Please note that this syllabus is subject to change and will be updated for the current semester.

MCB/PMB C134

Genome organization and nuclear dynamics

Spring

Course format: in person

3 semester credits

Course Description

This course focuses on the structure, functions, and dynamics of eukaryotic chromosomes and their organization within cell nuclei. All life on earth relies on genetic information, which is encoded within nucleic acids (DNA and RNA). Most organisms have DNA-based genomes; bacterial and archaeal genomes typically comprise a single circular DNA molecule, while the genomes of most eukaryotes are divided into a variable number of linear DNA molecules. These contiguous DNA strands, along with the associated proteins and other components that contribute to their organization and function, are known as "chromosomes."

This is a small, seminar-style course. We will have two interactive lectures per week and one student-led discussion, which will focus on an assigned research paper. We will cover diverse topics related to chromosome structure and function, and the experimental approaches that are used to investigate it. **Attendance and participation in the lectures and discussion sections is expected and is included in the final grade.**

Prerequisites

MCB/PMB C134 is intended to be a "deep dive" into a central and complex topic in biology. Chromosome biology incorporates aspects of genetics, molecular biology, biochemistry, biophysics and cell biology. Although there are no specific prerequisites for this course, some prior coursework in genetics, cell biology, and/or molecular biology (e.g., MCB 100, 102, 140, &/or 104) is strongly recommended.

We will assume that you already understand the "central dogma" of molecular biology; i.e., that genetic information is encoded in DNA, that most genes contain both regulatory elements and protein coding sequences which are transcribed into mRNAs, which in turn are translated to make proteins. In addition, a basic understanding of cell organization and compartmentalization, and DNA replication, transcription, and repair will be important, although we will cover additional details in the course. **We encourage you to make liberal use of online resources (Google searches, Wikipedia, iBiology etc.) to help fill in gaps in your knowledge, as working scientists do every day!**

Course Learning Objectives

Students will develop an understanding of key topics in chromosome biology including:

• Spatial organization and dynamics of the cell nucleus
• Epigenetic regulation: histone modifications, the proteins that "read" and "write" them, their roles in genome organization, gene expression, dosage compensation, and specification of chromosomal functions such as centromere activity
• Chromosome dynamics during mitosis and meiosis
• Regulation of DNA replication and repair
• Transposable elements and their contributions to genome organization and functions
• Intracellular phase separation and its roles in nuclear organization and function
• How chromosome (dis)organization and (dys)function can lead to cancer and other diseases
• Historical and contemporary methods for investigating chromosome structure and function

In addition, through assignments and exams, students will

• Demonstrate understanding of topics through clear and concise answers to conceptual questions
• Read and understand contemporary research papers in the field of chromosome biology
• Present a research paper to their peers, including background information, experimental approaches, conclusions, and interpretations
• Develop confidence in their ability to navigate and master complex concepts

This course should not be taken passively; it is essential that you keep up and engage with the material. Lectures will build on material from previous lectures/discussion, so reviewing the material only before exams is a very poor strategy. Numerous optional resources and readings (e.g. animations, videos, and background reading) are listed in the syllabus. While exams will focus on material presented in lectures and discussions, these will also help you to develop a deeper understanding.

Do not hesitate to ask questions! They help the instructors to know when we need to elaborate. We will be exploring concepts that are new to everyone in the course (in some cases even to us) and we encourage everyone to approach the subject with a "beginner's mind."

Instructor Information and Communication

Course Instructor

Gary Karpen | gkarpen@berkeley.edu

Graduate Student Instructors (GSIs)

While the instructor will interact with the whole class and will oversee all activities and grading, as well as being available to resolve any issues that may arise, the GSIs will be your main point of contact. Your GSIs are responsible for assisting you directly with

questions about assignments and course requirements. The GSIs will also facilitate ongoing discussion and interaction with you on major topics in each module.

Anna Horacek | annahoracek@berkeley.edu

Discussion Sections

At the beginning of the semester, everyone will indicate their preference for discussion dates. On Fridays, pairs of students (occasionally 3) will work together to present an assigned paper and lead a discussion. This is a significant component of the final grade (75 pts, including 15 points for preparation and engagement in a preparatory meeting with the GSI). Everyone is expected to read the paper before the presentation, and to work with a small group to think of relevant questions to stimulate discussion.

