CHE 488: Molecular and Cellular Bioengineering (3 Units)
Fall 2013

Mork Family Department of Chemical Engineering & Materials Science

Course Description:
Design, synthesis and analysis of biological molecules; routes to understand and engineer living systems at the molecular and cellular level; systems and synthetic biology.

Lectures: Two one hour and twenty minute lectures a week.

Location: VHE 214 2:00-3:20pm WF

Homework: Reading assignments for each class period, homework assigned each week, and project--an NSF style fellowship application.

Grading; 2 Midterms (100 pts each), 1 final (100 pts), Project (100 Pts), Homework (100 pts). 500 Pts total.

Instructor: Professor Richard Roberts

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Prerequisite: BISC 320 or equivalent.

Text: Biotechnology: Academic Cell Update Edition
Publication Date: January 12, 2011 | ISBN-10: 0123850630

Reference Text and other Material:

Biochemistry by Berg, Tymocko & Stryer (7th ed. 2010)

PDF versions of assigned articles, audio-visual source material, and lectures will be posted on Blackboard.

Course Overview:

CHE 488 is an introduction and survey of molecular and cellular bioengineering. The course is intended to provide an understanding of the design, synthesis, and analysis of biological molecules as well as routes to engineer and understand living systems at the molecular and cellular level, and to introduce concepts in both systems and synthetic biology. Topics for the course include DNA sequencing, protein sequencing, sequence databases, chemical, enzymatic, and biological synthesis of DNA, RNA, peptides and proteins; biological synthesis of fermentation products; engineered production of chemical feedstocks and biofuels; genetically modified crops; computational and functional approaches to protein and nucleic acid design; thermodynamic prediction of DNA, RNA and protein stability and folding; use of biological molecules in nanotechnology; use of biological molecules in human therapies. Throughout the course, current public policies toward these technologies, business aspects (e.g., start-up companies), and related ethics issues raised will be discussed.

Learning objectives:

A major underlying objective of this course is to familiarize upper level undergraduates and $1^{st}/2^{nd}$ year graduate students with both the knowledge and basic skills needed to be successful in pursuing an advanced degree (Ph.D., M.D., Masters) at the interface between engineering and biology -- specifically regarding problems in bio-molecular design.

Exams:

There will be two mid-terms and one final exam, each worth 100 points. Exams 2 and the final will be cumulative in the sense that knowledge of material from previous work is assumed in the design of questions for current examination material.

Project:

You will be expected to complete an NSF-style graduate fellowship application in practice for future possible actual applications. This will include you picking out a faculty member at a research university (USC or other) and designing a basic project that aligns with his/her research program as though you plan to pursue a Ph.D. in that person's lab. You will also need to construct an essay detailing why you think you would like to pursue graduate work in that particular area. Your total project grade will be worth 100 pts, equivalent to one exam. You will also be expected to give an in-class presentation on your project.

Grading:

Grades from the three exams and project will be summed and the course grade assigned based on total points (i.e. 25 % for each of the 3 exams and the project).

Course Outline:

Week 1:
- Introduction/Review. Why should engineers care about biological systems?

Introduction to selected results and promise of molecular and cellular bioengineering.

- Summary of expectations for the course.
- Nucleic acid sequencing. Cloning, plasmids, PCR, and phage, antibiotic selection.
- Restriction enzymes. Manual and robotic colony picking. Electrophoresis, capillary electrophoresis. Maxam-Gilbert, Sanger (dideoxy), sequencing of DNA and RNA.

Reading: Chapter 3 of text.

Week 2:

- Nucleic acid sequencing continued. Automated sequencing. FRET, FRET dyes. High throughput sequencing (454, Illumina and others).
- Relative genome sizes. Approaches to determining the genome of an organism. Sequence and structural databases. Depositing and searching online sequence databases.
- Algorithms for comparing sequences. Phylogenetic trees and the universal tree of life.

Reading: Chapter 4 of text and posted material.

Week 3:

- Relative genome sizes. Approaches to determining the genome sequence of an organism. Sequence databases. Relatedness of proteins through evolution. Depositing and searching online sequence databases. Phylogenetic trees and the universal tree of life.
- Diversity of culturable life.

Reading: Chapters 3 & 8 of text.

Week 4:

- Protein sequencing and Proteomics. 1-D and 2-D protein gels, proteolytic enzymes, visualization. Sanger and Edman based sequencing. Mass spectrometry based protein sequencing. Isotopic labeling.
- Control circuits in eukaryotic and prokaryotic systems. Model organisms, phage, bacteria, c. elegans, drosophila, arabadopsis, zebrafish, mice, human tissues. Classical negative and positive control. Inducible promoters in bacteria, eukaryotes.

Reading: Chapter 9 of text

Week 5:

- Systems biology, the cell cycle and cellular state. Chip-based analysis of tissue-specific mRNA levels. Mass spectrometry based analysis of protein expression.

Databases for expression data. Expression as a diagnostic tool. (Nano)Technologies for diagnosis.

- Systems Biology and Cancer. Creating tumors from defined genetic elements. Hallmarks of cancer.

