## Dr. Evan E. Seitz

CONTACT

INFORMATION Postdoctoral Researcher Phone: +1-404-964-9821

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RESEARCH INTERESTS Navigating biological complexity through the application of machine learning models augmented by advanced interpretation techniques.

CURRENT ACADEMIC APPOINTMENT Cold Spring Harbor Laboratory, Cold Spring Harbor, NY

## Computational Postdoctoral Fellow, March 2022 – present

- Mentors: Justin Kinney and Peter Koo (co-P.I.s)
- Affiliations:

Simons Center for Quantitative Biology

- Summary: My postdoctoral work aims to develop advanced interpretation techniques to understand gene-regulatory mechanisms learned by black-box deep neural networks.
- Awards
  - F32 Individual Postdoctoral Fellowship (2024). Awarded by the National Human Genome Research Institute of the National Institutes of Health. Award Number: F32HG013265.

### EDUCATION Columbia University, New York, NY

#### **Doctor of Philosophy** with distinction, May 2017 – January 2022

- Doctoral Thesis: Analysis of Conformational Continuum and Free-energy Landscapes from Manifold Embedding of Single-particle Cryo-EM Ensembles of Biomolecules
- Mentor: Joachim Frank
- Affiliations:

Department of Biological Sciences

Department of Biochemistry and Molecular Biophysics

- Summary: My thesis work focused on the development, interpretation and refinement of a geometric machine-learning approach, called ManifoldEM, using manifold embedding to obtain the energy landscape and corresponding continuum of 3D structures of a molecular machine from an ensemble of cryo-EM images afflicted by low signal-to-noise ratio, random rotations and orientations in 3D space, and distortions introduced by microscopy aberrations. A complete description of my accomplishments is available in my thesis [1].
- Awards:

John S. Newberry Prize (2022). Awarded to the graduate student in the Department who, in the opinion of the faculty, is the "most promising student of the year in the field of vertebrate zoology". The awardee was chosen by faculty and staff nominations and consideration by the departmental faculty committee for graduate affairs.

Master of Philosophy, May 2017 – October 2020

Master of Arts, May 2017 - May 2019

- Cumulative GPA: 3.74
- Core Courses: Advanced Genetic Analysis; Cell Biology; Eukaryotic Gene Expression;
   Genomics of Gene Regulation; Protein Thermodynamics; Structural Biology
- Elective Courses: Computational Linear Algebra; Cryo-Electron Microscopy; Statistical Mechanics; Topology

#### Pre-thesis Rotations:

- Califano Lab, Fall 2017: I conducted research under the guidance of Dr. Andrea Califano, exploring cell regulatory networks using information-theoretic algorithms (ARACNE, FIRE) to identify a set of maximally-informative DNA sequence motifs associated with the FOXM1 master-regulator pathway implicated in tumorigenesis.
- Gautier Lab, Summer 2017: I conducted research under guidance of Dr. Jean Gautier, investigating the role of genome instability in cancer using various wet lab experiments—such as plasma purification, spectrophotometry, and electrophoresis—to isolate and analyze specific protein-gene interactions responsible for cellular response to DNA damage.

### Georgia Institute of Technology, Atlanta, GA

**Bachelor of Science** in Physics with *Highest Honor*, May 2015 – May 2017

Cumulative GPA: 3.90

- Core Courses: Classical Mechanics; Differential Equations; Electro and Magnetostatics; Electrodynamics; Linear Algebra for Calculus; Modern Physics; Quantum Mechanics I; Quantum Mechanics II; Statistical Mechanics; Thermodynamics
- Elective Courses: Biophysics; Computational Physics; Neurophysics; Nuclei, Particles and Fields; Physics of Living Systems; Probability and Statistics

## Undergraduate Research

- Supervisor: Professor James Gumbart
- Summary: My undergraduate research in Computational Biophysics, supervised by Dr.
  James Gumbart, focused on simulating the molecular dynamics of the Light Harvesting
  Complex-II using NAMD and VMD.