Discussion questions: Each week, non-presenters will randomly be placed in groups of 3-4 students. Each group will be responsible for submitting at least one question they would like presenters to address during their presentations on bcourses by **Thursday at 3pm**. Individual students will then like at least two questions they want to see addressed by **Thursday at 5pm** to give presenters adequate time to formulate answers for the most popular questions. You are encouraged to meet outside of class in your groups to discuss the paper before submitting a question as a group!

Office Hours

The course instructor and GSIs will offer in person office hours, and if requested can also make appointments via Zoom. These office hours allow for interaction with the instructor and GSI, and are a good opportunity to discuss your questions relevant to the course.

Instructor: Day/Hour (Pacific Time) TBD

GSI: Day/Hour (Pacific Time) TBD

Course Mail

You can also contact your GSI and instructor using the bCourses emailing system, accessed via your Inbox (in global navigation on the left). You can also choose to have your bCourses mail forwarded as text (SMS) or to your personal email.

Course Help

You're not alone in this course; the instructor and GSI are here to support you as you learn the material. It's expected that some aspects of this course will take time to grasp, and the best way to grasp challenging material is to ask questions.

To ask a question, use bCourses or Ed Discussion, or attend office hours. The instructor and GSIs will monitor this discussion forum, but you should also feel free to answer questions posted by other students. You can also reach out to the course staff in office hours, during live discussion sections, and/or via email.

Students with Disabilities

If you require course accommodations due to a physical, emotional, or learning disability, contact UC Berkeley's Disabled Students' Program (DSP). Notify the instructor and GSI through course email of the accommodations you would like to use. You must have a Letter of Accommodation on file with UC Berkeley to have accommodations made in the course.

UC Berkeley is committed to providing robust educational experiences for all learners. With this goal in mind, we have activated the ALLY tool for this course. You will now be able to download reading materials in a format that best fits your learning preference (i.e., PDF, HTML, EPUB, and MP3). For more information, visit the alternative formats link or watch the video entitled, "Ally in bCourses."

Course Materials and Technical Requirements

Readings (all readings are posted on the syllabus and bcourses):

The course is largely based on primary literature (research papers). For background reading in chromosome biology, you can refer to general cell biology and/or genetics textbooks. Recommended options include Alberts et al., Molecular Biology of the Cell, Chapters 4, 5 or Hartwell et al., Genetics: From Genes to Genomes, 3rd edition, Chapters 4, 13, 14, 18, 20. A variety of online resources are available to supplement the information presented in class. We particularly encourage you to take advantage of online videos and other resources such as those available through iBiology. **One or more review articles addressing the topic of each lecture will be posted on the syllabus and bCourses.** We will provide guidance on what to focus on in your readings. Reading assignments may be modified during *the semester, so please check/download the current version of the syllabus.*

Additional Materials

You'll find links to additional reading materials in the syllabus and on bCourses.

Technical Requirements

This course is built on a Learning Management System (LMS) called Canvas (UC Berkeley's instance of Canvas is called bCourses). You'll need to meet these computer specifications to participate within this online platform.

Technical Support

If you're having technical difficulties please alert one of the GSIs immediately. However, understand that neither the GSIs, nor the instructor can assist you with technical problems. You must call or email tech support to resolve any technical issues.

To contact tech support, click on the "Help" button on the bottom left of the global navigation menu in bCourses. Be sure to document all interactions (save emails and transaction numbers).

Grading

Your final course grade will be calculated as follows, letter grades are curved:

Component	Points
Discussion presentation	75
Discussion questions	22
Midterm	100
Final	100
Participation	28
Total	**325**

Strategies for Successful Learning

View the Center for Teaching and Learning's page on (meta)cognitive strategies for student learning to help you effectively study the material.

Take Care of Yourself

Do your best to maintain a healthy lifestyle this semester by eating well, exercising, getting enough sleep, and taking time to recharge your mental health. Taking time to care for yourself, and avoiding academic burnout, will help you achieve your academic, professional, and personal goals.

