BIOSCIENCES 741 - GENOMICS
FALL SEMESTER, 2023

Dr. Karl J. Fryxell
School of Systems Biology, and the
Interdisciplinary Program in Neurosciences

Contact Information

Online Lectures: Tuesdays at 4:30 - 7:10 pm, online. Log into the Blackboard course website (section DL1). Some students in this course have enrolled in the in-person section (section 001). These students should be able to see both sections in Blackboard, and they should log in to the Blackboard DL1 section to join class meetings, listen to lectures, and access course materials. After opening the DL1 section, click on the "Tools" menu (left panel, below "assessments"), then click on "Class Collaborate Ultra" tool, then click on the "unlocked course room" icon (near the top left of the window).

In-person exams: Midterm and final exams in this class will be held in person, in K. Johnson Hall, room 248 (GMU SciTech campus).

Online office hours (most weeks, except in-person hours listed below): Fridays, 1:00 - 2:00 pm, online via Zoom: https://gmu.zoom.us/j/7931936280?pwd=RWV1OC9oVmRpQUNQb3Y5czhURG91UT09#success

In-person office hours: Fridays, 1:00 - 2:00 pm. On Oct 6 and Dec 1, in Exploratory Hall room L509 (GMU Fairfax campus). On Oct 20, in K. Johnson Hall, room 248 (GMU SciTech campus).

E-mail: kfryxell@gmu.edu *(Please use "BIOS 741" as the subject line of your e-mails)*

Telephone: 703-993-1069 *(Please leave a detailed message including your name, class, a callback phone number, and dates/times when you are available for me to call you back.*

Course web site: GMU Blackboard web site - includes lecture notes, study questions, and other materials.

Course Summary: Biology reached a turning point with the publication of the DNA sequence of the euchromatic portion of the human genome. Progress since then in genetics, medicine, biotechnology, pharmacology, and many other fields has been increasingly dependent on the data, techniques and concepts of genomics. The basic facts of biology rely upon the molecular anatomy of our chromosomes, just as basic facts of physiology rely upon the anatomy of our nerves and muscles. However, the volume and complexity of genomic sequence data pose significant problems of interpretation, which will occupy biologists for generations to come.

Prerequisites: Graduate standing, plus at least one undergraduate course in genetics and one undergraduate course in molecular biology.

Readings: There is one required textbook for this class: Pevsner (2015) *Bioinformatics and Functional Genomics* (3rd edition, Wiley). The assigned readings from this text are listed below. An additional, introductory text that may be helpful is Gibson and Muse (2009) *A Primer of Genome Science* (3rd edition, Sinauer, Sunderland, MA). Additional readings from the primary research literature will be assigned, and are listed below. These papers are generally available to registered students through the GMU library web site (library.gmu.edu). If not, copies will be posted on Blackboard.

Grading: Grades will be based on midterm (45%) and final (45%) examinations, plus attendance and active participation in class discussions (10%). Midterm and final exams will be short essay, in-class, closed book exams. The midterm exam will cover the first half of the course; the final exam will cover the second half of the course. Midterm and final exams typically consist of about 5 questions, each of which requires an answer about one page in length. These exam questions will focus on the main points in the lectures and assigned readings, as identified by questions at the end of each chapter in the text, and particularly Study Questions that are posted weekly on Blackboard. Students are expected to do the assigned readings before coming to class, and be prepared to participate in class discussions on these subjects. Makeup exams are not given in this course; excused absences from exams require prior permission from the instructor (that means a two-way conversation, not one-way voice mail or e-mail). The use of cell phones (spoken or texting) or internet resources during exams is not allowed.

Class Schedule

<u>Week 1 (August 22) Introduction to genomics</u>

Pevsner text: pp. 720-727.

van Nimwegen, E. (2003) Scaling laws in the functional content of genomes. *Trends Genet* 19, 479-484.

Week 2 (August 29) Sequencing methods, BAC fingerprinting, physical maps and FISH

Pevsner text: pp. 377-387; 399-403; 728-737; 966-968.

Lander, E.S. *et al*. (2001) Initial sequencing and analysis of the human genome. *Nature* 409, 860-921 (we will focus this week on pp. 860-875)

Week 3 (September 5) cDNA libraries, EST clusters, gene prediction and functional annotation

Pevsner text: pp. 433-459; 737-745.

Nekrutenko, A. (2004) Reconciling the numbers: ESTs versus protein-coding genes. *Mol Biol Evol* 21, 1278-1282.

Lander, E.S. et al. (2001) Initial sequencing and analysis of the human genome. *Nature* 409, 860-921. (we will focus this week on pp. 894-903).

Week 4 (September 12) Bacterial genomes

Pevsner text: pp. 307-309; 797-837.

Novick, R. P. and G. Ram (2016) The floating (pathogenicity) island: a genomic dessert. *Trends Genet* 32, 114-126.

