Griffin Chure | Curriculum Vitae

Current as of August 27, 2019

Division of Biology and Biological Engineering
California Institute of Technology
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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 2020*

- *Thesis topic:* The Molecular Biophysics of Physiological and Evolutionary Adaptation
- *Thesis adviser:* Professor Rob Phillips

Professional Employment

January 2010 - May 2013: Research assistant, Department of Biology, University of Utah. Biochemical assembly and architectural consequences of the bacterial flagellar motor. *Supervisor:* Prof. David F. Blair

May 2014 - Present: Graduate Student, Department of Chemistry & Chemical Engineering, California Institute of Technology. Faculty of both Physiology and Physical Biology of the Cell Summer Courses at the Marine Biological Laboratory, where we teach students the principles of computer programming and practical optics. *Supervisor:* Prof. Rob Phillips.

Academic Honors and Fellowships

University of Utah (2009 - 2013):

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

California Institute of Technology (2013 - Present):

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

Research Accomplishments

A predictive theory of allosteric induction

In this work, we present 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. *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.

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

Rapid changes in extracellular osmolarity is a potentially fatal insult that microbes face on a daily basis. One mechanism to counter the flux of water across the cell membrane from a 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 it's 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. *Research performed with Heun Jin Lee and Rob Phillips. Manuscript published as Chure et al. in Journal of Bacteriology 200(23), 2018.*

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

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. In this work, we present a framework to link individual mutations in a transcriptional repressor to the parameters which govern its response through measuring changes in the free energy of the system. Our findings are 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 experimentally well-characterized LacI repressor of *Escherichia coli*, probing 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. *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 2019.*

Current Research

Physiological perturbations and thermodynamic models in Biology

Much of our theoretical work on transcriptional regulation has been tested in bacteria growing in a minimal medium supplemented with glucose held at 37℃ while shaking at 225 RPM. However, none of these specific growth conditions are captured in our models. I am currently trying to perturb some of these "standard" growth conditions in a predictive manner such that changing to different carbon sources or temperatures does not require complete redetermination of the biophysical parameters. *Research performed with Zofii Kaczmarek and Rob Phillips.*

Quantitative dissection of a simple activation genetic circuit

Though the simple repression motif is the most common regulatory architecture found in bacteria, the maximum level of gene expression is limited by the strength of the promoter. However, regulation through transcriptional activation are effectively unbounded and can effectively boost expression by several orders of magnitude. This jump in gene expression is dependent on the interaction energy strength between the transcriptional activator and the the RNA polymerase directly. I am currently developing theoretical models of this unique transcriptional architecture and designing genetic circuits to experimentally test these predictions.

Research performed with Charlotte Strandkvist, Muir Morrison, and Rob Phillips.

Future Research Interests

The physical biology of populations and spatio-temporal evolutionary dynamics

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

Publications

† *indicates equal contribution*

1. **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*. doi: 10.1073/pnas.1907869116
2. 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
3. **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
    - Selected as "an article of significant interest" for the December 2018 issue.
4. 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.
    - Featured in "Splitting the World with Absolute Measurements: A Call for Collaborations in Physical Biology" by Quincey Justman. *Cell Systems* (6), 2018.

Conference Presentations and Posters

1. "The Energetics of Molecular Adaptation". Oral Presentation at the summer course "From Molecular Basis to Predictability and Control of Evolution" at NORDITA, 2019.
2. "Mutations, Epistasis, and Allostery from a thermodynamic perspective: A predictive theory for transcriptional regulatory networks." American Society of Cell Biology 2018. *Poster Presentation*
3. "A Predictive Theory of Allosteric Regulation in Transcription." American Physical Society 2018 March Meeting. *Poster Presentation*

Teaching

California Institute of Technology

- Evolution (with Rob Phillips and Victoria Orphan) - TA - *2020*
- Physical Biology of the Cell (with Justin Bois) - TA - *2018*
- Physical Biology Bootcamp (with Rob Phillips) - Optics TA - *2017, 2018, 2019*

- Bi1: Principles of Biology (with Rob Phillips) - Head TA - *2017*
- Data Analysis in the Biological Sciences (with Justin Bois) - TA - *2016, 2017*
- Programming for the Biological Sciences (with Justin Bois) - TA - *2016*
- Bi1x: The Great Ideas of Biology (with Justin Bois) - TA - *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) - TA - *2013*
- Principles of Genetics (with J.S. Parkinson) - TA - *Sp. 2012, Fa. 2012*
- Biosciences Research Bootcamp (with Rosemary Gray) - TA - *2010*
- Introduction to Biology (with Tanya Vickers) - TA - *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*

Technical Skills

- Wet-lab molecular biology including PCR, multi-fragment Gibson assembly, chromosomal integration, and other skills of genetic engineering.
- High-through put flow cytometry and single-cell time-lapse microscopy.
- Bayesian and frequentist statistical inference including high-dimensional hierarchical modeling with Markov chain Monte Carlo
- Computer programming. Fluent in Python, Stan, Matlab, and shell scripting. Intermediate knowledge of R and Javascript. Fluent in web-development languages such as Liquid, HTML/CSS.