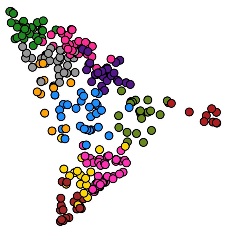
School of Molecular & Cellular Biology

MCB 545, Spring 2024

Functional Genomics in Principle and Practice
3 credit hours



Instructor

Kevin Van Bortle
B521 CLSL
kvbortle@illinois.edu
217-333-3797

Class Meeting Schedule

M,W 10 – 11:20 AM
Location: Nevada Building Computer Lab (1203 ½ W. Nevada St.)
Office Hours: By appointment

Course Overview and Description

This course introduces the experimental and analytical foundations of functional genomics, tailored to experimental biologists who are interested in using high-throughput sequencing technologies to analyze function in animal genomes. The overarching structure of this course tasks students with exploring the regulation and function of a specific RNA-binding protein (RBP) through analysis of multiple genomic assays. Students are tasked with retrieving publicly available sequencing data and executing differential and integrative data analyses through programming in R. This course combines lectures, which cover basic principles (e.g. genome assembly, gene/transcript annotation, functional genomic methods, statistics for genomic data), with in-class programming and assignments. Students present updates at specific intervals during the semester and submit a written synthesis of their findings at the conclusion of the course.

Course Prerequisites

Students are strongly encouraged to familiarize themselves with RStudio and the basics of programming in R prior to taking this class.

Student Learning Outcomes

At the end of the course, through assignments, discussions, activities and assessments, students will be able to:

- Understand basic principles of modern functional genomics methods and current sequencing and computational approaches
- Interpret common data visualization techniques and apply these approaches using R

- Navigate and utilize a high-performance computing (HPC) cluster environment
- Integrate multi-omic data to generate quantitative analyses related to the regulation and function of a specific gene of interest.

Course Text/Materials Information

Hands-on programming with R. Garrett Grolemund. O'Reilly Media. 2014
https://rstudio-education.github.io/hopr/basics.html
Student assignments will also include reading primary literature and reviews related to topics over the course of the semester.

Course Tools

MCB545 will utilize a Slack workspace as a resource for course communication between students, instructor, and between team members for group projects (https://slack.com).

Grading Information and Breakdown

30% Class participation: includes attendance and participation (30 points total)
15% Graded homework assignments (15 points total, 3 points each)
30% Graded project assignments/presentations (2 total, 15 points each)
25% Final project assignment (25 points total)

100 Total points

Grade format

97-100%	(A+)	93-96%	(A)	90-92%	(A-)
87-89%	(B+)	83-86%	(B)	80-82%	(B-)
77-79%	(C+)	73-76%	(C)	70-72%	(C-)
67-69%	(D+)	63-66%	(D)	60-62%	(D-)
0-59%	(F)				

COURSE CALENDAR (2024)

SECTION I. INTRODUCTION TO GENOMICS | INTRO TO PROGRAMMING IN R

January 17	Lecture Topic: **Course overview, Intro to genomics, RBP selection** Week 1 Reading: https://rstudio-education.github.io/hopr/basics.html Assignment: Intro Poll (RNA-binding protein selection); install Rstudio
January 22	Lecture Topic: **The Human Genome, Gene Annotation; Intro to IGV** Week 2 Reading: Rood & Regev 2021 | Mudge and Harrow, 2016
January 24	Lecture Topic: **Introduction to Programming in R** Week 2 Exercise: Importing data in R; R functions; R packages
January 29	Lecture Topic: **Sequencing Platforms; Read Alignment**
January 31	Lecture Topic: **Introduction to Programming in R (continued)** Week 3 Exercise: Plotting in R; Distributions; Gene/Transcript features
HW 1 Assignment – RBP gene/transcript annotation features: **Due Feb. 8** (3 pts)	

SECTION II. TRANSCRIPTION & RNA PROCESSING (BIRTH OF AN RNA)

February 4	Lecture Topic: **Transcription; RNA-seq methods** Week 4 Reading: Stark et al., 2019 | Wissink et al., 2019
February 6	Lecture Topic: **The Regulome: Enhancers, Silencers, and Insulators** Week 4 Exercise: Data wrangling; For loops; Gene expression profiles
February 12	Lecture Topic: **Architecture: Loops, Domains, Compartments** Week 5 Reading: Kempfer & Pombo, 2020 | Jerkovic & Cavalli, 2021
February 14	Lecture Topic: **Location: Nuclear position (e.g. LADs, Speckles)** Week 5 Exercise: Working with genomic intervals; Chromatin features
HW 2 Assignment – Expression patterns & features of your (RBP) gene: **Due Feb. 23** (3 pts)	
February 19	Lecture Topic: **RNA modifications, processing, splicing** Week 6 Reading: Neil et al., 2022; Rogalska, Vivori, Valcarcel 2023; Mitschka & Mayr, 2022; Childs-Disney et al., 2022
February 21	Lecture Topic: **RNA cont'd (Alternative splicing)** Week 6 Exercise: Intron retention and transcript splicing features

SECTION III. TRANSLATION (BIRTH OF A PROTEIN)

February 26	Lecture Topic: **Translation; Ribosome-profiling methods** Week 7 Reading: Brar & Weissman, 2015
February 28	Lecture Topic: **Translation regulation** Week 7 Exercise: Transcript G4 structures; codon usage
HW 3 Assignment – RNA features and splicing of your RBP transcript: **Due Mar. 8** (3 pts)	
March 4	Lecture Topic: **RBP structure and function; protein interactions** Week 8 Reading: Hentze et al., 2018
March 6	PRESENTATION #1: **INTRODUCTION OF YOUR RBP FEATURES** (15 pts)

