Connecting Industry to Mathematics Instruction

NSF ATE Award # 1954291

Student Activity Sheet - Virus Maximus

Virus Growth and Vaccine Production

In partnership with WAKE TECH, WAKE COUNTY PUBLIC SCHOOL SYSTEM, WakeEd PARTNERSHIP

Hemagglutinin (**HA**) is an antigenic glycoprotein found on the surface of influenza viruses. It is responsible for binding the virus to the cell that is being infected.

Overview: Below are sets of data showing viral HA protein percent yield for three different virus strains being considered for use in the upcoming flu vaccine production process, and a control. Seqirus needs to maximize the yield of the virus in order to use it to create as many doses of vaccines as possible. Calculate which strains, if any, showed a significant **difference** ($p<0.05$) in HA percent yield compared to the control. Based on the results, make a recommendation to manufacturing on which strain(s) to use, or to stick with the control strain. The sample for each run is 100.

Part 1:

1. Look at the data and compare each strain to the control. Estimate which strain you think is the least effective. Why do you think it is the least effective?
2. Estimate the strain that you think will be the most effective. Why do you think it is the most effective?

Control		Strain A		Strain B		Strain C	
Run	HA Percent Yield	Run	HA Percent Yield	Run	HA Percent Yield	Run	HA Percent Yield
1	41%	1	43%	1	54%	1	59%
2	38%	2	34%	2	61%	2	55%
3	37%	3	39%	3	56%	3	53%

3. What would be used as the population parameter for this situation?

4. Using the **median** values for the control and each strand, what is your null hypothesis and what alternate hypothesis will you be testing?

5. Using the **median** values for the control and each strand, complete the following table.

Strain	H_o	H_a	Calculations to find Probability (show work - What you typed into Desmos)	Probability	Significant?
A					
B					
C					

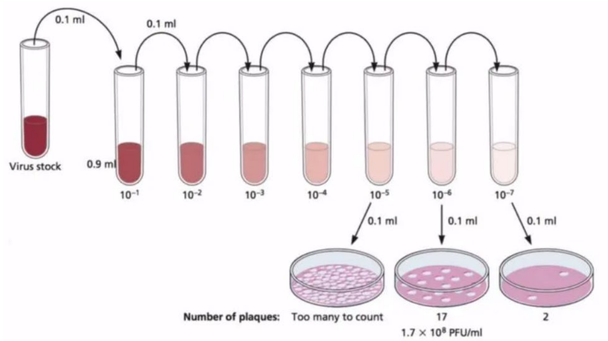
6. Based on your calculated probability, which strain do you feel can be discarded? Why?

7. Looking at the other two strains, does the differences in their probability justify using one over the other or do you feel that they are both similarly effective? Explain your conclusion with complete sentences.

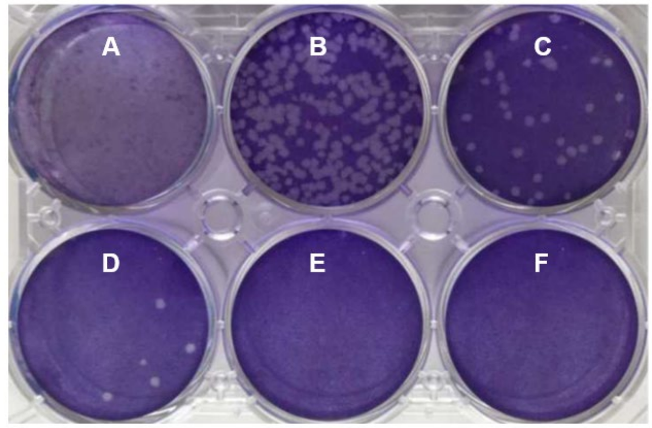
8. In the context of this question, why would a probability of 0.03 be considered significant when 0.20 is not?

Part 2:

Seqirus wants to produce the maximum amount of virus cells so they can use them in their vaccines. When counting the amount of virus cells, which is called calculating viral titer, dilution is necessary to get a countable number. Shown below is an image of a sample of a virus showing the stages of dilution from a high concentration of the white virus cells to a low concentration of the cells. (The white is the virus cells and the purple is the dilution agent)



