BIOGRAPHICAL SKETCH

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NAME:

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POSITION TITLE: Fred and Nancy Morris Professor of Biophysics and Biology

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
University of Minnesota (by independent study)	B.S	05/1986	Physics
Washington University	Ph.D	05/1989	Physics
Sandia National Laboratories	Postdoctoral	08/1991	Materials Physics
Cornell University	Postdoctoral	07/1993	Physics

A. Personal Statement

From the age of 17, my life has been driven primarily by science, coloring everything from the books I read to the destinations I choose for travel, which now includes having led 15+ field trips in evolutionary biology all around the world. My adventures in learning physics included working my way from a several year stint as an electrician to becoming a physics graduate student. Although my first love was physics and mathematics, as I learned more about the living world, it seemed that many of the most exciting problems in science are found there. As a result, I made the switch from materials physics to biology when I moved from a faculty position at Brown University to Caltech. The NIH Director's Pioneer Award gave me the chance to become a full-time physical biologist, with a group that aims to be equally adept at theory and experiments, and the MIRA award has been similarly transformative. Much of my biological education and taste in biological questions has come from the privilege of teaching and doing research with a host of fantastic collaborators including Steve Quake (physical biology laboratory), Dianne Newman (freshman biology), Victoria Orphan (evolution), Doug Rees (structural biology and physiology), David Baltimore (virology and immunology) and Eric Davidson (gene regulatory networks) and in my decade long association with the Marine Biological Laboratory in Woods Hole. Until recently, I served as Physiology Course co-director with Wallace Marshall and Jennifer Lippincott-Schwartz. Most importantly, my nearly two decades of work with Jane Kondev (Brandeis University), Julie Theriot (University of Washington), Hernan Garcia (UC Berkeley), Christina Hueschen (Stanford University), Thomas Lecuit (College de France), Wallace Marshall (UCSF), and Ron Milo (Weizmann Institute) on our books "Physical Biology of the Cell" , "Cell Biology by the Numbers" and "The Principles of Biological Shape" has shown me how quantitative thinking can serve as an engine of biological discovery. Stimulated by these experiences, my laboratory has focused on careful predictive modeling in physical biology complemented by precision measurements at both the single-molecule and single-cell level to precisely test those predictions.

a. Phillips, R., Kondev, J., Theriot J. and Garcia HG, (2012). Physical Biology of the Cell, Garland Press
b. Milo R. and Phillips, R., (2016). Cell Biology by the Numbers, Garland Press, New York.
c. Milo, R. and Phillips, R., A feeling for the numbers in biology, Proc. Nat. Acad. Sci.,106, 21465 (2009).
d. Moran, U., Phillips, R. and Milo, R., Snapshot: Key Numbers in Cell Biology, Cell, 141, 1262 (2010).

B. Positions and Honors

Positions and Employment

2020 – visiting professor College de France
2019-present Chan Zuckerberg Biohub scientific advisory board

2012-present Fred and Nancy Morris Professor of Biophysics and Biology, Caltech
2011-2012 Professor of Applied Physics and Biology, Caltech
2009-2012 Pierre Gilles de Gennes Visiting Professor, ESPCI
2000-present Professor; California Institute of Technology
2000-2001 Visiting Professor; Institut National Polytechnique de Grenoble
2000 Professor; Brown University
1998-2000 Associate Professor; Brown University
1997 Clark Millikan Visiting Asst. Professor; California Institute of Technology
1996-1998 Manning Assistant Professor; Brown University
1996 Visiting Professor; Institut National Polytechnique de Grenoble
1993-1996 Assistant Professor of Engineering; Brown University
1991-1993 Postdoctoral Research Associate; Cornell University
1989-1991 Postdoctoral Research Associate; Sandia National Laboratories

