Modeling the *lac* Operon to Understand the Regulation of Gene Expression in Prokaryotes

This week we are exploring control mechanisms of gene expression in prokaryotes. We will do this with a simulation of the "*lac* operon" as an example of how bacterial cells can control the production of proteins in response to environmental changes. An operon is a set of genes that are transcribed together and thus are under the control of the same regulatory mechanism. The *lac* operon contains genes that function in the metabolism of lactose, an energy source for some bacteria.

We will explore the *lac* operon by working with a simulation. A simulation is tool for exploring the dynamics of complex processes. It is a model built on a set of mathematical rules that define how the elements of the system interact with one another. While every simulation simplifies some of the biology it models they are important learning and research tools because they allow us to explore the model and compare its behaviors to the real world system.

Be careful not to conflate simulations with animations. Animations help us visualize complex systems but they do not allow us to ask "what if" questions. This simulation has a graphical output, so it looks like an animation, but unlike an animation the graphics are controlled by the underlying model.

http://bit.ly/lac_operon

Getting Oriented to the Model:

Build a complete system by putting all of the genetic elements into place and observing the simulation. You should recognize how the following molecules and processes are represented:

- Turn on the legend and compare the model to the genetic elements and proteins in figures 16.4 & 16.5.
- **transcription**, **translation**, **binding** & **unbinding**, **degradation** (mRNA and proteins), & **diffusion**.
- Set the Lactose Injector to Auto and compare the two conditions (lactose absent / lactose present) to Figure 16.5 A and B.
- Write out a sentence describing how and why the gene expression changes when you shift from lactose absent to lactose present. Practice using the correct technical terms.
- Write out a sentence describing how and why the gene expression changes when you shift from lactose present to lactose absent. Practice using the correct technical terms.

Control of Lac Z production:

1. Study the dynamics of the system in response to the introduction of lactose. Run your simulation in the lactose absent condition at a fast speed. Pause the simulation and introduce 20 lactose molecules. Restart the simulation and track the number of lactose and LacZ molecules over time (every 10 seconds) until they are all gone.
    a. Before you run the experiment predict what your graph will look like.
    b. Make a data table to collect your data.
    c. Using the pause button to stop the simulation will make it easier to count the lactose molecules.
    d. Sketch a graph of your results.
    e. Describe the dynamics by explaining what was going in different parts of the graph.
    f. Is your graph consistent with Figure 16.2 in the text?
2. Control of the *lac* operon:
    - Use the following terms to describe this part of the control system for the *lac* operon
        - **negative control**, **repressor**, **inducer**, **operator**, **promoter** & **operon**.
    - In the intact system what is **constitutively** produced? What is induced?
    - Find 3 ways to change the system (mutations) that makes the *lac* Z gene constitutively expressed.
    - Describe 3 changes to the system that would make it so that the cell couldn't use lactose as an energy source (the third change will require you to move to the second model – "Lactose transport" tab).

Lactose Transport Across the membrane: (Lactose Transport Model)

1. What is different about this simulation?
2. Model an intact cell without lactose present. Can you predict what will happen when lactose is available?
3. Provide a pulse of lactose outside of the cell. How does the lactose get into the cell if the repressor is not being bound by lactose?