNA, the side railing helps stabilize and maintain the structure of the entire molecule. This side railing is referred to as the **sugar-phosphate backbone**. The backbone of DNA was given this name because of its composition. Each nucleotide contains a five-carbon sugar and a phosphate group. These chemical groups maintain the rigidity of the double-helical property of DNA, while allowing flexibility for folding. DNA is an **antiparallel** molecule, meaning that each DNA molecule is composed of two strands that run in opposite directions. Because of this, the ends of the DNA strands differ in their chemical composition. The two ends of the DNA strands are referred to as the **3’** and **5’ ends**. The 5’ end contains a nucleotide with a free phosphate group. The 3’ end has a free -OH group, able to bind new nucleotides. Ultimately, the chemical properties of the sugar-phosphate backbone stabilize DNA and set the stage for the composition of the interior of the molecule.

When examined in more detail, DNA is composed of four different nucleic acid bases: **Adenine, Guanine, Cytosine**, and **Thymine**. These nucleic acids make up the rungs of the ladder in the DNA double helix. Like the socks on your feet, these bases always come in pairs. Adenine is always paired with thymine, and cytosine is always paired with guanine. This characteristic of DNA is referred to as **complimentary base pairing**, and allows new DNA to be synthesized from one of the existing strands. These bases are the source of true information in DNA. They are responsible for encoding the specifics of our bodies’ functions and appearance. To understand the role of the nucleic acids better, consider typing on a computer. When you press a specific letter, that letter is displayed on the computer screen. Like the keys on a keyboard provide functional information to the computer, the nucleic acids tell our bodies how to function properly. These functions range from directing your heart to beat to determining the color of your hair. Knowing this, it is easy to understand why DNA is so important and vital to our survival. So, where does our DNA come from?

Although you look much different than your mother or father, you do share DNA with your parents. This explains why you may resemble them or other family members. DNA is passed on from generation to generation, from your grandparents, to your parents, to you. You receive half of your DNA, or genetic information, from your mother and half from your father. However, the genetic information is somewhat scrambled. As you have learned, this occurs during meiosis and ensures that you are not a clone of either of your parents. As you consider your more distant relatives, you probably resemble them less than your siblings or parents. This is because, while you share genetic information with all of your relatives, significantly less genetic information is shared with your great aunt than with your sister. This also explains why you and your friend do not seem to look alike at all. Ultimately, while the way DNA works and its structure may seem complicated, DNA is what makes you, you.

Test Your Understanding

1. What is the name given to the shape of DNA, and what chemical bonds maintain this shape? Provide a drawing to illustrate your answer.
2. What is meant by the term complimentary base paring? Name the nucleic acids present in DNA and state their correct pairings.
	1. How DNA Controls the Functions of the Body

While DNA does provide instructions for how our bodies should function, DNA itself does not carry out these orders. The functional workers of our bodies that follow these instructions are proteins. The genetic information in DNA determines which proteins go where in the body. These proteins are the visible expression of DNA, causing everything from your height to your eye color. However, these proteins still require DNA as the blueprint or instruction manual. Specific regions of DNA are responsible for defined functions and their associated proteins. In this way, DNA is able to collectively make and instruct proteins to carry out the functions of the body correctly.

In living organisms, DNA is divided into **chromosomes**. Collectively, all of the chromosomes in an organism make up the **genome**. Chromosomes are bundles of our genetic information. In the body, DNA is organized into compact chromosomes, allowing the entirety of our genetic information to fit in the nucleus of each cell. Every somatic cell in the body has the same number of chromosomes as the other members of its species. We, as humans, have 46. Some species have many more chromosomes, while others have less. One species of ants only has one chromosome in every cell, while hermit crabs have 254. The number of chromosomes varies vastly among species, but the number of chromosomes does not necessarily reflect the level of genetic complexity. This is because not every region on DNA is used to make and direct proteins. The specific regions on every chromosome that are used to make proteins are called **genes**. Every chromosome contains multiple genes. The proteins made from our genes will provide various functions such as transporting material in and out of our cells.

1.2 Vocabulary

* Chromosome
* Genome
* Gene

To gain a better understanding of the structure of our genomes, consider the city of Stillwater. One DNA molecule, or one nucleic acid is like a house. By itself, it is small and cannot make a large impact. A gene, or a protein coding section of DNA is analogous to one street of houses in a neighborhood. This street composes one part of the neighborhood, as a gene makes up a small part of a chromosome. A whole chromosome can be represented by all the streets in one neighborhood of Stillwater. The specifics of the neighborhood are detailed and complex but collectively compose one thing. This is true also of all the genes and genetic information composing one chromosome. Finally, all the neighborhoods in the city of Stillwater are representative of the entire genome of an organism. Just as each level, from a house to collective neighborhoods, is important to the Stillwater society, every part of DNA in the genome is vital to the function of the body. Ultimately, all the working pieces of our genomes are important for our bodies to function properly.

