BE.010 Spring 2005
Session #8 notes

Bioengineering Research in Chemical Engineering

Outline of this session:

- definition of Chemical Engineering (ChE) and an overview of its undergraduate requirements at MIT
- discussion of ChE starting salaries and of the place ChE holds among other disciplines
- overview of ChE research groups at MIT

Introduction

Patrick S. Doyle is a Charles & Roddey Assistant Professor in Chemical Engineering at MIT. His current research in the dynamics of polymers and complex fluids under the influence of forces and fields lies at the interface of biophysics, polymer physics, and transport phenomena.

What is Chemical Engineering?

The American Institute of Chemical Engineers (AIChE), founded in 1908, is a professional organization that encourages undergraduate student activities and participation around the country and works to help students in the field to further their careers. The AIChE at MIT takes part in departmental decision making and offers sessions on the graduate school application process and on how to find jobs. This slide states the AIChE definition of ChE.

This is a fermentation-based process flow sheet for a particular biological product. As you can see, many different steps are involved. One must understand how each step functions separately and in relation to the rest of the process.

Overview of the Chemical Engineering and Chemical-Biological Engineering Majors

Both the Chemical Engineering curriculum (course 10) and the Chemical-Biological Engineering curriculum (course 10B) are built on the MIT general institute science requirements of chemistry, biology, physics, and single and multi-variable calculus. Upon the fundamental sciences, the chemical engineering curriculum adds the classes listed below, most of which are taken during the student's sophomore and junior years:

5.60 Thermodynamics and Kinetics

7.03 Genetics

7.05 General Biochemistry

7.06 Cell Biology

10.10 Introduction to Chemical Engineering

10.213 Chemical Engineering Thermodynamics

10.28 Biological Engineering Laboratory

10.29 Biological Engineering Projects Laboratory

10.301 Fluid Mechanics

10.302 Transport Processes

10.702 Introductory Experimental Biology and Communication

The 10B curriculum exchanges some of the traditional ChE classes for ones that are more biology based. Students are free to switch between the two tracks up to the end of their sophomore year. During senior year, students in both tracks take four capstone process chemical/biological engineering classes.

These are some examples of projects undertaken by students in 10.28, the Biological Engineering Laboratory during their junior year.

The 10B curriculum at MIT satisfies most of the Premed requirements. Students in 10B can obtain a Biomedical Engineering minor degree by choosing to take two additional classes from the core subject selections. Students can obtain an additional major in biology by taking three additional classes.

ChE in Relation to Other Fields

Chemical engineering, like biological engineering, lies at the interface of many fields. In recent decades, the molecular sciences have gradually overlapped more and more with traditional engineering disciplines, resulting in greater needs for interdisciplinary work. This Venn diagram categorizes the research areas of the various faculty in the ChE department. As you can see, chemical engineering is a product of the integration of the chemical, biological and physical aspects of the world.

The following slides show the present and potential contributions of chemical engineers to biological engineering.

Langer Lab: Novel Approaches to Drug Delivery

Chemical and Biomedical Professor Robert S. Langer is most well-known for his work in the development of new drug delivery techniques that allow for the release of large molecules into the body at a steady manner. Langer, MIT’s newest Institute professor, gives credit to risk taking and non-conventionality as two traits that helped to further his own career. This slide shows present uses of biomaterials in medicine. As you can see, polymers traditionally unassociated with medicine now have medical uses.

These two slides show two different types of erosion. Bulk erosion leads to burst drug release which can be fatal for potent drugs, in addition to being harmful to the patient receiving the medication. Surface erosion, on the other hand, leads to a much smoother delivery. Increasingly, polyanhydride biodegradable polymers have been used to treat cancer patients. The degradation of these block polymers, which can be adjusted by varying the ratio of X to Y, resemble surface erosion in that the matrixes degrade at a steady rate and that the block polymer themselves degrade as they release the drug.

This graph shows the percentage degradation of different block polymers. The numbers 0, 15, 55, 79 represent polymers with different chemical compositions. Block polymers 79, 15 and 0 all steadily degrade during the given time interval, but at different rates. 55 degrades unsteadily, proceeding faster in the beginning and slowing down as time passes.

The World Health Organization (WHO) classifies Glioblastoma multiforme (GBM) as the most common primary brain tumor in adults around the world. Most of these tumors quickly become malignant, leading to a uniformly fatal disease with an untreated, median life expectancy of four weeks. Death results from tumor enlargement and its pressure effects on the brain. Most patients die before the tumor metastasizes in another part of the body.

