BIOL 8300: Integrative Studies of the Phenotype

Description

This course will explore research on the mechanistic bases, origins, and evolution of phenotypes with an emphasis on the insights gained through integrative approaches. The 2023 offering will be loosely organized around the theme of understanding how complex phenotypes originate and change over time. Students will be introduced to the inferences possible when a problem is attacked across the spectrum of practical and conceptual approaches through guided reading and self-exploration of the literature. Study design and chalk talk exercises will provide practice in project design and presentation skills. Readings and laboratory tours will introduce students to techniques and approaches available in life sciences labs and how they can be applied across disciplines.

Format

The primary goal of the course is to introduce students to the value of integrative studies of any given topic and to see how researchers in different subfields approach fundamental questions in the life sciences. We have chosen to focus on case studies investigating how complex phenotypes of multiple types arise to emphasize this approach. We will discuss how concepts and methods from developmental and cell biology, ecology, evolution, and genetics can provide insights into these questions. During this semester, we will learn about topics including the origins of multicellular animals, how morphologies develop and evolve, and phenotypic interactions across levels of biological organization. The learning goals are not focused on specific content – our primary goals are to promote integrative science and explore a range of experimental frameworks used to approach fundamental questions and concepts in biology.

This is a graduate level course that spans a range of subdisciplines and includes both first-year and advanced students. Instructors will guide topics and some discussion, but students are expected to invest in taking each idea further and in new directions based on their own background and interests. Everyone should expect to find themselves a bit out of their depth at times (including the instructors), so we expect everyone to help other members of the group explore unfamiliar ideas, jargon, and approaches. **Learning goals**:

1) Understand fundamental questions and concepts related to the origins and evolution of novel phenotypes at different levels of biological organization
2) Appreciate the unique insights that can be gained through integrative and curiosity-driven studies
3) Gain familiarity with a range of experimental approaches and how they can be used to address questions in the life sciences
4) Practice presentation and project design skills

General Structure

Most class periods will have one research paper assigned to be read before class that will form the basis of the activities for that period. Many class periods will also have an accompanying article, commentary, or review that provides additional context or more recent advances. Class activities will include group discussions, secondary reading discussions, chalk talks, and micro-rotations.
Group discussions – based on the assigned reading, will focus on the conceptual and historical bases for the work, the level of question(s) addressed, empirical or theoretical techniques used, and potential limitations and/or future directions. Readings will involve various model and non-model organisms and a range of experimental methods. Students (and instructors) should not expect to understand everything immediately, and should expect to research the systems and techniques used on their own to fully understand the readings.

Secondary reading discussion - each class member chooses a secondary reading of their interest and briefly presents their paper and explains why they picked it in the context of the assigned reading.

Micro-rotations – We will orchestrate visits to different labs at UVA to introduce students to approaches, systems, methodologies, and people that they might not know about. “Micro-rotation” activities may vary from those originally envisioned due to scheduling (or other) reasons.

Assignments (in order of appearance)

Attendance and Participation

Your active participation in discussions and in-class activities is essential to your own learning and that of your classmates. Participation will require reading the materials ahead of time, coming prepared to discuss them, and engaging during class.

Secondary Readings

Everyone chooses a second paper to present to the class based on the assigned reading for the day. Each student should plan a very brief presentation of the paper, focusing on whatever key features led them to choose it (technique, hypothesis, study system, etc.). Secondary readings should be peer-reviewed papers or preprints posted to bioRxiv or a similar preprint server.
Students will be split into two groups that present secondary readings on alternating days/topics to ensure that everyone has time to talk. Students should post the citations for their secondary readings to the course Canvas site ahead of class along with a brief (2-3 sentence) summary of why they chose the paper.

NIH RePORTER Summary

This assignment is intended to help see how biologists frame their research for a broader audience, convey the significance of basic science to non-specialists, and define their short- and long-term goals. Your assignment is to use the NIH RePORTER website (https://reporter.nih.gov) to read at least three summaries (public abstracts) from awarded NIH projects that address integrative questions or use integrative methods (broadly defined). Your summaries should include at least one predoctoral or postdoctoral award (e.g. F31, F32, K99) and at least one research project grant (e.g. R01, R35). In class, we will discuss similarities and differences in how the researchers conveyed the significance and potential implications of their work and how they defined their questions and goals.