In order for children to grow, cuts to repair themselves, and organs to function properly, our cells must divide. During cell division, the genome must be copied to ensure that each cell has a copy of the organism’s DNA. The DNA replication process occurs before the cell begins to divide and involves many complex enzymes. These enzymes perform many different functions such as unwinding the strong bonds between nucleotides and adding bases to the new strand of DNA. When replication is finished, the cell contains two copies of the genome and will begin dividing. DNA replication is a complex and important process, as it ultimately enables our bodies to grow and function.

Test Your Understanding

1. What is the role of proteins and DNA in the body? How do they impact each other?
2. Provide and explain your own analogy for the relationship between one DNA nucleotide, a gene, a chromosome, and a genome.
	1. DNA Replication

Over our lifetimes, the growth of our bodies is obvious. Our height, hair, fingernails, feet, and hands all grow over various periods in our lives. At a biological level, this is made possible by cell division and DNA replication. When our cells divide, it is imperative that our DNA is replicated in each cell. DNA is replicated in a **semiconservative** manner. This means that the two molecules of DNA produced from replication each contain one strain of the DNA molecule that was originally replicated. In order for this to be possible, the strands of the DNA molecule are separated, and each strand becomes the **template strand**. A template strand of DNA provides enough information for certain enzymes to add the correct nucleotides to the molecule, synthesizing the complimentary strand. Recall that the nucleic acids of DNA are complimentary, meaning that an adenine nucleic acid on a template strand leads to a thymine nucleic acid opposing it. This makes the synthesis of a new strand of DNA from a template strand possible.

1.3 Vocabulary

* Semiconservative
* Template strand
* Helicase
* Leading strand
* Single-strand binding proteins
* Origin of replication
* Replication fork
* 3’ primers
* Primase
* DNA polymerase III
* Lagging strand
* Okazaki fragments
* DNA polymerase I
* Ligase

To begin replication, the template molecule of DNA must be unzipped, or partially unwound to allow for the addition of new nucleotides. This is accomplished by the enzyme **helicase**. Helicases bind to one strand of DNA, moving along the strand to unwind it. This strand becomes the **leading strand**. The leading strand is the site of continuous replication and runs in the 3’ to 5’ direction. Recall that the structure of DNA is very stable due to its specific chemical bonds. Because of this, helicases must stabilize the separated strands while they are unbound from each other. To assist helicases in stabilization, **single-strand binding proteins** are recruited. These proteins bind to the single strand not bound by helicases. When bound, the single-strand binding proteins prevent the strand from breaking while also ensuring the strands remain unwound. As helicases unwind and stabilize the strand, the nucleic acids become unpaired, leaving open areas for replication to begin. These areas are referred to as **origins of replication** and create **replication forks**, where replication will eventually take place. DNA replication begins at multiple locations on a chromosome. This requires multiple enzymes to add new nucleotides to the existing strand of DNA.

 Before nucleotides can be added to the separated strands of DNA, primers must bind to each of the strands. These primers are referred to as **3’ primers** and are short sequences of nucleotides attached complimentarily to the DNA strands being replicated. Primers are responsible for recruiting the enzyme complex responsible for synthesizing the new strand of DNA. The enzyme **primase** adds the primers to various areas near the origin of replication. These primers are important, as they prevent errors in replication. Primers highlight their sections of newly synthesized DNA as temporary. This means that the primers will later be removed and checked, allowing the cell to excise any small area of DNA that was copied incorrectly. After primase has finished its task, replication may finally begin.

Figure 1.3.1 Enzymes of DNA Replication

 The star enzyme of DNA replication is **DNA polymerase III**. This enzyme adds nucleotides complimentarily to the replication fork of the leading and **lagging strands** of DNA. DNA polymerase III works in a very specific way, reading both strands in the 3’ to 5’ direction and synthesizing the new strand in the 5’ to 3’ prime direction. The leading strand of DNA runs in the 3’ to 5’ direction and is able to be replicated continuously. In order to replicate the lagging strand, which runs in the 5’ to 3’ direction, DNA polymerase III must add nucleotides to the parent strand in fragments. These fragments are called **Okazaki fragments** and are synthesized discontinuously. Because the lagging strand runs 5’ to 3’, in the opposite direction of the leading strand, it must bend in a particular shape to be correctly read by DNA polymerase III. The lagging strand loops around the enzyme complex, while the leading strand remains fairly straight. This allows DNA polymerase III to move along the leading and lagging strand at the same time, adding complementary sequences of nucleotides to both strands. This exemplifies the importance of the flexibility of DNA, as it allows DNA polymerase III to move quickly, making the replication process efficient.

