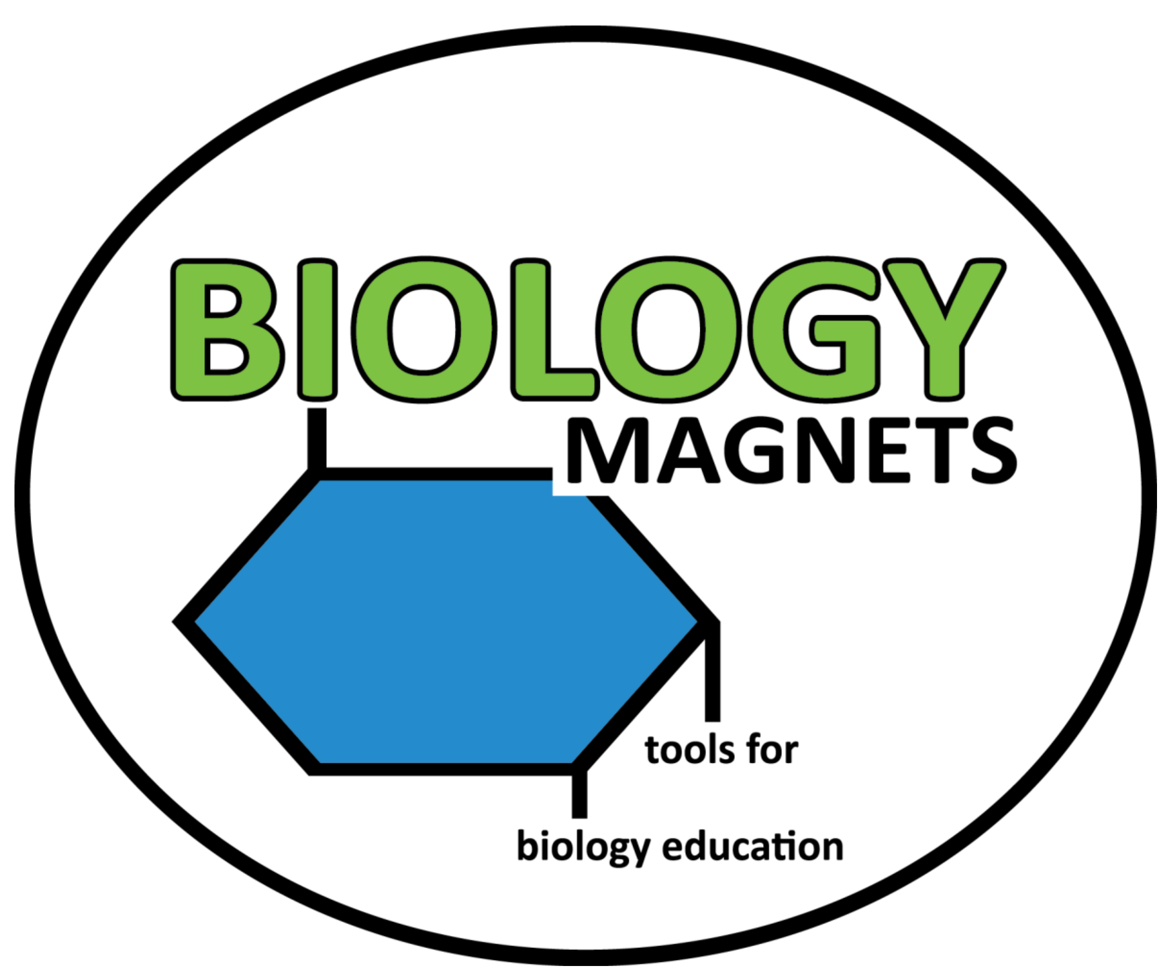
Biology Magnets Module 5: DNA Replication - Teacher and Student Guides



Teacher Information

This module uses magnets designed for teacher and student interaction to guide learning DNA replication. Contained in this guide are different lesson ideas that can last from 10-20 minutes each to an entire class period, depending upon teacher preference. Each lesson has both teacher-centered and student-centered activities. The student-centered activities are most effective if students are in small groups. It may be necessary to have multiple magnet sets for large classes. A student guide is provided that can be printed out and given to each student group to help guide their progress as they work with the magnets. If budget or white board space is limited, groups can alternate between using a set of magnets and doing other activities. Teachers can refer to the videos posted at the Biology Magnet web site at **Biology Magnets.com** for guided teaching and ordering information.

Magnet Care and Maintenance

Biology magnets are made to last for years. Periodically magnets will fall off or are knocked off the plastic. A piece of magnetic tape is included with each module, which should be able to replace around 10-12 magnets if necessary. Simply cut a new magnet and peel off the back to replace. Magnetic tape can be purchased from a hobby store to replace magnets lost over time. Laminate may peel off, especially on small pieces. Transparent tape can be used as a replacement or to re-attach laminate that comes loose by curling the tape over the back of the magnet. The machines used to cut Biology Magnets are not always perfectly accurate. Sometimes a bit of white or black outline on the edges occurs or a cut might be slightly off center. Use scissors to remove extra outline that is unnecessary if desired. Store magnets in the clasp envelopes in which they arrived for easy organization.

Copyright Information – Module 5 – DNA Replication

DNA/RNA nucleotides, ddNTPs: ©2020 Tom Willis all rights reserved

DNA Helicase: By Deposition authors: Yamada, K., Miyata, T., Tsuchiya, D., Oyama, T., Fujiwara, Y., Ohnishi, T., Iwasaki, H., Shinagawa, H. et al.;visualization author: User:Astrojan - http://www.rcsb.org/pdb/explore/explore.do?structureId=1ixr, CC BY-SA 4.0, https://commons.wikimedia.org/w/index.php?curid=65016810. This file is licensed under the Creative Commons Attribution-Share Alike 4.0 International license. Background and border added. Distributed under the same license as above.

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Biology Magnets Module 5 - DNA Replication - Materials List

Magnet Name	Quantity	Picture
DNA Nucleotide	66 – 30 on two strings, 36 free	
RNA Nucleotide	12	
DNA Helicase	2	
DNA Ligase	1	
DNA Polymerase I	1	
DNA Polymerase III	2	
Topoisomerase	1	
Exonuclease	1	
DNA Primase	1	
3" Magnetic Tape Strip	1	
Total Quantity	**87**	

Biology Magnets Module 5 Sanger Sequencing/

Meselson and Stahl Supplement Materials List

Magnet Name	Quantity	Picture
Guanine ddNTP	3	
Adenine ddNTP	3	
Thymine ddNTP	3	
Cytosine ddNTP	3	
DNA Primer	6	
15N Heavy DNA strand	2	
14N Light DNA strand	6	
Total Quantity	**26**	

Lesson 5A – DNA Replication (20-80 minutes)

Teacher Centered Activity (20-30 minutes): This lesson utilizes the Biology Magnets to model DNA replication. Start by placing the two strands of DNA attached to strings on the board so they link together in the center (**Figure 5.A.1**). Using DNA helicase, unzip the DNA strand down the middle. Topoisomerase is an enzyme that moves in front of the helicase that prevents supercoiling of the DNA. DNA Primase puts down an RNA primer in the 5'->3' direction to start the replication of the leading strand according to the pairing rules, G-C and A-U (T instead of U for DNA) (**Figure 5.A.2**).