Research Outlines

Research outlines are written documents that accompany each chalk talk. For this assignment, each student will write a summary in the format of an NIH Specific Aims page describing the research they will propose in their chalk talk. Our goal is for students to explore systems and methods that are outside their own research area, but you should run your ideas past other people with knowledge of the field to make sure the proposed research is technically and theoretically sound. Additional details will be provided in class.

Chalk Talks

Toward the middle and the end of the semester, each participant will give a “chalk talk” style presentation of a research proposal that takes an integrative approach to understanding a question of interest. EXPAND fellows should present the first chalk talk on the research they proposed in their fellowship application. First-year students may present one chalk talk related to their rotation research (if applicable) if they wish. The second chalk talk should be on an unrelated topic. Instructors will provide additional advice on how to plan and execute an effective chalk talk during class.

Grading

Grades will be based on completion, quality, and effort invested in oral and written assignments (50%), and participation and leadership in class meetings (50%).

Class participation and leadership (50 points):

You will earn all points for class participation if you actively and consistently engage in class, by for instance asking meaningful questions, responding to prompts, and making substantive contributions to discussions. Points will be reduced for infrequently engaging in class or lack of preparation. Everyone should expect to be out of their element with some of the material but should invest effort into understanding the key concepts and approaches ahead of class. This category includes overall participation in class discussions along with secondary reading presentations, which will give every student a regular outlet for participation.

Chalk talks and research outlines (50 points):
You will receive full credit for the research outline (10 points each) and chalk talk assignments (15 points each) if you propose thoughtful and scientifically sound research that uses integrative approaches. Points will be reduced for projects that lack scientific rigor, novelty, clarity, or significance. The overall grade for chalk talk assignments will incorporate an assessment of both the proposed research and your responses to questions, but the most important element is that you make a clear attempt to employ a creative and thoughtful approach and engage with an idea.

Class schedule

Full citations for course readings are provided at the end of the syllabus. Citations for commentaries and reviews related to research papers are listed under the article they accompany.

Date	Day	Theme	Topic	Reading(s)	Assignment
8/22	T	Course overview	Introduction to the course and our goals	None	
8/24	Th	Origins of complexity	Experimental evolution of multicellularity	**Research paper:** Bozdag, *et al.,* 2023 https://pubmed.ncbi.nlm.nih.gov/37165189/; **Commentary**, Shalev & Ratzke, 2023 https://pubmed.ncbi.nlm.nih.gov/37586948/	
8/29	T	Origins of complexity	Origins of animal multicellularity	**Research paper,** Brunet, *et al.,* 2021 https://pubmed.ncbi.nlm.nih.gov/33448265/; **Commentary**, Velle & Fritz-Laylin, 2021 https://pubmed.ncbi.nlm.nih.gov/33848494/; **Review,** Brunet & King 2017 https://pubmed.ncbi.nlm.nih.gov/29065305/	Secondary readings (Group 1)
8/31	Th	Origins of novel body plans	Body plan organization in echinoderms	**Research paper,** Formery, *et al.,* 2023 https://doi.org/10.1101/2023.02.05.527185	Secondary readings (Group 2)
9/5	T	Origins of novel structures	Origins of vertebrate limb developmental programs	**Research paper,** Letelier, *et al.,* 2018, https://pubmed.ncbi.nlm.nih.gov/29556077/; **Review**, Shubin, *et al.,* 2009 https://pubmed.ncbi.nlm.nih.gov/19212399/	
9/7	Th	Micro-rotation			
9/12	T	Evolution of complex phenotypes	Regulatory convergence in cichlid coloration	**Research,** Kratochwil, *et al.,* 2019 https://www.science.org/doi/full/10.1126/science.aao6809 ; **Commentary,** Gante 2019 https://www.science.org/doi/10.1126/science.aav3373	Secondary readings (Group 1)
9/14	Th	Evolution of complex phenotypes	Functional convergence versus genetic convergence in avian hemoglobin	**Research,** Natarajan, *et al*., 2016 https://www.science.org/doi/full/10.1126/science.aaf9070; **Commentary,** Bridgham, 2016 https://www.science.org/doi/10.1126/science.aai7394	Secondary readings (Group 2)
9/19	T	Genes to phenotypes to fitness	Natural selection on genes and phenotypes for mouse color	**Research,** Barrett, *et al.,* 2019 https://www.science.org/doi/10.1126/science.aav3824	Secondary readings (Group 1)

