Welcome and Orientation

Date: June 1, 2021

Instructors: The 2021 UQBIO Summer School Team

e-mail: qbio_summer_school@colostate.edu
Welcome to the 2021 UQ-BIO Summer School

Outline:

- Welcome
- Meet the UQBIO Organizers:
  - Brian
  - Doug
- Overview of the 2021 UQBIO Program
- Meet the 2021 UQBIO Lecturing Team
- Overview of 2021 UQBIO Projects:
  - Optogenetic Yeast with Zachary Fox
  - Single-Cell Transcription with Huy Vo
  - Single-mRNA Translation with Luis Aguilera
- Questions

Outline:

- Welcome
- Zoom Etiquette
- CSU Land Acknowledgement
- Finding and accessing UQBIO Materials
- Goals of the 2021 UQBIO Summer School

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Hello and Zoom Etiquette

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Attendee controls:
- Please MUTE your microphone!
- Enter questions in chat or raise your hand in reactions
- Turn your video ON if you don’t mind

Rename yourself: Click participants, hover over your name, Click More, and choose Rename
Name, University, Pronouns
Example:
Penelope Smith, CSU, (she hers)
Desmond Fletcher, ETH (they their)

CSU Land Acknowledgement

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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.
- Where are you from?  Where are you now?  Where do you hope to go next?

- Click View Options near the top of your zoom screen.
- Then, select Annotate at the top
- You will see these annotation tools:

  ![Annotation Tools](image)

- Where are you from?  Where are you now?  Where do you hope to go next?

- Click View Options then Annotate.
- Use a Stamp for your answers and Draw lines to connect the dots.
## The 2021 UQBIO Website and Resources

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

### Schedule: [https://q-bio.org/wp/schedule/](https://q-bio.org/wp/schedule/)
This shows all the upcoming events and provides zoom links. (Look through your welcome email for passwords).

### 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 or if you have a colleague that wants to join for a lecture or two.

### GitHub Page: [https://github.com/MunskyGroup/uqbio2021](https://github.com/MunskyGroup/uqbio2021)
This is where you will find example codes and lesson workbooks.

### Slack: [https://join.slack.com/t/uq-bio2021/shared_invite/zt-qi1lqqrr-t2CaZld0Wr4dO~HhhsdCGg](https://join.slack.com/t/uq-bio2021/shared_invite/zt-qi1lqqrr-t2CaZld0Wr4dO~HhhsdCGg)
This is where most of our day-to-day communication is going to be conducted.

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## About QBIO

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The Quantitative Biology Summer School (qbioSS) is an annual event intended to help students acquire essential skills to advance predictive modeling of cellular regulatory systems. Participants will be exposed to a survey of work in quantitative biology and provided with in-depth instruction in selected techniques.

### History:
- **qbioSS started in 2007** at Los Alamos National Laboratory, Los Alamos NM and jointly organized with the annual q-bio Conference on Cellular Information Processing.
- **qbioSS moved** to St. Johns College (Santa Fe NM) in 2010-2013 and at the University of New Mexico (2014-2017).
- **University of California, San Diego** Branch run 2012-2017
- **Colorado State University, Fort Collins** Branch run 2015-2017
- **Rice University, Houston** Branch run 2018-2019

More than **500 students have participated from >150 different institutions worldwide**, and dozens of qbioSS alumni now hold faculty positions around the world.

The key feature that makes q-bio stand out among other scientific conferences is the emphasis placed on encouraging participation by junior scientists.

This is the **first annual Undergraduate Quantitative Biology Summer School**.
Meet the 2021 UQ-BIO Summer School Organizers

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Brian Munsky and his Random Walk to UQBIO.

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

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

Studied *gene expression noise* (and surfing) for a Ph.D. in Mechanical Engineering student at UC Santa Barbara.

