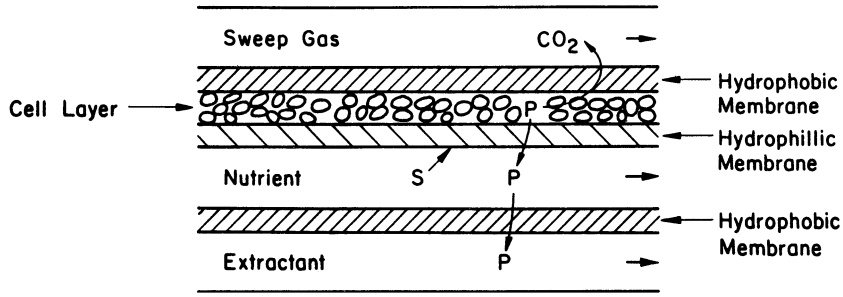


**Figure 11.33.** Example of a multimember reactor. The extractant fills the pores of the hydrophobic membrane but cannot pass into the nutrient solution if the pressure on the nutrient side is higher than on the extractant side. S is the substrate and P is the product. (With permission, from T. Cho and M. L. Shuler, Biotechnol. Prog. 2:53–60, 1986.)

an attractive solvent for this purpose, its direct use for *in situ* extraction was thought to be impossible due to toxicity. However, further work led to the recognition that a solvent could be toxic due to two features: (1) a chemical or molecular level toxicity due to solvent dissolved in aqueous broth, and (2) a physical or phase toxicity due to direct interaction of yeast with droplets of emulsified solvent. It turned out that TBP's toxicity was solely due to phase toxicity. One way to circumvent this is to immobilize cells in a manner that allows entry of nutrients and exit of product while excluding droplets of solvent. One device that can do this is a *multimembrane bioreactor* (Fig. 11.33).

With a hydrophobic membrane, the solvent will readily fill the pores of the membrane. If the aqueous solution is at a pressure higher than the solvent, but less than the critical entry pressure of the aqueous solution into the membrane pores, then the solvent is effectively immobilized in the membrane. Such a system allows *in situ* solvent extraction of product while preventing the emulsification of solvent and phase toxicity. The primary advantages for this type of bioreactor are the use of more concentrated feeds, relief of feedback inhibition, and reduced distillation or separation costs (e.g., for ethanol recovery).

Not only can this integrated view be expressed through the addition of extracting agents, but it can be expressed at the molecular level. Several groups have worked on protein excretion into the extracellular compartment from *E. coli* using appropriately constructed plasmids. The motivation for this approach has been to greatly simplify recovery and purification, rather than any potential increases in reactor productivity.

It is important for the bioprocess engineer to consider the whole system. The design or choice of culture, reactor configuration, and separation and purification train must be made carefully. Small changes in the upstream process can either greatly simplify or complicate the design of the downstream process.

## 11.7. SUMMARY

The recovery and purification of products at the end of fermentation processes is an essential step. Product separation can be accomplished either integrated with or following the fermentation step. The major categories of separation of fermentation products are