				Commentary, Pellier, 2019 https://www.science.org/doi/10.1126/science.aaw3097	
9/21	Th	Genes to phenotypes to fitness	Selection on neural basis for sexual fidelity in voles	**Research,** Okhovat, *et al.,* 2015 https://www.science.org/doi/full/10.1126/science.aac5791 **Commentary,** Robinson, 2015 https://www.science.org/doi/10.1126/science.aad8071	Secondary readings (Group 2)
9/26	T	Project/presentation design	Chalk talk and project design overview	Self-directed reading of NIH Project Summaries	NIH Reporter Summary
9/28	Th	Evolution of behavior	Neuroendocrinology and genetics of parental care in mice	**Research,** Bensky, *et al.,* 2017 https://www.nature.com/articles/nature22074; **Commentary,** Phelps, 2017 https://www.nature.com/articles/nature22486	
10/3	T	Reading Day			
10/5	Th	Micro-rotation			
10/10	T	Chalk Talks, Research outlines due			
10/12	Th	Chalk Talks			
10/17	T	Chalk Talks			
10/19	Th	Species interactions	Prey diversity and snake venome evolution	**Research,** Holding, *et al.,* 2021 https://www.pnas.org/doi/full/10.1073/pnas.2015579118	
10/24	T	Species inteartions	Monarchs and mikweed... and flies?	**Research,** Karageori, *et al.,* 2019 https://www.nature.com/articles/s41586-019-1610-8	Secondary readings (Group 1)
10/26	Th	Species interactions	Cooperative hunting	**Research paper 1,** Vail, *et al.,* 2014 https://pubmed.ncbi.nlm.nih.gov/25202866/ ; **Research paper 2,** Spottiswoode, *et al.,* 2016 https://pubmed.ncbi.nlm.nih.gov/27463674/	Secondary readings (Group 2)
10/31	T	Regeneration	Regeneration in an evolutionary context	**Review,** Bely & Nyberg, 2010 https://pubmed.ncbi.nlm.nih.gov/19800144/	Secondary readings (Group 1)
11/2	Th	Regeneration	Developmental origins of adult pluripotent cells	**Research,** Kimura, *et al.,* 2023 https://pubmed.ncbi.nlm.nih.gov/36493754/; **Commentary,** Davies, 2022 https://pubmed.ncbi.nlm.nih.gov/36493749/	Secondary readings (Group 2)
11/7	T	Election Day			
11/9	Th	Wild card	Topics TBD with class input	Papers TBD	
11/14	T	Wild card	Topics TBD with class input	Papers TBD	
11/16	Th	Wild card	Topics TBD with class input	Papers TBD	
11/21	T	Micro-rotation			
11/23	Th	Thanksgiving recess			
11/28	T	Chalk Talks, Research outlines due			
11/30	Th	Chalk Talks			
12/5	T	Chalk Talks			

Academic Integrity: All assignments must be the student's original work. While the ideas and writing must be your own, you are highly encouraged to discuss your ideas and seek input from others. All sources must be properly cited. Use of generative AI must be acknowledged, including the prompts used. It is the responsibility of the student to understand what constitutes plagiarism and to ensure that all submitted work is their own. Please contact the instructors if you have a question about what is or is not allowed for an assignment.

How to Access Scientific Literature: You will need online access to scientific journals for course readings and assignments. When connecting from off-grounds, some journal websites have paywalls. *Do not pay* to read any scientific articles. The UVA Libraries provide off-grounds access to scientific literature through EZproxy, UVA Anywhere, and UVA Anywhere-Lite. A description of these services and how to use them is here: https://www.library.virginia.edu/services/off-grounds-access/

Honor Statement: We trust that every student will comply fully with all provisions of the UVA honor system. All alleged honor violations brought to our attention may be forwarded to the Honor Committee. Any student who is caught cheating or committing academic fraud will receive an "F" on the assignment, irrespective of any subsequent action taken by the Honor Committee.

