

Ultrastable atomic force microscope for structural biology

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Determining the structure of membrane proteins and membrane protein assemblies is difficult by traditional means. The atomic force microscope is a powerful tool for structural biology that has achieved 0.6 nm lateral proteins in native membranes. Yet, lateral drift remains a critical, largely unaddressed issue that limits tip-sample registration, signal-to-noise ratio, and image resolution. This is particularly true in biologically relevant conditions (room temperature in fluid), which are highly perturbative. By measuring the positions of the sample and the tip in 3D with focused laser beams, we reduced drift to approximately 0.2 nm over one hour of imaging. We are currently performing initial measurements on membrane proteins. Ultimately, we expect to be able to determine binding sites for drugs on membrane proteins and ligand-induced conformational changes.