

SCOTT M. COYLE

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EDUCATION

- 2009-2015 **Ph.D., Biochemistry, University of California, San Francisco, CA**
Graduate GPA: 4.0
Dissertation advisor: Prof. Wendell A. Lim
Dissertation title:
Reconstituting signaling networks to interrogate the molecular and evolutionary logic of cellular decision making.
- 2003-2007 **B.A., Molecular and Cellular Biology, University of California, Berkeley, CA**
Highest Distinction and Honors
GPA 3.99 Major GPA: 4.0
Thesis advisor: Prof. Jennifer A. Doudna
Honors Thesis Title:
*Roles for RACK1 in the regulation of translation and the transition to invasive growth in the yeast *Saccharomyces cerevisiae*.*

RESEARCH EXPERIENCE & ACCOMPLISHMENTS

Prakash Lab, Stanford University

Postdoctoral Scholar

Summer 2017– Present

I am currently studying how mechanical behaviors are molecularly specified and programmed in ciliates, a diverse group of single-celled protozoans that perform an array of dazzling mechanical responses such as jumping, twisting, reorientation and hunting. Remarkably, this wide-range of behaviors arises through coordinating the actuation of common ciliary and contractile activities with signaling programs. By combining techniques from computer vision and machine learning with traditional cell biology and biochemistry, I am charting the design principles that govern the systems biology and biodynamics of these complex behaviors. My analysis of the hunting strategy of the unicellular predator *Lacrymaria olor* revealed a new paradigm for encoding a cellular search algorithm in the emergent mechanics of coupled active systems, suggesting alternative paths forward for engineering these behaviors. In parallel, I am using reconstitution approaches to construct new materials, devices, and networks that are inspired by the control strategies and design principles that we identify in these organisms.

CellDesignLabs, San Francisco / Emeryville

Scientific Consultant

Senior Founding Scientist

Founding Scientist

Scientific Consultant

Spring 2017 – Present

Winter 2016 – Spring 2017

Spring 2016 – Winter 2016

Summer 2015 – Spring 2016

As a founder of CellDesignLabs, I was involved in the initial conception and early stage business development to commercialize a number of technologies I developed during my time as a graduate student and post-doc in Prof. Wendell Lim's lab. As a scientist at the company, I developed the scientific research plan for our partnership with Kite Pharmaceuticals to design a new protein heterodimerization system that operates with FDA-approved drugs so as to engineer an inducible ON-switch Chimeric Antigen Receptor (CAR) for the treatment of acute myeloid leukemia (AML). I oversaw a team of RAs and technicians responsible for executing this research plan, and I coordinated with Kite and CDL clinical teams to

optimize reagents for therapeutic applications. In addition, I directed an internal research & development program to engineer new synthetic receptors and cellular circuits that performed diverse functions for applications in cell therapy and patented the intellectual property around the resulting technologies. CellDesignLabs was acquired by Gilead Pharmaceuticals in December 2017 for \$567M.

Lim Lab, University of California at San Francisco
Postdoctoral Scholar

Summer 2015 – Spring 2016

I developed a novel multi-turnover microscopy-based *in vitro* reconstitution of Ras signaling systems to investigate how cells specify complex dynamic Ras effector programs. I used this assay to study systems-level behavior of Ras signaling networks operating far from equilibrium for the first time. Additionally, I created and patented a method for the combinatorial assembly of barcoded chimeric antigen receptors and the high-throughput analysis of their signaling behaviors using an innovative next-generation sequencing assay. I applied evolutionary principles to facilitate the design of new synthetic signaling receptors based on the proto-Notch scaffold.

Graduate Student

Summer 2010 – Summer 2015

I investigated the role of conformational control of the signaling scaffold protein Ste5 in ensuring pathway insulation and controlling signaling fates in the budding yeast MAP kinase network. I developed this allosteric-based control system into a model system for interrogating the mechanisms that underlie the evolution of complex new allosteric regulators in cell signaling pathways, identifying latent allosteric features in ancestral proteins that provide toe-holds that simplify the evolution of new regulators.

