

Lesson Summary:

The DNA Replication Fork model will help you to simulate the process of DNA replication that occurs in every living thing as part of mitosis and meiosis. By manipulating the simulation, you will help different proteins work together to copy DNA. You will also learn how DNA relies upon patterns to replicate correctly and how mistakes in replication sometimes occur.

Challenge 1: Unwind the DNA (1/7)

Please read the instructions below, before you use the model.

Start by **specifying the following settings in the simulator:**

DNA-strand-length: 30

Speed: Normal

Enzyme labels: checked

Substitutions: unchecked

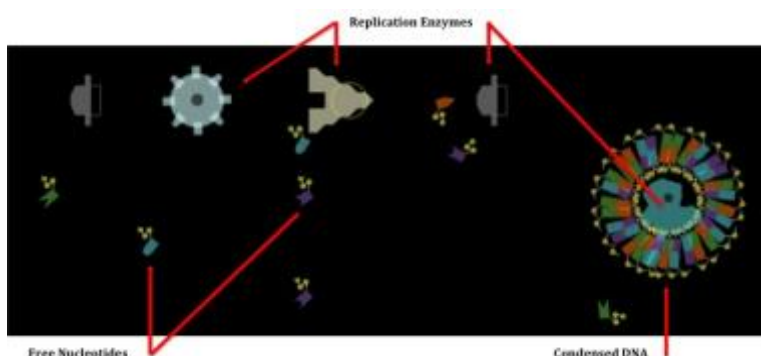
Nucleo labels: unchecked

Free-nucleosides: 50

Time-limit: None

When you have chosen the correct settings, press **SETUP**.

The simulation setup shows the tools you will need to replicate DNA. You have a strand of **Condensed DNA**, **Free Nucleotides** and **Replication Enzymes**:



Your **GOAL** in **PART 1** is to replicate (copy) a length of DNA by completing four **CHALLENGES**.

EXPLORE THE BIOLOGY:

Enzymes are proteins that perform chemical reactions in cells. This simulation shows you four *different* enzymes that are integral to DNA replication.

Press **GO/STOP** to start the simulation!

You can drag and drop molecules inside the cell using your mouse cursor.

Question 1: Which enzyme unwinds condensed DNA?

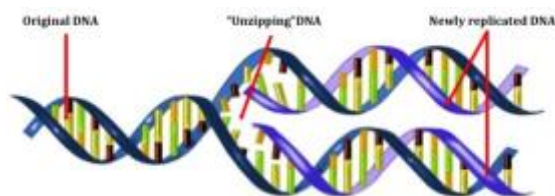
Hint: Try moving the different enzymes to the condensed DNA.

[Note: you may have to “let an enzyme go” with your mouse in order to see the enzyme work.]

Challenge 2: Unzip the DNA (2/7)

EXPLORE THE BIOLOGY:

DNA (DeoxyriboNucleic Acid) is made of two strands which wind around each other in a **double helix**. When DNA is replicated, the DNA strands are separated and each serves as a **template** (i.e. the basis for a pattern) for a new double helix.



DNA-strand-length: 30

Speed: Normal

Enzyme labels: checked

Substitutions: unchecked

Nucleo labels: unchecked

Free-nucleosides: 50

Time-limit: None

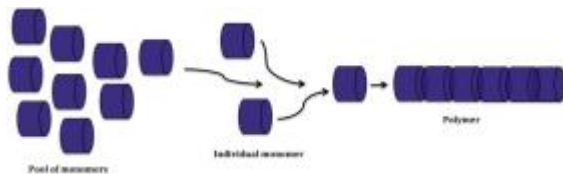
NOTE: Even though you are moving the proteins in this simulated cell by hand, in a real cell the proteins move randomly. This model allows the movement of molecules using the mouse to observe the effects faster. You would see the same behavior in the model but at a very slow pace if you do not move the molecules by hand.

Question 2: Which enzyme unzips the double stranded DNA? (Use the model to answer.)

