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Accoustic Force Microscopy in Aqueous Environments to Determine Protein Folding Dynamics STEFAN ZAUSCHER, ZEHRA PARLAK, JIANMING ZHANG, TERRY OAS, Duke University — Characterizing the dynamic mechanical response of (bio)molecular thin films can give insight into the dynamics of biomolecules on surfaces. Here, acoustic atomic force microscopy (AFM) methods are promising tools since they enable sensitive mapping of the mechanical properties of samples by introducing high frequency modulation while imaging the topography. We are among the first to show that it is possible to utilize acoustic AFM methods in aqueous environments. Accounting for the indentation dependent, off-resonance cantilever dynamics, we are able to obtain spatially resolved elasticity maps of organic thin films in water. Encouraged by these results, we are testing the hypothesis that the rapid unfolding/refolding cycles of the five B domains of SpA-N, a 291 residue protein, composed of five nearly identical 56 to 61 residue domains, confer a unique form of flexibility to the molecule. To this end we employ a non-resonant, acoustic AFM method in a frequency spectroscopy mode, and measure the viscoelastic properties of SpA-N monolayers quantitatively under physiological conditions. We present evidence that the apparent, frequency-dependent stiffness of SpA-N coincides with the kinetics of individual domain folding cycles.

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