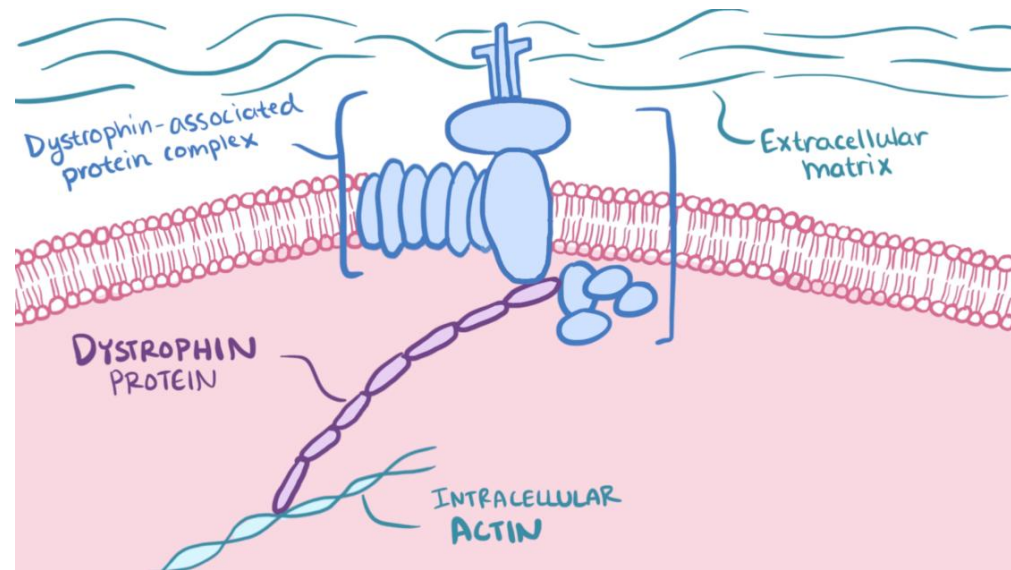


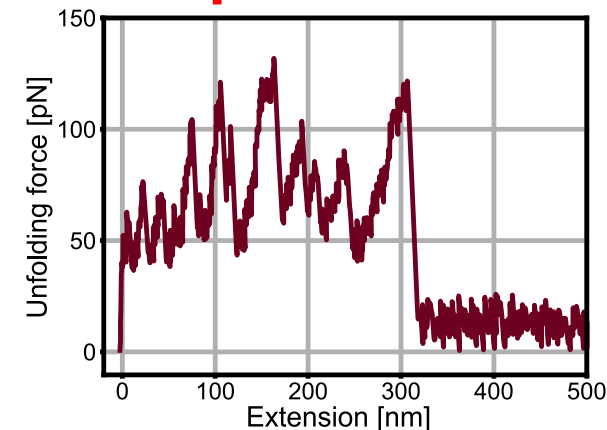
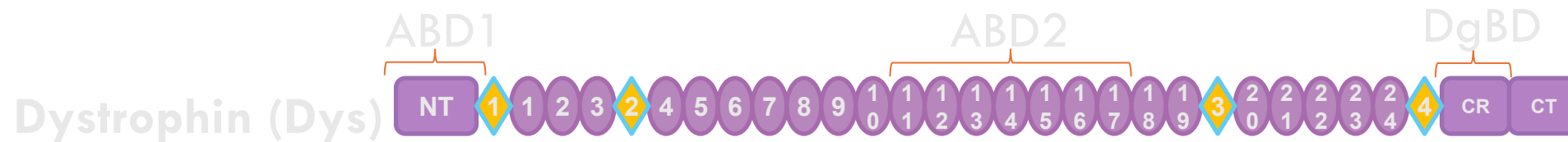
Machine Learning Enabling Single Molecule Physics



