AMERICAN CHEMICAL SOCIETY

MULTIPLE CONSIDERATIONS FOR SEPARATIONS

NEW YORK—Many of the separations technologies used by biotechnologists stem from developments within the chemical industry. For instance, reverse osmosis, adapted for concentration or separation, was originally developed as a membrane process for desalination of sea and brackish water. And ultrafiltration, a membrane process used to remove small macromolecules from solution, came into its own when the automotive industry used it to recover paint. In fact, ultrafiltration's widest industrial use is still in separating colloids, according to William Eykamp, president of Koch Membrane Systems (Wilmington, MA).

Whatever technology is used for large-scale separations, the process must be controllable. As Eykamp pointed out at the American Chemical Society's First International Conference on Separations Science and Technology here, to control a process, one must understand it—not as straightforward a task as it would appear from first principles. Eykamp emphasized that any such process must be "adequate." Adequacy is determined by economics, and this

changes with the particular application. In true molecular separations, for instance, 95-percent purity might be quite adequate if there were no competing product on the market. In this situation, the dependability of the process becomes the critical factor, and noncontamination is generally absolute. In colloid separations, on the other hand, noncontamination is not important except in a gross sense, but 100 percent purity is absolute.

When chromatography is used for the large-scale purification of biopolymers, the type of column-packing material becomes the economic pivot point. From a process point of view, according to J.-C. Janson (Pharmacia Biotechnology, Uppsala, Sweden), there are two aspects to consider: the life span of the column packing material and the throughput obtained under optimum operating conditions. The life span is a consequence of chemical stability: the material must be able to stand up to frequent cleaning regimens. Throughput (the amount of a purified fraction that can be recovered in a certain period of time) is a direct consequence of the dynamic capacity

of the matrix for the compound. If all other parameters are kept constant, the dynamic capacity can be improved by decreasing the average particle diameter of the column packing material. This can be done with the new rigid matrices available—including cross-linked agarose, cross-linked cellulose, and resins made from synthetic polymers (allyldextran, poly-bisacrylamide, and vinyl polymers with hydroxyl groups).

In process chromatography, it is critical to the economics to achieve maximal use of the column's capacity. The column is continually fed with solution until product first appears in the eluate (the breakthrough point). If the breakthrough is not a step function, producing an abrupt rather than gradual accumulation of product in the eluate, then sample is being wasted or the column is not being used to its full capacity. If the flow rate can be kept low, the dynamic capacity of the column is increased. This flow rate dependence varies considerably from one matrix type to another and depends on the polymer type and the pore distribution.

—Jennifer Van Brunt

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