Griffin Chure, PhD | Curriculum Vitae

Current as of December 31, 2020

Postdoctoral Scholar
Department of Applied Physics
California Institute of Technology
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Education

PhD. Biochemistry & Molecular Biophysics – California Institute of Technology, *2020*
Thesis topic: The Molecular Biophysics of Physiological and Evolutionary Adaptation
Thesis adviser: Professor Rob Phillips

BSc. Chemistry – Biological Emphasis & Minor Physics, University of Utah, *2013*

BSc. Biology – Cell & Molecular Emphasis (Honors), University of Utah, *2013*

ASc. General Studies, Utah State University, *2009*

Professional Employment

January 2021 – Present: NSF Postdoctoral Research Fellow – Department of Biology, Stanford University, Stanford, CA, USA.
Supervisor: Asst. Prof. Jonas Cremer.

July 2020 – December 2020: Postdoctoral Scholar – Department of Applied Physics and Materials Science, California Institute of Technology, Pasadena, CA, USA.
Supervisor: Prof. Rob Phillips.

September 2013 – June 2020: 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.

Postdoctoral Research Accomplishments

Quantitative Assessment of Fundamental Limits on Bacterial Growth
Research performed with Nathan Belliveau, Christina L. Heuschen, Hernan G. Garcia, Jane Kondev, Daniel S. Fisher, Julie A. Theriot, and Rob Phillips. Preprint on bioRxiv.

Recent years have seen a deluge of experiments dissecting the relationship between bacterial growth rate, cell size, and protein content, quantifying the abundance of proteins across growth conditions with unprecedented resolution. However, we still lack a rigorous understanding of what sets the scale of these quantities and when protein abundances should (or should not) depend on growth rate. In this work, we aimed to quantitatively understand this relationship across a collection of *E. coli* proteomic data sets covering $\approx$ 4000 proteins and 31 growth conditions. We estimate the basic requirements for steady-state growth by considering key processes in nutrient transport, energy generation, cell envelope biogenesis, and the central dogma, from which ribosome biogenesis emerges as a primary determinant of growth rate. We ultimately synthesize these estimates into a model of ribosomal regulation as a function of the nutrient supply, revealing a mechanism that ties cell size and growth rate to ribosomal content.

Human Impacts by the Numbers

Research performed with Avi Flamholz, Nicholas S. Sarai, Tine Valencic, Yinon Bar-On, Ron Milo, and Rob Phillips. Manuscript in preparation

The greatest experiment of the last 10,000 years is the presence and action of modern human beings on planet Earth. At this point, the consequences of this experiment are being felt on many fronts. Yet, many people still hold the view that because the world is so "huge", humans cannot really make a substantial impact. In this forthcoming publication, we present a collection of what we have come to view as essential numbers that summarize the broad reach of human action across the planet, presenting a view of the impact of human presence on Earth. These numbers include recent estimates/measurements of the volume of meltwater released from ice-sheets on an annual basis, the year change in ocean acidity from the absorption of CO_2, the background plutonium isotope reactivity found in soils stemming from nuclear weapons testing in the 1960's, to the number of livestock on the planet to give a few of many examples. In collecting and scrutinizing these data, we are also establishing the 'Human Impacts Database', a internet database similar in spirit to the BioNumbers website that we hope will be used by scientists and the general public alike.

Graduate 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.

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.

Understanding physiological adaptation through thermodynamic modeling

Research performed with Zofii Kaczmarek and Rob Phillips. Preprint on bioRxiv. Currently in revision at Cell Systems

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.

Publications

ⱥ contributed equally

Forthcoming Publications and Preprints

3. **Griffin Chure**, Avi Flamholz, Nicholas S. Sarai, Tine Valencic, Yinon Bar-On, Ron Milo, and Rob Phillips (2020). "Human Impacts by the Numbers". *Manuscript in preparation*.

2. Nathan M. Belliveauⱥ, **Griffin Chure**ⱥ, Christina L. Heuschen, Hernan G. Garcia, Jane Kondev, Daniel S. Fisher, Julie A. Theriot, and Rob Phillips (2020). "Fundamental Limits on the Rate of Bacterial Growth" *Preprint in bioRxiv*. doi: 10.1101/2020.10.18.344382. Paper website and GitHub repository.

1. **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

Peer Reviewed Publications

7. 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." *Physical Review E*. **102**, 022404. doi: 10.1103/PhysRevE.102.022404. Paper website and GitHub repository

    - Identified as an "Editor's Suggestion" for August 2020 issue

6. 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." *Nucleic Acids Research*. doi: 10.1093/nar/gkaa418. Paper website and GitHub repository

5. 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

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**ⱥ, Heun Jin Leeⱥ, 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-Mejiaⱥ, Stephanie L. Barnesⱥ, Nathan M. Belliveauⱥ, **Griffin Chure**ⱥ, Tal Einavⱥ, 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.

Doctoral Thesis

1. **Griffin Chure** (2020). "The Molecular Biophysics of Evolutionary and Physiological Adaptation." California Institute of Technology. doi: 10.7907/q8h6-xr92. Open Access PDF, Online Version, and GitHub Repository

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.

Academic Honors and Fellowships

Stanford University (beginning Jan. 2021):

- National Science Foundation – Postdoctoral Research Fellowship in Biology (beginning Jan. 1, 2021)

California Institute of Technology (2013 – 2020):

- National Institutes of Health – Molecular Biology Training Grant (2014 – 2016)
- Amgen – Research Fellowship (2015)
- National Science Foundation – Graduate Research Fellowship 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)

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, Django, 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.
- 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.

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*