Bacteriophage Plaque Assay



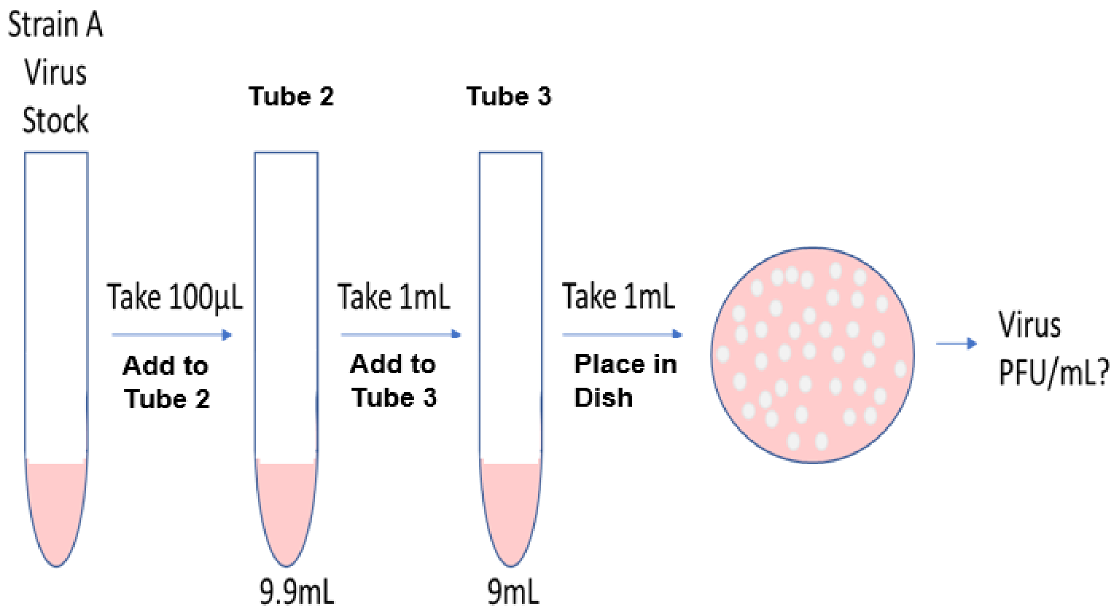
1. Which dilution sample do you think would be the best to count the number of cells? Why? Reminder: Dr. Johnstone gave parameters in the video for how many cells needed to be present in a sample. **(Video Link** should say the number of cells should be between 30 and 300)

Pictured below is the experimental overview and results of stocks using the control and three strains from Part 1. Each dot in the dish represents one virus unit called a “plaque forming unit (PFU)”.

Calculate the amount of PFUs per milliliter (PFU/mL) for each viral stock being tested.

µL means 1 microliter. A microliter is a unit of volume equal to 1/1,000,000th of a liter.

Note: 1mL=1000µL. You will notice that on the diagrams the units are sometimes in mL and other times in µL. Make sure you convert to mL when necessary.



Calculations for Strain A:

First you must calculate the dilution factor- To do this you are starting with your virus stock and taking a small amount of the Strain A Stock, placing it into Tube B and mixing it together. You then will take a small amount of the sample in Tube B and mix it into Tube C. Finally you take a small amount of sample from C and count the virus cells. You will then use this number to calculate how many virus cells were in the original Stock.

Take 100 µL from the stock and place in Tube 2:

First convert 100µL into mL: $\frac{1mL}{1000\mu L} = \frac{x}{100\mu L}$ Solve the proportion to get x = 0.1 mL

Find the total amount of solution in Tube 2: 9.9 mL + 0.1mL = 10mL

In Tube 2 there was 0.1 mL of stock so the total ratio of stock to solution is $\frac{0.1}{10} = 0.01 \text{ or } 10^{-2}$

Take 1mL from the Tube 2 and place in Tube 3:

Find the total amount of solution in Tube 3: 9mL + 1mL = 10mL

In Tube 3 there is 1mL from Tube 2 so the total ratio of Tube 2 to Tube 3 is $\frac{1}{10} = 0.1 \text{ or } 10^{-1}$

