

Classroom Paper Simulation of Shotgun Sequencing

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Background: The last 10 years has witnessed an explosion of DNA sequencing as techniques for determining the order of bases in DNA have improved. This wealth of sequencing information is revolutionizing the study of biology, providing insights into mechanisms of evolution and answering many longstanding questions about how organisms are constructed. These techniques rely on a process known as “shotgun” sequencing. Millions of identical copies of DNA molecules are purified and randomly sheared or cut into smaller pieces. The small pieces are cloned and sequenced. Then computer programs are put together (assembled) by their overlaps. By aligning the overlapping regions in the small sequence segments, the entire genome is reassembled. In practice, sequence reads ~900 base pairs in length are commonly achieved and the depth of sequence coverage is 8-10 fold, allowing accurate reconstruction of the genome.

The following activity was developed by researchers and educators at the University of Pittsburgh’s Pittsburgh Bacteriophage Institute, and tested by 19 high school teachers at a summer workshop. The activity provides 10 copies of a genomic sequence of 25 color-coded bases (A’s, T’s, C’s, and G’s) in landscape format. The teacher cuts the genomes and puts the fragments into a container, from which students reconstruct the entire sequence by assembling the overlapping fragments. The file is available as a pdf.

How to use this activity: (Preparation) You have two accompanying pdfs. The first is the actual activity page. The second shows you how to cut it.

1. Print as many copies of the activity page as you have students (or pairs of students).
2. Print one copy of the “with cuts” as a guide for how to cut the sequence. Do not use this version to cut and distribute. This is extremely labor intensive, so we recommend laminating the page before you cut and collecting it at the end of the activity for next year.
3. Put each page of cut sequences in a sandwich bag or 50mL plastic tube. We recommend using a 50 mL tube, so that the project has more substance and definition (than an plastic sandwich bag).

Student Instructions: This is a one-word set of instructions: ASSEMBLE!!!

Notes:

- Do not tell your students this was made from an 8 x 11 sheet of paper.
- Do not tell them how many copies of the sequence are present. (This would be a true reflection of the way sequences are generated.
- The best reconstruction of this assembly took a group of high school students about 20 minutes. Most students can get there in about 40 minutes. All the while, you can lead them to think about how this is comparable to what is happening with their phages’ DNA.
- As a summative assignment to this activity you can ask for a written compare/contrast of this activity (analogy) with real sequencing.