

A New Cellular and Molecular Engineering Curriculum at Rice University

Ka-Yiu San, Larry V. McIntire, Ann Saterbak

Department of Bioengineering, Rice University
Houston, Texas 77005

Abstract

The tremendous advances in cellular and molecular biology over the last 25 years have fundamentally changed our understanding of living organisms. This new understanding at the level of cells and their array of associated molecules is having a tremendous impact on both medicine and technology. Appreciating the complexities of the cell and its inner workings will be crucial to turning our knowledge into effective treatment strategies at the tissue, organ and whole individual levels. Because of its tradition of applying the fundamentals of physics and mathematics to the understanding and control of biological systems, biomedical engineering is especially well positioned to advance cellular and molecular-based medicine and technology. To accomplish this, the Bioengineering Department at Rice University is developing a curriculum that educates students in cellular and molecular processes and their control.

In this talk, we will describe the structure of a bioengineering undergraduate program at Rice University begun in 1998. We will present the development of a series of new courses for the cell and molecular engineering program. This series of courses starts with the basic concepts of engineering fundamentals at the sophomore level. This introductory course provides the foundation for the more advanced quantitative treatment of cell structure and function at the cellular and tissue levels taught in the junior and senior levels. In particular, we will discuss the development of three specific courses that cover topics ranging from molecular to tissue level: molecular engineering, cellular engineering and tissue engineering. This sequence of courses exposes students to the cutting-edge synthesis of molecular and cellular information into design of tissue systems. Coupled with these lecture-based courses is a hands-on tissue culture laboratory course. With the emphasis on cellular and molecular engineering, we believe our bioengineering undergraduate students will obtain the necessary training to become leaders in this rapidly emerging field of the biomedical/biotechnology industry.

Introduction

The Bioengineering undergraduate program at Rice University is designed to prepare students for careers in rapidly developing areas of biomedical engineering and bioprocessing. The undergraduate educational program in Bioengineering (BIOE) has the goal of producing a new type of biomedical engineer, fully conversant with modern biochemistry and cell and molecular biology. This type of biomedical engineer will translate bench-scale scientific advances in biological sciences into cost-effective new products and processes. New and innovative curricula are being developed to educate biomedical engineers who will not only create new tissues and cell-based therapies but also deliver them at a cost affordable to our health care system.

Bioengineering Curriculum at Rice University

The educational program objectives of the B.S. degree in Bioengineering at Rice University are to:

- Provide students with a fundamental understanding of the life and medical sciences;
- Teach students to apply engineering principles in the life and medical sciences;
- Develop their critical problem solving skills in bioengineering;
- Develop their ability to communicate effectively and participate in interdisciplinary teams;
- Expose students to a broad education that prepares them for diverse careers.

Graduates will be prepared to pursue further education in graduate school or medical school or begin a career in the biotechnology industry.

Bioengineering students follow the typical engineering curriculum during their freshman year with two semesters of calculus, two semesters of general chemistry, an introductory programming course and two semesters of physics. The introduction of the students to the fundamentals of life sciences begins with organic chemistry and introductory biology in the sophomore year. Biochemistry and cell biology are critical for our program and are taken in the junior year. Because of the increasing importance of computational science and mathematical modeling in bioengineering, students take two more semesters of mathematics and one semester of engineering computational methods, which was especially designed to provide engineering majors with a rigorous introduction to analytical and numerical methods.

Students obtaining a B.S. in Bioengineering are required to take seven core courses in Bioengineering. The core courses include the following (1 semester each):

- Bioengineering Fundamentals - conservation of mass, energy, momentum and charge in biological systems
- Biosystems Transport and Reaction Processes - momentum, heat and mass transport and reaction processes in human body
- Systems Physiology - physiology of organism, tissue and cellular levels
- Biomechanics/Biomaterials - force analysis, mechanics of deformation, biomechanics of tissue, physical and chemical properties of biomaterials
- Tissue Culture Laboratory - sterile technique; proliferation and transfection assays
- Bioengineering Design - design of process or product, FDA regulations, economics
- Advanced Bioengineering Laboratory - modules in biomaterials, biomechanics, systems physiology, instrumentation, bioprocessing, ethics

To enhance knowledge in one area of Bioengineering, students select one of three emphasis areas or tracks: (a) Cellular and Molecular Engineering; (b) Systems Engineering and Biomedical Instrumentation; and (c) Biomaterials and Biomechanics. Students take a minimum of five elective courses that expose them to important problems in their chosen track.

