CSHL School of Biological Sciences
Core Course on Specialized Disciplines, Fall 2022
Course Outline

Module: Quantitative Biology

Course Faculty

Organizers:	Justin Kinney
Invited Experts:	Alex Dobin Ivan Iossifov Peter Koo Adam Siepel David McCandlish Saket Navlakha Jon Preall Hannah Meyer
Course TAs:	Carlos Marti Gomez Aldaravi Armin Scheben

Lecture 1: Kinney
Statistics I

Lecture 2: Kinney
Statistics II

Lecture 3: Kinney
Statistics III

Lecture 4: Kinney
Statistics IV

Lecture 5: Kinney
Statistics V

Lecture 6: Kinney
Statistics VI

Lecture 7: Dobin
Machine Learning I

Lecture 8: Dobin
Machine Learning II

Lecture 9: Koo
Machine Learning III

Lecture 10: Koo
Machine Learning IV

Lecture 11: Siepel
Algorithms I

Lecture 12: Siepel
Algorithms II

Lecture 13: Navlakha
Algorithms III

Lecture 14: Navlakha
Evolution I

Lecture 15: Preall
Genomics I

Lecture 16: Preall
Genomics II

Lecture 17: Meyer
Genomics III

Lecture 18: Meyer
Genomics IV

Lecture 19: McCandlish
Evolution II

Lecture 20: McCandlish
Evolution III

Lecture 21: Kinney
Biophysics I

Lecture 22: Kinney
Biophysics II

Quantitative reasoning is a powerful means of understanding biological systems and uncovering biological principles. With the advent of high-throughput technologies, it has become increasingly necessary for researchers in Biology to be able to analyze and interpret large data sets and to quantitatively frame biological hypotheses. To this end, the 2022 Quantitative Biology Course will aim to equip the students with a working knowledge of statistics and Python programming, as well as provide exposure to more advanced topics in machine learning, algorithms, evolution, genomics, and biophysics.

Homework: Problem sets will be due on Friday each week–specifically, on Friday the week after the lectures that cover the relevant material. Optional problem sessions will be held by the TAs each week that a problem set is due. Unless otherwise stated, problem sets should be completed as Jupyter notebooks and emailed to the TAs. Generally, an assignment submitted after the specified date will be accepted with a late penalty of 30% off of the final grade, and will not be accepted after one week past the deadline. If you will be unable to turn in your assignment on time due to an emergency or other unavoidable circumstance, please contact Justin Kinney.

Student Evaluation: Problem sets: 80%, Lecture participation: 20%

Learning Objectives

- Acquire a working knowledge of standard statistics and Python programming
- Exposure to more advanced topics in machine learning, genomics, population genetics, neuroscience and biophysics

Learning Outcomes

- Be able to analyze and interpret large data sets
- Be able to frame biological hypotheses quantitatively

Background reading:
Núñez, M.A.B., Nuckolls, N.L., and Zanders, S.E. 2018. Genetic villains: killer meiotic drives. *Trends in Genetics* 34: 424-433.

Reference Material
There is a GitHub repository for the QB course
https://github.com/jbkinney/22e_qbbootcamp

CSHL School of Biological Sciences
Core Course on Specialized Disciplines, Fall 2022

Module: Genetics and Plant Biology

Lead Instructor: Dr. Ullas Pedmale

Invited Experts: Dr. Dave Jackson
Dr. Zach Lippman
Dr. Rob Martienssen
Dr. Sophie Zebell

Teaching Assistant: Dr. Sophie Zebell

Lecture 1: Pedmale
Topic: Plant anatomy and photosynthesis

Lecture 2: Pedmale
Topic: Genetics basics, Principles of genetic screens, mapping, and gene identification
a. Background reading: Griffiths Ch. 1-3
b. Background reading: Griffiths Ch. 4, and
c. Nüsslein-Volhard, C., and Wieschaus E. 1980. Mutations affecting segment number and polarity in Drosophila. *Nature* 287: 795-801, and,
d. Mayer, U., Torres-Ruiz, R. A., Berleth, T., Miséra, S. and Jürgens, G. 1991. Mutations affecting body organisation in the Arabidopsis embryo. *Nature* **353**: 402–407.