March 9-17 Spring Break

SECTION IV. FUNCTIONAL GENOMICS (TOWARDS PROTEIN FUNCTION)

March 18	Lecture Topic: **Functional genomics: CRISPR and other approaches** Week 8 Reading: Dowdy, 2017; Adli, 2018
March 20	Lecture Topic: **Introduction to High Performance Computing (HPC)** Week 8 Exercise: Using bioinformatic software in linux (crash course!) Week 8 Resource: Stothard, linux for bioinformatics. 2016
March 25	Lecture Topic: **Differential RNA-seq analysis (DGE part 1)** Week 9 Reading: Van den Berge et al., 2019
March 27	Lecture Topic: **Differential RNA-seq analysis (DGE part 2)** Week 9 Exercise: Differential Gene Expression Analysis; Visualization
	HW 4 Assignment – Differential expression survey: **Due Apr. 7** (3 pts)
April 1	Lecture Topic: **Mapping Protein-DNA and Protein-RNA interactions** Week 10 Reading: Hafner et al., 2021 (CLIP and complement. methods)
April 5	Lecture Topic: **Peak calling, motif discovery** Week 10 Exercise: Read pileup / signal plots
April 8	Lecture Topic: **Enrichment Analysis (part 1: Permutations)** Week 11 Reading: Phipson & Smyth, 2010
April 10	Lecture Topic: **Enrichment Analysis (part 2: Gene Set Enrichment)** Week 11 Exercise: Gene Set Enrich. Analyses
	HW 5 Assignment – Overlap and gene set enrichment analysis: **Due Apr. 19** (3pts)
April 15	Lecture Topic: **Machine Learning; Dimension Reduction; Clustering** Week 12 Reading: Greener et al., 2022
April 17	PRESENTATION #2: **RBP ANALYSIS, HYPOTHESIS** (15 pts)

SECTION V. GENE / PROTEIN DYSFUNCTION & TURNOVER MECHANISMS (DEMISE)

April 22	Lecture Topic: **Pathogenic Repeats | Genome-wide QTL mapping** Week 13 Reading: Malik et al., 2021; Uffelmann et al., 2021
April 24	Lecture Topic: **Cancer Genomics: mutations, CNVs, expression** Week 13 Exercise: Survival analysis
Final Project Assignment – Synthesis of RBP findings and future directions: **Due May 8** (25pts)	
April 29	Lecture Topic: **Targeted RNA and protein degradation** Week 14 Reading: Wolin & Maquat, 2019; Zhao et al., 2022
May 1	**Special Topic: Careers in Genomics**

Classes end May 1, Final project due May 8

Assignments, due dates, and course expectations

MCB545 is geared towards the practical application of functional genomic data analysis and will function as a hybrid lecture and hands-on lab course series. Attendance and in-class participation (maximum 30 points, 30% of total) is critical for actively learning this broad subject area. Students must contact me immediately or in advance if it becomes necessary to be absent from class to identify a reasonable action plan. Lecture topics will be linked to learning programming in-class and through multiple homework assignments that will be submitted electronically (maximum 15 points, 15% of total). This course encourages team-learning, including regular communication and group work on the MCB545 Slack workspace. However, homework assignments must be written up and submitted independently. Presentation assignments will feature opportunities to analyze, discover, and finally present novel genomic findings through short presentations (maximum 30 points, 30% of total). Towards the completion of the semester, a final project assignment will require each student to independently apply data processing tools and data analysis methods taught during the semester, as well as integrate and synthesize all data analyzed throughout the course to establish a hypothesis about the regulation and function of a specific gene (maximum 25 points, 25% of total).

Academic integrity

Students are expected to be familiar with the code of policies and regulations applied in all instances of academic misconduct. Please refer to http://studentcode.illinois.edu, and, in particular, Article 1 part 4: http://studentcode.illinois.edu/article1/part4/1-401/

Accommodations

To obtain disability-related academic adjustments and/or auxiliary aids, students with disabilities must contact the course instructor and the Disability Resources and Educational Services (DRES) as soon as possible. To contact DRES, you may visit 1207 S. Oak St., Champaign, call 333-4603 (V/TDD), or e-mail a message to disability@uiuc.edu. http://www.disability.illinois.edu/.

Inclusive classroom statement

The effectiveness of this course is dependent upon the creation of an encouraging and safe classroom environment. Exclusionary, offensive or harmful speech, such as racism, sexism, homophobia, and transphobia, will not be tolerated and in some cases will be subject to University harassment procedures. We are all responsible for creating a positive and safe environment that allows all students equal respect and comfort. We expect each of you to help establish and maintain an environment where you and your peers can contribute without fear of ridicule or intolerant or offensive language.

Sexual misconduct policy and reporting

The University of Illinois is committed to combating sexual misconduct. Faculty and staff members are required to report any instances of sexual misconduct to the University's Title IX and Disability Office. In turn, an individual with the Title IX and Disability Office will provide information about rights and options, including accommodations, support services, the campus disciplinary process, and law enforcement options. A list of the designated University employees who, as counselors, confidential advisors, and medical professionals, do not have this reporting responsibility and can maintain confidentiality, can be found here: wecare.illinois.edu/resources/students/#confidential. Other information about resources and reporting is available here: wecare.illinois.edu.