Hi everyone! I hope you’re all enjoying your first few weeks of Biology 1305 ICB! My name is Mahita Maddukuri and I’ll be the master tutor for this course for this semester. I’m a Cell and Molecular Biology Major with a minor in Business Administration on the pre-med track. I took ICB Bio my freshman year, so I know that even though the ICB text can be challenging, with the right approach, it can also be a valuable tool!

I will be creating weekly resources which you can use as additional study tools to better understand the concepts that you are covering each week in class. As you have already seen, this course utilizes the Integrating Concepts in Biology (ICB) textbook, which looks a little different from the traditional BIO 1305 textbook. Throughout this course, it will be important for us to understand and analyze the data that the textbook presents in order to better grasp the main concepts.

I will also be leading weekly Group Tutoring sessions from 5:15 PM to 6:15 PM in room 75 of the Sid Richardson building basement. Please see Tutoring | Center for Academic Success and Engagement for more information on how to sign up for sessions and how to access the many other resources that the Baylor Tutoring Center provides. You can always feel free to contact me at Mahita_Maddukuri1@baylor.edu if you would like to reach out with questions or feedback!

KEYWORDS: Cell, Heritable Information, Experimental Design, DNA

TOPIC OF THE WEEK

DNA as the Heritable Material

The first case study introduced by this book focuses on Dr. Fred Griffith’s attempt to answer the question: “What is the heritable material that is passed from one generation to the next?”
While conducting tests with \textit{S. pneumoniae}, Griffith noticed that these bacteria could be classified into two strains: \textbf{rough (R) and smooth (S)}, which could be distinguished from each other visually. He also discovered that injecting bacteria from \textit{R} colonies into mice did not kill them, but injecting bacterial \textit{S} colonies did. From all his experimentation, he was convinced that \textbf{\textit{S}} and \textit{R} colonies were \textit{two variant strains of the same species}.

He then performed the following experiment:

\begin{center}
\includegraphics[width=\textwidth]{experiment_diagram.png}
\end{center}

When mice were injected with \textit{S} cells, they died. When mice were injected with dead \textit{S} cells, they lived. When mice were injected with \textit{R} cells, they lived. \textbf{But when the mice were injected with \textit{R} cells AND dead \textit{S} cells, the mice died.} The new \textit{S} cells that were produced in the fourth experiment also reproduced to create more \textit{S} cells that were identical to the original \textit{S} strain, demonstrating that \textbf{the information from the \textit{S} cells was being preserved and passed on from generation to generation}. This fourth experiment led him to hypothesize that there was a component of the \textit{S} cells which was somehow communicated to the \textit{R} cells, and that this component, which he called the “\textit{S} factor,” was the “heritable material for all of life.”

The next question that scientists needed to tackle was \textit{“What is the \textit{‘S} factor?””}

Another scientist, O Avery, extracted all soluble material (including nucleic acids and proteins) from bacteria and treated the material with proteases, RNases, and DNases. \textbf{Proteases} are enzymes that destroy proteins but not nucleic acids, \textbf{RNases} are enzymes that destroy RNA, and \textbf{DNases} are enzymes which destroy DNA.

\textbf{Results:}
\begin{itemize}
\item \textbf{Material treated with proteases} = \textit{R} cells transformed into \textit{S} cells and killed mice
\item \textbf{Material treated with RNases} = \textit{R} cells transformed into \textit{S} cells and killed mice
\end{itemize}
Material treated with DNases = R cells did not transform into S cells and did not kill mice

What does this mean?

In treatments where DNA was still intact, R cells transformed to the virulent S form and killed mice, whereas in treatments where DNA was destroyed, R cells did not become virulent. This experiment did not PROVE that the heritable genetic material was not protein, but it provided evidence that supported the theory that DNA, and not protein, was the material that was being transferred from S cells to R cells.

Note: In Biology, we don’t use the word “prove!” Instead, we can only say that results or data support a particular conclusion. In science, it is impossible to truly PROVE something, but it IS possible to DISPROVE something.

Next, we look at Hershey and Chase, who wanted to demonstrate beyond a reasonable doubt that protein was not the heritable material. How did they set up their experiment?

1) Isotopes: Atomic elements which can decay and emit radiation

Hershey and Chase used a radioactive isotope of Sulfur (S-35) to make proteins and a radioactive isotope of Phosphorus (P-32) to make DNA. This is because proteins contain sulfur, while DNA contains phosphates. Each of these radioactive isotopes emits a different energy level, which would allow them to determine if DNA or protein was present based on which type of radiation was emitted.

2) Phages: Viruses that infect bacteria

Hersey and Chase selected the T2 phage as the model system for their experiment. This virus consists of a protein coat surrounding a DNA genome, which meant that the protein coat could be radioactively tagged, or labeled, with S-35, while the viral DNA could be labeled with the P-32. They grew the phages with either radioactive amino acids or radioactive nucleotides and then allowed the phage to inject its DNA into the bacteria E. coli. Then, they used a blender to pull the phage head away from the infected E. coli cell.
The above graph shows the results of their initial experiment. The data that is in purple represents the percentage of Sulfur, or protein, that was outside of the cell as they ran the blender, and the blue curve is showing the percentage of Phosphorus, or DNA, that was outside the cell as they ran the blender. Their results showed that about 80% of the radioactive protein was still in the media, which meant that it did not enter the bacteria. On the other hand, 70% of the DNA was found in the bacteria, and only 30% was found in the extracellular media. This meant that it was extremely unlikely that protein was the transforming factor, since the majority of it did not enter the cell.