#### Activities and Awards

- Sigma Pi Sigma Physics Honor Society
- Faculty Honors

## Georgia State University, Atlanta, GA

Initiated my pursuit towards a second degree (in Physics), May 2014 – May 2015. Transferred from Georgia State University (without degree) to the Georgia Institute of Technology

Cumulative GPA: 4.00

- Core Courses: Calculus of One Variable I; Calculus of One Variable II; Multivariate Calculus; Principles of Chemistry I; Principles of Chemistry II; Principles of Physics I; Principles of Physics II
- Elective Courses: Computer Programming in Python

#### Activities and Awards

President's List

### Georgia College, Milledgeville, GA

Bachelor of Arts in Mass Communication, May 2005 – May 2009

### Activities and Awards

- Lambda Pi Eta Honor Society
- National Chair of International Business Club

## REFEREED PUBLICATIONS

[1] E. Seitz, D. McCandlish, J. Kinney and P. Koo, "Interpreting cis-regulatory mechanisms from genomic deep neural networks using surrogate models." Nat Mach Intell, 2024. https://doi.org/10.1038/s42256-024-00851-5

[2] E. Seitz, J. Frank and P. Schwander, "Beyond ManifoldEM: Geometric relationships between manifold embeddings of a continuum of 3D molecular structures and their 2D projections." RSC Digital Discovery, vol. 2, no. 3, pp. 702–717, 2023. https://doi.org/10.1039/D2DD00128D

[3] E. Seitz, F. Acosta-Reyes, S. Maji, P. Schwander and J. Frank, "Recovery of conformational continuum from single-particle cryo-EM images: Optimization of ManifoldEM informed by ground truth." IEEE Trans Comput Imaging, vol. 8, pp. 462-78, 2022. https://ieeexplore.ieee.org/document/9773954

[4] T. Sztain et al., "A glycan gate controls opening of the SARS-CoV-2 spike protein," Nat Chem, vol. 13, pp. 963–8, 2021. https://www.nature.com/articles/s41557-021-00758-3

[5] E. Seitz and J. Frank, "POLARIS: Path of least action analysis on energy landscapes," ACS J Chem Inf Model, vol. 60, no. 5, pp. 2581–90, 2020. https://pubs.acs.org/doi/10.1021/acs.jcim.9b01108

## CONFERENCE TALKS

- [6] E. Seitz, D. McCandlish, J. Kinney and P. Koo. "Decoding the Mechanistic Impact of Genetic Variation on Regulatory Sequences with Deep Learning," Generative and Experimental Perspectives for Biomolecular Design (GEM) Workshop, International Conference on Learning Representations (ICLR), Singapore, April 2025.
  - E. Seitz, D. McCandlish, J. Kinney, and P. Koo. Decoding the Mechanistic Impact of Genetic Variation on Regulatory Sequences with Deep Learning. Workshop on Generative and Experimental Perspectives for Biomolecular Design, International Conference on Learning Representations, April 15, 2025.
  - URL: https://openreview.net/forum?id=PtjMeyHcTt

#### CONFERENCE POSTERS

- [7] E. Seitz, J. Kinney and P. Koo. A surrogate modeling framework for interpreting deep neural networks in functional genomics. The Biology of Genomes, Cold Spring Harbor Laboratory, May 2023.
- [8] E. Seitz, D. McCandlish, J. Kinney and P. Koo. A surrogate modeling framework for interpreting deep neural networks in functional genomics. Genome Informatics, Cold Spring Harbor Laboratory, December 2023.
- [9] E. Seitz, D. McCandlish, J. Kinney and P. Koo. Deciphering the determinants of mechanistic variation in regulatory sequences. Biological Data Science, Cold Spring Harbor Laboratory, November 2024.
- [10] E. Seitz, D. McCandlish, J. Kinney and P. Koo. Deciphering the determinants of mechanistic variation in regulatory sequences. 2025 In-House Symposium, Cold Spring Harbor Laboratory, January 2025.
- [11] E. Seitz, D. McCandlish, J. Kinney and P. Koo. Deciphering the determinants of mechanistic variation in regulatory sequences.
  Probabilistic Modeling in Genomics, Cold Spring Harbor Laboratory, March 2025.

[12] E. Seitz, D. McCandlish, J. Kinney and P. Koo. Decoding the Mechanistic Impact of Genetic Variation on Regulatory Sequences with Deep Learning. Biology of Genomes, Cold Spring Harbor Laboratory, May 2025.