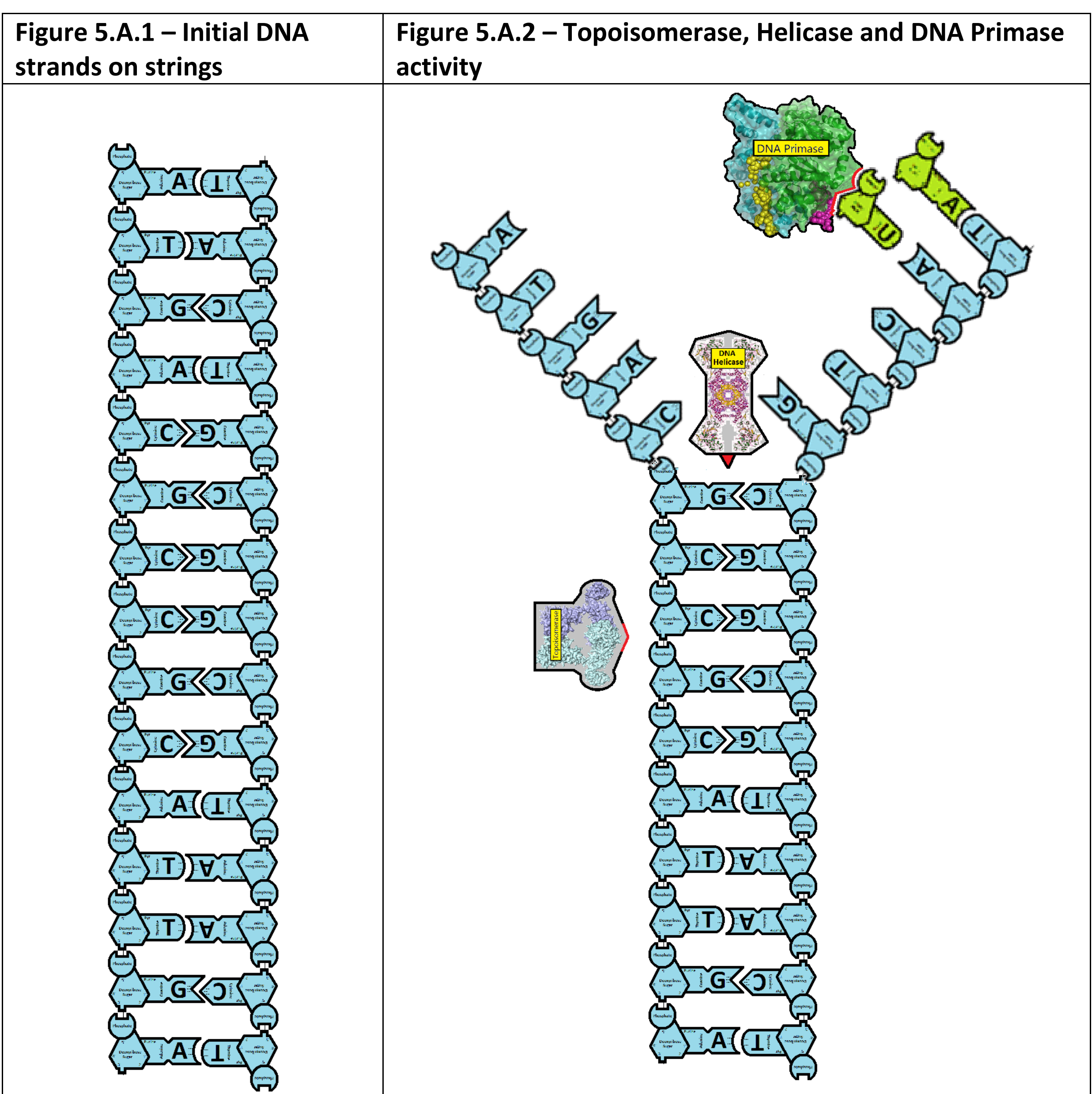


Figure 5.A.1 – Initial DNA strands on strings

Figure 5.A.2 – Topoisomerase, Helicase and DNA Primase activity

Move helicase and further unzip the strand. Add complementary DNA nucleotides after the RNA primer using the DNA Polymerase III enzyme. On the lagging strand, add RNA primers and DNA nucleotides in the same manner, still 5" -> 3', but in the opposite direction moving away from the helicase enzyme. These shorter fragments of DNA are called Okazaki fragments (**Figure 5.A.3**). After the strands are completed, use the exonuclease enzyme to remove the RNA primers, and then use DNA polymerase I to replace them with DNA nucleotides. Finally, DNA ligase will be needed to splice together the 3' end of the replacement chain with the 5' end of the adjacent DNA nucleotide (**Figure 5.A.4**).

Figure 5.A.3 – Activity of DNA Polymerase III and formation of Okazaki Fragments

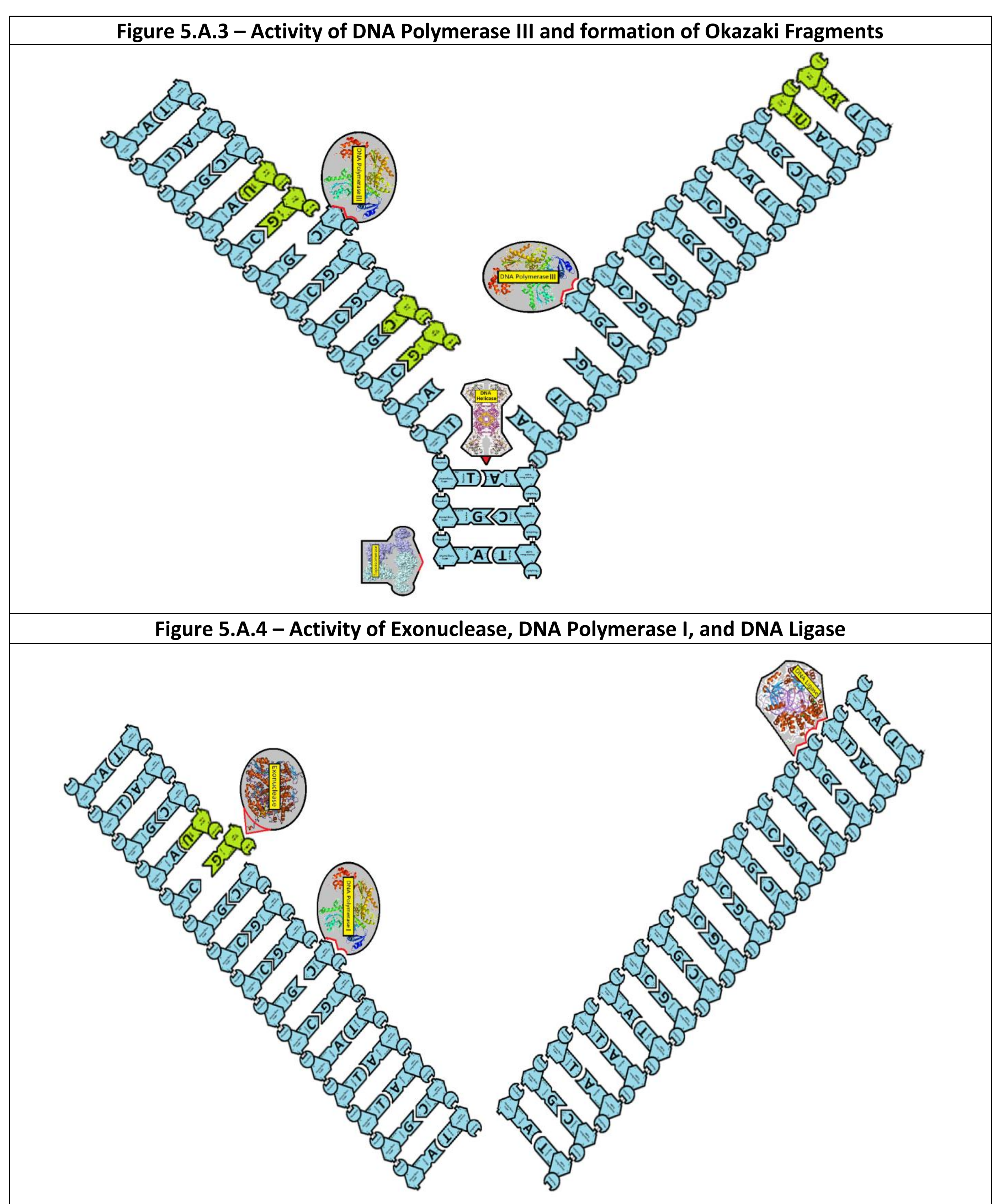


Figure 5.A.4 – Activity of Exonuclease, DNA Polymerase I, and DNA Ligase

Student centered activity (20-50 minutes): After teaching DNA replication, put students into small groups. A copy of the student guide for the lesson may be given to each group if necessary. Have the students take turns moving the Biology Magnets to accurately model the process of DNA replication. Allow the students to correct and help one another. Continue to practice until each student can model DNA replication without looking at the guide.

Extra exercises:

Mutations: Mutations can form when a nucleotide with a mismatched base is mistakenly placed in the replicated strand of DNA. Transversion mutations occur when a purine is substituted for a pyrimidine or vice-versa. This causes a change in the width of the DNA strand, either too wide (purine-purine) or too thin (purine-pyrimidine). Transition mutations occur when a purine is substituted with a different purine (or pyrimidine with a pyrimidine). This does not change the width of the DNA chain. Transition mutations are about twice as common as transversion mutations (**Figure 5.A.5**). Have the students model several of the mutations while they are replicating the DNA. Students could simulate DNA repair by using repair enzymes such as exonuclease to remove mismatched bases and DNA polymerase and ligase to replace the bases.

Replication bubble: In order to speed up the process of DNA replication, replication bubbles form within each chromosome, where the unzipping of the DNA occurs in both directions of the DNA chain. Have the students use the second DNA helicase enzyme to form a replication bubble (**Figure 5.A.6**). Have the students determine which side of each fork is the lagging strand and the leading strand. Have them use the Biology Magnets to model the replication of a few nucleotides on each strand at both ends of the fork.

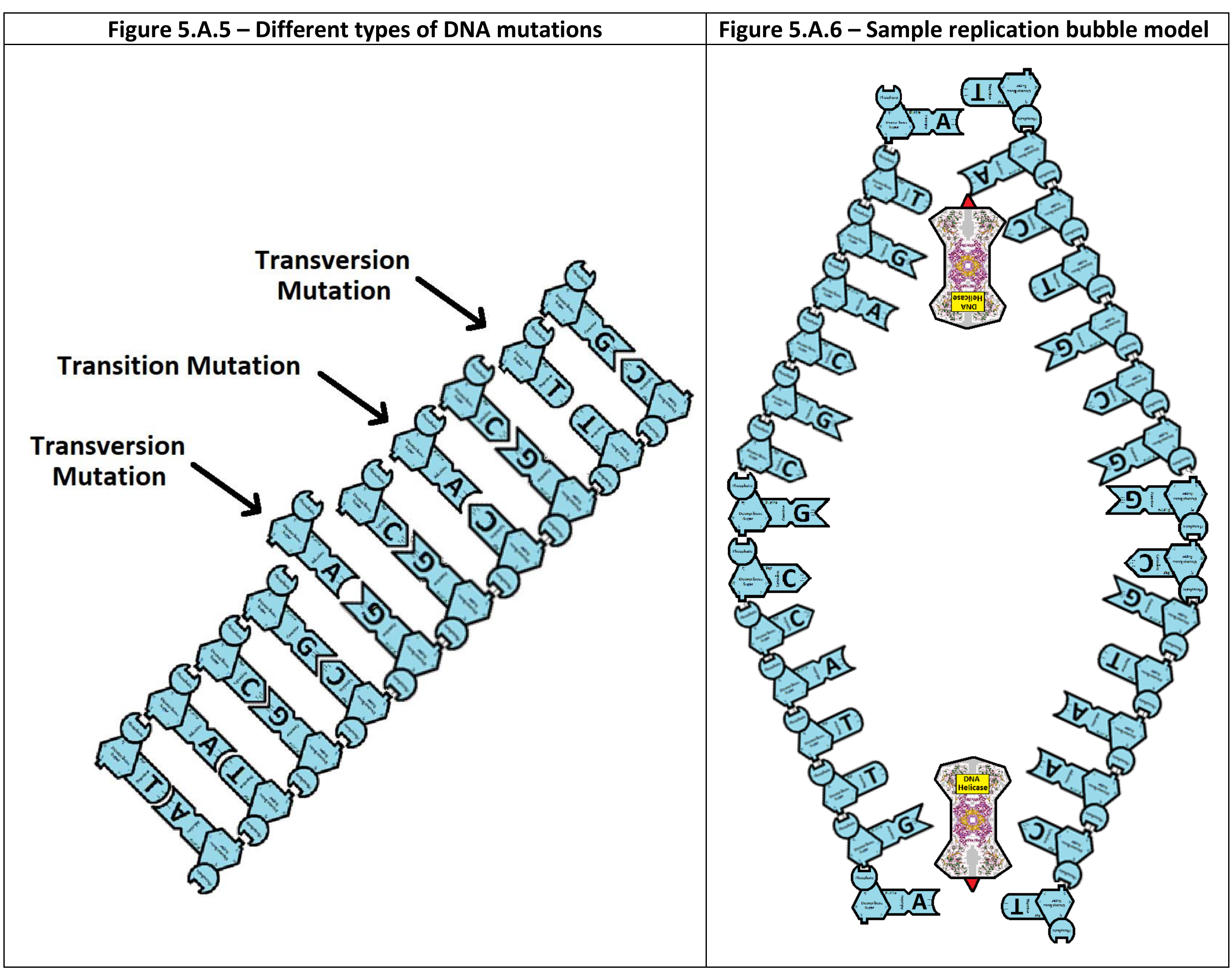


Figure 5.A.5 – Different types of DNA mutations

Figure 5.A.6 – Sample replication bubble model

Lesson 5B – Meselson and Stahl Experiment (10-40 minutes)

