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Toward Nanoscale Imaging of Biomolecular Systems

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Biological cells fabricate and assemble molecular building blocks into diverse molecular networks with striking complexity and functionality. As such, they are model integrated nanosystems whose study should yield important information for optimizing specific cellular functions, and for engineering functional synthetic nano-systems. To study biological systems in this context, it is crucial to observe their molecular machinery at work in a physiologically relevant environment. Currently, there are no techniques that can accomplish this.To study these systems at the molecular length scale, we have developed a near-field microscopy technique called tip-enhanced fluorescence microscopy (TEFM) that combines tapping-mode atomic force microscopy (AFM) with confocal fluorescence microscopy. Briefly, a strong axial field is produced at the focus of a laser beam and an AFM probe is positioned into the focus. This creates a localized dipole field at the tip apex, which can strongly excite fluorescence of nearby chromophores. Scanning the illuminated tip over a surface leads to high-fidelity fluorescence images with resolution limited only by the sharpness of the tip. In contrast to AFM, TEFM also provides single-molecule sensitivity and biochemical specificity when combined with fluorescence labeling. We recently demonstrated $\sim$10 nm resolution in TEFM images of quantum dots in air and we are now working to extend its capabilities to liquid imaging and to improve the resolution yet further by attaching carbon nanotubes to the ends of the AFM tips.