HOWEVER, critics could still argue that the 20% of the protein that made it into the cell was the transforming factor! This is an example of why we can’t truly prove things in Biology.

After their initial experiment, Hershey and Chase refined their methodology to account for almost all of the missing protein and to reduce errors as much as possible. The first two rows of the below table display their initial data (which we saw in the graph above), while the final two rows display their final set of data.

<table>
<thead>
<tr>
<th>Sample Source</th>
<th>Extracellular</th>
<th>Intracellular</th>
</tr>
</thead>
<tbody>
<tr>
<td>(^{35}\text{S}-\text{Protein Figure 1.8})</td>
<td>~80%</td>
<td>~20%</td>
</tr>
<tr>
<td>(^{32}\text{P}-\text{DNA Figure 1.8})</td>
<td>~30%</td>
<td>~70%</td>
</tr>
<tr>
<td>(^{35}\text{S}-\text{Protein refined experiment})</td>
<td>~99%</td>
<td>~1%</td>
</tr>
<tr>
<td>(^{32}\text{P}-\text{DNA refined experiment})</td>
<td>~30%</td>
<td>~70%</td>
</tr>
</tbody>
</table>

We can see that while in the initial experiment, they could only find 80% of the Sulfur in the extracellular media, in their final experiments, they were able to account for 99% of the Sulfur. This drastically reduced the possibility that protein was the transforming factor, since it wasn’t entering the cell!
Hershey and Chase’s experiment provided strong evidence that DNA, and not protein, was not the transforming material.

**HOWEVER, what arguments could be made by critics who still weren’t convinced by this data?**

Some counter arguments could be:

- the one percent of Sulfur that was not found in the extracellular media was inside the cell, and those proteins were the transforming factor *(this is extremely unlikely!)*
- Protein is still the transforming factor, but the heritable material is a type of protein that doesn’t contain Sulfur *(Hershey and Chase understood that this was a potential alternate explanation, but it was still unlikely)*

Although alternate explanations exist, the DNA hypothesis was finally accepted by the majority of the scientists of the time because of Hershey and Chase’s work.

For more information on Hershey and Chase’s experiment: [https://youtu.be/ZtSfFqqhEIY](https://youtu.be/ZtSfFqqhEIY)

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**HIGHLIGHT #1: Biological Information**

Although there are many definitions of the word “information,” the two most relevant ones for this course are:

1) communication or reception of knowledge
2) signal representing data that justifies a change

As you study the next chapters, think about how each of the experiments we are looking at are focused on studying the exchange of, organization of, or communication of biological information in some way.

**HIGHLIGHT #2: What is a Cell?**

The formal definition is that a cell is the fundamental structural and functional unit of life. It is composed of different organelles, organic macromolecules and a wide variety of chemical and biological molecules that help in cell functioning. However, in this course, we will see that a cell is very difficult to define. Section 8.1 looks at several examples which challenge our definition of what a cell is.
Why did people think that proteins were more likely to be the code for the heritable material?

**Multiplication Principle:** the number of possible outcomes of a multi-step process is the product of the number of possible outcomes of each step.

In a DNA sequence with three bases, there are 4 possible nucleotides that the first base could be, 4 for the second base, and 4 for the third base: $4 \times 4 \times 4 = 64$ possible outcomes.

In a protein sequence of the same length, because there are 20 amino acids while there are only 4 DNA nucleotides, the number of possible outcomes would equal: $20 \times 20 \times 20 = 8000$ possible outcomes.

A protein of the same length as a DNA strand can be composed of exponentially more combinations of information than DNA.

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**CHECK YOUR LEARNING**

(Answers below)

1) What was Griffith’s “S factor”?
2) What was the purpose of Avery’s experiment?
3) Why was the phage system chosen by Hershey and Chase so effective for their experiment?
4) How many possible combinations exist for a DNA strand with a length of 5 base pairs? What about for a protein of the same length?

**THINGS YOU MAY STRUGGLE WITH**

- We can’t prove things in science through experimentation; we can only support or disprove them.
- Griffith injecting S cells into the mice was his positive control. Injecting R cells into the mice was his negative control. However, the name of the control can vary depending on how you look at it. The important thing is that he demonstrated that the first three experiments worked the way they were supposed to so that he could compare them to the fourth and final scenario.
• Hershey and Chase used radioactive isotopes which emitted energy at different levels in a way that could be detected. This allowed them to find the location of the protein and DNA, because these radioactive isotopes were incorporated into these molecules.

**ANSWERS:**

1) DNA
2) To determine what the S factor was
3) The phage had a fast generation time and only contained DNA and protein, which were the two molecules they were studying
4) 1024.
   3,200,000.

**That’s it for this week! Please feel free to reach out with questions or check out Baylor Tutoring Center’s website for more resources!**