If you start to feel overwhelmed, be kind to yourself and reach out for support. Remember that seeking help is a courageous thing to do—for yourself and for those who care about you.

Support Resources include emotional, physical, safety, social, and other basic wellbeing resources for students. Academic resources can be found at the Student Learning Center and English Language Resource sites. Berkeley's Office of Emergency Management has resources to prepare for emergencies.

Course Policies

All assignments must be submitted by the indicated deadlines, unless you receive permission in advance. **Please notify us in writing by the second week of the term about any known or potential academic or extracurricular conflicts**. We will try our best to help you with making accommodations, but cannot promise them in all cases.

Academic Integrity

You're a member of an academic community at one of the world's leading research universities. Berkeley creates knowledge that has a lasting impact in the world of ideas and on the lives of others; such knowledge can come from an undergraduate paper as well as the lab of an internationally known professor. One of the most important values of an academic community is the balance between the free flow of ideas and the respect for the intellectual property of others. Scholars and students always use proper citations in papers; professors may not circulate or publish student papers without the writer's permission; and students may not circulate or post materials (handouts, exams, syllabi—any class materials) from their classes without the written permission of the instructor.

Any test, paper or report submitted by you and that bears your name is presumed to be your own original work that has not previously been submitted for credit in another course unless you obtain prior written approval to do so from your instructor. In all of your assignments, including your homework or drafts of papers, you may use words or ideas written by other individuals in publications, websites, or other sources, but only with proper attribution. If you're unclear about the expectations for completing an assignment or taking a test or examination, be sure to seek clarification from your instructor or GSI beforehand. For additional information on plagiarism and how to avoid it, read the UC Berkeley Library Citation Page, Plagiarism Section.

As a member of the campus community, you're expected to demonstrate integrity in all of your academic endeavors and will be evaluated on your own merits. The consequences of

cheating and academic dishonesty—including a formal discipline file, possible loss of future internship, scholarship, or employment opportunities, and denial of admission to graduate school—are simply not worth it. Read more about Berkeley's Honor Code.

Incomplete Course Grade

Students who have substantially completed the course but for serious extenuating circumstances, are unable to complete the final assignments or exams, may request an Incomplete grade. This request must be submitted in writing to the GSI and instructor. You must provide verifiable documentation for the seriousness of the extenuating circumstances.

Refer to the Office of the Registrar's website for more information on the university's policy on Incomplete Grades.

End of Course Evaluation

UC Berkeley is committed to improving our courses and instruction. Before your course ends, please take a few minutes to participate in the course evaluation. We are interested in your online learning experience, and your feedback will help us plan for the future and make improvements. The evaluation does not request any personal information, and your responses will remain strictly confidential. Information about the course evaluation will be made available in bCourses.

Course Outline

Below is the weekly course schedule/syllabus. All readings are provided in bCourses for the assigned week. Check bCourses for specific assignment due dates.

