Three-Dimensional (3D) Bioprinting

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Office: Discovery Park K240K
Office hours: Friday 1:00 – 3:00 pm
Lecture hours: Tuesday, 11:30 am – 2:20 pm
Classrooms: NTDP D201 (lecture) and K270 (lab)
Prerequisite(s): Graduate standing in biomedical engineering, material science and engineering, biology, chemistry, physics or permission of instructor.

Catalog Description:
There have been great advances made recently in three-dimensional (3D) bioprinting, which is a robotic additive manufacturing of functional human tissue constructs using living cells and hydrogels, similar to their tissue structure *in vivo*. This practical course will introduce the basic principles and applications of 3D bioprinting of human cells in biomimetic hydrogels (a.k.a. "bioinks") to create multicellular tissue constructs used in biomedical and biological research.

Course Description:
Recent advances in 3D bioprinting offer new opportunities for creating highly organized multicellular tissue constructs *in vitro* by using printing robots to precisely dispense multiple cell types in biomimetic hydrogels layer-by-layer, thereby potentially revolutionizing regenerative medicine, oncology, and drug discovery. The 3D-printed tissue constructs with cells obtained from patients can be used as promising disease models for screening therapeutic drugs for individuals. This practical course will introduce the overview of 3D bioprinting in the context of tissue engineering. Emphasis for this course will be on the fundamental concepts of 3D bioprinting processes, including extrusion, inkjet printing, solenoid valve-based printing, and laser printing, as well as hydrogels and cell sources used in 3D bioprinting. Students will learn how to culture mammalian cells in 3D, perform cell-based assays and operate instruments used for compound screening. In addition to the fundamental concepts of computational design and simulation, students will also learn potential applications of 3D bioprinting and its challenges. The overall objective of this course is to have students understand complex human cell printing processes for applications in tissue engineering and drug discovery. Demonstrations on a few experiments will be provided in the laboratory (K270). Finally, students will work on 3D bioprinting projects selected from their own research topic, or from literature. The students are expected to identify critical needs for new tissues for human disease modeling, explore existing cell/tissue models for problem solving, study the principles of the existing cell-based assays and analytical instrument used, propose a new/improved method, and write standard operating protocols for 3D bioprinting of human cells. The students are also expected to present their work in class, and critically evaluate peer's work with regard to its significance, innovation, and approach for disease modeling.

* Cell phone use in class is strongly prohibited.
* There will be no midterm exam and no make-up exam. In case a student cannot take the final exam for medical reasons with official documents provided by hospitals, 75% of the score obtained from the student project will be used instead of the final exam.
* During the exam, phones and bio-breaks are not allowed.
* All purses and bags must be completely zipped up and closed during the exam.
* Students are required to pull back all head coverings to display their ears during exams to prevent academic misconduct: As part of the University's ongoing efforts to prevent cheating, and based on evidence of increased use of headphones and earpiece devices to permit cheating on exams, all

students are required to display their ears for the duration of any exam. The policy may require adjustment to hair or clothing. Any student not complying with this policy will, after a warning, be issued a zero on the exam. Students with concerns about their compliance with this policy, please contact Academic Integrity Officer at academic.integrity@unt.edu or 940-565-2856.

Course Goal:

- Understand basics of tissue engineering
- Introduce the overview of 3D bioprinting in tissue engineering
- Introduce the fundamental concepts of 3D bioprinting processes, including extrusion, inkjet printing, solenoid valve-based printing, and laser printing
- Overview hydrogels and cell sources used in 3D bioprinting
- Learn how to culture mammalian cells in 3D
- Introduce cell-based assays and instruments used for compound screening
- Learn the fundamental concepts of computational design and simulation
- Learn potential applications of 3D bioprinting and its challenges

Course Materials:

Textbooks

- Bioprinting: Principles and Applications, Chee Kai Chua and Wai Yee Yeong, World Scientific, ISBN # 978-9-814-61210-4 (2015)
- Microarray Bioprinting Technology: Fundamentals and Practices, Moo-Yeal Lee, Springer, ISBN # 978-3-319-46803-7 (2016)

Reference books

- 3D Bioprinting: Fundamentals, Principles and Applications, Ibrahim Ozbolat, Academic Press, ISBN # 978-0-128-03030-1 (2016)
- Cell and Organ Printing, Bradley R. Ringeisen, Barry J. Spargo, and Peter K. Wu (Editors), Springer, ISBN # 978-90-481-9144-4 (2010)

These books are only suggestions, and there is no need to purchase them. The material covered in the course will be drawn from these books and other sources, and lecture notes will be provided to students.

