## **LAND ACKNOWLEDGEMENT**

UBC’s Point Grey Campus is located on the traditional, ancestral, and unceded territory of the xwməθkwəy̓əm (Musqueam) people. The land it is situated on has always been a place of learning for the Musqueam people, who for millennia have passed on their culture, history, and traditions from one generation to the next on this site.

##

## **COURSE INFORMATION**

|  |  |  |
| --- | --- | --- |
| **Course Title** | **Course Code Number** | **Credit Value** |
| Advanced Topics in Protein Chemistry II | BIOC 559 | 1.5 |

###

### **PREREQUISITES**

### This course is restricted to students in one of these programs: BSC with one of these specializations: HON BIOC -OR- in one of these faculties: GRAD -OR- in one of these programs: BSC with one of these specializations: HON \*\*\*\* not with any of these specializations: \*\*\*\*CHEM -OR- in one of these programs: BSC with one of these specializations: CHN BIOC

### **COREQUISITES**

## See above.

### **COURSE LOCATION AND TIME**

|  |  |
| --- | --- |
| **Time** (Day(s), Hour) | **Room** |
| Tuesdays and Thursdays, 3:30pm – 5:00pm | DMCBH Meeting Room 3402A/B/C |

##

## **COURSE CHAIR**

|  |  |
| --- | --- |
| **Course Chair** | **Contact Details** |
| Prof. Sriram Subramaniam (he/him/his) | sriram.subramaniam@ubc.ca |

##

## **COURSE INSTRUCTOR(S)**

|  |  |  |  |
| --- | --- | --- | --- |
| **Course Instructor(s)** | **Contact Details** | **Office Location** | **Office Hours** |
| Prof. Sriram Subramaniam (he/him/his) and colleagues | sriram.subramaniam@ubc.ca | DMCBH 3406  | By appointment |

## **LEARNING OUTCOMES**

At the conclusion of the course, students will have an understanding of principles of cryo-electron microscopy and cryo-electron tomography and will develop critical insights into the types of problems in modern structural and cell biology that can be addressed using these methods.

## **COURSE OUTLINE**

This course is intended to provide a broad introduction to the principles of 3D electron microscopy and its application to important problems in biology. One half of the course will cover lectures on the principles and use of cryo-electron microscopy, electron tomography and focused ion beam technology in structural biology. The material will be introduced via lectures as well as in-class tutorials spanning some aspects of data processing. The other half of the course will involve student presentations of recently published papers to give them experience in critically reading current literature in the field. Grading will be based on the presentations and in-class participation. This course will be offered once every two years starting in Fall 2022.

**COURSE SCHEDULE**

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| --- |
| Term 1 (12 lectures | TUESday/THURSDAY | 3:30pm-5:00pm | DMCBH 3402A: |
| **Oct 25 (T)** Lecture 1: Introduction to Cryo-EM Part 1 (Sriram Subramaniam) |
| **Oct 27 (Th)** Lecture 2\*:  Introduction to Cryo-EM Part 2 (Sriram Subramaniam) & Visit to EM Lab   |
| **Nov 1 (T)** Lecture 3\*:  Cryo-EM Image Analysis Examples and Tutorial (Dhiraj Mannar + Geoffrey Woollard)  |
| **Nov 3 (Th)** Lecture 4\*:  Cryo-EM Image Analysis : Theory (Khanh Dao Duc) and Practice (James Saville and  Spencer Cholak) |
| **Nov 8 (T)** Lecture 5:  Student Presentations #1 |
| **Nov 10 (Th)**  **No class because of Reading Week****Nov 15 (T)** Lecture 6: Cryo-Electron Tomography (Cryo-ET) (Elitza Tocheva)**Nov 17 (Th)** Lecture 7: Student Presentations #2 **Nov 22 (T)** Lecture 8: Student Presentations #3**Nov 24 (Th)** Lecture 9: Student Presentations #4**Nov 29 (T)** Lecture 10: Student Presentations #5**Dec 1 (Th)** Lecture 11: Student Presentations #6 + course wrap-up (Sriram Subramaniam) **\* On these three days, the class will be extended by 30 minutes to make up for the lost day of classes on Nov. 10**  |

