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# Book Review

**Biological Reaction Engineering**. By I. J. Dunn, E. Heinzle, J. Ingham, and J. E. Prenosil, Second Edition with CD-ROM, Wiley-VCH, Verlag GmbH & Co., Weinheim, Germany, 2003, 508 pages, Hardcover, ISBN: 3-527-30759-1

Occasionally an older, albeit evolving field takes on a wholly new importance as other emerging technologies recognizes its utility. *Biological reaction engineering* is just such a field and *bioMEMS** is an emerging technology that may depend on it for the next generation of medical microdevices. Let us first consider *what* this field is all about, *how* this book addresses it, and *why* then this is so important.

The book is an advanced presentation of modeling and simulation in the field of bioreaction processes, historically known as *fermentation processes*. This field is important to the food, pharmacological and chemical industries. Many products, including wine, cheese, bread, sugars, organic acids and medications depend on these processes. At first glance the book seems to appeal to chemical and biochemical engineers, with its emphasis on mass and energy balances, and rate processes in the design of optimally performing bioreactors. It is however approachable by biomedical engineers, microbiologists, and other laboratory scientists, and it is from this perspective that the book is reviewed. It is a reference book and presumes some knowledge of the field by the reader.

The book is divided into two parts, the first concerns the principles of bioreactor modeling, the second dynamic process simulation examples using the Berkeley Madonna simulation language. The latter is left for the reader to explore, and includes a CD-ROM with various application programs.

Perhaps in its most blasé context biological reaction engineering deals with the biochemical processes of *bioreactors* — vessels that support a biologically active environment in which microorganisms (bacteria, yeast and fungi), cells (human, animal and plant), and other substances (enzymes, biocatalysts) interact. These biomaterials are cultivated in a controlled manner and converted or transformed through specific reactions. Designing a bioreactor is a complex process, and *performance* depends on many variables.

The book examines closely the reaction kinetics of fermentation, including such variables as biomass, substrate and product concentrations, and reactor volume. Derivation of the balance equations is performed in an understandable manner, and begins with the conservation of mass in the steady-state flow process. *The rate of mass flow into the system must equal the rate of mass flow out of the system.* From there dynamic systems are considered at the component level. *The rate of accumulation of mass of a component in the system equals the mass flow into the system, less the mass flow of the component out of the system, plus the rate of production of the component by the reaction.*

Next energy balancing is considered. The fundamental relationship is this: *the accumulation rate of energy equals the rate of energy in by flow, less the rate of energy out by flow and transfer, plus the rate of energy generated by reaction and agitation.* Having explained these concepts in mathematical terms, the book then introduces bioreactor operation, including *batch, semicontinuous or fed batch*, and *continuous* operation systems. The variables, reaction kinetics and ultimately the advantages and disadvantages of each reactor mode are discussed.

Recognition is given to factors other than the mass balance equations that contribute to modeling of the entire system. These include for example reaction rates as functions of concentration, temperature and pH; stoichiometric or yield relationships; ideal gas behavior; pressure variations as a function of flow rate; dynamics of measurement instruments as a function of the instrument response time; equilibrium relationships; and system physical properties.

Modeling requires an understanding of biochemical reactions, including enzyme reaction kinetics. The Michaelis-Menten equation describes the rate of reaction catalyzed by a soluble enzyme. This and other enzyme kinetic models are explored, and simple microbial kinetics is considered, with interesting case studies (for example, growth and product formation of an oxygen-sensitive *Bacillus subtilis* culture). Other concepts dealt with include oxygen balance and oxidation; diffusion and biological reaction in immobilized biocatalysts systems; and bioprocess control.

It was mentioned earlier that biological reaction engineering is important for the next generation of medical microdevices. For example, tissue engineering incorporates *scaffolds* and other systems that support cell and tissue growth. These devices are essentially bioreactors. BioMEMS have a least one dimension between 100 nm and 200 $\mu$m, while other dimensions may be several mm or more. These include *lab-on-chip* devices (LOC), *micro-total-analysis systems* ($\mu$TAS), *DNA and protein microar-*

*Biomedical Microelectromechanical Systems.

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*rays*, novel sensors and actuators, diagnostic tools, and therapeutic devices. Lab-on-a-chip devices may be fabricated to function as micro-bioreactors. As a science bioMEMS includes an expansion into a host of new polymer materials, microfluidic physics, surface chemistries and modification, "soft" fabrication techniques (including polymers and biological components) and a new understanding of biocompatibility.

There is much greater potential though, and this has to do with evolution of "artificial organs" to "synthetic organs" – the natural consequence of *large-scale bioMEMS integration* (assembly of macro systems through multiple units of microfabricated components). It is primarily through this technology that we will see the next generation of bioreactor-based extracorporeal filters; and even implantable synthetic livers, kidneys, endocrine glands and other organ systems that require *synergy* between an *implantable* bioreactor and a living host. While much work needs to be done to achieve these lofty goals, this book successfully imparts the mathematical foundations for bioreactor operation and design.

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