Bio 5703: Experimental Design and Analysis **Fall 2019**

Instructors:

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Course Objectives:

The ability to identify important biological questions, develop testable hypotheses, design experiments tailored to particular questions, and evaluate results is critical for scientific research success. Presenting data clearly and concisely both in written and oral formats is critical for a successful career in research.

At the end of the course students will be able to formulate testable hypotheses, design practical ways to address scientific problems, and organize and present scientific data and insights to a professional audience.

Course Description

This course takes advantage of research articles—old and new--to highlight different approaches for problem solving in biology and, in doing so, develop skills for the critical analysis of the primary literature. The last three weeks of class will be devoted to student presentations on topics related to these landmark papers, providing students the opportunity to hone their public speaking skills.

Class will meet for two hours once a week, Mondays 2PM.

Please do not use cellphones or other technology during class. Please bring printouts of the papers being discussed with you to class.

Landmark Research Articles

Landmark papers were selected for their excellence and their impact on the field, and represent the best of the best. They are thus also not representative of the majority of articles you will read during the course of your studies. Of course, despite their status as landmark articles, these papers are also not without flaws. While we encourage you to look for these flaws, we prefer you focus on honing your ability to recognize 1) clever strategies; 2) the logical progression from the initial observation to the last experiment; and 3) the use of multiple approaches, combined with published background data, to reach sound conclusions.

All research is constrained by available methodologies and on-going paradigms; many important papers introduce new technologies or paradigms. As you read the “old” papers, consider how the research might have been done or interpreted differently in present times. How have the “new” papers addressed questions first raised by the “old” papers?

Expectations:
Students are expected to work independently unless otherwise instructed.

Read and Participate:

- Each week, students will be assigned landmark and current papers in prokaryotic and eukaryotic microbiology. Papers will be available to download from the course website on Canvas.

- Discussions will focus on analysis of the biological question(s) addressed in the week's reading material and the approaches used to answer the question. Possible alternative approaches will be evaluated.

- Every student is expected to come to class prepared to discuss the entire paper. Students should be able to: 1) identify the biological question(s) being addressed; 2) describe the approaches used to address the question; 3) summarize the data presenting in figures and tables; 4) assess the significance and/or validity of the authors' conclusions; and where appropriate, 5) propose follow-on experiments.

- Class participation will count towards 40% of the final grade.

Write:

- With the exception of the first class meeting, three days prior to class (i.e. by midnight Friday), students are expected to email to the appropriate instructor (plevin@wustl.edu or abose@wustl.edu) a one-page "Specific Aims" document that includes: i) a 250-word summary of relevant background; ii) a statement of the question to be addressed and their hypothesis; and iii) three experimental approaches (Aims) designed to test their hypothesis. These will be evaluated by the instructors and returned with constructive feedback.

- The first class will include a discussion of what makes a good set of specific aims, how to structure your specific aims page etc. Examples of specific aims pages will be available on blackboard.

- The first set of specific aims will focus on a topic of the student's choosing. The remaining three sets of aims will be based on an assigned topic.

- After receiving the aims, the instructors will provide constructive criticism on the first set of aims. Students are then expected to revise their specific aims page based on this critique for submission three days prior to the following class (i.e. by midnight Friday) by email to appropriate instructor as above. As per the schedule below, submission of new specific aims will alternate with submission of revised specific aims.

- Performance on specific aims and revisions will count towards 40% of the final grade.

Present:

- The last three weeks of the course will be devoted to student led presentations. Students will select one set of their specific aims for a 30-minute in-class presentation. The student will be expected to complete an extensive literature review on the topic and, in consultation with Dr. Levin and Dr. Bose, develop a 30-minute PowerPoint lecture, including graphics, that establishes the significance of the biological problem they are seeking to address and describing the approaches they propose to use.

- Revising is an essential part of writing and speaking. To help students hone their public speaking skills, students will submit a detailed outline and list of slides to Drs. Bose and Levin and for critique two weeks before their scheduled presentation. One week prior to their presentation, the student will schedule a practice talk with either Dr. Bose or Dr. Levin.