Inclusive Environment: As instructors, we are working to create a learning environment that respects and affirms the full range of students' experiences, perspectives, and accessibilities. We are learners in this process, and can do a much better job if you share with us any concerns or challenges of accessibility that you might have. We ask that you, as students, help us make the classroom a welcoming and inclusive learning environment for everyone by being kind, respectful, and thoughtful in all of our class interactions. There will be zero tolerance for offensive or inappropriate language in class, chats, or forums. If you ever feel uncomfortable, upset, or targeted, please bring it to the attention of course instructors immediately.

Support for undoc+ students: Students of all immigration statuses are welcomed and valued in our class, including undocumented students, students from mixed-status families, and students with Temporary Protected Status. If your status is impacting your success in the course, please contact the instructors to discuss appropriate accommodations. We pledge to keep your status confidential unless required by judicial warrant.

Accessibility: Our goal as instructors is to make materials in this course accessible to all students. If you find that this isn't the case, please let us know and we will do our best to adjust accordingly. For students who may benefit from additional support for assignments, please contact the Student Disability Access Center (SDAC). They will be happy to help, and we work directly with them regularly.

Safety and Well-being: We are committed to creating a safe, welcoming, equitable and inclusive classroom environment. All members of our UVA community should be treated with respect and compassion, and we expect you to uphold these ideals at all times. We understand that the learning environment is challenging in the best of times, and even more recently. As course instructors, we are here to support you and direct you towards resources to help you cope with challenges in your academic and personal life.

If you or someone you know is feeling overwhelmed, uncomfortable or stressed out, please reach out to ask for guidance and support. The Student Health Center has Counseling and Psychological Services (CAPS) available for all students; call 434-243-5150 or 434-297-4261 after hours and on weekends. You can also call Madison House's HELP line to speak to someone anonymously any time of day at 434-295-8255.

If you or someone you know is experiencing gender, sexual, or domestic violence, you can find help through the Office of the Dean of Students, Sexual Assault Resource Agency (SARA), Shelter for Help in Emergency (SHE) or the UVA Women's Center. For more information, contact the Director of Sexual and Domestic Violence Services at 434-982-2774.

Readings

* indicates review or commentary articles related to the primary reading(s). These are not required reading but may provide useful context.

Barrett, *et al.* (2019) Linking a mutation to survival in wild mice. *Science* https://www.science.org/doi/10.1126/science.aav3824

*Pellier (2019) Testing evolutionary predictions in wild mice. *Science* https://www.science.org/doi/10.1126/science.aaw3097

Bely AE, Nyberg KG, 2010. Evolution of animal regeneration: re-emergence of a field. *Trends in Ecology & Evolution* 25, 161-170. https://pubmed.ncbi.nlm.nih.gov/19800144/

Bensky, *et al.* (2017) The genetic basis of parental care evolution in monogamous mice. *Nature* https://www.nature.com/articles/nature22074

*Phelps (2017) How to build a better dad. *Nature* https://www.nature.com/articles/nature22486

Bozdag GO, Zamani-Dahaj SA, Day TC, Kahn PC, Burnetti AJ, Lac DT, Tong K, Conlin PL, Balwani AH, Dyer EL, Yunker PJ, Ratcliff WC (2023) *De novo* evolution of macroscopic multicellularity. *Nature* 617(7962):747754. doi: 10.1038/s41586-023-06052-1 https://pubmed.ncbi.nlm.nih.gov/37165189/

*Shalev O, Ye X, Ratzke C (2023) Replaying the evolution of multicellularity. *Trends in Ecology & Evolution* S0169-5347(23)00209-4. doi: 10.1016/j.tree.2023.07.007 https://pubmed.ncbi.nlm.nih.gov/37586948/

Brunet T, Albert M, Roman W, Coyle MC, Spitzer DC, King N, 2021. A flagellate-to-amoeboid switch in the closest living relatives of animals. *eLife* 10, e61037. https://pubmed.ncbi.nlm.nih.gov/33448265/

