lems would need to be solved. Another analytical method that offers a good potential for on-line determination of solutes is Fourier transform infrared (FTIR) spectra analysis. Finally, the use of spectra analysis combined with optical fibers may offer a good technique to determine cell mass in the presence of other suspended solids.

In summary, current instrumentation to monitor fermenters on line is very limited. However, many techniques currently under development promise to solve this problem.

10.3.3. Using the Information Obtained

Having information is one thing; using it wisely is another. Current fermenter design and control techniques are rather limited. We do not have a fully satisfactory approach to the effective use of information on the extracellular and intracellular chemical environment.

Computer-controlled fermenters are fairly common, particularly at the pilot-plant scale. Figure 10.10 displays an overview of the software functions for a typical antibiotic fermentation facility, and Fig. 10.11 shows the relationship of primary measurements to secondary parameters.

An important function of such systems is *data logging*. This information is unusually important in the food and pharmaceutical industries. An actual record for the manufacture of each product batch is required by regulatory agencies. If the product is later found to be unsafe, such information can be used to trace the problem. Beyond the regulatory concerns, the lack of good high-level control strategies leads to a control strategy based on exactly duplicating a particular recipe. Consistency from batch to batch is an important consideration. Expert control systems may be useful in such situations.

In many cases, fermentation control schemes have begun to move beyond simple open-loop environmental control strategies. The use of computers allows the rapid manipulation of information from the data-logging operation to yield estimates of secondary parameters. For example, a secondary parameter may be cell concentration estimated from estimates of oxygen consumption or carbon dioxide evolution based on primary measurements of off-gas composition and dissolved-gas concentrations. Essentially, cell mass is estimated from mass balances using information from what have been termed *gateway sensors*. The main limitation to this approach is the accumulation of error. For example, in estimating cell mass X at time t, the value of X at time $t - \Delta t$ must be known. Any systematic errors in cell mass estimates or the inability of an algorithm to respond to an unusual perturbation can lead to significant difficulties over the length of a typical culture cycle. Data-handling procedures to mitigate this problem have been suggested (e.g., Kalman filters).

In some cases our partial knowledge of cellular metabolism is sufficient to solve important bioreactor problems. For many years it was thought impossible to grow *E. coli* to high cell densities (> 15 or 20 g/l). An improved understanding of cell physiology led to the observation that it was the buildup of toxic metabolic by-products (primarily acetate) that inhibited growth. Acetate is formed in *E. coli* when a good carbon source, such as glucose, is available in high concentrations. Control strategies that feed glucose at a rate sufficient to maintain at least moderately good growth without forming acetate were seen as possibilities to improve reactor volumetric productivities.

Thus, several possible control strategies are immediately apparent. The simplest perhaps would be to measure acetate concentration on line and reduce nutrient feed rates