BE 207: Special Topics – Biomaterials for Medical Device Design

Instructor: Professor Brian Aguado, baguado@eng.ucsd.edu

Term: Spring 2022

Pre-requisites: General chemistry, biology, and/or materials science

Class Time: Tuesdays and Thursdays, 8:00 – 9:20 AM

Instructor Office Hours: Wednesdays, 1-2 PM or by appointment (SCRM 4003 or Zoom on request)

Teaching Assistants (TA): Talia Baddour (PhD Student, Bioengineering), tbaddour@ucsd.edu
Rayyan Gorashi (PhD Student, Bioengineering), rgorashi@ucsd.edu

TA Office Hours: Mondays, 4-5 pm, or by appointment

Location: PFBH 161

Format: Classes will be in-person per university guidance. When necessary due to new or unforeseen pandemic constraints, some classes may be virtual and/or previously recorded. As much advance notice as possible will be provided if a transition to virtual instruction is necessary.

Reference textbook: Biomaterials Science: An Introduction to Materials in Medicine, Edited by W.R. Wagner, S.E. Sakiyama-Elbert, G. Zhang, M.J. Yazemski, 4th Edition, 2020. Available online from the UCSD library. Suggested readings are provided but not required.

Course description: This course will introduce design principles for biomaterials, including considerations for protein and cell delivery, cell-instructive biomaterials, drug delivery systems, material-tissue interactions (e.g., host immune response), and material characterization. Current literature in the field will be discussed in a journal club-style format. Students will complete a final project to design/use a biomaterial for a specific application (e.g., tissue repair, biosensing, immune-modulation, etc.) and write a grant proposal to develop this biomaterial that addresses a potential path to commercialization and clinical use. Students will gain experience writing and addressing peer reviews for grant proposals and participate in a mock grant review panel.

Course objectives: At the conclusion of this course, students will be able to:

1. Explain the relationship between biomaterial properties and performance in biological environments.
2. Select appropriate techniques for biomaterial characterization based on desired material properties and applications.
3. Identify design criteria and appropriate in vitro / in vivo experiments to use biomaterials for specific applications.
4. Read and critique primary literature and research proposals in the biomaterials, regenerative medicine, and medical device fields.
5. Apply knowledge of current biomaterials literature, materials characterization, and design criteria to develop an NIH-style grant proposal.
6. Demonstrate knowledge of biomaterials through oral and written communication activities.

Grading Scheme:

Project	Assignments	Weight
Journal Club (40%)	Group presentation (author or reviewer)	15%
	Audience participation	10%
	Question/critique submissions	15%
Grant Proposal (60%)	5-minute project pitch	5%
	Specific Aims page	5%
	Significance and Innovation	10%
	Final proposal	20%
	Peer review of proposals	5%
	Mock study section	10%
	Response to reviewers	5%

Schedule:

Week	Dates	Class Topic	Reading	Assignment Due
1	3/29	Lecture 1 – Course Intro History of Biomaterials	Section 1.1	
	3/31	Lecture 2 – Polymers / Hydrogels	Sections 1.3.2, 1.3.6	Submit "slide about you" Sign up for (1) journal club group and (2) grant proposal group on Canvas
2	4/5	Lecture 3 – Fabrication, modification, degradation, sterilization	Sections 1.4, 2.4	
	4/7	Journal Club – Group 1	Paper 1	Question/critique submission
3	4/12	Lecture 4 – Cell Material Interactions	Section 2.1	
	4/14	Journal Club – Group 2	Paper 2	Question/critique submission
4	4/19	5 min Project Pitches	NA	Project pitch presentations (in class)
	4/21	Journal Club – Group 3	Paper 3	Question/critique submission
5	4/26	Lecture 5 – Immune Response	Section 2.2	Significance / Innovation due (5 PM PT)
	4/28	TBD Guest Lecture		
6	5/3	Lecture 6 – Tissue Engineering	Section 2.6	Specific Aims Page due (5 PM PT)
	5/5	Journal Club – Group 4	Paper 4	Question/critique submission
7	5/10	Journal Club – Group 5	Paper 5	Question/critique submission
	5/12	Journal Club – Group 6	Paper 6	Question/critique submission
8	5/17	Lecture 7 – Clinical translation	Sections 3.1.1-3.1.11	
	5/19	Journal Club – Group 7	Paper 7	Question/critique submission
9	5/24	Journal Club – Group 8	Paper 8	Full Proposals Due (5 PM PT) Question/critique submission
	5/26	Lecture 8 – Precision Biomaterials	Selected Papers	
10	5/31	Mock Study Section – Proposals 1, 2, 3 reviewed	Proposals	Peer reviews (in class) – submit final rubrics by 5 PM PT
	6/2	Mock Study Section – Proposals 4, 5 reviewed	Proposals	Peer reviews (in class) – submit final rubrics by 5 PM PT
11	6/9	Finals Week (No final)	NA	Responses to reviews due (5 PM PT)