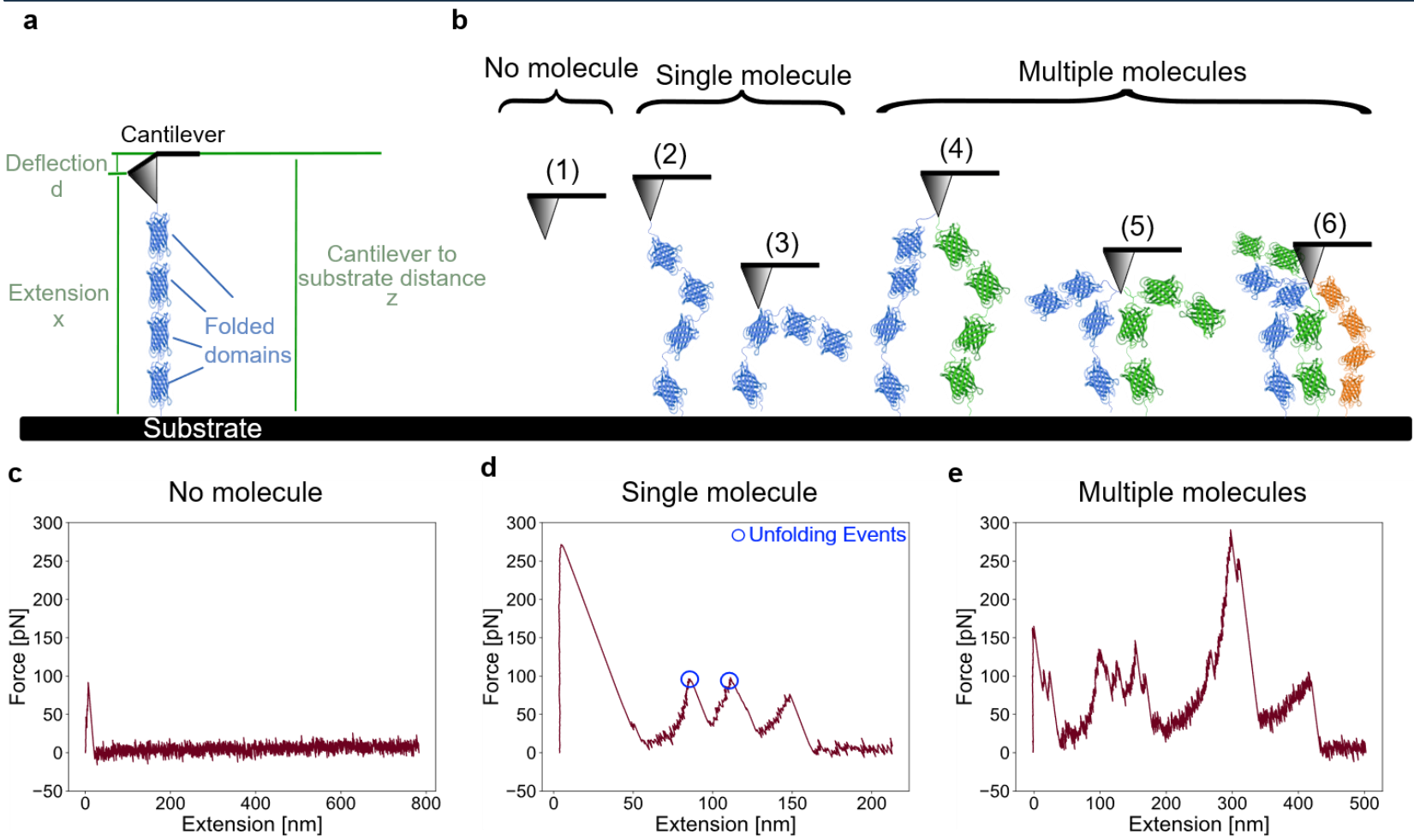
Duchenne Muscular Dystrophy (DMD) affects 1 in 5000 male births, no cure.

- Cause: loss of dystrophin.
- Dystrophin as molecular shock absorber.
- Mechanical forces play a critical role and needs to understand.

Predict force profile from domain sequence.



