

Cellular Imaging in Pathobiology

Course# LMP1006H

Department of Laboratory of Medicine and Pathobiology (LMP)
Faculty of Medicine, University of Toronto

Summary

This course explores the powerful intersection of Physics, Biological science, and Imaging technologies. Basic principles of optics such as the nature of light, diffraction, refraction, the nature of lenses, and the design of the light microscope will be covered in this course. We will discuss phase contrast, dark field, interference contrast, and modulation contrast, as well as polarization and fluorescence microscopy. Different types of microscopes and imaging technologies and their use in biological sciences including dissecting, compound, scanning and transmission electron microscopes, positron emission tomography, single photon emission computed tomography, nuclear magnetic resonance imaging, ultrasound, optical imaging, stereology and 3D imaging, optical microscopy, nanoscopy, live cell and whole animal imaging techniques, cytogenetics, X-ray crystallography and imaging in forensic science and their use in diagnostic pathology will be discussed. Some of the lectures will be complemented by laboratory sessions demonstrating these systems. As a result, students will have the opportunity for hands-on experience with state-of-the-art optical, electronic, and digital imaging equipment guided by an experienced staff from the University, hospitals, research facilities, government agencies as well as the industry. This course will focus on the theory, application and implementation of different imaging techniques, and more importantly, on application of biological experimentation relevant to modern biological research or clinical biochemical studies and the common real-life research goal in the industry, hospitals and research laboratories.

Objective

At the end of this course participants are expected to have acquired knowledge about different types of microscopes and imaging technologies, their functionality and use in biological sciences. The course will provide students with the knowledge and expertise to implement cutting edge microscopic and imaging methods within their own laboratories.

Format

13 weeks, two-hour lecture and/or a laboratory session per week

Course Schedule

The course is scheduled for spring 2011.

Tuesdays between 10 AM to 12 PM (except March 29th from 9 AM to 1 PM).

Curriculum

Each lecture consists of theory and/or hands on microscopy, imaging instrument, research facility tour, laboratory sessions, and technology or instrument demonstrations.

Prerequisite

No specific courses are required; however, students should have successfully completed advanced courses in molecular biology, cell biology and/or biochemistry. Priority will be given to more senior PhD students.

Evaluation

Four methods of evaluation will be used:

(I) 10% Participation in Lectures and Laboratory Sessions

(II) 25% Midterm Test

The mark will be based on a 40-minute short multiple-choice midterm test (before the course drop-deadline). The exam would be based on the first four lectures.

(III) 35% Written Grant Proposal

The grant proposal will be in IRAP (Industrial Research Assistance Program) Small Project Grant-format. The grant proposal should include at least one imaging technology (max 4000 words). The application will be assessed on the basis of scientific merit and will be reviewed and judged based on: (1) how original the project is, (2) how well the project is planned, (3) how well the proposal budget is developed, and (4) what are the benefits that may result from this project? Course participants are encouraged to seek mentorship from an imaging technology expert for the specific method used in their grant proposal.

(IV) 30% Oral Presentation

The mark will be based on oral presentation of the grant application. The presentation will be judged based on: (1) is the message of the presentation concise and well articulated? (2) is the presentation well structured? (3) does the presenter present her own point of view in an appropriate manner? (4) is the response to questions and comments competent, accurate and adequate? (5) is there sufficient evidence presented to support the argument? (6) is there evidence of acceptable critical thinking? (7) is the presentation original or creative in some way? (8) is time keeping managed well?

Course Coordinator

Sima Salahshor, PhD

Science & Hypothesis Accelerator Inc. (ScienceHA)

Email: salahshor@scienceha.com | Tel: 416-841-7959

Course Schedule

January 11th -April 5th 2011

Tuesdays 10 AM-12 PM (March 29th from 9 AM to 1 PM)

Lecture 1 (Jan 11)

Dr. Sima Salahshor

Department of Laboratory of Medicine and Pathobiology (LMP)
and Science & Hypothesis Accelerator Inc. (ScienceHA)

Title: Course and grant proposal introduction

Synopsis: Course content will be summarized and format and requirements for completing the grant proposal will be discussed.