Expectations:

1. Active participation and classroom engagement is important to learning the fundamentals of biomaterials and becoming comfortable discussing and critiquing journal articles. Everyone is expected to participate in lectures and journal paper discussions.

2. Academic dishonesty will not be tolerated. The Department of Bioengineering adheres to the UCSD Policy on Integrity of Scholarship. An excerpt of this Policy states that "Students are expected to complete the course in compliance with the instructor's standards. No student shall engage in any activity that involves attempting to receive a grade by means other than honest effort...." Any suspected incident (including but not limited to plagiarism on writing assignments) will be dealt with in accordance with UCSD policy, which includes reporting the misconduct to the Dean. More information on UCSD's academic dishonesty policy can be found at: http://senate.ucsd.edu/Operating-Procedures/Senate-Manual/Appendices/2

Graded assignment instructions:

1. **Journal club:** Many labs/research organizations use "journal clubs" to learn about the latest and greatest research in the field. We will use journal clubs in our class to present a research article and important findings, and then critically evaluate the article to assess its validity and impact on the field.

    - **Group presentation:** Groups of 3 will be assigned to read a pre-selected journal article. The entire class will also be expected to read the article. Journal club discussions will be led by groups of students split up into "author" and "reviewer" roles. For each paper, two students will serve as authors and one student will serve as the reviewer. Role assignments will be up to group members. All students will participate in facilitating the presentation. An example slide deck will be posted (Journal Club – Example), in addition to a grading rubric (Journal Club Presentation – Rubric).

      Authors: 2 group members will play the role of author for the discussion. Authors will make a PowerPoint presentation (~45 minutes including Q&A) including the following:
        - *Introduce the real authors (2 mins):* The first author is typically the scientist that performed most of the work in the laboratory, offered the most intellectual contribution, and wrote the manuscript. The last authors (1-2) on a research article are known as the "corresponding authors." The corresponding author(s) usually provides the funding and lab space where the research was performed. Please search for the first and last authors over Google and briefly introduce their backgrounds, education, institutions, and research interests (include the first authors if you can find them in your searches, they may be harder to find and that's ok). The goal is to appreciate the people behind the science that was conducted.
        - *Background (10 mins)*: Now acting as "authors", provide for your audience sufficient background knowledge important to understand the concepts and experiments of the paper. Read references cited in the introduction of your assigned paper to build more background knowledge and context for your presentation. Describe the current "state of the art" in the field, and limitations with current approaches.
            - *Motivation:* Describe the reasons why the research is being conducted. Think: why should we care? For example, is there a specific clinical need to address? A key biological mechanism that is still misunderstood/unknown?
            - *Problem/limitations*: Describe the problem or gaps in knowledge in the field. Describe technical limitations, lack of basic knowledge, etc.
            - *Solution*: Describe the proposed solution you are exploring as "authors" for the article. As an author, what prompted you to take the described approach?
            - *Hypotheses*: Clearly state your overarching (1) research question and (2) hypothesis (proposed answer to the research question).
        - *Approach (30 mins):* Most of your presentation will be spent discussing in detail the experiments conducted in the manuscript, the techniques used, the results obtained, and the implications of each result in the field.

