The reader should now see how the cellular control strategy emerges. If the cell has an energetically favorable carbon–energy source available, it will not expend significant energy to create a pathway for utilization of a less favorable carbon–energy source. If, however, energy levels are low, then it seeks an alternative carbon–energy source. If and only if lactose is present will it activate the pathway necessary to utilize it.

Catabolite repression is a global response that affects more than lactose utilization. Furthermore, even for lactose, the glucose effect can work at levels other than genetic. The presence of glucose inhibits the uptake of lactose, even when an active uptake system exists. This is called *inducer exclusion*.

The role of global regulatory systems is still emerging. One concept is that of a *regulon*. Many noncontiguous gene products under the control of separate promoters can be coordinately expressed in a regulon. The best studied regulon is the *heat shock regulon*. The cell has a specific response to a sudden increase in temperature,[†] which results in the elevated synthesis of specific proteins. Evidence now exists that this regulon works by employing the induction of an alternative sigma factor, which leads to high levels of transcription from promoters that do not readily recognize the normal *E. coli* sigma factor. Examples of other regulons involve nitrogen and phosphate starvation, as well as a switch from aerobic to anaerobic conditions.

Although many genes are regulated, others are not. Unregulated genes are termed *constitutive*, which means that their gene products are made at a relatively constant rate irrespective of changes in growth conditions. Constitutive gene products are those that a cell expects to utilize under almost any condition; the enzymes involved in glycolysis are an example.

Example 4.1.

Diauxic growth is a term to describe the sequential use of two different carbon–energy sources. Industrially, diauxic growth is observed when fermenting a mixture of sugars, such as might result from the hydrolysis of biomass. The classic example of diauxic growth is growth of *E. coli* on a glucose–lactose mixture. Observations on this system led to formulation of the operon hypothesis and the basis for a Nobel prize (for J. Monod and F. Jacob). Consider the plot in Fig. 4.11, where the utilization of glucose and lactose and the growth of a culture are depicted for a batch culture (batch reactor). As we will discuss in more detail in Chapter 6, the amount of biomass in a culture, X, accumulates exponentially. Note that at 2 h after inoculation, cells are growing rapidly, glucose is being consumed, and lactose is not being utilized. At 7 h, cell mass accumulation is zero. All the glucose has been consumed. At 10 h the culture is growing and lactose is being consumed, but the rate of growth (cell mass accumulation) is less than at 2 h.

Explain what is happening with intracellular control to account for the observations at 2, 7, and 10 h. What rate of β-galactosidase formation would you expect to find in the culture at these times in comparison to the basal rate (which is < 1% of the maximum rate)?

Solution

At 2 h the lac operon is fully induced, since lactose converted to allolactose combines with the *lac i* repressor protein, inactivating it. With the repressor protein deactivated, RNA polymerase is free to bind to the promoter, but does so inefficiently. Glucose

[†]Or other stresses that result in abnormal protein formation or membrane disruption.