$K = G/L$ (the gas-to-liquid ratio), the following model is obtained for the three-stage absorber:

$$\tau\frac{dx_1}{dt} = K(y_f - b) - (1 + \mathcal{S})x_1 + x_2 \qquad (2\text{-}73)$$

$$\tau\frac{dx_2}{dt} = \mathcal{S}x_1 - (1 + \mathcal{S})x_2 + x_3 \qquad (2\text{-}74)$$

$$\tau\frac{dx_3}{dt} = \mathcal{S}x_2 - (1 + \mathcal{S})x_3 + x_f \qquad (2\text{-}75)$$

In the model of Eqs. 2-73 to 2-75, note that the individual equations are linear but also coupled, meaning that each output variable—x_1, x_2, x_3—appears in more than one equation. This feature can make it difficult to convert these three equations into a single higher-order equation in one of the outputs, as was done in Eq. 2-49.

2.4.8 Fed-Batch Bioreactor

Biological reactions that involve microorganisms and enzyme catalysts are pervasive and play a crucial role in the natural world. Without such bioreactions, plant and animal life, as we know it, simply could not exist. Bioreactions also provide the basis for production of a wide variety of pharmaceuticals and healthcare and food products. Other important industrial processes that involve bioreactions include fermentation and wastewater treatment. Chemical engineers are heavily involved with biochemical and biomedical processes. In this section we present a dynamic model for a representative process, a bioreactor operated in a semi-batch mode. Additional biochemical and biomedical applications appear in other chapters.

In general, bioreactions are characterized by the conversion of feed material (or *substrate*) into products and cell mass (or *biomass*). The reactions are typically catalyzed by enzymes (Bailey and Ollis, 1986; Fogler, 2006). When the objective is to produce cells, a small amount of cells (*inoculum*) is added to initiate subsequent cell growth. A broad class of bioreactions can be represented in simplified form as

$$\text{cells} + \text{substrate} \rightarrow \text{more cells} + \text{products} \qquad (2\text{-}76)$$

The stoichiometry of bioreactions can be very complex and depends on many factors that include the environmental conditions in the vicinity of the cells. For simplicity we consider the class of bioreactions where the substrate contains a single limiting nutrient and only one product results. The following *yield coefficients* are based on the reaction stoichiometry:

$$Y_{X/S} = \frac{\textit{mass of new cells formed}}{\textit{mass of substrate consumed to form new cells}} \qquad (2\text{-}77)$$

$$Y_{P/S} = \frac{\textit{mass of product formed}}{\textit{mass of substrate consumed to form product}} \qquad (2\text{-}78)$$

$$Y_{P/X} = \frac{\textit{mass of product formed}}{\textit{mass of new cells formed}} \qquad (2\text{-}79)$$

Many important bioreactors are operated in a semi-continuous manner that is referred to as *fed-batch* operation, which is illustrated in Fig. 2.11. A feed stream containing substrate is introduced to the fed-batch reactor continually. The mass flow rate is denoted by F and the substrate mass concentration by S_f. Because there is no exit stream, the volume V of the bioreactor contents increases during the batch. The advantage of fed-batch operation is that it allows the substrate concentration to be maintained at a desired level, in contrast to batch reactors where the substrate concentration varies continually throughout the batch (Shuler and Kargi, 2002).

Fed-batch operation is used to manufacture many important industrial products, including antibiotics and protein pharmaceuticals (Chapter 23). In batch and fed-batch reactors, cell growth occurs in different stages after the inoculum is introduced. We will consider only the exponential growth stage where the cell growth rate is autocatalytic and is assumed to be proportional to the cell concentration. A standard reaction rate expression to describe the rate of cell growth with a single limiting substrate is given by (Bailey and Ollis, 1986; Fogler, 2006)

$$r_g = \mu X \qquad (2\text{-}80)$$

where r_g is the rate of cell growth per unit volume, X is the cell mass, and μ is the *specific growth rate*, which is well described by the *Monod equation*:

$$\mu = \mu_{\max}\frac{S}{K_S + S} \qquad (2\text{-}81)$$

Note that μ has units of reciprocal time—for example, h^{-1}. Model parameter $\mu_{\max}$ is referred to as the *maximum growth rate,* because μ has a maximum value of $\mu_{\max}$ when $S \gg K_S$. The second model parameter, K_S, is called the *Monod constant*. The Monod equation has the same form as the Michaelis–Menten equation, a standard rate expression for enzyme reactions (Bailey and Ollis, 1986; Fogler, 2006). More complex versions of the

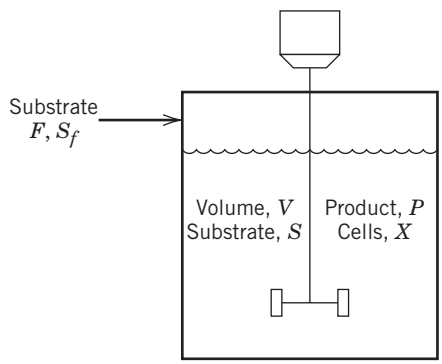

Figure 2.11 Fed-batch reactor for a bioreaction.

specific growth rate are possible including, for example, product inhibition.

