

BIOGRAPHICAL SKETCH

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NAME: Jena, Siddhartha Gautama

eRA COMMONS USER NAME (credential, e.g., agency login): SiddharthaJena

POSITION TITLE: Postdoctoral Fellow

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)	Start Date MM/YYYY	Completion Date MM/YYYY	FIELD OF STUDY
Harvard College	BA	09/2012	06/2016	Chemistry, Physics, Mathematics, minor in Biology
Princeton University	PhD	09/2016	07/2021	Molecular Biology
Harvard University/Broad Institute	N/A	08/2021	TBD	Epigenomics, Chromatin Biology

A. Personal Statement

My interests lie at the intersection of signaling and gene regulation, with an eye towards understanding mechanisms in basic cell biology that may inform processes at a tissue- or organismal-level. I approach these questions with a multifaceted approach informed by a quantitatively rigorous background in systems biology, theoretical chemical physics and pure mathematics. In my graduate work at Princeton, advised by Jared Toettcher, I grew interested in the nascent field of signaling dynamics, focusing on the Ras/ERK pathway, which displays rapid pulses of activity seemingly independent of any external pulsatile stimulation. My dissertation work leveraged a broad set of experimental and computational tools to unearth two new modes of information transfer through signaling dynamics. First, I studied cell-to-cell transcriptional heterogeneity as a fundamental feature of ERK-mediated immediate-early gene expression in mammalian cells and tissues, identifying that pulse amplitude and duration, as well as synergistic activation of parallel MAP kinase pathways, can modulate the responsive fraction of a stimulated population, thereby encoding a potentially wide range of outcomes in a single pathway activation event (Jena et. al. 2021). Second, I analyzed live-cell videos of thousands of pulsatile epidermal stem cells and other epithelial cell types and developed a machine learning-based approach to deconvolve self-excitation from spatially coupled signaling events (Verma*, Jena* 2021). My interest in signaling-regulated gene expression also extended to whole-organism approaches, where I investigated the spatiotemporal interpretation of upstream morphogen gradient dynamics by enhancers in *Drosophila* (Keller*, Jena*, et. al. 2020).

I am currently a postdoctoral fellow in Jason Buenrostro's lab at Harvard and the Broad Institute. My work synthesizes my continuing interest in signaling and dynamic cellular processes with methods that allow for precise and genome-wide measurements and perturbation of epigenetic changes, with a focus on chromatin domains. The combination of these approaches will allow me to link two important and inextricable avenues of biology: the recognition of environmental cues by the cell and the conversion of those cues into rapid and persisting changes in post-translational modifications on histones that mold genome structure and gene expression. I am also interested in how to control changes in chromatin domains through controlled synthetic perturbations such as engineered histones and transcription factors. As an independent investigator, I will combine genomic approaches with synthetic biology, live-cell imaging modalities and state-of-the-art computational analysis to uncover the basic biology underlying chromatin domain establishment and how to control it.

B. Positions, Scientific Appointments and Honors

Positions and Employment

2021-present Postdoctoral Fellow, Buenrostro Lab, Harvard University
2017-2021 Graduate Student, Toettcher Lab, Princeton University
2017 Rotation Student, Toettcher Lab, Princeton University
2016 Rotation Student, Levine Lab, Princeton University
2016 Rotation Student, Wingreen Lab, Princeton University
2015-2016 Undergraduate Researcher, Szostak Lab, Harvard University
2013-2016 Undergraduate Researcher, Karplus Lab, Harvard University
2012-2013 Undergraduate Researcher, Melton Lab, Harvard University

Teaching Experience

Spring 2019 Section TA, MOL 375: Genetics, Princeton University
Spring 2018 Lab TA, MOL 101: From DNA to Human Complexity, Princeton University
Spring 2016 Course TA/Grader, Physics 15b, Electricity and Magnetism, Harvard University
Spring 2015 Course TA/Grader, Physics 15b: Electricity and Magnetism, Harvard University

Other Experience

2020-2021 Mentor, Polygence
2015 Mentor, Research Science Institute
2014-2016 Harvard College Undergraduate Representative Board for the Sciences

Honors

2019-2021 NIH NIAMS F31 Fellowship, "Cracking the signaling code: how ERK activity dynamics coordinate gene expression and differentiation in keratinocytes"
2017 Francis Boyer Fellowship in the Life Sciences, Princeton University
2016 Honors in Chemistry and Physics Major, Harvard University Physics Department
2014 Origins of Life Initiative Summer Research Fellowship, Harvard University
2013, 2015 Fellowship, Harvard College Undergraduate Research Program

Doctoral Mentoring (with Jared Toettcher)

2019-2021 Catherine Yu, Undergraduate (Current: Research Assistant, NYU)
2018 Brittany Williams, University of Arizona Undergraduate (Current: PhD student at University of Washington)
2017-2019 Danielle Isakov, Undergraduate (Current: MD-PhD student, Tri-I program)

Postdoctoral Mentoring (with Jason Buenrostro)

2022 Wilson Gomarga, Rotation Student
2022 Ena Oreskovic, Rotation Student
2022 Michael Quezada, MD-PhD Rotation Student
2021-present Amalia Driller-Colangelo, Graduate Student

Other Mentoring

2020-2021 Pranav Avadhanam, middle school student. Mentored through Polygence
2020-present Teoman Toprak, high school student. Mentored through Polygence
2019-2021 served as Residential Graduate Student, Butler College, Princeton University
2018 LeeRoy Borders Rutgers University Undergrad. Mentored through the Prison Teaching Initiative summer program.