DATE	LECTURE	TOPIC	DISCUSSION	READINGS
1/17/2024	**1**	**Introduction to Class & History of Chromosome Biology**		
1/19/2022			**0**	How to Read a Scientific Paper; Watson and Crick 1953
1/22/2024	**2**	**Genes and Genomes 1**		Blommaert J. 2020 Genome size evolution: towards new model systems for old questions. Proc. R. Soc. B 287: 20201441. LINK (READ THE WHOLE THING BUT FOCUS ON PARTS 1 A,C AND 2 A,B,C)
1/24/2024	**3**	**Genes and Genomes 2**		*Optional review*: Wells, J. N. & Feschotte, C. A Field Guide to Eukaryotic Transposable Elements. *Annu Rev Genet* **54**, 1–23 (2020). (Note section on genome size p. 548) LINK
1/26/2022		*Transposons drive evolution of genome size*	**1**	Naville, M. et al. Massive Changes of Genome Size Driven by Expansions of Non-autonomous Transposable Elements. Curr Biol 29, 1161-1168.e6 (2019). LINK *Minireview:* Suh, A. Genome Size Evolution: Small Transposons with Large Consequences. *Curr Biol* **29**, R241–R243 (2019). LINK
1/29/2024	**4**	**Chromosome Dynamics in the Cell Cycle: Mitosis**		Batty P, Gerlich DW. Mitotic Chromosome Mechanics: How Cells Segregate Their Genome. Trends Cell Biol. 2019 Sep;29(9):717-726. LINK
1/31/2024	**5**	**Chromatin and Epigenetics 1**		Allis CD, Jenuwein T. (2016) The molecular hallmarks of epigenetic control. Nature 17(8):487-500. LINK (up to p 493, use lecture as guide to most important parts) *Optional, just in case you want to read about ChIP* Park, P.J. (2009). ChIP-seq: advantages and challenges of a maturing technology. Nat Rev Genet 10, 669–680 (especially Fig 1, 2, 4 and associated text) LINK
2/2/2024		*The histone code and epigenetic regulation*	**2**	Hirota, T., Lipp, J., Toh, BH. et al. Histone H3 serine 10 phosphorylation by Aurora B causes HP1 dissociation from heterochromatin. Nature 438, 1176–1180 (2005). LINK *Minireview:* Eissenberg, J., Elgin, S. Antagonizing the neighbours. Nature 438, 1090–1091 (2005). LINK
2/5/2024	**6**	**Chromatin and Epigenetics 2**		(Same reading as for L5)
2/7/2024	**7**	**Chromatin and Epigenetics 3**		McKinley, K.L., and I.M. Cheeseman. 2016. The molecular basis for centromere identity and function. Nat Rev Mol Cell Biol. 17:16–29. LINK (Box 1, Fig 3 and associated text)
2/9/2024		*Epigenetic regulation of centromeres*	**3**	Marina Murillo-Pineda, Luis P. Valente, Marie Dumont, João F. Mata, Daniele Fachinetti, Lars E.T. Jansen; Induction of spontaneous human neocentromere formation and long-term maturation. J Cell Biol 1 March 2021; 220 (3): e202007210. LINK *Minireview:* Carty and Dunleavy 2021 J. Cell Biol. 2021 Vol. 220 No. 3 e202101027 LINK (also see McKinley et al for background)