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

Spent a lot of time hanging out with quantum physicists as a Richard P Feynman Fellow at Los Alamos National Lab.
Acknowledgments and Collaborators (2018-2020)

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Hog Signaling/Transcription Activation
- Gregor Neuhauser, Vanderbilt
- Guiliana Li, Vanderbilt
- Hossein Jahmsaz, Vanderbilt
- Jason Hughes, Vanderbilt
- Douglas Shepherd, CU Denver

Single-mRNA Translation
- Tim Stasevich, CSU
- Tatsuya Morisaki, CSU
- Kenneth Lyon, CSU
- Amanda Koch, CSU

Single-Cell Projects:

- Optogenetic Yeast with Zachary Fox
- Huy Vo
- Luis Aguilera

Postdocs:
- Luis Aguilera
- Linda Forero Quintero
- Huy Vo

Graduate Students:
- Lisa Weber
- Will Raymond
- Eric Ron
- Joshua Cook
- Brooke Silagy

Alumni:
- Torin Moore (BS 2020)
- Zach Haigh (BS 2020)
- Rachel Keating (BS 2021)
- Katie Davis (BS 2021)
- Stuart McKnight (BS 2021)

Zachary Fox (PhD 2019)
- Jaron Thompson (MS 2020)
- Mohammad Tahmasebi (MS 2020)
- Elisa Djokic (BS 2019)
- Charlotte Mitchell (BS 2018)
- Charis Ellis (BS 2019)

Cell Heterogeneity in Algal Biofuels:
- Sabrina Leslie, McGill University
- Shane Scott, McGill University

In vitro Single-BioMolecule Kinetics:
- Ana Sastri, CalTech

Thomas Catanach, Sandia

Soil Microbiome Machine Learning:
- John Dunbar, LANL
- Micheline Albright, LANL
- Nick Lubbers, LANL

Inflammation driven mRNA expression:
- James Werner, LANL
- Elizabeth Hong Geller, LANL
- Dan Kells, LANL

q-bio Training and Textbooks:
- William S. Hlavacek, LANL
- Lev S. Tsimring, UCSD
- Marek Kimmel, Rice University
- Douglas Shepherd, ASU

Munsky Group Objectives

Combining data-driven modeling and model-driven design of experiments to uncover new mechanisms of single-cell gene regulation.

Funding:
- DTRA
- WAKF
- NH/VGMS
- DOE/BER
- NSF CAREER
Listening to the Noise of Gene Regulation

The “Central Dogma of Molecular Biology”

Molecular signals → Gene activation → Transcription → mRNA → Translation → Protein

0-1 copies → 0-60 copies → 0-10^5 copies

Even for genetically identical cells in identical environments, these mechanisms produce stochastic, spatial, temporal fluctuations.

In the UQ-BIO Summer School, you are going to learn how we measure, model and predict, each stage of these fluctuations.

Neuert, Munsky, et al, Science 2013
Munsky, Li, Fox, Shepherd, Neuert, PNAS, 2018
Central Dogma

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Forero, Raymond, et al, Nature Communications, 2021

Central Dogma

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Lyon, Aguilera, et al, Molecular Cell, 2019
Aguilera et al, PLoS Computational Biology, 2019
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Doug Shepherd and his delayed walk to UQBIO.

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Doug Shepherd
- Grew up all over the USA, spending a lot of time in the mountains.
- Earned a BS in Physics at UC Santa Barbara
- Postdoc at Los Alamos National Lab. Started working in quantitative imaging and modeling of gene expression. Was able to travel to some more remote mountains.
- Spent some time away from academia in the mountains
- Earned a PhD in Physics from Colorado State University working on single-molecule spectroscopy. Escaped to the local mountains as much as possible
- Now an Assistant Professor of Physics at Arizona State University. Still spend a lot of time in the mountains.
Quantitative Imaging and Inference Lab (qi2lab)

Peter Brown
Katelyn Hernandez
Rory Krulhoff
Dominik Stich
CU Anschutz

Jessica Ullom
Steven Sheppard
Lei Zhou

What do we think goes into quantitative (bio)-imaging and inference?