*Velle, KB, Fritz-Laylin LK, 2021. Evolutionary cell biology: Closest unicellular relatives of animals crawl when squeezed. *Current Biology* 31, R353-R355. https://pubmed.ncbi.nlm.nih.gov/33848494/

Brunet, T., King, N., 2017. The Origin of Animal Multicellularity and Cell Differentiation. *Developmental Cell* 43, 124-140. https://pubmed.ncbi.nlm.nih.gov/29065305/

Formery L, Peluso P, Kohnle I, Malnick J, Pitel M, Uhlinger KR, Rokhsar DS, Rank DR, Lowe CJ (2023) Molecular evidence of anteroposterior patterning in adult echinoderms. *bioRxiv* 2023.02.05.527185; doi: https://doi.org/10.1101/2023.02.05.527185

Holding, *et al.* (2021) Phylogenetically diverse diets favor more complex venoms in North American pit vipers. *PNAS* https://www.pnas.org/doi/full/10.1073/pnas.2015579118

Kimura JO, Bolaños DM, Ricci L, Srivastava M (2023) Embryonic origins of adult pluripotent stem cells. *Cell* 185(25):4756-4769.e13. doi: 10.1016/j.cell.2022.11.008 https://pubmed.ncbi.nlm.nih.gov/36493754/

*Davies EL (2022) Tracing the origin of everything. *Cell* 185, 4677-4679. https://pubmed.ncbi.nlm.nih.gov/36493749/

Kratochwil, *et al.* (2019) Agouti-related peptide 2 facilitates convergent evolution of stripe patterns across cichlid fish radiations. *Science* https://www.science.org/doi/full/10.1126/science.aao6809

*Gante (2019) How fish get their stripes - again and again. https://www.science.org/doi/10.1126/science.aav3373

Karageorgi M, Groen SC, Sumbul F, Pelaez JN, Verster KI, Aguilar JM, Hastings AP, Bernstein SL, Matsunaga T, Astourian M, Guerra G, Rico F, Dobler S, Agrawal AA, Whiteman NK (2019) Genome editing retraces the evolution of toxin resistance in the monarch butterfly. *Nature* 574(7778):409-412. doi: 10.1038/s41586-0191610-8 https://pubmed.ncbi.nlm.nih.gov/31578524/

Letelier J, de la Calle-Mustienes E, Pieretti J, Naranjo S, Maeso I, Nakamura T, Pascual-Anaya J, Shubin NH, Schneider I, Martinez-Morales JR, Gomez-Skarmeta JL (2018) A conserved Shh cis-regulatory module highlights a common developmental origin of unpaired and paired fins. *Nature Genetics* 50, 504-509. https://pubmed.ncbi.nlm.nih.gov/29556077/

*Shubin N, Tabin C, Carroll S (2009) Deep homology and the origins of evolutionary novelty. *Nature* 457, 818-823. https://pubmed.ncbi.nlm.nih.gov/19212399/

Natarajan et al. (2016) Predictable convergence in hemoglobin function has unpredictable molecular underpinnings. *Science* https://www.science.org/doi/full/10.1126/science.aaf9070

* Bridgham (2019) Predicting the basis of convergent evolution. *Science* https://www.science.org/doi/10.1126/science.aai7394

Okhovat, *et al*. (2015) Sexual fidelity tradeoffs promote regulatory variation in the prairie vole brain. *Science* https://www.science.org/doi/full/10.1126/science.aac5791

*Robinson (2015) Dissecting diversity in the social brain. *Science* https://www.science.org/doi/10.1126/science.aad8071

Spottiswoode CN, Begg KS, Begg CM (2016) Reciprocal signaling in honeyguide-human mutualism. *Science* 353(6297):387-9. doi: 10.1126/science.aaf4885 https://pubmed.ncbi.nlm.nih.gov/27463674/

Vail AL, Manica A, Bshary R (2014) Fish choose appropriately when and with whom to collaborate. *Current Biology* 24(17):R791-3. doi: 10.1016/j.cub.2014.07.033 https://pubmed.ncbi.nlm.nih.gov/25202866/