## **COURSE MATERIALS**

The cryo-EM field is relatively new and continues to evolve rapidly. Here are some useful references to material that you will find useful, probably more so after an initial introduction to the subject in the class. The first two have dozens of hours of videos and that will serve you as a reference for a long time to come, while the third is more like a current textbook that provides a very good overview of concepts and applications.

1. <https://em-learning.com/>
2. <https://cryoemprinciples.yale.edu/video-lectures>
3. <https://iopscience.iop.org/book/edit/978-0-7503-3039-8>

## **GRADING SCHEME**

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| --- | --- |
| **Assignment**  | **Grade Weight** |
| Student presentation of assigned paper | 60 % |
| Class participation | 40 % |

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## **GRADING AND COURSE POLICY**

## Students are expected to be present to all classes, unless excused, and participate in each lecture by either asking questions, answering questions raised by the course instructor or sharing their points of view.

## Students with disabilities and ongoing medical conditions have the option to request an [accommodation](https://students.ubc.ca/enrolment/academic-learning-resources/academic-accommodations-disabilities) for the course assessments after registering with the [Centre for Accessibility](https://students.ubc.ca/about-student-services/centre-for-accessibility/registering-centre-accessibility).

## **If you are ill, please do not attend class. If you do miss class/assessments because of illness, you will still have access to the material presented and can arrange to meet with the course chair for any further clarification.**

**If the instructor is sick:** We will all do our best to stay well, but if one of the instructors falls ill then they will not come to class. If that happens, all efforts will be made to communicate that to students in a timely manner prior to class time, usually via an announcement in Canvas. Depending on the situation a substitute lecturer will take over, the lecture may take place over zoom, or the class may be cancelled.

##

## **STUDENT PRESENTATIONS**

Papers for presentation will be grouped thematically and provide an opportunity for students to get a first-hand experience in reading, understanding and presenting current papers that communicate important results. For each of the six days that are allocated for student presentations, three students will make presentations. Each student will have a chance to select a day from the set of six days (see below) for presentations, with each day covering a specific topic. For each topic, a set of several papers is available (see below), and students are encouraged to browse through the topics and papers before the start of the course. When the course begins, students will have access to a spreadsheet where they can select the paper of their choice on a first-come first-served basis. Each student should plan for a presentation of approximately 15-20 minutes on the day of their presentation, with 10-15 minutes reserved for questions and discussion.

Topics for student presentations:

1. Cryo-EM and COVID-19 (November 8)
2. Cryo-EM of ion channels and transporters (November 17)
3. Cryo-EM of DNA-protein complexes (November 22)
4. Cryo-ET of prokaryotic cells (November 24)
5. Focused ion beams, cryo-ET and light/electron correlative imaging (November 29)
6. Integrative structural biology with cryo-EM, cryo-ET and AI/machine learning (December 1)

| 1. **Cryo-EM and COVID-19**
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| --- |
| [SARS-CoV-2 neutralizing antibody structures inform therapeutic strategies](https://www.nature.com/articles/s41586-020-2852-1) |
| [Defining variant-resistant epitopes targeted by SARS-CoV-2 antibodies: A global consortium study](https://www.science.org/doi/10.1126/science.abh2315?url_ver=Z39.88-2003&rfr_id=ori:rid:crossref.org&rfr_dat=cr_pub%20%200pubmed) |
| [Receptor binding and priming of the spike protein of SARS-CoV-2 for membrane fusion](https://www.nature.com/articles/s41586-020-2772-0) |
| [Structural basis for backtracking by the SARS-CoV-2 replication–transcription complex](https://www.pnas.org/doi/abs/10.1073/pnas.2102516118?url_ver=Z39.88-2003&rfr_id=ori:rid:crossref.org&rfr_dat=cr_pub%20%200pubmed) |
| [Structural basis for inhibition of the RNA-dependent RNA polymerase from SARS-CoV-2 by remdesivir](https://www.science.org/doi/10.1126/science.abc1560?url_ver=Z39.88-2003&rfr_id=ori:rid:crossref.org&rfr_dat=cr_pub%20%200pubmed) |
| [Structure of SARS-CoV-2 membrane protein essential for virus assembly](https://www.nature.com/articles/s41467-022-32019-3) |