10.1038/s41596-021-00502-8
Modeling the molecular labeling, photon emission, optical physics, image formation, and noise sources allows us to build full pipelines from sample preparation to data analysis.

One example: fast 3D spatial “–omics” in human lung tissue

Nuclei, HTII-280 protein, TMPRSS2 mRNA, ACE2 mRNA
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Module 0 (June 1-4) Basic Scientific Computing in Python.
  • learn to create variables and tensors to represent single-cell data;
  • modify images using algebraic & logical transformations;
  • visualize & share single-cell data

Module 1 (June 7-11) Single-Cell Image Processing.
  • learn about different fluorescent labeling approaches;
  • explore different fluorescence microscopy approaches;
  • use image processing and tracking software to quantify single-cell data.

  • learn important statistical tools to analyze single-cell data;
  • practice regression and supervised ML to relate cell properties;
  • use clustering and unsupervised ML to explore phenotype behaviors.
Overview of the 2021 UQBIO Program

Module 3 (June 21-25) Stochastic Simulations
- learn to simulate discrete chemical reactions and single-cell fluctuations;
- explore how non-linearity and noise combine to create surprising single-cell phenotype behaviors.

Module 4 (June 28 - July 2) Chemical Master Equation
- learn how to predict distributions of single-cell responses in fluctuating environments
- learn how to quantitatively compare stochastic models and single-cell data.

Module 5 (July 5-9) Integrating Single-Cell Data and Stochastic Models
- learn to apply Bayesian statistics to single-cell data;
- write MCMC codes to quantify uncertainties;
- see how Fisher Information can be used to design better single-cell experiments.

Weekly schedules and events

Weekly schedules are posted at: https://q-bio.org/wp/schedule/

All Participants are welcome to attend:
- 11 Invited Talks (one in week 0 and two in weeks 1-5)
- 12 Tutorials using Python in Google Colab
- 5 Career Discussion Sessions (Tuesdays at 9:30 PACIFIC starting next June 8)

Full Participants only can also attend:
- 6 Python Help and Hacking Sessions
- 6 Student Introduction or Project Presentation Sessions
- Weekly mentored project sessions with Learning Assistants (Teams will form on Thursday morning, June 4)
- FIRST HOMEWORK – Prepare a 2-minute presentation to introduce yourself on Friday June 4:
  - Who are you and what are your hobbies/interests?
  - Where are you from? Where are you going next?
  - What are you studying?
  - What are you hoping to learn at UQ-BIO?
  - What is your favorite algorithm or coding language and why?
Meet the 2021 UQ-BIO Lecturing Team

Lecturers:
- **Prof. Brian Munsky**, Chemical and Biological Engineering, Colorado State University, Fort Collins, CO
- **Prof. Doug Shepherd**, Physics, Arizona State University, Tempe, AZ
- Dr. Luis Aguilera, Chemical and Biological Engineering, Colorado State University, Fort Collins, CO
- Dr. Linda Forero-Quintero, Chemical and Biological Engineering, Colorado State University, Fort Collins, CO
- Dr. Zachary Fox, Center for Non-Linear Studies, Los Alamos National Laboratory, Los Alamos, NM
- **Prof. Carlos Lopez**, Vanderbilt University, Nashville, TN
- Michael May, Ph.D. Student, Biomedical Engineering, Colorado State University
- William Raymond, Ph.D. Student, Biomedical Engineering, Colorado State University
- Dr. Huy Vo, Chemical and Biological Engineering, Colorado State University, Fort Collins, CO
- Lisa Weber, Ph.D. Student, Chemical and Biological Engineering, Colorado State University

