(1) separation of biomass or other insoluble products, (2) concentration or primary isolation of product, and (3) purification.

When the product is the biomass, the separation strategy is relatively simple and involves filtration or centrifugation following coagulation–flocculation of the cells. Drying is required for a marketable biomass, such as a single-cell protein (SCP) source.

For soluble products such as antibiotics, enzymes, and organic acids, the separation strategy depends on whether the products are extracellular or intracellular. Some products can be both. For intracellular products, the cells need to be disrupted for the release of the products. Mechanical, chemical, and enzymatic methods can be used for cell disruption. Products need to be separated from the other cell and medium components after cell disruption. Depending on the type and the molecular weight of the product, separation methods involve the removal of cell debris by centrifugation or filtration, followed by extraction or precipitation (for protein products) of the product. The separation strategy for extracellular products is simpler than that for intracellular products, since cell disruption is not required. After the separation of the biomass from the fermentation medium, the product is separated from the broth by one or a combination of the following methods: liquid–liquid extraction (antibiotics), two-aqueous-phase extraction (enzymes), adsorption (antibiotics), or precipitation (proteins).

Protein (enzymes, hormones) separations usually require a special strategy. Proteins are usually precipitated from the media either by salting-out or by the addition of organic solvents. The desired protein is crudely separated from other protein components, usually by ultrafiltration on the basis of its molecular weight. Then some chromatographic methods, such as ion-exchange or affinity chromatography, need to be used for further purification. After elution of the protein from the chromatographic column, the product must be dried and crystallized, if necessary, before packaging. Depending on the chemical nature of the desired protein and the composition of the protein mixture, sometimes special protein separation methods, such as isoelectric focusing or electrophoresis (for charged proteins), may need to be used.

Simultaneous separation and fermentation schemes offer special advantages over consecutive schemes, since they may overcome product inhibition and provide a more compact and economical alternative. Membrane, adsorptive, or extractive separation schemes can be utilized for the simultaneous separation of products during fermentation.

SUGGESTIONS FOR FURTHER READING

AIBA, S., A. E. HUMPHREY, AND N. F. MILLIS, *Biochemical Engineering*, 2d ed., Academic Press, New York, 1973.

ATKINSON, B., AND F. MAVITUNA, *Biochemical Engineering and Biotechnology Handbook*, 2d ed., Stockton Press, New York, 1991.

BAILEY, J. E., AND D. F. OLLIS, *Biochemical Engineering Fundamentals*, 2d ed., McGraw-Hill, New York, 1986.

BELTER, P. A., E. L. CUSSLER, AND W. S. HU, *Bioseparations*, John Wiley & Sons, New York, 1988.

BLANCH, H. W., AND D. S. CLARK, *Biochemical Engineering,* Marcel Dekker, New York, 1996.