Reading: Chapters 7 &18 of text

Week 6:

- Synthetic biology I. Approaches to create genetically modified and synthetic organisms, e.g., Transgenic plants and animals. Altering the genome of prokaryotes. Altering the genomes of eukaryotes. Artemesinin, Dupont Feedstock, Biofuels.
- Synthetic Biology II. Engineered control circuits. Oscillatory circuits. Circuits built out of synthetic parts. iGEM. Biological molecules for performing logical operations. Rewiring existing controls.

Reading: Chapters 14 & 15 of text and posted material.

Week 7

- The structure and energetics of proteins. Amino acid structure, protein secondary structure, Ramachandran plots, similarity and conservation of structural elements through evolution, Introduction to the protein database and structural tools for visualizing proteins.
- Rational prediction of protein structure and energetics. Cho and Fasman, GOR and other methods for predicting secondary structure methods. Thermodynamics of protein folding, the hydrophobic effect, Ponder and Richards approach to packing protein cores.

Reading: Chapter 11 of text and posted material.

Mid-term I

Week 8.

- Susceptibility of proteins to mutations. The Genetic code. Mutations through evolution, PAM and BLOSUM analysis of evolutionarily related proteins. Mutations on existing proteins. Purposeful mutations and directed evolution of altered/new/improved function (methods and results).
- Computational approaches to predict/design protein structure. Levinthal's paradox. Protein folding funnels. CASP, Rosetta, Dead end elimination, protein design automation. Examples of computationally designed proteins.

Reading: Chapter 11 of text and posted material.

Week 9:

- Functional approaches to design new proteins I. Antibody selection and evolution in vivo. The structure of the antibody and T-cell repertoire. Similarity of mammalian antibodies (mouse, horse, human).
- Functional approaches to design new proteins II. History of antibody therapeutics. MHC Class I and Class II. Humanization of murine antibodies. The big successes. The big failures.

  Chapter 6 of text.

Week 10:

- Non-human approaches to produce human antibodies and other proteins. Human-mouse hybrids. Phage display, the yeast two hybrid method, yeast display, mRNA display, ribosome display, emulsion-based encapsulation.
- Getting your proteins (or other biomolecules) into an organism. Oral availability, injection, intravenous infusion, bioformulations/gels, Virus and Gene therapy-based delivery.

  Reading: Chapter 17 of text

Week 11:

- Issues related to library design, including diversity, scaffold, avidity, selectivity and specificity. Thermodynamics of binding. Statistical mechanical approach to multiple equilibria. Analytical and computational approaches to treat avidity, and multiple binding events.
- The business of biotechnology. Key historical developments in biotechnology. Raising money, intellectual property, patents, claims, interferences, royalties, stock options, products—is there a billion dollars in your future? Raising money, venture capital, IPOs, exit strategy.

  Reading: posted material.

Mid-term 2

Week 12.

- Something from nothing: Bioengineering and the origin of life. The age of the earth, formation of the oceans, and the worst engineer ever. The origin of life, the last common ancestor, and attempting to bridge this chasm.
- Evolution in a test tube before humans walk on the moon (Q beta replicase), evolution to fight viruses, evolution to resurrect ancient biochemistry, evolution to drive nanotechnology.

  Reading: Chapter 11 of text.

Week 13:

- RNA and DNA aptamers. Predicting RNA and DNA structure thermodynamically, topologically, and phylogenetically—ribosomes, tRNAs and more.
- Building with RNA and DNA. Helical repeat, crossovers, topology. Large DNA structures, DNA Origami.

  Reading: Chapter 11 of text and posted material.

Week 14:

- Integrated devices made with biomolecules. Calculating with DNA. Hybrid devices made with semiconductors and biomolecules.

  Reading: Chapter 7 and posted material.

Week 15:

- In-class presentations

Academic Integrity Policy

All USC students are responsible for reading and following the Student Conduct Code, which appears in the SCampus and at http://www.usc.edu/dept/publications/SCAMPUS/goverance.

The USC Student Conduct Code prohibits plagiarism. Some examples of what is not allowed by the conduct code: copying all or part of someone else's work (by hand or by looking at others' files, either secretly or if shown), and submitting it as your own; giving another student in the class a copy of your assignment solution; consulting with another student during an exam. If you have questions about what is allowed, please discuss it with the instructor. Students who violate University standards of academic integrity are subject to disciplinary sanctions, including failure in the course and suspension from the University. Since dishonesty in any form harms the individual, other students, and the University, policies on academic integrity will be strictly enforced. We expect you to familiarize yourself with the Academic Integrity guidelines found in the current SCampus. Violations of the Student Conduct Code will be filed with the Office of Student Conduct, and appropriate sanctions will be given.

Disability Policy Statement

Any Student requesting academic accommodations based on a disability is required to register with Disability Services and Programs (DSP) each semester. A letter of verification for approved accommodations can be obtained from DSP. Please be sure the letter is delivered to the instructor or to the TA as early in the semester as possible. DSP is located in STU 301 and is open 8:30 a.m. – 5:00 pm., Monday through Friday. The phone number for DSP is (213) 740-0776.