- Peer review is an essential component of modern science. To this end, students will be expected to fill out a brief evaluation for each of their colleagues' talks. The evaluation form will ask students to briefly address overall performance as well as organization, clarity, and slide "aesthetics." As a final project, the presenting student will write a one page summary detailing their "response to reviewers" and noting how they would modify their talk for future presentations, being as specific as possible.

- Oral Presentation will count towards 20% of the final grade (10% content; 10% presentation design and implementation)

Course Web Site:

All materials will be available on Canvas.

Rules to Read By: Reading and evaluating a scientific research article in four simple steps

1) Read through the Abstract and Introduction to ascertain background, premises, and major conclusions.

At the end of this step you should be able to succinctly state the question being addressed or hypothesis being tested.

2) Look through all Figures and Tables and their legends, consulting Methods if those used are unfamiliar, to get a sense of the kind and quality of the data.

3) Read Results carefully in conjunction with Figures and Tables, comparing claims about what the data is showing with what the data actually shows, again consulting Methods when necessary.

After completing steps 2 and 3 you should be able to summarize the important findings of the paper in four or five sentences.

4) Read Discussion, evaluating whether the conclusions drawn are supported by the data or whether some are tenuous; where tenuous, do the authors acknowledge this and indicate that further experiments are needed?

Other criteria for evaluation. 1) Have previous published articles been adequately acknowledged? If the results refute previous publications, are explanations offered for the discrepancies? 2) Are Methods sufficiently detailed that you believe you could repeat the experiments?

You should also take note of what you like and don't like about the presentation style. 1) Is some of the data presented in an informative fashion (e.g. accessible graphics) that you might wish to emulate in your own publications? Reciprocally, is some of the data presented in a confusing fashion that you would want to avoid? 2) If you find the writing particularly lucid and engaging, try to identify what goes into that for future emulation. If it's turgid and boring, notice what generates that outcome for future avoidance.

At the end of Step 4 you should be able to summarize the merit of the paper both experimentally (i.e. are the experiments well designed and properly controlled) and in terms of contribution to the field (i.e. what are the implication of the authors' findings for the field) in one or two sentences.

Date	Topic	Reading
8/26	**DNA as the molecule of heredity (Petra)**	Avery, O. T., Macleod, C. M., & McCarty, M. (1944). Studies on the chemical nature of the substance inducing transformation of pneumococcal types. Inductions of transformation by a desoxyribonucleic acid fraction isolated from pneumococcus type III. J. Ex. Med. 149: 297–326. Hershey, A. D. and Martha Chase, (1952) Independent functions of vial protein and nucleic acid in growth of a bacteriophage, The Journal of General Physiology, 36: 39-56.
8/30	**To both Petra and Arpita**	**Specific Aims 1 Due**
9/2	**Labor Day**	**NO CLASS**
9/9	**Prokaryotic Gene Regulation (Arpita)**	Pardee, Arthur B., François Jacob, and Jacques Monod. (1959) The genetic control and cytoplasmic expression of "inducibility" in the synthesis of β-galactosidase by *E. coli*. J. Mol. Biol. 1: 165-178. Somvanshi, Vishal S., et al. (2012) A single promoter inversion switches Photorhabdus between pathogenic and mutualistic states." *Science* 337: 88-93.
9/13	**To both Petra and Arpita**	**Specific Aims 1 REVISED Due**
9/16	**Prokaryotic Secretion (Arpita)**	Oliver, Donald B., and Jon Beckwith. (1981)*E. coli* mutant pleiotropically defective in the export of secreted proteins. *Cell* 25: 765-772. Guttman, David S., et al. (2002)A functional screen for the type III (Hrp) secretome of the plant pathogen Pseudomonas syringae." *Science* 295: 1722-1726.
9/20	**To both Petra and Arpita**	**Specific Aims 2 Due** TOPIC: Genetic and biochemical analysis of a molecular machine
9/23	**Antibiotic Discovery (Petra)**	Fleming, A. (1929). On the Antibacterial Action of Cultures of a Penicillium, with Special Reference to their Use in the Isolation of *B. influenzæ*. British Journal of Experimental Pathology, 10(3), 226. Abraham, E. P., & Chain, E. (1940). An Enzyme from Bacteria able to Destroy Penicillin. Nature, 146: 837–837. Hover, et al. (2018)Culture-independent discovery of the malacidins as calcium-dependent antibiotics with activity against multidrug-resistant Gram-positive pathogens." Nature Microbiology 3: 415.