## BOOK CHAPTERS

- [13] E. Seitz, J. Frank, POLARIS: Path of Least Action Analysis on Energy Landscapes. In: J. Frank, Novel Developments in Cryo-EM of Biological Molecules: Resolution in Time and State Space, Jenny Stanford Publishing, ch. 8, pp. 151–175, 2023. ISBN: 9781003456100.
- [14] T. Sztain, S. Ahn, A. Bogetti, L. Casalino, J. Goldsmith, E. Seitz, R. McCool, F. Kearns, F. Acosta-Reyes, S. Maji, G. Mashayekhi, J. McCammon, A. Ourmazd, J. Frank, J. McLellan, L. Chong, R. Amaro, A Glycan Gate Controls Opening of the SARS-CoV-2 Spike Protein. In: J. Frank, *Novel Developments in Cryo-EM of Biological Molecules: Resolution in Time and State Space*, Jenny Stanford Publishing, ch. 11, pp. 241–256, 2023. ISBN: 9781003456100.
- [15] E. Seitz, F. Acosta-Reyes, S. Maji, P. Schwander, J. Frank, Recovery of Conformational Continuum from Single-Particle Cryo-EM Images: Optimization of ManifoldEM Informed by Ground Truth. In: J. Frank, Novel Developments in Cryo-EM of Biological Molecules: Resolution in Time and State Space, Jenny Stanford Publishing, ch. 12, pp. 242–288, 2023. ISBN: 9781003456100.

# OTHER PUBLICATIONS

[16] E. Seitz. Analysis of Conformational Continuum and Free-energy Landscapes from Manifold Embedding of Single-particle Cryo-EM Ensembles of Biomolecules. PhD thesis. Columbia Libraries Academic Commons, 2022. https://doi.org/10.7916/4n0v-wa24

#### **GRANTS**

#### Awarded

[1] F32 Individual Postdoctoral Fellowship, Awarded by the National Human Genome Research Institute of the National Institutes of Health. Award Number: F32HG013265. June 1, 2024 to May 31, 2027.

# Advising and Mentoring

## **Undergraduate Research**

## Nika Chuzhoy

Undergraduate student in Computer Science, California Institute of Technology. Computational research on surrogate modeling for interpreting genomic DNNs (2023)

### **High School Research**

#### • Tinu Yu

High school student attending Syosset High School, NY. Computational research on surrogate modeling for interpreting genomic DNNs (2024)

### TEACHING EXPERIENCE

#### Cold Spring Harbor Laboratory, Cold Spring Harbor, NY

Invited Lecturer March 5, 2025

 "Decoding the Mechanistic Impact of Genetic Variation on Regulatory Sequences with Deep Learning", Quantitative Biology and Artificial Intelligence In-house Seminar Series Invited Lecturer July 19, 2024

• "From Data to Discovery: Navigating Biological Complexity with Interpretable Machine Learning", Bioinformatics and Computational Neuroscience Lecture Series

Invited Lecturer March 6, 2024

• "Deciphering the Regulatory Landscape Encoded by Genomic Deep Neural Networks", Quantitative Biology and Artificial Intelligence In-house Seminar Series

Invited Lecturer July 21, 2023

• "From Data to Discovery: Navigating Biological Complexity with Interpretable Machine Learning", Bioinformatics and Computational Neuroscience Lecture Series

Invited Lecturer April 12, 2023

• "A Surrogate Modeling Framework for Interpreting Deep Neural Networks in Functional Genomics", Quantitative Biology and Artificial Intelligence In-house Seminar Series

## Columbia University, New York, NY

Invited Lecturer November 9, 2021

• Cryo-EM Microscopy Center (CEMC) 2021 Fall Workshop

Teaching Assistant, R1 University

August 2018 – December 2019

- Assistant Instructor for BCHM GU4323: Biophysical Chemistry (Professors: Dr. John Hunt and Dr. Art Palmer)
  - Fall 2019
  - Responsible for weekly 1-hour recitation lecture, proctoring and grading. This course
    covered a rigorous introduction to the theory underlying widely used biophysical
    methods to understand the behavior of molecules and develop related analytical tools,
    including applications to biomedical research problems.
- Grader for BIOL UN2005 Intro Biology: Biochemistry, Genetics & Molecular Biology
  - Fall 2018
  - Proctored and graded exams.

## Georgia Institute of Technology, Atlanta, GA

Creative Director & Animator, R1 University

May 2016 - February 2017

- Assisted the Department of Physics with the design and animation of educational content
  for Georgia Tech MOOC (massive online open courses) under advisement of Dr. Michael
  Schatz. Topics ranged from *Introductory Mechanics* to *Electromagnetism*. Duties included both scientific and artistic, beginning with the translation of physical concepts
  and theories into a visual language, and ending in the full production of animated video
  content for semester-long courses. After initial production, served as project lead on a
  team of animators for creating an extensive library of related videos for the university.
- Lesson 1 Introduction to Electric Fields: https://vimeo.com/237845454

### Georgia State University, Atlanta, GA

Physics Learning Assistant, R1 University

**Spring 2015** 

Recruited into the Learning Assistant program to aid in the education of students taking *Principles of Physics* under advisement of Dr. Joshua Von Korff. Duties included instruction of two one-hour Physics labs each week, attendance of weekly pedagogy lessons taught by Physics professors, and execution of a weekly theoretical practice lecture with graduate students.

