

COURSE TITLE: Experimental Biology

COURSE NUMBER: G302

CREDITS: 5

COURSE DIRECTOR: Mary Baylies, Ph.D.

COURSE PREREQUISITES: None; Open to first year PhD students

GRADING POLICY: Pass/Fail

COURSE DESCRIPTION AND LEARNING OBJECTIVES

Experimental Biology teaches conceptual and practical aspects of four different research disciplines: imaging, genetics, genomics, and biochemistry. Each topic will be covered for one week through a combination of workshops, research paper discussions, and lectures. The purpose of this course is to hold discussions about different research disciplines and their methods, but not to teach each topic comprehensively. Each week will introduce new concepts and may not connect directly to the previous week. Questions that will be considered in the course include:

- How is imaging performed at different length scales, and what can be learned through different techniques?
- How have imaging technologies pushed the boundaries of knowledge?
- How are genetic principles and applied technologies used to make new discoveries?
- What techniques allow for the experimental manipulation of DNA, RNA and protein, and how do they work?
- How do the “kits” on my research bench actually work?

COURSE STRUCTURE

This course meets four to five days a week for four weeks. Each day includes a 2 hour lecture/discussion followed by a 2 hour afternoon session. Total in-class time includes approximately 75 hrs. Students are also expected to spend considerable time reading the pre-assigned articles and background assignments prior to class.

Teaching Fellows

Each topic will have a teaching fellow, who is an advanced GSK Student. The teaching fellow's responsibilities will include setting up for the course, helping organize group projects, creating and evaluating student problem sets and reflection papers.

ASSIGNMENTS AND METHODS FOR ASSESSING STUDENT ACHIEVEMENT

The course is structured so that each morning lecture/discussion is followed by a group presentation or assignment that will test the students' knowledge of the topics discussed in the morning. Projects will include paper discussions, problem sets, and explanations of how certain biological research tools work. Students will receive real-time feedback from the faculty director during their presentations.

In addition, some weeks will have either a reflection paper or problem sets assigned, which will be reviewed by the teaching fellows. These assignments will be due during the week following that section.

BASIS FOR GRADE DETERMINATION

Students will receive a pass/fail grade for this course. To receive a passing grade, students must attend all morning and afternoon sessions, actively participate in class discussions, and complete all group and individual assignments outlined by each week's faculty leader. Students are permitted to miss one morning and afternoon session. Any more absences will be brought to the attention to the Dean to determine how this will impact the final grade.

COURSE EVALUATION

Students will be encouraged to complete anonymous post course surveys that will evaluate the effectiveness of the course. This survey is used to improve future course offerings.

COURSE SCHEDULE

The following schedule shows planned activities for each week. Please take note of assignments for paper introductions and a small group project in week 2.

Week 1: Introduction/Imaging

8/25/2025; 9/2/2025 – 9/5/2025

- Lectures each morning (10am-12pm)
- Discussion sessions each afternoon (1-3pm)

Teaching Fellow: Achuth Nair

Monday 8/25

Morning Breakfast session: Dr. Selwyn Vickers, lecture: "The impact of Research on the Mission of MSK" – This session will meet from 9:00-11:00 am

Tuesday 9/2

Morning Session: Introduction to the Year – From Basic Biology to Cancer

Afternoon Session: Group Paper discussion

Cheung KJ, Padmanaban V, Silvestri V, Schipper K, Cohen JD, Fairchild AN, Gorin MA, Verdone JE, Pienta KJ, Bader JS, Ewald AJ. Polyclonal breast cancer metastases arise from collective dissemination of keratin 14-expressing tumor cell clusters. Proc Natl Acad Sci U S A. 2016 Feb 16;113(7):E854-63. doi: 10.1073/pnas.1508541113. Epub 2016 Feb 1. PMID: 26831077; PMCID: PMC4763783.

