

Nanodiamonds are promising quantum probes of living cells

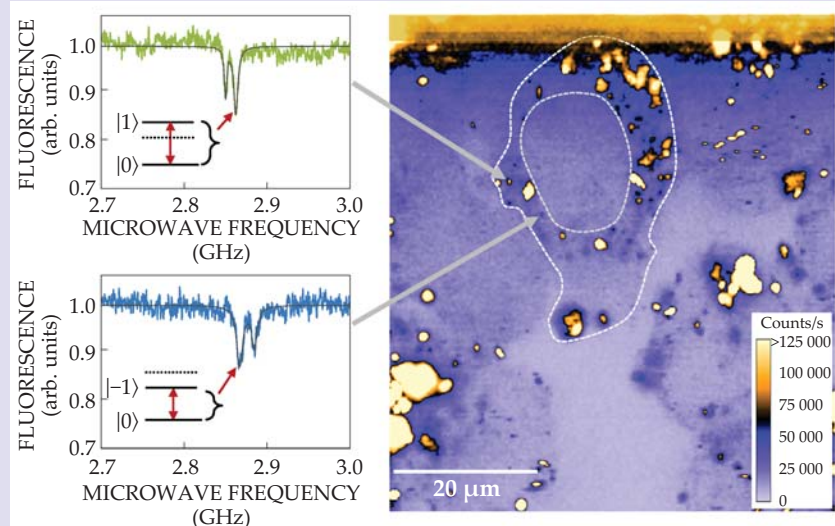
Even in a complex electromagnetic environment, the spin of a single point defect in diamond can be used as a sensitive magnetometer.

Magnetic resonance techniques work by detecting the response of electronic or nuclear spins as they are manipulated by an applied magnetic field. But magnetic resonance imaging and spectroscopy remain notoriously insensitive to faint magnetic moments at small length scales. The performance of induction coils, the standard detectors, scales poorly with decreasing size, and billions of spins are required to yield a recognizable signal. In 2004 Daniel Rugar and his IBM colleagues overcame the problem by combining magnetic resonance with force microscopy. Using a chunk of cobalt at the end of a cantilever, his group was able to locate a single electron spin inside a glass slab (see *PHYSICS TODAY*, September 2004, page 21).

Four years later, two research groups—one led by Mikhail Lukin, Ronald Walsworth, and Amir Yacoby from Harvard University, the other led by Fedor Jelezko and Jörg Wrachtrup from the University of Stuttgart—independently demonstrated an alternative approach that combines magnetic resonance with optical microscopy.^{1,2} Their method exploits the spin state of a crystal defect in diamond known as an NV center—a nitrogen atom substituted for carbon with an adjacent lattice vacancy. The atomically small defect can, if it's embedded in a nanoscale diamond, be brought extremely close to a microscopic sample. And thanks to the NV center's long spin-coherence time, which exceeds a millisecond in nearly pure crystals at room temperature, even tiny magnetic variations on the scale of nanoteslas perceptibly shift the defect's spin resonance frequency.

When optically excited, an NV center exhibits a stable fluorescence, even in a diamond crystal as small as 5 nm. Because of interactions among its electrons, the defect has magnetically sensitive spin sublevels in its ground state: a spin-zero level $|0\rangle$ split from nearly degenerate spin-1 levels $|\pm 1\rangle$ by a microwave transition of 2.9 GHz. That sensitivity allows one to detect weak magnetic fields by observing the spin state, which can be manipulated by microwave pulses and then read out by monitoring the fluorescence intensity. (The intensity depends on which of the spin states is populated.)

Researchers led by the University of



Point defects known as nitrogen-vacancy (NV) centers in diamond absorb green laser light and fluoresce in the red. In this confocal microscope image (right) of nanodiamonds in living cancer cells, the fluorescence intensity reveals a defect's spin state, either $m_s = 0$ (brighter) or $m_s = \pm 1$ (darker). Dashed lines mark the boundaries of a cell and its nucleus. Because each nanodiamond has its own unique size and shape, each NV center experiences a unique strain that breaks the degeneracy of $|\pm 1\rangle$ spin states and subtly alters the fluorescence spectrum. The spectra (left) thus act as fingerprints to identify, track, and sense the NV centers over hours. (Adapted from ref. 3.)

Melbourne's Lloyd Hollenberg have now performed such magnetic-resonance experiments on individual nanodiamonds inside human cancer cells.³ Fluorescent particles have long been used as markers to probe biological processes, but unlike many quantum dots, nanodiamonds are nontoxic and don't blink, and unlike fluorescent proteins, they don't bleach under long-term exposure to laser light. That photostability makes nanodiamonds particularly useful for tracking specific organelles, say, or molecular motors in vivo. But Hollenberg wondered if the NV center's remarkable quantum coherence could be maintained in a cell's noisy electromagnetic environment. His group's proof-of-principle experiments demonstrated that it could, albeit with coherence times on the scale of microseconds.

Once the cells ingested the nanodiamonds, the Melbourne team demonstrated how the defects' spin levels acted both as local magnetometers and as fingerprints to spectrally distinguish each nanodiamond from the others. Although NV centers are chemically sta-

ble enough to survive just nanometers from the crystal surface, they experience strain when so confined. Fortunately, the strain subtly alters each defect's energy levels and thus its fluorescence spectrum, as shown in the figure. Potentially thousands of NV centers can be uniquely identified and tracked with a precision of 20 nm, and their spin states repeatedly measured for hours.

Although it's possible to anchor a nanodiamond by chemically attaching ligands or proteins that latch onto cellular structures, the researchers allowed their nanodiamonds to freely tumble around the cell. To track that rotational component of the motion, they applied a fixed magnetic field while continuing to measure the spin resonance optically. The resulting orientation-dependent Zeeman shift in energy levels allowed them to deduce the particle's orientation to within 1° .

