



Magnetic resonance force microscopy: A frontier for quantum system engineering

Some people say that the 21st Century will be the “Century of Biology.” But there an equally strong case can be made that it will be the “Century of Quantum Engineering.” At the University of Washington, a team of researchers is working to make both visions come true.

Members of the UW Quantum System Engineering Group are pursuing one of the oldest dreams of science: a microscope technology that can image individual atoms within biological molecules, in 3-D, non-destructively, with Angstrom-scale resolution. Such microscope technology would revolutionize structural biology as thoroughly as DNA sequencers have revolutionized the study of the genome.

Back in the 1940s and 1950s, many prominent scientists worked on atomic-resolution microscopy, including Linus Pauling, John von Neumann, and Richard Feynman. In a famous 1959 lecture entitled *There’s Plenty of Room at the Bottom*, Feynman¹ called for new ideas:

I put this out as a challenge: Is there no way to make the electron microscope more powerful? ... Make the microscope one hundred times more powerful, and many problems of biology would be made very much easier.

Feynman’s lecture is widely credited with having launched the field of nanotechnology, but it did not ignite a revolution in electron microscopy. Instead, over the next several decades, it gradually became apparent that biological molecules are simply too fragile to stand up to the brutal impact of high-energy electrons and x-rays. As a 1995 review article by Henderson² concluded:

Radiation damage ... prevents the determination of the structure of a single biological macromolecule at atomic resolution using any kind of microscopy. This is true whether neutrons, electrons, or x-rays are used as the illumination.

But this was not the end of the story. In the 1980s and 1990s, several new technologies came on-line, which together offer new promise of achieving the long-

cherished dream of true molecular microscopy. Three ideas were particularly important. First, the advent of magnetic resonance imaging in medicine proved that high-resolution images can be obtained with low energy (non-ionizing, and hence non-destructive) quanta.

Second, the advent of scanning probe microscopy proved that for a broad class of sensors, making the sensor smaller makes it work better. And third, the advent of trapped-atom experiments proved that quantum mechanics is true, in the sense that all the peculiar predictions that quantum mechanics makes for continuously observed single atoms are true.

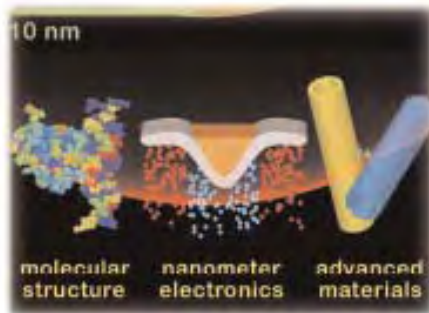


Figure 1: MRFM spin imaging targets.

Combining these ideas leads to magnetic resonance force microscopy (MRFM) (fig.1). As in medical magnetic resonance imaging, MRFM exploits spin resonance to create high-resolution images. In MRFM the magnetic environment is created by a micron-scale magnetic tip on a force microscope. The MRFM signal is not electrical, but is the attractive force between the spin(s) being observed and the tip. This mechanical detection strategy is hopeless at macroscopic scales, because the signal force is too small and the force microscope cantilever is too heavy.

As the cantilever and the tip are made smaller, the signal force gets stronger, and the cantilever gets lighter (and hence easier to move and more sensitive to the spin force).

One further ingredient is necessary: make the system cold. This reduces the thermal noise of the cantilever, stops the Brownian motion of the biological molecules observed and, lengthens the quantum coherence time of the spins being observed.

By following the general strategy of “smaller, colder, sharper, cleaner”, the MRFM community has improved sensitivity by 160 decibels during 1992-2003. Single-electron-spin sensitivity is now being approached.

There is, however, a substantial gap between single-electron sensitivity and single-proton sensitivity, because the electron magnetic moment is 650 times larger than the proton moment. Unpaired electrons are very rare in biological molecules, while protons are ubiquitous, so it would be very advantageous to be able to image protons. This means having come 160 decibels since 1992, the MRFM community still has about 56 more decibels to go.

How much farther can “smaller, colder, sharper, cleaner” be pushed? Relative to fundamental quantum limits, it appears that there is plenty of room for improvement. But there is often a big gap between theory and practice. What everyone in the MRFM community wants (and what we look to companies like Oxford Instruments to supply), is a robust, compact, closed-cycle 100 mK refrigerator, to serve as a test bed for the next generation of cantilevers, magnetic tips, and sensing and control technologies.

If the molecular imaging dreams of MRFM researchers can be realized, such that the quantum limits to biomolecular imaging can be approached in practice, then we can look forward to a world in which table-top scale cryogenic refrigerators are found in every biology laboratory, where they busily observe all the atoms and molecules within living cells and tissues.

References:

1. Feynman R. P., ‘*There’s plenty of room at the bottom*’, *Journal of Microelectromechanical Systems*, 1992; vol. 1 no. 1 pp. 60-66
2. Henderson R., ‘*The potential and limitations of neutrons, electrons and X-rays for atomic resolution microscopy of unstained biological molecules*’, *Quarterly Reviews of Biophysics*, 1995; vol. 28. no. 2, pp.171-193

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