 After DNA polymerase III has reached the end of both strands, it dissociates from the DNA molecules. Before DNA replication can be formally complete, the small areas of discontinuous DNA must be attended to. These include the primers and the Okazaki fragments. A new enzyme, **DNA polymerase I** removes the primer and replaces these areas with nucleotides on both the leading and lagging strands. DNA polymerase I also fills in gaps between the Okazaki fragments on the leading strand. After these areas are filled in, another enzyme, DNA **ligase** joins the Okazaki fragments with the lagging parent strand. Finally, all the enzymes involved in DNA replication are able to dissociate from the two molecules of DNA. At the conclusion of replication, the DNA condenses back into chromosomes. Now, two nuclei form around the newly synthesized DNA, and your cells are ready to divide.

Test Your Understanding

1. What gives DNA the ability to be flexible, and how is the importance of this trait exemplified in the replication process?
2. Name three different enzymes involved in DNA replication. State their functions and the order in which they perform these functions.
	1. What Happens when DNA Replication Goes Wrong?

Have you ever picked up a bag of clementines and wondered what the GMO sticker means? Do you wish you understood why certain diseases occur? Genetically modified organisms and many illnesses can be explained by disruptions in our genetic information. Recall that every nucleotide composing our genetic information is important in determining everything about you, from your appearance to your body’s function. Because of this, any variant nucleotide that is wrongly placed during DNA replication can be detrimental to one of the body’s functions. These disruptions are generally referred to as **mutations**. A mutation is any alteration in the nucleotide sequence of a DNA strand that subsequently causes a change in the genetic message that is carried in the genetic information. However, not all mutations damage the organism. Some genetic mutations lead to positive changes that may benefit the organism or even create a new form of that organism. Exemplified in the case of clementines, mutations have the ability to make a sour fruit sweeter, or even change its size. It is apparent that mutations can be categorized in many different ways. Let’s explore the different types of mutations further.

1.4 Vocabulary

* Mutation
* Substitution
* Deletion
* Insertion
* Amino acid
* Nonsynonymous mutation
* Synonymous mutation

There are three overall categories of genetic mutations. The first is called a **substitution**. A substitution occurs when one nucleotide is substituted for a different nucleotide. Substitutions can be harmful, but generally cause the least damage between the three mutation types. A **deletion** occurs when a part of the nucleotide sequence is removed from the DNA strand during replication. This can affect anywhere from one nucleotide to hundreds and is understandably capable of causing largely aversive effects. The final type of mutation is an insertion. As the name suggests, an **insertion** mutation occurs when additional nucleotides are added to the DNA sequence during replication. As with deletion mutations, insertions can effect varying numbers of nucleotides. It is clear that the effects of different mutations vary greatly, but how do these mutations actually change functions in the body?

 Recall that DNA is used as a template to make proteins. These proteins go on to perform all the functions of our bodies. Proteins are composed of **amino acids**, and the order of these amino acids determines the function of the protein, just as the nucleotide sequence is important for the function of DNA. Like letters must be arranged correctly to form words, amino acids must be placed in a certain order. If this order is jumbled, shortened, or elongated, the resulting protein not only may lack its function, but could also impact the body negatively. Substitutions may cause the replacement of the correct amino acid with an incorrect amino acid. Similarly, insertions and deletions lead to too many or not enough amino acids. Understandably, this can be detrimental to the function of the protein. Mutations that cause the protein to have a change in function are called **nonsynonymous mutations**. Conversely, substitution mutations may actually lead to a protein that has not experienced a change in function. This type of mutation is referred to as a **synonymous mutation**. Ultimately, DNA replication is a vital process in our bodies, but if done incorrectly may prove to harm us as well.

Test Your Understanding

1. How does DNA provide information for protein synthesis? What specific part of DNA is used to produce amino acids?
2. Name the three types of mutations and state which can lead to synonymous mutations and which lead to nonsynonymous mutations.

References

Glencoe Science. (2007). *Reading Essentials for Biology: The Dynamics of Life.* Columbus, OH: McGraw-Hill.