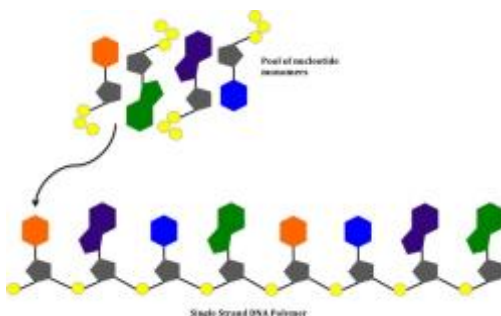
Challenge 3: Polymerize DNA (3/7)

EXPLORE THE BIOLOGY:

DNA is a polymer. **Polymers** (*poly* = many) are large molecules made of smaller, linked units called **monomers** (*mono* = one).



DNA is made up of many, individual **nucleotides** (monomers) that are connected to each other to form both single strands and helical, double strands (polymers). Nucleotides are attached to a growing strand by an enzyme.



DNA-strand-length: 30

Speed: Normal

Enzyme labels: checked

Substitutions: unchecked

Nucleo labels: unchecked

Free-nucleosides: 50

Time-limit: None

Question 3: What enzyme will attach nucleotides to form double stranded DNA?

Hint: You will need to move an enzyme and nucleotides into one place together to form new DNA.

Question 4: What do you notice about the shapes of the nucleotides?

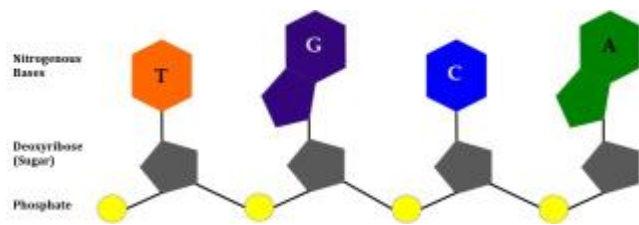
Challenge 4: Completely Replicate DNA (4/7)

EXPLORE THE BIOLOGY:

Nucleotides are made of 3 parts: a sugar attached to a phosphate group and a nitrogen-containing base. Human DNA is made of MANY nucleotides (about 3.2 billion base pairs) and there are *different types of nucleotides* because they are made with *different types of **bases***.

T = THYMINE G = GUANINE C = CYTOSINE A = ADENINE





DNA-strand-length: 30

Speed: Normal

Enzyme labels: checked

Substitutions: unchecked

Nucleo labels: unchecked

Free-nucleosides: 50

Time-limit: None

Play with the model to answer the following questions:

Question 5: Can polymerase attach *any nucleotide, anywhere* on a DNA strand?

(Hint: Try out different bases at different locations; note what works and what doesn't.)

Question 6: Which nucleotides (colors, labels) will pair together? (Turn **NUCLEO-LABELS on)**

Question 7: Why do you think only certain nucleotides will pair up, but others won't?

(Hint: Review your answer to Question 4 in CHALLENGE #3 on the page 4.)

Reflection Question 1:

Before scientists had discovered that nucleotides form the base pairs you observed with the model today, one biochemist, Edwin Chargaff, discovered something unexpected. He was studying DNA samples from humans, other animals and bacteria. Chargaff discovered that, in every sample, the percent of cytosine was about the same as the percent of guanine AND the percent of adenine was about the same as the percent of thymine. This observation became known as *Chargaff's Rule*.

Explain how Chargaff's observation relates to the base pairings you saw today.

Question:

The percentages of A & T and C & G were *about* the same, but not exactly equal. For example, in a sample of human DNA, Chargaff noted that the percentages of nucleotides were: Adenine = 30.9% Thymine = 29.4% Guanine = 19.9% Cytosine = 19.8%

Why do you think the percentages of A & T and C & G are not EXACTLY the same?

Reflection Question 2:

In this model, you moved enzymes and nucleotides around to replicate DNA. But, in real, living cells, no tiny person is there to move enzymes and nucleotides into position to replicate DNA.

So, how do you think enzymes and nucleotides “know” where to go to create new DNA? How do enzymes “know” what to do? How does polymerase “know” which nucleotide is the right one to add to a growing DNA strand?