Teacher Centered Activity (10-20 minutes): For this exercise, you will need the Biology Magnet Module 5 supplement packet. In the experiment, the bacteria were first grown in a medium with heavy 15N DNA, then transferred to a medium with only light 14N DNA nucleotides. Meselson and Stahl used a centrifuge to “weigh” the bacteria after each generation. If the replication were conservative, after one generation, one light DNA strand and one heavy DNA strand would result and there would be two bands in a centrifuge tube (**Figure 5.B.1**). If the replication were semiconservative, two hybrid DNA strands would result and there would be only one band in a centrifuge tube (**Figure 5.B.2**). Meselson and Stahl found that DNA replication was semiconservative, not conservative. Use the Biology Magnets to show the two possibilities, and use a marker to draw the centrifuge results on the board. In the experiment, a second generation of bacteria was produced as well. The results obtained were two bands, one with 14N light DNA, and one with 14-15N hybrid DNA. Demonstrate the second generation using the Biology Magnets (**Figure 5.B.3**).

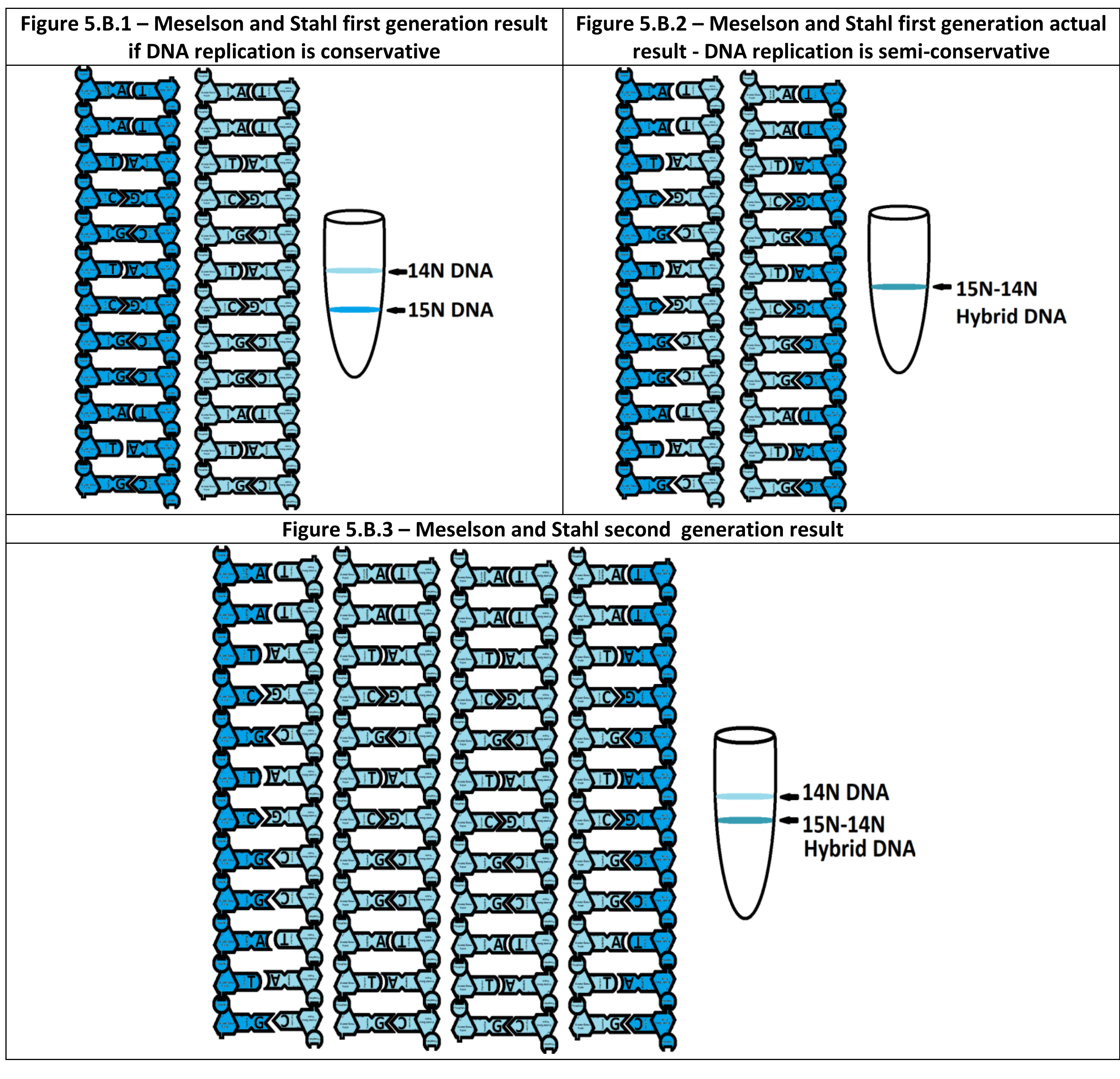


Figure 5.B.1 – Meselson and Stahl first generation result if DNA replication is conservative

Figure 5.B.2 – Meselson and Stahl first generation actual result - DNA replication is semi-conservative

Figure 5.B.3 – Meselson and Stahl second generation result

Student Centered Activity: (10-20 minutes): After teaching the Meselson and Stahl experiment, put students into small groups. A copy of the student guide for the lesson may be given to each group if necessary. Have the students take turns moving the Biology Magnets to accurately model the Meselson and Stahl experiment. Allow the students to correct and help one another. Continue to practice until each student can model the experiment without looking at the guide.

Extra exercises:

Second generation conservative replication: See if the students can predict what bands would have resulted if the second replication were conservative instead of semiconservative. Have the students use the magnets to show the resulting DNA strands. Have them use a marker to draw what bands would have resulted upon centrifuging the bacteria. (Answer: A heavy 15N band and a light 14N band, but no hybrid band).

Dispersive replication: Another hypothesis that Meselson and Stahl had was that perhaps DNA replication is dispersive, in which the new DNA strand is a mottled patchwork of old and new nucleotides (**Figure 5.B.4**). Have students predict what the second generation centrifuge results would have been if DNA replication is dispersive. How is that different from the semiconservative results? (**Figure 5.B.5**)

