Metagenomics

BIMM 194 / BGGN 283 – Fall 2023
3010 York Hall
Thursdays 11:00 – 12:20 pm

DATE	LECTURE & PRESENTATION TOPIC
Introduction to Metagenomic Approaches and Analysis	
Oct 03	1) Course Description & Introduction
Oct 10	2) The Metagenomic Approach
Oct 17	3) Bioinformatics: Assembly, Binning, & Annotation
Metagenomics in Action	
Oct 24	4) Environmental Gene Inventories
	5) Community & Population Genomics
Nov 07	6) Metatranscriptomics, Proteomics, & Metabolomics
Nov 14	7) Functional Metagenomics
Nov 21	No class – (early) Thanksgiving Holiday!
Nov 28	8) Host-associated Microbiomes
Dec 05	9) Single Cell Genomics
Dec 15	****Reports due via email****

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Shuttle information: https://transportation.ucsd.edu/campus/shuttles/sio.html

Course Web Site: https://canvas.ucsd.edu/courses/48778 (lectures, assigned readings, etc.)

Course Prospectus: The field of metagenomics is a rapidly evolving discipline driven by advances in computational biology, DNA sequencing technologies, and the techniques of modern systems biology. The application of genomic methods to environmental samples are being exploited to understand the microbial biology of diverse habitats ranging from the human body to the oceans and extreme environments. Ultimately, the goal of this line of research is to discover the form, function, and diversity of environmental microorganisms. The field cuts across many disciplines with metagenomic approaches being utilized in diverse areas including biomedicine, biotechnology, bioenergy, agriculture, biogeochemistry, phylogenetics, evolution and molecular ecology. From this class, you will gain an admiration of the immense taxonomic, genetic, and metabolic diversity of microorganisms and an appreciation of the tools, both computational and molecular, that can be deployed to analyze the biology of environmental microorganisms.

Textbook: Nope. An authoritative textbook on the topic does not exist. Instead, we will rely on the primary literature to dive into various topics and themes. All primary assigned readings (journal articles and reviews) will be posted on the course Canvas website as .pdf files under "Required Readings".

Grading & Evaluation Criteria: Our weekly 80-minute meetings will conform to the following schedule:

35 minute lecture covering various topics led by Professor Allen
30 minute student-led group presentation of primary research article(s) to the class (beginning in Wk3)
15 minute interactive discussion about the day's lecture & presentation

******* The final grade in the class will be based on one of two possible options, (A) or (B) below, in addition to class participation.

(Option A) Oral Presentation:

Participate in leading a 30-minute presentation to the class covering a contemporary journal article (or multiple articles) that utilizes metagenomic approaches as a tool for biological discovery. In consultation with Professor Allen, choose a paper that is of interest. Prepare a PowerPoint (or other media such as Google Slides) presentation that provides an introduction to the scientific question being addressed, a description of the methods used, and an analysis of the results from the study. Be prepared to field questions from the class and engage in discussion! It is recommended that you use ancillary references (additional papers) to research the topic as you prepare your presentation. To accommodate as many students as possible, **presentations will be team-led**, i.e. two or three, maybe four, students per presentation.

Presentation Format: Each member of the presenting team should prepare 3-5 slides or whiteboard sketches. It is recommended that presenting teams coordinate their efforts by organizing meetings (the more the better) to discuss the order of presentation and determine who is responsible for what material. Also, decide who in the group is bringing a laptop and be sure that everyone has included their content into a single presentation file. As noted above, each group should prepare a cumulative presentation of approximately 30 minutes.

Guidelines for Oral Presentations: The oral presentations should hit upon several essential elements. By following the guidelines below, you will be able to strategically prepare an effective presentation that will be applauded by all! Importantly, focus on preparing clear visual aids to present the data and illustrate your points. This will assist your audience in grasping the topics being presented.

I. Introduction/Background Information
It is important to set the appropriate stage to introduce the research being presented. Familiarize yourself with background information on the topic so as to project a clear and concise rationale for why the research was conducted. Questions to ask in preparing introductory slide materials include: Why is this system interesting? What is already known regarding this environment/organism/system? What is the question or problem being addressed? What is the motivation for this research? What is the big picture of this scientific endeavor?

II. Experimental Approach
Now that you have introduced the context of the research, explain the methodology and experimental protocols used in this study to dissect a biological problem or explore a novel biological system. What approaches were used? Why did the authors choose this approach and these methods?

III. Results
When presenting the results, it is important to reiterate the methods used to generate the data. The data should be summarized to allow a reviewer (or in this case your audience) to begin to consider conclusions on her/his own without interjecting the author's interpretations. You should also consider the integrity of the experimental results.

Please feel free to include your opinions, likes, or dislikes of the data and begin to describe some conclusions about the results that can be drawn.

IV. Conclusions
Present the major conclusions of the study revealed by the authors. Be sure to also include your independent interpretations of the data and provide these in concert with the authors' interpretations. What is the significance of the results? Do you believe the author's conclusions? What additional experiments might have been performed to strengthen the conclusions? In wrapping up your presentations, discuss the long-term implications of the research. What might be done next?

(Option B) Research Proposal:

After 10 arduous weeks of learning about metagenomic methods and applications to ecological and/or applied questions, it is time to put all that you have learned together and run with it. Once you have learned all of the wonderful opportunities and analyses available to your genomically-enabled mind, you are well armed to design a project and venture forth as an independent researcher.

