Looking Inside Single Cells and Tissue Using Nanoscale Infrared Spectroscopy

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Abstract

Infrared (IR) spectroscopy is a powerful tool for obtaining chemical information about materials. Unfortunately, the wavelength of light used to make the measurement limits the size of structures that can be reliably identified by IR spectroscopy. Diffraction typically limits the spatial resolution of IR microspectroscopy to 3-10 μm, making this technique problematic for identifying small structures in samples such as tissue sections and single cells. Atomic force microscopy (AFM), on the other hand, provides exquisite spatial resolution (as small as one nanometer), but this technique does not provide any chemical information. A new technique which combines AFM and IR spectroscopy is described. It is based on the combination of a tunable infrared laser with an atomic force microscope that can locally map and measure thermal expansion of nanoscale regions of a sample resulting from the absorption of infrared radiation. Because the AFM probe tip can map the thermal expansion on very fine length scales, the AFM-IR technique provides a robust way to obtain interpretable IR absorption spectra at spatial resolution scales well below the diffraction limit. Several types of tissue samples, including hair, skin, and bone cross sections have been examined by AFM-IR spectroscopy and imaging. The technique has also been shown to be useful for chemically characterizing structures inside single cells and for identifying secondary structure and orientation of sub-micrometer-diameter protein fibers.