9/27	**To both Petra and Arpita**	**Specific Aims 2 REVISED Due**
9/30	**Genetics for the win! (Petra)**	Luria, S. E., & Delbruck, M. (1943). Mutations of Bacteria from Virus Sensitivity to Virus Resistance. Genetics, 28(6), 491–511. Lederberg, J. and E. M. Lederberg (1951) Replica plating and the indirect selection of bacterial mutants, J. Bacteriol., 63:399-406. Giver et al (1998) Directed evolution of a thermostable esterase, Proc, Nat. Acad. Sci. 95: 12809–12813.
10/4	**To both Petra and Arpita**	**Specific Aims 3 Due** Topic: Genetic and Molecular Analysis of an Essential Process in Bacteria
10/7	**Characterization of essential processes (Petra)**	Hirota, Y., Ryter, A., & Jacob, F. (1968). Thermosensitive Mutants of E. coli Affected in the Processes of DNA Synthesis and Cellular Division. Cold Spring Harbor Symposia on Quantitative Biology, 33(0), 677–693. doi:10.1101/SQB.1968.033.01.077 Fuller, R. S., & Kornberg, A. (1983). Purified DnaA protein in initiation of replication at the *Escherichia coli* chromosomal origin of replication. Proceedings of the National Academy of Science, U S A, 80(19), 5817–5821. Peters, J. et al. (2016). A Comprehensive, CRISPR-based Functional Analysis of Essential Genes in Bacteria. Cell, 2016 vol. 165 (6) pp. 1493-1506
10/11	**To both Petra and Arpita**	**Specific Aims 3 REVISED Due**
10/14	**FALL BREAK**	Find a cool story on the ASM blog “small things considered” and come back and tell us all about it next week! http://schaechter.asmblog.org/schaechter/
10/21	**One gene one enzyme (Arpita)**	Beadle, G. W., & Tatum, E. L. (1941). Genetic control of biochemical reactions in Neurospora. Proc Natl Acad Sci U S A, 27: 499-506 Helliwell K.E., Wheeler G.L. & Smith A.G. (2013). Widespread decay of vitamin-related pathways: coincidence or consequence? Trends Genetics 29: 469-478. [Note: This is a review article, so discussion will focus on concepts rather than on data interpretation.]

10/25	**To both Petra and Arpita**	**Specific Aims 4 Due** Topic: Microbe-host interaction
10/28	**CRISPr (Petra)**	Marraffini, L. A., & Sontheimer, E. J. (2008). CRISPR Interference Limits Horizontal Gene Transfer in *Staphylococci* by Targeting DNA. Science, 322(5909), 1843–1845. doi:10.1126/science.1165771 Jinek et al, (2013) RNA-programmed genome editing in human cells, eLife 2013;2:e00471 DOI: 10.7554/eLife.00471
11/1	**To both Petra and Arpita**	**Specific Aims 4 Revised Due**
11/4	**Microbial Physiology (Arpita)**	Bryant, M. P., et al. (1967) *Methanobacillus omelianskii*, a symbiotic association of two species of bacteria." *Archives of microbiology* 59: 20-31. Boetius, Antje, et al. (2000) A marine microbial consortium apparently mediating anaerobic oxidation of methane." *Nature* 407: 623.
11/8	**To both Petra and Arpita**	**Slide List for Final Presentation Due**
11/11	**Three kingdoms and eukaryotic origins (Arpita)**	Woese, C.R., & Fox, G.E. (1977). Phylogenetic structure of the prokaryotic domain: The primary kingdoms. Proc Natl Acad Sci U S A, 74:, 5088-5090. Alvarez-Ponce, D., Lopez, P., Baptiste, E., & McInemey, O. (2013). Gene similarity networks provide tools for understanding eukaryotic origins and evolution. Proc Natl Acad Sci U S A, 110: E1594-E1603.
11/18		**THANKSGIVING BREAK WEEK** **Polish your presentations – amaze your family and friends!**
11/25	**STUDENT PRESENTATIONS**	
12/2	**STUDENT PRESENTATIONS**	