The ratio for rates of biomass formation is

$$\frac{r_{c,\text{opt}}}{r_b} = \ln \frac{X_m}{X_0} + \mu_m t_l \tag{9.7}$$

Most commercial fermentations operate with $X_m/X_0 \approx 10$ to 20. Thus, we would expect continuous systems to always have a significant productivity advantage for primary products. For example, an *E. coli* fermentation with $X_m/X_0 = 20$, $t_l = 5$ h, and $\mu_m = 1.0\ h^{-1}$ would yield $r_{c,\text{opt}}/r_b = 8$.

Based on this productivity advantage we might be surprised to learn that most commercial bioprocesses are batch systems. Why? There are several answers.

The first is that eq. 9.7 applies only to growth-associated products. Many secondary products are not made by growing cells; growth represses product formation. Under such circumstances, product is made only at very low dilution rates, far below those values optimal for biomass formation. For secondary products, the productivity in a batch reactor may significantly exceed that in a simple chemostat.

Another primary reason for the choice of batch systems over chemostats is *genetic instability*. The biocatalyst in most bioprocesses has undergone extensive selection. These highly "bred" organisms often grow less well than the parental strain. A chemostat imposes strong selection pressure for the most rapidly growing cell. Back-mutation from the productive specialized strain to one similar to the less productive parental strain (i.e., a revertant) is always present. In the chemostat the less productive variant will become dominant, decreasing productivity. In the batch culture the number of generations available (< 25 from slant cultures to a commercial-scale fermenter) for the revertant cell to outgrow the more productive strain is limited. Cells at the end of the batch are not reused. These considerations of genetic stability are very important for cells with recombinant DNA and are discussed in detail in Chapter 14.

Another consideration is operability and reliability. Batch cultures can suffer great variability from one run to another. Variations in product quality and concentration create problems in downstream processing and are undesirable. However, long-term continuous culture can be problematic; pumps may break, controllers may fail, and so on. Maintenance of sterility (absence of detectable foreign organisms) can be very difficult to achieve for periods of months, and the consequences of a loss of sterility are more severe than with batch culture.

One other factor determining reactor choice is market economics. A continuous system forms the basis of a dedicated processing system—dedicated to a single product. Many fermentation products are required in small amounts, and demand is difficult to project. Batch systems provide much greater flexibility. The same reactor can be used for two months to make product A and then for the next three for product B and the rest of the year for product C.

Most bioprocesses are based on batch reactors. Continuous systems are used to make single-cell protein (SCP), and modified forms of continuous culture are used in waste treatment, in ethanol production, and for some other large-volume, growth-associated products such as latic acid.

Let us consider some modifications to these reactor modes.