# Jeffrey Ruffolo, PhD

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#### Professional <sup>2024</sup> **Profluent Bio**, Head of Protein Design Building and leading team of protein design scientists. **Profluent Bio**, Machine Learning Scientist Contributed to OpenCRISPR initiative, aimed at designing a novel Cas9-like nuclease protein for genome editing applications. Developed structure-conditioned language model (proseLM) for usage across diverse design projects. <u>2022</u> **Ably Bio**, Founder and CEO 2023 Co-founded company to apply machine learning methods to therapeutic antibody design. Won Microsoft Innovation Acceleration Award. Accepted into Microsoft for Startups program. 2022 Generate: Biomedicines, Machine Learning Scientist Intern Developed diffusion models for protein complex prediction. 2019 Microsoft, Software Engineer Intern Developed efficient process for migrating large quantities of user metadata for the Microsoft Reworked architecture of globally-distributed metadata storage service to reduce load in hightraffic regions and increase resiliency to bursts of increased demand. 2018 Microsoft, Software Engineer Intern Developed initial implementation of GraphQL service layer, providing backend service abstraction for Microsoft Teams product. Built representative metrics for analyzing performance impact resulting from additional layer between client and distributed services. 2017 IBM, Software Developer Intern Performed exploratory analysis of Spring web framework and its compatibility with IBM Cloud Published ten articles on official IBM Cloud blog, aimed at providing support for Spring community and establishing IBM Cloud as a preferred choice for enterprise Java development. Education 2019 Doctor of Philosophy, Johns Hopkins University, Baltimore, MD 2023 **Program** Molecular Biophysics

Advised by Prof. Jeffrey Gray and Prof. Jeremias Sulam

Bachelor of Science, University of Missouri, Columbia, MO

Johns Hopkins-AstraZeneca Scholar

Summa Cum Laude (GPA 3.979)

Minor in Mathematics

Majors Biochemistry, Computer Science

2019

## Research

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Graduate Student, Johns Hopkins University

- Adviser Prof. Jeffrey Gray
- Developed first deep learning methods for antibody  $F_V$  structure prediction (DeepH3, DeepAb), which significantly improved performance on the critical CDR H3 loop over prior approaches.
- Developed antibody-specific language models for representation learning and synthetic library
- Developed fast, accurate method for antibody structure prediction (IgFold), leveraging 558M natural antibody sequences.

#### **Graduate Student**, Johns Hopkins University

- Adviser Prof. Jeremias Sulam
- Applied protein language models and weakly supervised learning to identify specific antibodies within immune repertoires.

# Johns Hopkins-AstraZeneca Scholar, AstraZeneca

- Adviser Dr. Gilad Kaplan
- Experimentally validated designed antibodies and received industry mentorship as part of joint training program between Johns Hopkins and AstraZeneca.

#### Undergraduate Researcher, University of Missouri

- Adviser Prof. Yi Shang
- Developed TPCref, a method for refinement of protein contact-map predictions using the results of predictions by the same method on template structures.

#### **Undergraduate Researcher**, *University of Missouri*

- Adviser Prof. Andrew McClellan
- Used parallel dual-annealing exploration strategy to demonstrate that diverse combinations of parameters can produce realistic neuronal behavior for a multi-compartmental neuron model.

### **Publications**



2015

2019

Sai Pooja Mahajan, Fátima A Davila-Hernandez, Jeffrey A Ruffolo, and Jeffrey J Gray. "How well do contextual protein encodings learn structure, function, and evolutionary context?" Cell Systems (2025)

Jason Yang, Aadyot Bhatnagar, Jeffrey A Ruffolo, and Ali Madani. "Conditional enzyme generation using protein language models with adapters". arXiv (2024)

2024

Jeffrey A Ruffolo, Aadyot Bhatnagar, Joel Beazer, Stephen Nayfach, Jordan Russ, Emily Hill, Riffat Hussain, Joseph Gallagher, and Ali Madani. "Adapting protein language models for structure-conditioned design". bioRxiv (2024)

2024

Jeffrey A Ruffolo\*, Stephen Nayfach\*, Joseph Gallagher\*, Aadyot Bhatnagar\*, Joel Beazer, Riffat Hussain, Jordan Russ, Jennifer Yip, Emily Hill, Martin Pacesa, Alexander J Meeske, Peter Cameron, and Ali Madani. "Design of highly functional genome editors by modeling the universe of CRISPR-Cas sequences". bioRxiv (2024)

2024

Jeffrey A Ruffolo and Ali Madani. "Designing proteins with language models". Nature Biotechnology (2024)