2/12/2024	**8**	**Nuclear Architecture and Dynamics 1**		Beagan, J.A., Phillips-Cremins, J.E. On the existence and functionality of topologically associating domains. Nat Genet 52, 8–16 (2020). LINK (focus on p8-11 top left section, Figs 1 and 2) Video:https://www.youtube.com/watch?v=Tn5qgEqWgW8
2/14/2024	**9**	**Nuclear Architecture and Dynamics 2**		Staněk, D. & Fox, A. Nuclear bodies: news insights into structure and function. *Curr Opin Cell Biol* **46**, 94–101 (2017). LINK
2/16/2024		*Chromosome architecture and loop extrusion*	**4**	Dai et al. Loop extrusion mediates physiological Igh locus contraction for RAG scanning. Nature. 2021 Feb;590(7845):338-343. LINK. *Review:* Jan-Michael Peters, How DNA loop extrusion mediated by cohesin enables V(D)J recombination, Current Opinion in Cell Biology, Volume 70, 2021, 75-83. LINK Video: https://www.youtube.com/watch?v=bzXAKX6j-hg
2/19/2024		**No Class-Presidents's Day**		
2/21/2024	**10**	**Nuclear Architecture and Dynamics 3**		Strom and Brangwynne 2019 The liquid nucleome – phase transitions in the nucleus at a glance. Journal of Cell Science 2019 132: LINK https://www.wired.com/story/a-newfound-source-of-cellular-order-in-the-chemistry-of-life/ *Optional review: Lyon, A. S., Peeples, W. B. & Rosen, M. K. A framework for understanding the functions of biomolecular condensates across scales. Nat Rev Mol Cell Bio **22**, 215–235 (2021).*LINK
2/23/2024		*Nuclear architecture impacts night vision*	**5**	Solovei I, Kreysing M, LanctOt C, et al. Nuclear architecture of rod photoreceptor cells adapts to vision in mammalian evolution. Cell. 2009;137(2):356-368. LINK *Minireview:* Eskiw, C., and Fraser, P. (2009). Inverted rod nuclei see the light. Nat Cell Biol 11, 680–681 LINK
2/26/2024	**11**	**Nuclear Architecture and Dynamics 4**		(Same readings as for L10)
2/28/2024	**12**	**Nuclear Architecture and Dynamics 5**		(Same readings as for L10)
3/1/2024		*Nuclear architecture empowers smell*	**6**	Monahan K, Horta A, Lomvardas S. LHX2- and LDB1-mediated trans interactions regulate olfactory receptor choice. Nature. 2019;565(7740):448-453. LINK *Minireview:* Spitz F. Chromosomes come together to help mice distinguish odours. Nature. January 2019:439-440 LINK *Optional review:* Pourmorady, A. & Lomvardas, S. Olfactory receptor choice: a case study for gene regulation in a multi-enhancer system. *Curr Opin Genet Dev* **72**, 101–109 (2022). LINK
3/4/2024		**CATCHUP or REVIEW**		
3/6/2024		**REVIEW**		
3/8/2024		**MIDTERM**		
3/11/2024	**13**	**DNA Damage and Repair 1**		Clouaire, Thomas et al. 2019 A Snapshot on the Cis Chromatin Response to DNA Double-Strand Breaks.Trends in Genetics, Volume 35, Issue 5, 330 - 345 LINK (Focus on 330-336, Fig 1-3; will cover Figs 4 and 5 briefly in lecture)
3/13/2024	**14**	**DNA Damage and Repair 2**		Lamm, N., Rogers, S. & Cesare, A. J. Chromatin mobility and relocation in DNA repair. Trends Cell Biol 31, 843–855 (2021). LINK
3/15/2024		*DNA repair dynamics in 4D*	**7**	Caridi, C.P., D'Agostino, C., et al. (2018). Nuclear F-actin and myosins drive relocalization of heterochromatic breaks. Nature 559, 54–60. LINK *Minireview:* Roukos, V. (2018). Actin proteins assemble to protect the genome. Nature 559, 35–37. LINK
3/18/2024	**15**	**Meiosis 1**		See Meiosis 'cheat sheet' on bcourses
3/20/2024	**16**	**Meiosis 2**		Paige and Petkov. PRDM9 and its role in genetic recombination. Trends Genet. 2018 April ; 34(4): 291–300. LINK Andreas Hochwagen, Gabriel A.B. Marais, Meiosis: A PRDM9 Guide to the Hotspots of Recombination, Current Biology, Volume 20, Issue 6, 2010, Pages R271-R274 LINK
3/22/2024		*Control of meiotic chromosome segregation*	**8**	Akera, T., Chmátal, L., Trimm, E., Yang, K., Aonbangkhen, C., Chenoweth, D.M., Janke, C., Schultz, R.M., and Lampson, M.A. (2017). Spindle asymmetry drives non-Mendelian chromosome segregation. Science 358, 668–672. LINK *Review-*(focus on parts relevant to the Akera paper) Kursel and Malik (2018) The cellular mechanisms and consequences of centromere drive. Current Opinion in Cell Biology. LINK
3/25-29/2024		**No Class-Spring Break**		
4/1/2024	**17**	**Sex Determination**		Graves, J. Evolution of vertebrate sex chromosomes and dosage compensation. Nat Rev Genet 17, 33–46 (2016). LINK
4/3/2024	**18**	**Dosage Compensation**		Ditto
4/5/2024		*X inactivation by XIST RNA*	**9**	Dossin, F. et al. SPEN integrates transcriptional and epigenetic control of X-inactivation. Nature 578, 455–460 (2020) LINK *Minireview:* Trotman, J. B. & Calabrese, J. M. How to silence an X chromosome. *Nature* **578**, 365–366 (2020). LINK
4/8/2024	**19**	**Chromosomes and Cancer 1**		
4/10/2024	**20**	**Chromosomes and Cancer 2**	:	Ly and Cleveland. 2017. Trends in Cell Biology Vol. 27, No. 12. LINK *Optional (if you want to read about clinical impact of Chromothripsis):* Cortés-Ciriano, I., Lee, J.JK., Xi, R. et al. Comprehensive analysis of chromothripsis in 2,658 human cancers using whole-genome sequencing. Nat Genet 52, 331–341 (2020). LINK
4/12/2024		*Cancer, CIN and aneuploidy*	**10**	Cohen-Sharir, Y. *et al.* Aneuploidy renders cancer cells vulnerable to mitotic checkpoint inhibition. *Nature* **590**, 486–491 (2021). LINK *Minireview:* Bielski, C. M. & Taylor, B. S. Homing in on genomic instability as a therapeutic target in cancer. Nat Commun **12**, 3663 (2021). LINK *Optional deep review:* Ben-David, U. & Amon, A. Context is everything: aneuploidy in cancer. Nat Rev Genet 21, 44–62 (2020). LINK
4/15/2024	**21**	**Chromosomes and Cancer 3**		
4/17/2024	**22**	**Environmental Epigenomics 1**		Cavalli, G., Heard, E. Advances in epigenetics link genetics to the environment and disease. Nature 571, 489–499 (2019). LINK (FROM Environmental Epigenetics (p. 492) to the end)
4/19/2024		*Condensates control flowering*	**11**	Zhu, P., Lister, C. & Dean, C. Cold-induced Arabidopsis FRIGIDA nuclear condensates for FLC repression. *Nature* **599**, 657–661 (2021). LINK *Minireview:* Osman, S. Changing of the seasons — transcriptional buffers against flowering in the cold. Nat Struct Mol Biol 28, 963 (2021). LINK *Optional deep review:* Whittaker and Dean. Annual Review of Cell and Developmental Biology 2017 33:1, 555-575 LINK

