Introduction
The Meselson–Stahl experiment has been called “the most beautiful experiment in biology” due to its essential simplicity. In 1957, Meselson and Stahl proposed and tested three different models for DNA replication: conservative, semi-conservative, and dispersive. They grew bacterial cells in heavy nitrogen \(^{15}\text{N}\); in the original paper written \(^{15}\text{N}\)) media and then transferred these cells to light nitrogen \(^{14}\text{N}\); in the original paper written \(^{14}\text{N}\)) media. As outlined, samples of the bacteria were taken immediately prior to transfer and after one and two rounds of replication. The DNA molecules were subjected to centrifugation using a cesium chloride gradient to separate the labeled molecules based on density. After the first round of replication, all of the DNA was of intermediate density, proving the conservative model false. After the second round of replication, half of the DNA was intermediate and half was light only, proving the dispersive model false. These results were, however, consistent with a semi-conservative model of replication and the structure of DNA that had been proposed by Watson and Crick a few years earlier. The semi-conservative model maintains that the original double helix serves as a template for, but does not contribute to, a new double helix. Thus, if Meselson and Stahl were to continue their experiment for two more generations, the number of intermediate DNA strands would not increase, but
rather stay the same, whereas the number of light DNA strands would increase with each generation.

Original Paper

http://www.pnas.org/cgi/reprint/44/7/671

Links
(For additional links on this topic, refer to the Chapter 13 Experiment Links.)

*DNA from the Beginning: Matthew Meselson and Franklin Stahl*
http://www.dnaftb.org/dnaftb/concept_20/con20bio.html

*John Kimball's Home Page: The Meselson–Stahl Experiment*
http://home.comcast.net/~john.kimball1/BiologyPages/M/Meselson_Stahl.html

*Michigan State University: Meselson–Stahl Experiment Proving Semi-Conservative Replication of DNA*
http://www.msu.edu/course/lbs/333/fall/meselson-stahl.html

*A fascinating commentary on how these two scientists did what some have called the “most beautiful experiment in modern biology.”*
http://www.pnas.org/content/101/52/17895.full

Analyze the Data

A key experimental method was the separation of DNA that contained ^14^N (“light DNA”) and ^15^N (“heavy DNA”). This was done using an ultracentrifuge in which the samples were spun until they reached their own density (See Figure 1).
Figure 1

Figure 2 shows the “data,” photographically and as traces of DNA content.

Figure 2

Question 1
You can approximate these data quantitatively by measuring the heights of the peaks of heavy, intermediate, and light DNA as a percentage of the total DNA in the experiment. Create a table summarizing these calculations and discuss whether they support the authors’ conclusions.

Question 2
What would the data look like if the bacteria had been allowed to divide for three more generations?

Question 3
If Meselson and Stahl had done their experiment starting with “light” DNA and then added $^{15}$N for succeeding generations, what would the bands look like? Draw them alongside the actual data, above.