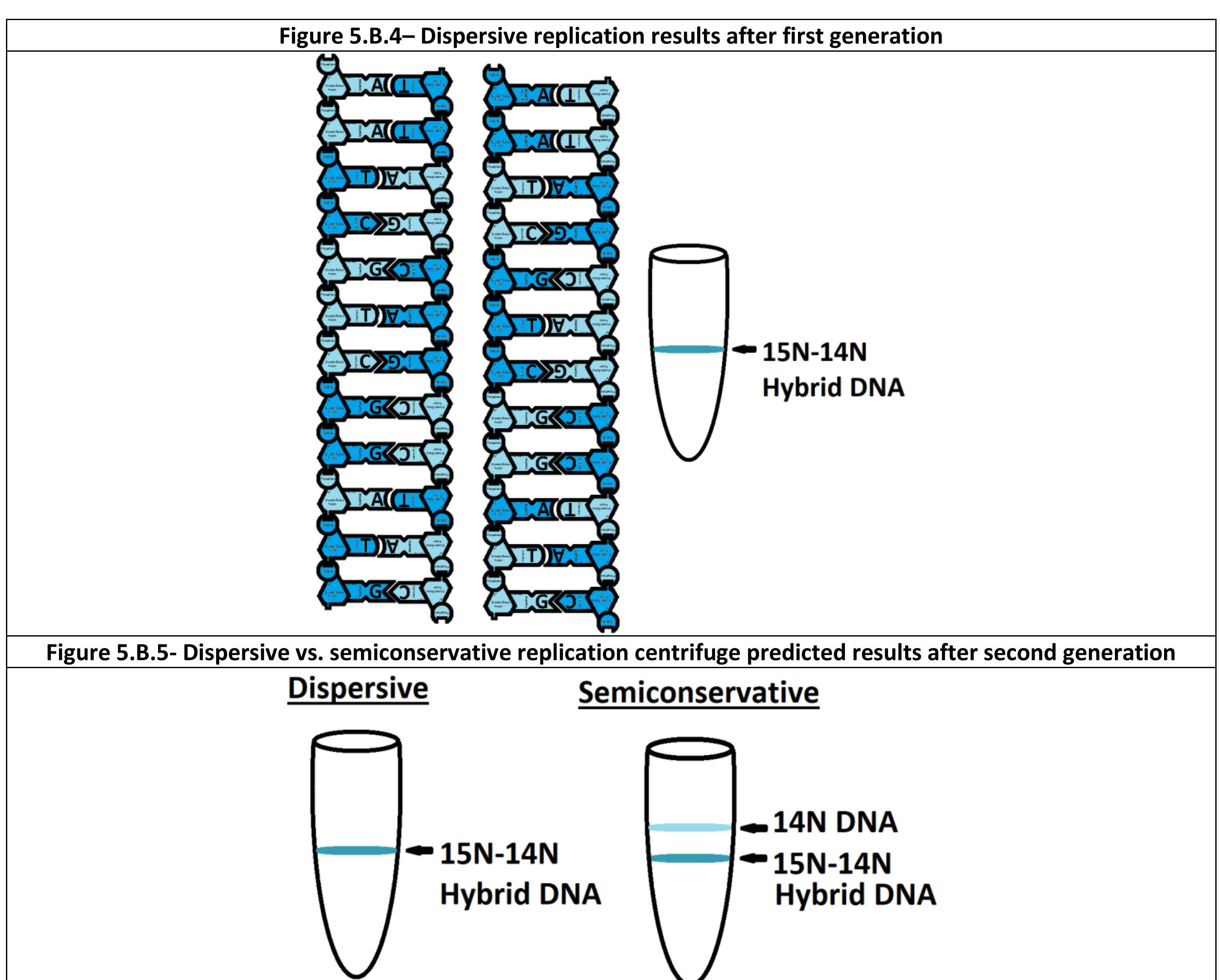


Figure 5.B.4– Dispersive replication results after first generation

Figure 5.B.5- Dispersive vs. semiconservative replication centrifuge predicted results after second generation

Lesson 5C – Sanger Sequencing (10-40 minutes)

Teacher Centered Activity (10-20 minutes): For this exercise, use the Biology Magnet Module 5 supplement packet. Sanger sequencing involves using specially modified nucleotides (ddNTPs) to stop the process of DNA replication at each nucleotide and use the resulting replicated strands to determine the DNA sequence through gel electrophoresis. Use the DNA strands on a string and arrange those lying horizontally at the bottom of the white board, with the strand starting TCA 5’->3’ on bottom. Place free DNA nucleotides, ddNTPs, DNA primers, and DNA polymerase enzyme above the strand (**Figure 5.C.1**). First, simulate heating the test tube by separating the strands and removing the top strand. When the test tube holding the ingredients is cooled, the DNA primer binds to the chain at the end, ATG to CAT. DNA polymerase then copies the template strand with the free nucleotides available. By random chance, the DNA polymerase will place a ddNTP nucleotide at some point, which terminates the chain (**Figure 5.C.2**). The test tube is then heated and the resulting replicated DNA strand breaks free. This process is repeated until many replicated strands of various length exist in the tube. Demonstrate the formation of different length strands with the Biology Magnets (**Figure 5.C.3**). The replicated strands are then pulled through a capillary tube filled with agar using an electrophoresis apparatus. Shorter strands move faster through the tube, and a laser at the end of the tube identifies the ddNTPs, which fluoresce different colors when they are struck with the laser beam. Adenine fluoresces green, thymine red, cytosine violet, and guanine yellow. A computer reads the colors as the strands pass and determines the sequence. Draw a capillary tube on the board and move the magnets through the tube to demonstrate the procedure. Note that the sequence determined is actually the sequence of the opposite strand to the template strand.

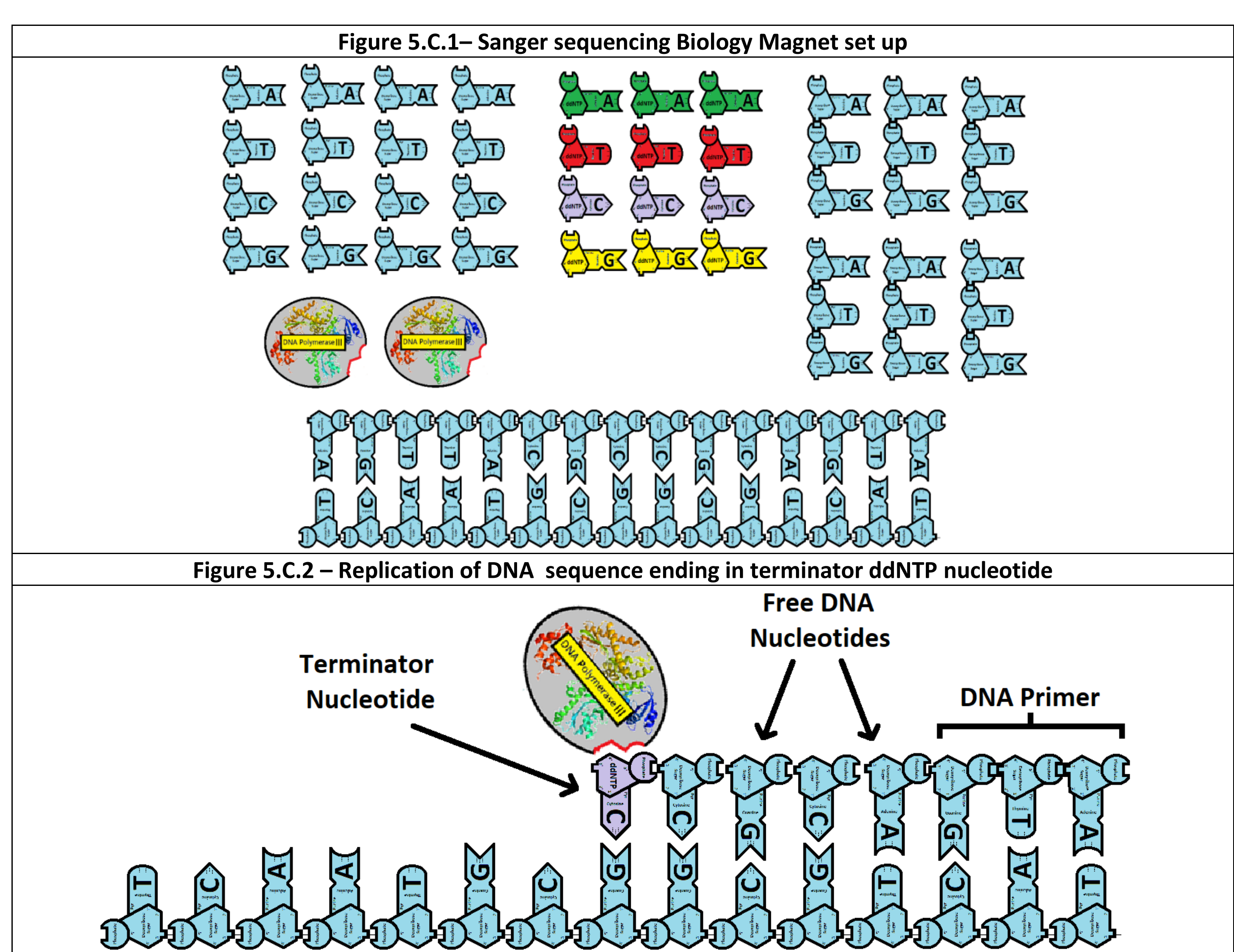
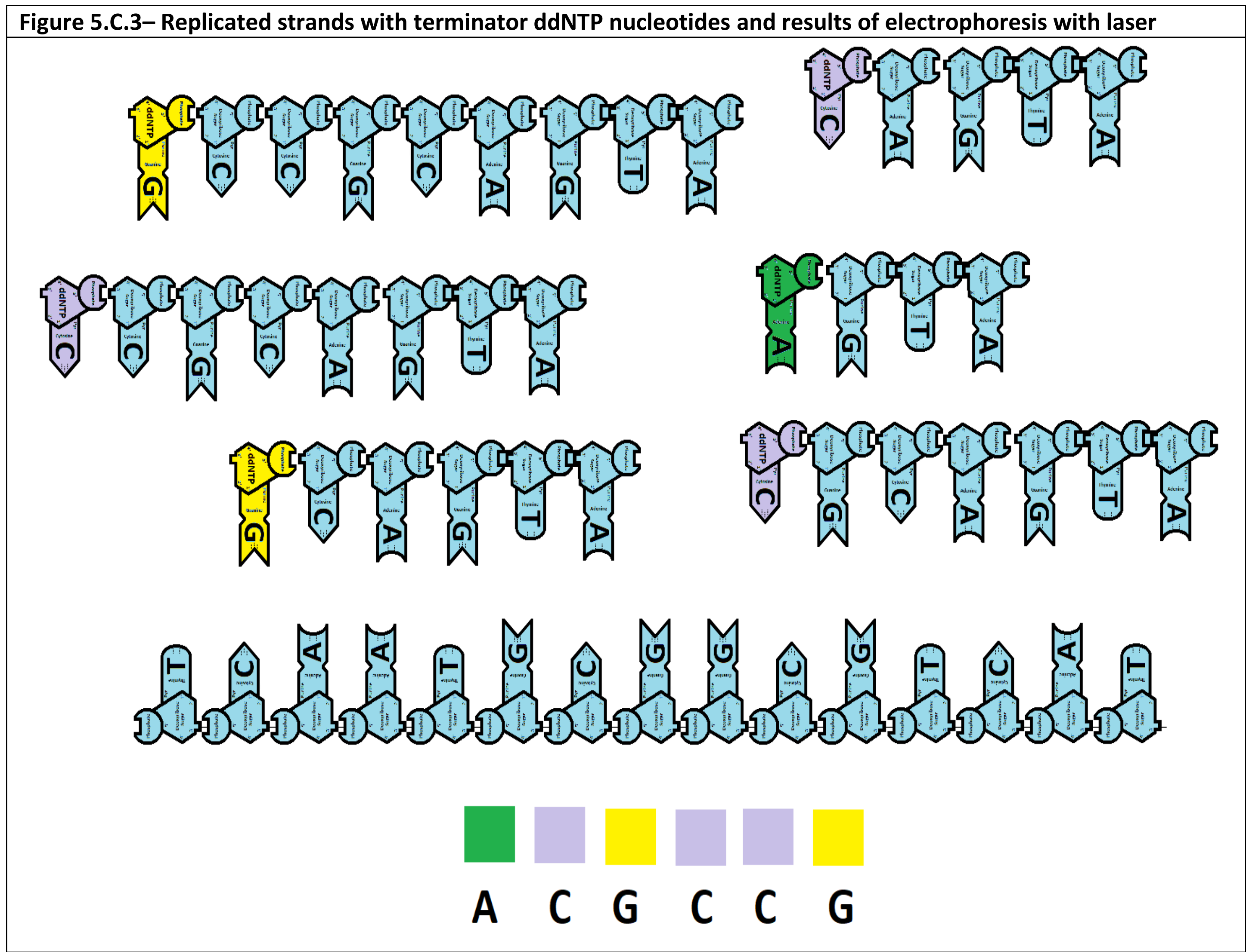


