

Dr. Evan E. Seitz

CONTACT INFORMATION

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RESEARCH INTERESTS

Complex biophysical systems: quantitative biology; unsupervised machine learning; deep learning; neural networks; kernel methods; dimensionality reduction; manifold embedding; spectral geometry; energy landscapes; algorithm design, development and optimization

CURRENT ACADEMIC APPOINTMENT

Computational Postdoctoral Fellow, Cold Spring Harbor Laboratory

In March 2022, I joined the [Simons Center for Quantitative Biology](#) at Cold Spring Harbor Laboratory as a Computational Postdoctoral Fellow. The research is formed in collaboration between the [Kinney](#) and [Koo](#) labs, with the goal to bridge the divide between "black-box" deep neural network models in genomics and mechanistically interpretable biophysical models of gene regulation.

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](#), Ph.D.
- Affiliations:
 - [Department of Biological Sciences](#)
 - [Department of Biochemistry and Molecular Biophysics](#)
- Summary: My thesis work is based on a geometric machine-learning approach using manifold embedding to obtain the energy landscape and corresponding continuum of 3D structures of a molecular machine. This information comes buried among typically hundreds of thousands of unorganized single-particle cryo-EM images formed under extremely noisy conditions and microscopy aberrations. An ability to obtain the desired information from cryo-EM data has been shown possible on two experimental systems—the 80S ribosome and ryanodine receptor—through a previously-established framework termed ManifoldEM. I first incorporated ManifoldEM into an advanced graphic user interface (+10,000 lines of code) for public release [7], and augmented it with a new method, POLARIS [3], for determining minimum-energy pathways. I next applied ManifoldEM on two new systems: vacuolar ATPase and the SARS-CoV-2 spike protein [4], and for both systems, discovered several novel aspects of the machine's function.

Throughout the development and use of ManifoldEM—including my extensive coding, troubleshooting, and supervision of an alpha-user testing group—our team discovered several critical limitations and uncertainties in the ManifoldEM framework. However, in the absence of ground-truth data, testing and validation of ManifoldEM was infeasible, with its implementation largely understood as a black box. As recourse, I created a protocol for generating simulated cryo-EM data from an atomic model subjected to multiple conformational changes and experimental conditions [6], with several Hsp90 synthetic ensembles generated for analysis by ManifoldEM. Guided by heuristic results of these ground-truth studies, new insights were made into the origin of longstanding ManifoldEM problems, further motivating and informing my development of a new, comprehensive method for correcting them, termed ESPER [5]. The ESPER method operates within the ManifoldEM framework and, as I have shown using both synthetic and experimentally-obtained data, ultimately results in substantial improvements to the

previous work [2]. A thorough description of these accomplishments is available in my thesis [1].

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: Under guidance of Dr. Andrea Califano, I investigated cell regulatory networks using systems biology principles, aimed at understanding tumorigenesis and cellular heterogeneity. Specifically, I applied pre-established algorithms (ARACNE, FIRE) based on information theory, and analyzed their outputs to determine a collection of maximally-informative DNA sequence motifs corresponding to the FOXM1 master-regulator pathway
- **Gautier Lab**, Summer 2017: Under guidance of Dr. Jean Gautier, I employed a diverse set of experimental approaches on *Xenopus* cell-free extracts to investigate the role of genome instability in cancer. This task required the development of crucial wet-lab skills—such as plasma purification, spectrophotometry, electrophoresis, and chromatin immunoprecipitation—which I trained for and applied in order to isolate and analyze specific protein-gene interactions responsible for cellular response to DNA damage.

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.

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**, Ph.D.
- Topic: Computational simulations involving biophysics of proteins and other biomolecules
- Summary: My undergraduate research was done in Computational Biophysics under the advisement of Dr. James Gumbart, with intent to simulate the physical mechanisms underlying processes and organization in living systems on the molecular scale. Of specific interest was the Light Harvesting Complex-II, the pigment-protein complex responsible for the initiation of photosynthetic processes within the chromatophores of purple bacteria. Programming was done through the structural analysis programs NAMD and VMD, with a computer model of the LH-II produced capable of accurately simulating the molecular dynamics of the system.

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

PUBLICATIONS

Doctoral Thesis

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

Journal Publications

- [2] E. Seitz, D. McCandlish, J. Kinney and P. Koo, "Interpreting cis-regulatory mechanisms from genomic deep neural networks using surrogate models." bioRxiv, 2023.
<https://doi.org/10.1101/2023.11.14.567120>
- [3] 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>
- [4] 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>
- [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>
- [6] 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>

Software Distributions

- [7] 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

CONFERENCES

Posters

- [8] 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.

ADVISING AND MENTORING

Undergraduate Research

- **Nika Chuzhoy**
Undergraduate student in Computer Science, California Institute of Technology. Computational research on surrogate modeling in functional genomics. 2023

TEACHING EXPERIENCE

Cold Spring Harbor Laboratory, Cold Spring Harbor, NY

Guest Lecturer

July 21, 2023

- Bioinformatics and Computational Neuroscience Lecture Series

Columbia University, New York, NY

Teaching Assistant

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

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

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

- Oversaw artistic vision for a series of animations detailing scientific research done by [Dr. Jennifer Aaker](#) and colleagues at Stanford on topics including empathy, humor, and purpose. Responsibilities included storyboarding, creation of animated assets, and unification of artistic vision as it related to the use of visual elements, artistic style, and motion to elicit the relevant emotional responses required to inspire positive change.
- The Happiness Narrative (2015): <https://vimeo.com/210360824>
- Persuasion and the Power of Story (2013): <https://vimeo.com/74576399>

PROFESSIONAL
SERVICE

Referee Service

- *Journal of Chemical Information and Modeling* (2020)
- *Nature Machine Intelligence* (2023)
- *Genome Research* (2023)
- *ICML Workshop on Computational Biology* (2023)
- *Nature*(2023)
- *NeurIPS Generative AI and Biology Workshop*(2023)
- *NeurIPS AI4Science Workshop*(2023)

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>

PROFESSIONAL
EXPERIENCE

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

Related 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)

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, including libraries: Anaconda, NumPy, Scipy, Pandas, Matplotlib, Mayavi, PyQt, TraitsUI, TensorFlow; among others
- Experience in Matlab, R

Scientific Software:

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

Visualization Software:

- Adobe Creative Suite: Illustrator, Photoshop, After Effects
- GIMP
- Cinema4D
- Final Cut Pro

Productivity Software:

- T_EX (L^AT_EX, B^BT_EX),
- Microsoft Office, Excel, and PowerPoint
- GitHub

Operating Systems:

- Apple OS X
- Linux
- Microsoft Windows family

REFERENCES
AVAILABLE TO
CONTACT

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. 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

Additional references available upon request.