Atomic force spectroscopy of single molecules and surfaces

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Force spectroscopy techniques possess the ability to detect subtle details in protein dynamics at sub-nanometer resolution, bridge physics, chemistry, biology and engineering. My lab interweaves studies of atomic-scale friction and dynamic behavior of single proteins under external forces.

Main research interests

1. Dynamical behavior of proteins using force spectroscopy:

Recent advances in single molecule force spectroscopy permit measuring the folding and unfolding kinetics of a protein and their coil-to-globule transition in great detail while the protein performs under a mechanical force. The Atomic Force Microscope (AFM) is capable of picking up and holding a single protein for long periods of time, while the mechanical pulling force can be changed over wide ranges, in order to examine how the protein responds (as shown in Figure 1).

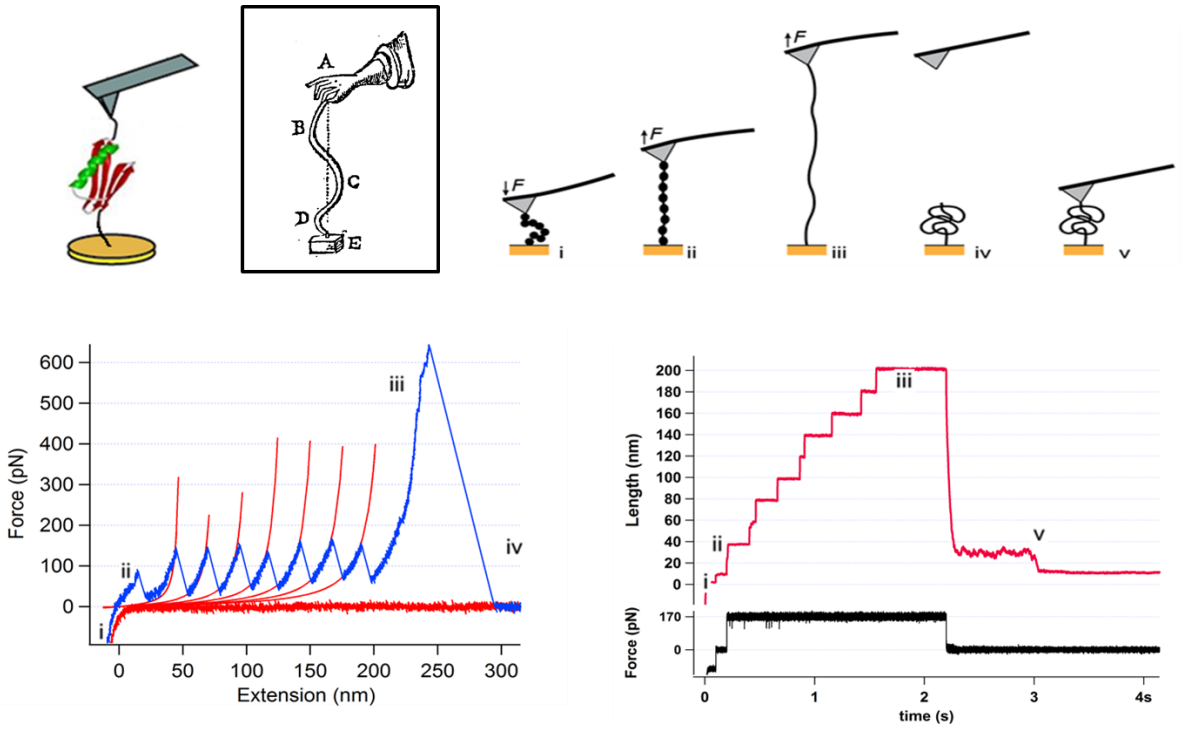

Figure 1. The upper panel shows a schematic of a force-spectroscopy experiment of a single protein (left) and a polyprotein. The lower panel exemplifies the two modes of force application in such experiments: left – Force

extension (FX) of poly-(I27), displaying an unfolding sequence of the molecule as it being stretched at constant velocity, and right: Force-clamp (FC) unfolding sequence of poly-ubiquitin under a constant force constant force of 170 pN, and its collapse when the force is released to zero.

These manipulations enable the study of mechanical properties and the dynamical behavior of various proteins and polymer with regards to varying conditions and conformations. The data output of these experiments will be analyzed using theoretical tools that are based on statistical-mechanics models, extracting information such as the free energy landscape (or potential of mean force) of the collapsing protein (Figure 2).