Figure 5.C.1– Sanger sequencing Biology Magnet set up

Figure 5.C.2 – Replication of DNA sequence ending in terminator ddNTP nucleotide

Figure 5.C.3– Replicated strands with terminator ddNTP nucleotides and results of electrophoresis with laser



Student Centered Activity: (10-20 minutes): After teaching Sanger sequencing, put students into small groups. A copy of the student guide for the lesson may be given to each group if necessary. Have the students take turns moving the Biology Magnets to accurately model Sanger sequencing. Allow the students to correct and help one another. Continue to practice until each student can model the process without looking at the guide.

Extra exercises:

Opposite strand template: Have the students try to use the opposite DNA strand (which starts ATG 5’-> 3’) as a template for the Sanger method. Is it possible to determine the sequence using the same Biology Magnet tools? Why or why not? **Answer**: It is not possible to sequence the entire other strand because the DNA primer that is used for the opposite strand binds to a site in the middle of the strand but not on the end. To copy the entire opposite strand, a different DNA primer (TCA) would have to be developed. Have students develop that primer using free nucleotides and then sequence the opposite strand.

Research Sequencing Techniques: There are many techniques other than the Sanger method for sequencing DNA. Have students research various techniques online and present their findings to the rest of the class. Use Biology Magnets in the presentations if possible.

Lesson 5A – DNA Replication – Student Guide

Student centered activity: This lesson utilizes the Biology Magnets to model DNA replication. Start by placing the two strands of DNA attached to strings on the board so they link together in the center (**Figure 5.A.1**). Using DNA helicase, unzip the DNA strand down the middle. Place Topoisomerase in front of the helicase to prevent supercoiling of the DNA. Use the DNA primase enzyme to put down a short RNA primer in the 5'->3' direction to start the replication of the leading strand according to the pairing rules, G-C and A-U (T instead of U for DNA) (**Figure 5.A.2**).

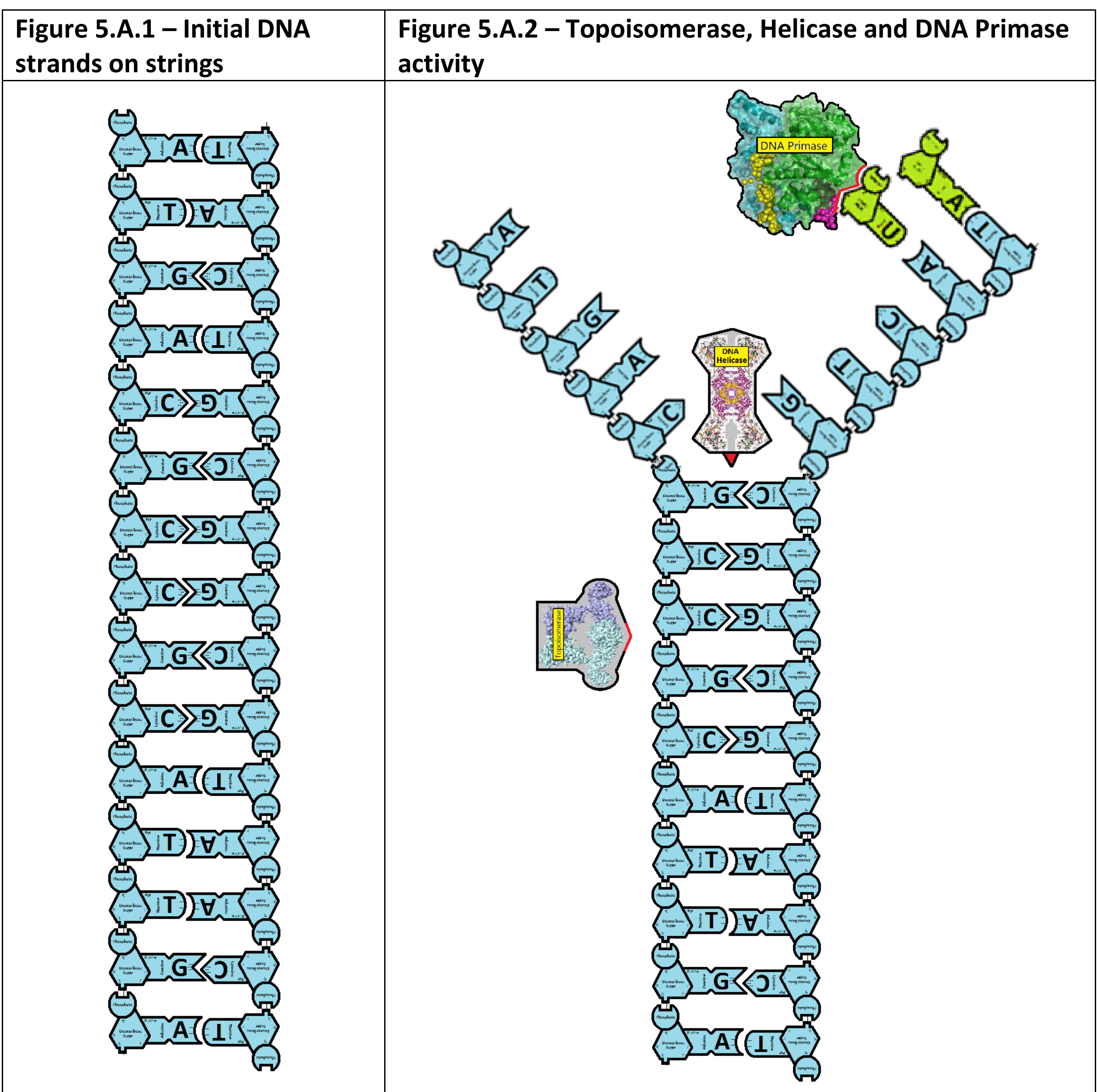


Figure 5.A.1 – Initial DNA strands on strings | **Figure 5.A.2 – Topoisomerase, Helicase and DNA Primase activity**

Move helicase and further unzip the strand. Add complementary DNA nucleotides after the RNA primer using the DNA Polymerase III enzyme. On the lagging strand, add RNA primers and DNA nucleotides in the same manner, still 5" -> 3', but in the opposite direction moving away from the helicase enzyme. These shorter fragments of DNA are called Okazaki fragments (**Figure 5.A.3**). After the strands are completed, use the exonuclease enzyme to remove the RNA primers, and then use DNA polymerase I to replace them with DNA nucleotides. Finally, use DNA ligase to splice together the 3' end of the replacement chain with the 5' end of the adjacent DNA nucleotide (**Figure 5.A.4**). Each student should practice modeling until the process can be done without looking at the student guide.