To measure an NV center's rate of decoherence, they used a microwave-pulse sequence to place a defect's spin in a coherent state—a superposition of $|0\rangle$ and $|+1\rangle$, for example—and then

made repeated measurements to monitor the characteristic time over which the spin-state oscillations decayed. That work now sets the stage for statistical studies that explore the link between an NV center's decoherence and local magnetic fluctuations in processes such as the charge transport through ion

channels in a cell membrane. Last year Hollenberg and colleagues calculated that ion-channel dynamics could, in principle, be detected with millisecond resolution by monitoring the probe's decoherence.⁴ The issue is not just academic; ion channels are important drug targets.

Mark Wilson

References

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2. G. Balasubramanian et al., *Nature* **455**, 648 (2008).
3. L. P. McGuinness et al., *Nat. Nanotechnol.* **6**, 358 (2011).
4. L. T. Hall et al., *Proc. Natl. Acad. Sci. USA* **107**, 18777 (2010).

Kinetic experiments shed light on protein-folding thermodynamics

Perturbing biomolecules and then watching them relax may be the kind and gentle way to determine their free-energy landscapes.

In its native state, the treasure trove of nutrients and biochemical machinery known as egg white is a slimy, translucent soup of proteins. Heat it atop a stove, however, and the proteins unfold, coagulate, and collectively morph into an opaque white solid. The unraveled proteins are said to have denatured. The enzymes among them, although well-suited for a cheese omelet, are in no shape to usher along biochemical reactions.

The proteins would have suffered a similar fate had the egg white been whipped into a foamy meringue or soaked in lime juice. Indeed, the precise biological work of folding a protein can be undone by any number of environmental stresses, including heat, acidity, and mechanical strain. Proteins, like all molecules, tend to adopt the shape that minimizes their free energy. In some circumstances, a compactly folded state makes thermo-

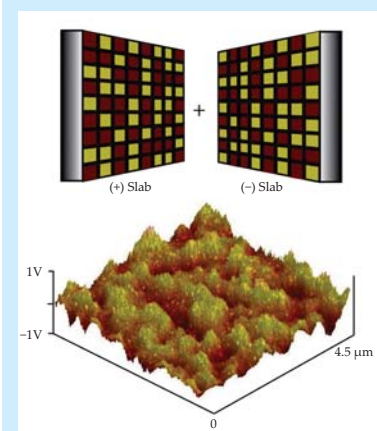
dynamic sense; in others, it doesn't.

To characterize the influence of environment on a protein's shape, biologists construct a free-energy landscape. They typically do so by performing titrations, experiments not all that dissimilar to frying an egg: A protein solution is subjected to a gradual ramp in some input variable—perhaps temperature, perhaps some other quantity—and monitored for physical changes indicative of folding or unfolding.

physics update

These items, with supplementary material, first appeared at <http://www.physicstoday.org>.

A nanoscale mosaic model of static electricity. Rub a balloon against your hair or rub any two nonconducting materials together, and as any high school physics student knows, the surfaces develop opposing static charges. Theoretical models of that process, known formally as contact electrification, have long assumed that the material properties of each surface are spatially homogeneous and that the post-contact charge distributions are uniform. If those assumptions were correct, then identical materials rubbed together should not transfer any charge. But



they do, as was demonstrated by Northwestern University researcher Bartosz Grzybowski and colleagues roughly two years ago with identical polymer slabs. They predicted then that charge is transferred through a random mosaic of oppositely charged sub-micron-scale domains, shown in the schematic, generated by inhomogeneities in the materials' surface properties.

Now, Grzybowski and other Northwestern researchers have experimentally verified the mosaic model by imaging contact-electrified polymer slabs with an atomic force microscope; the AFM-generated surface potential map shown here revealed multiple positively and negatively charged nanometer-sized domains. Probing further, the researchers found possible evi-

dence of surface inhomogeneities: Raman spectra indicated that some bonds were cleaved or oxidized, and x-ray photoelectron spectra of dissimilar polymer slabs that had been in contact revealed nonnative elemental peaks, which suggests material transfer. Their next goal is to probe other local surface properties to find out how bond breaking and material transfer influence domain size and overall charge. (H. T. Baytekin et al., *Science*, in press, doi:10.1126/science.1201512.)

—JNAM

Tantalizing and rare neutrino oscillation. The first appearance of electron neutrinos amidst an underground beam of muon neutrinos has been reported by Japan's T2K collaboration. The three "flavors" of neutrinos—electron, muon, and tau—can quantum mechanically swap identities in transit as long as all three neutrino masses are different. To date, those so-called flavor oscillations have been detected mainly by observing the disappearance, rather than the appearance, of neutrinos of a given flavor; the assumption is that some of the missing neutrinos changed identity en route from their source. Originating at the Japan Proton Accelerator Research Complex (J-PARC), the T2K muon-neutrino beam traveled 295 km to Japan's Super-Kamiokande detector, where 88 neutrino-interaction events were detected. Of those 88 events, 6 appear to come from electron-type neutrinos. Only 1.5 such events would be expected if the elusive flavor-mixing parameter θ_{13} were zero. The θ_{13} result, based on only 2% of the data originally expected from the experiment, is considered preliminary. But it is being published because J-PARC was damaged by eastern Japan's massive earthquake and tsunami on 11 March 2011 and will remain offline for many more months. If confirmed, the result will have profound implications: A nonzero θ_{13} makes possible CP violation with leptons, which might then explain the cosmic matter-antimatter imbalance. (K. Abe et al.: T2K collaboration, <http://arxiv.org/abs/1106.2822>.)

—SGB

Houston's structures thwart cleansing breezes. On 30 August 2000, as the Sun beat down on Texas's largest city, ozone