10.3. BIOREACTOR INSTRUMENTATION AND CONTROL

10.3.1. Introduction

The maintenance of optimal conditions for product formation in the complex environment in a bioreactor requires the control and measurement of at least a few parameters. Almost all fermenters have pH, temperature, and dissolved-oxygen control (by control of agitator rotational speed). New probes and techniques for the measurement of various ions, substrates, and products are being developed and have been implemented in particular situations. Actual process-control strategies for bioreactors are very primitive in comparison to the petrochemical industry, because of a lack of sensors for on-line measurements and of reliable, quantitative, dynamically accurate models. In this section we will summarize briefly not only the state of the art but some ideas on opportunities to improve the control of bioreactors.

10.3.2. Instrumentation for Measurements of Active Fermentation

The maintenance of sterility in a fermenter imposes a severe limitation on obtaining on-line measurements of fermentation parameters. Some probes (e.g., pH and dissolved oxygen) enter the reactor through penetrations in the fermenter shell. Each penetration significantly increases the probability of contamination. Thus, the benefit in increased productivity from the use of each probe must outweigh the economic losses that result from an increased number of contamination events. The probes themselves must also be sterilizable, preferably with steam. Thus, probes must ideally be able to withstand moderately high temperatures (121°C) in the presence of 100% humidity. Chemical sterilization, which is less desirable, may allow the use of a temperature-sensitive device if it has sufficient chemical resistance. Any general technique for monitoring fermentations must be compatible with the limitations imposed by sterility requirements.

Techniques to monitor the physical environment are summarized in Table 10.5. Except for viscosity and turbidity, these parameters would be monitored on most pilot-plant fermenters and many industrial fermenters. Each parameter is generally subject to its own closed-loop control system. These individual control loops may be integrated into an overall control package, especially at the pilot-plant scale, but in many cases higher-level control is not practiced, owing to the difficulty of measuring key parameters (e.g., product concentration) and the lack of dynamically accurate process models.

On-line measurements of concentrations beyond pH and dissolved oxygen are difficult, although exciting progress is being made. Table 10.6 summarizes techniques that have been considered for determining the concentrations of key components.

With insertable probes, we need to worry not only about probe performance but also about probe placement. The heterogeneity in a large fermenter means that dissolved oxygen and substrate levels (and to a lesser extent pH) will be position dependent (see Example 10.4). Although placement in the midsection of the vessel often gives the most representative values, mechanical design considerations may dictate placement elsewhere. Because probe fouling is a potential problem, the probe should be inserted in a region