Invited Speakers:
- **Prof. Mary Dunlop**, Biomedical Engineering, Boston University, Boston, MA
- **Prof. Khuloud Jaqaman**, Biophysics and Bioinformatics, University of Texas Southwestern Medical Center, Dallas, TX
- **Prof. Steve Presse**, Physics and School of Molecular Sciences, Arizona State University, Tempe, AZ
- **Prof. Zaida (Zan) Luthey-Schulten**, Chemistry, University of Illinois Urbana-Champaign
- **Prof. Gregor Neuert**, Molecular Physiology and Biophysics, Vanderbilt University, Nashville, TN
- **Prof. Linda Petzold**, Computer Science, University of California Santa Barbara, Santa Barbara, CA
- **Prof. Steve Presse**, Physics and School of Molecular Sciences, Arizona State University, Tempe, AZ
- **Prof Jesse Wilson**, Electrical and Computer Engineering, Colorado State University, Fort Collins, CO
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Project Managers:
- Dr. Luis Aguilera, Chemical and Biological Engineering, Colorado State University
- Dr. Zachary Fox, Center for Non-Linear Studies, Los Alamos National Laboratory
- Dr. Huy Vo, Chemical and Biological Engineering, Colorado State University

Learning Assistants:
- Dr. Bryce Assay, Utah Public Health Laboratory
- Joshua Cook, M.S. Student, Biomedical Engineering, Colorado State University
- Kaan Öcal, Ph.D. Student, Edinburgh University
- Jafar Anafi, M.S. Student, Numerical Analysis, University of Germany
- Dr. Heidi Klumpe, Chemical Engineering, Caltech
- Dr. Nava Leibovich, Physics, University of Toronto
- Dr. Keisha Cook, Mathematics, Tulane University
- Eric Ron, M.S. Student, Biomedical Engineering, Colorado State University
- Brooke Silagy, M.E. Student, Chemical Engineering, Colorado State University

Career Discussion Topics and Panelists

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Career Discussions
Tuesdays at 9:30 am (PACIFIC)

June 8: Applying for and choosing the right graduate program

June 15: Working in an interdisciplinary research environment

June 22: There is more to life and science than academics

June 29: Navigating the treacherous waters of graduate school

July 6: Justice, Equity, Diversity and Inclusion in STEM

Panelists:
- Ilya Nemenman, Emory University
- Balgopal, Meena, Colorado State University
- Douglas Shepherd, Arizona State University
- Steve Presse, Arizona State University
- Stuart Tobet, Colorado State University
- Tim Stasevich, Colorado State University
- Melissa Burt, Colorado State University
- Colleen Webb, Colorado State University
- Amanda Koch, Colorado State University
- Mary Dunlop, Boston University
- Linda Petzold, University of California Santa Barbara
- Carol Wilusz, Colorado State University
- Khuloud Jaqaman, UT Southwestern Medical Center
- Erin Nishimura, Colorado State University
Overview of the 2021 UQ-BIO Course Projects

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Optogenetic Yeast with Zachary Fox

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- Questions
Project 1: Single Cell Yeast Response Dynamics

Instructor: Zach Fox

e-mail: zachfox@lanl.gov

About me

From: Harrisburg, Pennsylvania

Undergraduate research with Abhyudai Singh in stochastic sys bio

PhD with Brian Munsky, "Integrating Discrete Stochastic Models with Single Cell Data"

Post-doc I with Gregory Batt and Jakob Ruess at Institut Pasteur

Post-doc II CNLS/Info Sciences, Yen Ting Lin and Anatoly Zlotnik Los Alamos National Laboratory
Meet the Learning Assistant Team for Project 1!

Dr. Heidi Klumpe
Caltech
Learning Assistant Team 1A

Dr. Bryce Asay
Utah Department of Health/Viden Technologies
Learning Assistant Team 1A

Jafar Anafi
Usman Danfodio University
Learning Assistant Team 1B

PhD St. Kaan Öcal
Universiy of Edinburgh
Learning Assistant Team 1B

What is optogenetic gene expression?

