Proteins Crystal Tips for Atomic Force Microscopy

JASON HAFNER, NISSANKA WICKREMASINGHE, Dept. of Physics and Astronomy, Rice University — Protein crystals are being tested as tip materials for biological atomic force microscopy (AFM) with molecular recognition. A critical limitation of AFM for biological imaging is that it only reveals molecular “topography”, making it impossible to distinguish similar size proteins or to identify specific proteins in an aggregate. Recognition-AFM combines topographic AFM imaging and biomolecular specificity through the use of antibodies tethered to AFM tips through flexible polymer linkers. [Stroh, et al, PNAS 2004, v101 p12503] The linker is required to allow the antibody to achieve the proper orientation for specific interactions with the sample, and to increase the likelihood of having an active Fab at the tip apex. However, this method of tip functionalization is not highly robust, and the linker can degrade the imaging resolution. The presence of an oriented antibody at the tip apex will be guaranteed with a tip made of a protein crystal. Initial work has been carried out with lysozyme crystals grown directly onto commercial AFM tips. Their mechanical rigidity is sufficient for routine imaging, and the resolution is being optimized. Recognition AFM with these tips is being tested by imaging patterned anti-lysozyme and non-specific serum antibodies.

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