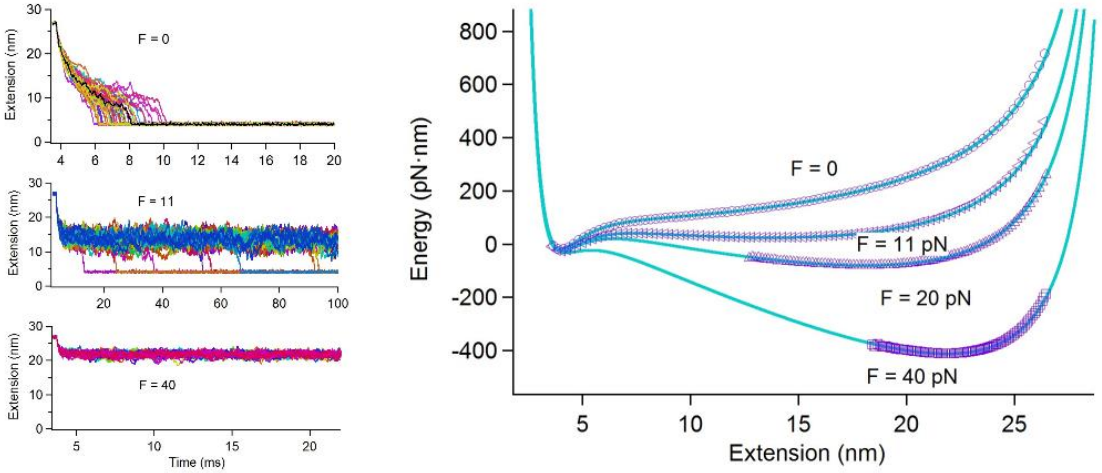

Figure 2: Free energy landscape reconstruction from force-quench Brownian-dynamics simulations: Reconstructed free energy profiles (open purple symbols) from the simulated collapse trajectories of an unfolded protein held at high extension (F = 250 pN) and then quenched to F = 0, 11 and 40 pN (shown on the left). From an ensemble of these trajectories, the free energy landscapes were reconstructed (open purple symbols), showing that they matched the original potentials (light blue lines) perfectly according to the regime in the phase-space that their trajectories sampled.

The overall purpose will be to understand scaling laws, specific-ion effects on phase transitions and properties that are related to unstructured proteins that are related to neurodegenerative diseases.

2. Atomic friction of surfaces

The AFM is known to image surface topologies with exceptional resolution, providing atomic-scale details of various surfaces. Through the interaction between the sharp AFM cantilever tip and the surface, various forces can be measured during the scanning experiment. The measured interaction forces eventually result in a three dimensional image of the probed surface with a sub-nanometer resolution. One

of the key features for understanding the activity various materials lies in their surface energy. Here we are interested in the application of *Jarzynsky*'s nonequilibrium work relation to reconstruct the surface potential from nano-tribological measurements of mono-crystals and catalysts.

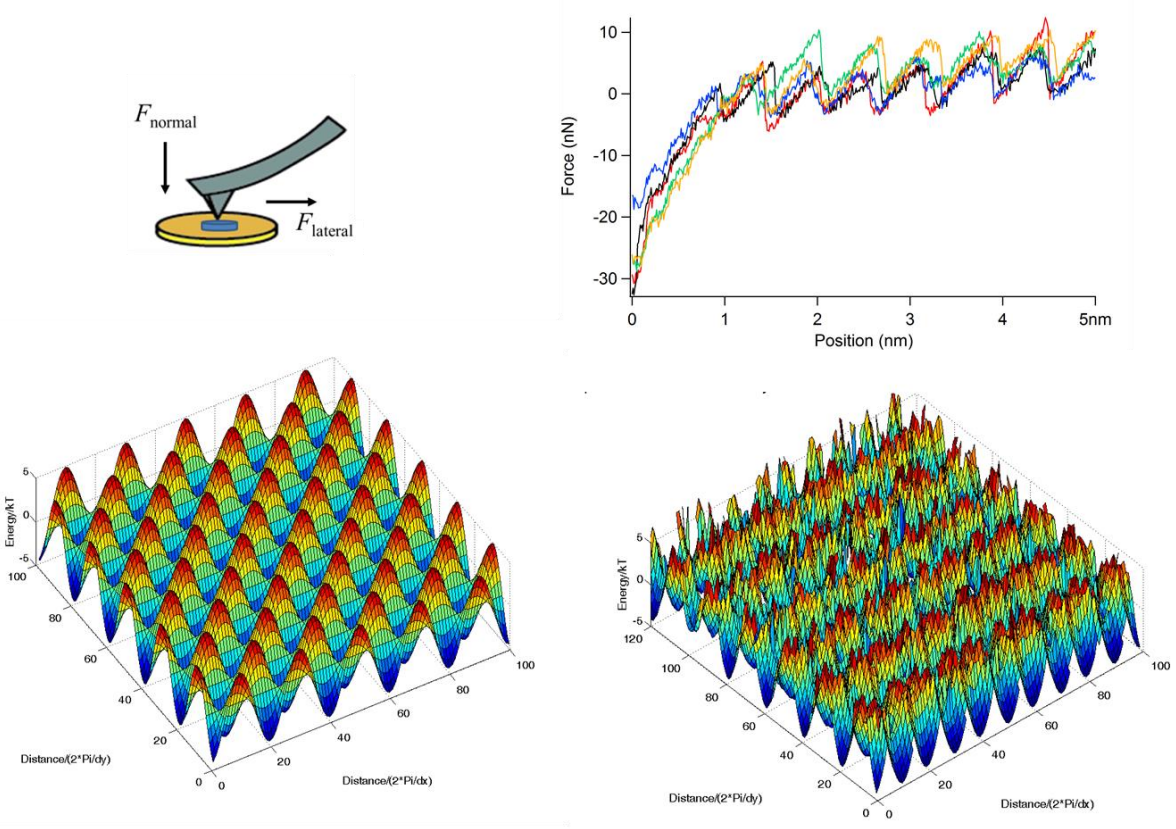

Figure 3: Measured friction force traces of NaCl (Halite) with atomic resolution (upper panel). Reconstructed surface potential of a lattice (lower panel, rigth) using the *Jarzynsky*'s nonequilibrium work relation from simulated atomic-friction experiments over a model potential (lower panel ,left)