Bioinformatics for Microbial Genomics and Metagenomics

I609 Bioinformatics Seminar I
Spring 2010
School of Informatics and Computing,
Indiana University
**Key Words**

- *Bioinformatics*
- *Microbe (microorganism):* a microbe is an organism that is microscopic (too small to be seen by the naked human eye alone)
- *Genomics:* study of an organism's *entire* genome
  - Sequencing
  - Functional Genomics
- *Metagenomics (environmental genomics):* study of microbial communities, often unculturable, by analyzing the pooled genomes of all the organisms present in the community (study of the totality of genetic material of a community)
  - Metagenome: the totality of genetic information of a community
  - Microbiome: the totality of microbes, their genetic elements (genomes), and environmental interactions in a defined environment (e.g., human microbiome)
Basic Information

- Class meets (Tuesdays 1:00-3:45 PM)
- Instructor: Yuzhen Ye (yye@indiana.edu)
  - Office I 201B
- Office hour: by appointment, or you may just stop by my office and see if I am available.
- Course website:
  - http://mendel.informatics.indiana.edu/~yye/lab/teaching/spring2010mg.php
Overview of the Course

Recommended text books

Grading
- Paper summary (40%)
- Paper presentation (30%)
- Course project (proposal)* (30%)
Tentative Schedule of the Course

- Week 1 (overview & play some puzzles!)
- Week 2 (read a review article & select two papers that sound most interesting to you)
- Week 3-5 (lectures given by the instructor)
- Weeks after (paper presentations by students; possible guest lectures)
- Final week (project/proposal presentation)
Paper Presentations

- Each class covers a particular topic
- 2 (or 3) related research articles for each topic
- Papers are selected by the instructor (and the students)
- Students present the papers, and lead the discussions. Preparation of powerpoint slides needs to be done by the weekend before the paper is going to be presented.
- All students are required to write a summary for each of the papers; due by the noon of the Tuesday the papers are going to be presented.
Paper Presentation Topics

- Species diversity estimation (how many, and what are they)
- Functional annotation (what are they doing)
- Evolutionary studies
- Comparative metagenomics
- Microbe-host interactions, and microbe-environment interactions, etc
Why Metagenomics?

- Many good reasons
  - “Studying microbial communities through metagenomics can help biologists tackle fundamental scientific questions and address related social, environmental, and economic problems”
  - “...under the radar of public attention, or even that of most biologists, microbiology is undergoing a renaissance”
  - “METAGENOMICS AS A MODEL FOR EDUCATION-RESEARCH INTEGRATION”

First Peek at Microbes

Bacteria Morphological Diversity: from http://ag.arizona.edu/plp/courses/plp329/micdivintro.ppt
Microbes are Small

The basic unit of length is the meter (m), and all other units are fractions of a meter.

nanometer (nm) = 10^-9 meter = .000000001 meter  
micrometer (μm) = 10^-6 meter = .000001 meter  
millimeter (mm) = 10^-3 meter = .001 meter  
1 meter = 39.4 inches

These units of measurement correspond to units in an older but still widely used convention.

1 angstrom (Å) = 10^-10 meter  
1 micron (μ) = 10^-6 meter

(source: http://www.mansfield.ohio-state.edu/~sabedon/lectures/index.html)
Bacterial Anatomy

Figure 1
Microbes Run the World

- The Earth is a “microbial planet”
  - microorganisms predate other life forms (have evolved for some 3.8 billion years)
  - they are the most abundant -- both in terms of numbers and distribution
  - Microbial activities have profound influence on the integrity and functioning of global ecosystems.