- *Figures*: For each figure (and supplemental figures/videos), walk through the motivation for the experiment, the experimental set up, negative/positive controls, sample sizes (technical vs. biological replicates), key observations/data/results, and conclusion for each experiment. Scientific or research techniques should be explained in detail – assume no prior knowledge of biomaterials research techniques - remember your audience, we are here to learn.
- *Techniques*: Describe in sufficient detail the techniques used in the article if they are not common techniques. For example, tissue immunostaining does not need to be explained, since the technique is quite common in bioscience research. On the other hand, article-specific techniques (e.g., nanoparticle fabrication, polymer synthesis strategies, single cell seq analyses, etc) must be explained so that everyone in class can be on the same page.

▪ *Conclusions (3 mins)*: Discuss your conclusions and contextualize the importance and relevance of your results in the field. What did your contribution as "authors" add to the existing knowledge in the field?

Reviewers: Using the "Step by Step Guide to Reviewing a Manuscript" as a guide (Journal Club – Reviewer Guide document uploaded on Canvas), one group member will play the role of reviewers for the discussion. The goal of the reviewer is to provide critical yet constructive feedback on how to improve the paper and suggest areas for improvement. Reviewers will work together to make a PowerPoint presentation (~30 minutes including Q&A) that include (but not limited to) the following discussion points:

- *Summary* (10 minutes)
  - Give positive feedback first. Authors are more likely to acknowledge your feedback.
  - Briefly summarize what the paper is about and what the findings are
  - Try to put the findings of the paper into the context of the existing literature and current knowledge
  - Indicate the significance of the work and if it is novel or mainly confirmatory
  - Indicate the work's strengths, its quality and completeness
  - State any major flaws or weaknesses and note any special considerations. For example, if previously held theories are being overlooked

- *Major Issues* (10 minutes)
  - Are there any major flaws? State what they are and what the severity of their impact is on the paper
  - Has similar work already been published without the authors acknowledging this?
  - Are the authors presenting findings that challenge current thinking? Is the evidence they present strong enough to prove their case? Have they cited all the relevant work that would contradict their thinking and addressed it appropriately?
  - If major revisions are required, try to indicate clearly what they are
  - Are there any major presentational problems? Are figures & tables, language and manuscript structure all clear enough for you to accurately assess the work?
  - Are there any ethical issues? If you are unsure it may be better to disclose these in the confidential comments section

- *Minor Issues* (10 minutes)
  - Are there places where meaning is ambiguous? How can this be corrected?
  - Are the correct references cited? If not, which should be cited instead/also? Are citations excessive, limited, or biased?
  - Are there any factual, numerical or unit errors? If so, what are they?
  - Are all tables and figures appropriate, sufficient, and correctly labelled? If not, say which are not

- **Audience participation**: On journal club days, all students are required to participate in journal club discussions. Each student will be provided with a name tag for class discussions. The TAs will keep track of student participation with a checkmark on a sheet. Suggestions for participation include asking questions during presentations, clarification of concepts, suggestions for future research, providing unique perspectives on the research, etc.

- **Question/critique submissions:** To encourage participation during journal club days, you will need to read the assigned journal article and prepare (1) at least one question and (2) at least one critique on the paper to be submitted on Canvas for credit. You can then ask the question during the journal club discussion. Submitted questions/critiques may be read aloud in class to stimulate discussion.

2. **Grant proposal:** Biomaterials engineers must learn how to write effective research proposals to obtain funding for projects in various career roles (academia, industry, government, etc.). In your teams of 4-5, you will be writing a 12-page original proposal (NIH R01 style). Proposals will be evaluated based on NIH evaluation criteria and will also be peer-reviewed by your classmates. You will also write responses to reviewer feedback. More instructions for each step are provided in separate documents, as well as grading rubrics.

