



Theory Research Assistant Position at Shakhnovich Lab, Harvard University

Topic: Protein Evolution Through Modeling, Simulation and Machine Learning

Context and Objective:

In the wake of the COVID-19 pandemic, the need to comprehend viral protein evolution has never been greater. We are an interdisciplinary team that uses statistical mechanics, mathematical modeling, and various machine learning methods to investigate the complex dynamics of protein evolution. We aim to develop predictive tools that assess how mutations alter the biophysical properties of proteins and, consequently, impact protein fitness. Physically, we use statistical mechanics to model the fitness landscape on 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 molecular dynamics⁴ (MD) to predict these biophysical properties. Mathematically, we model the evolutionary dynamics to explore the trajectories of viral protein escape.⁵

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

- Developing **machine learning** methods for **protein function prediction**
- Developing **physical based methods** for **protein binding prediction**
- Developing **mathematical models** for viral **trajectories sampling and prediction**

Selected scholars can meet regularly with Prof. Shakhnovich and will be working with a group of senior PhD students and postdocs. Scholars are encouraged to explore their own project.

Qualifications:

1. Have a basic understanding of thermodynamics and protein biophysics, or be able to absorb concepts quickly
2. Pursuing or having a degree in Applied Math, Computer Science, Computational Biology, Physics, Bioinformatics, Chemistry or a related field. Successful candidates usually have an interdisciplinary background or skill sets. Prior experience with modeling, MD simulation and/or machine learning is a plus
3. Be proficient in programming in Python or other languages
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. Non-Harvard interns will have access to 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] Di Bari, Leonardo, et al. "Emergent time scales of epistasis in protein evolution", biorxiv (2024)