Lecture 2 (Jan 18)

Dr. William Geddie

University Health Network, Department of Laboratory of Medicine and Pathobiology and
Princess Margaret Hospital, Ontario Cancer Institute

Title: Optical microscopy techniques and their application in diagnostic pathology

Synopsis: This 90 minute lecture will address the ways in which cells and tissues are imaged by either transmitting visible light through them, or reflecting it from their surfaces. Topics to be covered include the basic physics of optical microscopy in its most common form, bright field microscopy, and other ways in which the light microscope can be used to create contrast: polarized light, darkfield, phase, and differential interference contrast microscopy. Each of these topics will be illustrated with examples that illustrate how the development of light microscopy (and concomitant means of creating contrast by staining) revolutionized our concept of the cell, and how light microscopy remains the most essential technique used in diagnostic pathology. Some common problems encountered in microscope set-up, digital imaging, measurement, and preparation of digital photomicrographs for publication will also be presented.

Lecture 3 (Jan 25)

Dr. Kenichi Okamoto and Dr. Jeff Lee

Samuel Lunenfeld Research Institute, MT Sinai Hospital
Princess Margaret Hospital, Ontario Cancer Institute, Department of Medical Biophysics,
University of Toronto, Department of Laboratory Medicine and Pathobiology

Title: Introduction to 2-photon laser scanning microscopy techniques and applications (Dr. Okamoto)

Synopsis: This lecture will outline the principle of 2-photon laser scanning microscopy and applications of live imaging techniques combined with fluorescence probes. The live imaging

techniques that will be discussed include: molecular and cellular imaging, protein activity and interaction imaging using 2-photon laser microscopy. Also, this lecture will introduce recent photo-activation techniques using 2-photon laser light which can be used to manipulate specific molecular and protein functions in living tissue.

Title: X-ray crystallography: principles and applications (Dr. Lee)

Synopsis: X-ray crystallography has become the most common method to obtain three-dimensional structures of proteins and protein-protein complexes. This lecture will briefly describe the fundamentals of X-ray crystallography and its applications in medical research. Topics to be covered include background to structural biology and the techniques involved in structure determination. In addition, students will learn to critically examine crystal structures deposited in the Protein Data Bank. Finally, the importance of protein structures to drug development and biomedical research will be illustrated with real life examples.

Lecture 4 (Feb 1)

Dr. Sergio Grinstein and Dr. Brian Wilson

The Hospital for Sick Children, Department of Biochemistry, U of T
Department of Medical Biophysics, Ontario Cancer Research, Princess Margaret Hospital

Title: An overview of the fundamentals of fluorescence microscopy (Dr. Grinstein)

Synopsis: This lecture will cover the basic principles and will describe the equipment necessary to visualize fluorescently labeled specimens (both live and fixed). The topics featured will include the fundamentals of fluorophore absorption/excitation/emission, and microscope and camera optics. The goal is to familiarize students with the theoretical and practical aspects behind fluorescence microscopy, with a focus on cellular imaging.

Title: Advanced and Emerging Optical Microscopy Techniques (Dr. Wilson)

Synopsis: This lecture will cover some of the newest advances in optical microscopy that are likely to become important in studying normal and pathological cell structure and function. These include advanced confocal and hyperspectral techniques, super-resolution microscopy ('nanoscopy'), Raman microscopy, and the use of targeted molecular and nanoparticle-based optical reporters. The status, potential advantages and current limitations of each technique will be considered.

Mid Term Exam (Feb 8)

10 AM to 11 AM

Dr. Sima Salahshor

Department of Laboratory of Medicine and Pathobiology and ScienceHA

Mid-term Exam

Lecture 5 (Feb 8)

Dr. Grinstein, Paul Paroutis and Michael Woodside

The Hospital for Sick Children, Imaging Facility, McMaster North Annex and TMDT

Title: Basic and advanced live cell imaging: principles and applications (Paroutis and Grinstein)

Synopsis: This lecture will focus on four specialized fluorescence microscopy techniques pertaining to live cell imaging. More specifically, techniques such as total internal reflection microscopy (TIR-FM), fluorescence lifetime imaging (FLIM), fluorescence recovery after photobleaching (FRAP) and Forster resonance energy transfer (FRET) will be described, with a view to establishing quantitative measurements of protein mobility, protein-protein interactions and vesicle fusion.

