Modeling Sequencing by Synthesis

**Purpose:** The students should have just been introduced to sequencing by synthesis and have some idea of how it works. This activity will help them solidify their knowledge and give them an active role in learning from and teaching their peers. Students will act out the different parts involved in sequencing by synthesis together as a class. The students should be discussing among themselves what step occurs next and guiding their peers to complete the right actions. If they are struggling, the instructor can walk them through the first 1-2 cycles, then slowly give them more responsibility for doing it on their own.

**Set up:** Explain to the entire class what each student’s role is as they are assigned.
- One student to represent the beginning of the sequence that the primer will anneal to (hold a sheet of paper with the beginning sequence)
- One student to represent the primer that anneals to the student above (hold a sheet of paper with the beginning sequence that is complementary)
- ~4 students to represent the original, unknown DNA sequence. Each student will be given a piece of paper telling them what nucleotide they represent, and which nucleotide they are complementary to and that nucleotide’s color. This will be kept secret from anyone else in the class.
- One student to hold a flashlight to represent the laser.
- One student to hold a camera or binoculars as the camera, recording the sequences on a piece of paper
- At least one student as the deblocker
- One student as the DNA polymerase
- The rest of the students as the dNTPs, each holding a flag with a color of either blue, green, yellow, or red
  A = blue, G = green, C = yellow, T = red

**Procedure:**
- Have the students representing the original DNA sequence line up at the front of the class
- The students representing dNTPs will walk around
- The student representing DNA Polymerase will bring random students to the original sequence
- The original sequence will either accept or reject the nucleotide brought to them. They will say yes to the first nucleotide with the correct color that is complementary to them. Otherwise, they will reject the rest.
- The first nucleotide that is complementary will link arms with the primer while holding the flag in the other hand.
- The rest of the nucleotides and the DNA polymerase will be washed away to one side of the class, out of the way.
- The student with the flashlight will represent the laser and shine their flashlight on the flag to illuminate its color.
- The student representing the camera will "take a picture" (either by taking a real picture or looking through the binoculars, etc.), then record the color they see.
- The deblocker(s) flow in, removing the flag from that nucleotide's hand.
- The deblockers are washed away to one side of the class, out of the way.
- The nucleotides holding flags will be flown in again to repeat steps 2-10. The next one will link arms with the nucleotide that just had its flag removed, since their arm is now free to link to someone else with. Each round of step 2-10 is considered a cycle.
- When the entire sequence has been synthesized, the camera shares with the class what colors they saw and the class can interpret that into nucleotides, then from that information discover what the original sequence was. E.g. red, red, green, blue, yellow means that the newly synthesized complementary strand was TTGAC. Therefore, the original strand must be AACTG.