Lecture 3: Pedmale
Topic: Paper Discussion:
a. Xin, X.F., Nomura, K., Aung, K., Velásquez, A.C., Yao, J., Boutrot, F., Chang, J.H., Zipfel, C., and He, S.Y. 2016. Bacteria establish an aqueous living space in plants crucial for virulence. *Nature* **539**:524-529.
b. Tao Y, Ferrer JL, Ljung K, Pojer F, Hong F, Long JA, Li L, Moreno JE, Bowman ME, Ivans LJ, Cheng Y, Lim J, Zhao Y, Ballaré CL, Sandberg G, Noel JP, Chory J. 2008. Rapid synthesis of auxin via a new tryptophan-dependent. *Cell* **133**: 164-176.

Lecture 4: Zebell
Topic: Plant Immunity

Lecture 5: Zebell
Topic: Quantitative Genetics, Epistasis, GWAS

Lecture 6: Lippman
Topic: Fundamentals (molecular and genetic) of flowering in development, evolution, domestication and breeding.

Lecture 7: Zebell
Topic: Non-Mendelian Inheritance – epigenetics and strange genetics
a. Background reading: Núñez, M.A.B., Nuckolls, N.L., and Zanders, S.E. 2018. Genetic villains: killer meiotic drives. *Trends in Genetics* **34**: 424-433.

Lecture 8: Jackson
Topic: genetics and signaling of the plant meristem.

Lecture 9: Martienssen
Topic: Transposons and gene silencing

Lecture 10: Pedmale

Topic: Hormones and light signaling

Lecture 11: Pedmale

Topic: Epistasis, Clinical Genetics or genetic basis of diseases.

a. Background reading: Griffiths Ch. 6.
b. Background reading: Griffiths pp. 749-755.

Lecture 12: **Pedmale**

Topic: Paper Discussion:

a. Bomblies K, Lempe J, Epple P, Warthmann N, Lanz C, Dangl JL, Weigel D. 2007. Autoimmune response as a mechanism for a Dobzhansky-Muller-type incompatibility syndrome in plants. *PLoS Biol*. **5**: e236.
b. Cadieu E, Neff MW, Quignon P, Walsh K, Chase K, Parker HG, Vonholdt BM, Rhue A, Boyko A, Byers A, Wong A, Mosher DS, Elkahloun AG, Spady TC, André C, Lark KG, Cargill M, Bustamante CD, Wayne RK, Ostrander EA. 2009. Coat variation in the domestic dog is governed by variants in three genes. *Science* **326**: 150-153.

Student Evaluation:

- Problem sets: 40%; Journal club discussions: 30%; Lecture participation: 30%

Learning Objectives:

- To place modern genetics and genomics into the context of classical genetics.
- Genetic basis of diseases.
- History, technique, and perspective of genetic inference along with four levels of analysis: forward genetics, natural genetic variation, gene interaction, and genomics.
- Integration of classical with modern questions of genetic analysis: How are genes mapped and "cloned"? How do gene mutations help to define biological processes? How are more complex traits genetically dissected into their component parts? What concepts and techniques are used to organize genes into pathways and networks? What defines a gene and what gene variation exists in natural populations? What are the functional consequences of gene variation, and how is it detected? How are genomes organized and coordinately regulated? How can genomic information be catalogued, organized and mined?

Learning Outcomes:

- Apply the principles of genetics
- Demonstrate an understanding of the concept of Mendelian and non-Mendelian inheritance
- Describe tools and techniques used in genetics and genomics.
- Demonstrate an understanding of the genetic basis of phenotype and complex phenotypes

Reference Material:

- Textbooks: Griffiths, A.J.F, Wessler, S.R., Carroll, S.B., and Doebley, J. *Introduction to Genetic Analysis*. W.H. Freeman, 2015.

