9.3.4. Perfusion Systems

An alternative to fed-batch culture is a perfusion system. Such systems are used most often with animal cell cultures (see Chapter 12). The basic characteristic is constant medium flow, cell retention, and in some cases selective removal of dead cells. High cell density can be achieved. Cell retention is usually achieved by membranes or screens or by a centrifuge capable of selective cell removal. When a membrane is used, the system has characteristics of an immobilized cell system (see Section 9.4) except the cells are usually maintained in suspension and mixed. With a selective removal/recycle the system approaches the cell recycle reactor discussed earlier in this chapter. Figure 9.10 depicts one type of perfusion system.

The potential advantages of a perfusion system is the potential removal of cell debris and inhibitory by-products, removal of enzymes released by dead cells that may destroy product, shorter exposure time of product to potentially harsh production conditions (compared to batch or fed-batch operation), high per-unit volumetric productivity (due to high cell density and metabolism), and a rather constant environment.

The primary disadvantage is that a large amount of medium is typically used and the nutrients in the medium are less completely utilized than in batch or fed-batch systems. High medium usage is expensive, owing not only to the high cost of raw materials but also to the costs to prepare and sterilize the medium. Additionally, costs for waste treatment increase. Typically the bioprocess engineer must consider the trade-off of improved product quality and reactor productivity with the extra costs associated with a more complex reactor system (membranes, pumps, centrifugal separator, etc.) and increased medium usage. The best choice depends on the specific situation.
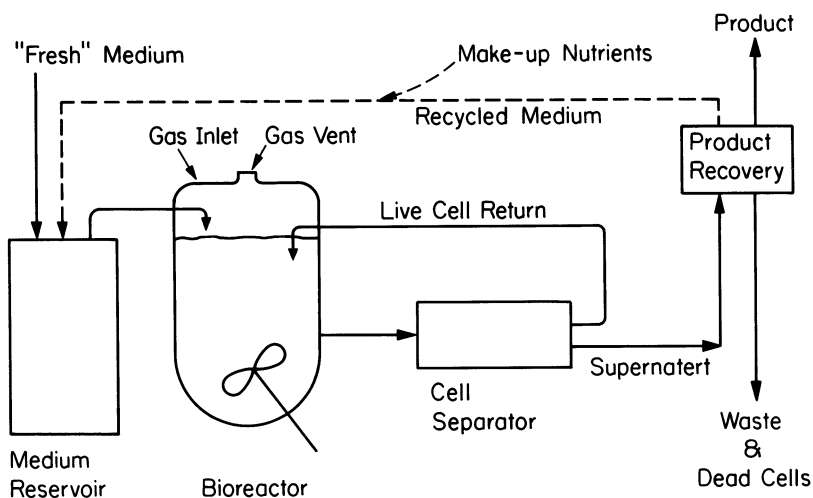

Fig. 9.10. Schematic of a perfusion system with external centrifugation and return of cells. Internal retention of cells is also possible. Return of spent medium is optional.