| 1. **Cryo-EM of ion channels and transporters**
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| --- |
| [Structures of the T cell potassium channel Kv1.3 with immunoglobulin modulators](https://www.nature.com/articles/s41467-022-31285-5) |
| [Structural and electrophysiological basis for the modulation of KCNQ1 channel currents by ML277](https://www.nature.com/articles/s41467-022-31526-7) |
| [Architecture of the human erythrocyte ankyrin-1 complex](https://www.nature.com/articles/s41594-022-00792-w) |
| [Cryo-EM structure of human glucose transporter GLUT4](https://www.nature.com/articles/s41467-022-30235-5) |
| [Methotrexate recognition by the human reduced folate carrier SLC19A1](https://www.nature.com/articles/s41586-022-05168-0) |
| [Cryo-EM structure and electrophysiological characterization of ALMT from Glycine max reveal a previously uncharacterized class of anion channels](https://www.science.org/doi/10.1126/sciadv.abm3238?url_ver=Z39.88-2003&rfr_id=ori:rid:crossref.org&rfr_dat=cr_pub%20%200pubmed) |

| 1. **Cryo-EM of DNA-protein complexes**
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| --- |
| [Structure of a nucleosome-bound MuvB transcription factor complex reveals DNA remodelling](https://www.nature.com/articles/s41467-022-32798-9) |
| [Structure of the Dicer-2–R2D2 heterodimer bound to a small RNA duplex](https://www.nature.com/articles/s41586-022-04790-2) |
| [Mechanism of AAA+ ATPase-mediated RuvAB–Holliday junction branch migration](https://www.nature.com/articles/s41586-022-05121-1) |
| [Mechanism of replication origin melting nucleated by CMG helicase assembly](https://www.nature.com/articles/s41586-022-04829-4) |
| [Cryo-EM structure of MukBEF reveals DNA loop entrapment at chromosomal unloading sites](https://www.sciencedirect.com/science/article/pii/S1097276521008406) |
| [Cryo-EM structure of DNA-bound Smc5/6 reveals DNA clamping enabled by multi-subunit conformational changes](https://www.pnas.org/doi/10.1073/pnas.2202799119%22%20%5Cl%20%22sec-1) |

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| 1. **Cryo-ET of prokaryotic cells**
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| --- |
| [Visualizing translation dynamics at atomic detail inside a bacterial cell](https://www.nature.com/articles/s41586-022-05255-2) |
| [Cryo-Electron Tomography Reveals the Complex Ultrastructural Organization of Multicellular Filamentous Chloroflexota (Chloroflexi) Bacteria](https://www.frontiersin.org/articles/10.3389/fmicb.2020.01373/full) |
| [Flagellar Structures from the Bacterium Caulobacter crescentus and Implications for Phage ϕCbK Predation of Multiflagellin Bacteria](https://journals.asm.org/doi/10.1128/JB.00399-20) |
| [Cell Surface Filaments of the Gliding Bacterium *Flavobacterium johnsoniae* Revealed by Cryo-Electron Tomography](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2168446/) |
| [Structural dynamics of bacteriophage P22 infection initiation revealed by cryo-electron tomography](https://www.nature.com/articles/s41564-019-0403-z) |
| [Molecular mechanism for rotational switching of the bacterial flagellar motor](https://www.nature.com/articles/s41594-020-0497-2) |
| [Visualization of the type III secretion mediated Salmonella–host cell interface using cryo-electron tomography](https://elifesciences.org/articles/39514) |