Lecture 6 (Feb 15)

Dr. Sergio Grinstein, Paul Paroutis and Michael Woodside

The Hospital for Sick Children, Imaging Facility, McMaster North Annex and TMDT

Title: Live cell imaging

Synopsis: This laboratory session will build on previous lectures pertaining to fluorescence microscopy using a hands-on approach. Students will have the opportunity to use advanced imaging technology, including spinning-disk confocals, to image live cell samples. The basics of image acquisition will be examined and some basic image analysis tools will be employed, including three-dimensional reconstructions.

Lecture 7 (Feb 22)

Dr. Mary Ann George and Dr. Mary Shago

Cytogenomics Laboratory, Department of Paediatric Lab Medicine, and Cytogenomics & Genome Resources Facility, The Centre for Applied Genomics, The Hospital for sick Children

Title: Cytogenomic technologies to investigate genomic organization and structural alterations

Synopsis: This lecture will briefly introduce the field of cytogenetics and molecular cytogenetics and then outline the current major technologies that are used to detect both intra and interchromosomal rearrangements. These include methods used for bright field microscopy such as G-banding, C-banding as well as those used for fluorescence microscopy. There will be a focus on Fluorescence in situ Hybridization (FISH) applications including interphase and metaphase FISH, Spectral Karyotyping (SKY) and whole chromosome painting. The most appropriate choice of technology for validation, detection or characterization of specific chromosomal alterations will be discussed. Illustrative cases or projects from research and clinical settings will be presented.

Lecture 8 (March 1)

Dr. Rita Kandel and Douglas Holmyard

Mount Sinai Hospital, Department of Pathology and Laboratory Medicine and Advanced Bioimaging Centre

Title: Principle of Scanning (SEM) and Transmission Electron Microscopy (TEM)

Synopsis: General principles underlying electron microscope and differences between scanning and transmission microscopes will be discussed.

Lecture 9 (March 8)

Dr. Isabelle Aubert, Dr. Bojana Stefanovic and Cory Glowinski

Sunnybrook Health Sciences Centre, Imaging Research
Sunnybrook Research Institute

Title: In vivo imaging of brain hemodynamics (Dr. Stefanovic)

Synopsis: This lecture will present the physical basis of 2 imaging modalities for imaging of cerebral hemodynamics in preclinical models- two photon laser scanning microscopy and functional magnetic resonance imaging. The source of contrast, signal equation, system hardware, and basic tradeoffs of respective modalities will be presented; the experimental design described, and sample images shown.

Title: It's your data: Make it count, Make it shine. Introduction to unbiased stereology and virtual slices (Dr. Aubert)

Synopsis: This lecture will provide an introduction to a set of methods designed to rigorously quantify and present imaging data. Stereology is used to quantify the size, length, volume and number of objects (i.e. cells). Two-dimensional (2D) and three-dimensional (3D) virtual slide acquisition, analysis and presentation will also be discussed.

Lecture 10 (March 15)

Dr. David Jaffray and Lisa Di Diodato

STTARR Innovation Centre - part of the Radiation Medicine Program at Princess Margaret Hospital, located in the MaRS Toronto Medical Discovery Tower (TMDT)

Title: Introduction to Preclinical Imaging and STTARR Facility Tour

Synopsis: This lecture will explore the application of in-vivo imaging techniques (anatomical and/or functional MRI, CT, PET, SPECT, ultrasound, and optical imaging) in preclinical research. Scaled down, high resolution versions of these imaging systems are used at STTARR to visualize small-animal models of disease and evaluate the efficacy of corresponding diagnostic and therapeutic methods.

Lecture 11 (March 22)

Dr. Michael S. Pollanen and Dr. David A. Chiasson
Ontario Forensic Pathology, Service Chief Forensic Pathologist
The Hospital for Sick Children, Department of Paediatric Laboratory Medicine

Title: Forensic Pathobiology (Dr. Pollanen)

Title: Imaging techniques in medico-legal death investigation (Dr. Chiasson)

Synopsis: This lecture will explore how a variety of light microscopic and radiographic imaging techniques are utilized in medico-legal death investigation.

Final Exam (March 29)

9 AM to 1 PM, TMDT Rm 4-204

Dr. Sima Salahshor
Department of Laboratory of Medicine and Pathobiology
and Science & Hypothesis Accelerator (ScienceHA) Inc.

Final Evaluation: Grant proposal submission and oral presentation of the small grant application.