Reviews:

- Benzer, S. 1955. Fine structure of a genetic region in bacteriophage. *PNAS* **41**: 344-354.
- Cadieu, E. *et. al.,* 2009. Coat Variation in the Domestic Dog Is Governed by Variants in Three Genes. *Science* **326**: 150-153.
- Miki, Y. *et al.,* 1994. A Strong Candidate for the Breast and Ovarian Cancer Susceptibility Gene BRCA1. *Science* **266**:66-71.
- Bomblies, K., Lempe, J., Epple, P., Warthmann, N., Lanz, C., Dangl, J.L., and Weigel, D. 2007. Autoimmune response as a mechanism for a Dobzhansky-Muller-type incompatibility syndrome in plants. *PLoS Biol* **5**: e236
- Blount, Z., Borland, C., Lenski, E. 2008. Historical contingency and the evolution of a key innovation in an experimental population of Escherichia coli. *PNAS* **105**: 7899-7906
- Hou J., *et al.,* 2018. Global impacts of chromosomal imbalance on gene expression in Arabidopsis and other taxa. *PNAS* **115:** E11321-11330.
- Birchler J.A*., et al.,* 2016. Kinetics genetics: Incorporating the concept of genomic balance into an understanding of quantitative traits. *Plant Science* **245**:128-134.

CSHL School of Biological Sciences
Core Course on Specialized Disciplines, Fall 2022
Course Outline

Module: Cancer

Course Faculty

Organizers:	Mikala Egeblad
	Christopher Vakoc
Invited Experts:	Corina Amor
	Semir Beyaz
	Jeremy Borniger
	Camila dos Santos
	Tobias Janowitz
	Michael Lukey
	David Tuveson
	Linda Van Aelst
	Peter Westcott
Tutor:	Ledong Wan wan@cshl.edu

Lecture 1: Egeblad
The Hallmarks of Cancer

Lecture 2: Vakoc
The Cancer Genome

Lecture 3: dos Santos
Cancer Epigenetics

Lecture 4: Tuveson
Cancer Models

Lecture 5: Westcott
Paper Discussion

Lecture 6: Vakoc
Targeted Cancer

Lecture 8: Egeblad
Tumor microenvironment

Lecture 9: Beyaz
Tumor Immunology

Lecture 10: Amor & Beyaz
Paper Discussion

Lecture 11: Borniger & Janowitz
Host response to cancer

Lecture 12: Egeblad & Van Aelst
Metastasis

Lecture 13: Janowitz & Lukey
Cancer Metabolism

Lecture 14: Lukey
Paper Discussion

Lecture 15: Egeblad & Vakoc
Course Round Up

Student Evaluation:

- 40% participation in daily discussions during lectures
- 40% based on paper discussions
- 20% based on problem set

Learning Objectives

Gain proficiency in the following:

- Hallmarks of cancer
- Tumor progression
- Cancer genome
- Cancer microenvironment
- Tumor immunology
- Metastasis
- Approaches to treating cancer, including targeted therapy

Learning Outcomes

- Elaborate on an understanding of cancer as a pathological process
- Discuss how cancer progresses
- Contemplate how to expand on current methods to treat cancer
- Design tractable methods to investigate fundamental aspects of cancer biology
- Discuss translational approaches to defeating cancer

Reference Material

Textbooks:

- Weinberg, RA 2014. The Biology of Cancer

Reviews:

- Hanahan, D., and Weinberg, R.A. 2011. Hallmarks of cancer: the next generation. *Cell* **144**: 646-674.
- Harper, J.W., and Elledge, S.J. 2007. The DNA damage response: ten years after. *Mol Cell* **28**: 739-745.
- Lowe, S.W., Cepero, E., Evan, G. 2004. Intrinsic tumor suppression. *Nature* **432**: 307-315.
- Kaelin, W.G., 2005. The concept of synthetic lethality in the context of anticancer therapy. *Nat Rev Cancer* **5**: 689-698.
- Meacham, C.E. and Morrison, S.J. 2013. Tumor heterogeneity and cancer cell plasticity. *Nature* **501:** 328–337.
- Holohan, C., Van Schaeybroeck, S, Longley, D.B, and Johnston, P.G. 2013. Cancer drug resistance: an evolving paradigm. *Nat Rev Cancer* **13**: 714-726.