    - **5-minute project pitch**: The project pitch should be on the same idea you plan to submit your grant proposal on. It should be a broad overview of the clinical/scientific problem, biomaterial strategy/solution you are proposing, the aims of the proposal, and the methods you will use to test and characterize your biomaterial. The purpose of this presentation is to get feedback and suggestions from the instructor, TA, and the other students about your idea before finalizing the details you will include in your grant proposal. An example slide deck (Project Pitch – Example) and a scoring rubric (Project Pitch – Rubric) will be provided.

    - **Significance and Innovation section**: In 3-4 pages, you will detail the significance and innovation of your proposal. Significance is the impact that your research will have on the field, and innovation is your new and substantively different way of considering/addressing a given problem. Instructions on how to approach this section are provided in the Grant Proposal – Instructions document. An example Significance and Innovation section can be found in the Grant Proposal – Example document.

        - *Significance*: The idea here is to get your reader "hooked" on the conceptual, exciting parts of the proposal to the extent that your reviewers will want to continue reading the details of your proposal and subsequently convince them to recommend funding your proposal. A core review criterion is to address an important problem and/or critical barrier to progress in the field. Does the prior research conducted in the field support the new area of study?
        - *Innovation*: In this section, you will describe how your proposal challenges and seeks o chipt current research or clinical practice paradigms. Describe here any novel theoretical conceptrs, approaches, or methodologies, and any advantage over existing methods/approaches. A core review criterion is whether or not your concepts, approaches, and methods are novel to your field of research.

    - **Specific aims page**: You will submit a 1-page "specific aims" page that highlights the motivation, milestones, and overall outcomes of the work. Typically, three aims will be proposed, and the three aims could be completed within a reasonable time frame (approximately 5 years). The instructor and TA will provide additional feedback on this aims page so that you can adjust before you write the rest of your grant proposal. Appropriate references should be included and are not counted in the page limit. Please use Arial 11 pt font with 0.5 inch margins, single spacing. Instructions on how to approach this section are provided in a separate document (Specific Aims – Instructions) along with a rubric (Specific Aims – Rubric) and example (Specific Aims – Example).

    - **Final proposal**: Your final proposal will allow you to learn about a specific medical disease or condition of interest to you and your group, review the latest advancements in biomaterials to propose a solution/treatment for the disease, and propose a new and/or innovative solution using biomaterials

and/or novel medical devices as tools. One proposal will be submitted per group (12 pages max). Please use Arial 11 pt font with 0.5-inch margins, single spacing. Figures and figure captions count toward the page limit. Figures may include (but not limited to) previously published datasets (please cite), conceptual/experimental setups, tables, equations, etc. Instructions on how to outline your proposal are provided in a separate document. An example proposal will be provided (Grant Proposal – Example).

- **Peer review of proposals**: Part of this course will be to learn more about the peer review process that goes into reviewing proposals and recommending them for funding. Groups will complete written reviews of 5 grant proposals from other students in the class. Written peer-review will follow NIH guidelines and involve scoring the significance, innovation, and approach of the proposal. On review days (Week 10), one group will lead the discussion for one proposal (e.g. Group 1 leads the discussion for Group 5's proposal) for ~15 minutes to discuss the aims of the proposal, pros/cons of the approach, suggestions for improving the proposal, provide an overall impact score, etc. Additional resources for effective peer review of proposals will be provided, including example rubrics and a word document to provide your own feedback.