Doudna Lab, University of California at Berkeley
Research Technician

Summer 2007 - Summer 2009

I served as a technical consultant to Gilead Sciences to aid in the development of a high-throughput screen for inhibitors of the Hepatitis-C Virus. I assisted in the structural characterization of CAS1, a conserved protein involved in the prokaryotic CRISPR immune system. I participated in the biochemical and structural characterization of the exonuclease Xrn1, a GW182/PAB interaction critical for miRNA mediated silencing, and piRNA and rasiRNA biogenesis proteins from *Drosophila melanogaster*. I also served as lab systems administrator and webmaster.

Independent Undergraduate Researcher

Summer 2005 - Spring 2007

I independently employed biochemical, genetic and structural methods to explore roles for the ribosomally-associated scaffold RACK1 in signaling to the ribosome and the regulation of translation. I used structure/activity relationships to design mutations that exclusively disrupt RACK1 interaction with ribosomes. I used these mutants to discover the first evidence that RACK1's location on the ribosome was important for its biological functions in cell signaling.

The Molecular Sciences Institute, Berkeley, California USA
Independent Undergraduate Researcher

Summer 2003 - January 2005

I worked under Dr. Evgueny Kroll to elucidate the molecular mechanisms of eukaryotic adaptation to changing environments and the molecular basis of speciation in the yeast *S. cerevisiae*.

AWARDS & FELLOWSHIPS

Helen Hay Whitney Foundation Postdoctoral Fellowship (2018)
Harold M. Weintraub Graduate Student Achievement Award (2015)
UCSF Discovery Fellow, 2014-2015
ASCB Beckman Coulter Distinguished Graduate Student Achievement Prize, 2013
UCSF Outstanding Teaching Assistant Award, 2011
National Science Foundation Graduate Research Fellowship, 2010
MCB Outstanding Scholar for the Class of 2007, *Spring 2007*
Phi Beta Kappa, *Spring 2006*
Dean's Honor List, *Spring 2004, Fall 2004, Spring 2005, Fall 2005*
UC Summer Undergraduate Research Fellow (SURF), *Summer 2006*
Howard Hughes Medical Institute Internship, *Summer 2005*

TEACHING EXPERIENCE

MCB 11: Of Molecules & Man, University of California, Berkeley
Teaching Assistant and Discussion Section Leader **Spring 2005**

MCB 11 was an undergraduate course that taught biochemical and genetic concepts to non-science majors with the goal of providing students with a rigorous foundation on which to consider pressing questions facing our society as it enters a new era of biological understanding. I prepared discussion sections based on lectures, taught a weekly review session, held office hours, and was responsible for grading exams.

NSF-GRFP Fellowship Writing Workshop, University of California, San Francisco
Student Workshop Leader **Fall 2010**

I led a weekly fellowship-writing workshop with Prof. Bob Farese in which we helped students prepare their written applications for the NSF Graduate Research Fellowship Program. In addition to helping students prepare well-written sound research proposals, I helped students become familiar more broadly with the process of applying for funding sources and awards. This included working with students to identify the "broader impacts" of their work and to understand the multi-faceted nature of strong proposals.

Bioregulatory Mechanisms, University of California, San Francisco
Teaching Assistant and Discussion Section Leader **Spring 2011**

Bioregulatory Mechanisms is UCSF's "methods & logic" course that trains students how to pose testable hypotheses, design experiments, and evaluate and interpret data to draw conclusions. Students must write an original research proposal outside their own specialization and defend their ideas in an oral examination administered by senior faculty. My responsibilities included holding weekly discussion sections to review lecture material and to hold twice-weekly office hours to assist students with writing of their proposals. In addition, I helped students prepare for their oral examinations by holding several mock exams for each student. My commitment to this course was recognized with UCSF's Outstanding TA Award for 2010.

Physical Underpinnings of Biological Systems (PUBS), University of California, San Francisco
Guest Lecturer **Spring 2014**

UCSF has developed an innovative approach to enriching the first-year graduate student experience through an experiment-oriented course called "Physical Underpinnings of Biological Systems". Students in this course work as a team to execute a semester-long research project that integrates traditional wet-

lab work with computational analysis and modeling. I prepared a guest lecture for this course in which I surveyed techniques for generating combinatorial libraries of synthetic proteins and methods to screen them efficiently using next-generation sequencing technologies.

