stage, the inducer is added and large quantities of product are made. Cells defective in product synthesis should not overtake the culture (at least not completely), because fresh genetically unaltered cells are being continuously fed to the reactor. Thus, the two-stage system can allow the stable continuous production of the target protein when it would be impossible in a simple chemostat.

Perhaps an easier situation to consider is the production of a secondary product (e.g., ethanol or an antibiotic). Here we worry not so much about a mixture of subpopulations, but that conditions that promote growth completely repress product formation. A very large scale multistage system for ethanol production is currently in use. A multistage system of CFSTR approaches PFR behavior. A PFR mimics the batch system, where space time (the time it takes the culture fluid to reach a specific location in the PFR) replaces culture time. A multistage system is much like taking the batch growth curve and dividing it into sections, with each section being "frozen" in a corresponding stage of the multistage system. As in the batch reactor, the culture's physiological state progresses from one stage to the next.

The mathematical analysis of the multistage system that we present here is imperfect. Growth in the second and subsequent stages is intrinsically unbalanced growth, even though it is steady-state growth. New cells entering the second or subsequent stage are continuously adapting to the new conditions in that stage. Consequently, unstructured models are not expected to give completely accurate predictions. However, we use unstructured models here due to their simplicity and to illustrate at least some aspects of multistage systems.

A two-stage chemostat system is depicted in Fig. 9.3. Biomass and substrate balances on the first stage yield the following equations (ignoring endogeneous metabolism):

$$S_1 = \frac{K_s D_1}{\mu_m - D_1} \tag{9.15}$$

$$X_1 = Y^M_{X/S}(S_0 - S_1) \tag{9.16}$$

The biomass balance for the second stage yields

$$FX_1 - FX_2 + \mu_2 V_2 X_2 = V_2 \frac{dX_2}{dt} \tag{9.17}$$

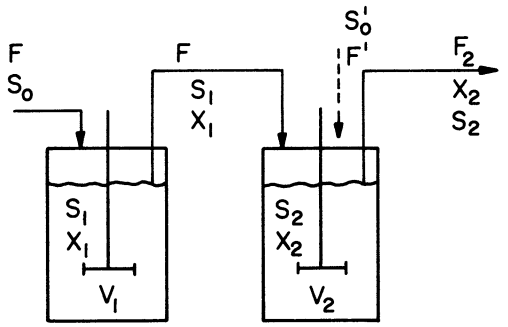

Figure 9.3. Two-stage chemostat system.