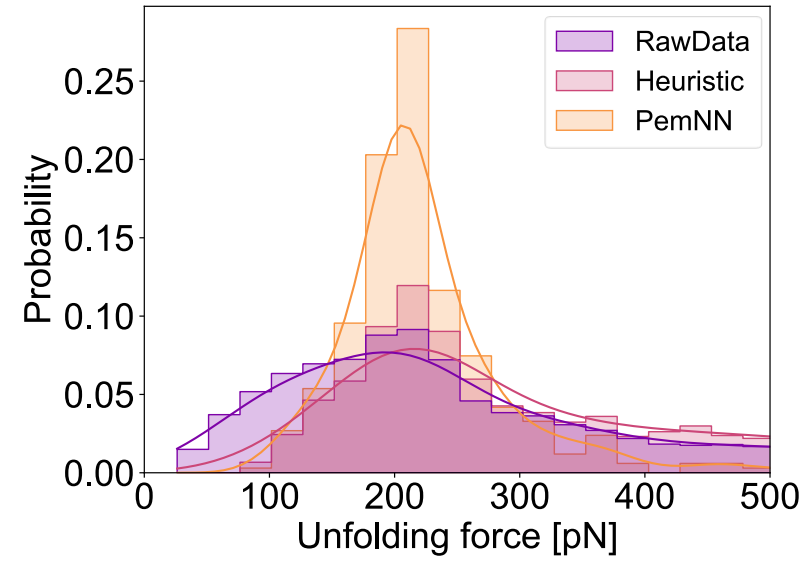
NIH: 5R01AR042423



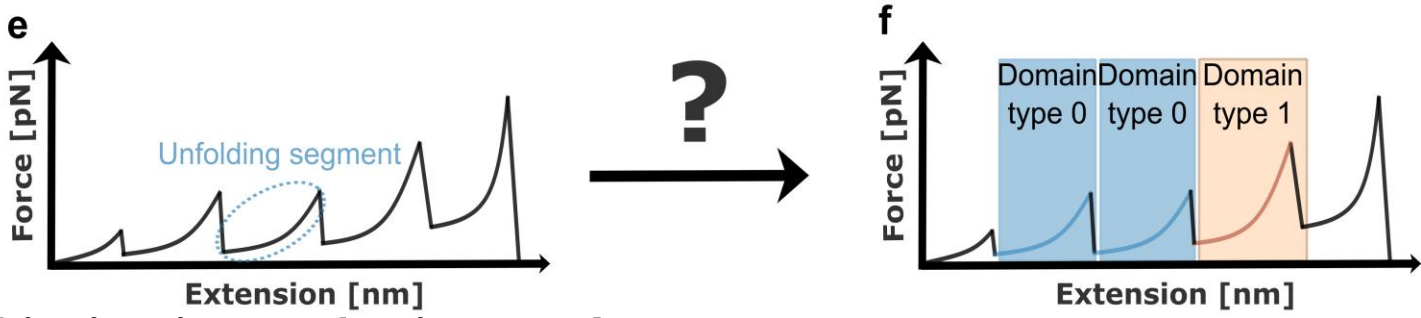
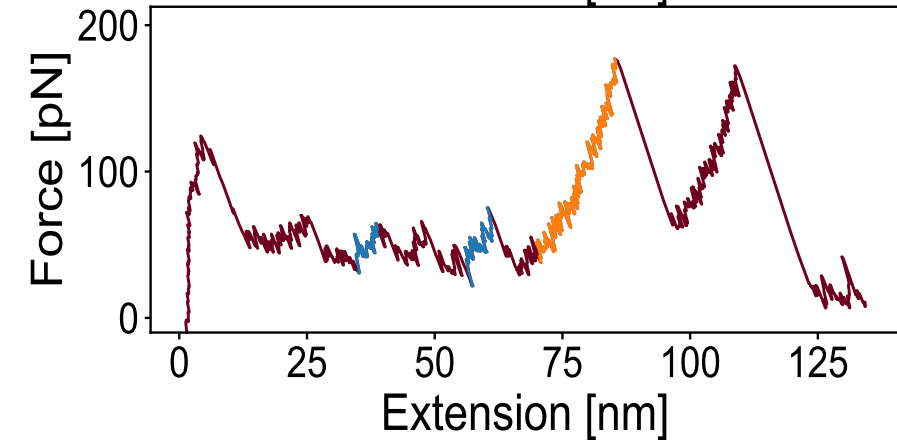
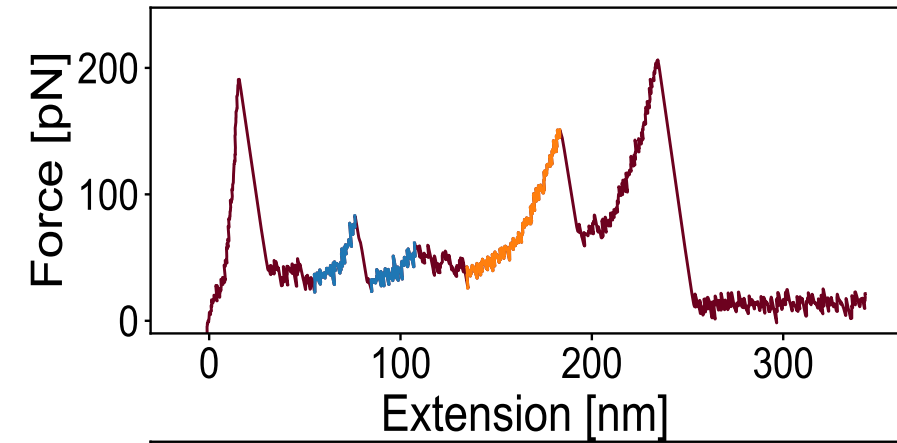
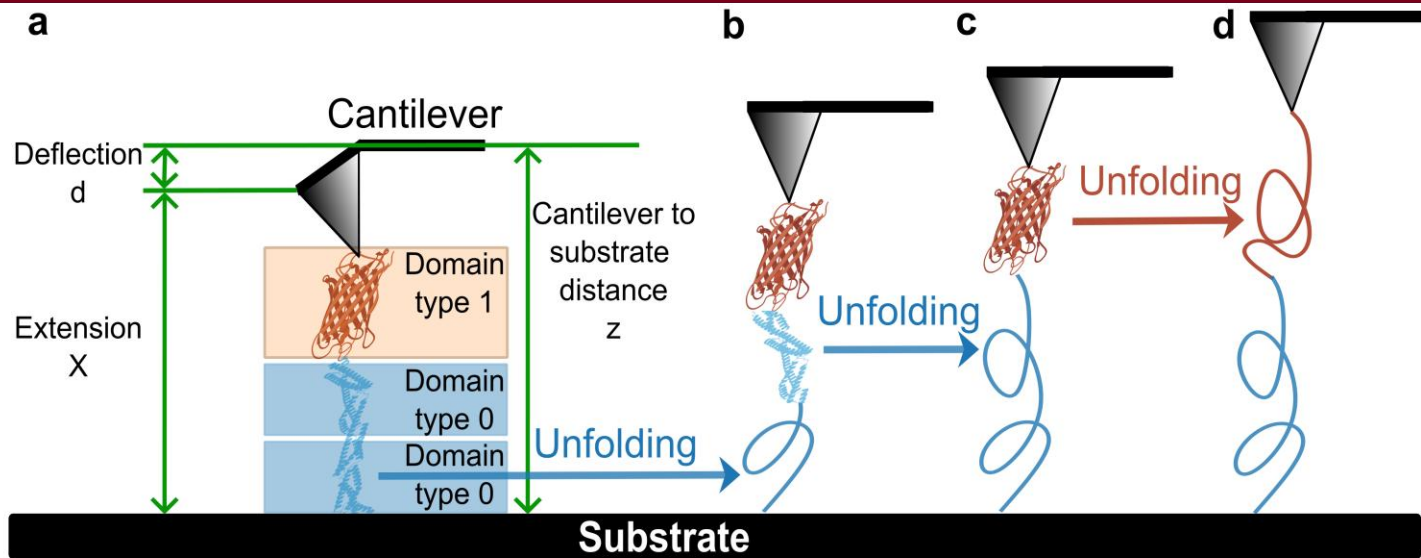
Visual inspection remains the standard approach

- Time-consuming (12-24 hours)
- Expertise

Critical Need:
An automation tool to filter data that results from single molecule.



Hua, Cailong, Sivaraman Rajaganapathy, Rebecca A. Slick, Joseph Vavra, Joseph M. Muretta, James M. Ervasti, and Murti Salapaka. "A Physics-Augmented Deep Learning Framework for Classifying Single Molecule Force Spectroscopy Data." In *Forty-second International Conference on Machine Learning*.

