Welcome to the 2024 UQ-Bio Summer School!

Outline of This Morning’s Presentation:

- Welcome from Dr. Ken Reardon (WSCOE Associate Dean for Research)
- The CSU Land Grant Acknowledgement
- Brief introduction to course Organizers and Learning Assistants
- Short discussion of UQ-Bio Summer School Goals.
- Quick review of where to find important crucial UQ-Bio Materials
- Preview of the UQ-Bio Summer School Schedule
- Overview of Course Requirements
- Preview of Key Concepts for the 2024 UQ BIO Summer School:
  - Central Dogma of Molecular Biology
  - Measuring Gene Regulation at Single-Cell Resolution
  - Predicting Gene Regulation at Single-Cell Resolution

Have Questions?
Ask on Slack
(Use Technical Questions Channel)
Colorado State University acknowledges, with respect, that the land we are on today is the traditional and ancestral homelands of the Arapaho, Cheyenne, and Ute Nations and peoples. This was also a site of trade, gathering, and healing for numerous other Native tribes. We recognize the Indigenous peoples as original stewards of this land and all the relatives within it. As these words of acknowledgment are spoken and heard, the ties Nations have to their traditional homelands are renewed and reaffirmed.

CSU is founded as a land-grant institution, and we accept that our mission must encompass access to education and inclusion. And, significantly, that our founding came at a dire cost to Native Nations and peoples whose land this University was built upon. This acknowledgment is the education and inclusion we must practice in recognizing our institutional history, responsibility, and commitment.

Brian Munsky and his Random Walk to UQ-Bio.

Grew up playing soccer and writing terrible poetry in Pittsburgh, Pennsylvania.

Started as an English major but later earned BS/MS in Aerospace Engineering studying *helicopter noise* at Penn State.

Now Associate Professor of Chemical Engineering (and trail runner / birdwatcher) at the Colorado State University.

Studied *gene expression noise* (and surfing) for a Ph.D. in Mechanical Engineering student at UC Santa Barbara.
UQ-Bio Summer School Goals

The Goals of the 2024 UQ-Bio Summer School are:

1. To advance the integration of experimental, mathematical and computational tools and principles needed to achieve rigorous, reproducible, and quantitatively predictive understanding for the mechanisms of biological processes.

2. To provide students with helpful resources and networking opportunities to advance their careers in quantitative biology, and to promote increased diversity, equity and inclusion among teams and networks that seek quantitative and mechanistic understanding of biological and biomedical phenomena.
UQ-Bio Website and Resources

Outline
- Website
- Slack
- Schedule
- Contact Email
- GitHub Page

Website: [https://q-bio.org/wp/](https://q-bio.org/wp/)
- This is where you will find general information about the programs and where we are heading over the next few weeks.

Slack: [Use the QR code (bottom left) to join.](#)
- This is where online questions and discussions will be conducted.

- This shows all the upcoming events. Look through your welcome email or scroll through the Slack ‘General’ Channel for links to recordings.

Contact Email: [qbio_summer_school@colostate.edu](mailto:qbio_summer_school@colostate.edu)
- This is how you get in touch if you are having trouble getting access to the Slack channel

GitHub Page: [https://github.com/MunskyGroup/uqbio2024](https://github.com/MunskyGroup/uqbio2024)
- This is where you will find example codes and links to lesson workbooks.

UQ-Bio - Required Online Accounts

Outline
- GitHub (https://github.com/MunskyGroup/uqbio2024)
- Anaconda Python and VS Code.

GitHub (https://github.com/MunskyGroup/uqbio2024)
- We will frequently need to use or share codes over GitHub.
- If you have not done so before, I strongly recommend getting familiar with using GitHub to share and keep track of changes in computational projects. Please see the uqbio2024 GitHub page for instructions on getting started.
- Sign up for the GitHub Student Developer Pack as soon as possible. When you are granted access, activate the GitHub Co-Pilot Extension.