2024

Lee-Shin Chu, Ruffolo, Jeffrey A, Ameya Harmalkar, and Jeffrey J Gray. "Flexible protein-protein docking with a multitrack iterative transformer". Protein Science (2024)

2023

Mark Hutchinson\*, Jeffrey A Ruffolo\*, Nantaporn Haskins, Michael Iannotti, Giuliana Vozza, Tony Pham, Nurjahan Mehzabeen, Harini Shandilya, Keith Rickert, Rebecca Croasdale-Wood, Melissa Damschroder, Ying Fu, Andrew Dippel, Jeffrey J. Gray, and Gilad Kaplan. "Enhancement of antibody thermostability and affinity by computational design in the absence of antigen". bioRxiv (2023)

2023

Alex Morehead, Jeffrey A Ruffolo, Aadyot Bhatnagar, and Ali Madani. "Towards Joint Sequence-Structure Generation of Nucleic Acid and Protein Complexes with SE(3)-Discrete Diffusion". Arxiv (2023)

2023	Michael F Chungyoun, <b>Jeffrey A Ruffolo</b> , and Jeffrey J. Gray. "FLAb: Benchmarking deep learning methods for antibody fitness prediction". <i>bioRxiv</i> (2023)
2023	Erik Nijkamp*, <b>Jeffrey A Ruffolo</b> *, Eli N. Weinstein, Nikhil Naik, and Ali Madani. "ProGen2: Exploring the Boundaries of Protein Language Models". <i>Cell Systems</i> (2023)
2023	Richard W. Shuai*, <b>Jeffrey A Ruffolo*</b> , and Jeffrey J. Gray. "IgLM: infilling language modeling for antibody sequence design". <i>Cell Systems</i> (2023)
2023	<b>Jeffrey A Ruffolo</b> , Lee-Shin Chu, Sai Pooja Mahajan, and Jeffrey J. Gray. "Fast, accurate antibody structure from deep learning on massive set of natural antibodies". <i>Nature Communications</i> (2023)
2022	Sai Pooja Mahajan, <b>Jeffrey A Ruffolo</b> , Rahel Frick, and Jeffrey J. Gray. "Hallucinating structure-conditioned antibody libraries for target-specific binders". <i>Frontiers in Immunology</i> (2022)
2022	Seth D. Ludwig*, Zachart J. Bernstein*, Christian Agatemor, Kris Dammen-Brower, <b>Jeffrey Ruffolo</b> , Jonah M. Rosas, Jeremey D. Post, Robert N. Cole, Kevin J. Yarema, and Jamie B. Spangler. "A versatile design platform for glycoengineering therapeutic antibodies". <i>mAbs</i> (2022)
2022	Deniz Akpinaroglu, <b>Jeffrey A Ruffolo</b> , Sai Pooja Mahajan, and Jeffrey J. Gray. "Simultaneous prediction of antibody backbone and side-chain conformations with deep learning". <i>PLOS One</i> (2022)
2022	<b>Jeffrey A Ruffolo</b> , Jeremias Sulam, and Jeffrey J. Gray. "Antibody structure prediction using interpretable deep learning". <i>Patterns</i> (2022)
2021	<b>Jeffrey A Ruffolo</b> , Jeffrey J. Gray, and Jeremias Sulam. "Deciphering antibody affinity maturation with language models and weakly supervised learning". <i>arXiv</i> (2021)
2020	<b>Jeffrey A Ruffolo</b> and Andrew D. McClellan. "Modeling of lamprey reticulospinal neurons: multiple distinct parameter sets yield realistic simulations". <i>Journal of Neurophysiology</i> (2020)
2020	<b>Jeffrey A Ruffolo</b> , Carlos Guerra, Sai Pooja Mahajan, Jeremias Sulam, and Jeffrey J. Gray. "Geometric potentials from deep learning improve prediction of CDR H3 loop structures". <i>Bioinformatics</i> (2020)
2019	<b>Jeffrey A Ruffolo</b> , Zhaoyu Li, and Yi Shang. "MUFold-Contact and TPCref: New Methods for Protein Structure Contact Prediction and Refinement". <i>IEEE International Conference on Bioinformatics and Biomedicine</i> (2019)
	Invited Talks
2025	BioLogic Summit, San Diego, CA, USA  - "Steering protein language models for functional protein design"  - January 14, 2025
2024	<ul> <li>Stanford AI + Biomedicine Seminar, San Diego, CA, USA</li> <li>"OpenCRISPR: Design of highly functional genome editors by modeling the universe of CRISPR-Cas sequences"</li> <li>July 23, 2024</li> </ul>
2024	<ul> <li>PEGS Boston, Boston, MA, USA</li> <li>"Design of highly functional genome editors by modeling the universe of CRISPR-Cas proteins"</li> <li>May 17, 2024</li> </ul>
2024	ML Protein Engineering Seminar Series, Virtual  - "Design of highly functional genome editors by modeling the universe of CRISPR-Cas proteins"  - May 7, 2024  - Video recording
2023	<ul><li>PEGS Europe, Lisbon, Portugal</li><li>"Generative modeling for functional protein design"</li><li>November 15, 2023</li></ul>

