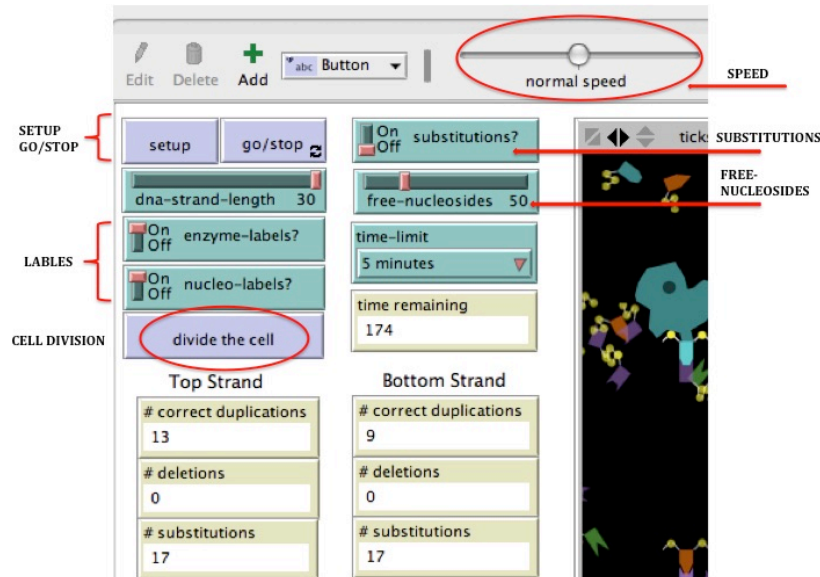


USING THE SIMULATION & TROUBLE-SHOOTING

USING THE SIMULATION:

Students will use the control panel to set parameters for the simulation. These parameters are variables that will effect how quickly and accurately students can complete their task: replicating a strand of DNA.



VARIABLES:

Speed: manipulates the time in the simulation, which is also called “ticks”

Substitutions: “on” permits base mis-pairing; “off” prevents incorrect bases from being incorporated into the growing DNA strand

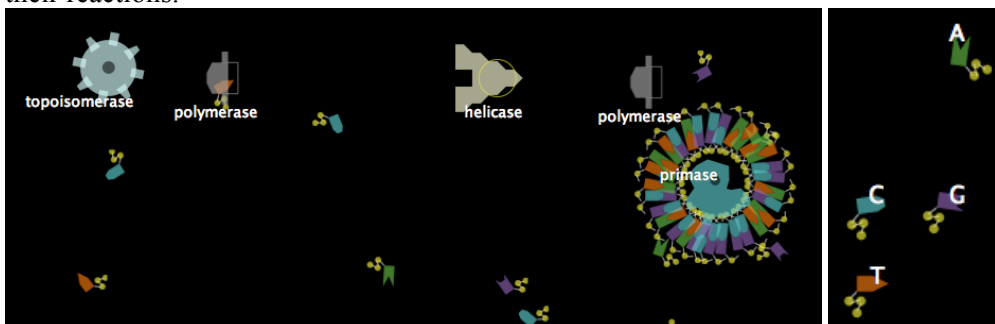
Number of free nucleosides: increases or decreases the number of available nucleoside bases

Time: operate with or without a time limit on DNA replication

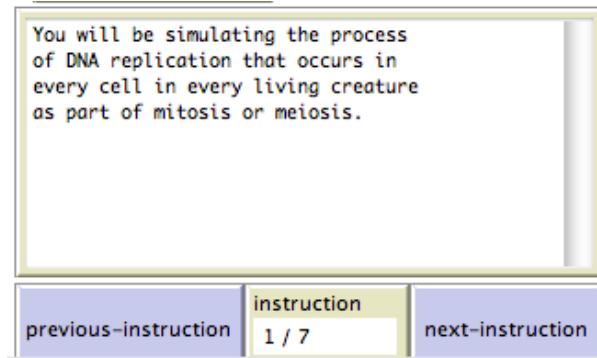
DNA strand length: choose the length of the DNA strand you have to replicate

DNA REPLICATION:

Once simulation parameters have been chosen, clicking **SETUP** will display the DNA strand, enzymes and nucleosides. Students may choose to display labels for the enzymes (below left) and nucleosides (below right) or not. Students will facilitate DNA replication by using their mouse to drag the enzymes and nucleosides into the correct positions for the enzymes to catalyze their reactions.

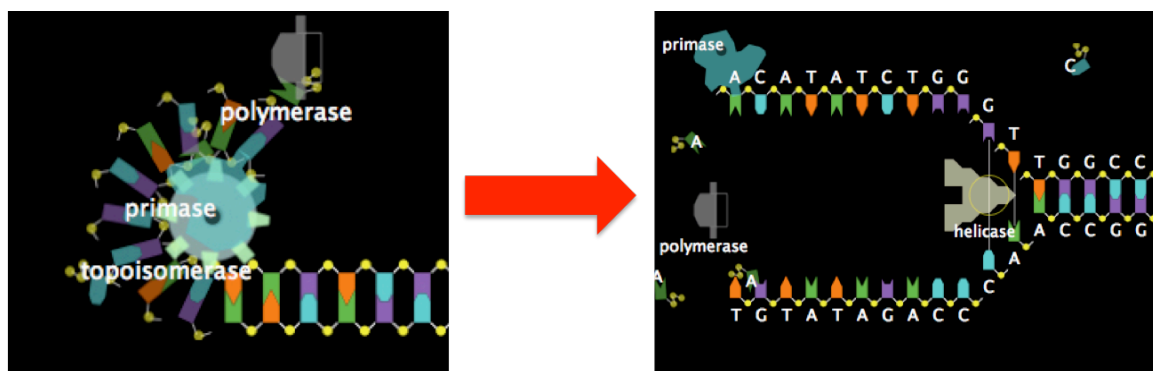


INSTRUCTION reminders are provided in an box below the control panel so students may check steps in the middle of a replication run. Press **GO/STOP** to start and stop the simulation.

