

Mechanisms of Gene Expression

2021 Coordinator:

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Course website: <https://zach-hensel.github.io/gem2021/>

Objectives

- To familiarize students with some mechanisms of regulating gene expression at the transcription and post-transcription levels including production and degradation processes;
- To offer study of selected topics at the cutting edge of advancing knowledge on gene expression;
- To teach critical analysis of original experimental data and the scientific literature;
- To familiarize students with peer review of gene expression literature;
- To introduce stochastic simulation and machine learning techniques that can be applied by non-expert scientists;
- To demonstrate how knowledge of gene expression mechanisms is being deployed in synthetic biology.

Lectures

T1 – Introduction: Foundations in genetics and evolution for molecular studies and recent developments in post-transcriptional regulation

T2 – The operon and transcriptional regulation: Transcription factors and other aspects of gene regulation in bacteriophage lysis/lysogeny

T3 – Bacterial gene expression mechanisms – size, activation, translation, degradation

T4 – Insights into gene expression from single-molecule studies

T5 – Synthetic biology: How do we get from simple gene circuits to engineering synthetic organisms?

T6 – Machine Learning: How are machine learning techniques changing studies of gene expression?

Homework: Machine learning tutorial “TensorFlow, Keras and deep learning, without a PhD”

SCAN Seminar – Francisco Nascimento

T7 – Topics in eukaryotic gene regulation: chromatin folding at different scales and predicting binding from sequence using machine learning

T8 – Stochastic simulations: an easy (really!) method that can be applied to almost any problem in biology

Homework: Perform a stochastic simulation of a simple gene circuit using Tellurium

T9 – Movies: *The Scientist: The Race for the Repressor* (ABC News; provided by CSHL Library), *Decoding Watson* (PBS)

TP1 – Introduction to preprint peer review, team introductions, paper selections.

TP2 – Group work focusing on highlight article

TP3, TP4 – Group work focusing on preparing preprint journal club and reviews

Evaluation: A passing grade requires (1) active participation in class discussions, (2) participation in the team project, (3) completing homework assignments, (4) attending all lectures.

Team Projects

Overview: Teams will review the recent preprint literature, briefly summarize two recent research articles *broadly* relevant to the topic “Gene Expression Mechanisms” and of interest to all team members, prepare a “highlights” article to distribute to the class, and present the article to the class in a journal club format.

Preprint Requirements

- Must NOT be published in a peer reviewed journal (bioRxiv lists if articles are already published)
- The articles should be, roughly, “letter” length: ~1500–2500 words, ~3–5 figures (not including supplements)

Assignment deadlines: send written assignments to zach.hensel@itqb.unl.pt (.pdf or .docx please). The timelines for work on this are short and I do not expect a polished product!

- 23:59 1 March: **Summaries of 2 articles.** Each 3 sentences (1) What is the main question being asked, (2) What is the main method used to answer it, (3) What is the answer + why is it important. Also include links to the articles. Example (for doi [10.1073/pnas.1811589116](https://doi.org/10.1073/pnas.1811589116) from Arraiano lab):

This paper asks the question: what RNAs interact with the mRNA encoding the transcription terminator protein Rho? The authors used pulldown and sequencing to identify interacting RNAs, and in vivo and in vitro methods to characterize the interaction. They found that the noncoding RNA SraL interacts with the 5' UTR of the rho mRNA to protect it from premature termination, which is important for tuning transcription termination in different growth conditions.

- 23:59 3 March: **Highlight article.** One page (12 pt font single spaced) including 1 figure. The figure can be a composite of figures from the text with or without your own illustrations.

Whenever you read a paper, ask yourself, “What questions are the authors trying to ask?” Ask yourself also, “What questions have they managed to answer?” which may not at all be the same as those they think they’re asking, those they say they’re asking, or those they are, in effect, asking. And ask yourself also, “What questions have they left unresolved” or “What questions get posed by the paper?” – Wally Gilbert

- 09:00 5 March: **Read.** Highlight articles will be distributed on Thursday morning. Read them all to have some familiarity with material to be presented on Friday.
- **Evaluation:** Fill out evaluation Google form during the talks.
- **Preprint review:** Post a positive/constructive comment on bioRxiv/medRxiv

Recommended Schedule

TP1 — Discuss with team members to identify team members’ areas of expertise. List tasks that need to be done and assign them to group members with deadlines. Search the preprint literature using tools provided in class to identify 2 articles. Skim the articles, write three-sentence summaries, and e-mail them to zach.hensel@itqb.unl.pt

TP2 — Read the assigned article closely and discuss it with the group. Agree on tasks/deadlines required for the highlight article and preprint review presentation and begin work.

TP3 — Complete highlight article. Also distribute tasks for journal club presentation. Every team member should play some role for both the highlight article and the journal club presentation.

TP4 — Focus on completing journal club presentation. Key points: What are the claims made by the abstract? Are they proven in the paper? What if any experiments/analysis are missing? What is the next experiment that you would do? See the rubric on the course website for more information.