# Evan E. Seitz

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# Summary

Computational biologist with expertise in interpretable machine learning for regulatory genomics and structural biology, seeking research-focused roles that bridge deep learning and biology.

### Education

**PhD in Biological Sciences**, with Distinction – Columbia University Departments of Biological Sciences & Biochemistry and Molecular Biophysics

MPhil and MA – Columbia University

BS in Physics, with Highest Honors – Georgia Institute of Technology
BA in Mass Communication – Georgia College

# Experience

Cold Spring Harbor Laboratory, Postdoctoral Fellow with Drs. Peter Koo and Justin Kinney
Simons Center for Quantitative Biology

Mar 2022 – Present

Developed a surrogate modeling framework—SQUID—to mechanistically interpret deep neural networks trained on genomic data, enabling robust dissection of cis-regulatory logic in high-throughput functional assays.

- Modeled additive and higher-order interactions between sequence features while removing confounding effects from nonlinearities and experimental noise using shallow neural networks as interpretable surrogates.
- Demonstrated that this framework identifies more consistent motifs across genomic loci and improves singlenucleotide variant effect prediction, outperforming established attribution methods like DeepSHAP.

Invented a meta-explainability framework—SEAM—that systematically investigates how mutations reshape regulatory mechanisms, enabling interpretable insights into mutational effects on gene regulation.

- Enabled systematic and unbiased exploration of the reprogrammability of cis-regulatory mechanisms
- Revealed the remarkable evolvability of human regulatory elements, disentangled transcription factor-specific effects from broader sequence context, and advanced decoding of the cis-regulatory code
- Illuminated evolutionary trajectories and supported the rational design of synthetic regulatory sequences

Columbia University, PhD Researcher with Nobel laureate Dr. Joachim Frank Departments of Biological Sciences & Biochemistry and Molecular Biophysics

2017 - 2022

Invented a geometric machine learning method—ESPER—to interpret latent manifolds derived from cryo-EM ensembles of macromolecular complexes, enabling accurate reconstruction of 3D structures across the free-energy landscape.

- Improved the interpretability of spectral embeddings by introducing a novel eigenbasis realignment procedure that extracts conformational degrees of freedom along eigenfunctions of the Laplace–Beltrami operator.
- Enabled reconstruction of conformational continua and free-energy landscapes in key biomolecular systems, including the 80S ribosome, V-ATPase, and SARS-CoV-2 Spike protein.

### Awards

NIH F32 Postdoctoral Fellowship, National Human Genome Research Institute (F32HG013265), 2024–2027 John S. Newberry Prize, Columbia University, 2022 — most promising PhD student by faculty nomination PhD with Distinction, Columbia University, 2022 — dissertation excellence by thesis committee nomination

BS with Highest Honors, Georgia Institute of Technology, 2017 — awarded for minimum GPA of 3.55 (3.74) Sigma Pi Sigma, National Physics Honor Society

### Skills

- Supervised and unsupervised learning, deep neural networks, convolutional neural networks, surrogate modeling, attribution analysis, global interpretability, explainable AI (XAI), meta-explainability, data visualization, dimensionality reduction, manifold learning, data wrangling/munging
- Python, Tensorflow, PyTorch, Bash, High Performance Computing, LaTeX, NumPy, SciPy, Pandas, Conda, GitHub, ReadTheDocs, UCSF Chimera, PyMOL, VMD, RELION, Phenix, Adobe Illustrator, Adobe After Effects, Adobe Photoshop, Cinema4D, Matplotlib, Mayavi

## **Select Publications**

Seitz et al., ICLR GEM Workshop, 2025 — Decoding the mechanistic impact of genetic variation with deep learning. Seitz et al., Nat Mach Intell, 2024 — Interpreting genomic deep neural networks using surrogate models. Seitz et al., RSC Digital Discovery, 2023 — Geometric relationships between manifolds of cryo-EM conformers. Seitz et al., IEEE Trans Comput Imaging, 2022 — Recovery of cryo-EM conformations using manifold embedding. Sztain et al., Nat Chem, 2021 — Conformational mapping of the SARS-CoV-2 spike protein receptor binding domain.

A complete publication list is available on my Google Scholar profile.

# **Presentations**

Talks: ICLR GEM Workshop (2025), Quantitative Biology and AI In-house Seminar Series (2023–2025), Bioinformatics and Computational Neuroscience Lecture Series (2023, 2024), Cryo-EM Microscopy Center Fall Workshop (2021) Posters: CSHL Biology of Genomes (2023, 2025), Genome Informatics (2023), Biological Data Science (2024), Probabilistic Modeling in Genomics (2025) and In-House Symposium (2024, 2025)

# Teaching and Mentoring

#### Teaching Assistant, Columbia University

2018-2019

BCHM GU4323: Biophysical Chemistry — Recitation instructor (Prof. John Hunt and Prof. Art Palmer)

### Learning Assistant, Georgia State University

Spring 2015

PHYS 1111K: Introductory Physics — Lab instructor (Prof. Joshua Von Korff)

# **Educational Media and Animation**

Georgia Institute of Technology — Creative Director for physics MOOCs (Prof. Michael Schatz, 2016–2017) Stanford University — Creative Director for behavioral science education (Prof. Jennifer Aaker, 2013–2015)

## Undergraduate Research Advisor

2023

Nika Chuzhoy (Computer Science, Caltech) — Research on surrogate modeling for interpreting genomic DNNs

### **High School Research Mentor**

2024

Tinu Yu (Syosset High School, NY) — Research on surrogate modeling for interpreting genomic DNNs

#### Referee Service

2024: Nature (×2), Nature Genetics (×2), American Journal of Human Genetics, RECOMB, ICML AI4Science 2023: Nature, Nature Machine Intelligence, Genome Research, Cold Spring Harbor Perspectives in Biology, NeurIPS AI4Science Workshop, NeurIPS Generative AI and Biology Workshop, ICML Workshop on Computational Biology 2020: Journal of Chemical Information and Modeling