Intel ISEF Foldscope Workshop, Stanford University
Workshop Leader

Spring 2017

I attended the 2017 Intel International Science and Engineering Fair in Los Angeles and helped lead a workshop in which we made and distributed over one thousand paper microscopes to middle school and high school students from underserved areas in the Los Angeles area. I taught students simple principles that underlie the function of a microscope — like why you need to have light passing through your sample to see it—and explored a variety of biological questions and concepts with students based on the discoveries they made exploring samples of their own creation.

PREPRINTS

1. **Coyle, S. M.**, Flaum, E., Li, H., Krishnamurthy, C., Prakash, M. Coupled active systems encode emergent behavioral dynamics of the unicellular predator *Lacrymaria olor*. *BioRxiv* 406595 [Preprint]. September 3, 2018. Available from <https://doi.org/10.1101/406595>.

PUBLICATIONS

** denotes equal contribution*

15. **Coyle, S.M.** Reverse engineering GTPase programming languages with reconstituted signaling networks. *Small GTPases* 7 (3), 168-172 (2016).

14. Morsut, L., Roybal, K.T., Xiong, X., Gordley, R.M., **Coyle, S.M.**, Thomson, M., Lim, W.A. Engineering customized cell sensing and response behaviors using synthetic notch receptors. *Cell* **164**, 780-791 (2016).

13. **Coyle, S.M.**, Lim, W.A. Mapping the functional versatility and fragility of Ras GTPase signaling circuits through in vitro network reconstitution. *eLife*, 5:e12345 (2016).

- Faculty of 1000 recommended selection.
- Striking image highlighted on eLife front page.

12. Dumesic, P.A., Homer, C.M., Moresco, J.J., Pack, L.R., **Coyle, S.M.**, Strahl, B.D., Fujimori, D.G., Yates, J.R., Madhani, H.D. Product binding directs genomic specificity of a yeast Polycomb repressive complex. *Cell* 160, 204-216 (2015).

11. Van Anken, E., Pincus, D., **Coyle, S.M.**, Aragon, T., Osman, C., Lari, F., Puerta, S.G., Korennykh, A.V., Walter, P. Specificity in endoplasmic reticulum stress signaling entails a step-wise engagement of HAC1 mRNA to Ire1 clusters. *eLife*, 3:e05031 (2014).

10. **Coyle S.M.**, Flores J., Lim W.A. Exploitation of latent allosterity enables the evolution of new modes of MAP kinase regulation. *Cell* **154**, 875-887 (2013).

9. Kroll E., **Coyle S.**, Dunn B., Koniges G., Aragon A., Edwards J., Rosenzweig F. Starvation-associated genome restructuring can lead to reproductive isolation in yeast. *PLoS ONE* **8**, e66414 (2013).

8. Zalatan J.G.*, **Coyle S.M.***, Rajan S., Sidhu S.S., Lim W.A. Conformational control of the Ste5 scaffold protein insulates against MAP kinase misactivation. *Science* **337**, 1218-1222 (2012).
 - Perspective in *Science* by Roger Davis.
 - Editor's Choice, *Science Signaling*.
7. Rougemaille M., Braun S.*, **Coyle S.***, Dumesic P.A.*, Garcia J.F.*, Isaac R.S.*, Libri D., Narlikar G.J., Madhani H.D. Ers1 links HP1 to RNAi. *Proc. Natl. Acad. Sci.* **109**, 11258-11263 (2012).
6. Jinek M., **Coyle S.M.**, Doudna J.A. Coupled 5' nucleotide recognition and processivity in Xrn1-mediated mRNA decay. *Mol. Cell* **41**, 600-608 (2011).
5. Weeks A.M., **Coyle S.M.**, Jinek M., Doudna J.A., Chang M.C.Y. Structural and biochemical studies of a fluoroacetyl-CoA-specific thioesterase reveal a molecular basis for fluorine selectivity. *Biochemistry* **49**, 9269-9279 (2010).
4. Jinek M., Fabian R.M., **Coyle S.M.**, Sonenberg N., Doudna J.A. Structural and biochemical analysis of the human GW182-PABC interaction in microRNA-mediated silencing. *Nat. Struct. Mol. Biol.* **17**, 238-240 (2010).
3. Wiedenheft B., Zhou K., Jinek M., **Coyle S.M.**, Ma W., Doudna J.A. Structural basis for DNase activity of a conserved protein implicated in CRISPR-mediated genome defense. *Structure* **17**, 904-912 (2009).
2. **Coyle S.M.**, Gilbert W.V., Doudna J.A. Direct link between RACK1 function and localization at the ribosome in vivo. *Mol. Cell. Biol.* **29**, 1626-1634 (2009).
1. **Coyle S.**, Kröll E. Starvation induces genomic rearrangements and starvation-resilient phenotypes in yeast. *Mol. Biol. and Evol.* **25**, 310-318 (2008).