Student Presenter: Lange, Matthew

Wednesday 9/3

Morning session: Rich Hite, lecture

Introduction to imaging at different scales

1. What types of imaging are useful in biological sciences?
 - a. Start small with electrons
 - b. Light has diverse roles in imaging
 - c. How to image whole organisms?
2. How can information at different scales be combined to better understand complex biological questions?
 - a. Dynamic vs. static images
 - b. Time-resolved effect of perturbations
 - c. Steady-state vs non-equilibrium

Afternoon session: Rich Hite, lecture

Electron microscopy

1. Electron optics viewed through the lens of light optics
2. Physics of converting a 3D object into a 2D image
 - a. Central section theorem
 - b. Fourier transforms
3. Practical applications of electron microscopy in biological sciences
 - a. Traditional electron microscopy
 - b. Single-particle cryo-EM
 - c. Cryo-ET
 - d. Electron crystallography (micro-ED)
4. Limitations of electron microscopy
 - a. Static structures
 - b. Heterogeneity

Thursday 9/4

Morning session: Christina Pyrgaki, lecture

Light microscopy: Visualization of cells and cellular components

Afternoon session: Instrument Tours – meet in Z668

Group 1:

Afroz, Jalwa
Beattie, Kai
Cherkas, Shelby
Hanselman, Olivia
Li, Ruofei

Group 2:

Illouz, Sylvia
Lange, Matthew
Magnus, Karina
McIlhenny, Lauren
Tarrab, Stephanie

Group 3:

Ahmed, Nibras
Levin, Bailey
Mutaher, Mohammed
Perea del Angel, Ana
Pope, Eleanor

Group 4:

Prabakaran, Adithya
Styers, Hannah
Sussman, Carleigh
Ta, Christina
Volpe, Christina

Friday 9/5 (10:00-12:00 and 1:00-4:00)

Morning session: Jason Lewis, lecture

Whole body imaging

Afternoon session (1:00-4:00): Organized visits to imaging facilities at MSK – meet in Z138 at 12:45.

Tours will be organized in 3 groups, each group visiting 3 of the imaging facilities for 1 hour, beginning at 1:00 pm.

Groups as follows:

Group 1:

Afroz, Jalwa
Ahmed, Nibras
Beattie, Kai
Cherkas, Shelby
Hanselman, Olivia
Illouz, Sylvia

Group 2:

Lange, Matthew
Levin, Bailey
Li, Ruofei
Magnus, Karina
McIlhenny, Lauren
Mutaher, Mohammed
Perea del Angel, Ana

Group 3:

Pope, Eleanor
Prabakaran, Adithya
Styers, Hannah
Sussman, Carleigh
Ta, Christina
Tarrab, Stephanie
Volpe, Christina

Evaluation project:

Students are to write a 1–2-page paper on how imaging can be used to answer a research question. These papers are to be emailed directly to the teaching fellow by Tuesday September 9, 2025.

Week 2: Genetics

9/8/2025 – 9/12/2025

- Sessions each morning and afternoon (10am-12pm and 1-3)

Teaching Fellow: James Rodrigues

Monday 9/8

Morning session: Danwei Huangfu, lecture

CRISPR techniques and application

1. Basic concepts of CRISPR technologies
2. Different applications of CRISPR technologies in genetic studies.
 - a. CRISPR/Cas-mediated genome editing
 - b. The expanding CRISPR toolbox
 - c. Diverse applications and beyond

Afternoon session: Student small group presentations

Using CRISPR technology to study and/or combat COVID-19: Prepare to discuss ideas using CRISPR technology to study and/or combat COVID-19. Your ideas can be creative and involve anything from the development of diagnostic tests, to foundational research or the development of treatments. You may search the literature, but you are also encouraged present your own original ideas. Please prepare a 10 minute presentation to discuss the technical and applied aspects of your idea(s). Consider both the potential benefits and also the limitations of your approaches.

Working groups:

Group 1:

Afroz, Jalwa
Beattie, Kai
Cherkas, Shelby
Hanselman, Olivia

Group 2:

Illouz, Sylvia
Lange, Matthew
Magnus, Karina
McIlhenny, Lauren

Group 3:

Levin, Bailey
Mutaher, Mohammed
Perea del Angel, Ana
Pope, Eleanor

Group 4:

Prabakaran, Adithya
Styers, Hannah
Sussman, Carleigh
Ta, Christina

Group 5:

Ahmed, Nibras
Li, Ruofei
Tarrab, Stephanie
Volpe, Christina

Tuesday 9/9

Morning Session:

Advanced genetic approaches -1 Xiaolan Zhao

Generate informative alleles

Conditional alleles

- Temperature sensitive alleles
- Chemical induced degron
- Analog-sensitive alleles & small molecular inhibitors
- Transcription and translation turn off)

Separation-of-functional alleles

Use suppressors to discover new factors, pathways, and mechanisms

Dosage suppressors

Second site mutations

Afternoon session: Paper discussion on synthetic viability screening

Synthetic viability screen

- Puddu, F. *et al.* Chromatin determinants impart camptothecin sensitivity. *EMBO Rep* (2017).