Figure 5.A.3 – Activity of DNA Polymerase III and formation of Okazaki Fragments

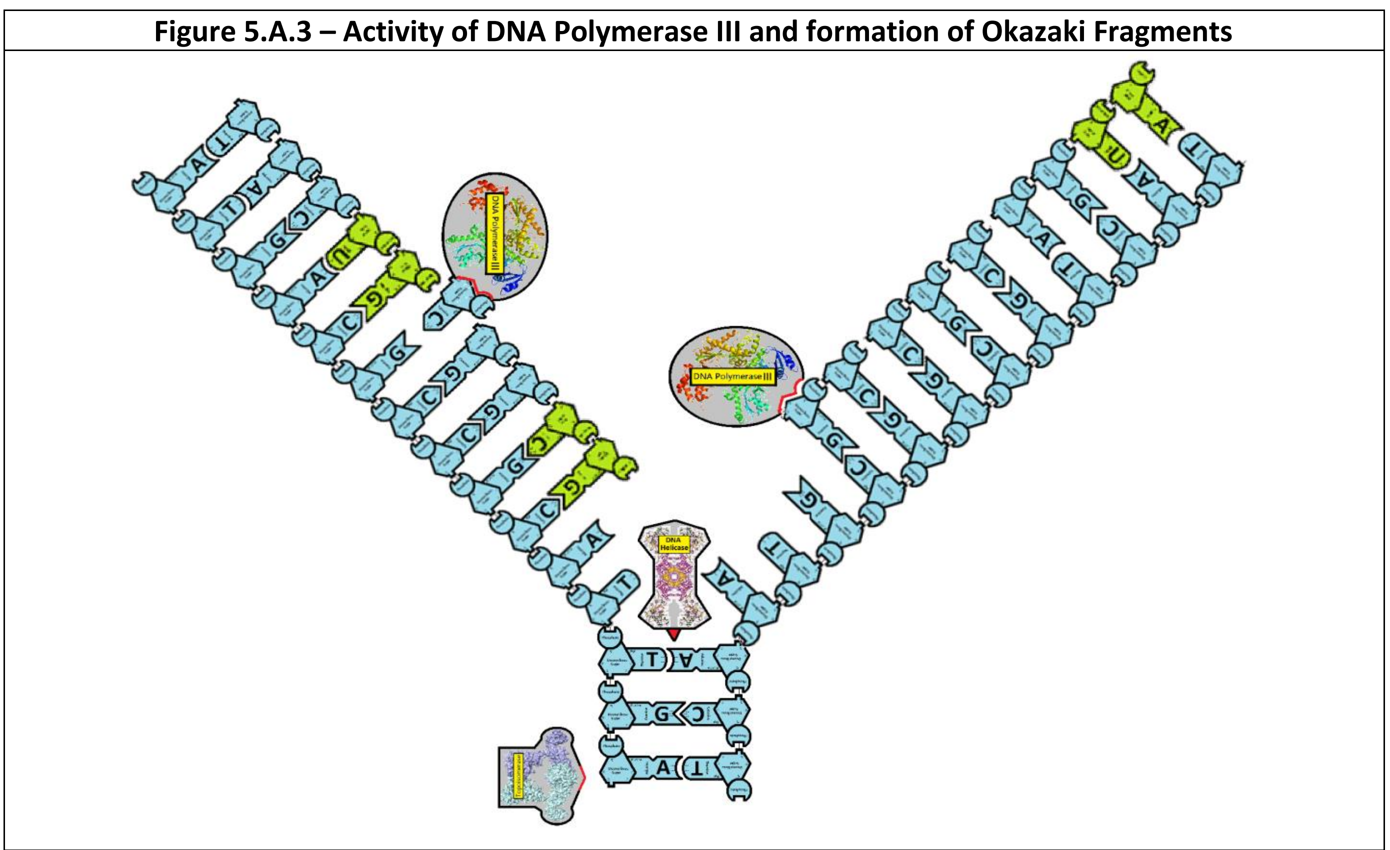
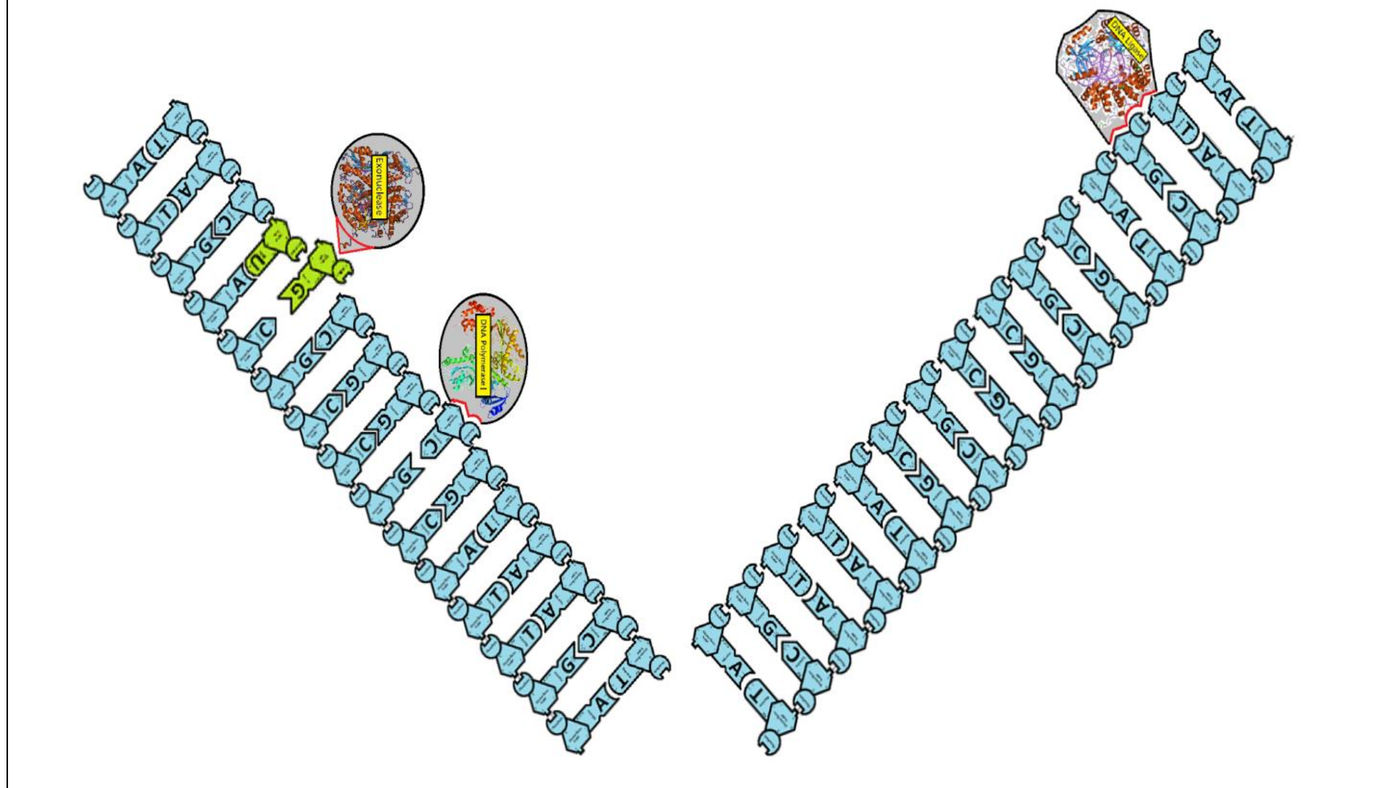


Figure 5.A.4 – Activity of Exonuclease, DNA Polymerase I, and DNA Ligase



Extra exercises:

Mutations: Mutations can form when a nucleotide with a mismatched base is mistakenly placed in the replicated strand of DNA. Transversion mutations occur when a purine is substituted for a pyrimidine or vice-versa. This causes a change in the width of the DNA strand, either too wide (purine-purine) or too thin (purine-pyrimidine). Transition mutations occur when a purine is substituted with a different purine (or pyrimidine with a pyrimidine). This does not change the width of the DNA chain. Transition mutations are about twice as common as transversion mutations (**Figure 5.A.5**). Model several of the mutations while the group is replicating the DNA. Simulate DNA repair by using repair enzymes such as exonuclease to remove mismatched bases and DNA polymerase and ligase to replace the bases. Show the teacher the mutations and repair process.

Replication bubble: In order to speed up the process of DNA replication, replication bubbles form within each chromosome, where the unzipping of the DNA occurs in both directions of the DNA chain.   Use the second DNA helicase enzyme to form a replication bubble (**Figure 5.A.6**). Determine which side of each fork is the lagging strand and the leading strand. Use the Biology Magnets to model the replication of nucleotides on each strand at both ends of the fork.

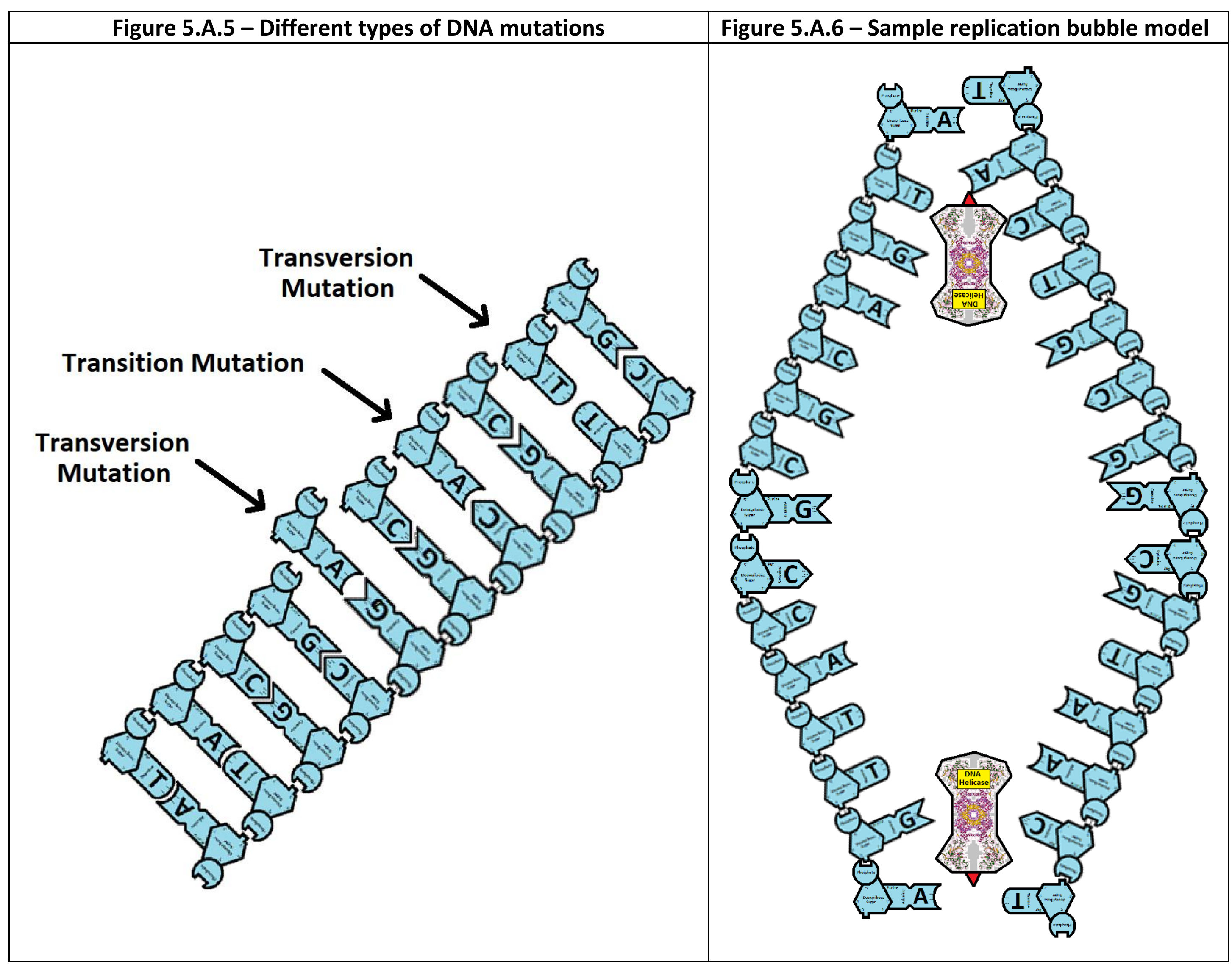


Figure 5.A.5 – Different types of DNA mutations

Figure 5.A.6 – Sample replication bubble model

Lesson 5B – Meselson and Stahl Experiment – Student Guide

Student Centered Activity: For this exercise, you will need the Biology Magnet Module 5 supplement packet. In the experiment, the bacteria were first grown in a medium with heavy 15N DNA, then transferred to a medium with only light 14N DNA nucleotides. Meselson and Stahl used a centrifuge to “weigh” the bacteria after each generation. If the replication were conservative, after one generation, one light DNA strand and one heavy DNA strand would result and there would be two bands in a centrifuge tube (**Figure 5.B.1**). If the replication were semiconservative, two hybrid DNA strands would result and there would be only one band in a centrifuge tube (**Figure 5.B.2**). Meselson and Stahl found that DNA replication was semiconservative, not conservative. Use the Biology Magnets to show the two possibilities, and use a marker to draw the centrifuge results on the board. In the experiment, a second generation of bacteria was produced as well. The results obtained were two bands, one with 14N light DNA, and one with 14-15N hybrid DNA. Demonstrate the second generation using the Biology Magnets (**Figure 5.B.3**). Continue to practice until each student can model the experiment without looking at the guide.

