Microbiology 424

Fall term 2015

Microbial Cellular Dynamics – The organization and regulation of higher order processes in bacterial cells

General description

An upper level undergraduate course intended for students planning to pursue careers that require a high level understanding of how the bacterial cell works. Such an understanding is essential to developing novel approaches to fighting infection and useful microbial processes for biotechnological applications. Students will in addition acquire an understanding of cutting-edge methods and develop their abilities to critically evaluate the literature. The underlying approaches are applicable to a wide range of biological systems. At least 50% of the course material will be taken from recent landmark publications and will require the students to synthesize concepts presented in such publications and use them to solve problems.

Learning objectives

At the end of this course, students should be able to:

1. Compare and contrast detection and signaling strategies used by bacteria to sense and respond to metabolic and environmental cues.

2. Describe the impact of signaling processes on cytoskeleton organization and the function and localization of macromolecular machines.

3. Outline the hierarchical organization of regulatory networks (*e.g.*, RpoS, Crp modulon, stringent response) and explain how they are coordinated under different conditions of cell growth.

4. Formulate hypotheses about the roles of genes and their products and propose experiments to test these hypotheses using cutting-edge genomic, molecular genetic and biochemical approaches. Explain the limitations of such approaches.

5. Critically evaluate different methods for studying bacterial physiology, adaptation and response in environmental and pathogenic bacteria.

6. Critically evaluate original literature pertaining to bacterial physiology (i.e., appreciate the evidence).

7. Explain the concept of physiology-driven systems biology and its impact on understanding how bacterial systems function.

Grading:

In-class discussion	5%	
Commentary on readings	10%	
Research paper	15% oral, 20% written	
Midterm exam	25%	[October 19. Covers material to October 16.]
Final exam	25%	

Assigned and suggested readings:

Most sections will have suggested or assigned readings from the primary literature. These will be indicated in advance and are available free of charge through the UBC library. You will be responsible for obtaining this material.

Readings requiring written commentary will be indicated at least two classes in advance. A hard copy will be due at the beginning of the class and an electronic file before noon the same day. The commentary should not exceed 2500 characters with spaces (~1 page, double-spaced) and should address the following aspects in one sentence each:

- the study's (or review article's) objectives (i.e., "Take Home Message")
- why the study was done (background and/or rationale)

- the primary experimental approach(es); not relevant for review-type article
- major finding(s), two or three sentences okay here if appropriate
- critical analysis - greatest strength, most significant weakness (if any), logical next step (or missing piece)

Course Outline

1. Metabolic regulation
   - importance, simple illustration, levels at which it occurs, basic considerations in studying bacterial physiology
2. Enzyme levels
   - transcription, mRNA stability, translation, protein degradation, ncRNAs
3. Regulatory enzymes (allostery)
   - allostery, post translational modification
4. Phosphorelay systems
5. Sigma-antisigma factors
6. Signal integration
   - robustness, integral feedback
7. Higher order prokaryotic cell structures
   - Compartmentalization - formal structures, subcellular addresses (approaches)
   - Macromolecular complexes and machines, studying macromolecular complexes
8. Cytoskeletal elements
9. Global regulation
   - Multigene systems, hierarchical organization, Stimulus-response pathway
   - coordination devices, examples of global networks (Crp modulon, stringent control)
10. Systems Biology
    - Annotation, Metabolic reconstruction, BioCyc
    - Transcriptomics, Proteomics, Metabolomics
    - Gene inactivation and labeling (overview)
    - *Mycoplasma pneumoniaie* (case study)
11. Pts and CCR
    - Interplay between transport, signal transduction and regulation
12. Physiology-driven systems biology – the case of cAMP
13. Stasis
    - experimental approaches to dissect interconnection with Crp and stringent response
14. Global coordination of bacterial metabolism

Required background

Bacterial physiology (MICB 201, MICB 301)

- structure and composition of the bacterial cell
- exponential growth, balanced growth
- Central metabolism, catabolism, biosynthesis (energy and metabolic pools), respiration
- transport (primary, secondary)

Bacterial genetics (MICB 325)

- chromosome structure and organization, operons, transcriptional regulation, targeted gene deletion

Research paper critique

- increase knowledge of current aspects of bacterial physiology and how they are studied
- develop your abilities to understand and critically analyze published literature.
- develop your abilities to think creatively and to communicate emerging concepts.