Syllabus QBIO 481 Fall 2024

Structural Bioinformatics from Atoms to Cells

Time and Location:

Lectures: TTh 11:00 am – 12:20 pm RRI 101

Discussion: F 4:00 – 5:00 pm RRI 301

Instructors:

Dr. Tsu-Pei Chiu	RRI 413J	tsupeich@usc.edu

Teaching Assistants:

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Description:

This course will introduce the principles of computational structural biology ranging in scope from the molecular structures of biological macromolecules to their structural organization at the cellular level. Structural bioinformatics methods are introduced for the analysis and structural prediction of proteins, nucleic acids and their assemblies. The principles of molecular interactions and recognition are illustrated. We will exemplify all computational and theoretical approaches with practical examples, and introduce related software packages and databases.

Goals:

The students shall obtain necessary skills to analyze and predict structural properties of biological macromolecules and complexes, which includes proteins and nucleic acids. Our students shall gain a good understanding of key concepts of structure and dynamics of biological assemblies at the atomic, molecular, and cellular level. Prior programming experience is not required for this course.

Required reading:

The Molecules of Life – Physical and Chemical Principles. First Edition, 2012. John Kuriyan, Boyana Konforti, and David Wemmer. Garland Science. Taylor & Francis. The book can be rented or purchased on amazon.com, or required Chapters can be purchased directly from Garland Science.

Recommended reading:

Introduction to Proteins – Structure, Function, and Motion. Second Edition, 2018. Amit Kessel and Nir Ben-Tal. CRC Press. Taylor & Francis Group.

Structural Bioinformatics, Vol. 44, Series: Methods of Biochemical Analysis; 2005, Editor(s): Philip E. Bourne, Helge Weissig. Print ISBN: 9780471202004; Online ISBN: 9780471721208; DOI: 10.1002/0471721204

Course contents:

Biological web resources, structure databases, structure alignment, protein, DNA, and RNA structure, molecular recognition, machine learning methods for modeling DNA and protein structure and their interactions, dynamics, and nucleic acid binding, and computational approaches for structural analysis and molecular simulation.

Grade:

Course grade will be based on homework, a mid-term and final examination as follows:

Percentage of final grade:
Homework Projects: 40 %
Mid-term Examination: 30 %
Final Examination: 30 %

The final and mid-term examinations will be comprehensive written tests. Four homework projects will be assigned by the instructors. You should hand in your projects by the due date specified by the instructors. Points will be subtracted for projects submitted after the due date.

Tentative Schedule:

Weekly discussion sections will be held every Friday 4-5 pm (led by TA). These discussion sections are not obligatory but rather offered to complement the lectures. We also plan to provide a Q&A Forum for accessibility of the course.

Week 1: Lectures 1 and 2 08/27/24-08/29/24

Topics: Introduction to Structural Bioinformatics / Molecular structure / Energy and intermolecular forces / Visualization of molecular structures / Protein Data Bank
Reading: The Molecules of Life, Ch. 1

Week 2: Lectures 3 and 4 09/03/24-09/05/24

Topics: Protein structure / Calculation of bond and torsion angles / Secondary structure elements / Ramachandran plot / Hierarchy of protein structure
Reading: The Molecules of Life, Ch. 4A-B and 6C

Week 3: Lectures 5 and 6 09/10/24-09/12/24

Topics: Nucleic acid structure / Calculation of helical parameters / RNA vs. DNA

Reading: The Molecules of Life, Ch. 2

Release of Assignment 1

Week 4: Lectures 7 and 8 09/17/24-09/19/24

Topics: Electrostatics / Electrostatics calculations and solvation models / Poisson-Boltzmann equation

Reading: Honig & Nicholls Science 268, 1144-1149, 1995 (will be on Brightspace)

Week 5: Lectures 9 and 10 09/24/24-09/26/24

Topics: Force fields / Structure prediction / Molecular dynamics and Monte Carlo simulations / Data mining and high-throughput DNA shape prediction

Reading: Rohs et al. Nature 461, 1248-1253, 2009 and Zhou et al. NAR, 41, W56-W62, 2013 (will be on Brightspace)

Week 6: Lectures 11 and 12 10/01/24-10/03/24

Topics: Structure determination / X-ray crystallography and NMR spectroscopy / Cryo electron microscopy

Release of Assignment 2

Week 7: Lectures 13 10/08/24

Topics: Affinity and specificity in molecular interactions / Cooperativity through cofactor and oligomerization / Energetic of binding / Protein-nucleic acid recognition / Transcription factors / Nucleosome

Reading: The Molecules of Life, Ch. 13A+13C

Review for Midterm

Week 8: Lecture 14 10/15/24, 11 am – 1 pm (RRI 221 and 321)

Midterm Exam

Week 9: Lectures 15 and 16 10/22/24-10/24/24

Topics: High-throughput experiments for probing protein-DNA binding / Machine learning techniques for binding specificity predictions / Introduction to Machine Learning / Linear regression / Classification

Reading: Zhou et al. PNAS 112, 4654-4659, 2015 (will be on Brightspace)

Release of Assignment 3

Week 10: Lectures 17 and 18 10/29/24-10/31/24

Topics: Predicting DNA shape and protein-DNA binding specificity / Introduction to Neural Network and deep learning

Reading: Li et al. Nat. Commun. 15, 1243, 2024 and Chiu et al. PNAS 120, e2205796120, 2023 (will be on Brightspace)

Week 11: Lectures 19 and 20 11/05/24-11/07/24

Topics: Protein folding problem / Energy and kinetics of folding / Protein structure modeling / Advanced modeling methods using AlphaFold and RoseTTAFold