4/22/2024	**23**	**Environmental Epigenomics 2**		Casas, E. & Vavouri, T. Mechanisms of epigenetic inheritance of variable traits through the germline. *Reproduction* **159**, R251–R263 (2020). LINK Focus on info/systems mentioned in this lecture.
4/24/2024	**24**	**Chromosomes and Society**		**Please read/view the following (and any other info on this topic if you like; *Center for Genetics and Society* is a great 'local' organization and site for bioethics topics)** **Come to class prepared to discuss different perspectives on the general topics of 'genome engineering and society'.** Since some of the videos are long, I provide a guide for which sections of the material to focus on. You should be able to view/read all within an hour. Of course feel free to watch additional parts as desired. Enjoy! 1. CRISPR/Future of gene editing(8 min) 2. Gene editing/designer babies(12 min) 3. Future of genetics(11:00-23:00; 30:26-46:00) 4. *The Disability Critique* by Marsha Saxton (PDF). pls read the intro up to "The Medical Model" of Disability and the Need for Screening; continue if interested in learning more about perspectives on the topic. *optional:* *Climate Crisis, Designer Babies and Pandemics: Challenging the Techno-Utopianism of the Genetically Engineered Age* long but interesting, broad discussion of technology and society. at least watch the end 52:30-60:00 We will not focus on eugenics directly (though it does drive some perspectives on genome engineering), but if you are unaware of the the history of eugenics (and how it still drives many societal choices) please become informed. If you can find a copy of the documentary "A Dangerous Idea: Eugenics, Genetics, and the American Dream" view it...alternatively there is a great discussion in this video, and you can see clips from the documentary throughout (eg starting ~38min) *LINK*
4/26/2024		*Environmental epigenetics and transgenerational inheritance*	**12**	Klosin, A., Casas, E., Hidalgo-Carcedo, C., Vavouri, T. & Lehner, B. Transgenerational transmission of environmental information in C. elegans. Science 356, 320–323 (2017). LINK Minireview: See summary in L23 review (Casas 2020) R254-255, 'Heritable responses to environmental stimuli'
4/29-5/3/2024		**RRR WEEK**		**Review Sessions M W 9-10**
5/6/2022		**FINAL**		**7-10PM (LOCATION TBD)**