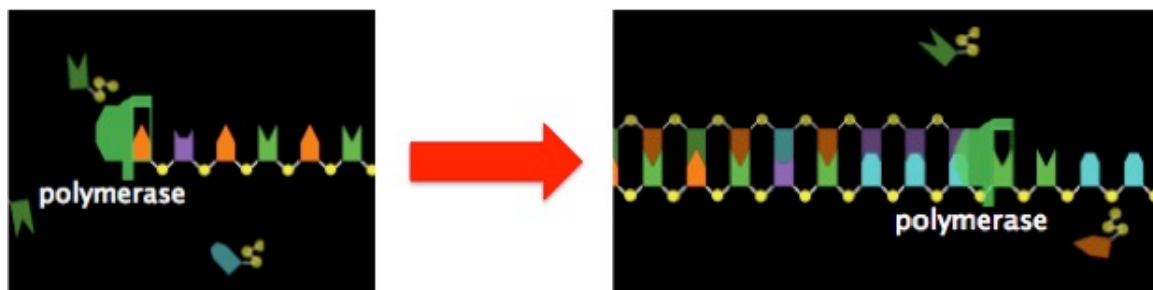


Replication consists of four steps:

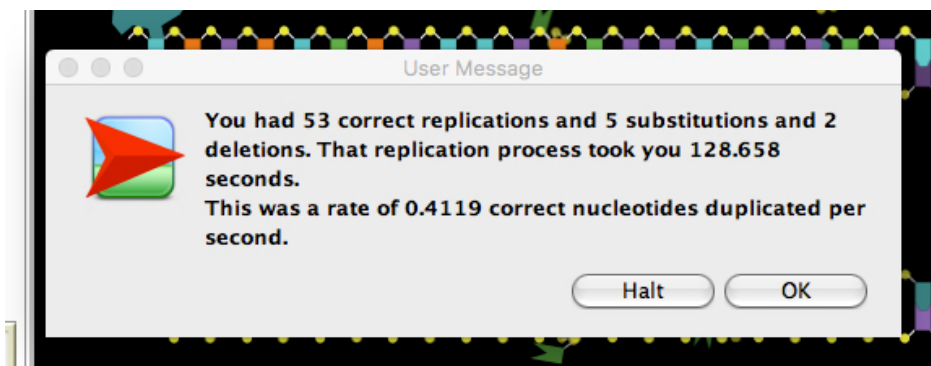
1. Unwind the DNA double helix by placing topoisomerase on top of primase (below left).
2. Separate the two strands using helicase (below right).



3. Place a polymerase at a free nucleotide (below left) and drag the correct nucleoside base pair to polymerase for it to be added to form new, double stranded DNA (below left).
4. Repeat STEP 3 until both DNA strands are replicated.



Press **DIVIDE THE CELL** to trigger cell division and obtain the results of the replication. The readout provides a tally of correct replications, substitution and deletion mutations, the time taken to replicate the DNA and the rate of correct nucleotides duplicated per second.



ALTERING VARIABLES:

Students will manipulate several variables as part of the replication scenarios. It is important for students to understand the effect of altering these variables on the speed and accuracy of DNA replication as they will be required to propose their own ideal parameters for DNA replication as their last experiment.

SUBSTITUTIONS – when substitutions are turned “off”, polymerase (below, red) will reject any incorrect nucleoside bases which attempt to pair with the original strand. When substitutions are turned “on”, polymerase will accept any base to pair with the original strand.



FREE NUCLEOSIDES – A new nucleoside is generated each time one is paired by polymerase to the original DNA strand. However, too few free nucleosides will make it impossible to complete DNA replication due to lack of variety. Too many free nucleosides creates clutter and may result in numerous substitution mutations.

SPEED – Movement in the simulation becomes stochastic at either speed extreme. Speed a little slower than normal may make it easier for students to pair bases and avoid errors. Speeds faster than normal may increase the number of substitution mutations.

DNA STRAND LENGTH – Shorter DNA strand lengths are quicker to replicate and can be helpful for students who want to experiment with parameters. Fewer mutation events may occur with shorter DNA strands as there are fewer base pairing events.

TIME – Setting a time limit may encourage greater speeds but also a greater number of substitution mutations.

TROUBLE-SHOOTING THE SIMULATION:

If **topoisomerase “won’t unwind the DNA”**, release topoisomerase with your mouse (i.e. “let the enzyme go”) on top of primase. You will know that topoisomerase is interacting successfully with primase when topoisomerase starts to spin faster.

If **polymerase won’t add a chosen base**, likely the base pairing is incorrect. Choose the correct base; it will have a compatible shape.

If **you run out of the correct bases**, this is likely because there are too few free nucleosides. Either increase the number of free nucleosides or replicate other parts of the DNA for which there are compatible, free nucleosides available.

If **you do not get a readout when you DIVIDE THE CELL**, likely the simulation is stopped. Press **GO/STOP**, then press **DIVIDE THE CELL**.

If **the simulation is “flashing” or “jumping”**, rather than moving smoothly, likely the simulation speed is too fast. Decrease the simulation speed and the molecules should move more smoothly. (The same is true if the simulation speed is too slow.)