tions such as lactic acid and other plant cell and mammalian cell fermentations, where the rate of product formation is maximal at low nutrient concentrations.

Fed-batch culture is important for *E. coli* fermentations to make proteins from recombinant DNA technology. To make a high concentration of product, it is desirable to grow the culture to very high cell density before inducing production of the target protein. If *E. coli* has an unlimited supply of glucose it will grow at a maximal rate, but produce organic acids (e.g., acetic acid) as by-products. The accumulation of these by-products inhibits growth. If glucose is fed at a rate that substains the growth rate at slightly less than maximal, *E. coli* uses the glucose more efficiently, making less by-product. Very high cell densities (50 to 100 g/l) can be achieved. Fed-batch culture may benefit from active process control. For example, the feed rate of glucose could be controlled by measuring glucose concentration in the medium or the CO_2 evolution rate using a feedback controller.

Example 9.3

In a fed-batch culture operating with intermittent addition of glucose solution, values of the following parameters are given at time $t = 2$ h, when the system is at quasi-steady state.

$$V = 1000 \text{ ml} \qquad F = \frac{dV}{dt} = 200 \text{ ml/h}$$

$$S_0 = 100 \text{ g glucose/l} \qquad \mu_m = 0.3 \text{ h}^{-1}$$

$$K_s = 0.1 \text{ g glucose/l} \qquad Y_{X/S}^M = 0.5 \text{ gdw cells/g glucose}$$

$$X_0^t = 30 \text{ g}$$

a. Find V_0 (the initial volume of the culture).
b. Determine the concentration of growth-limiting substrate in the vessel at quasi-steady state.
c. Determine the concentration and total amount of biomass in the vessel at $t = 2$ h (at quasi-steady state).
d. If $q_P = 0.2$ g product/g cells, $P_0 = 0$, determine the concentration of product in the vessel at $t = 2$ h.

Solution

a. $V = V_0 + Ft$

$V_0 = 1000 - 200(2) = 600$ ml

b. $D = F/V = 0.2 \text{ h}^{-1}$

$$S \approx \frac{K_s D}{\mu_m - D} = \frac{(0.1)(0.2)}{0.3 - 0.2} = 0.2 \text{ g glucose/l}$$

c. $$X^t = X_0^t + F Y_{X/S}^M S_0 t$$
$$= 30 + (0.2)(0.5)(100)(2) = 50 \text{ g}$$

d. $$P = P_0 \frac{V_0}{V} + q_P X_m \left(\frac{V_0}{V} + \frac{Dt}{2} \right) t$$

$$= 0 + (0.2)(50) \left(\frac{600}{1000} + \frac{(0.2)(2)}{2} \right) (2)$$
$$= 16 \text{ g/l}$$