

# Sophia Tang

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## EDUCATION

### University of Pennsylvania

Dual Degree with Bachelor of Science in Engineering and Bachelor of Science in Economics

Philadelphia, PA

Sept 2023 - May 2027

Jerome Fisher Program in Management & Technology; Major in Computer Science & Statistics

**Relevant Coursework:** Algorithms, Programming Languages and Techniques I and II, Mathematics of Computer Science, Multivariable Calculus, Linear Algebra, Machine Learning, Computer Systems, Automata Computability and Complexity, Corporate Finance, Database & Information Systems, Statistical Inference

## RESEARCH EXPERIENCE

### Chatterjee Lab, University of Pennsylvania.

Philadelphia, PA

Undergraduate Researcher. **Advised by Dr. Pranam Chatterjee.**

Sept 2024 - Present

- Developing theoretical ML frameworks for generative modeling with applications in biological design and simulation.
- First-author paper presented at main ICML 2025 and multiple first-author papers under review at top ML venues (see below).

### Mitchell Lab, University of Pennsylvania.

Philadelphia, PA

Undergraduate Researcher. **Advised by Dr. Michael Mitchell.**

Sept 2023 - Present

- Developed novel targeted lipid nanoparticle (LNP)-encapsulated mRNA therapeutics with high transport across the blood-brain barrier after systemic administration and transfection into brain cell types.
- Synthesized and characterized ionizable LNPs with targeted peptide groups for in vitro and in vivo experiments. Evaluated relevant literature on targeted brain delivery techniques and planned experiments.
- Several co-authored papers and a first-author review paper published (see below)

## MACHINE LEARNING PUBLICATIONS (\*denotes equal contribution; † denotes advising role)

### [1] PepTune: De Novo Generation of Therapeutic Peptides with Multi-Objective-Guided Discrete Diffusion.

**Sophia Tang\***, Yinuo Zhang\*, Pranam Chatterjee†.

42nd International Conference on Machine Learning (ICML 2025), Dec 2024. <https://openreview.net/forum?id=FQoy1Y1Hd8>

**Description:** We introduce PepTune, a multi-objective discrete diffusion model for simultaneous generation and optimization of therapeutic peptide SMILES. Built on the Masked Discrete Language Model (MDLM) framework, PepTune ensures valid peptide structures with a novel bond-dependent masking schedule and invalid loss function. To guide the diffusion process, we introduce Monte Carlo Tree Guidance (MCTG), an inference-time multi-objective guidance algorithm that balances exploration and exploitation to iteratively refine Pareto-optimal sequences. MCTG integrates classifier-based rewards with search-tree expansion, overcoming gradient estimation challenges and data sparsity.

### [2] Branched Schrödinger Bridge Matching.

**Sophia Tang**, Yinuo Zhang, Alexander Tong†, Pranam Chatterjee†.

Preprint. Jun 2025. <https://doi.org/10.48550/arXiv.2506.09007>

**Description:** We introduce Branched Schrödinger Bridge Matching (BranchSBM), a novel framework that learns branched Schrödinger bridges. BranchSBM parameterizes multiple time-dependent velocity fields and growth processes, enabling the representation of population-level divergence into multiple terminal distributions. We show that BranchSBM is not only more expressive but also essential for tasks involving multi-path surface navigation, modeling cell fate bifurcations from homogeneous progenitor states, and simulating diverging cellular responses to perturbations.

### [3] TR2-D2: Tree Search Guided Trajectory-Aware Fine-Tuning for Discrete Diffusion.

**Sophia Tang\***, Yuchen Zhu\*, Molei Tao†, Pranam Chatterjee†.

Preprint. Sept 2025. <https://doi.org/10.48550/arXiv.2509.25171>

**Description:** We introduce a novel framework that optimizes reward-guided discrete diffusion trajectories with tree search to construct replay buffers for trajectory-aware fine-tuning. These buffers are generated using Monte Carlo Tree Search (MCTS) and subsequently used to fine-tune a pre-trained discrete diffusion model under a stochastic optimal control objective. We validate our framework on single- and multi-objective fine-tuning of biological sequence diffusion models, highlighting the overall effectiveness of TR2-D2 for reliable reward-guided fine-tuning in discrete sequence generation.

### [4] Entangled Schrödinger Bridge Matching.

**Sophia Tang**, Yinuo Zhang, Pranam Chatterjee†.

Preprint. Oct 2025. <https://doi.org/10.48550/arXiv.2511.07406>

**Description:** We introduce a framework that learns the first- and second-order stochastic dynamics of interacting, multi-particle systems where the direction and magnitude of each particle's path depend dynamically on the paths of the other particles. We define the Entangled Schrödinger Bridge problem as solving a coupled system of bias forces that entangle particle velocities. We show that our framework accurately simulates heterogeneous cell populations under perturbations and rare transitions in high-dimensional biomolecular systems.