2023	GSK Seminar, Virtual
	<ul><li>- "Harnessing immune repertoire data for antibody understanding and design"</li><li>- February 28, 2023</li></ul>
2022	iReceptor+ Seminar Series, Virtual
	- "Language models for protein generation and fitness prediction"
	<ul><li>September 22, 2022</li><li>Video recording</li></ul>
2022	Absci Invites, Virtual
	- "Fast, accurate antibody structure prediction from deep learning on massive set of natural
	antibodies"
	<ul><li>May 26, 2022</li><li>Video recording</li></ul>
2022	Boston Protein Modeling and Design Club, Virtual
	<ul> <li>"Learning from natural antibodies for sequence generation and fast structure prediction"</li> </ul>
	- March 2, 2022
	<ul> <li>Video recording</li> </ul>
	Presentations
2024	RosettaCon, Oral
	- "Steering protein language models for functional protein design"
	- Jeffrey A. Ruffolo
2023	Computational Design and Modeling of Biomolecules, Poster
	- "Harnessing immune repertoire data for antibody understanding and design"
2022	<ul> <li>Jeffrey A. Ruffolo, Richard W. Shuai, Jeremias Sulam, Jeffrey J. Gray</li> <li>RosettaCon, Oral</li> </ul>
	- "Language models for protein generation and fitness prediction"
	- Jeffrey A. Ruffolo
2022	Biophysical Society Annual Meeting, Oral
	<ul> <li>"Fast, accurate antibody structure prediction from deep learning on massive set of natural antibodies"</li> </ul>
	<ul> <li>Jeffrey A. Ruffolo and Jeffrey J. Gray</li> </ul>
2021	Antibody Engineering & Therapeutics (The Antibody Society), Poster
	<ul> <li>"Antibody structure prediction using interpretable deep learning"</li> </ul>
2021	- Jeffrey A. Ruffolo, Jeremias Sulam, and Jeffrey J. Gray
	<ul> <li>Machine Learning for Structural Biology (NeurIPS workshop), Oral</li> <li>"Deciphering antibody affinity maturation with language models and weakly supervised learning"</li> </ul>
	<ul> <li>Jeffrey A. Ruffolo, Jeffrey J. Gray, and Jeremias Sulam</li> </ul>
2021	<ul> <li>Video recording</li> </ul>
2021	Machine Learning for Structural Biology (NeurIPS workshop), Poster
	<ul> <li>"Generative language modeling for antibody design"</li> <li>Richard Shuai, Jeffrey A. Ruffolo, and Jeffrey J. Gray</li> </ul>
2021	Winter RosettaCon, Poster
	<ul> <li>"Improved antibody structure prediction using repertoire sequence data and neural attention"</li> </ul>
2020	<ul> <li>Jeffrey A. Ruffolo, Jeremias Sulam, and Jeffrey J. Gray</li> </ul>
2020	Computational Drug Discovery & Development for Biologics Summit, Poster
	<ul> <li>"Deep learning improves prediction of antibody CDR H3 loop structures"</li> <li>Jeffrey A. Ruffolo, Sai Pooja Mahajan, Jeremias Sulam, and Jeffrey J. Gray</li> </ul>
2020	RosettaCon, Oral
	- "Geometric potentials from deep learning improve prediction of CDR H3 Loop structures"
2020	- <b>Jeffrey A. Ruffolo</b> , Carlos Guerra, Sai Pooja Mahajan, Jeremias Sulam, and Jeffrey J. Gray
2020	Intelligent Systems for Molecular Biology, Oral
	<ul> <li>"Geometric potentials from deep learning improve prediction of CDR H3 Loop structures"</li> <li>Jeffrey A. Ruffolo, Carlos Guerra, Sai Pooja Mahajan, Jeremias Sulam, and Jeffrey J. Gray</li> </ul>
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## MU Undergraduate Research Forum, Poster

- "Computer model of reticulospinal neurons in the lamprey"
  Jeffrey A. Ruffolo and Andrew D. McClellan

2016

# MU Undergraduate Research Forum, Poster

- "User-friendly computer model of reticulospinal neurons in the lamprey"
- Jeffrey A. Ruffolo and Andrew D. McClellan