Summary:
Although bacteria reproduce asexually, recombination occurs commonly. Recombination plays an important role in maintaining a genetically cohesive population and in facilitating adaptation. Recombination-seeded adaptive events may be especially important in complex communities like the microbiome because co-existing species and strains may serve as a reservoir for adaptive genetic material. However, recent evidence in the literature suggests that recombination in host-associated bacteria may be more complex than in a freely recombining population. In this seminar, students will read and discuss key papers on recombination in bacteria, including classic papers and recent literature on the microbiome. Important, outstanding questions will be discussed from reading these papers.

Course Objectives:
1. Explain how bacteria recombine.
2. Explain how recombination impacts genetic diversity.
3. Explain why recombination is important for the ecological structure of a community of bacteria.
4. Explain how to quantify recombination.
5. Pose new questions about recombination in bacteria.
6. Present complex, technical information.
7. Critically read and analyze primary literature.

Expected Participation:
1) Each student is expected to read the papers each week and be prepared to contribute to discussion. Students should be prepared to discuss the questions posed for each week (most weeks have a question).

2) In addition, to facilitate the discussion and ensure that students understand the papers, students are required to prepare at least one question per week and/or propose an extension of the work that they read about. The questions could be about a confusing point in the paper or about a broader question for the field. Extensions of the work presented in the paper
could be about a future direction or follow up to the work. Please fill out this form with your question/idea prior to class so that we can make sure to discuss it!
https://docs.google.com/forms/d/e/1FAIpQLSd9bNWImXiperZtfwegr6imsWTTeJy7cNG5zOFem--xO7hFA/viewform?usp=sf_link

3) Each student will be **allowed one absence or class session where they do not have to have a question prepared without affecting their grade.**

4) Each student will **present at least one paper in one session.** The presentation should be a powerpoint that goes through all elements of the paper. For some of the shorter papers, please present key elements of the supplement (e.g., tables, figures, and methods). The presentation should help us understand: what are the key questions being addressed in the paper? What methodology was used? What were the key findings and their meanings? What assumptions were made? What are the open questions?

The presentations should set the stage for discussion with other students and invite discussion and questions. The presenters should pose relevant questions about the paper and invite answers from students. The presenters should be prepared to lead a productive discussion.

Please sign up here for your presentation date(s): https://docs.google.com/spreadsheets/d/1-1G0PQzLlf8KgbM94tEADBiha79-v5Oh8WmChMaVZ0/edit?usp=sharing
(There may be more people than spots – if so, please double up on the weeks where there are two papers).

5) **The students presenting for a particular week are expected to meet me ahead of the discussion to share a draft of their presentations.** The purpose of this meeting is to ensure that the right topics receive enough emphasis. I may suggest additional references that contain background material to help students understand and enhance certain papers.

**Grading**
The following composition will be used to determine the grades:
Questions and participation each week: 50%
Presentation: 50%

**Office Hours:**
Fridays 4-5pm (this could be a good opportunity to go over material for the presentation the next week).
Please email me if you want to meet at another time at ngarud@ucla.edu
My office: 4304 Life Sciences Building.

**Schedule**
Papers available here:
https://www.dropbox.com/sh/7jmpqem6dj6pvry/AACpqRC-tWrpAWUKHHJcWZg9a?dl=0

**Week 1 – Sept 30**
Introduction to recombination in bacteria
- Redfield et al. 2001 – Do bacteria have sex?
- Hanage et al. 2016 – Not so simple after all: Bacteria, their population genetics, and recombination.
- Questions: what are the different modes of recombination in bacteria?

Week 2 – Oct 7
How clonal are bacteria?
- John Maynard Smith 1993 -- How clonal are bacteria?
- Jesse Shapiro 2016 -- How clonal are bacteria over time?
- Questions: What can generate linkage disequilibrium? Is it appropriate to draw a tree for a panmictic population?

Week 3 – Oct 14
Quasi-sexual bacteria
- Rosen et al. 2015 -- Fine-scale diversity and extensive recombination in a quasisexual bacterial population occupying a broad niche
- Addendum: Rosen et al. 2018 -- Probing the ecological and evolutionary history of a thermophilic cyanobacterial population via statistical properties of its microdiversity
- Questions: What is a quasi-sexual species? What confusions does Figure 1 in Rosen 2018 pose (Hint: the distributions make it look like the bacteria are asexual, but actually they aren’t).

Week 4 – Oct 21
Are bacteria freely recombining?
- Sakoparnig et al. 2019 -- Whole genome phylogenies reflect long-tailed distributions of recombination rates in many bacterial species
- Questions: What does scale free mean? What does exchangeable mean (look up exchangeability in statistics)? What is the 4-gamete test? How can we use phylogenetic inconsistencies to detect recombination? What is a key assumption that the authors make with regards to bi vs tri allelic SNPs?

Week 5 – Oct 28
Costs of sex
- San Millan & Maclean 2017 – Fitness Costs of Plasmids: a Limit to Plasmid Transmission
- Otto & Lenormand 2002 – Resolving the paradox of sex and recombination

Week 6 – Nov 4
Recombination in microbiomes across species boundaries
- Smillie, Smith et al. 2011: Ecology drives a global network of gene exchange connecting the human microbiome
- Brito et al. 2016: Mobile genes in the human microbiome are structured from global to individual scales
Week 7 – Nov 11 (Veterans Day, off)

Week 8 – Nov 18
Measurements of recombination with rho/mu
- Didelot 2010 -- Inference of Homologous Recombination in Bacteria Using Whole-Genome Sequences
- Vos & Didelot 2009 -- A comparison of homologous recombination rates in bacteria and archaea
- Questions: What does rho/mu mean? How does recombination vary across species?

Week 9 – Nov 25
Ecotypes
**Note: we will not be meeting for this class. Please write at least two paragraphs summarizing the papers below, and in these paragraphs pose either a question or future direction for each paper.
- Shapiro et al. 2012 -- Population Genomics of Early Events in the Ecological Differentiation of Bacteria
- Cohan 2017 -- Transmission in the Origins of Bacterial Diversity, From Ecotypes to Phyla
- Questions: What is a gene-specific sweep and what is a genome-wide sweep? How does recombination (or lack of) generate ecological niches? What is an ecotype?

Week 10 – Dec 2
Linkage disequilibrium
- Lin and Kussell 2019 -- Inferring bacterial recombination rates from large-scale sequencing datasets
- Question: How can we use LD to detect recombination?