Jeffrey Ruffolo

Berkeley, CA, USA jeffreyruffolo.com github.com/jeffreyruffolo linkedin.com/in/jeffreyruffolo

Professional ²⁰²⁴Profluent 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. **Ably Bio**, Founder and CEO 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 Teams product. 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 **Program** Molecular Biophysics Advised by Prof. Jeffrey Gray and Prof. Jeremias Sulam Johns Hopkins-AstraZeneca Scholar Bachelor of Science, University of Missouri, Columbia, MO

Research

Minor in Mathematics

Majors Biochemistry, Computer Science

Summa Cum Laude (GPA 3.979)

2019



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 design.
- Developed fast, accurate method for antibody structure prediction (IgFold), leveraging 558M natural antibody sequences.

2020

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.

2015

Undergraduate Researcher, *University of Missouri*

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

2024

2024

2024

2023

Publications

- Jason Yang, Aadyot Bhatnagar, **Jeffrey A Ruffolo**, and Ali Madani. "Conditional enzyme generation using protein language models with adapters". In: *arXiv* (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". In: *bioRxiv* (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". In: bioRxiv (2024)
- Jeffrey A Ruffolo and Ali Madani. "Designing proteins with language models". In: Nature Biotechnology (2024)
 - Lee-Shin Chu, **Ruffolo**, **Jeffrey A**, Ameya Harmalkar, and Jeffrey J Gray. "Flexible protein–protein docking with a multitrack iterative transformer". In: *Protein Science* (2024)
 - 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". In: *bioRxiv* (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". In: *Arxiv* (2023)
 - Michael F Chungyoun, **Jeffrey A Ruffolo**, and Jeffrey J. Gray. "FLAb: Benchmarking deep learning methods for antibody fitness prediction". In: *bioRxiv* (2023)
- Sai Pooja Mahajan, **Jeffrey A Ruffolo**, and Jeffrey J Gray. "Contextual protein and antibody encodings from equivariant graph transformers". In: *bioRxiv* (2023)



2022	Absci Invites, Virtual
	$$ $$ $$ $$ $$ $$ $$ $$ $$
	antibodies"
	- May 26, 2022
2022	- Video recording
	Boston Protein Modeling and Design Club, Virtual
	 "Learning from natural antibodies for sequence generation and fast structure prediction" March 2, 2022
	- Video recording
	video recording
	Presentations
2023	
2023	Computational Design and Modeling of Biomolecules, Poster
	- "Harnessing immune repertoire data for antibody understanding and design"
2022	- Jeffrey A. Ruffolo, Richard W. Shuai, Jeremias Sulam, Jeffrey J. Gray
	Summer Rosetta Conference, Oral
	 "Language models for protein generation and fitness prediction" Jeffrey A. Ruffolo
2022	•
•	Biophysical Society Annual Meeting, <i>Oral</i> - "Fast, accurate antibody structure prediction from deep learning on massive set of natural
	antibodies"
	- Jeffrey A. Ruffolo and Jeffrey J. Gray
2021	Antibody Engineering & Therapeutics (The Antibody Society), Poster
	 "Antibody structure prediction using interpretable deep learning"
	- Jeffrey A. Ruffolo , Jeremias Sulam, and Jeffrey J. Gray
2021	Machine Learning for Structural Biology (NeurIPS workshop), Oral
	- "Deciphering antibody affinity maturation with language models and weakly supervised learning"
	 Jeffrey A. Ruffolo, Jeffrey J. Gray, and Jeremias Sulam
2021	 Video recording
2021	Machine Learning for Structural Biology (NeurIPS workshop), Poster
	- "Generative language modeling for antibody design"
2021	- Richard Shuai, Jeffrey A. Ruffolo , and Jeffrey J. Gray
2021	Winter Rosetta Conference, Poster
	- "Improved antibody structure prediction using repertoire sequence data and neural attention"
2020	- Jeffrey A. Ruffolo, Jeremias Sulam, and Jeffrey J. Gray
	Computational Drug Discovery & Development for Biologics Summit, Poster
	 "Deep learning improves prediction of antibody CDR H3 loop structures" Jeffrey A. Ruffolo, Sai Pooja Mahajan, Jeremias Sulam, and Jeffrey J. Gray
2020	Summer Rosetta Conference, Oral
•	- "Geometric potentials from deep learning improve prediction of CDR H3 Loop structures"
	 Jeffrey A. Ruffolo, Carlos Guerra, Sai Pooja Mahajan, Jeremias Sulam, and Jeffrey J. Gray
2020	Intelligent Systems for Molecular Biology, Oral
	 "Geometric potentials from deep learning improve prediction of CDR H3 Loop structures"
	 Jeffrey A. Ruffolo, Carlos Guerra, Sai Pooja Mahajan, Jeremias Sulam, and Jeffrey J. Gray
2017	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
	Software
2022	IgFold
• —	- Fast, accurate antibody structure prediction from deep learning on massive set of natural

antibodies.

- https://github.com/Graylab/IgFold

4/5



Gamma Chapter