# 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

March 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 single-nucleotide 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 unbiased discovery of mutations poised to reprogram cis-regulatory mechanisms and function.
- Disentangled co-occurring regulatory elements from broader sequence context and revealed epistatic interactions between them—insights inaccessible to conventional attribution or mutagenesis tools.
- 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

May 2017 – February 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 — awarded to the most promising PhD student, Columbia University, 2022 PhD with Distinction — awarded for dissertation excellence by faculty committee, Columbia University, 2022

BS with Highest Honors — top distinction for academic excellence in physics (GPA 3.74/4), Georgia Tech, 2017 Sigma Pi Sigma — National Physics Honor Society

#### Skills

- Supervised learning: Deep neural networks, convolutional neural networks, nonlinear regression
- Unsupervised learning: Dimensionality reduction, spectral methods, manifold learning, latent space analysis
- Model interpretability: Explainable AI (XAI), attribution analysis, surrogate modeling, meta-explainability, global importance analysis, high-dimensional data visualization
- Computational tools:

Languages and frameworks — Python, Bash, LaTeX, TensorFlow, PyTorch, NumPy, SciPy, Pandas, Conda Development and reproducibility — GitHub, ReadTheDocs, HPC environments

Molecular modeling — UCSF Chimera, PyMOL, VMD, RELION, Phenix

Visualization and media — Adobe Creative Suite, Cinema4D, Final Cut Pro, 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