Topical Outline:

- Introduction to tissue engineering
- Bioprinting techniques
  - ✓ Extrusion
  - ✓ Inkjet printing
  - ✓ Solenoid valve-based printing
  - ✓ Laser printing
- Materials for bioprinting
- Cell sources for bioprinting
- Three-dimensional cell culture
- Computational design and simulation
- Applications of bioprinting: Challenges and potential
- Student project presentations

Lab Component:

There are lab components in this class, which will be carried out at K270 (Bioprinting Lab). Students will have a great opportunity to learn in-depth knowledge of 3D bioprinting of human cells on a pillar plate platform *via* several experiments with a microarray spotter and a chip scanner. By performing hands-on experiments, students will learn fundamental principles of aseptic cell culture techniques, human cell printing and culture in 3D, and cell staining and analysis that are routinely used in hospitals, biomedical

labs, R&D centers, and industries. After each experiment, students will write a report (3 – 5 pages long) in terms of background information (35%), experimental methods (45%), and data analysis (20%). Below is a list of experiments that will be performed at K270.

1. Lab #1: Human cell culture and passaging
2. Lab #2: Surface coating of a 36PillarPlate and preparation of hydrogels
3. Lab #3: Miniature 3D printing of human cells on the 36PillarPlate for 3D culture
4. Lab #4: Preparation of compound solutions for toxicity tests
5. Lab #5: Cell staining and imaging
6. Lab #6: Data analysis

*Specific demonstration schedules will be announced later.

Student Project:

In terms of student projects, multiple human tissue models, including skins, bones, vascular grafts, hearts, cartilages, and mini-tissues derived from pluripotent stem cells (a.k.a., organoids) used for tissue engineering and drug discovery are suggested. Each student is expected to identify critical needs of tissues for human diseases, provide current cell/tissue models available for disease modeling, describe experimental approaches developed to simulate human diseases, discuss advantages and limitations of experimental approaches, explain basic principles of 3D bioprinting approaches used for the tissue models, describe what experimental instrument is being used for 3D bioprinting and image acquisition, provide standard operating protocols for 3D bioprinting of human tissues as well as cell image acquisition and analysis, and draw proper conclusions. The students are also expected to present their work in class, participate in class discussion, and critically evaluate peer's work with regard to its significance, innovation, and approach for disease modeling. Since this is a split-level course, Master's and doctoral students will be graded separately. Doctoral students are expected to submit more in-depth student project reports and PowerPoint slide decks than Master's students. For example, doctoral students will submit a project report ranging from 15 – 20 pages (Arial 11 and line spacing 1.5) and a PowerPoint slide deck (up to 25 min presentation and 5 min Q&A) whereas master's students will submit a report ranging from 10 – 15 pages and a PowerPoint slide deck (up to 20 min presentation and 5 min Q&A). In terms of the format, both project reports should include cover page with title and student name, introduction, experimental approaches, conclusions, literature cited, and future direction. Specific grading rubrics will be provided.

A. Introduction

- ✓ Identify critical needs of tissues for human diseases
- ✓ Provide current cell/tissue models available for disease modeling
- ✓ Describe experimental approaches (including animal models, *in vitro* tissue models, and computational methods) developed to simulate human diseases
- ✓ Discuss advantages and limitations of experimental approaches

B. Experimental approaches for 3D bioprinting

- ✓ Explain basic principles of 3D bioprinting approaches used for the tissue models
- ✓ Describe what experimental instrument is being used for 3D bioprinting and image acquisition
- ✓ Provide standard operating protocols for 3D bioprinting of human tissues as well as cell image acquisition and analysis

C. Conclusions

- ✓ Draw proper conclusions

D. References cited

- ✓ Provide relevant literature

E. Future direction (bonus points if addressed properly)

- ✓ Propose new/improved methods to better simulate human diseases

Grading Policy:
Students are expected to attend lectures, submit homework assignments on time, perform experiments, submit lab reports, present student projects in class, submit reports on student projects, and take the final exam. All scores on class attendance, assignments, lab reports, student projects, and exams will be based on 100 points. The final score will be calculated by the percentage given below.