### Stanford University, Stanford, CA

Creative Director, Animator

2013, 2015

- Directed a team of animators for creating a series of educational videos detailing scientific research done by Dr. Jennifer Aaker and colleagues at Stanford on topics including empathy, humor, and purpose.
- The Happiness Narrative (2015): https://vimeo.com/210360824
- Persuasion and the Power of Story (2013): https://vimeo.com/74576399

## PROFESSIONAL SERVICE

#### Referee Service

- RECOMB (2024)
- Nature Genetics (2024)
- Nature Genetics (2024)
- Nature (2024)
- Nature (2024)
- The American Journal of Human Genetics (2024)
- ICML AI4Science Workshop (2024)
- Cold Spring Harbor Perspectives in Biology (2023)
- NeurIPS AI4Science Workshop (2023)
- NeurIPS Generative AI and Biology Workshop (2023)
- Nature (2023)
- ICML Workshop on Computational Biology (2023)
- Genome Research (2023)
- Nature Machine Intelligence (2023)
- Journal of Chemical Information and Modeling (2020)

#### **Scientific Illustrations**

- Illustrated journal cover for *JCIM: Special Issue on Frontiers in Cryo-EM Modeling*, Volume 60, Issue 5, May 2020: https://pubs.acs.org/toc/jcisd8/60/5
- Illustrated cover for *Simons Center for Quantitative Biology: 2024 Annual Report*, December 2024: https://www.cshl.edu/wp-content/uploads/2025/01/2024\_SCQB\_Annual\_Report.pdf

# PROFESSIONAL EXPERIENCE

The following are some of my experiences in the arts, previous to my scientific career. More information on each of these, and others in between, is provided in my **LinkedIn** profile

#### 22squared, Atlanta, GA

Editor, Motion Graphics Designer

May 2013 - May 2014

• Designed digital content for major corporate advertising clientele, including Toyota, Baskin-Robbins, PGA Superstore, Buffalo Wild Wings, Costa Rica Tourism Board, and American Standard. (Full-time position).

#### Indigo Studios, Atlanta, GA

Motion Graphics Designer

May 2011 – August 2012

- Created 2D and 3D computer animations for a variety of clients, including American Cancer Society, Coca-Cola, Georgia Pacific, Southern Company, Infiniti, Cirque du Soleil, Caterpillar, ABF, Ariba, Discovery Channel, and Cartoon Network. (Freelance position)
- Awarded 32nd Annual Telly Award (Bronze) for American Cancer Society animation "Marketing Excellence"

#### Fuzebox, Inc., Atlanta, GA

Editor, Motion Graphics Designer

**January 2010 - June 2012** 

• Editor and motion graphics artist on "Submit", a documentary on cyberbullying. Duties included storyboarding, editing, compositing, 2D and 3D animation, and color correction. (Freelance position).

## Georgia Public Broadcasting, Atlanta, GA

Editor, Motion Graphics Designer

**January 2009 - May 2010** 

Supervised post-production activities for daily statewide television broadcasts of "Law-makers", providing in-depth coverage of state legislature and related issues. Responsibilities included creation of original show open, animation of graphics, and editing of news segments. (Freelance position).

## Artistic Honors and Awards, 2012 - 2015

- 2015 "The Happiness Narrative" featured at Future of StoryTelling Summit in NYC
- 2013 "The Power of Story" featured at Future of StoryTelling Summit, NYC
- 2013 Vimeo Staff Pick, "ABCinema: Take 2" (>100,000 views)
- 2013 Vimeo Staff Pick, "Alphagames" (>350,000 views)
- 2012 "ABCinema" featured at SXSW, PauseFest, Athfest, and Tribeca
- 2012 Vimeo Staff Pick, "ABCinema" (>500,000 views)

## ADDITIONAL

## TRAINING

## **Invited Participant**

- CIFAR Deep Learning + Reinforcement Learning Summer School (July 25–29, 2022)
- CSHL Computational Genomics course (Nov. 29–Dec. 6, 2023)