P A T E N T S

Coyle, S.M., Rupp, L., Santoro S. "Chimeric Polypeptides and Methods of Altering the Membrane Localization of the Same." US Patent application 62/477,733. Filed March 28, 2017. Patent pending.

Lim, W.A., **Coyle, S.M.**, Gordley, R., Roybal, K. "Modular Polypeptide Libraries and Methods of Making and Using Same." US Patent application 62/212,999. Filed September 1, 2015. Patent pending.

P R E S E N T A T I O N S

*Coupled active systems encode emergent behavioral dynamics of the unicellular predator *Lacrymaria olor*.* IOP Workshop on Physics of Cells Poster Presentation, September 2018.

*Unicellular microcontrollers: how calcium signaling programs the complex hunting behaviors of the predatory ciliate *Lacrymaria olor*.* ASCB Annual Meeting Poster Presentation, December 2017.

Reconstituting signaling networks to interrogate the molecular and evolutionary logic of cellular decision making. Harold M. Weintraub Graduate Student Achievement Award Symposium, May 2015

Reconstituted signaling networks reveal molecular and evolutionary bases of complex cellular decision making. HHMI Meeting Poster Session, Chevy Chase, MD, March 2014.

Exploitation of latent protein allostery enables the evolution of new modes of MAP kinase regulation, Breakthrough Prize in Life Sciences Poster Session, San Francisco, CA, December 2013.

Exploitation of latent protein allostery enables the evolution of new modes of MAP kinase regulation, “Proteins” Gordon Research Conference, Holderness, NH, June 2013.

Evolution of novel and divergent modes of MAP kinase regulation by exploitation of latent protein allostery. UCSF Evolution Seminar, San Francisco, CA, May 2013.

Roles for RACK1 in the transition to invasive growth, UC Berkeley Biochemistry and Molecular Biology Retreat, Pacific Grove, CA, January 2007; January 2008.

Structural and biochemical basis of RACK1 association with ribosomes in yeast, EMBO 2007 Conference on Protein Synthesis and Translational Control, Heidelberg, Germany, September 2007.

Starvation induces genomic rearrangements in yeast, MSI Alpha-Project Symposium, Berkeley, CA, June 2004.

OUTREACH & MENTORSHIP

Foldscope Workshop, 2017 California Academy of Sciences Nightlife Event
Foldscope Workshop, 2017 International Science and Engineering Fair
Science Demo Booth at UCSF Byers Lecture, Spring 2015
Guest Lecturer for new UCSF Physical Underpinnings of Biological Systems (PUBS) Course; 2014.
Mentorship for High School Research Intern; Summer 2013
UCSF Summer Research Training Program Mentor; Summer 2012
Organization of and participation in UCSF “Science and Cooking” public seminar; Summer 2012
Undergraduate Student Instructor for UC Berkeley MCB 11 course; Spring 2005
Mentorship of Molecular Sciences Institute summer interns; Summer 2004, 2005, 2006
Alameda County Regional Intel Science and Engineering Fair (ISEF) Judge 2004, 2005

REFERENCES

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