C. Contributions to Science

1. Exploring and engineering mechanisms of gene regulation: Cells employ various methods to activate and deactivate genes in response to different environmental or physiological cues. My graduate work uncovered a set of amplitude, duration, and context-dependent rules for fractional transcriptional responses to transient Erk signaling (Jena et. al. 2021). My work connecting time-dependent signaling to gene regulation has also extended to developmental, whole-animal contexts, where I dissected the contributing enhancer elements that allow for rapid interpretation of an upstream transcription factor gradient in the fly embryo (Keller*, Jena* et. al. 2020).

- a. **Jena S.G.**, Yu C., Toettcher J.E. Dynamics and heterogeneity of Erk-induced immediate-early gene expression. *bioRxiv*, 2021.
- b. Keller S.H.*, **Jena S.G.***, Yamazaki Y., Lim B. Regulation of spatiotemporal limits of developmental gene expression via enhancer grammar. *PNAS* 117 (26) 15096-15103 (2020).
- c. Ravindran P.T., Wilson M.Z., **Jena S.G.**, Toettcher J.E. Engineering combinatorial and dynamic decoders using synthetic immediate-early genes. *Comms. Biol.* 2020.

2. Measuring and modeling signaling dynamics: One of the focuses of my graduate work was the recently discovered phenomenon of Erk signaling dynamics, where the Erk pathway activates and deactivates in a pulsatile fashion. In addition to my work linking dynamics to gene regulation, my collaborators and I established a set of models and accompanying machine learning tools for inferring signaling behavior and signaling-dependent gene regulation from live-cell imaging (Verma*, Jena* et. al. 2021).

- a. **Jena S.G.***, Goglia A.G., Engelhardt B.E. Towards 'end-to-end' analysis and understanding of biological timecourse data. *Biochem J.* (2022) 479 (11): 1257–1263.
- b. Verma A.*, **Jena S.G.***, Isakov D.R., Aoki K., Toettcher J.E., Engelhardt B.E. A self-exciting point process to study multi-cellular spatial signaling patterns. *PNAS* 118 (32)
- c. **Jena S.G.**, Toettcher J.E. The role of timing in biological perception and actuation. *Phys. Biol.* (2021)
- d. Goglia A.G.*, Wilson M.Z.*, **Jena S.G.**, Silbert J., Basta L.P., Devenport D., Toettcher J.E. A Live-Cell Screen for Altered Erk Dynamics Reveals Principles of Proliferative Control. *Cell Syst.* 10 (3) (2020).

3. Biophysical regulation of membrane protein behavior: My undergrad thesis, completed under the mentorship of Martin Karplus, was focused on using molecular dynamics to simulate the effect of membrane lipid composition on the behavior of embedded proteins. I also studied models of protocellular membrane evolution with Jack Szostak (Lin*, Kamat* et. al. 2018). Later in my graduate work, I engineered membrane-bound optogenetic tools for cellular activation of signaling activity.

- a. Golonka D., Fischbach P., **Jena S.G.**, Kleeberg J.R.W., Essen L., Toettcher J.E., Zurbriggen M.D., Moglich A. Deconstructing and repurposing the light-regulated interplay between Arabidopsis phytochromes and interacting factors. *Comms. Biol.* 2 (2019).
- b. Jin L.*, Kamat N.P.*, **Jena S.G.**, Szostak J.W. Fatty Acid/Phospholipid Blended Membranes: A Potential Intermediate State in Protocellular Evolution. *Small* 14.15 (2018).
- c. **Jena S.G.** (2013) Involvement of potassium channel in AQP1-mediated water and gas transport in erythrocytes. *J. Biol Phys Chem* 13: 12-17.
- d. **Jena S.G.**, Lee, J-S. (2010) High Cholesterol Impairs Water and Gas Transport in Red Blood Cells and is Ameliorated by the PLA2 Inhibitor ONO-RS-082. *J. Biol Phys Chem* 10: 127-134.

4. Mathematics/mathematical biology: I have taken the opportunity to build on my background in mathematics and undertake pure mathematics research as well as mathematics applied to biology.

- a. **Jena S.G.***, Verma A.*, Engelhardt B.E. Answering open questions in biology using spatial genomics and structured methods. arXiv:2310.09482. 2023.
- b. Avadhanam P.*, **Jena S.G.*** Restricted Positional Games. arXiv:2108.12839. 2021.
- c. **Jena S.G.** (2016) A Random Graph Model of Density Thresholds in Swarming Cells. *J. Cell. Mol. Med.* 20(3): 413-421.

5. Selected scientific presentations:

- a. 2021 American Society for Biochemistry and Molecular Biology Conference. **Jena, S.G.** Dynamics and heterogeneity of Erk-induced immediate-early gene expression. (Invited Talk)
- b. 2020 Keystone Symposium on Gene Regulation. **Jena, S.G.**, Isakov, D.R., Toettcher, J.E. Dynamic signaling and stochastic transcription intersect to modulate heterogeneity. (Poster)
- c. 2017 American Physical Society March Meeting (Volume 62, Number 4). **Jena, S.G.**, Levine, M.S. Information Propagation in Developmental Enhancers. (Talk)
- d. 2016 Origins of Life Symposium, Harvard University. **Jena, S.G.**, Jin, L., Kamat, N., Szostak, J. Cation Stability of Blended Phospholipid/Fatty Acid Vesicles. (Poster)

References

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