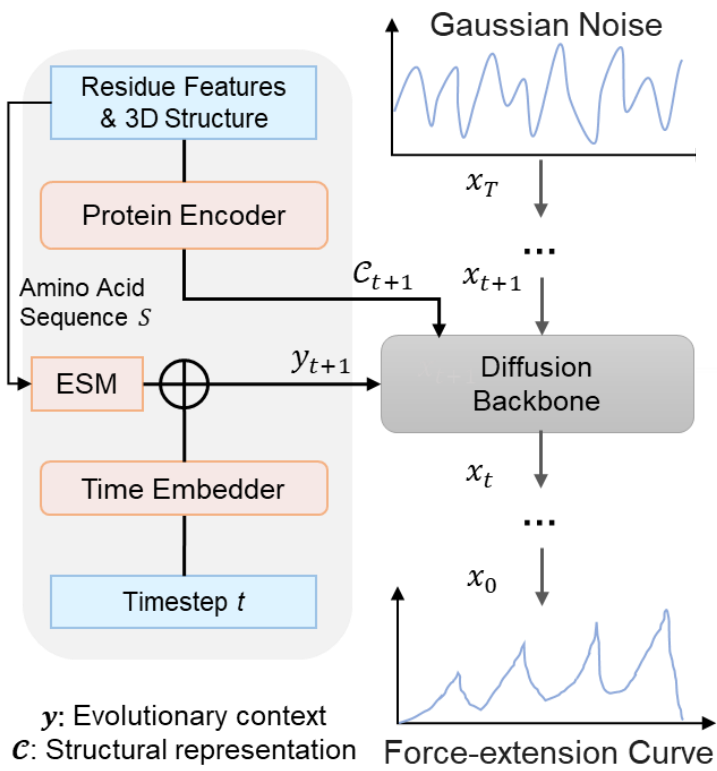


Limitations of prior work:

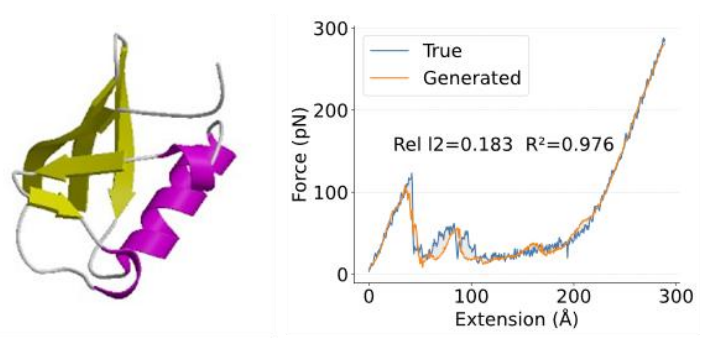
- Draw limited biological inferences in an average sense without accounting for the impact of heterogeneity.

Goal:

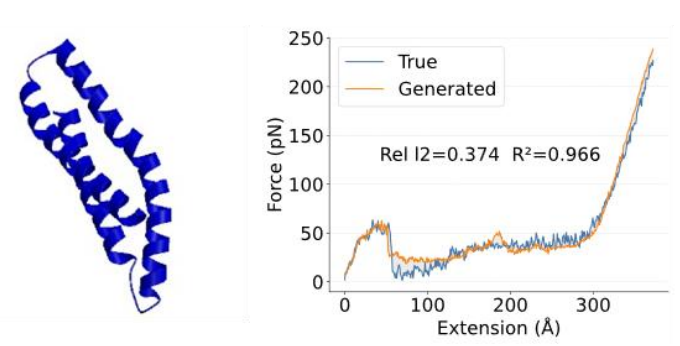
- Automated, data-driven tools for identifying heterogeneous protein domains



(a) PDB: 1ubq (Alpha Helix & Beta Sheet Structure)



(b) PDB: 1aj3 (Mainly Alpha Helix Structure)



Rapidly generate force curves via generative diffusion models and probe the mechanical properties of proteins.

Yiyuan Zhang, Cailong Hua, Vinitendra Singh, Joseph M. Mureta, James M. Ervasti, and Murti Salapaka. "GenUnfold: Rapidly Predict Protein Mechanical Unfolding Trajectory via a Physics-Guided Diffusion Model." *Submitted to Forty-Third International Conference on Machine Learning.*

Limitation:
Physical experiment is labor-intensive and time-consuming.

Scientific significance :
High-throughput protein screening tool for force-targeted therapeutics.

