Stanford

Grant M. Rotskoff

Assistant Professor of Chemistry

Bio

BIO

Grant Rotskoff studies the nonequilibrium dynamics of living matter with a particular focus on self-organization from the molecular to the cellular scale. His work involves developing theoretical and computational tools that can probe and predict the properties of physical systems driven away from equilibrium. Recently, he has focused on characterizing and designing physically accurate machine learning techniques for biophysical modeling. Prior to his current position, Grant was a James S. McDonnell Fellow working at the Courant Institute of Mathematical Sciences at New York University. He completed his Ph.D. at the University of California, Berkeley in the Biophysics graduate group supported by an NSF Graduate Research Fellowship. His thesis, which was advised by Phillip Geissler and Gavin Crooks, developed theoretical tools for understanding nonequilibrium control of the small, fluctuating systems, such as those encountered in molecular biophysics. He also worked on coarsegrained models of the hydrophobic effect and self-assembly. Grant received an S.B. in Mathematics from the University of Chicago, where he became interested in biophysics as an undergraduate while working on free energy methods for large-scale molecular dynamics simulations.

Research Summary

My research focuses on theoretical and computational approaches to "mesoscale" biophysics. Many of the cellular phenomena that we consider the hallmarks of living systems occur at the scale of hundreds or thousands of proteins. Processes like the self-assembly of organelle-sized structures, the dynamics of cell division, and the transduction of signals from the environment to the machinery of the cell are not macroscopic phenomena—they are the result of a fluctuating, nonequilibrium dynamics. Experimentally probing mesoscale systems remains extremely difficult, though it is continuing to benefit from advances in cryo-electron microscopy and super-resolution imaging, among many other techniques. Predictive and explanatory models that resolve the essential physics at these intermediate scales have the power to both aid and enrich the understanding we are presently deriving from these experimental developments.

Major parts of my research include:

1. Dynamics of mesoscale biophysical assembly and response.— Biophysical processes involve chemical gradients and time-dependent external signals. These inherently nonequilibrium stimuli drive supermolecular organization within the cell. We develop models of active assembly processes and protein-membrane interactions as a foundation for the broad goal of characterizing the properties of nonequilibrium biomaterials.

2. Machine learning and dimensionality reduction for physical models.— Machine learning techniques are rapidly becoming a central statistical tool in all domains of scientific research. We apply machine learning techniques to sampling problems that arise in computational chemistry and develop approaches for systematically coarse-graining physical models. Recently, we have also been exploring reinforcement learning in the context of nonequilibrium control problems.

3. Methods for nonequilibrium simulation, optimization, and control.— We lack well-established theoretical frameworks for describing nonequilibrium states, even seemingly simple situations in which there are chemical or thermal gradients. Additionally, there are limited tools for predicting the response of nonequilibrium systems to external perturbations, even when the perturbations are small. Both of these problems pose key technical challenges for a theory of active biomaterials. We work on optimal control, nonequilibrium statistical mechanics, and simulation methodology, with a particular interest in developing techniques for importance sampling configurations from nonequilibrium ensembles.

ACADEMIC APPOINTMENTS

- Assistant Professor, Chemistry
- Member, Bio-X
- Member, Institute for Computational and Mathematical Engineering (ICME)

HONORS AND AWARDS

- Early Career Research Program Award, Department of Energy (2022-2027)
- Research Scholar Award, Google (2022)
- Terman Faculty Fellow, Stanford University (2020-2022)

Teaching

COURSES

2023-24

- Advanced Physical Chemistry: CHEM 273 (Win)
- Machine Learning for Chemical and Dynamical Data: CHEM 263 (Aut)
- Physical Chemistry III: CHEM 175 (Win)

2022-23

- Advanced Physical Chemistry: CHEM 273 (Win)
- Exploring Chemical Research at Stanford: CHEM 91 (Win)
- Physical Chemistry III: CHEM 175 (Win)

2021-22

- Advanced Physical Chemistry: CHEM 273 (Win)
- Machine Learning for Chemical and Dynamical Data: CHEM 263 (Aut)
- Physical Chemistry III: CHEM 175 (Win)

