Syllabus QBIO 481 Fall 2023 **Updated**

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. Remo Rohs (1st part)	RRI 413H; (213) 740-0552	rohs@usc.edu
Dr. Vsevolod Katritch (2nd part)	MCB 317; (213) 821-1488	katritch@usc.edu

Teaching Assistants:

Raktim Mitra (1st part)	RRI 413M	raktimmi@usc.edu
Ao Xu (2nd part)	MCB 320	aoxu@usc.edu

Short Course Description:
Introduction to physical and statistical methods, molecular simulations, machine learning and AI for structural bioinformatics studies of proteins, nucleic acids, molecular complexes, and whole cells.

Course 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 the structure and dynamics of biological assemblies at the atomic, molecular, and cellular levels. 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 the 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, threading, deep learning methods for modeling protein structure and interactions, dynamics, and nucleic acid binding, and computational approaches for structural analysis and molecular simulation.

Grade:
The course grade will be based on homework, the mid-term, and the final examination as follows:

Percentage of final grade:	
Homework Projects:	33 %
Mid-term Examination:	33 %
Final Examination:	33 %

The final and mid-term examinations will be comprehensive written tests. Six 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 the accessibility of the course.

Week 1: Lectures 1 and 2 (Rohs) 08/22/23-08/24/23

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

Week 2: Lectures 3 and 4 (Rohs) 08/29/23 -08/31/23

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 (Rohs) 09/05/23-09/07/23

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

Reading: The Molecules of Life, Ch. 2

Week 4: Lectures 7 and 8 (Rohs) 09/12/23-09/14/23

Guest Lecture 9/12 "Coevolution of Structural Biology and the Protein Data Bank" by Dr. Helen Berman, Founder of the Protein Data Bank, Member of the National Academy of Sciences

Guest Lecture 9/14 "Artificial Intelligence and Bioinformatics – A 30-year Personal Journey" by Dr. Soheil Shams, Founder of BioDiscovery, CIO of Bionano Genomics, Founder of TESA Research

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

Week 5: Lectures 9 and 10 (Rohs) 09/19/23-09/21/23

Guest Lecture 9/19 "Modeling Protein-DNA Binding Using Machine Learning Techniques" by Dr. Tsu-Pei Chiu, Postdoc in Rohs Lab, QCB Department

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

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

Week 6: Lectures 11 and 12 (Rohs) 09/26/23-09/28/23

Topics: Force fields / Structure prediction / Molecular dynamics and Monte Carlo simulations

Reading: Rohs et al. Nature 461, 1248-1253, 2009 (will be on Blackboard)

Week 7: Lectures 13 and 14 (Rohs) 10/03/23-10/05/23

Topics: Structure determination / X-ray crystallography and NMR spectroscopy / Cooperativity / Transcription factors / Nucleosome / Review for Midterm

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

Week 8: Midterm Exam (Rohs), 10/10/22, 11 am – 1 pm (RRI 221 and 321)

Fall Recess

Week 9: Lectures 16 and 17 (Katritch) 10/17/23-10/19/23

Topics: Overview structural biology of the cell – historic perspective - breakthrough discoveries. Protein structure motifs / Protein structure variation and structure space

Week 10: Lectures 18 and 19 (Katritch) 10/24/23-10/26/23

Topics: Protein sequence similarity / Sequence alignment and dynamic programming / Protein structure alignment and RMSD/ Protein classification/ Fold recognition

Week 11: Lectures 20 and 21 (Katritch) 10/31/23-11/02/23

Topics: Protein folding problem / Energy and kinetics of folding/ MD simulations / Protein structure modeling/ Comparative modeling and ab initio methods/ Deep learning prediction of protein structures

Reading: Jumper et al. Highly accurate protein structure prediction with AlphaFold. Nature. 2021;596(7873):583-9

Week 12: Lectures 22 and 23 (Katritch) 11/07/23-11/09/23

Topics: Protein interactions: Detection of interactions and principles of protein recognition / Structure determination of protein complexes / Interaction Networks

Week 13: Lectures 24 and 25 (Katritch) 11/14/23-11/16/23

Topics: Modeling of protein complexes / Prediction of protein interactions / Protein docking methods / Deep learning prediction of protein interactions

Structural modeling of membrane proteins/ organization of the membrane / Conformational plasticity / Allosteric modulation models

Reading: Evans Protein complex prediction with AlphaFold-Multimer. bioRxiv. 2022:2021.10.04.463034. doi: 10.1101/2021.10.04.463034.

Optional: Fontana et al Structure of cytoplasmic ring of the nuclear pore complex by integrative cryo-EM and AlphaFold. Science. 2022;376(6598)

Week 14: Lecture 26 (Katritch) 11/21/23

Topics: / Methods for determining the ultrastructures of cells and the cellular distribution of proteins and complexes / Cryo-electron tomography

Week 15: Lectures 28 and 29 (Katritch) 11/28/23-11/30/23

Approaches to modeling cell organelles and whole cells.

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

Review for the Final Exam.

Study Days: 12/02/23-12/05/23

Final Exam (Katritch), 12/12/23, 8 – 10 am (place TBA)

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.