Student Presenter: Afroz, Jalwa

Wednesday 9/10

Morning Session:

Advanced genetic approaches- 2 Xiaolan Zhao

- **Enrichment strategy**
- **Use synthetic lethality or sickness method to unravel new biology**
- **E-map**
- **Synthetic dosage suppression**
- **Biochemical readouts used in genetic screens**
- **Convert biochemical questions to genetic questions**
- **Overview of model organisms**
- **Emerging Genetic Approaches**

Afternoon Session: Group Exercise.

Group 1:

Afroz, Jalwa
Beattie, Kai
Cherkas, Shelby
Lange, Matthew
Levin, Bailey

Group 2:

Ahmed, Nibras
Hanselman, Olivia
Illouz, Sylvia
McIlhenny, Lauren
Mutaher, Mohammed

Group 3:

Perea del Angel, Ana
Styers, Hannah
Ta, Christina
Tarrab, Stephanie
Volpe, Christina

Group 4:

Li, Ruofei
Magnus, Karina
Pope, Eleanor
Prabakaran, Adithya
Sussman, Carleigh

Thursday 9/11 – Morning Session

Morning session: Mary Baylies, lecture

Genetics on the Fly: Drosophila Model Systems

1. Analysis of mutations in fly
 - a. LOS
 - b. nulls
 - c. hypermorphs
 - d. hypomorphs
2. Genetic analyses in fly
 - a. complementation tests, pathway analysis (are genes in the same pathway for the specific function)
 - b. autonomous/nonautonomous functions of a gene (mosaic analysis);
 - c. epistasis
 - d. gene dosage
3. Genetic screens (using fly eye as an example):
 - a. recessive screens,
 - b. sensitized screens,
 - c. tissue specific screens RNAi/ Overexpression,
4. Usefulness of the fly
 - a. Conservation to human,
 - b. Conservation of processes, using to find new processes.

Afternoon Session: Logic and Critical Analysis Session 1
Dr. Lydia Finley

Discussion Paper Group A:

Sullivan, et al. Supporting Aspartate Biosynthesis Is an Essential Function of Respiration in Proliferating Cells. *Cell*. 2015; 162, 552–563 July 30.

Discussion Paper Group B:

Birsoy, et al. An Essential Role of the Mitochondrial Electron Transport Chain in Cell Proliferation Is to Enable Aspartate Synthesis. *Cell*. 2015; 162, 540–551 July 30.

Group A:

Afroz, Jalwa
Ahmed, Nibras – **Student Presenter**
Cherkas, Shelby
Hanselman, Olivia
Illouz, Sylvia
Lange, Matthew
Levin, Bailey
Li, Ruofei
Magnus, Karina
McIlhenny, Lauren

Group B:

Beattie, Kai – **Student Presenter**
Mutaher, Mohammed
Perea del Angel, Ana
Pope, Eleanor
Prabakaran, Adithya
Styers, Hannah
Sussman, Carleigh
Ta, Christina
Tarrab, Stephanie
Volpe, Christina

Friday 9/12

Morning session: Kat Hadjantonakis, lecture

Mouse genetics

1. Overview of embryonic stem cells, mouse chimeras, and transgenic mouse models.
2. Generation and analysis of genetically engineered mouse models (GEMMs): nulls, hypermorphs, hypomorphs...
3. Genetic analyses in mice:
 - a. complementation tests
 - b. pathway analysis (are genes in the same pathway for the specific function)
 - c. autonomous/nonautonomous functions of a gene (chimera analysis);
4. Genetic screens: dominant and recessive screens
5. The International Mouse Phenotyping Consortium (IMPC)
 - a. unbiased comprehensive catalog of mammalian gene function
 - b. conservation to human

Afternoon session: Yas Furuta***Development of Genetically Engineered Mouse (GEM) Models***

1. Practical considerations in choosing platforms for germ line genome modifications in the mouse
2. One size hardly fits all – complex realities in common approaches to targeted genome modifications
3. Cheating genetics to expedite complex in vivo genetic studies
4. Genome editing and germ line gene modifications today, tomorrow and beyond

Evaluation project:

In class group projects will be used for evaluation.