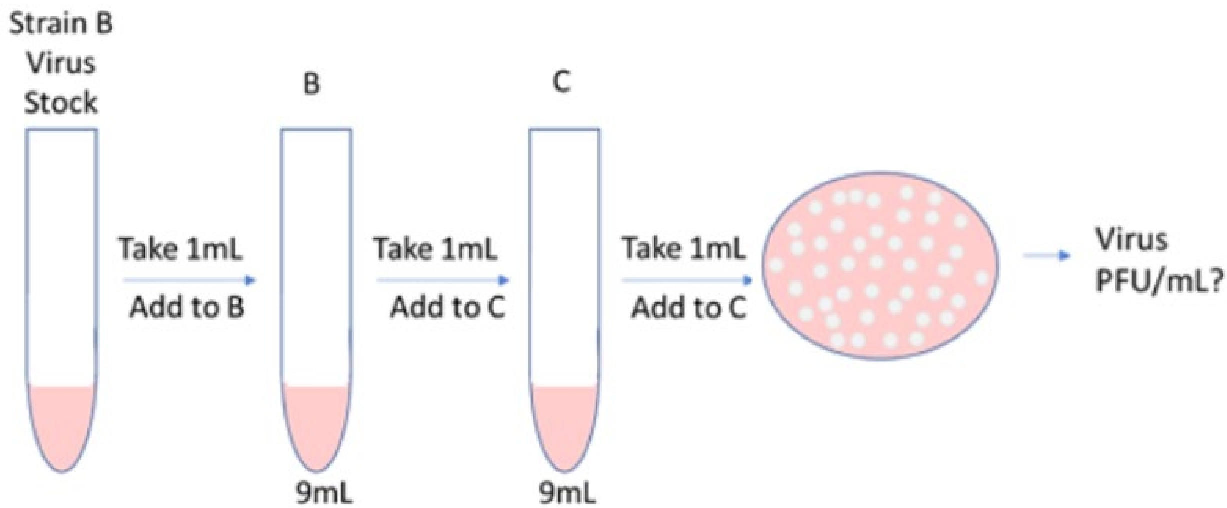
Total Dilution and Final Count

The total dilution is then $10^{-2} \cdot 10^{-1} \cdot 1 = 10^{-3}$

Count the virus cells in your diagram above: 39 cells

Final count: 39 PFU ÷ 10^{-3} = 39,000 PFU

Convert to scientific notation: 39,000 = 3.9 x 10^{4} PFU/mL



Take 1mL from the stock and place in Tube 2:

No need to convert since you start with mL.

Find the total amount of solution in Tube 2:

The total ratio of stock to solution is:

Take 1mL from the Tube 2 and place in Tube 3:

Find the total amount of solution in Tube 3:

The total ratio of Tube 2 to Tube 3 is:

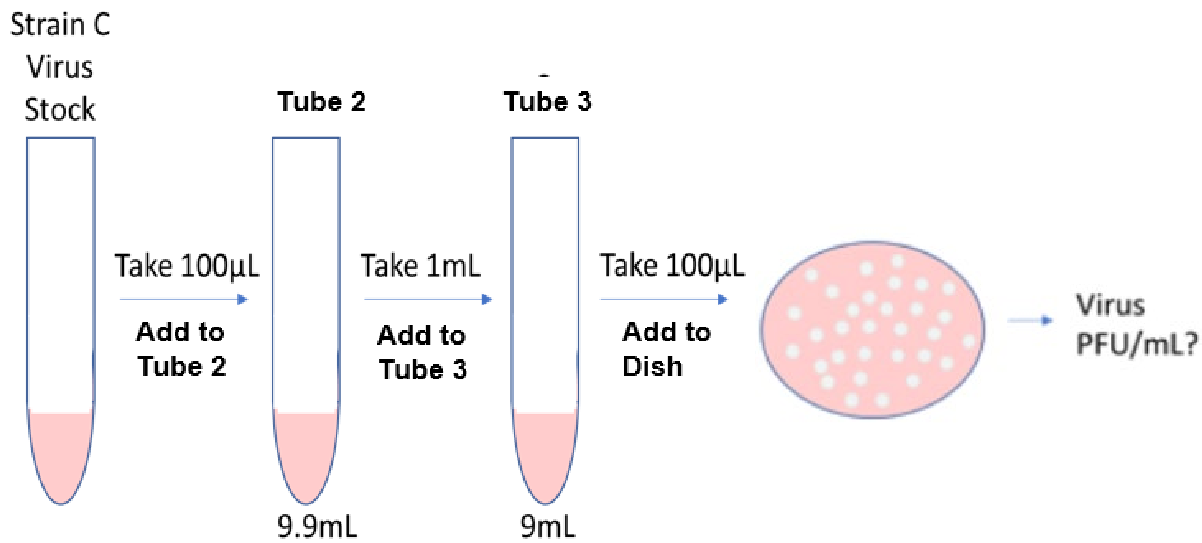
Total Dilution and Final Count

The total dilution is:

Count the virus cells in your diagram above:

Final count:

Convert to scientific notation:



Take 100 µL from the stock and place in Tube 2:

First convert 100µL into mL:

Find the total amount of solution in Tube 2:

The total ratio of stock to solution is:

Take 1mL from the Tube 2 and place in Tube 3:

Find the total amount of solution in Tube 3:

The total ratio of Tube B to Tube 3 is:

Total Dilution and Final Count (Note: there is not 1 mL of tube C used, but 100µL and you must convert to mL)

The total dilution is:

Count the virus cells in your diagram above:

Final count:

Convert to scientific notation:

Conclusion:
Seqirus produces a flu vaccine that requires maximal viral HA protein yield and virus production for manufacturing the vaccine efficiently. Using the information from part #1 and #2, make a recommendation to Dr. Johnstone for which strain Seqirus should use to produce the vaccine. Remember that you are presenting your written conclusion to a scientist and you should use complete sentences and proper grammar in your explanation of why you picked a certain strain and support your recommendation with the mathematics.