

$$c) \quad Pr_x = DX = DY_{X/S}(S_0 - S) = 0.1D \left(10 - \frac{6D}{0.5 - D} \right)$$

6.4.4. The Chemostat as a Tool

The chemostat can be used as a tool to study the mutation and selection of cultures and also to study the effect of changes in the environment on cell physiology. The molecular aspects of mutation and selection will be discussed in Chapter 8.

Natural or induced *mutations* can take place in a chemostat culture. Errors in DNA replication take place with an average frequency of about 10^{-6} to 10^{-8} gene per generation. With a cell concentration of 10^9 cells/ml in culture, the probability is high in a chemostat that a wide variety of mutant cells will be formed. The vast majority of natural mutations in a chemostat are of little significance, unless the mutation alters the function of a protein involved in growth in the chemostat environment. If the specific growth rate of the mutant is larger than that of the wild type, then the mutant outgrows the wild type in a chemostat. This selection for a variant cell type can be accomplished by creating a more favorable environment for growth of the mutant organism.

A chemostat culture can be used for the selection of special organisms. Selection or enrichment nutrient media need to be used for this purpose. For example, if it is desired to select an organism growing on ethanol, a nutrient medium containing ethanol and mineral salts is used as a feed to a chemostat culture. An organism capable of oxidizing some toxic refractory compounds can be selected from a mixed culture by slowly feeding this compound to a chemostat. A thermophilic organism can be selected from a natural population by operating a chemostat at an elevated temperature (e.g., 50° to 60°C). Selection in chemostats also presents significant problems in the culture of cells containing recombinant DNA. The most productive cells often grow more slowly and are displaced by less productive cells. We will discuss this problem in more detail in Chapter 14.

6.4.5. Deviations from Ideality

In fermentations such as the utilization or production of polysaccharides or mycelial fermentations, the fermentation broth may be highly viscous and it may be difficult to maintain complete mixing. Also, certain cells tend to grow in the form of a film on solid surfaces in fermenters, such as on fermenter walls or probe surfaces. Incomplete mixing is the rule in industrial-scale fermenters. The presence of incompletely mixed regions in a “chemostat” culture is common. The term “chemostat” is actually applicable only to perfectly mixed vessels. Here we denote nonideality by putting chemostat in quotation marks. A segregated reactor model can be used to analyze an incompletely mixed continuous-flow fermenter.

A simple, two-compartmental model of a “chemostat” culture is depicted in Fig. 6.20, where the reactor is divided into two regions: a well-mixed region and a stagnant region. Feed and effluent streams pass through the well-mixed region 1, and mass exchange takes place between the two regions. The biomass and substrate balances for both regions at steady state are as follows: