ENGR 499 Course Syllabus

Microscope design and construction

Instructors:

Prof. Andrea Armani, Dept. of Chemical Engineering and Materials Science, VHE 712, armani@usc.edu

Prof. Scott Fraser, Dept. of Biological Sciences and Biomedical Engineering, RRI 401, sfraser@provost.USC.edu

Registration:

Because the course has limited enrollment, to register for the course, you must first receive approval from Prof. Armani. To receive D-clearance approval, email the following items to Prof. Armani by the first Wednesday of the semester:

- Stars report
- CV/resume
- 1 paragraph (4-6 sentences) explaining why you are interested in the project

A decision will be made by the end of the first week.

Textbook/Reference material:

There is no specific textbook. Reference materials will be posted periodically on Blackboard.

Course Objective:

One of the NAE Grand Challenges is engineering tools for scientific discovery. Additionally, past studies by the NAE have stated that engineering curriculums emphasize theory over practice. To address both issues, this section of directed research will bring together a small cross-disciplinary team of undergraduates with the specific objective of building a state-of-the-art optical project tomography microscope for imaging biological samples. This microscope will be integrated into the USC Imaging Center at the end of the semester. Students will participate in all aspects of the microscope design, construction and verification. Additionally, students will learn project management skills and will learn how to clearly and concisely present scientific results.

Grading

ENGR 491 is for a grade. The grade is determined based on the below:

- Proposal: 15%
- Progress Report: 15%
- Final Report: 25%
- Final Presentation: 25%
- Effort in Lab: 20% (determined by advisor)

Expectations/Information for Assignments:

Project Proposal:

By the end of week 2 of the semester, you must submit a 1-2 page project proposal to the Turn-It-In link on Blackboard. This proposal should include the following components: 1) 200-400wd abstract, 2) tasks to be accomplished (an itemized/bulleted list and an approach for accomplishing the list), and 3) timeline for tasks. Additional information and a sample proposal is posted on Blackboard.

Progress Report:

A 2 page progress report is due halfway through the semester. It should be submitted to the Turn-It-In link on Blackboard. This report should directly refer to the information included in the initial proposal. If the project is on-schedule, it should indicate as such. If the project is not on-schedule, explanations should be given. If possible, the inclusion of data is strongly encouraged. Additional information is posted on Blackboard.

Final report:

A final report is due by the last day of finals. It should be submitted to the Turn-It-In link on Blackboard, and it should be approved by your advisor. This report should directly refer to the information included in the initial proposal. If the project is on-schedule, it should indicate as such. If the project is not on-schedule, explanations should be given. Additional information is posted on Blackboard.

The final report should also include a user or operational manual explaining how the microscope works.

Final Presentation:

During finals week, you must give a presentation to Prof. Fraser, Prof. Armani, and Prof. McMahon The presentation should be approximately 1 hour long and will be open (you may bring your friends). It should also include a demonstration of the microscope or a video. A (optional) class will be held in November to discuss how to prepare a good presentation and what pitfalls to avoid. Additionally, you can mail your slides to Prof. Armani in advance (at least 72 hours) of the presentation for feedback. An electronic copy (pdf, <5MB) of your slides should be made available (emailed) to the committee at least two days before your presentation.

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 ones own academic work from misuse by others as well as to avoid using anothers work as ones 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/.

Plagiarism (copying or modifying someone else's work and presenting it as your own) and other forms of cheating will not be tolerated. Please ask the instructor if you have questions about proper behavior.

Statement of 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 me (or the TA) as early in the semester as possible. DSP is located in STU 301 and is open 8:30am – 5:00pm, Monday through Friday. The phone number for DSP is (213) 740-0776.

ENGR 499: Project Details

Project Overview:

This section of directed research will bring together a small cross-disciplinary team of undergraduates with the specific objective of building a state-of-the-art optical projection tomography (OPT) microscope for mesoscale imaging of biological samples.

While significant advances in light microscopy have enabled increasing sub-cellular resolution, OPT remains the most effective approach for many types of biological studies where the need is to resolve cells within the larger context of a tissue mass; for example, visualizing a rare complement of stem cells within a developing organ system.

Optical projection tomography uses the same processing algorithms as computer tomography (CT) X-rays to create three dimensional light microscope images of biological specimens. A large number of transmitted light images are collected as the specimen is rotated to slightly different tilt angles, and the images are processed to generate a 3D image with excellent resolution in all three dimensions. This approach solves one of the key challenges in imaging biological samples: the anisotropic resolution of conventional light microscopy. In other words, the resolution in depth is many times worse than the resolution in the imaging plane.

A proof of principle publication reporting images of complex biological specimens using optical projection tomography appeared in Science in 2002 (Sharpe et al., 2002. **Science** *296*, 541-545). Since this initial demonstration, numerous attempts have been made to commercialize this potentially groundbreaking instrument. These efforts have been hampered by: 1) the use of conventional microscope optics and 2) the limited means to make the specimen more translucent. The optics limited the accuracy of the reconstruction, which negatively impacted the overall resolution of the image. Light scattering from minimally translucent samples results in image blurring, thus restricting the ultimate size of the sample. By combining recent advances in optics and in bioengineering, both challenges can be overcome. Specifically, recently developed telecentric lenses can solve the imaging challenges and new clearing agents – such as Clarity – improve the transparency of samples (Chung et al., 2013. **Nat. Methods** *10*, 508-513). Indeed recent developments have rendered an entire mouse accessible to OPT-based imaging (Yang et al., 2014. **Cell** *158*, 945-958).

Project Goals:

The project is funded by Professor McMahon, director of the Eli and Edythe Broad Center for Regenerative Medicine and Stem Cell Research on the HSC campus and will be overseen by Prof. Armani and Prof. Fraser. The goal is for students to build a working, optimized OPT microscope guided by open source instructions. The student team would then perform a series of tests of the systems with the final goal of generating movies that display 3-D projections and virtual slices of mammalian kidney structures. An example of the computer rendering of this type of data can be visualized here (see movie: https://mcmahonlab.usc.edu/research/generation-and-repair-of-the-kidney). As the end of the project, the OPT machine will be placed within the Imaging Core facilities within the Eli and Edythe Broad Center for Regenerative Medicine and Stem Cell Research to facilitate multi-investigator analysis of stem cell research.

Project Expectations:

The project will involve the progressive optimization of the optical design, taking into account the limitations of the specimen and the image sensor, and the need for the microscope to reliable service a broad group of researchers where the need for reproducibility and simplicity of operation are critical. The expectation is that all students engaged in this project will understand and recognize the compromises inherent in the design and implementation of such a multi-user system, gain a first-hand experience in interdisciplinary project execution, and develop an understanding of front-line stem cell research using the kidney system as an imaging test-bed for the assembled OPT microscope. To aid in the design and development, several lectures/seminars will be held near the beginning of the semester.

Given the complexity of this project, the team (not any single member) should have a combined skill set which includes:

- Imaging and image analysis
- Programming
- Machining and multi-component design
- Cell culture analysis and cell imaging
- Optics

All students involved in the project are expected to contribute equally to its success. A portion of the work will be performed on the HSC campus. Given the research nature of this project, it will be necessary to be able to dedicate large, single blocks of time to this project.