Honors
Gavin Borden Lecturer, Cold Spring Harbor Laboratory, 2019
Widom Memorial Lecturer, Northwestern University, 2018
Friday Evening Lecturer, Marine Biological Laboratory, 2017
Winegard Visiting Lecturer in Soft Matter and Biological Physics, Univ. Guelph, 2017
Member American Academy of Arts and Sciences, 2016 – present
KITP Simons Distinguished Visiting Scholar – 2015
Makris Memorial Lecturer, University of Pennsylvania -2015
Resnick Lecturer, Johns Hopkins University - 2014
Book of the Year Award for “Physical Biology of the Cell” - Society of Biologists, 2013
Co-Director – Physiology Course, Marine Biological Laboratory, 2014 to 2018
Burroughs-Wellcome CASI Award Selection Committee Chair, 2013-2015
KAVLI Institute Theoretical Physics-Advisory Board, 2013-2015
Fred and Nancy Morris Professor of Biophysics and Biology, 2012 to present
EU International Distinguished Scientist, 2012
Member, Institute of Theoretical Physics, 1997, 2006, 2012, 2015
Burroughs-Wellcome CASI Award Selection Committee, 2011 to present
Ehrenfest Colloquium, Leiden, 2010
35th Annual Award for Excellence in Teaching, ASCIT, 2010-2011
Pierre Gilles de Gennes Fellowship 2010-2012– Paris, France
Course Director, Physical Biology, Cold Spring Harbor Laboratory, 2010 to present
APS Fellow 2009
Southwest Mechanics Lecturer, 2009
Lead Instructor, Physiology Course, Marine Biology Laboratory, 2006 to present
Editorial Board Annual Reviews of Biophysics, 2006-2012
NIH Director’s Pioneer Award, 2004-2009
Midwest Mechanics Lecturer, 2002-2003
Member, Isaac Newton Institute for Mathematical Sciences, 1999
First Chaired Manning Assistant Professor, Brown University
NSF CAREER Award
Washington University Fellow, 1986-1988
Washington University Dissertation Fellow, 1988-89

C. Contributions to Science
1. **Physical biology of the cell.** Work in my laboratory emphasizes the unity of perspective and predictive power that comes from formulating biological hypotheses in mathematical language and the interplay between the mathematicization of biological models and the use of careful measurements to test them. Just as sequence and function tell us about the relationship between regulatory genes (*pax6* and *eyeless*) for eye development in different organisms, physical and mathematical models have taught us about different kinds of unexpected unity. For example, our work on allostery has shown how examples as diverse as transcription factor induction and ligand-gated ion channel gating can be described by precisely the same underlying

model in a way that provides deep insights into the mutants that arise in both of these classes of molecules. The style and substance of our modeling efforts are reported in three books I have co-authored, *Physical Biology of the Cell* (20,000+ copies sold, used widely in teaching throughout the world and winner of the 2013 Society of Biology best book of the year award), *Cell Biology by the Numbers*, and *The Molecular Switc*h.

a. Phillips, R, Kondev, J., Theriot, J. and Garcia, H.G., Physical Biology of the Cell, Garland Press, 2012.
b. Phillips, R, The Molecular Switch, Princeton University Press, 2020.
c. Marzen, S, Garcia, HG and Phillips, R, Statistical mechanics of Monod-Wyman-Changeux (MWC) models, J. Mol. Biol., 425, 1433 (2013). PMCID: PMC3786005
d. Bintu, L, Buchler, NE, Garcia HG, Gerland, U, Hwa, T, Kondev, J and Phillips, R, Transcriptional Regulation by the Numbers 1: Models Current Opinion in Genetics & Development, 15(2):116-124 (2005). PMCID: PMC3482385
e. Wiggins, P and Phillips, R., Analytic models for mechanotransduction: Gating a mechanosensitive channel, Proc. Nat. Acad. Sci., 101: 4071-4076 (2004). PMCID: PMC384697

2. **Predictive studies in transcription.**
It is becoming increasingly feasible to predict the input-output relations of signaling and regulatory circuits and to design cell strains that tune the relevant molecular parameters to precisely test these predictions. We use a three-pronged dialogue between theory, single-molecule experiments and single-cell methods that has permitted us to make a number of insights into transcriptional regulation. For example, we predicted how mean expression and noise depend upon key molecular parameters and then tested these predictions using single-cell mRNA FISH experiments, revealing a remarkable agreement between theory and experiment (see Brewster et al., 2014; Jones et al, 2014). When viewed in terms of the natural variable (in this case, fugacity, a combined measure of TF affinity and concentration) of these problems, data from a broad spectrum of different regulatory circumstances fall on one master, parameter free curve (see Weinert et al, 2014).

a. Chure,G., Razo-Mejia, M., Belliveau, N.M., Einav,T.,Kaczmarek, Z. A., Barnes, S.L., Lewis, M. and Phillips, R., Predictive shifts in free energy couple mutations to their phenotypic consequences, Proc. Nat. Acad. Sci.,116, 18275-18284 (2019). PMCID: PMC6744869
b. Phillips, R., Belliveau, N.M., Chure, G., Garcia, H.G., Razo-Mejia, M. and Scholes, C., Figure1 Theory Meets Figure 2 Experiments in the Study of Gene Expression, Ann. Rev. Biophys., 48, 121-163 (2019). PMID: 31084583
c. Belliveau, NM, Barnes, SL, Ireland, WT, Jones, DL, Sweredoski, J, Moradian, A, Hess, S, Kinney, JB, and Phillips, R, A systematic approach for dissection of the molecular mechanism of transcriptional regulation in bacteria, PNAS 115, 2018. PMCID: PMC6003448
d. Razo-Mejia, M., Barnes, S. L., Belliveau, N.M., Chure, G., Einav,T., Lewis, M. and Phillips, R., Tuning transcriptional regulation through signaling: A predictive theory of allosteric induction, Cell Systems, 6, 1-14 (2018). PMCID: PMC5991102