## **General Participant**

- CSHL Mentor Training Workshop based on the curriculum developed by CIMER (June 2023)
- SUNY Old Westbury Undergraduate Teaching and Pedagogy Workshop on course design, active learning, and inclusive teaching (Fall 2023)

# SOFTWARE SKILLS

#### Computer Programming:

- UNIX shell scripting
- Expertise in Python, with significant experience using TensorFlow, PyTorch, NumPy, Scipy, Pandas, Matplotlib, Mayavi, PyQt, TraitsUI and Anaconda, among others
- Experience in Matlab, R

#### Scientific Software:

- UCSF Chimera
- PyMOL
- Visual Molecular Dynamics
- RELION
- Phenix
- Prism
- Mathematica

#### Visualization Software:

- Adobe Illustrator, Photoshop, After Effects (2/2.5D illustration and animation)
- Cinema4D (3D illustration and animation)
- Final Cut Pro (Video editing)

#### Productivity Software:

- TEX (LATEX, BIBTEX),
- · Microsoft Office, Excel, and PowerPoint
- GitHub

## Operating Systems:

- Linux
- Apple OS X

# SOFTWARE DISTRIBUTIONS

- E. Seitz et al., "SEAM Python repository: Systematic explanation of attribution-based mechanisms for regulatory genomics," 2024-2025. https://github.com/evanseitz/seam-nn
  - Read the Docs: https://seam-nn.readthedocs.io
- E. Seitz et al., "SQUID Python repository: Interpreting sequence-based deep learning models for regulatory genomics," Zenodo, 2024.
  - doi:10.5281/zenodo.11060672, https://github.com/evanseitz/squid-nn
  - Read the Docs: https://squid-nn.readthedocs.io
- E. Seitz et al., "ManifoldEM Python repository," Zenodo, 2021. doi: 10.5281/zenodo.5578874, https://github.com/evanseitz/ManifoldEM\_Python
  - Video Demonstration:
    - https://www.dropbox.com/s/pe106oizw4p7uyb/GUI\_Overview\_VATPase.mp4?dl=0

## REFERENCES AVAILABLE TO CONTACT

#### Dr. Peter Koo (e-mail: koo@cshl.edu)

- I am currently working in Dr. Koo's lab as a Computational Postdoctoral Fellow
- Simons Center for Quantitative Biology, Cold Spring Harbor Laboratory, Cold Spring Harbor, NY 11724 USA

#### **Dr. Justin Kinney** (e-mail: jkinney@cshl.edu)

- I am currently working in Dr. Kinney's lab as a Computational Postdoctoral Fellow
- Simons Center for Quantitative Biology, Cold Spring Harbor Laboratory, Cold Spring Harbor, NY 11724 USA

## Dr. David McCandlish (e-mail: mccandlish@cshl.edu)

- I am currently collaborating with Dr. McCandlish during my postdoctoral fellowship
- Simons Center for Quantitative Biology, Cold Spring Harbor Laboratory, Cold Spring Harbor, NY 11724 USA

## **Dr. Joachim Frank** (e-mail: jf2192@cumc.columbia.edu; phone: +1-646-770-4527)

- Dr. Frank was my Ph.D. supervisor
- Department of Biochemistry and Molecular Biophysics, Columbia University Medical Center, New York, NY 10032 USA
- ★ Department of Biological Sciences, Columbia University, New York, NY 10027 USA

#### **Dr. Peter Schwander** (e-mail: pschwan@uwm.edu)

- Dr. Schwander was a member of my Ph.D. dissertation defense committee
- ♦ Department of Physics, University of Wisconsin-Milwaukee, Milwaukee, WI 53211 USA

## Dr. Rommie Amaro (e-mail: ramaro@ucsd.edu)

- Dr. Amaro was a member of my Ph.D. dissertation defense committee
- Department of Chemistry and Biochemistry, University of California-San Diego, La Jolla, CA 92093 USA

#### **Dr. John Hunt** (e-mail: jfh21@columbia.edu)

- Dr. Hunt was a member of my Ph.D. dissertation defense committee
- ♦ Department of Biological Sciences, Columbia University, New York, NY 10027 USA

## **Dr. Liang Tong** (e-mail: ltong@columbia.edu)

- Dr. Tong was a member of my Ph.D. dissertation defense committee
- ♦ Department of Biological Sciences, Columbia University, New York, NY 10027 USA

Additional references available upon request.