| 1. **Focused ion beams, cryo-ET and light/electron correlative imaging**
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| --- |
| [Correlative three-dimensional super-resolution and block-face electron microscopy of whole vitreously frozen cells](https://www.science.org/doi/10.1126/science.aaz5357?siteid=sci&keytype=ref&ijkey=RUgVXfsXwdF4o) |
| [Whole-cell organelle segmentation in volume electron microscopy](https://www.nature.com/articles/s41586-021-03977-3) |
| [DNA origami signposts for identifying proteins on cell membranes by electron cryotomography](https://www.cell.com/cell/fulltext/S0092-8674%2821%2900076-3?rss=yes) |
| [Three-Dimensional Analysis of Mitochondrial Crista Ultrastructure in a Patient with Leigh Syndrome by *In Situ* Cryoelectron Tomography](https://www.sciencedirect.com/science/article/pii/S2589004218301020) |
| [Super-resolution confocal cryo-CLEM with cryo-FIB milling for in situ imaging of Deinococcus radiodurans](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8688812/) |
| [Label-free 3D-CLEM Using Endogenous Tissue Landmarks](https://www.sciencedirect.com/science/article/pii/S2589004218301007) |
| [Post-correlation on-lamella cryo-CLEM reveals the membrane architecture of lamellar bodies](https://www.nature.com/articles/s42003-020-01567-z) |
| [In situ cryo-electron tomography reveals filamentous actin within the microtubule lumen](https://rupress.org/jcb/article/219/9/e201911154/151828/In-situ-cryo-electron-tomography-reveals) |

| 1. **Integrative structural biology with cryo-EM, cryo-ET and AI/machine learning**
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| --- |
| [Structure of the cytoplasmic ring of the *Xenopus laevis* nuclear pore complex](https://www.science.org/doi/10.1126/science.abl8280?intcmp=trendmd-sci) |
| [Structure of cytoplasmic ring of nuclear pore complex by integrative cryo-EM and AlphaFold](https://www.science.org/doi/full/10.1126/science.abm9326) |
| [Architecture of the cytoplasmic face of the nuclear pore](https://www.science.org/doi/full/10.1126/science.abm9129) |
| [AI-based structure prediction empowers integrative structural analysis of human nuclear pores](https://www.science.org/doi/full/10.1126/science.abm9506) |
| [From structure to sequence: Antibody discovery using cryoEM](https://www.science.org/doi/10.1126/sciadv.abk2039) |
| [PTX3 structure determination using a hybrid cryoelectron microscopy and AlphaFold approach offers insights into ligand binding and complement activation](https://www.pnas.org/doi/full/10.1073/pnas.2208144119) |
| [Artificial intelligence-assisted cryoEM structure of Bfr2-Lcp5 complex observed in the yeast small subunit processome](https://www.nature.com/articles/s42003-022-03500-y) |
| [Model building of protein complexes from intermediate-resolution cryo-EM maps with deep learning-guided automatic assembly](https://www.nature.com/articles/s41467-022-31748-9) |

## **ACADEMIC MISCONDUCT**

UBC and the Department of Biochemistry and Molecular Biology take the issue of academic misconduct very seriously; the honest assessment of student learning is key to both the success of the university and success for individual students. Cheating, in any form, undermines the value of a degree and can have serious consequences for your continued academic success. As such it is important to know what your responsibilities are, what constitutes misconduct and how you can avoid it. With some effort and forethought no student should ever have to find themselves facing discipline for academic misconduct; inform yourself as to the expectations placed on you and what your responsibilities are. UBC definition of academic misconduct can be found in the [UBC Calendar](https://www.calendar.ubc.ca/vancouver/?tree=3,54,111,959) and additional information is available in this [UBC resource link](https://learningcommons.ubc.ca/resource-guides/understand-academic-integrity/).

