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MICROSCOPES AREN'T JUST FOR MICROSCOPISTS, ANYMORE (CONTINUED)

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Microscopes are being used to obtain more and more information from a specimen. We are all acquainted with various ways to visualize structures, whether on the surface or embedded within a relatively translucent specimen. There are many ways to "tag" a molecule of interest so that the molecule can be positively identified within the specimen. Traditional microscopes are not able to identify a molecule for us. Other analytical tools are used for that. For example, the nuclear magnetic resonance (NMR) spectrum of a molecular species yields a "fingerprint" that gives a reliable identification. Wouldn't it be great to combine the sensitivity of a state-of-the-art microscope with the molecular analytical capabilities of NMR?

Well you guessed it, this has been done. This approach was first suggested by John A. Sidles at the University of Washington[2] and has recently been demonstrated by Dan Rugar and colleagues at the IBM Almaden Research Center in San Jose.[3] For this experiment they used an atomic force microscope (AFM) within a superconducting magnet with a radio-frequency (rf) coil that was essentially a NMR instrument. The AFM was used in an unconventional mode; to say unconventional is misleading, it was basically run backwards. Rather than scanning a cantilever with a stylus over the sample, the sample was glued to the cantilever. The cantilever was special in that it was fabricated to be ultrathin, with a spring constant less than 1/30 the standard used for typical AFM. This improved the force detection sensitivity to the femtonewton range, or below. The sample was suspended by the cantilever within the strong magnetic field of 2.35 Tesla provided by a superconducting magnet. The magnetic field was intentionally made to be non-uniform by positioning a small (1.5 by 4 mm) magnetized iron particle to within 700µm of the sample. This generated a measurable force on the sample and provided spatial resolution because the field gradient varied with the distance from the iron particle. A small (0.8 mm diameter) rf coil positioned at right angles to the iron particle provided a controllable perturbation within the magnetic field which was used to control the orientation of nuclei within the sample. They used a NMR modulation technique whereby a frequency modulated (FM, similar to the FM mode on your radio) radio signal interacts with the specimen. They chose a modulation frequency at the cantilever resonance frequency, thereby enhancing the resulting cantilever vibration amplitude.

To back up a moment, it should be pointed out that Rugar *et al.* chose a sample that contained a relatively large number of hydrogen nuclei (protons) that would react appropriately within the magnetic field gradient they designed. Specifically the sample was 12 ng of ammonium nitrate. When this sample was perturbed by the FM signal provided by the rf coil, it vibrated the cantilever in response to the changing magnetic moment of the protons within the sample. The vibration was on the order of angstroms and could be detected by a fiber optic interferometer that was coupled to a lock-in amplifier. Variations in vibration within the magnetic field gradient provided by the iron particle provided a spatial resolution of 2.6 µm in one dimension. They produced convincing evidence that as few as 1.6×10^{13} protons could be detected. This is roughly 100 times better sensitivity than conventional NMR imaging techniques.

This impressive demonstration of NMR microimaging is probably just the first step in a new direction. It will be exciting to see how modern microscopes are to be used as sensitive detectors to provide us with information on a smaller and smaller scale. ■

1. The author gratefully acknowledges the help of Dr. Dean Palmer, IBM Rochester, and Dr. Dan Rugar, IBM Almaden Research Center.

2. Sidles, J.A., Noninductive detection of single-proton magnetic resonance, *Appl. Phys. Lett.* 58:2854-2856, 1991.

3. Rugar, D., O. Zuger, S. Hoen, C.S. Yannoni, H.-M. Vieth, and R.D. Kendrick, Force detection of nuclear magnetic resonance, *Science* 264:1560-1563, 1994.

Front Page Image
Industrial Diamond Image

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Don Grimes, Editor

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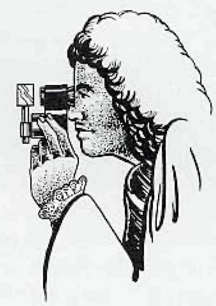

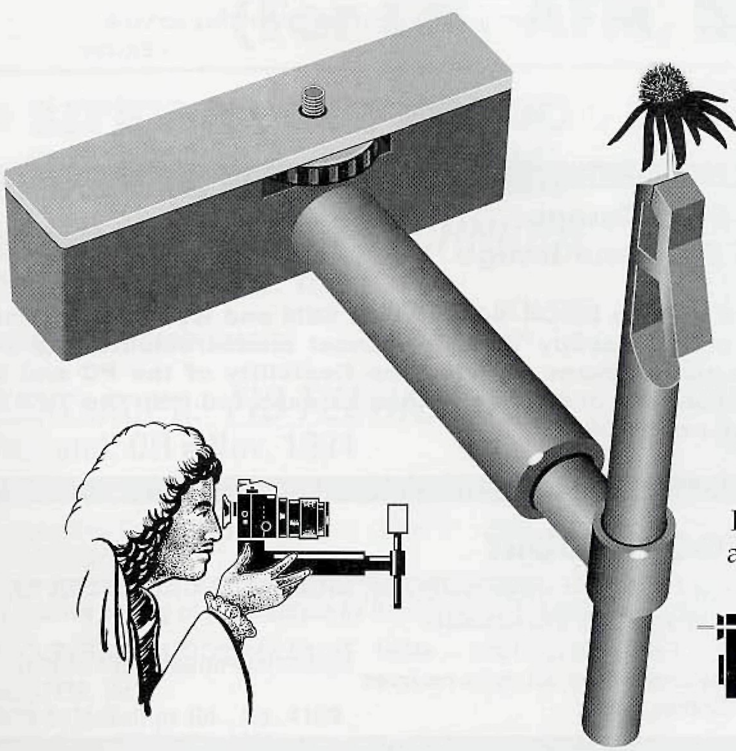

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