OEB 100 – Evolution in Action

Spring 2011 Course Syllabus

Instructor: Christopher Marx (cmarx@oeb.harvard.edu, Biolabs 3083)
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Weekly meeting: Northwest Building room 152
Time: M 4:00 – 5:30 pm

Laboratory: Northwest Building room 152
Time: 24/7/365 open access

Website: http://isites.harvard.edu/k77185

Goals: This course's primary aim is to teach students how to design, perform, interpret, and discuss independent research in a collaborative atmosphere. A second goal is to utilize the unique advantages of studying experimental populations of microbes in the laboratory as a means to explore evolution in 'real time'. Finally, this course will provide an opportunity to integrate within a single, hands-on class, concepts from genetics, biochemistry, systems biology, microbiology, evolution and ecology. **This year's project is rather extreme: adaptation to eating the toxic compound formaldehyde.**
(Note that this course can freely substitute for the Research experience requirement for an MCB concentration, the LS100r requirement for a Secondary Field in Microbial Sciences, or can count toward either an OEB Concentration or Secondary Field.)

Format: There are two pre-arranged meetings each week. Each Monday afternoon (4:00-5:30 pm) we will hold our weekly course meeting. This time will initially be used for lectures on fundamentals necessary for the course and training in a few key areas. Starting with the 4th week (2/14), this will transition to presentations by class members on recent results and planned next steps. A second meeting each week (time to be decided on Wed, Thu or Fri) will be one hour long devoted to detailed informal discussions about data interpretation, experimental design, etc. Beyond this, the lab is open 24/7/365 and students are responsible for scheduling as a team to propel the project forward.

Group structure: The class (max. of 12) will be divided into groups based upon research questions students find most interesting. All sub-projects will relate to the same broader theme (see below), but as ideas are suggested and discussed, students will volunteer to join in on specific efforts ('threads') depending upon their interests, the number of people needed for a task, and number of other threads that they are contributing to. As appropriate, we will ask for one student to serve as the leader of that research thread. Students will maintain their own section of the Goggle docs as their collective lab notebook. The hours that the TF will be present to aid in training and implementation of the project will be arranged on an ad hoc basis.

Project concept: The novel research project area for OEB 100 has been chosen to provide a balance between two different types of tradeoffs. The first is a balance between independence and a well-thought project with momentum that is ready to run from the first week. Each group will be responsible for making decisions regarding implementation of their goals, yet we wish for student groups to have well-formed projects with some momentum from the very beginning so that as much as possible of the semester can be spent performing interesting experiments. As such, we have outlined a broad research project below that has a great deal of flexibility in terms of scientific questions to ask and address by means of experiment. Since this project has been specifically designed in a manner that allows you to perform independent research and come up interesting conclusions we want to make it possible for creative ideas and hard work to perhaps even result in contributing to publishing your work.

The second tradeoff relates to an aspect that makes OEB 100 unique from other research-based courses: An explicit desire for intellectual continuity between a panel of inter-related research threads, all centered around using experimentally-evolved populations in the lab. On the other hand, the multi-disciplinary nature of the questions you will address will result in consideration and use of a great variety of instrumentation and techniques.

Project details: Using evolution to study bacterial ~~resistance~~ *growth* on the toxic chemical formaldehyde

The recent oil spill in the Gulf of Mexico has been in the news for several reasons. One among them is the fact that researchers recently found bacteria belonging to the genus *Oceanospiralles* that could actually degrade some of the toxic, even carcinogenic, aromatic hydrocarbons present in oil. These bacteria harbor genes that can degrade aromatic compounds like naphthalene into non-toxic products thereby using it as a source of energy, carbon or both. This phenomenon raises an obvious question: *How do bacteria develop resistance to the intracellular presence of toxic chemicals?* In other words - *How do bacteria withstand the harmful effects of toxic chemicals within the cell before they get degraded?*

In this project, we have taken a novel approach that seeks to use adaptation as a tool to answer the aforementioned question. *Methylobacterium* is a bacteria that can use single carbon compounds (such as methanol, methylamine) as growth substrate. Interestingly enough, these bacteria produce intracellular formaldehyde as an intermediate whilst growing on single carbon compounds but become really sick if they are asked to grow on formaldehyde itself. This is because formaldehyde is not just very toxic, but is a potential carcinogen, and also a known mutagen (induces mutations).

To understand how these bacteria have evolved to withstand intracellular formaldehyde we have already evolved populations of *Methylobacterium* in the lab that can now grow on pretty high formaldehyde concentrations (>30 mM). We have also found that some of these isolates can hardly grow on anything else!

From here, we already have several exciting directions to propose (and welcome your ideas for more):

- How specific is adaptation to the concentration of formaldehyde itself? Has becoming able to grow at super high levels compromised growth at lower levels? Does this allow both strategies to coexist in the population?
  - How much has evolution to formaldehyde growth helped or hurt their ability to grow on other carbon compounds or in the presence of other stresses such as salt, ethanol, peroxide, antibiotics, etc.? For this we will take advantage of the course's automated, robotic growth system available. Thes quantitative growth profiles thus obtained will reveal changes in niche breadth to reveal whether there are other tradeoffs beyond those already found.
  - Given that we already know there have been some massive tradeoffs involved in adapting to formaldehyde, we can evolve new populations from these strains to recover growth in alternative environments. Will this cause them to consequently lose some of their ability in formaldehyde?
  - What is the genetic basis of improvement on formaldehyde? We will be using pyrosequencing to re-sequence the genome of a few of the evolved strains. This will allow us to determine the genetic loci that have undergone mutations over the course of evolution, examine these loci in other populations to look for parallelism, determine the order of mutational events, and begin to reintroduce these alleles to address which of these cause the phenotypic changes observed.
  - How dramatic and parallel is the change in the global gene expression profile of these evolved isolates? We could use either microarrays or RNA sequencing to determine these patterns and use them as guide for further experiments.

Schedule

		Class Meeting	**Assignments due**
January	24	Broad introduction to class	
	31	Detailed description of possible initial project threads, general background	
February	7	Further background	
	14	Group Presentations	Presentations/videos
	21	No class –	

		Presidents' Day	
	28	Group Presentations	
March	7	Group Presentations	
	14	No class - Spring Break	
	21	Group Presentations	
	28	Group Presentations	
April	4	Group Presentations	
	11	Group Presentations	
	18	Group Presentations	
	25	Final Group Presentations	Final composite video
May	5	(Reading Period ends)	Pre-proposal

Grading & assessment

Weekly presentations	20%
Final group presentation	10%
Active participation in course meetings	10%
Contribution to group's research	20%
Synopses in Google docs	10%
Contribution to class video	15%
Brief (3 page) final proposal	15%

Given that this is a course without exams, assessment will be based upon a multiplicity of different components. Some of these are relatively straight-forward, such as presentations of final proposals (and will be discussed further in class). The most unusual type of project will be the creation of a video that describes the over-arching biological question being addressed, gives an overview of the model system and approach taken, summarizes the results of each thread, and captures the broad significance of work in this area. The target audience for this is the general public. This will reinforce central concepts through the process of having to simplify and distill them at a fundamental level for non-experts. Thankfully, video production using tools such as iMovie is remarkably easy and powerful. In order to build expertise, there will be a series of stages in which individual segments of each group's video will be due throughout the term.