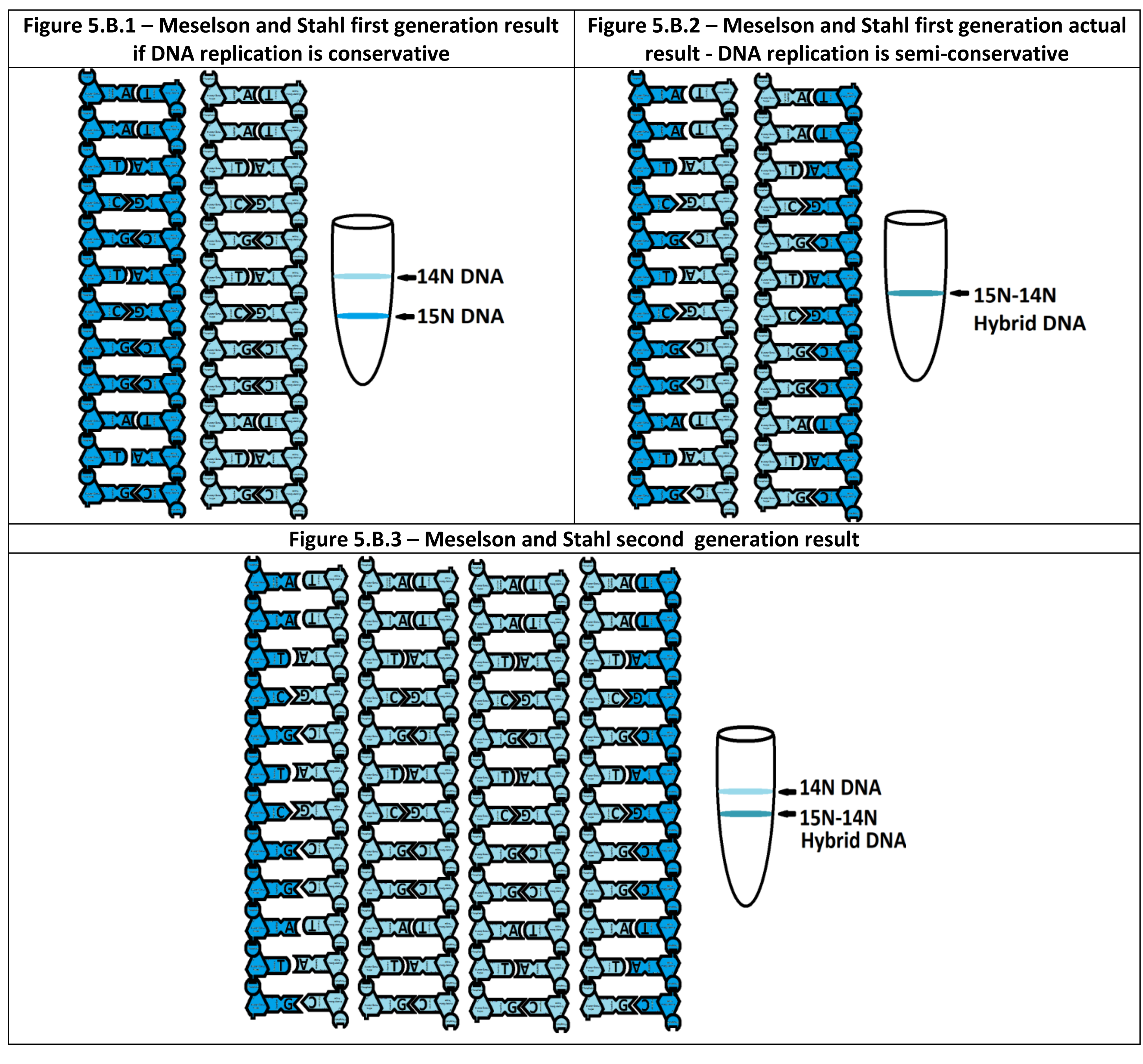


Figure 5.B.1 – Meselson and Stahl first generation result if DNA replication is conservative

Figure 5.B.2 – Meselson and Stahl first generation actual result - DNA replication is semi-conservative

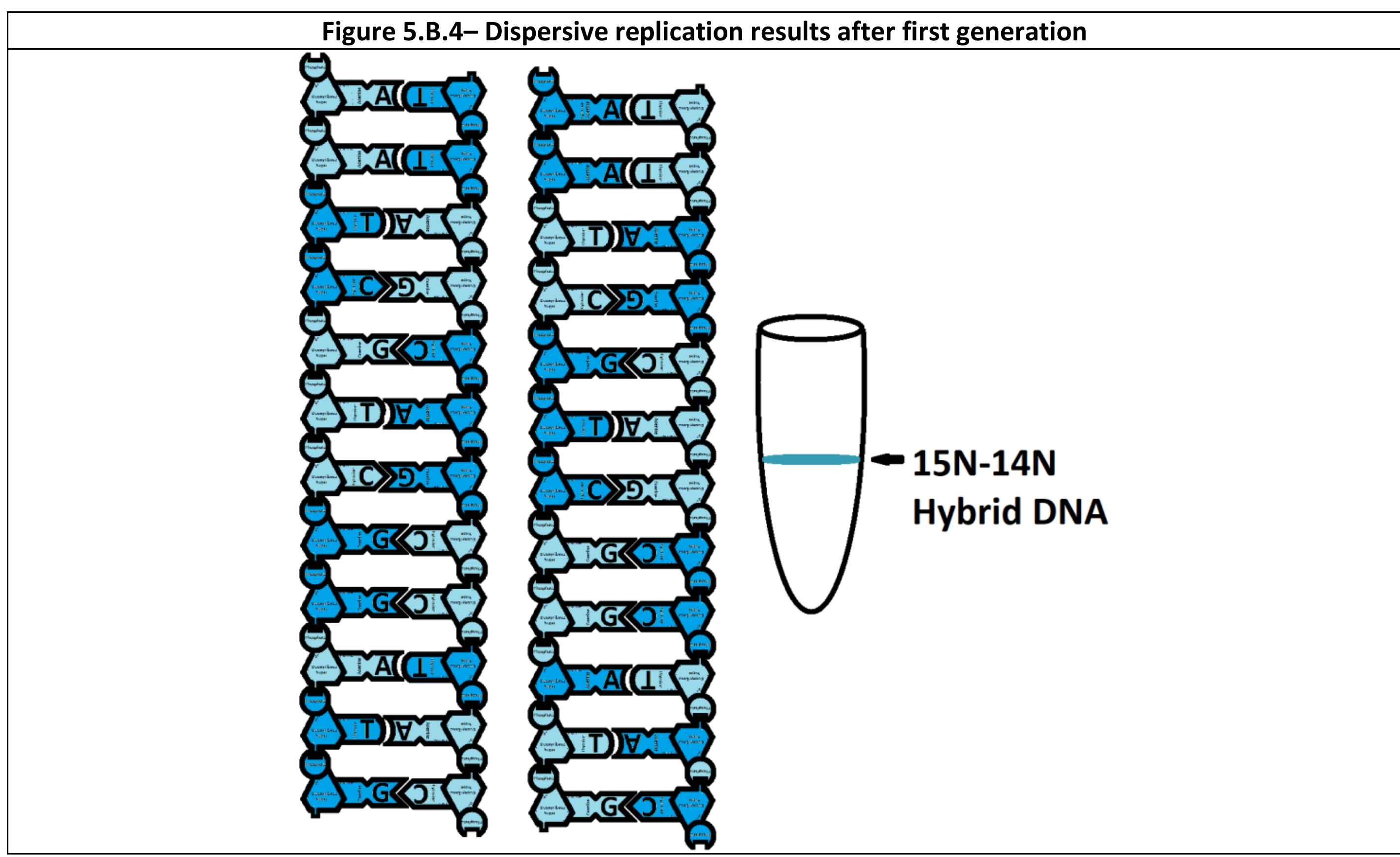
Figure 5.B.3 – Meselson and Stahl second generation result

Extra exercises:

Second generation conservative replication: Predict what DNA strands would have resulted if the second replication were conservative instead of semiconservative. Use the magnets to show the resulting DNA strands. Use a marker to draw what bands would have resulted upon centrifuging the bacteria.

Dispersive replication: Another hypothesis that Meselson and Stahl had was that perhaps DNA replication is dispersive, in which the new DNA strand is a mottled patchwork of old and new nucleotides (**Figure 5.B.4**). Predict what the second generation centrifuge results would have been if DNA replication is dispersive. How is that different from the semiconservative results?