Reading: Jumper et al. Nature 596, 583-589, 2021 (will be on Brightspace)

Week 12: Lectures 21 and 22 11/12/24-11/14/24

Topics: Prediction of protein-DNA contact and binding specificity / Introduction to geometric deep learning

Reading: Mitra et al. Nature Methods, https://doi.org/10.1038/s41592-024-02372-w, 2024, and Sagendorf et al. Biophysical Review, 16, 297-314, 2024 (will be on Brightspace)

Release of Assignment 4

Week 13: Lectures 23 and 24 11/19/24-11/21/24

Topics: Genome architecture / Chromatin structure and organization / Predicting chromatin states / Enhancer-promoter interactions / Hi-C data analysis and 3D genome reconstruction

Week 14: Lecture 25 11/26/24

Topics: Approaches to modeling cell organells and whole cells / Cryo electron tomography

Reading: Thornburg et al, 2022. Fundamental behaviors emerge from simulations of a living minimal cell. Cell.185(2):345-60.e28. 2022 (will be on Brightspace).

Week 15: Lectures 26 and 27 12/03/24-12/05/24

Guest speaker

Review for the Final Exam.

Study Days: 12/07/24-12/10/24

Final Exam, 12/12/22, 8-10 am

Please note that some reading assignments and homework due dates will be announced at a later time.

Statement for Observance of Religious Holidays:

The university's policy grants students excused absences from class to observe religious holidays (http://orl.usc.edu/religiouslife/holydays/absences.html). In this case, please contact your instructor in advance to agree on alternative course requirements.

Statement for Students with Disabilities:

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 your instructor as early in the semester as possible. DSP is located in STU 301 and is open 8:30 a.m.–5:00 p.m., Monday through Friday. The phone number for DSP is (213) 740-0776.

Statement on Academic Integrity:

USC seeks to maintain an optimal learning environment. General principles of academic honesty include the concept of respect for the intellectual property of others, the expectation that individual work will be submitted unless otherwise allowed by an instructor, and the obligations both to protect one's own academic work from misuse by others as well as to avoid using another's work as one's own. All students are expected to understand and abide by these principles. SCampus, the Student Guidebook, contains the Student Conduct Code in Section 11.00, while the recommended sanctions are located in Appendix A: http://www.usc.edu/dept/publications/SCAMPUS/gov/. Students will be referred to the Office of Student Judicial Affairs and Community Standards for further review, should there be any suspicion of academic dishonesty. The Review process can be found at: http://www.usc.edu/student-affairs/SJACS/.

Statement on Academic Conduct and Support Systems

Academic Conduct:

Plagiarism – presenting someone else's ideas as your own, either verbatim or recast in your own words – is a serious academic offense with serious consequences. Please familiarize yourself with the discussion of plagiarism in SCampus in Part B, Section 11, "Behavior Violating University Standards" policy.usc.edu/scampus-part-b. Other forms of academic dishonesty are equally unacceptable. See additional information in SCampus and university policies on scientific misconduct, policy.usc.edu/scientific-misconduct.

Support Systems:

Student Health Counseling Services - (213) 740-7711 – 24/7 on call
engemannshc.usc.edu/counseling
Free and confidential mental health treatment for students, including short-term psychotherapy, group counseling, stress fitness workshops, and crisis intervention.
National Suicide Prevention Lifeline - 1 (800) 273-8255 – 24/7 on call suicidepreventionlifeline.org
Free and confidential emotional support to people in suicidal crisis or emotional distress 24 hours a day, 7 days a week.
Relationship and Sexual Violence Prevention Services (RSVP) - (213) 740-4900 – 24/7 on call
engemannshc.usc.edu/rsvp
Free and confidential therapy services, workshops, and training for situations related to gender-based harm.

Office of Equity and Diversity (OED) | Title IX - (213) 740-5086 equity.usc.edu, titleix.usc.edu
Information about how to get help or help a survivor of harassment or discrimination, rights of protected classes, reporting options, and additional resources for students, faculty, staff, visitors, and applicants. The university prohibits discrimination or harassment based on the following protected characteristics: race, color, national origin, ancestry, religion, sex, gender, gender identity, gender expression, sexual orientation, age, physical disability, medical condition, mental disability, marital status, pregnancy, veteran status, genetic information, and any other characteristic which may be specified in applicable laws and governmental regulations.

Bias Assessment Response and Support - (213) 740-2421
studentaffairs.usc.edu/bias-assessment-response-support
Avenue to report incidents of bias, hate crimes, and microaggressions for appropriate investigation and response.
The Office of Disability Services and Programs - (213) 740-0776 dsp.usc.edu
Support and accommodations for students with disabilities. Services include assistance in providing readers/notetakers/interpreters, special accommodations for test taking needs, assistance with architectural barriers, assistive technology, and support for individual needs.
USC Support and Advocacy - (213) 821-4710

studentaffairs.usc.edu/ssa
Assists students and families in resolving complex personal, financial, and academic issues adversely affecting their success as a student.

Diversity at USC - (213) 740-2101
diversity.usc.edu
Information on events, programs and training, the Provost's Diversity and Inclusion Council, Diversity Liaisons for each academic school, chronology, participation, and various resources for students.

USC Emergency - UPC: (213) 740-4321, HSC: (323) 442-1000 – 24/7 on call
dps.usc.edu, emergency.usc.edu
Emergency assistance and avenue to report a crime. Latest updates regarding safety, including ways in which instruction will be continued if an officially declared emergency makes travel to campus infeasible.

USC Department of Public Safety - UPC: (213) 740-6000, HSC: (323) 442-120 – 24/7 on call
dps.usc.edu
Non-emergency assistance or information.