models for dynamic response, feedforward control strategies are ineffective. Because of the highly nonlinear nature of most culture systems, black-box techniques to develop dynamic models are usually ineffective. Good process control for fermentations awaits improved models of cultures, more sophisticated sensors, and advances in nonlinear control theory.

In addition to reactor control, a computer monitored and controlled process involves the control of medium preparation, sterilization, and some downstream recovery processes. An important factor in bioprocesses is the predominance of batch processing. The scheduling of equipment is critical, and these tasks are being done increasingly with the aid of in-house computers.

In summary, exciting progress is being made in instrumentation and modeling, but the possible contributions of process control to bioprocesses have been only marginally realized.

10.4. STERILIZATION OF PROCESS FLUIDS

10.4.1. Introduction and the Kinetics of Death

Modern fermenters consume large amounts of media and gas. The tens of thousands of liters of medium and millions of liters of air used in a typical antibiotic fermentation must be absolutely devoid of any contaminating organism. The economic penalty for contamination is high. With bioprocesses to make proteins from recombinant DNA, the exit streams must also be treated to prevent the discharge of any living cell. The ability to ensure the destruction of viable organisms is critical.

Sterility is an absolute concept; a system is never partially or almost sterile. However, with a 100,000-l fermenter, we cannot sample every drop of fluid for a foreign organism. On a practical basis, sterility means the absence of any detectable viable organism, and a *pure culture* means that only the desired organism is detectably present.

Disinfection differs from sterilization. A disinfecting agent will greatly reduce the number of viable organisms, often a specific type of organism, to a low, but nonzero value.

Fluid streams can be sterilized through the physical removal of cells and viruses or the inactivation of living particles by heat, radiation, or chemicals. If sterilization is accomplished by inactivating living cells, spores, or viruses, we need to understand the kinetics of death. *Death* in this case means the failure of the cell, spore, or virus to reproduce or germinate when placed in a favorable environment. When dealing with sterilization, the probabilistic nature of cell death cannot be ignored.

The simplest case presumes that all the viable cells or spores are identical. The *probability of extinction* of the total population, $P_0(t)$, is

$$P_0(t) = \left[1 - p(t)\right]^{N_0} \tag{10.12}$$

where $p(t)$ is the probability that an individual will still be viable at time t, and N_0 is the number of individuals initially present. The expected value of the number of individuals present at time t, $E[N(t)]$, is