3. **Biology by the Numbers:**
Quantitative sciences and their partner engineering disciplines rely on a wellspring of quantitative factual knowledge of the parameters that govern the phenomena. It has become increasingly clear that the experimental revolution in the life sciences invites a similar characterization of the phenomena of the living world, ranging from the speeds of the enzymes of the central dogma to the concentrations of phage in the sea. In collaboration with noted biologist/physicist/data scientist Ron Milo and my book coauthor team for Physical Biology of the Cell (Jane Kondev, Julie Theriot, Hernan Garcia, Christina Hueschen) we have been engaged in creating reliable data sets (see BNID – Bionumbers website, accessed 40,000+ times per month) and an associated set of order of magnitude estimates that provide intuition for these magnitudes. In conjunction with my interactions with the Chan-Zuckerberg Biohub, I have been increasingly interested in the relation between human impacts on Earth and the implications for human health and developing a new round of Bionumbers to describe these problems.

a. Bar-On, YM, Phillips, R, and Milo, R, The biomass distribution on Earth, PNAS June 19, 2018 115 (25) 6506-6511. PMCID: PMC6016768
b. Shamir, M, Bar-On, YM, Phillips, R, and Milo, R, SnapShot: Timescales in Cell Biology, Cell 164 (6) 2016. PMID: 26967295

c. Flamholz, A, Phillips, R and Milo, R, The quantified cell, Molecular Biology of the Cell 25 (22) 2014. PMCID: PMC4230611

4. **Biophysics of Cellular organization:**
One of the defining characteristics of living organisms is the expenditure of free energy to maintain their structures in a state of disequilibrium. A particularly fertile test bed that permits a rich interplay between theory and experiment for these kinds of questions is provided by “active matter”. We have developed an optogenetic system (see collaboration letter from Matt Thomson) that permits us to control when and where molecular motors crosslink cytoskeletal filaments, resulting in the emergence of structures such as asters. In parallel, we have been developing chemical master equations that allow us to calculate and predict how these structures evolve in space and time.

a. Ross, TD, Lee, HJ, Qu, Z, Banks, R, Phillips, R, and Thomson, M, Controlling organization and forces in Active Matter through optically-defined boundaries, Nature, 572, 224-229 (2019). PMCID: PMC6719720
b. Hueschen, CL, Galstyan, V, Amouzgar, M, Phillips, R and Dumont, S, Microtubule end-clustering maintains a steady-state spindle shape, Current Biology, 2019,. PMCID: PMC6383811
c. Mohapatra, L, Goode, BL, Jelenovic, P, Phillips, R, and Kondev, Jane, Design principles of length control of cytoskeletal structures, Annual Reviews of Biophysics, 45 (2016). PMCID: PMC5466818

5. **The life cycles of bacterial viruses.** My initial jump to physical biology was sparked by questions on the mechanism of DNA packaging in viruses. Inspired by single-molecule experiments aimed at measuring how force builds up inside viruses, we worked out a number of predictions for how tightly packaged DNA affects both viral assembly and infection. This led to a long-standing experimental program within my laboratory aimed at measuring the DNA injection process by bacteriophage (see attached figure which shows the ejection process measured using fluorescence) and the subsequent viral assembly. These experiments tested our understanding of the free energy of DNA packaging and challenged the field’s understanding of the kinetics of DNA ejection and the mechanism of infection. This then led us to investigate the underlying evolutionary variability of the viral molecular machinery. Past and current efforts in my lab aim to understand the complexity of the virus-host relations in environments such as termite-gut and the human mouth. The bioinformatics side of this work led to the discovery of ubiquitous phage markers that are now being used to study phage biogeography in the human mouth.

a. Van Valen, D., Wu, D., Chen, Y.-J., Tuson, H., Wiggins, P. and Phillips, R., A Single-Molecule Hershey-Chase Experiment, Curr. Biol., 22, 1 (2012). PMCID: PMC3462812
b. Tadmor, AD., Ottesen, EA, Leadbetter, JR. and Phillips, R., Probing Individual Environmental Bacteria for Viruses by Using Microfluidic Digital PCR, Science, 333, 58, (2012). PMCID: PMC3261838
c.Mahmoudabadi, G, Milo, R, and Phillips, R, The energetic cost of building a virus, PNAS 114 (22) 2017. PMCID: PMC5465929
d. Mahmoudabadi, G. and Phillips, R, A comprehensive exploration of thousands of viral genomes, eLife 7:e31955, 2018. PMCID: PMC5908442