**What consequences can arise from academic misconduct?**

The severity of the discipline can range from a letter of reprimand or a zero on the assignment in question all the way to expulsion from the University. Perhaps the most common outcome in these cases are grades of zero in the course in which the misconduct occurred.

**EQUITY DIVERSITY AND INCLUSION (EDI) POLICIES**

It is our goal that students from all diverse backgrounds and perspectives be well-served by this course, that students' learning needs be addressed both in and out of class, and diversity that the students bring to this class be viewed as a resource, strength and benefit. We make a commitment to present materials and activities that are respectful of diversity: gender identity, sexuality, disability, age, socioeconomic status, ethnicity, race, nationality, religion, and culture. We will foster a climate within the classroom where students of diverse backgrounds and identities feel comfortable sharing their opinions and experience with varied topics throughout the class. We (like many people) are learning about diverse perspectives and identities. If something was said in class (by anyone) that made you feel uncomfortable or if you observe a situation where someone else is made to feel uncomfortable, please talk to us about it. This includes concerns about any class-related interactions that lead to feelings of exclusion or marginalization. We welcome and encourage your feedback on how we can better cultivate a sense of inclusion in our course. This can be done through meetings, email or anonymous feedback through canvas. We aim to do our best to address each situation as it arises and effect meaningful changes moving forward. For more information visit our [departmental EDI webpage](https://biochem.ubc.ca/equity-diversity-inclusion/).

## **STUDENT RESOURCES**

UBC provides resources to support student learning and to maintain healthy lifestyles but recognizes that sometimes crises arise and so there are additional resources to access including those for survivors of sexual violence. UBC values respect for the person and ideas of all members of the academic community. Harassment and discrimination are not tolerated nor is suppression of academic freedom. UBC provides appropriate accommodation for students with disabilities and for religious observances. UBC values academic honesty and students are expected to acknowledge the ideas generated by others and to uphold the highest academic standards in all of their actions. Details of the policies and how to access support are available on[the UBC Senate website](https://senate.ubc.ca/policies-resources-support-student-success).

**Mental Health Resources**

In case you are struggling with mental health, or are feeling stressed or anxious, [UBC Counselling services](https://students.ubc.ca/health/counselling-services) provides information about a number of resources for students to use. Additionally, UBC students receive [mental health coverage of up to $1500](https://www.studentcare.ca/rte/en/UniversityofBritishColumbiaAMSGSS_Health_HealthCoverage_HealthPractitioners_Psychologists) under the AMS Health & Dental Plan (more information about coverage [here](https://www.studentcare.ca/rte/en/UniversityofBritishColumbiaAMSGSS_Health_HealthCoverage_HealthPractitioners_Psychologists)).

[Here2Talk](https://here2talk.ca/) is available for BC post-secondary students to talk with trained counsellors 24/7 (via voice call or text messages). If you are a student living in UBC residence, [Counsellors in Residence](https://vancouver.housing.ubc.ca/counsellor-in-residence/) can also be a valuable resource to provide mental health support. If you have a UBC email address, [Therapy Assistance Online (TAO)](https://ca.taoconnect.org/register) is a free online resource that provides tools to manage stress, relationship problems, substance use, etc.

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## **COVID RELATED POLICIES**

For UBC’s latest response to COVID-19, please visit [covid19.ubc.ca](https://covid19.ubc.ca/). For our in-person meetings in this class, it is important that all of us feel as comfortable as possible engaging in class activities while sharing an indoor space. Non-medical masks that cover our noses and mouths are a primary tool to make it harder for COVID-19 to find a new host. The higher the rate of vaccination is in our community overall, the lower the chance of spreading this virus. You are an important part of the UBC community. Please arrange to get vaccinated if you have not already done so. **If you’re sick, it’s important that you stay home – no matter what you think you may be sick with (e.g., cold, flu, other).**

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