Research Assistant Position at Shakhnovich Lab, Harvard University

Topic: *Predicting and Safeguarding Protein Evolution in the Age of AI*

Context and Objective:
With AI breakthroughs in molecular biology such as AlphaFold and ESM, new possibilities in protein design have been unlocked. We are an interdisciplinary team that uses statistical mechanics, mathematical modeling, and various **AI tools** to investigate the complex dynamics of **protein evolution**, with an eye toward **biosecurity**. Our goal is twofold:

1. To develop predictive tools that assess **how mutations alter the biophysical properties** of proteins and, consequently, impact protein fitness.
2. To safeguard emerging protein design and prediction technologies against **biosecurity risks**.

Physically, we use statistical mechanics and machine learning to model the fitness landscape of viruses based on its biophysical properties such as folding energy and antibody evasion.[1] Computationally, we integrate state-of-the-art protein language models[2,3] with biophysical priors[4] to learn and predict these biophysical properties, as well as safeguarding these capabilities.[5] Mathematically, we model the evolutionary dynamics to explore the trajectories of viral protein evolution.[6]

We are seeking talented scholars to study one or more of the following topics:

- Developing **machine learning** methods for **protein function prediction**
- Developing **safeguards** for **protein design tools**
- Research on **mechanistic interpretability** for prediction models

Selected scholars will have the opportunity to meet regularly with Prof. Shakhnovich and collaborate closely with senior PhD students, postdoctoral researchers, and industry leaders. Scholars are also encouraged to pursue their own independent projects

Qualifications:

1. Have a good understanding of thermodynamics and/or protein biophysics, or be able to absorb concepts quickly
2. Pursuing or having a degree in Applied Math, Computer Science,Computational Biology, Physics, Bioinformatics, or a related field. Successful candidates usually have an interdisciplinary background or skill sets. Prior experience with modeling, and machine learning is a plus
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5. Be able to commit to **at least 4 months** of in-person work, a longer commitment more than 6 months is preferable

Supervisor: Prof. Eugene Shakhnovich, Department of Chemistry and Chemical Biology, Harvard University

Funding and resources: Financial support is currently ***NOT*** available for non-Harvard students because of regulation changes. While there is a chance the policy might change, interns should secure their own funding. Interns will have access to all Harvard facilities and resources as visiting scholars.

Application materials: Please email your English CV, transcripts and a brief description of your background and interests to shakhnovichlab@gmail.com, CC Prof. Shakhnovich at shakhnovich@chemistry.harvard.edu. Please also include your intended time of visiting. Offers will be granted on a rolling basis.

References:

[1] Wang, Dianzhuo, et al. "Biophysical principles predict fitness of SARS-CoV-2 variants" PNAS (2024)
[2] Hie, Brian, et al. "Learning the language of viral evolution and escape" Science (2021)
[3] Han, Wenkai, et al. "Predicting the antigenic evolution of SARS-COV-2 with deep learning" Nature Communications (2023)
[4] Bussi, Giovanni, et al. “Using metadynamics to explore complex free-energy landscapes” Nature Review Physics (2020)
[5] Wang, Dianzhuo, et al. “ Without Safeguards, AI-Biology Integration Risks Accelerating Future Pandemics”
[6] Di Bari, Leonardo, et al. “Emergent time scales of epistasis in protein evolution”, biorxiv (2024)