BCNU/BiCNU is the trade name for 1,3-bis(2-chloroethyl)-1-nitrosourea, which by itself is very lethal. The drug, when coated with a polymer, is commonly used in chemotherapy to stop the growth of cancer cells, particularly those in the brain. It is administrated through an injection into the vein over a period of one to two hours. A person's appropriate dosage is dependent on body weight and prior food intake.

In 1980, the therapy proposed to combat GBM focused on the development of a novel approach in getting BCNU-polymers into the body. With a half life in vivo of 12 minutes, BCNU is susceptible to attack and degradation by the body's enzymes and cannot survive for prolonged periods by itself. Langer worked on the development of a novel polymer to protect BCNU in its journey, to prolong the effects of the drug, and to allow it to be delivered in a periodic manner.

As with all novel approaches, the idea was met with a lot of resistance. Even as each objection listed was overturned through the years, more were generated to take its place.

These are pictures of the final product. These polymer wafers can be administrated directly at the site of the brain tumor. Delivery is made exactly to where it is needed, getting rid of other unnecessary complications. This innovation marked the beginning of pioneering work in local chemotherapy.

The survival statistics on this slide show that the lifespan of patients treated with the drug is considerably longer than that of the control.

Trout Group: Stabilization of Proteins

The Trout group, led by Associate Professor of Chemical Engineering Bernhardt L. Trout, is currently involved in the stabilization of therapeutic proteins for medical use. The many motivations of the project lie not only in the financial rewards of the industry but also in

the vast potential uses of the discovery. The current approach, based mainly on the experimentation and evaluation that comes along with trial and error, is not very efficient. The Trout group chose to use physics to describe protein interactions and then to use that understanding in the design of new stabilization approaches.

Currently, arginine, one of the twenty essential amino acids, is used to prevent aggregation and to promote proper refolding in the body. The goal is to study the reaction mechanics of arginine in order to understand how it works in the body and then to design new additives which are much more effective.

Jensen Group: Microfluidic Devices for Biological Analysis

Professor of Chemical Engineering and Material Science and Engineering Klavs F. Jensen designs microfluidic devices to increase the efficiency and effectiveness of laboratory processes.

These are some examples of the current microfabrications and microelectronic mechanical systems (MEMS). The first two chips are products of the Jensen lab. The last two are products of Caliper Tech. Co. The usefulness of the chip lies in its ability to integrate many different processes together into a chain reaction which can be carried out in a device. The chip is put into a machine, which functions much like an ATM receiving a card. The entire process is automated.

This is an outline of a typical system approach, which may take the lab technician much time to perform. Here are a summary of the processes:

1. Cells are cultured
2. Cells are sorted based on fluorescence characteristics
3. Cells are lysed- exploded, broken open
4. Inner contents (organelles) are further separated
5. Organelles are lysed
6. Proteins in the organelles are separated
7. Certain proteins are detected

The circled step, step 4, is discussed in detail.

Isoelectric focusing operates based on the presence of an electric field and a pH gradient. Depending on their pH, many molecules, especially proteins, can be positively or negatively charged. In this example, let the red and blue dots represent arbitrary organelles. The red dot is positioned below its IpH. Thus, it accelerates toward the cathode. Additional red dots would accelerate in the same direction and eventually form a vertical stream. The blue dot is positioned above its IpH. It accelerates in the opposite direction. Separation is made possible by a flow field perpendicular to the force field. In

the final device, particles are continually fed from the bottom and separated out at the top. This slide shows a detailed mathematical modeling of the system, describing how different variables in the conservation and transport equations vary in time and space.

This computer simulation with the field lines aligned parallel to the plates A, B, and C resulted in well-defined focusing of the mitochondria and serves as a proof of principles.

This is a cartoon layout of the actual device. The electric contact pad connects the battery to the external world. Ohmic heating due to resistance is disregarded. This slide shows the movement of different particles to separate exits. The result of an actual experiment is shown here.

Doyle Group: Magnetosensitive Self-Organizing Arrays for DNA Separation

The traditional method of gel electrophoresis is replaced by DNA electrophoresis in the separation of large DNA molecules.

Superparamagnetic beads are created to serve as a custom obstacle course that allows some molecules to pass through while blocking others. The magnets orient themselves head to tail in the direction of the field. When the magnetic field is on, the beads are relatively ordered. The different chemistries on the outside of the beads cause the selective permeability of different molecules. As statistics show, the method pursued by the Doyle Group is much less time consuming.

This last slide shows the movement of a single molecule through the presence of an electric field. There is an obstacle at the beginning of the path. The disentanglement time of the molecule depends on its chain size.