Cellular Imaging in Pathobiology

Department of Laboratory of Medicine and Pathobiology, Faculty of Medicine, University of Toronto
(January 11, 2011- March 29, 2011)

LMP1006H: Cellular Imaging in Pathobiology (Tuesdays 10 AM-12 PM)

Final Exam: March 29th from 9:00 AM to 1:00 PM

Coordinator: Dr. Sima Salahshor | Email: salahshor@scienceha.com | Tel: 416-841-7959

Lecture	Day	Time	Type	Location	Title	Professor/Instructor
1	Jan 11	10-12	Seminar	MaRS, TMDT Rm 4-204	Course and Grant Proposal Introduction & Review	Salahshor
2	Jan 18	10-12	Seminar	MSB, Rm 2290	Microscopy Techniques and their Application in Diagnostic Pathology	Geddie
3	Jan 25	10-11	Seminar	MSB, Rm 2290	2-photon laser scanning microscopy techniques and applications	Okamoto
3	Jan 25	11-12	Seminar	MSB, Rm 2290	X-ray Crystallography: Principles and Applications	Lee
4	Feb 1	10-11	Seminar	HSC, McMaster W, Rm 5008	An overview of the fundamentals of fluorescence microscopy	Grinstein
4	Feb 1	11-12	Seminar	HSC, McMaster W, Rm 5008	Advanced and Emerging Optical Microscopy Techniques	Wilson
5	Feb 8	10-11	Mid-Term	HSC, McMaster W, Rm 5008	Multiple-Choice Test	Salahshor
5	Feb 8	11-12	Seminar	HSC, McMaster W, Rm 5008	Basic and Advanced Live Cell imaging: Principles and Applications	Grinstein, Paroutis
6	Feb 15	10-12	Laboratory	HSC, McMaster Bld, North Annex	Live Cell Imaging	Woodside, Paroutis
7	Feb 22	10-11	Seminar	MaRS, TMDT Rm 14-203	Cytogenomic Technologies to Investigate Genomic Organization	George, Shago
7	Feb 22	11-12	Laboratory	MaRS, TMDT Rm 14-204	Cytogenomic Technologies to Investigate Structural Alterations	George, Shago
8	Mar 1	10-11	Seminar	MSH, Rm 6-412	Principle of Scanning and Transmission Electron Microscopy	Kandel, Holmyard
8	Mar 1	11-12	Laboratory	MSH, Rm 6-409	Scanning and Transmission Electron Microscopy Application	Kandel, Holmyard
9	Mar 8	10-11	Seminar	MaRS, TMDT, Rm 4-204	In Vivo Imaging of Brain Hemodynamics	Stefanovic
9	Mar 8	11-12	Seminar	MaRS, TMDT, Rm 4-204	Introduction to Unbiased Stereology and Virtual Slices	Aubert
10	Mar 15	10-11	Seminar	MaRS, TMDT, Rm 7-211	Introduction to Preclinical Imaging	Jaffray, Di Diodato
10	Mar 15	11-12	Laboratory	MaRS, TMDT, Rm 7-211	STTARR Facility Instruments	Di Diodato
11	Mar 22	10-11	Seminar	HSC, Elm St W, Rm 3-3108	Forensic Pathobiology	Pollanen
11	Mar 22	11-12	Seminar	HSC, Elm St W, Rm 3-3108	Imaging Techniques in Medico-Legal Death Investigation	Chiasson
12	Mar 29	09-13	Final Exam	MaRS, TMDT, Rm 4-204	Grant Proposal Submission and Oral Presentation of the Application	Salahshor

MSB = Medical Science Building, 1 King's College Circle

MSH = Mount Sinai Hospital, 600 University Avenue

STTARR = Spatio-Temporal Targeting and Amplification of Radiation Response, 101 College Street, Toronto Medical Discovery Tower , 7th Floor

TMDT = Toronto Medical Discovery Tower, 101 College Street

MaRS = Medical and Related Sciences, 101 College Street

HSC = Hospital for Sick Children, 555 University Avenue

Feb 1 and Feb 8: HSC, McMaster Bld., Room 5008 (Library). NB: McMaster Building is located on the north east corner of Elizabeth St and Elm St.

Feb 15: HSC, McMaster Bld, North Annex. NB: North Annex entrance is via the North Annex door at the McMaster Bld, at the east south corner of Elizabeth St. and Walton St. Please ring bell for entrance.

Course Schedule

Last updated March 2011