- Class attendance: 5%
- Homework assignments: 6%
- Lab reports: 24%
- Student project: 30% - presentation + report
- Final exam: 35%

Total: 100%

The final grade will be determined by a grading guideline chosen by the instructor. The following grading guideline exemplifies the relationships between the final score calculated from the formula above and the letter grade assigned. Final grades will be balanced between the grading guideline and a student grade distribution.

- A: 89.5 – 100%
- B: 79.5 – 89.4%
- C: 69.5 – 79.4%
- D: 59.5 – 69.4%
- F: below 59.4%

Registration, Drop and Withdrawal Policy

Drop: It is the student's responsibility, and not the instructor's, to drop the course. You may find important details about how dropping a class can affect your GPA and your Financial Aid here: http://registrar.unt.edu/registration/dropping-class

Withdrawal: It is the student's responsibility to withdraw from the course by either going to their academic advisor's office (which should be the first stop when considering a withdraw), the Registrar's office, or the Department. If you can't complete the course, you must withdraw for a "W" (after this date, you'd receive either a "WP" or a "WF"). Withdrawing from a course is a formal procedure which YOU must initiate. I can't do it for you. If you simply stop attending and do not withdraw, you will receive a performance grade, usually an "F." All deadlines can be found at: http://registrar.unt.edu/registration/fall-registration-guide

University Policy on Academic Misconduct

Academic Misconduct (Sec. 3.4 from the Student Handbook): Any act that violates the academic integrity of the institution is considered academic misconduct. The procedures used to resolve suspected acts of academic misconduct are available in the Office of Academic Deans and the Office of Campus Life. Specific examples include, but are not limited to:

Cheating: Copying from another student's test paper, written assignment, other report, or computer files and listings; Using, during any academic exercise, material and/or devices not authorized by the person in charge of the test; Collaborating with or seeking aid from another student during a test or laboratory without permission; Knowingly using, buying, selling, stealing, transporting, or soliciting in its entirety or in part, the contents of a test or other assignment unauthorized for release; Substituting for another student or permitting another student to substitute for oneself.

Plagiarism: The appropriation, theft, purchase or obtaining by any means another's work, and the unacknowledged submission or incorporation of that work as one's own offered for credit. Appropriation includes the quoting or paraphrasing of another's work without giving credit (especially online resources). Turnitin will be utilized to ensure online resources are not misappropriated.

Any work not meeting this standard will be evaluated and subject to either a re-write, if the Instructor concludes that the assignment was unintentionally plagiarized or a zero for the assignment. Egregious forms of academic conduct are subject to a formal hearing. For more information on paper writing,

including how to avoid plagiarism, and how to use citations, see http://anthropology.unt.edu/resources-writingpaper.php. For information on the University's policies regarding academic integrity and dishonesty, see the UNT Center for Student Rights and Responsibilities, http://www.unt.edu/csrr/.
Collusion: The unauthorized collaboration with another in preparing work offered for credit.

Sexual Discrimination, Harassment and Assault

UNT is committed to providing an environment free of all forms of discrimination and sexual harassment, including sexual assault, domestic violence, dating violence, and stalking. If you (or someone you know) has experienced or experiences any of these acts of aggression, please know that you are not alone. The federal Title IX law makes it clear that violence and harassment based on sex and gender are Civil Rights offenses. UNT has staff members trained to support you in navigating campus life, accessing health and counseling services, providing academic and housing accommodations, helping with legal protective orders, and more.

Personal Distress

Excerpts from http://studentaffairs.unt.edu/care "The University of North Texas cares about our students' success, not only academically, but emotionally and physically…. Because of our commitment, we provide literally hundreds of departments and services across campus that respond to our students' unique needs…. UNT believes it is important to foster an environment that encourages students to maintain a standard of responsibility for self-care which includes the ability to respond adequately to one's emotional, physical, and educational needs. If you are experiencing physical or emotional distress which adversely affects your ability to succeed in class, please see me as soon as possible. Together, we will point you towards the appropriate resources.