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1 Introduction

This First–Year Inquiry seminar, is based primarily on research being conducted in my group, placed in context with the work of others at Northeastern and in the international biomedical optics community.

The optical microscope, having reached its nominal limit of resolution in the 19th century, and now ubiquitous in research, pathology, manufacturing, and education, seems an unlikely topic for exciting research. However, at the turn of the 21st century, lasers provided new light sources, chemistry provided new contrast agents, and improved computers provided the ability to process large amounts of imaging data. These three technologies fostered revolution in the field of microscopy providing exciting research opportunities for electrical, mechanical, and chemical engineers, as well as biologists and physicists. Even more recently, techniques combining light with ultrasound have opened the door for deeper penetration of light for therapy and imaging.

The seminar will present just enough of the principles of optics to allow students to consider questions such as

- Is it possible to see a person's thoughts?
- Can blue light cure acne?
- How deep can we see inside the human body with light?
- How does oxygen go from the air to the lung to the blood to a muscle when we exercise?
- How is it that the connective tissue in our bodies can grow and strengthen while we are using it?

2 Schedule

We will meet for 65 minutes Tuesdays at 3:25 (Sequence 7) in 126RY.

3 Expectations

This seminar is mostly intended for undeclared engineering students, as well as students in Electrical and Computer, Mechanical and Industrial, and Chemical Engineering. Students in physics or chemistry might also find it of interest.

This is a one–semester–hour course, consisting mostly of readings and discussions. The discussions consist of about an hour per week for 12 weeks, so attendance is unusually important in this course. If you must miss a week, let me know ahead of time and do your best to get information from your fellow students about the material you missed. You will be asked to sign in each week.

You are expected to arrive promptly by the start of the meeting time, stay through the end, and avoid distractions during the discussion. Keep your phone in silent mode, and do not use it during the discussion. You may use a laptop for taking notes or researching discussion topics during the

discussion, but please don't use it for other work. You are welcome to bring snacks and drinks to the discussion.

It is important to do the reading before coming to the discussion, so that you can learn and contribute. You will be reading mostly technical papers that are written and read mostly by graduate students and faculty, so there will be a lot that you don't understand. Don't be intimidated by the depth of these papers. We will work to extract the information we want from these papers. In the early weeks of the course, we will discuss some guidelines for thinking about the topics, and what to look for in the readings.

I will maintain a discussion group on Blackboard where you can communicate with me and with each other. That is normally the best forum for questions and comments. However, feel free to ask me questions by email at any time during the term.

4 Special Needs

The university will make reasonable accommodations for persons with documented disabilities. Students should notify the Disability Resource Center located in 20 Dodge Hall and their instructors of any special needs. Instructors should be notified the first day of classes.

5 Topics and Course Material

The seminar will begin with a simple discussion of optics and different types of optical contrast that are used in biology and medicine. We will briefly trace the development of the field of microscopy to the 20th century, and then discuss some new techniques developed at the turn of the 21st century, with special attention to those being used at Northeastern, and how our own faculty and students (including undergraduates) have influenced the field. We will read a few technical papers, with an emphasis not on in–depth understanding, but on being able to extract a few key facts. The proposed

topics of twelve sessions are enumerated below. Work that is specifically related to Northeastern is highlighted in **bold type**.

For the first three weeks, I will present ideas on the board. After that, we will read a series of papers, and discuss them. The papers are listed below. You can obtain them from the library electronically.

1. Basic optics: a survival guide to geometric optics, ray tracing, polarization, diffraction and interference.

2. Finding and reading (and a bit about writing) technical papers: Library tools, Google Scholar, Pub Med.

3. Why do we choose a particular technique? How do we know what we are seeing? Optical contrast: Absorption, scatter, phase, fluorescence, Raman spectroscopy, non–linear processes. Molecular tags. Just a little bit of spectroscopy.

4. The first few hundred years of microscopy. Köhler illumination. Transmission, reflection, brightfield, darkfield. (Microscopy Notes to be posted)

5, 6. Looking under the skin: Optical sectioning: Confocal, multi–photon, and multi–modal microscopy. Applications to skin cancers. (Northeastern and Memorial Sloan Kettering Cancer Center) [1, 2]

7. Take a deep breath: A look into the lung with optical coherence tomography. (Northeastern ECE and MIE) [3]

8. Understanding how our bodies grow while we are using them: Harmonic microscopy and light scattering in collagen. (Northeastern ECE and MIE) [4, 5]

9. Can you see someone's thoughts?: Diffusive optics including brain imaging and other applications. (Lie detectors?) [Paper TBD: Boas?]

10. Computational microscopy: Generating synthetic images with a computer. (Northeastern ECE) [6]

11. Light–and–sound, sound–and–light, light–and–sound–and–light: Photo–acoustic tomography, acousto–optical imaging and more. (Northeastern, BU) [7]

12. Phase conjugation: Making the tissue transparent. (Northeastern and Caltech). [8]

Note: If possible, we will prepare a short hands–on experience in the microscope facility for each enrolled student. This activity would be conducted in the evening, outside the regular seminar time.

References

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[3] A. Gouldstone, N. Caner, T. Swedish, S. Kalkhoran, and C. DiMarzio. Mechanical and optical dynamic model of lung. *IEEE transactions on bio-medical engineering*, June 2011.

[4] M.C. Robitaille, R. Zareian, C.A. DiMarzio, K.T. Wan, and J.W. Ruberti. Small-angle light scattering to detect strain-directed collagen degradation in native tissue. *Interface Focus*, 1(5):767, 2011.

[5] Yair Mega, Mike Robitaille, Ramin Zareian, James McLean, Jeffrey Ruberti, and Charles DiMarzio. Quantification of lamellar orientation in corneal collagen using second harmonic generation images. *Opt. Lett.*, 37(16):3312–3314, Aug 2012.

[6] T.B. Swedish, J.P. Robinson, M.R. Silva, A. Gouldstone, D. Kaeli, and C.A. DiMarzio. Computational model of optical scattering by elastin in

lung. In *Proceedings of SPIE*, volume 7904, pages 79040H–1 – 79040H–7, 2011.

[7] Todd W. Murray, Lei Sui, Gopi Maguluri, Ronald A. Roy, Alex Nieva, Florian Blonigen, and Charles A. Dimarzio. Detection of ultrasound-modulated photons in diffuse media using the photorefractive effect. *Optics Letters*, 29(21):2509 – 2511, 2004.

[8] Ying Min Wang, Benjamin Judkewitz, Charles A. DiMarzio, and Changhuei Yang. Deep-tissue focal fluorescence imaging with digitally time-reversed ultrasound-encoded light. *Nature Communications*, 3:928, June 2012.