

## **BMB 803/805: Protein Structure, Design, and Mechanism, Spring 2026**

**Classroom:** 101 Biochemistry Bldg.

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

**BMB 803 Dates:** Jan. 12 – Mar. 25; 28 lectures/labs by Hu & Dickson

**BMB 805 Dates:** Jan. 13 – Apr. 24; BMB 803 + 13 lectures by Hu & Lohman

### **Instructors**

Jian Hu, 501 Biochemistry, 353-8680, [hujian1@msu.edu](mailto:hujian1@msu.edu)

Alex Dickson, 310C Biochemistry, 884-8985, [alexrd@msu.edu](mailto:alexrd@msu.edu)

Jeremy Lohman, 517 Biochemistry, 353-7751, [jlohman@msu.edu](mailto:jlohman@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 (2<sup>nd</sup> 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 individual presentation.

For BMB 805, the total of points is 410, including 280 from Drs. Hu and Dickson (BMB803) and 130 from Drs. Hu and Lohman. Of the 130 points for the materials of Drs. Hu and Lohman, 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 Lohman in BMB805. The exams are not cumulative.

Exam 1: Monday, Feb. 13, 9:00-10:00 am, group presentations

Exam 2: Monday, Mar. 16, 9:10-10:00 am, individual presentations

Exam 3: Tuesday, Apr. 28 12:45pm - 2:45pm, open book exam, 101 Biochemistry Bldg.

### **Holidays and Breaks**

Martin Luther King Day Jan. 19; No class held Feb. 13; Spring break Feb. 28 - Mar. 8. No class on these days.

## Schedule

Dr. Hu (14 lectures + in-class group presentations, Jan. 12 – Feb. 16)

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. **Directed Evolution:** theory, approaches, and examples
15. **Group Presentations**

Dr. Dickson (6 lectures + 3 labs + in-class individual presentations, Feb. 18 – Mar. 18)

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

Dr. Hu (3 lectures, Mar. 20 – Mar. 25)

26. **General Catalytic Mechanisms of Enzymes**

27. **Transition State Theory and Transition State Determination:** theory, kinetic isotope effects and transition state analog in drug design
28. **Enzyme Kinetics and Inhibition:** theory and enzyme inhibitors
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*End of BMB 803*

Dr. Hu (8 lectures, Mar. 27 – Apr. 13)

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<sub>2</sub> fixation (carboxylation) with an inevitable oxygenation side reaction
36. **Biotin and biotin synthase:** biotin-dependent enzymes, radical SAM enzymes, and Fe-S clusters

Dr. Lohman (5 lectures, Apr. 15 – Apr. 24)

37. **Introduction to pyridoxal phosphate (PLP) chemistry:** Ornithine decarboxylase and mechanism-based inhibitors
38. **Other PLP-dependent chemistries:** Racemase, transaminase,  $\beta$ -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*