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Why do I think this is cool?

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Hybrid bio-digital systems

Control transcription dynamics

Study feedback mechanisms
Using digital micromirrors to target individual cells

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EL222 is the system we will be working with

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Fox, Fletcher et al. bioRxiv, 2021
Week by week plan for the project

- **Week 0:**
  - Get comfortable with Python

- **Week 1:**
  - Use single-cell segmentation and tracking to extract individual cells and their statistic from fluorescence time-lapse microscopy images.

- **Week 2:**
  - Use multivariate clustering analyses to discover the optogenetic input cells received.
  - Learn population growth rates from segmented images.

- **Week 3:**
  - Simulate a model of optogenetic gene expression using the stochastic simulation algorithm.

- **Week 4:**
  - Simulate the FSP version of the optogenetic stimulation model.
  - Qualitatively compare to simulations and data

- **Week 5:**
  - Quantitatively compare FSP models to single-cell simulations and data.
  - Design optogenetic inputs to learn about model parameters

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Single-Cell Transcription Analysis with Huy Vo

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Project 2: Extracting data and building models from single-cell transcription imaging data

Instructor: Huy Vo

e-mail: huy.vo@colostate.edu

About me

PhD in Math at University of Alabama

with Prof. Roger Sidje, Numerical solution of the chemical master equation

Undergrad Math Major in Vietnam

Postdoc at Colorado State University with Prof. Brian Munsky, Model identification from fluorescent microscopy data, experiment design, machine learning
Meet the Learning Assistant Team for Project 2!

Dr. Huy Vo
Colorado State University
Learning Assistant Team 2A

Dr. Linda Forero
Colorado State University
Learning Assistant Team 2B

PhD St. Michael May
Colorado State University
Learning Assistant Team 2A

PhD St. Lisa Weber,
Colorado State University
Learning Assistant Team 2B

Visualizing transcription at the single-cell level

What do these histograms tell us about the genes’ transcriptional activities?
What can give rise to those histograms?

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How certain am I about my fit?

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Why is this cool?

Cool data and experiments:
- Help you appreciate heterogeneity at one of the most fundamental cellular processes.
- Single-cell, single-molecule resolution for tens of thousands of cells.
- Visualize and quantify transcriptional response under different conditions (nutrition, drugs, light stimulation).

Help you get started on mastering highly transferrable skills:
- Computer vision.
- Statistics.
- Monte Carlo simulation, numerical analysis.
- Bayesian inference, MCMC, model selection.
- And obviously, Python.

Week by week plan for the project

- **Week 0:**
  - Get comfortable with Python.
- **Week 1:**
  - Understand the structure of a typical smFISH imaging dataset (example from Doug Shepherd’s experiments).
  - Pip install image processing tools to your colab environment (specific toolbox to be detailed).
  - Identify RNA spots and output mRNA counts per cell using Python.
- **Week 2:**
  - From mRNA counts per cell data, plot mRNA histograms.
  - Compute summary statistics from the data.
- **Week 3:**
  - Use Gillespie algorithm to simulate single-cell trajectories predicted by each model.
- **Week 4:**
  - Use FSP to compute the time-varying distributions predicted by each model at different parameter sets.
  - Use FSP-computed likelihoods to estimate best parameters for each model.
- **Week 5:**
  - Use Bayesian Information Criteria to decide the best model.
  - Use MCMC to quantify uncertainty in parameters and predictions.
Outline:
• Welcome
• Meet the UQBIO Organizers
• Overview of the 2021 UQBIO Program
• Meet the 2021 UQBIO Lecturing Team
• Overview of 2021 UQBIO Course Projects
  • Optogenetic Yeast with Zachary Fox
  • Single-Cell Transcription with Huy Vo
  • Single-mRNA Translation with Luis Aguilera
• Questions

