BMB 803/805: Protein Structure, Design, and Mechanism, Spring 2025

Classroom: 101 Biochemistry Bldg.

Class Hours: 9:10 am – 10:00 am, Monday, Wednesday, & Friday

BMB 803 Dates: Jan. 13 – Mar. 26; 28 lectures/labs by Hu & Dickson

BMB 805 Dates: Jan. 13 – Apr. 25; BMB 803 + 13 lectures by Hu & Hausinger

Instructors

Jian Hu, Jan. 13 – Feb. 14, and Mar. 19 – Apr. 14, 501 Biochemistry Bldg., 353-8680, hujian1@msu.edu
Alex Dickson, Feb. 17 – Mar. 17, 310C Biochemistry, 884-8985, alexrd@msu.edu
Robert Hausinger, Apr. 16 – Apr. 25, 6193 BPS Bldg., 884-5404, hausinge@msu.edu

Office Hours

There are no defined office hours, and students are encouraged to meet with the instructors whenever necessary by arranging a meeting time.

Recommend Materials

Introduction to Proteins: Structure, Function, and Motion by Amit Kessel and Nir Ben-Tal (2nd Edition, ISBN: 1498747175) for BMB803 (electronic version and a hard copy available at the MSU library). Enzymatic Reaction Mechanisms by Perry A. Frey and Adrian D. Hegeman (ISBN: 0195122585) for BMB805 (electronic version is available at the MSU library).

Grading

For BMB 803, the total of points is 280 (10 points per lecture). Dr. Hu's materials count 18/28, 180 points in total: 50% points from homework assignment and 50% points from the final group presentation. Dr. Dickson's materials count 10/28 (100 points) of the course grade, 50% from assignments and 50% for the final presentation.
For BMB 805, the total of points is 410, including 280 from Drs. Hu and Dickson (BMB803) and 130 from Drs. Hu and Hausinger. Of the 130 points for the materials of Drs. Hu and Hausinger, 60% will be from Exam 3 (given at the official final exam time – see below) and 40% points from homework.
There will be three examinations in the course: the first is a group presentation; the second is an individual presentation based on the materials provided by Dr. Dickson in BMB803; and the third exam covers the materials provided by Drs. Hu and Hausinger in BMB805. The exams are not cumulative.

Exam 1: Monday, Feb. 14, 9:00-10:00 am, group presentations
Exam 2: Monday, Mar. 24, 9:10-10:00 am, individual presentations
Exam 3: Tuesday, Apr. 29 12:45pm - 2:45pm, open book exam, 101 Biochemistry Bldg.

Holidays and Breaks

Martin Luther King Day Jan. 20; Spring break Mar. 2 - Mar. 9. No class on these days.

Schedule

Dr. Hu (13 lectures + group presentations, Jan. 13 – Feb. 14)

1. ***Course Introduction and Overview of Protein Functions***
2. ***Primary, Secondary, and Tertiary Structure:*** properties and covalent modifications of amino acids, types of secondary structure and intrinsically disordered proteins/regions, super-secondary structures, and tertiary structures
3. ***Primary, Secondary, and Tertiary Structure (Continued)***
4. ***Proteins Structure Determination:*** general strategy, approaches of structure determination (NMR, X-ray crystallography, and cryo-EM)
5. ***Noncovalent Forces in Protein Structure:*** electrostatic, nonpolar, hydrogen bonds, hydrophobic effects
6. ***Conformational Changes and Dynamics:*** motion at different time scales and methods of detection
7. ***Protein-Ligand and Protein-Protein Interactions:*** biological functions, binding constants, cooperativity, binding constant measurement
8. ***Protein Folding and Protein Stability:*** folding landscape and kinetics, folding models, folding intermediate, molecular chaperones
9. ***Membrane Proteins:*** classification, protein-membrane interactions, structure features, and biological functions
10. ***Membrane Mimetics in Membrane Protein Research***
11. ***Channels:*** potassium channels, voltage-gating mechanism
12. ***Carriers:*** glucose transporters, P-type ATPases
13. ***Receptors:*** glutamate receptors (ligand-gated ion channel and GPCR)
14. ***Group Presentations***

Dr. Dickson (7 lectures + 3 labs + in-class presentations, Feb. 17 – Mar. 17)

15. ***Review of protein structure concepts, digital representations of chemical structure***
16. ***Sequence analysis:*** sequence vs. structural homology; homologs, orthologs and paralogs; evolutionary conservation; tools for quantify sequence homology (BLAST)
17. ***Lab 1: Introduction to VMD (Visual Molecular Dynamics):*** loading biomolecular coordinates and topologies; constructing representations; changing viewpoints; rendering images
18. ***Structural analysis:*** Protein Data Bank; root mean squared distance; alignment and rotation matrices; TM-SCORE; alignment of heterogeneous structures
19. ***UniProt and online databases:*** GO terms; ChEMBL; DisGenNET; BioMUTA; DrugBank; BioGRID
20. ***Lab 2: Building molecular environments with CHARMM-GUI:*** Chain selection; post-translational modifications; loop modeling; multi-component assembler
21. ***Homology Modeling and Structure Prediction:*** CASP competitions; PSI-BLAST; SWISS-MODEL; multiple sequence alignments; AlphaFold
22. ***Structure and Model-Based Drug Design:*** Binding free energy; receptor-based vs ligand-based screening; top-performing algorithms; pharmacophore screening example
23. ***Lab 3: Predicting protein complexes with AlphaFold***
24. ***Project presentations***

Dr. Hu (4 lectures, Mar. 19 – Mar. 26)

25. ***General Catalytic Mechanisms of Enzymes***
26. ***Transition State Theory and Transition State Determination:*** theory, kinetic isotope effects and transition state analog in drug design

27. ***Enzyme Kinetics and Inhibition:*** theory and enzyme inhibitors
28. ***Directed Evolution:*** theory, approaches, and examples

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End of BMB 803

Dr. Hu (8 lectures, Mar. 28 – Apr. 14)

29. ***Types of enzymatic reactions***
30. ***Acyl transfer:*** serine proteases and inhibitors
31. ***Acyl transfer (continued):*** cysteine protease, aspartic protease and metalloprotease, and protease inhibitors
32. ***Phosphoryl transfer:*** kinases and phosphatases
33. ***Aldolases:*** C-C bond formation/cleavage
34. ***Thiamine pyrophosphate (TPP)-dependent enzymes:*** C-C bond formation/cleavage and decarboxylation
35. ***RuBisCO:*** CO_2 fixation (carboxylation) with an inevitable oxygenation side reaction
36. ***Biotin and biotin synthase:*** biotin-dependent enzymes, radical SAM enzymes, and Fe-S clusters

Dr. Hausinger (5 lectures, Apr. 16 – Apr. 25)

37. ***Introduction to pyridoxal phosphate (PLP) chemistry:*** Ornithine decarboxylase and mechanism-based inhibitors
38. ***Other PLP-dependent chemistries:*** Racemase, transaminase, β-elimination/replacement
39. ***Introduction to NAD(P)-dependent hydride-transfer enzymes:*** Glyceraldehyde phosphate (GAP) dehydrogenase
40. ***Methylation and Demethylation chemistry: focused on epigenetics***
41. ***Other FAD-dependent chemistries:*** Oxidases, dehydrogenases, and additional examples

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End of BMB 805