

determined from either cell number or cell mass would be the same. Since the nutrient concentrations are large in this phase, the growth rate is independent of nutrient concentration. The exponential growth rate is first order:

$$\frac{dX}{dt} = \mu_{\text{net}} X, \quad X = X_0 \quad \text{at} \quad t = 0 \quad (6.5)$$

Integration of eq. 6.5 yields

$$\ln \frac{X}{X_0} = \mu_{\text{net}} t, \quad \text{or} \quad X = X_0 e^{\mu_{\text{net}} t} \quad (6.6)$$

where  $X$  and  $X_0$  are cell concentrations at time  $t$  and  $t = 0$ .

The time required to double the microbial mass is given by eq. 6.6. The exponential growth is characterized by a straight line on a semilogarithm plot of  $\ln X$  versus time:

$$\tau_d = \frac{\ln 2}{\mu_{\text{net}}} = \frac{0.693}{\mu_{\text{net}}} \quad (6.7)$$

where  $\tau_d$  is the doubling time of cell mass.

Similarly, we can calculate a doubling time based on cell numbers and the net specific rate of replication. Thus

$$\tau'_d = \frac{\ln 2}{\mu_R} \quad (6.8)$$

where  $\tau'_d$  is the doubling time based on the replication rate. During balanced growth  $\tau_d$  will equal  $\tau'_d$ , since the average cell composition and size will not change with time.

The *deceleration growth phase* follows the exponential phase. In this phase, growth decelerates due to either depletion of one or more essential nutrients or the accumulation of toxic by-products of growth. For a typical bacterial culture, these changes occur over a very short period of time. The rapidly changing environment results in *unbalanced growth*. During unbalanced growth, cell composition and size will change and  $\tau_d$  and  $\tau'_d$  will not be equal. In the exponential phase, the cellular metabolic control system is set to achieve maximum rates of reproduction. In the deceleration phase, the stresses induced by nutrient depletion or waste accumulation cause a restructuring of the cell to increase the prospects of cellular survival in a hostile environment. These observable changes are the result of the molecular mechanisms of repression and induction that we discussed in Chapter 4. Because of the rapidity of these changes, cell physiology under conditions of nutrient limitation is more easily studied in continuous culture, as discussed later in this chapter.

The *stationary phase* starts at the end of the deceleration phase, when the net growth rate is zero (no cell division) or when the growth rate is equal to the death rate. Even though the net growth rate is zero during the stationary phase, cells are still metabolically active and produce secondary metabolites. *Primary metabolites* are growth-related products and *secondary metabolites* are nongrowth-related. In fact, the production of certain metabolites is enhanced during the stationary phase (e.g., antibiotics, some hormones) due to metabolite deregulation. During the course of the stationary phase, one or more of the following phenomena may take place: