Griffin Chure | Curriculum Vitae

Current as of May 11, 2020
Division of Biology and Biological Engineering
California Institute of Technology
1200 E. California Blvd. MC11496
Pasadena, CA 91125
website: gchure.github.io
email: gchure@caltech.edu
GitHub: gchure
ORCID: 0000-0002-2216-2057
Tel: +1-801-703-1316

Education

ASc. General Studies, Utah State University, *2009*
BSc. Biology – Cell & Molecular Emphasis (Honors), University of Utah, *2013*
BSc. Chemistry – Biological Emphasis & Minor Physics, University of Utah, *2013*
PhD. Biochemistry & Molecular Biophysics – California Institute of Technology, *expected May 2020*
Thesis topic: The Molecular Biophysics of Physiological and Evolutionary Adaptation
Thesis adviser: Professor Rob Phillips

Professional Employment

September 2013 – Present: Graduate Student, Division of Biology and Biological Engineering, California Institute of Technology, Pasadena, CA, USA. *Supervisor:* Prof. Rob Phillips.
January 2010 – May 2013: Research assistant, Department of Biology, University of Utah, Salt Lake City, UT, USA. *Supervisor:* Prof. David F. Blair.

Academic Honors and Fellowships

California Institute of Technology (2013 – Present):

- NIH Molecular Biology Training Grant (2014 – 2016)
- Amgen Research Fellowship (2015)
- NSF GRFP Honorable Mention (2015)

University of Utah (2009 – 2013):

- Honors at Entrance Scholarship (2009 – 2013)
- Robert C. Byrd Scholarship (2009 – 2011)
- New Century Scholarship (2009 – 2013)

Research Accomplishments

A predictive theory of allosteric induction
Research performed with Manuel Razo-Mejia, Nathan M. Belliveau, Stephanie L. Barnes, Tal Einav, Mitchell Lewis, and Rob Phillips. Manuscript published as Razo-Mejia et al. in Cell Systems (6), 2018.

Allosteric regulation is found across all domains of life, yet we still lack simple, predictive theories that directly link the experimentally tunable parameters of a system to its input-output response. To that end, I, along with several collaborators, developed a statistical mechanical model of allostery in the context of transcriptional regulation using the Monod-Wyman-Changeux model. We rigorously tested predictions resulting from this model experimentally using a ubiquitous regulatory architecture found in bacteria, the simple repression motif. The model quantitatively captures the diverse phenomenology of the induction profiles, allowing us to collapse all data onto a single master curve. This theory is presented in general terms, allowing it to be applied to a wide range of regulatory architectures.

Mapping mechanosensitive channel abundance to single-cell survival after hypo-osmotic shock

Research performed with Heun Jin Lee and Rob Phillips. Manuscript published as Chure et al. in Journal of Bacteriology 200(23), 2018.

Rapid changes in extracellular osmolarity is a potentially fatal insult that microbes face on a daily basis. One mechanism to counter the massive flux of water across the cell membrane from a hypo-osmotic shock is through the opening of tension-sensing channels known as mechanosensitive channels. MscL is the most abundant mechanosensitive channel in *E. coli* and the most heavily studied, though its contribution to cell survival rates remains enigmatic. In this work, we use single-cell quantitative microscopy to count the number of MscL channels per cell and directly map the copy number to a cell's probability of survival under hypo-osmotic shock. Our results suggest that on the order of ~ 500 channels are needed for full protection from a strong osmotic shock, contradicting the current prediction from theory alone and suggesting that our current understanding of this mechanism is incomplete.

Using changes in free energy to classify mutational effects in allosteric regulation

Research performed with Manuel Razo-Mejia, Nathan M. Belliveau, Zofii A. Kaczmarek, Stephanie L. Barnes, Tal Einav, Mitch Lewis, and Rob Phillips. Manuscript published as Chure et al. in PNAS 116(35) 2019.

Mutation is a critical mechanism by which evolution explores the functional landscape of proteins. Despite our ability to experimentally inflict mutations at will, it remains difficult to link sequence-level perturbations to systems-level responses. This work presents a framework to link individual mutations in a transcriptional repressor to the parameters which govern the transcriptional response through measuring changes in the free energy of the system. We found that the energetic effects of the mutations can be categorized into several classes which have stereotypical curves as a function of the inducer concentration. These diagnostic predictions are tested using the experimentally well-characterized LacI repressor of *E. coli*, in which we probe several mutations in the DNA binding and inducer binding domains. We show that the induction profiles and resulting free energies associated with double mutants can be predicted with quantitative accuracy given knowledge of the single mutants, providing an avenue for identifying and quantifying epistatic interactions.

Single-molecule exploration of sequence dependence in V(D)J recombination

Research performed with Soichi Hirokawa, Nathan M. Belliveau, Geoffrey A. Lovely, Michael Anaya, David G. Schatz, David Baltimore, and Rob Phillips. Preprint on bioRxiv.

The antibody repertoire of jawed vertebrates is staggering with the number of possible unique epitopes dwarfing the number of antibody-encoding genes by eight orders of magnitude. Through a process known as V(D)J recombination, disparate gene segments are brought together to create a functional antibody-encoding gene through a genomic cut-and-paste process. This process is initiated by binding of an intricate protein complex to specific DNA sequences, known as Recombination Signal Sequences (RSSs), which dictate the efficiency with which the neighboring antibody encoding fragment is used. In this work, we explored the sequence landscape of a particular RSS using a single-molecule technique known as Tethered Particle Motion. We found that certain positions of the RSS are more important than others, sometimes in different steps of recombination. Some mutations completely abrogate all steps of the cut-and-paste process while others inhibit (or enhance) a single step while the others are unperturbed. This work opens the door towards understanding why different antibodies are used with different frequencies and presents a critical step forward towards engineering specific RSS sequences.

Understanding physiological adaptation through thermodynamic modeling

Research performed with Zofii Kaczmarek and Rob Phillips. Preprint on bioRxiv.

Much of our theoretical work on transcriptional regulation has been tested in bacteria growing in a minimal medium supplemented with glucose and held at 37° C while shaking at 225 RPM. However, none of these specific growth conditions are captured in our models nor are they similar to those found in nature. As the forces of evolution have sculpted regulatory architectures to retain their function in a variety of environments, it is reasonable to question how well these models perform when the cells are in a drastically different physiological state. To answer this question, we have quantitatively measured the level of gene expression in a variety of environmental conditions (such as varying temperature and carbon-source quality) from a single promoter in which the regulatory components are tightly controlled and the copy numbers are directly measured. We have found that, despite significant changes in cellular physiology, the biophysical parameters determined from one condition accurately predict the gene expression from another, suggesting that the values of the biophysical parameters are robust, further demonstrating their utility as a quantitative trait in understanding evolutionary dynamics.

Future Research Interests

The physical biology of populations and spatiotemporal eco-evolutionary dynamics

Much as the molecular revolution changed the face of cell biology and experimental biophysics, developments in microfluidics, high-throughput massively-parallel sequencing, and quantitative imaging hold the potential to revolutionize our understanding of evolution. Traditionally viewed as an observational science, evolutionary biology is rapidly becoming experimental where the evolutionary potential of populations can be predicted and tested with quantitative precision. I am interested in exploring the eco-evolutionary dynamics of spatially, temporally, or ecologically structured populations and how competition and cooperation at the level of individual cells sculpts the behavior of ensembles consisting of 10^9 or more individuals and leads to the remarkable collective behavior of populations. I hope to use my knowledge of physical

biology and statistical mechanics, Bayesian statistical inference, and quantitative experimental methods to dissect predictions of microbial evolution both theoretically and experimentally.

Publications

† *indicates equal contribution*

8. Manuel Razo-Mejia, Sarah S. Marzen, **Griffin Chure**, Muir Morrison, Rachel Taubman, and Rob Phillips (2020). "First-principles prediction of the information processing capacity of a simple genetic circuit." *Preprint on arXiv*. arXiv:2005.03214. Paper website and GitHub repository

7. Kathrin S. Laxhuber, Muir J. Morrison, **Griffin Chure**, Nathan M. Belliveau, Charlotte Strandkvist, Kyle L. Naughton, and Rob Phillips (2020). "Theoretical investigation of a genetic switch for metabolic adaptation." *PLoS ONE*. 15(5). doi: 10.1371/journal.pone.0226453.g001

6. **Griffin Chure**, Zofii A. Kaczmarek, and Rob Phillips (2019). "Physiological Adaptability and Parametric Versatility in a Simple Genetic Circuit." *Preprint on bioRxiv*. doi: 10.1101/2019.12.19.878462. Paper website and GitHub repository

5. Soichi Hirokawa, **Griffin Chure**, Nathan M. Belliveau, Geoffrey A. Lovely, Michael Anaya, David G. Schatz, David Baltimore, and Rob Phillips (2019). "Sequence-Dependent Dynamics of Synthetic and Endogenous RSSs in V(D)J Recombination." *Preprint on bioRxiv*. doi: 10.1101/791954. Paper website and GitHub repository

4. **Griffin Chure**, Manuel Razo-Mejia, Nathan M. Belliveau, Tal Einav, Zofii Kaczmarek, Stephanie L. Barnes, Mitchell Lewis, and Rob Phillips (2019). "Predictive shifts in free energy couple mutations to their phenotypic consequences." *PNAS*. 116(35). doi: 10.1073/pnas.1907869116. Paper website and GitHub repository

3. Rob Phillips, Nathan M. Belliveau, **Griffin Chure**, Manuel Razo-Mejia, Clarissa Scholes, and Hernan G. Garcia (2019). "Figure 1 Theory Meets Figure 2 Experiments in the Study of Gene Expression." *Annual Reviews of Biophysics*, Volume 48. doi:10.1146/annurev-biophys-052118-115525

2. **Griffin Chure**†, Heun Jin Lee†, Akiko Rasmussen, and Rob Phillips (2018). "Connecting the dots between osmotic shock, mechanosensitive channel abundance, and survival at single-cell resolution." *Journal of Bacteriology*. 200(23). doi: 10.1128/JB.00460-18. Paper website and GitHub repository

    - Selected as "an article of significant interest" for the December 2018 issue.

1. Manuel Razo-Mejia†, Stephanie L. Barnes†, Nathan M. Belliveau†, **Griffin Chure**†, Tal Einav†, Mitchell Lewis, Rob Phillips (2018) "Tuning transcriptional regulation through signaling: A predictive theory of allosteric induction." *Cell Systems* (6). doi:10.1101/111013. Paper website and GitHub repository

    - Featured in "Splitting the World with Absolute Measurements: A Call for Collaborations in Physical Biology." by Quincey Justman. *Cell Systems* (6), 2018.

Conference Presentations

4. "The Molecular Biophysics of Adaptation". Poster Presentation at the Biophysical Society Annual Meeting (San Diego, CA), 2020.

3. "The Energetics of Molecular Adaptation". Oral Presentation at the summer course "From Molecular Basis to Predictability and Control of Evolution" at NORDITA (Stockholm, Sweden), 2019.

2. "Mutations, Epistasis, and Allostery from a thermodynamic perspective: A predictive theory for transcriptional regulatory networks." Poster presentation at American Society of Cell Biology (San Diego, CA, USA) 2018.

1. "A Predictive Theory of Allosteric Regulation in Transcription." Poster presentation at the American Physical Society March Meeting (Los Angeles, CA, USA), 2018.

Wet-Lab Skills

- Molecular biology including PCR, multi-fragment Gibson assembly, chromosomal integration, and other skills of genetic engineering.
- High throughput flow cytometry and plate reader operation.
- Practical optics including the ground-up construction of optical tweezers, Total Internal Reflection Fluorescence (TIRF), and line-scan confocal microscopes.
- Extensive experience with time-lapse epifluorescence microscopy of microbial samples.
- Protocol optimization and efficient time management.

Dry-Lab Skills

- Knowledge of equilibrium statistical mechanics, kinetics, probability theory, and their various applications to biological questions.
- Proficient in Bayesian and frequentist statistical inference including high-dimensional hierarchical modeling with Markov chain Monte Carlo.
- Fluent computer programming in Python, Stan, JavaScript, Matlab, and Shell. Intermediate knowledge of R and Julia. Fluent in web-development languages such as Liquid, Sass, and HTML/CSS. Fluent in using LaTeX and MarkDown for typesetting.
- Skilled in data presentation/visualization. Can quickly build interactive dashboards for rapid exploration and presentation of high-dimensional data using Python/JavaScript. Examples of interactive widgets can be found on my personal website: `gchure.github.io/art/showcase`
- Experienced in computer-aided illustration. Fluent in using Adobe Illustrator to generate publication and textbook quality scientific illustrations. Examples of some of my illustrations can be found on my personal website: `gchure.github.io/art/showcase`

Teaching

California Institute of Technology

- The Great Human Experiment by the Numbers (with Rob Phillips) – *2020*
- Evolution (with Rob Phillips and Victoria Orphan) – *2020*
- Physical Biology of the Cell (with Justin Bois) – *2018*
- Physical Biology Bootcamp (with Rob Phillips) – Optics TA – *2017, 2018, 2019*
- Bi1: Principles of Biology (with Rob Phillips) – *2017*
- Data Analysis in the Biological Sciences (with Justin Bois) – *2015, 2016*
- Programming for the Biological Sciences (with Justin Bois) – *2016*
- Bi1x: The Great Ideas of Biology (with Justin Bois) – *2014, 2015*

Extramural

- IBDM (Marseille, FR) Cell Biology by the Numbers – Programming TA – *2018*
- MBL (Woods Hole, MA, USA) Physical Biology of the Cell – Optics TA – *2018*
- MBL (Woods Hole, MA, USA) Physiology Course – MATLAB Instructor (with James Boedicker)– *2017*
- MBL (Woods Hole, MA, USA) Physiology Course – Research TA – *2015, 2016, 2017, 2018*
- GIST (Gwangju, PRK) Physical Biology of the Cell – Programming TA – *2016, 2017*
- KITP (Santa Barbara, CA, USA) Evolutionary Cell Biology – Research and Programming TA – *2015*
- CSHL (Cold Spring Harbor, NY, USA) Physical Biology of the Cell – Programming TA – *2015*

University of Utah

- Advanced Biochemistry Lab (with David Goldenberg) – *2013*
- Principles of Genetics (with J.S. Parkinson) – *Sp. 2012, Fa. 2012*
- Biosciences Research Bootcamp (with Rosemary Gray) – *2010*
- Introduction to Biology (with Tanya Vickers) – *2010*

Service & Leadership

- Biochemistry & Molecular Biophysics Graduate Student Council – Co-chair – *2015-2018*
- Caltech RISE High School Mentoring Program – Biology & Physics Tutor – *2015-2016*
- Caltech SURF – Research Mentor – *2015*
- Caltech SURF – Presentation Judge – *2014*