Week 3: Genomics

9/15/2025 – 9/19/2025

- Sessions each morning and afternoon (10am-12pm and 1-3pm)

Teaching Fellow: Manisha Srinivas Raghavan

Monday 9/15

Morning session: Iestyn Whitehouse, discussion leader

1. Basic overview of genomes.
2. Intro to sequencing technologies.
3. What is a sequencing library, and how do you make one?

Afternoon session: Discussion and introduction to small group presentations. Dissecting a kit: commonly used “kits” from the research bench will be distributed to student groups as announced in class on Mon 9/15. Groups should then prepare to discuss on 9/16 how the individual components of their assigned kit actually work to achieve the desired technique.

Tuesday 9/16

Morning session: Iestyn Whitehouse

Small group presentations: dissecting a kit.

Afternoon session:

Continuation of group presentations (if needed).

Wednesday 9/17

Morning session: Neeman Mohibullah, discussion leader

1. Single cell DNA, Single cell RNA
2. Spatial transcriptomics
3. Single molecule transcriptomics

Afternoon session: IGO tour cohort 1/Tutorial on best practices for sample submission

Tour group for 9/17:

Afroz, Jalwa
Beattie, Kai
Cherkas, Shelby
Lange, Matthew
Li, Ruofei
Magnus, Karina
McIlhenny, Lauren
Perea del Angel, Ana
Styers, Hannah
Volpe, Christina

Thursday 9/18

Morning session: Cassidy Cobbs, Discussion leader:

1. Sequencing Technologies

Afternoon session: IGO tour cohort II/Tutorial on best practices for sample submission

Tour group for 9/18:

Ahmed, Nibras
Hanselman, Olivia
Illouz, Sylvia
Levin, Bailey
Mutaher, Mohammed
Pope, Eleanor
Prabakaran, Adithya
Sussman, Carleigh
Ta, Christina
Tarrab, Stephanie

Friday 9/19

Morning session (10:00-12:00): Logic and Critical Analysis Session 2

Dr. Agnel Sfeir – Groups

Group A:

Afroz, Jalwa
Hanselman, Olivia
Lange, Matthew
Levin, Bailey
Li, Ruofei
McIlhenny, Lauren
Mutaher, Mohammed
Pope, Eleanor
Ta, Christina
Volpe, Christina

Group B:

Ahmed, Nibras
Beattie, Kai
Cherkas, Shelby
Illouz, Sylvia
Magnus, Karina
Perea del Angel, Ana
Prabakaran, Adithya
Styers, Hannah
Sussman, Carleigh
Tarrab, Stephanie

Discussion Papers Group A (Classic Papers - 3):

Prusiner SB. Prions (Nobel Lecture). Proc. Natl. Acad. Sci. 1998; Nov (95):13363-13383.

Sparrer et al., Evidence for the prion hypothesis: induction of the yeast [PSI⁺] factor by in vitro-converted Sup35 protein. Science. 2000 Jul 28;289(5479):595-9.

Prusiner SB. Novel proteinaceous infectious particles cause scrapie. Science. 1982; Apr 9;216(4542):136-44.

Discussion Paper Group B (Contemporary Paper):

EN Neumann et al. Science 2024 Jun 28;384(6703). Brainwide silencing of prion protein by AAV-mediated delivery of an engineered compact epigenetic editor. PMID: 38935715

Afternoon session (1:00-4:00pm): Tobias Walther, lecture

Essential concepts in Lipid and Membrane Biology/Mass spectrometry analysis for biochemistry

Discussion Paper:

Abrams ME, Johnson KA, Perelman SS, Zhang LS, Endapally S, Mar KB, Thompson BM, McDonald JG, Schoggins JW, Radhakrishnan A, Alto NM. Oxysterols provide innate immunity to bacterial infection by mobilizing cell surface accessible cholesterol. Nat Microbiol. 2020 Jul;5(7):929-942. doi: 10.1038/s41564-020-0701-5. Epub 2020 Apr 13. PMID: 32284563; PMCID: PMC7442315.