The Rice University cellular and molecular engineering track has several distinct features:

- The general organization of the track consists of a set of core courses to cover the basic and fundamental bioengineering concepts, which provides breadth, followed by another set of more specialized area electives, which provides depth.

- The curriculum includes courses in biochemistry and cell biology taught by the biochemistry and cell biology faculty to provide knowledge in basic life sciences at the molecular and cellular level.
- A solid introductory sophomore foundation course (bioengineering fundamentals) covers the conservation laws of mass, momentum, charge and energy. Many example and homework problems highlight applications at the cellular and molecular level. This course includes case studies that demonstrate how applying the conservation law with different conserved properties can illuminate many different aspects of the same system. It provides the fundamental concepts that are reinforced by more advanced courses.
- Three specific courses are offered that cover topics ranging from molecular to tissue level: molecular engineering, cellular engineering and tissue engineering. These expose students to the cutting-edge synthesis of molecular and cellular information into design of tissue systems.
- A junior-level tissue culture laboratory focuses on learning sterile tissue culture techniques. The lab includes attachment and proliferation assays, as well as several staining techniques and use of GFP reporter genes.
- The advanced bioengineering laboratory contains several modules targeted toward the cellular and molecular engineering track, including biomaterials synthesis and characterization, cell function on biomaterials, bioprocessing and a laser tweezers lab. These reinforce concepts covered in other lecture-based courses as well as in the tissue culture lab.
- Undergraduate research opportunities expose students to state-of-the-art materials; they also provide a perspective of graduate student life. It is estimated that half the undergraduates will undertake research.
- Report writing and oral presentation are implemented as an integral component in most courses. Students work with communication specialists from our English department and the Cain Center to practice and improve these presentations. Both writing skills and technical expertise are evaluated and graded.

New courses in Cellular and Molecular Engineering Program

As mentioned, we have developed three specific courses that cover topics ranging from molecular to tissue level for the Cellular and Molecular Engineering Track. The sequence of courses is designed to expose students to the cutting-edge synthesis of molecular and cellular information into design of tissue systems. These three courses are Computational Molecular Engineering, Cellular Engineering and Tissue Engineering. The Computational Molecular Engineering course is designed for juniors while the Cellular Engineering and Tissue Engineering courses are intended for senior/graduate students. All three courses are lecture based. A special and common feature among these courses is the requirement of a term project. To further enhance the written and oral communication skill, a written report and an oral presentation is also required. Assessment is based on written evaluations by the students at the end of the semester. A brief description of each of the courses is provided below.

Cellular Engineering

The Cellular Engineering course consists of three major topics: cytomechanics, ligand-receptor interactions and signal transduction, and pathway and metabolic engineering. The cytomechanics portion deals with biomechanical issues related to cells and subcellular elements. A major objective is to provide a basic explanation of the effects of mechanical forces on cell synthetic or metabolic activities. Another aim is to describe the mathematical and experimental bases of biomechanical characterization techniques. These include the well-established micropipette aspiration method, as well as modern methods, such as cytoindentation, cytodetachment, atomic force microscopic techniques, and optical tweezers. The second portion, ligand-receptor interactions and signal transduction, emphasizes on the mathematical modeling of cell behavior regulated by receptor/ligand signaling. It emphasizes on the formulation of physical models and the development of kinetic balance equations. Various cell surface receptor binding modeling concepts are introduced to describe equilibrium and transient binding of ligand to cell surface receptors as well as subsequent intracellular trafficking processes. Methodologies, both graphical and numerical, are described for the determination of model parameters. The pathway and metabolic engineering portion deals with the analysis and design of large-scale reaction networks. Special emphasis is put on the effect of network structure and reaction kinetics on the final network behavior. The concept of metabolic flux analysis is introduced for the estimation of intracellular pathway fluxes. The resulting set of linear equations is solved by standard MatLab program. The concept of least squares estimation is used to deal with overdetermined systems. Finally, the concept of metabolic control theory is also introduced for the quantitative treatment of enzyme kinetics interactions and flux control. Finally, a design and analysis project is required for all students. They are divided into teams to work on projects related to cytomechanics. They students are required to turn in a written report and make an oral presentation at the end of the semester.