Fillol-Salom. A. et al. (2018) Phage-inducible chromosomal islands are ubiquitous within the bacterial universe. *ISME J*. 12, 2114-2128.

Week 5 (September 19) Gene expression analysis

Pevsner text: pp. 460-472; 479-533.

Lenhard, B., et al. (2012) Metazoan promoters: emerging characteristics and insights into transcriptional regulation. *Nat Rev Genet* 13, 233-245.

Davuluri, R. V. et al. (2008) The functional consequences of alternative promoter use in mammalian genomes. *Trends Genet* 24, 167-177.

Week 6 (September 26) Alternative splicing

Barbosa-Morais, N. L. et al. (2012) The evolutionary landscape of alternative splicing in vertebrate species. *Science* 338, 1587-1593.

Kalsotra, A. and Cooper, T. A. (2011) Functional consequences of developmentally regulated alternative splicing. *Nat Rev Genet* 12, 715-729.

Park, E. et al. (2018) The expanding landscape of alternative splicing in human populations. *Am. J. Hum. Genet*. 102, 11-26.

Week 7 (October 3) Midterm Examination - 4:30 pm to 7:10 pm in K. Johnson Hall, room 248 (GMU SciTech campus). covers weeks 1-6

Week 8 (October 10) Fall Break - Tuesday classes do not meet this week

Week 9 (October 17) Proteomics

Pevsner text: pp. 539-580.

Vogel, C. and E. M. Marcotte (2012) Insights into the regulation of protein abundance from proteomic and transcriptomic analysis. *Nat Rev Genet* 13, 227-232.

Boellner, S. and K.-F. Becker (2015) Reverse phase protein arrays – quantitative assessment of multiple biomarkers in biopsies for clinical use. *Microarrays* 4, 98-114.

Week 10 (October 24) The eukaryotic chromosome: noncoding and repetitive sequences, chromosome rearrangements and gene families

Pevsner text: pp. pp. 325-365; 957-965; 971-979.

Lander, E.S. et al. (2001) Initial sequencing and analysis of the human genome. *Nature* 409, 860-921. (we will focus this week on pp. 879-885; 887-889).

Waterston, R.H., K. Lindblad-Toh, E. Birney et al. (2002) Initial sequencing and comparative analysis of the mouse genome. *Nature* 420, 520-562.

Pehrsson, E. C. et al. (2019) The epigenomic landscape of transposable elements across normal human development and anatomy. *Nat Commun* 10, 5640.

Week 11 (October 31) Genetic polymorphisms, population genetics and human genetics

Pevsner text: pp. 408-410; 986-1004; 1036-1049.

Bentley, D. B. (2003) DNA sequence variation of *Homo sapiens*. *Cold Spring Harbor Symp Quant Biol*. 68, 55-63. (A PDF copy of this article will be posted on the course web site.)

Liao, W.-W. et al. (2023) A draft human pangenome reference. *Nature* 617, 312-324.

Week 12 (November 7) The human genome: codon bias, gene density, GC content, recombination, CpG islands

Pevsner text: pp. 806-808; 968-971; 981-986.

Lander, E.S. et al. (2001) Initial sequencing and analysis of the human genome. Nature 409, 860-921. (we will focus this week on pp. 875-879; 885-887; 892-894).

Hinch, A. G. et al. (2011) The landscape of recombination in African Americans. Nature 476, 170-175.

Week 13 (November 14) Class does not meet (Society for Neuroscience meetings)

Week 14 (November 21) Epigenetics – DNA methylation

Jones, P. A. (2012) Functions of DNA methylation: islands, start sites, gene bodies and beyond. *Nat Rev Genet* 13, 484-492.

Smith, Z. D. and Meissner, A. (2013) DNA methylation: roles in mammalian development. *Nat Rev Genet* 14, 204-220.

Mellen, M., P. Ayata and N. Heintz (2017) 5-hydroxycytosine accumulation in postmitotic neurons results in functional demethylation of expressed genes. *Proc. Natl. Acad. Sci. USA* 114(37), E7812-E7821.

Week 15 (November 28) Epigenetics - histone modifications.

Jin, C. et al. (2009) H3.3/H2A.Z double variant-containing nucleosomes mark 'nucleosome-free regions' of active promoters and other regulatory regions. *Nat Genet* 41, 941-945.

Ernst, J. et al. (2011) Mapping and analysis of chromatin state dynamics in nine human cell types. *Nature* 473, 43-49.

Petty E, Pillus L (2013) Balancing chromatin remodeling and histone modifications in transcription. *Trends Genet* 29, 621-629.

December 5 - Reading Day

December 12 - Final Exam - 4:30 pm to 7:10 pm in K. Johnson Hall, room 248 (GMU SciTech campus). Covers weeks 9-15.