Scan this QR Code to Reach the GitHub Page

Anaconda Python and VS Code.
- We will be using Python extensively in this course. We recommend Anaconda and VS Code for these tasks.
- Please see installation instructions on the uqbio2024 GitHub README.
UQ-Bio Summer School Schedule

The full schedule can be found at:

https://q-bio.org/wp/uq-bio-schedule-2024/

Schedule at a Glance (Broadcast Events)

• 09:00 - 10:00 — Lectures
• 10:15 - 12:15 — Python Tutorials
• 14:00 - 15:00 — Project Session Introductions or Updates
• 15:30 - 17:00:
  • Project Work Sessions June 4, 5, 7, 12, 14
  • Career Discussion Panels, June 6, 11, 13

Monday, June 10 — Lab tours and microscopy demo day.

UQ-Bio Course Completion Requirements

All students who complete the UQ-Bio summer school program will receive a certificate of completion.

Requirements for Online Students:

• Complete the six homework assignments in the course with an average score of 75% for the auto-graded components. You can submit as many times as you like, and there is no deadline.
• Email qbio_summer_school@colostate.edu with title “UQ-Bio 2024 – Request for Completion Certificate” and provide (1) the github account name through which you submitted your work, (2) your real name for the certificate, and (3) your home institution/company/organization.

Requirements for In Person Students:

• Attend all lectures, tutorials, and career discussions.
• Participate in all four stages of the course challenge.
• Electronic homework submissions are strongly encouraged, but optional.
Key Concepts

Central Dogma of Molecular Biology

Genes (0-2 copies) → Transcription (nucleus) → mRNA (0-100’s copies) → Translation (cytoplasm) → Protein (0-10^4’s copies)

Activation Signals (inter- and intra-cellular)

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Processing of Microscopy Images to Collect Quantitative Data

Using fluorescent proteins (left) or immunocytochemistry to measure the concentrations and location of key signaling molecules.

Signals → DNA → mRNA → Protein

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Munsky, et al, PNAS, 2018;
Jashnsaz, et al, iScience, 2020

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Processing of Microscopy Images to Collect Quantitative Data

Combining many small, co-localized labels to measure mRNA molecules at single-molecule resolution.

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Use fluorescence proteins (left) to quantify expression over time. Combine with mRNA tags and fragmented antibodies (right) to watch nascent translation in real time.

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Building Predictive Models to Predict Cellular Statistics

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Predicting Signaling Dynamics and Variations vs. time and Concentration

$\frac{k_{on}(Dex)}{k_{off}}$

DNA mRNA Protein

DNA mRNA Protein

Predicting Polymerase and Transcription Site Activation Statistics and Dynamics

RNAP2 cluster

Bursts (\(B_u\))

CTD + Serph

Escape (\(k_e\))

Residence CTD + Serph + mRNA

\(k_{burst}\)

\(k_{b} = \frac{\text{burst frequency}}{\text{burst size}}\)

\(k_{unsucc} = \frac{\text{unsuccesful}}{\text{total}}\)

\(k_{com} = \frac{\text{completion}}{\text{total}}\)

Intensity Distributions

Auto-Correlations CTD

Cross-Correlations Serph-CTD

Intensity vs. time

Log time [min]
Building Predictive Models to Predict Cellular Statistics

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Predicting mRNA Expression vs. Induction Concentration and Time,

Data -> Model

Number of Dusp1 mRNA per Cell

Predicting Nascent Translation Dynamics and Statistics

DNA mRNA Protein

Signals DNA mRNA Protein

UQ-Bio Materials Schedule Course Requirements Key Concepts

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Predicting Nascent Translation Dynamics and Statistics

DNA mRNA Protein

Signals DNA mRNA Protein

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Acknowledgment

Much of data presented contains analyses of HeLa cell lines that were established from tumor cells biopsied taken from Henrietta Lacks (1920-1951). Henrietta Lacks was a Black woman who lived her life in poverty and lack of opportunity driven by systemic racism, and the HeLa cell line was created without her knowledge, consent, or compensation. We want to express our gratitude and deep respect to Henrietta Lacks and her surviving family members for their tremendous contributions to scientific progress and advances in human health.

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