Tissue Engineering

The Tissue Engineering course focuses on the study of cell, cell interactions and the role of the extracellular matrix in the structure and function of normal and pathological tissues. The course also covers strategies to regenerate metabolic organs and to repair structural tissues, as well as cell-based therapies to deliver proteins and other therapeutic drugs, with emphasis on issues related to cell and tissue transplantation such as substrate properties, angiogenesis, growth stimulation, cell differentiation, and immunoprotection. The first half of the course provides background information on biomaterials, cell/tissue interactions with materials, tissue development and growth. The second half of the course deals with case studies of strategies for the creation of new tissues, including tissue induction, cell transplantation, biohybrid organs, blood substitutes and gene therapy. During these lectures, a brief overview of the existing options to replace human tissue is presented before each case study. In all cases, engineering principles of transport and reaction phenomena are used for the analysis and the understanding of the behavior of the new constructs. Finally, the students are required to do a group project. They are divided into group of two or three and are allowed to choose an organ or tissue which they investigate and for which they devise a tissue-engineering strategy. The students are also required to turn in a written report and make an oral presentation at the end of the semester.

Computational Molecular Engineering

The Computational Molecular Engineering course is designed to introduce the principles and methods used for the simulations and modeling of macromolecules of biological interest. Protein conformation and dynamics are emphasized. Empirical energy function and molecular dynamics calculations, as well as other approaches, are described. Specific biological problems are discussed to illustrate the methodology. Classic examples such as the cooperative mechanism of hemoglobin and more frontier topics such as the motional properties of molecular motors and ion channels as well as results derived from the current literature are covered. Other topics such as protein folding/predictions, the nature of reaction rate enhancement in enzyme catalysis, physical chemistry properties of biologically relevant nano-materials, simulations of free energy changes in mutations, electrostatic properties of protein, molecular recognition, and the properties of binding sites are also included. Particular emphasis is given to the applications of molecular graphics. During the final reading period, each student carries out an original research project that makes use of the techniques. The students are required to turn in a written report and make an oral presentation of the final projects at the end of the semester.

Biographical Information

KA-YIU SAN

Dr. San is a professor in the Departments of Bioengineering and Chemical Engineering at Rice University. Dr. San received his B.S. degree in chemical engineering from Rice University in 1978 and his M.S. and Ph.D. degrees in chemical engineering from the California Institute of Technology in 1981 and 1984, respectively. His research interests include genetic and metabolic engineering of microbial and plant cells, and modeling and optimization of bioreactors.

LARRY V. MCINTIRE

Dr. McIntire is the E.D. Butcher Professor of Bioengineering and Chemical Engineering and Chair of the Institute of Biosciences and Bioengineering. Dr. McIntire received his B.Ch.E. and M.S. degrees in chemical engineering from Cornell University in 1966 and his Ph.D. degree in chemical engineering from Princeton University in 1970. Dr. McIntire has edited two texts: *Biotechnology - Science, Engineering and Ethical Challenges for the Twenty-First Century* [Joseph Henry Press (NAS), 1996] and *Frontiers in Tissue Engineering* [Pergamon-Elsevier Science Ltd., 1998].

ANN SATERBAK

Dr. Saterbak is the laboratory coordinator and an instructor in the Department of Bioengineering at Rice University. She received her B.A. degree in chemical engineering and biochemistry from Rice University in 1990 and her Ph.D. degree in chemical engineering from University of Illinois at Urbana-Champaign in 1995. As a graduate student, Dr. Saterbak received two Excellence in Teaching Awards from the University of Illinois at Urbana-Champaign.