Supplemental reading

- Alberts, B et al. 2008. Molecular Biology of the Cell
- Mukherjee S. 2011. The Emperor of All Maladies: A Biography of Cancer

Discussion Paper 1: Westcott

Yang D, Jones MG, Naranjo S, Rideout WM 3rd, Min KHJ, Ho R, Wu W, Replogle JM, Page JL, Quinn JJ, Horns F, Qiu X, Chen MZ, Freed-Pastor WA, McGinnis CS, Patterson DM, Gartner ZJ, Chow ED, Bivona TG, Chan MM, Yosef N, Jacks T, Weissman JS. 2022. Lineage tracing reveals the phylodynamics, plasticity, and paths of tumor evolution. *Cell* **185**: 1905-1923.

Discussion Paper 2: Amor & Beyaz

Restifo NP, Smyth MJ, Snyder A. 2016. Acquired resistance to immunotherapy and future challenges. *Nat Rev Cancer* **162**:121-126.

Discussion Paper 3: Lukey

Diehl FF, Lewis CA, Fiske BP, Vander Heiden MG. 2019. Cellular redox state constrains serine synthesis and nucleotide production to impact cell proliferation. *Nat Metab.* **1**: 861-867.

CSHL School of Biological Sciences
Core Course on Specialized Disciplines, Fall 2022
Course Outline

Module: Systems Neuroscience

Course Faculty
Organizers: Stephen Shea
Florin Albeanu
Arka Banerjee

Tutor: Priyanka Gupta

Lecture 1: Shea
- Transduction, Conduction, and Excitability

Lecture 2: Shea
- Synapses, Plasticity, and Integration

Lecture 3: Banerjee
- How does your brain compute?

Lecture 4: Shea
- How do you recognize your grandmother?

Lecture 5: Albeanu
- How do you smell your favorite coffee?

Lecture 6: Banerjee
- How do you localize sounds?

Lecture 7: Shea
- How do you remember what you ate for breakfast?

Lecture 8: Shea
- How do you know what is important and learn from your mistakes

Lecture 9: Banerjee
- Why don't you keep falling on your head?

Lecture 10: Albeanu
- How do you build models of the world?

Lecture 11: All
- Paper Presentations

Lecture 12: All
- Paper Presentations

Student Evaluation: There will be three main components to the class: lectures, a problem set and paper presentations. Evaluation will be based on participation during the lectures and performance during paper presentations and the problem set.

Paper Presentations: 50%
Lecture participation: 25%
Problem set: 25%

Learning Objectives
Achieve fluency with the following topics:
- Neuronal excitability and sensory transduction
- Synaptic communication and modification
- Receptive field structure and single neuron and population coding
- Analysis of natural and trained behaviors

Learning Outcomes

- Understand the logic and tools of modern neuroscience
- Master experimental design in systems neuroscience
- Think critically about systems neuroscience literature
- Understand the basics of information representation in the brain
- Appreciate the importance of causal manipulations of brain activity to neuroscience as an experimental field

Reference Material

Textbooks:

- "Principles of Neurobiology" by Liqun Luo

Discussion Papers

- Keshavarzi S, Bracey EF, Faville RA, Campagner D, Tyson AL, Lenzi SC, Branco T, Margrie TW. 2022. Multisensory coding of angular head velocity in the retrosplenial cortex. *Neuron* **110**: 532-543.

- Jordan, R, Keller, GB. 2022. The locus coeruleus broadcasts prediction errors across the cortex to promote sensorimotor plasticity *bioRxiv* 11.08.515698.

- Evans DA, Stempel AV, Vale R, Ruehle S, Lefler Y, Branco T. 2018. A synaptic threshold mechanism for computing escape decisions. *Nature* **558**: 590-594.