- “. . .The diversity and range of their environmental adaptations indicate that microbes long ago ‘solved’ many problems for which scientists are still actively seeking solutions.” (Microbial genome program, US. Department of Energy; http://microbialgenomics.energy.gov/)
The global carbon cycle: Source: http://www.bigelow.org/foodweb/carbon_cycle.jpg
Microbes and Industry

- Industry: Fermentation products (ethanol, acetone, etc.)
- Food: Wine, cheese, yogurt, bread, half-sour pickles, etc.
- Biotech: Recombinant products (e.g., human insulin, vaccines)
- Environment: Bioremediation
  Bugs+Plus: to digest oil and other petroleum derivatives.
Microbes and You

- Every part of your body that normally comes in contact with outside world (deep lungs and stomach are exceptions)
- You are “what you eat”
  - Human gut microbes
- “Good” and “bad” microorganisms
Humans are 99% Bacteria?

human flora: the assemblage of microorganisms that reside on and within on human bodies

genes: 100 times more

human flora include bacteria (90%), fungi and archaea
**Helicobacter pylori** and Ulcers

- Ulcers were thought to be caused by stress or poor diet
- Disruptions to the human microbiome caused by a *Helicobacter pylori* that is not normally present or does not cause troubles (early 1980s).
- A Nobel Prize for Medicine was given to Robin Warren & Barry Marshall in 2005 for their discovery
Diseases Caused by Microbes

Bacillus anthracis  
Borrelia burgdorferi  
Brodetella pertussis  
Chlamydia trachomatis  
Clostridium botulinum  
Clostridium perfringens  
Clostridium tetani  
Corynebacterium diphtheriae  
Escherichia coli  
Gardinerella vaginalis  
Helicobacter pylori  
Haemophilus influenzae  
Klebsiella pneumoniae  
Legionella spp.  
Listeria monocytogenes

Anthrax  
Whooping cough (pertussis)  
Lyme disease  
Trachomas (blindness), etc.  
Botulism  
Gas gangrene & food poisoning  
Tetanus  
Diphtheria  
Typhoid fever  
Vaginitis  
Stomach ulcer  
Lung, ear infection, meningitis  
Atypical pneumoniae  
Legionnaire’s disease  
Damage to fetus
Hitchhikers?

- Not really
- The role of the microbiome may be summarized as mediating between the host and its environment
- Involved in a range of functions, from breaking down otherwise indigestible compounds (e.g., cellulose), to modulating immune responses against both invasive pathogens and members of the microbial community itself.
  - normal flora (commensals) versus pathogens (opportunistic pathogens)
Potential Microbial Applications

- **Environment**
  - Cleanup of toxic-waste sites worldwide
  - Management of environmental carbon dioxide, which is related to climate change
  - Detection of disease-causing organisms and monitoring of the safety of food and water supplies
  - Use of genetically altered bacteria as living sensors (biosensors) to detect harmful chemicals in soil, air, or water

- **Energy**
  - Energy generation and development of renewable energy sources (e.g., methane and hydrogen)

- **Health**
  - Production of novel therapeutic and preventive agents and pathways
  - Prebiotics (contains micronutrients designed to restore normal microbiota populations)
  - Probiotics (microorganisms themselves)

- **Industry**
  - Production of chemical catalysts, reagents, and enzymes to improve efficiency of industrial processes
Microbial Genomics Projects

- It is unthinkable to launch a major comprehensive initiative in the biology of any species without **sequencing its genome**
- JGI Microbial Genomics ([http://genome.jgi-psf.org/mic_home.html](http://genome.jgi-psf.org/mic_home.html))

![IMG Genomes](http://img.jgi.doe.gov/cgi-bin/pub/main.cgi)

As of Jan 4, 2010

IMG (integrated microbial genomes) ([http://img.jgi.doe.gov/cgi-bin/pub/main.cgi](http://img.jgi.doe.gov/cgi-bin/pub/main.cgi))
From Genomics to Metagenomics

- Majority of the microorganisms can not be cultured!
  - Metagenomics can in principle access 100% of the genetic resources in an environment
  - Traditional cultivation methods and traditional genomics can at best access 1%

- Advances of **sequencing technology** & computational methods for analyzing genomic sequences make it possible
Resources

- IMG (Integrated Microbial Genomics) (http://img.jgi.doe.gov/m)
- IMG/M (http://img.jgi.doe.gov/m)
- NCBI taxonomy browser
- CAMERA (metagenomics databases)