A dynamic model for the fed-batch bioreactor in Fig. 2.11 will be derived based on the following assumptions:

1. The cells are growing exponentially.
2. The fed-batch reactor is perfectly mixed.
3. Heat effects are small so that isothermal reactor operation can be assumed.
4. The liquid density is constant.
5. The *broth* in the bioreactor consists of liquid plus solid material (i.e., cell mass). This heterogeneous mixture can be approximated as a homogeneous liquid.
6. The rate of cell growth r_g is given by Eqs. 2-80 and 2-81.
7. The rate of product formation per unit volume r_p can be expressed as

$$r_P = Y_{P/X} rg \tag{2-82}$$

8. The feed stream is sterile and thus contains no cells.

The dynamic model of the fed-batch reactor consists of individual balances for substrate, cell mass, and product, plus an overall mass balance. The general form of each balance is

$$\{Rate\ of\ accumulation\} = \{rate\ in\} + \{rate\ of\ formation\} \tag{2-83}$$

The individual component balances are

$$Cells: \quad \frac{d(XV)}{dt} = Vr_g \tag{2-84}$$

$$Product: \quad \frac{d(PV)}{dt} = Vr_p \tag{2-85}$$

$$Substrate: \quad \frac{d(SV)}{dt} = FS_f - \frac{1}{Y_{X/S}} Vr_g - \frac{1}{Y_{P/S}} Vr_p \tag{2-86}$$

where P is the mass concentration of the product and V is reactor volume. Reaction rates r_g and r_p and yield coefficients were defined in Eqs. 2-77 through 2-82. The overall mass balance (assuming constant density) is

$$Mass: \quad \frac{dV}{dt} = F \tag{2-87}$$

The dynamic model is simulated for two different feed rates (0.02 and 0.05 L/h). Figure 2.12 shows the profile of cell, product, and substrate concentration, together with liquid volume in the reactor. The model parameters and simulation conditions are given in Table 2.4. For different feed rates, the bioreactor gives different responses; thus, the product can be maximized by varying F.

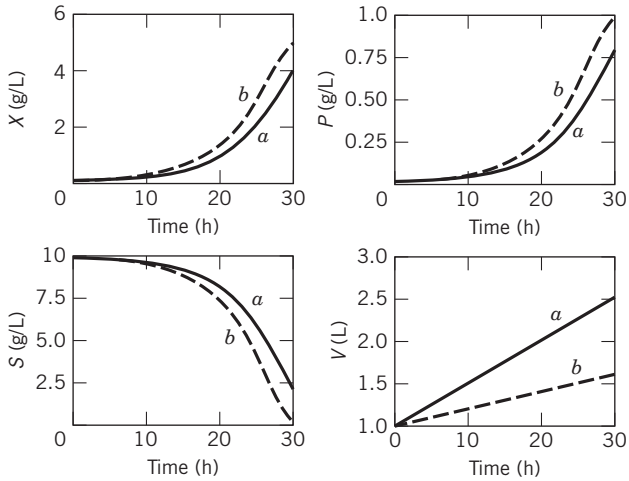

Figure 2.12 Fed-batch reaction profile (*a* (solid): $F = 0.05$ L/h; b (dashed): $F = 0.02$ L/h).

Table 2.4 Model Parameters and Simulation Conditions for Bioreactor

Model Parameters			Simulation Conditions		
μ_{max}	0.20	h^{-1}	S_f	10.0	g/L
K_S	1.0	g/L	$X(0)$	0.05	g/L
$Y_{X/S}$	0.5	g/g	$S(0)$	10.0	g/L
$Y_{P/X}$	0.2	g/g	$P(0)$	0.0	g/L
			$V(0)$	1.0	L

2.5 PROCESS DYNAMICS AND MATHEMATICAL MODELS

Once a dynamic model has been developed, it can be solved for a variety of conditions that include changes in the input variables or variations in the model parameters. The transient responses of the output variables as functions of time are calculated by numerical integration after specifying the initial conditions, the inputs and the time interval at which the system is to be integrated.

A large number of numerical integration techniques are available, ranging from simple techniques (e.g., the Euler and Runge–Kutta methods) to more complicated ones (e.g., the implicit Euler and Gear methods). All of these techniques represent some compromise between computational effort (computing time) and accuracy. Although a dynamic model can always be solved in