2020-21

- Physical Chemistry III: CHEM 175 (Win)

STANFORD ADVISEES

Doctoral Dissertation Reader (AC)

Alex Chang, Xiao Cui, Ethan Curtis, Joseph Kelly

Postdoctoral Faculty Sponsor

Clay Batton, Sreekanth Kizhakkumpurath Manikandan, Jeremie Klinger

Doctoral Dissertation Advisor (AC)

Shriram Chennakesavalu, Steven Dunne, Sebastian Ibarraran, Sherry Li, Andy Mitchell, Abigail Park, Emmit Pert

Doctoral Dissertation Co-Advisor (AC)

Yinuo Ren

Publications

PUBLICATIONS

- **Data-Efficient Generation of Protein Conformational Ensembles with Backbone-to-Side-Chain Transformers.** *The journal of physical chemistry. B*
  Chennakesavalu, S., Rotskoff, G. M.
  2024
- **Adaptive nonequilibrium design of actin-based metamaterials: Fundamental and practical limits of control.** *Proceedings of the National Academy of Sciences of the United States of America*
  Chennakesavalu, S., Manikandan, S. K., Hu, F., Rotskoff, G. M.
  2024; 121 (8): e2310238121
- **Computing equilibrium free energies through a nonequilibrium quench.** *The Journal of chemical physics*
  Liu, K., Rotskoff, G. M., Vanden-Eijnden, E., Hocky, G. M.
  2024; 160 (3)
- **Ensuring thermodynamic consistency with invertible coarse-graining.** *The Journal of chemical physics*
  Chennakesavalu, S., Toomer, D. J., Rotskoff, G. M.
  2023; 158 (12): 124126
- **Unified, Geometric Framework for Nonequilibrium Protocol Optimization.** *Physical review letters*
  Chennakesavalu, S., Rotskoff, G. M.
  2023; 130 (10): 107101
- **Trainability and Accuracy of Artificial Neural Networks: An Interacting Particle System Approach** *COMMUNICATIONS ON PURE AND APPLIED MATHEMATICS*
  Rotskoff, G. M., Vanden-Eijnden, E.
  2022; 75 (9): 1889-1935
- **Physics-informed graph neural networks enhance scalability of variational nonequilibrium optimal control** *JOURNAL OF CHEMICAL PHYSICS*
  Yan, J., Rotskoff, G. M.
  2022; 157 (7): 074101
- **Adaptive Monte Carlo augmented with normalizing flows.** *Proceedings of the National Academy of Sciences of the United States of America*
  Gabrie, M., Rotskoff, G. M., Vanden-Eijnden, E.
  2022; 119 (10): e2109420119
- **Learning nonequilibrium control forces to characterize dynamical phase transitions** *PHYSICAL REVIEW E*
  Yan, J., Touchette, H., Rotskoff, G. M.
  2022; 105 (2)
- **Learning nonequilibrium control forces to characterize dynamical phase transitions.** *Physical review. E*
  Yan, J., Touchette, H., Rotskoff, G. M.
  2022; 105 (2-1): 024115
- **Remembering the Work of Phillip L. Geissler: A Coda to His Scientific Trajectory.** *Annual review of physical chemistry*
  Bowman, G. R., Cox, S. J., Dellago, C., DuBay, K. H., Eaves, J. D., Fletcher, D. A., Frechette, L. B., Grünwald, M., Klymko, K., Ku, J., Omar, A., Rabani, E., Reichman, et al
  2022
- **Probing the theoretical and computational limits of dissipative design.** *The Journal of chemical physics*
  Chennakesavalu, S., Rotskoff, G. M.
  2021; 155 (19): 194114

- **A Dynamical Central Limit Theorem for Shallow Neural Networks**
  Chen, Z., Rotskoff, G. M., Bruna, J., Vanden-Eijnden, E., Larochelle, H., Ranzato, M., Hadsell, R., Balcan, M. F., Lin, H.
  NEURAL INFORMATION PROCESSING SYSTEMS (NIPS).2020