CELL CYCLE AND EXPONENTIAL GROWTH

Models:

1. Steps in the bacterial cell cycle
2. Binary fission and the exponential increase in cell number
3. Shape of growth curve during exponential growth
4. Semi-log plot of cells growing exponentially with a constant generation time

During growth, the cell number of most bacteria increases by binary fission, with one cell dividing to form two cells. The new cells then increase their mass until they divided again. The overall process is referred to as the cell cycle and is illustrated with **Model 1**. This model includes a collection of rod-shaped cells having different lengths. There is also a plate having troughs at different locations, with each trough matching the size of one of the cells. Orient the plate so that the label is at the top.

Place the shortest cells (there are two) in the trough at the left below the label. These represent new cells, those that have just arisen by cell division. The cell cycle is illustrated using one of these. Follow the arrow that points to another trough, which is upward and to the right. Place at this location the cell fitting the trough. This cell is larger than newly formed cells because the cell itself grows after division by an increase in mass. In particular, the new cell becomes longer, although notice that its diameter does not change. This is typical of rod-shaped cells, including those of *E. coli*. Growth is mostly in one direction, along the long axis of the rod. After this period of elongation, a constriction starts to form in the middle of the cell. Follow the arrow down to the next trough, and place in it the cell matching the length of the trough. If you pass your hand along the length of the cell you will notice a slight constriction at the middle. This indicates the beginning of cell division. As division proceeds, the constriction becomes more pronounced while the cell continues to grow. This is shown by the next model. Follow the arrow downward to the remaining empty tough and place in it the final cell model. This represents a cell late in the process of cell division. Eventually, the constriction leads to the separation of the two halves to form daughter cells. Follow the arrow upwards and to the left to the starting position in the cycle.

The cell cycle seems simple, but that appearance is deceptive when you think about some of its properties. For example, what causes a cell to start dividing? What mechanism ensures that division occurs in the middle of the cell and not at a randomly selected location? These questions have been the subject of intensive research and a lot has been learned.

The increase in cell number by binary fission is also called exponential growth, because the number of cells not only increases, but does so at an exponentially increasing rate. This is illustrated with **Model 2**. The label is at the bottom. At the top is a single cell. When it divides (follow the arrow downward) two cells are formed, a net increase of one cell. When these daughter cells divide, four cells are produced, a net increase of two cells. Division of these four cells then produces eight cells, an increase of four cells (again, follow the arrows downward). The number of cells produced after each cell in the population has divided is not constant but increases as the number of divisions increases. Starting with one cell, the number of cells after x divisions will be 2 raised to the x power. For example, after 10 divisions the number of cells will be 2 to the 10^{th} power or 1,024. 512 cells will have been added by the final division.

If we started with N cells, then the number of cells after x divisions is simply N times the quantity 2 raised to the x power.

In the laboratory, care is usually taken to culture bacteria under a set of conditions that does not change during the period of growth. In this case, the time between cell divisions, called the generation time, is constant. Notice that this is not a necessary characteristic of exponential growth, where the generation time can vary greatly depending on changes in environmental conditions such as the availability of nutrients or temperature. In the lab, it is frequently important to know the generation time of the cells in a culture. However, it is impossible to follow the division cycle of a single cell. In addition, the cells are all dividing at different times, even if the culture is started with a single cell. This is because of the cumulative effect of small fluctuations in the generation time. We can still define the generation time as the time required for the number of cells to double. This means that, on average, every cell in the population has divided once. If the number of cells is plotted with time, the generation time can be calculated.

Model 3 illustrates a problem with generating that kind of plot. In this model, there is a set of vertical tubes, which hold, from left to right, one, two, four, eight and sixteen cells. You can verify that the tubes are the correct height by adding small cells to each until they reach the top. The height of the tube thus represents the increase in cell number during exponential growth. The shape of the plotted curve is shown by the model piece that can be placed in front of the tubes. The graph is a curve that becomes more and more vertical with each generation. Drawing such a graph for many generations of growth is difficult because of the changing shape of the curve and the need for an enormous horizontal scale, quickly extending several orders of magnitude. For these reasons, microbiologists commonly generate instead a semi-log plot. When the logarithm of the number of cells is plotted against time, the result is a straight line and it is easy to graph many generations of growth with a single plot. Moreover, it is not necessary to convert the number of cells to their logarithmic equivalents. Instead, the actual cell numbers are used, but plotted according to their logarithmic values. Such a semi-log plot is illustrated with **Model 4**. The letter "T" refers to the top of the graph. The horizontal axis labelled at the bottom is the growing time in minutes. This is an ordinary, linear scale: equal distances along the scale represent the same number of minutes. For example, the distances along the axis between 0 and 40 minutes and 40 and 80 minutes are the same. The vertical axis is the number of cells, plotted according to their logarithmic value. Since there are a lot of cells at the start, the axis begins at 1 times 10 raised to the 5^{th} power. The horizontal lines moving upward then indicate 2 times 10 to the 5^{th}, 3 times 10 to the 5^{th} and so on. The varying distance between the horizontal lines form a pattern which is repeated for each order of magnitude.

Consider some real data and how it can be usefully displayed on a semi-log plot. A collection of pegs is included with the model. These fit into the holes on the graph and will be used to mark data points. At the start of growth (0 minutes) the number of cells was found to be 1.9 times 10 to the 5^{th} power. Locate the hole (make sure you understand its position) and place one of the plugs in it. Pause the recording if you need to.

The second data point was taken at 40 minutes and is 4.5 times 10 to the 5^{th} power. Place a peg at this position. The next two data points are 8.8 times 10 to the 5^{th} at 80 minutes and 1.7 times 10 to the 6^{th} at 120 minutes. After placing the pegs, use a straight edge to verify that the pegs lie along nearly a

straight line. They do not exactly fit a straight line due to measurement error. The numerical value for the slope of the line, which is easy to calculate, is the generation time.

QUESTIONS TO TEST YOUR UNDERSTANDING

1. Additional data points for the culture were taken at 160 and 180 minutes. Place pegs at these data points and estimate the number of cells for each.

2. Explain why the following is true:

For N number of cells at time t1 and 2N number of cells at t2, the generation time is t2 – t1.