We will have covered a fair amount of material this quarter:

- Sampling the environment
- Bioinformatic practices (assembly, phylogenetic binning, annotation, and analysis of genomic data)
- Functional metagenomics
- Environmental gene inventories
- Community and population genomics
- Environmental post-genomics (proteomics, transcriptomics, metabolomics)

Prepare a 3 - 4 page report (1.5 point spacing) describing a hypothetical research project of your choosing. Specifically, you will prepare a research proposal in which you will conceive of a research project and describe how you would go about exploring the biology of a system ("environment") using metagenomic methodologies. The report should identify a target community or environment and discuss the importance of this system, the methods to be used to examine the system and the expected outcomes of the research, i.e. what do you hope to learn? Proper citing of literature used in preparing your proposal MUST be included. If you are unfamiliar with how to properly cite primary literature (i.e. original research articles published in peer-reviewed scientific journals), please ask Professor Allen.

When designing a research topic, think about the project's goals and what hypotheses you set out to test. What kinds of organisms and what kinds of metabolisms do you expect to encounter? This could simply involve investigating the diversity of microbes that live in Antarctic sea ice (permanently cold environments) or microbes associated with the basalts of deep-sea hydrothermal vents (permanently hot environments) or the microbes associated with the gastrointestinal tract of Canadian newborn infants born on the Summer Soltice in odd years with parents who exclusively drive motorcycles (huh?). Alternatively, you may wish to be imaginative and explore perhaps less exotic, yet equally interesting, sites such the cooling towers of nuclear power plants, chlorine resistant microbes in your swimming pool, microbes associated algae ponds used for biofuel production, the flora found in the guts of koalas, or the zoo of microbes found on a shower curtain. Be creative!

The format of the report should include the following elements:

I. Title (20 words or less)
Be explicit as is necessary to adequately describe the proposed project.

II. Abstract (0.5 page)
Provide a brief overview of the project including the system to be explored, the methods used, and why this project is important.

III. Introduction (0.5 – 1 page)

Provide an introduction to the system ("environment") in the form of background information. The introduction should provide sufficient information to acquaint the reader with the importance of this particular biological system. It is important to justify why the environment you have chosen is of interest and there should be a scientific basis for exploring this environment's organismic and functional diversity. The point here is to get the people who read your proposal excited about what you plan to do!

IV. Specific Aims/Goals (< 0.5 page)
Explicitly state what you plan to accomplish with this research. This can be presented in the form of bullet points or a brief description of what the project aims to accomplish.

V. Project Description & Methods (1 – 2 pages)
You must logically progress through how you will go about performing the research. This includes sampling techniques and the methods used to assess the diversity of the environment (who is in there?) and gain insight into the metabolic abilities of these populations (what are they doing?). This section is the most important part of the proposal and should provide enough detail that the reader can evaluate if you know what you are talking about and if the proposed project is technically sound. Remember that this is a proposal – you are justifying WHY a project is worthy of being funded and thus you do not have answers yet. Answers are what you seek! You do however have access to PubMed and Google Scholar so you can research background reference information about your system before you begin to propose a study. Do it!

VI. References (no page limit)
In order to adequately prepare a proposal, you must know something about the system under investigation. To do so you will have to access primary scientific literature (e.g. PubMed or Google Scholar) and read through the relevant literature to obtain sufficient information to describe the system. No less than three references should be included in your report. Use the following reference style in your report:

Narasingarao P, Podell S, Ugalde JA, Brochier-Armanet C, Emerson J, Brocks JJ, Heidelberg KB, Banfield JF, Allen EE (2011) *De novo* metagenomic assembly reveals abundant novel major lineage of Archaea in hypersaline microbial communities. *ISME J.* 6:81-93.

Class Participation:

******* In addition to the grading criteria described above, you will be responsible for *active participation* in this class! After each lecture and presentation, we will have a brief discussion period where we will evaluate a paper's scientific methods, results and the author's interpretations. YOU SHOULD CRITICALLY READ THE ASSIGNED PAPERS BEFORE CLASS so that you are prepared to participate in the discussions.

General Guidelines for Reading Scientific Papers:

Familiarize yourself with the related topics:
Read and understand the Abstract and Introduction. Do background reading on related material (via PubMed or Google Scholar searches; see links below) in order to become familiar with the subject matter. Research papers are written for people who already know something about the subject matter!

Try to answer the following questions as you read the papers:

1. What questions were addressed in this paper?
   Frequently the introduction will present background information and raise the questions that will be addressed in the paper.
2. What were the main conclusions from the paper?
   The main conclusions will be summarized in the abstract, and further explained in the discussion section. Why were these conclusions important?

3. What experiments were performed to answer these questions?

   These will be briefly summarized in the abstract and discussed at length in the materials & methods and results sections of the paper.

4. For each experiment:

   What conclusions did the experiments allow? What were the caveats of each experiment? (i.e., were there alternative explanations?) What experiments ruled out these alternatives?

Useful Websites:

PubMed: http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?tool=cdl&holding=ucsdlib (journal literature portal)

Google Scholar: http://scholar.google.com (literature search portal)

Nature Reviews Microbiology: http://www.nature.com/nrmicro/index.html (microbial biology news and reviews)

Small Things Considered: http://schaechter.asmblog.org/schaechter/ (odds and ends from the microbial world)

Microbe wiki: http://microbewiki.kenyon.edu (resource for exploring a rich variety of microbes)

EBI-Metagenomics: https://www.ebi.ac.uk/metagenomics/ (metagenome analysis at EBI)