Student presenter: Cherkas, Shelby

Evaluation project:

Students will be emailed a 2-question problem set for completion in one week. Completed problem sets will be emailed to the Registrar.

Week 4: Biochemistry

9/22/2025-9/26/2025

- Sessions in mornings and afternoons (10am-12pm, and 1-3pm)

Teaching Fellow: Lucia Wang

Monday 9/22

Morning session (10am-12pm): Dirk Remus, lecture
Molecular techniques for the analysis of DNA

Afternoon session (1-3pm): Dirk Remus, Discussion

Tuesday 9/23

Morning session (10am-12pm): Chris Lima, lecture
Molecular techniques for the analysis of RNA

Afternoon session (1-3pm): Joshua Peter, paper discussion leader

Paper: Linder B, Grozhik AV, Olarerin-George AO, Meydan C, Mason CE, Jaffrey SR. Single-nucleotide-resolution mapping of m6A and m6Am throughout the transcriptome. *Nat Methods*. 2015 Aug;12(8):767-72. doi: 10.1038/nmeth.3453. Epub 2015 Jun 29. PMID: 26121403; PMCID: PMC4487409.

Student Presenter: Hanselman, Olivia

Wednesday 9/24

Morning session (10am-12pm): Stewart Shuman, lecture and group discussion
Molecular techniques for the analysis of Protein

Please read in advance: Protein production and purification. *Nature Methods*. Volume 5, Pages135–146 (2008).

Afternoon session (1-3pm): Stewart Shuman, Group Discussion

Thursday 9/25

Morning session (10am-12pm): Richard Hite, lecture
Alpha-fold and modern Protein structure determination.

Paper discussion

Jumper J, Evans R, Pritzel A, Green T, Figurnov M, Ronneberger O, Tunyasuvunakool K, Bates R, Žídek A, Potapenko A, Bridgland A, Meyer C, Kohl SAA, Ballard AJ, Cowie A, Romera-Paredes B, Nikolov S, Jain R, Adler J, Back T, Petersen S, Reiman D, Clancy E, Zielinski M, Steinegger M, Pacholska M, Berghammer T, Bodenstein S, Silver D, Vinyals O, Senior AW, Kavukcuoglu K, Kohli P, Hassabis D. Highly accurate protein structure prediction

with AlphaFold. Nature. 2021 Aug;596(7873):583-589. doi: 10.1038/s41586-021-03819-2. Epub 2021 Jul 15. PMID: 34265844; PMCID: PMC8371605.

Student Presenter: Illouz, Sylvia

Afternoon session (1-3pm):

Paper discussion

Abramson J, Adler J, Dunger J, Evans R, Green T, Pritzel A, Ronneberger O, Willmore L, Ballard AJ, Bambrick J, Bodenstein SW, Evans DA, Hung CC, O'Neill M, Reiman D, Tunyasuvunakool K, Wu Z, Žemgulytė A, Arvaniti E, Beattie C, Bertolli O, Bridgland A, Cherepanov A, Congreve M, Cowen-Rivers AI, Cowie A, Figurnov M, Fuchs FB, Gladman H, Jain R, Khan YA, Low CMR, Perlin K, Potapenko A, Savy P, Singh S, Stecula A, Thillaisundaram A, Tong C, Yakneen S, Zhong ED, Zielinski M, Žídek A, Bapst V, Kohli P, Jaderberg M, Hassabis D, Jumper JM. Accurate structure prediction of biomolecular interactions with AlphaFold 3. Nature. 2024 Jun;630(8016):493-500. doi: 10.1038/s41586-024-07487-w. Epub 2024 May 8. PMID: 38718835; PMCID: PMC11168924.

Student Presenter: Levin, Bailey

Evaluation project:

In class group projects will be used for evaluation.