Figure 5.B.4– Dispersive replication results after first generation



Lesson 5C – Sanger Sequencing – Student Guide

Student Centered Activity: For this exercise, use the Biology Magnet Module 5 supplement packet. Sanger sequencing involves using specially modified nucleotides (ddNTPs) to stop the process of DNA replication at each nucleotide and use the resulting replicated strands to determine the DNA sequence through gel electrophoresis. Use the DNA strands on a string and arrange those lying horizontally at the bottom of the white board, with the strand starting TCA 5'->3' on bottom. Place free DNA nucleotides, ddNTPs, DNA primers, and DNA polymerase enzyme above the strand (**Figure 5.C.1**). First, simulate heating the test tube by separating the strands and removing the top strand. When the test tube holding the ingredients is cooled, the DNA primer binds to the chain at the end, ATG to CAT. DNA polymerase then copies the template strand with the free nucleotides available. By random chance, the DNA polymerase will place a ddNTP nucleotide at some point, which terminates the chain (**Figure 5.C.2**). The test tube is then heated and the resulting replicated DNA strand breaks free. This process is repeated until many replicated strands of various length exist in the tube. Demonstrate the formation of different length strands with the Biology Magnets (**Figure 5.C.3**). The replicated strands are then pulled through a capillary tube filled with agar using an electrophoresis apparatus. Shorter strands move faster through the tube, and a laser at the end of the tube identifies the ddNTPs, which fluoresce different colors when they are struck with the laser beam. Adenine fluoresces green, thymine red, cytosine violet, and guanine yellow. A computer reads the colors as the strands pass and determines the sequence. Draw a capillary tube on the board and move the magnets through the tube to demonstrate the procedure. Have each student practice until everyone is able to model the process without looking at the student guide.

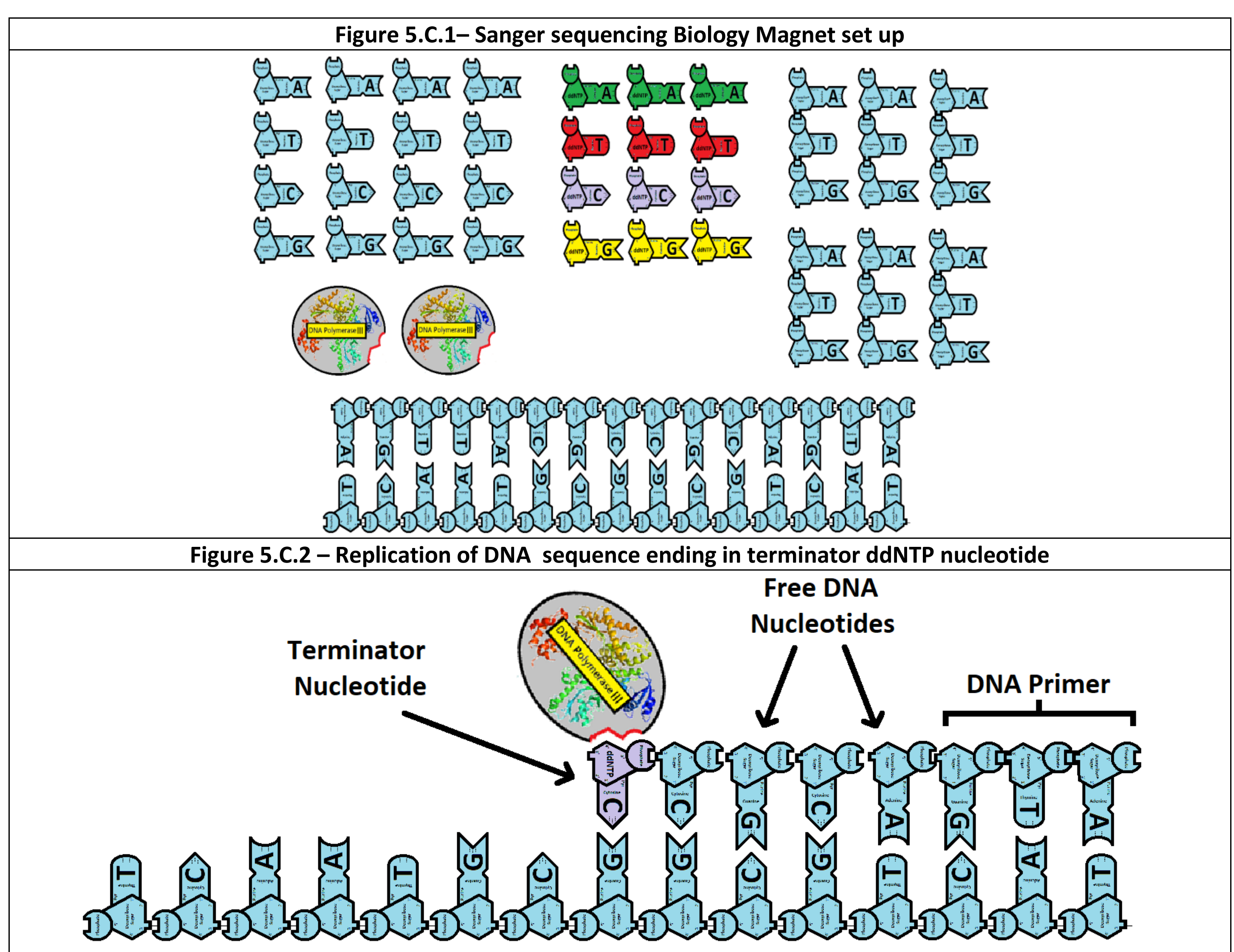


Figure 5.C.1– Sanger sequencing Biology Magnet set up

Figure 5.C.2 – Replication of DNA sequence ending in terminator ddNTP nucleotide

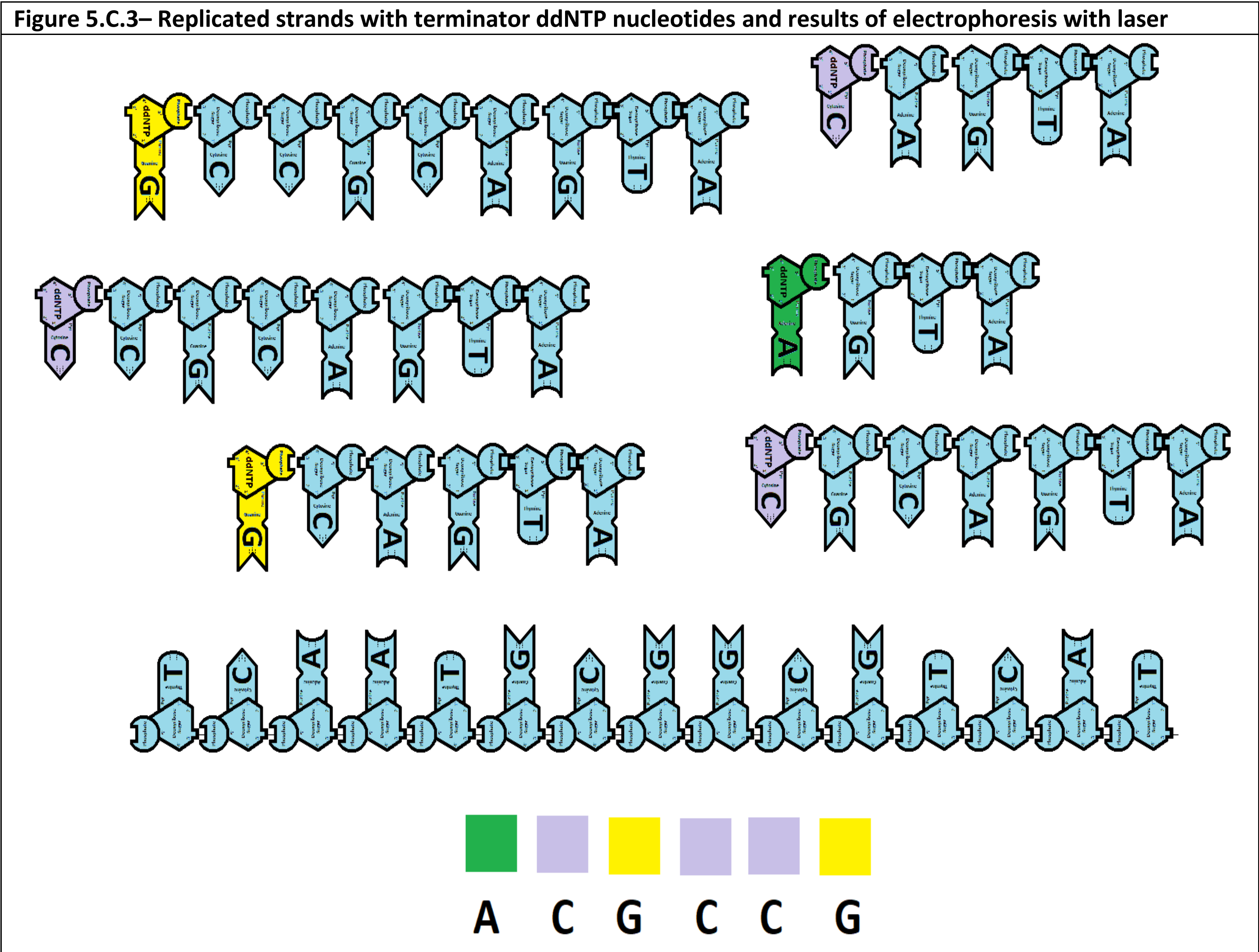


Figure 5.C.3– Replicated strands with terminator ddNTP nucleotides and results of electrophoresis with laser

Extra exercises:

Opposite strand template: Try to use the opposite DNA strand (which starts ATG 5’-> 3’) as a template for the Sanger method. Is it possible to determine the entire sequence using the same Biology Magnet tools? Why or why not? Use the Biology Magnets to investigate the problem. If not, try and invent a way to make the Sanger method work for that strand. Show the teacher the solution the group devised.

Research Sequencing Techniques: There are many techniques other than the Sanger method for sequencing DNA. Research various techniques online and present the findings to the rest of the class. Use Biology Magnets in the presentation if possible.