THE NEEDS FOR—AND OF—BIOCHEMICAL ENGINEERS

RESEARCH TRIANGLE PARK, N.C.—What do biochemical engineers do? How should a biochemical engineer be educated? In what directions is this emerging field headed, and are these the proper choices for future development? These were some of the questions discussed at a symposium on Initiatives for the Nineties for Biochemical Engineering held at Burroughs Wellcome here in late June.

Robert Kelly, associate professor of chemical engineering at The Johns Hopkins University (Baltimore, MD), in addressing the training of graduate students in biochemical engineering, strongly advocated an increased emphasis—at both the graduate and undergraduate levels—on training in the biological sciences. According to Kelly, if major markets are going to revolve around biological systems and biological molecules, then biochemical engineers must thoroughly understand the biochemistry of these molecules and processes, just as chemical engineers have to understand organic chemistry. Kelly believes that engineers need more than just a general familiarity with the biological sciences: they must obtain the experimental expertise and intellectual focus of a research biologist if they are to distinguish good science from the simply mediocre.

On the other hand, Robert Eltz, director of bioprocess development at Monsanto Co. (St. Louis, MO), deemphasized the need for strong biological training for industrial biochemical engineers. The primary concern of the engineer in industry is "How?" Exploring "Why?" is the responsibility of a basic scientific research group, he said. Biochemical engineers must be sufficiently fluent in biology to effectively pose questions to scientists and to understand the answers, but they are not expected to have the skills necessary to find those answers independently. A biochemical engineer's skills, Eltz contended, must be those of a classically trained engineer: analysis of experimental results; hands-on experience with equipment, instrumentation, and computers; strong logical reasoning; and organization and integration of the skills of disparate groups such as scientists, engineers, and economists.

Eltz proposed that the only undergraduate life science course requirements should be biochemistry and microbiology, provided the chemical engineering core curriculum incorporates biochemical engineering topics into lectures, problem sets, term papers, and a thesis. At the graduate level, he advised courses in microbiology, immunology, biochemistry, genetics, and molecular biology.

Other industry representatives also pointed out the importance of training in the life sciences. One of the distinguishing features of industrial R&D is the diversity of projects. Products are custom tailored to specific applications and customers. There may be formal teams assigned to large projects—a multidisciplinary approach. As a result, there is a need for more interaction at the interface of biochemistry, biology, and engineering: This is where the opportunities lie.

The degree to which engineering contributes to production processes depends primarily on the size of the market, which can vary over several orders of magnitude. Larger production volumes make efficiency more important. A number of opportunities exist to improve the development and manufacture of protein products, according to Barry Buckland, director of bioprocess development for Merck Sharp & Dohme (Rahway, NJ). The availability of on-line instrumentation will be key for process monitoring and control to obtain maximum performance. A major problem here is the limitation in real-time analysis of complex molecules: biological assays for activity take far too long to be useful in a process setting. Other process factors to evaluate, Buckland added, include assuring proper protein folding, cell line storage, and preparation of the inoculum for a large reactor from a very small archival sample. Also, regulatory and engineering concerns must be considered early.

James Walter, manager of biochemical engineering at W. R. Grace & Co. (Columbia, MD), added to the list of problems that need to be addressed, including reducing the costs of fermentations and improving on-line process sensors. Better criteria for selecting host cells and expression systems are needed, as are better methods to select antifoam (for the fermentation broth) and predict its effects on downstream processing equipment. There is also a need for ways to select the optimal filtration method for a given application, and to predict filter fouling in protein and cell separations.

Kim Nelson (United Engineers and Constructors, Philadelphia, PA) emphasized the importance of process monitoring and control, especially when a company is trying to validate its process to satisfy the Food and Drug Administration (Bethesda, MD). Nelson continued with a long list of areas where additional methods development and research would be beneficial to bioprocess design engineers. Biotechnology and pharmaceutical companies have a major need for a design database of physical properties (such as density, viscosity, and heat capacity) for fermentation broths, cell lines, and downstream fluids such as cell homogenates and concentrated protein solutions. Existing design correlations must be checked against these data, and new correlations created if necessary. Nelson suggested that the relevant technical societies agree on a standard set of cell lines, media compositions, and culture conditions. This would form the framework for a properties database which could be used for benchmark process comparisons and to which all labs could contribute reference data without disclosing their own proprietary information.

—**Steven Peretti and Robert Cherry**