Project 3: Single mRNA translation dynamics
Project Leader: Luis Aguilera
e-mail: luis.aguilera@colostate.edu
About me

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**Education**

<table>
<thead>
<tr>
<th>BSc Genomics and Bioinformatics</th>
<th>PhD Biomedical Eng. and Physics</th>
<th>Postdoc at CSU, USA</th>
</tr>
</thead>
<tbody>
<tr>
<td>UANL- Mexico</td>
<td>Nat. Polytechnic Institute, Mexico</td>
<td>Stochastic modeling and Image processing.</td>
</tr>
<tr>
<td>Universität Heidelberg, Germany</td>
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</tbody>
</table>

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The Single-mRNA Translation Project team

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Meet the Learning Assistant Team for Project 3!

- **Dr. Nava Leibovich**
  University of Toronto
  Learning Assistant Team 3A

- **Dr. Luis Aguilera**
  Colorado State University
  Project Leader

- **Dr. Keisha Cook**
  Tulane University
  Learning Assistant Team 3A

- **MS St. Brooke Silagy**
  Colorado State University
  Learning Assistant Team 3B

- **MS St. Joshua Cook**
  Colorado State University
  Learning Assistant Team 3A

- **PhD St. William Raymond**
  Colorado State University
  Learning Assistant Team 3B
Introduction to single-mRNA translation

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• Super-resolution fluorescence microscopy and modern molecular biology techniques allows to quantify single-molecule events.

Extracting information

• Large microscope data sets
• Mathematical modeling

Single-molecule translation


Aims of Project 3

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To learn and practice...

Bioinformatics

Image Processing

Stochastic Modeling

Quantifying biophysical parameters

Machine Learning
Aims of Project 3

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To learn and practice

Using synthetic data to easily train and test our codes

The simulation provides exact information for the spots’ intensity and location

20 translation spots

100 translation spots
Week by week plan for the project

- **Week 0:**
  - Contact the project team.
  - Get comfortable with Python
- **Week 1:**
  - Learn and practice image processing techniques.
- **Week 2:**
  - Learn and practice bioinformatics using biophyton.
- **Week 3:**
  - Learn and practice stochastic modeling using rSNAPsim.
- **Week 4:**
- **Week 5:**
  - Learn and practice parameter optimization and inference techniques.

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The Single-mRNA Translation Project team

Please feel free to reach out to us for any assistance

- Dr. Nava Leibovich
  - University of Toronto
  - Learning Assistant Team 3A

- MS St. Joshua Cook
  - Colorado State University
  - Learning Assistant Team 3A

- Dr. Keisha Cook
  - Tulane University
  - Learning Assistant Team 3A

- Dr. Luis Aguilera
  - Colorado State University
  - Project Leader

- MS St. Brooke Silagy
  - Colorado State University
  - Learning Assistant Team 3B

- PhD St. William Raymond,
  - Colorado State University
  - Learning Assistant Team 3B
Tips for getting the most out of UQ-BIO.

• Try the example questions and write your own codes in the Project notebooks.
  • The best (only?) way to learn is by doing the work. We’ll get you started, and we’re here to provide some hints, but you are in driver’s seat for this journey.

• Work in teams – start new collaborations.
  • Help one another and learn by teaching others!
  • Even if you are a partial participant, reach out to others on Slack to form your own teams and help each other to troubleshoot.

• Take Risks and ASK QUESTIONS.
  • It is extremely normal to feel overwhelmed or out of place when engaging in multidisciplinary science.
  • This year’s UQBIO participants have a very broad range of experience and skillsets, and the course will cover a lot of material from a lot of different fields and at many different levels of sophistication.
  • Every problem has multiple solutions, and after many decades in this field, none of us knows all the answers.

Questions?

If you have a question, raise your hand in zoom, or type it in chat.

Research is not about knowing the answers;… it is about finding the answers.

Even better – research is about asking the right questions, …. and that takes a ton of practice!

What time is better than now to practice?