- **Mock Study Section**: At the NIH, proposals are rigorously peer reviewed, discussed, and scored during a live roundtable discussion. We will emulate this process in our class. On a Mock Study section day, assigned proposals will be reviewed. One group (the "lead group") will lead the discussion for one proposal (~15 mins) that will evaluate the impact, significance, innovation, and approach of the proposed project. One person in the "lead" group will take notes of the discussion to be included in the summary statement. All other groups (the "supporting groups") will also provide feedback on the same proposal (2 points of critique) and participate in (but do not necessary lead) the discussion. All feedback from all groups will be compiled into one "summary statement" that will be distributed to the group that wrote the proposal. Mock study sections will be evaluated based on the rigor of the lead group's discussion points, completion of the supporting groups' comments, and overall participation of all groups in the discussion. At the end of the discussion, each group will provide their final overall impact score on the proposal. Examples of the peer review process can be viewed in these videos:

    - Virtual mock NIH study section (start video at 11:10) - https://www.youtube.com/watch?v=Vx6qO8z9swQ
    - Another mock NIH study section: https://www.youtube.com/watch?v=IzBhKeR6VIE
    - American Heart Association study section example: https://www.youtube.com/watch?v=DOQJUw1l4fk

- **Response to reviewers**: Each group will write a 1-page max response and/or rebuttal of their summary statement. The exercise here is to agree/disagree with critiques, suggest feasible future experiments, and identify further areas to improve the proposal as needed.

Journal Club Papers:

Paper 1 Blatchley, M. R. et al. In Situ Super-Resolution Imaging of Organoids and Extracellular Matrix Interactions via Phototransfer by Allyl Sulfide Exchange-Expansion Microscopy (PhASE-ExM). Advanced Materials n/a, 2109252, doi:https://doi.org/10.1002/adma.202109252. **Last author:** Kristi Anseth **Link**: https://onlinelibrary.wiley.com/doi/10.1002/adma.202109252
Paper 2 Doloff, J. C. et al. The surface topography of silicone breast implants mediates the foreign body response in mice, rabbits and humans. Nature Biomedical Engineering 5, 1115-1130, doi:10.1038/s41551-021-00739-4 (2021).

Last author: Robert Langer
Link: https://www.nature.com/articles/s41551-021-00739-4

Paper 3
Griffin, D. R. et al. Activating an adaptive immune response from a hydrogel scaffold imparts regenerative wound healing. Nature Materials 20, 560-569, doi:10.1038/s41563-020-00844-w (2021).

Last authors: Tatiana Segura and Philip Scumpia
Link: https://www.nature.com/articles/s41563-020-00844-w

Paper 4
Madl, C. M. et al. Maintenance of neural progenitor cell stemness in 3D hydrogels requires matrix remodelling. Nature Materials 16, 1233-1242, doi:10.1038/nmat5020 (2017).

Last author: Sarah Heilshorn
Link: https://www.nature.com/articles/nmat5020

Paper 5
Morris, A. H. et al. Engineered immunological niches to monitor disease activity and treatment efficacy in relapsing multiple sclerosis. Nature Communications 11, 3871, doi:10.1038/s41467-020-17629-z (2020).

Last author: Lonnie Shea
Link: https://www.nature.com/articles/s41467-020-17629-z

Paper 6
Li, W. et al. Rapidly separable microneedle patch for the sustained release of a contraceptive. Nature Biomedical Engineering 3, 220-229, doi:10.1038/s41551-018-0337-4 (2019).

Last author: Mark Prausnitz
Link: https://www.nature.com/articles/s41551-018-0337-4

Paper 7
Hong, C. et al. Modulating Nanoparticle Size to Understand Factors Affecting Hemostatic Efficacy and Maximize Survival in a Lethal Inferior Vena Cava Injury Model. ACS Nano 16, 2494-2510, doi:10.1021/acsnano.1c09108 (2022).

Last author: Paula Hammond
Link: https://pubs.acs.org/doi/10.1021/acsnano.1c09108

Paper 8
Anderson, A. E. et al. An immunologically active, adipose-derived extracellular matrix biomaterial for soft tissue reconstruction: concept to clinical trial. npj Regenerative Medicine 7, 6, doi:10.1038/s41536-021-00197-1 (2022).

Last author: Jennifer Ellisseff
Link: https://www.nature.com/articles/s41536-021-00197-1