Part 2 - Challenge 5: Changing the Pace (5/7)

In **PART 1**, you replicated DNA but did not change any settings. In **PART 2**, your **GOAL** is to investigate the effects of changing variables in the simulation on your DNA replication. To complete this goal, you will need to complete a second set of **CHALLENGES**.

[NOTE: If at any time in Challenges 5 through 7, you “run out of DNA” to replicate, just reset your simulation and continue with your challenge.]

1. Start by **specifying the following settings in the simulator:**

DNA-strand-length: 30

Speed: see below

Enzyme labels: checked

Substitutions: unchecked

Nucleo labels: unchecked

Free-nucleosides: 150

Time-limit: No Limit

2. When you have chosen the correct settings, press **SETUP**. Press **GO/STOP**.

3. Start DNA replication by unwinding and unzipping your DNA and attaching polymerase **ONLY** on the TOP strand.

4. First change the simulation speed by moving the slider to the left, to **FASTER**.

Do NOT move the nucleosides using mouse. Observe the random motion of nucleosides and DNA replication.



6. After you replicate the top strand, decrease the simulation speed by moving the slider to the left, to **SLOWER**.

Attach the polymerase to the bottom strand.



Now, observe the replication bottom strand of DNA. Press **GO/STOP** to end the simulation.

Question 8: How does increasing the simulation speed affect your DNA replication? Is it easier or harder? Why? Use your observations to justify the reason.

Question 9: How does decreasing the simulation speed affect your DNA replication? Is it easier or harder? Why? Use your observations to justify the reason.

1. Return the speed to **NORMAL** and **SETUP** the simulation, then press **GO/STOP**.
2. Unwind the DNA, separate the strands and attach polymerase. Increase the number of free nucleosides to approximately **150 bases**.
3. Observe the replication the TOP STRAND of DNA ONLY.
4. Now, decrease the number of free nucleosides to approximately **15 bases**.
5. Attach polymerase to the bottom strand. Observe the replication the bottom strand of DNA now. Press **GO/STOP** to end the simulation.

Question:

Question 10: How does increasing the number of nucleotides affect your DNA replication? Is it easier or harder? Why? Use your observations to justify the reason.

Question 11: How does decreasing the number of nucleotides affect your DNA replication? Is it easier or harder? Why? Use your observations to justify the reason.

Part 2 - Challenge 7: Breaking the Rules (7/7)

1. Return the free nucleotides to approximately 50 and **SETUP** the simulation, press **GO/STOP**.
2. Unwind the DNA, separate the stands, attach the polymerase to the TOP strand ONLY. Observe the top strand of DNA, now.
3. After the top strand is finished, turn **SUBSTITUTIONS** to **ON** and attach polymerase to the bottom strand. Observe replication of the bottom DNA strand.
4. Press **GO/STOP** to end the simulation.
5. Check the readout boxes for your top and bottom DNA strands (as in the picture below)

Top Strand	Bottom Strand
# correct duplications N/A	# correct duplications N/A
# deletions N/A	# deletions N/A
# substitutions N/A	# substitutions N/A

Question 12: Compare your top and bottom strands; what changed when you turned SUBSTITUTIONS on? What do you think SUBSTITUTIONS means?

Hint: You might want to compare this challenge to your results from Part 1 – Challenge 4.

Hint: In order to see your DNA more clearly, press **GO/STOP**, change **FREE-NUCLEOTIDES** to zero, and move the enzymes out of the way, then press **GO/STOP** again!

Question 13: What nucleotide pairings do you observe in the bottom strand but not in the top strand?

Question:

Reflection Question 3: The changes you observed in the sequence of nucleotides in your DNA strand are called **mutations**. There are several different types of mutations. You simulated *substitution* mutations, meaning that some nucleotides were paired incorrectly during replication, for example a Thymine might be substituted where a Cytosine should be, or a Guanine substituted for an Adenine. As a result, the two, new DNA strands that you made in **CHALLENGE 7** had different (mutated) sequences.

What other kinds of mutations do you think might happen to change the sequence of nucleotides in DNA?