## [5] Gumbel-Softmax Flow Matching with Straight-Through Guidance for Controllable Biological Sequence Generation.

*Sophia Tang, Yinuo Zhang, Alexander Tong<sup>†</sup>, Pranam Chatterjee<sup>†</sup>.*

Preprint. Mar 2025. <https://doi.org/10.48550/arXiv.2503.17361>

**Description:** We introduce a generative framework on the simplex based on a novel Gumbel-Softmax interpolant with a time-dependent temperature. Our framework enables high-quality, diverse generation and scales efficiently to higher-dimensional simplices.

## [6] Multi-Objective-Guided Generative Design of mRNA with Therapeutic Properties.

*Sawan Patel\*, Sophia Tang\*, Yinuo Zhang, Pranam Chatterjee<sup>†</sup>, and Sherwood Yao<sup>†</sup>.*

Preprint. Jul 2025. <https://openreview.net/pdf?id=Jiv4B97NAn>

**Description:** We introduce the first multi-objective guided generative model for simultaneous mRNA codon optimization and de novo design of untranslated region (UTR) sequences.

## [7] Multi-Objective-Guided Discrete Flow Matching for Controllable Biological Sequence Design.

*Tong Chen, Yinuo Zhang, Sophia Tang, and Pranam Chatterjee<sup>†</sup>.*

Preprint. May 2025. <https://doi.org/10.48550/arXiv.2505.07086>

**Description:** We introduce a multi-objective guidance method for discrete flow matching that leverages rank-based directional scoring and hypercone filtering to guide pre-trained discrete flow velocities to Pareto-optimal sequences.

## BIOENGINEERING PUBLICATIONS

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### [8] Peptide-functionalized nanoparticles for brain-targeted therapeutics.

*Sophia Tang, Emily L. Han, and Michael J. Mitchell<sup>†</sup>.*

Drug Delivery and Translational Research, Springer Nature. Mar 2025. <https://doi.org/10.1007/s13346-025-01840-w>

### [9] Peptide-Functionalized Lipid Nanoparticles for Targeted Systemic mRNA Delivery to the Brain.

*Emily L. Han, Sophia Tang, Dongyoon Kim, Amanda M. Murray, Kelsey L. Swingle, Alex G. Hamilton, Kaitlin Mrksich, Marshall S. Padilla, Rohan Palanki, Jacqueline J. Li, and Michael J. Mitchell<sup>†</sup>.*

ACS Nano Letters. Dec 2024. <https://doi.org/10.1021/acs.nanolett.4c05186>

### [10] Predictive High-Throughput Platform for Dual Screening of mRNA Lipid Nanoparticle Blood–Brain Barrier Transfection and Crossing.

*Emily L. Han, Marshall S. Padilla, Rohan Palanki, Dongyoon Kim, Kaitlin Mrksich, Jacqueline J. Li, Sophia Tang, Il-Chul Yoon, and Michael J. Mitchell<sup>†</sup>.*

ACS Nano Letters. Jan 2024. <https://doi.org/10.1021/acs.nanolett.3c03509>

### [11] Optimized microfluidic formulation and organic excipients for improved lipid nanoparticle-mediated genome editing.

*Rohan Palanki, Emily L. Han, Amanda M. Murray, Robin Maganti, Sophia Tang, Kelsey L. Swingle, Dongyoon Kim, Hannah Yamagata, Hannah C. Safford, Kaitlin Mrksich, William H. Peranteau, and Michael J. Mitchell<sup>†</sup>.*

Lab on a Chip, Royal Society of Chemistry. Jan 2024. <https://doi.org/10.1039/D4LC00283K>

## TECHNICAL ARTICLES

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### A Complete Guide to Spherical Equivariant Graph Transformers

<https://alchemybio.substack.com/p/spherical-equivariant-graph-transformer>

A 2.5-hour breakdown of the theory behind spherical equivariant ( $SE(3)$ ) graph neural networks (EGNNs) and the  $SE(3)$ -Transformer architecture.

### A Complete Guide to Protein Folding Prediction

<https://alchemybio.substack.com/p/a-complete-guide-to-protein-folding>

A 3-hour breakdown of the three-track RoseTTAFold protein prediction model that leverages multi-modal deep learning architectures to transform single sequences into dynamic 3D structures.

## INVITED TALKS

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### Discrete Diffusion Reading Group. Nov 2025.

[https://youtu.be/NX2Mth\\_Epvk?si=LsVS\\_bhzyD-RV03m](https://youtu.be/NX2Mth_Epvk?si=LsVS_bhzyD-RV03m)

### Starkly Speaking Reading Group. Jul 2025.

<https://youtu.be/inVYA0pQ4Wg?si=mdwhTE3wu0vXJ4ZX>

### Learning on Graphs and Geometry Reading Group. Jan 2025.

<https://youtu.be/KVr8ryclwdA?si=RdRPdqNqvmblk3Og>

## WORKSHOP PRESENTATIONS

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FPI, SPIGM (NeurIPS 2025)

GenBio, ExAIT, FM4LS, SIM (ICML 2025)

DeLTa, FPI, GEM, AI4NA (ICLR 2025)