Nanoscale Imaging of Chemical and Biological Systems

"There's Plenty of Room at the Bottom."

Richard Feynman
American Physical Society, Caltech, 1959

Course description

Imagine you are an atom. How big is a molecule to you? How big is a protein? About 30 times your size, maybe? Now, imagine you are a molecule. Then, the interior of a cell, at 1000-10'000 times your size, would seem absolutely huge. This is how one could interpret Feynman's visionary statement above that foresaw the dawn of nanotechnology. From atoms in molecules to molecules in cells, much of our present understanding of nature at these length scales has been made possible by high-resolution imaging experiments.

For hundreds of years, scientists and engineers have developed a variety of ever more powerful microscopes which can now access the nanometer length scales and an unprecedented variety of content in the specimen. These instruments are revolutionizing our understanding of the world around us. At the same time, this field is still very active and, as you read this, new technological innovations are being made in all areas of instrument design, sample preparation, and computational image analysis.

If imaging at the nanoscale kindles your imagination and you seek to become a competent and independent scientist, this course will help you on your journey. In the first half of the class, you will learn to integrate and apply your knowledge of biology, chemistry and physics to more fully understand how complex microscopes function. This skill will then allow you to think creatively about addressing current scientific problems related to high-resolution imaging in the second half of class.

Specific objectives

1) understand the anatomy of different types of microscopes.
2) explain the physical principles of how different types of images are formed.
3) use computational tools to process and analyze images.
4) explain the capabilities and limitations of different types of microscopes.
5) critically evaluate image data in the scientific literature.
6) understand how scientific breakthroughs in imaging have affected you personally.
7) think creatively about designing new microscopy experiments that shed light into the unknown.

Course activities

Throughout the course, we will evaluate your progress toward the above learning objectives. This will be done through the following activities:

Final Research Proposal (~40%). This is the final assignment. We will work on small components of it continually throughout the course, both individually and in groups. This assignment is designed to help you think outside the box and to dream big. First, you will pick an experimental problem that is interesting and relevant to you, but could be solved through imaging. It has to be a real problem in that it is just beyond what is experimentally accessible with today's imaging technology. However, you will get to play one card to your advantage: We will imagine that another research group has just overcome a key experimental obstacle. You realize that you are in a prime position to incorporate this breakthrough into a new type of imaging experiment, a new way to prepare a sample, and/or a new way to analyze imaging data. Now, you can finally see a way to access this out-of-reach experimental observable that you have been interested in. You will then develop this idea into a formal research proposal that you could pitch to governmental or venture capital funding entities of your choice. On several occasions, you will be able to enlist the help of your colleagues in the class to make your idea and the proposal as convincing as possible.

Historical Context Essay (~20%). Science is not done in isolation. Science is done by individual human beings and we all stand on the shoulders of those who came before us. The fundamental discoveries that we build upon to construct today's microscopes are significant in their own right and have won numerous Nobel Prizes over decades. In this assignment, you will choose one of these fundamental discoveries and describe its connection to imaging in detail. You will compare and contrast how the discovery was relevant at the time it was made and how it is relevant today.

Problem Sets (~20%). You will complete several homework sets both in and outside of class. They will include both instructional problems to solidify your understanding of the theoretical concepts we cover, and problems that you may face tomorrow in a research laboratory. For the latter type of problems you will primarily use Matlab and ImageJ to process and analyze images published in the literature. Although you can work on the problem sets individually, you are strongly encouraged to complete them in study groups. We will also work on some components of the problem sets in class, both as groups and individuals.

Participation/Self-reflection (~20%). We will engage in activities, both inside and outside of class that are designed for you to become a good colleague to your peers. This character trait is important because scientific progress is vastly accelerated if we can make each other better. To help you in the development of your scientific persona, your participation and your level of engagement in these activities will be assessed by yourself and by your peers.