

AFM INVESTIGATION OF ELASTICITY AND CONFORMATION MALEABILITY OF SINGLE PROTEINS AND SUPRAMOLECULAR STRUCTURES

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The atomic force microscope (AFM) is becoming increasingly useful for studying the structure and mechanical properties of proteins. AFM studies require that the protein be immobilized on a substrate, typically gold or mica. The choice of the substrate can have profound effects upon the images that one obtains and the ability to measure single molecule elasticity. We have studied several protein systems that clearly demonstrate the effects of the substrate and environment on the conformation and elasticity as determined via AFM. AdhE is a multienzyme from *E. coli* which forms supramolecular structures. These structures appear differently in AFM images depending upon the immobilization surface. Calmodulin is a small sensor protein that changes conformation upon binding calcium and its target peptides. We have demonstrated that it is also stretched by meniscus forces when immobilized on mica. Nebulin is a giant muscle protein with a molecular weight between 600 and 900 kDa depending upon the source. The protein, in part, functions as a ruler for the assembly of the F-actin thin filaments, and therefore takes on an extended conformation *in vivo*. Nebulin takes on both globular and extended conformations when immobilized on mica. Nebulin is also elastic when stretched between site-specific antibodies. PEVK is the elastic domain of the giant protein titin. The elastic properties of the PEVK domain depend greatly upon the environment in which it is studied. Our results demonstrate both the power of AFM and the precautions one must take when studying proteins.