SENSORS AND PROBES

Magnetic field imaging and more

Two reports demonstrate further advances in the use of nitrogen vacancies for very different imaging applications.

At the end of 2012 we highlighted the use of nitrogen-vacancy (NV) color centers as a Method to Watch, and 2013 is not disappointing us. These defects in the regular carbon structure of diamond generate a fluorescence signal that is remarkably photostable and highly sensitive to magnetic fields. But all magnetic sensing applications of NV color centers to date have been in nonliving samples, and adapting nanodiamonds to biological imaging applications has proven challenging.

Ronald Walsworth of Harvard University and his colleagues now report the use of NV color centers for imaging magnetic fields in living organisms, albeit microscopic ones (Le Sage *et al.*, 2013). Many organisms contain natural magnetic nanoparticles. For example, magnetotactic bacteria have membrane-bound organelles containing nanoparticles that allow the bacteria to orient themselves and move along magnetic field lines. A possibly similar system operates in vertebrates to allow some species to navigate based on Earth's magnetic field.

To detect the magnetic fields from magnetotactic bacteria, Walsworth and colleagues created a tiny magnetic field imaging array using a nanometer-scale layer of NV color centers implanted at the surface of a diamond chip. When they placed the magnetotactic bacteria on the chip, the magnetic fields produced by the bacteria altered the fluorescence of the NV color centers that the fields contacted. This allowed the researchers to use a fluorescence microscope to visualize the magnetic fields and obtain correlated bright-field optical images of the bacteria.

For imaging live bacteria, they used their microscope in a total-internal-reflection geometry that limited the high-intensity green excitation light to the diamond chip while allowing the red fluorescent signal for reading out the magnetic fields to pass through the bacteria and into the objective above. This allowed them to image the bacteria for several minutes while maintaining cell viability. However, the quality of the fluorescence signal was substantially improved when they used dead bacteria exposed to direct excitation in the absence of the poly(L-lysine) adhesion layer needed for live-cell imaging on the diamond chip. The next challenges will be adapting the method for application to more varied and complex biological systems.

Although Walsworth and colleagues relied on NV color centers localized outside the organism being imaged, nanodiamonds containing NV color centers have properties—such as photostability, biocompatibility and near-infrared fluorescence—that would facilitate many imaging applications. But particle aggregation and difficulty attaching biological molecules to the inert diamond surface have limited their use to date. To address these challenges, Keir Neuman, of the National Heart, Lung, and Blood Institute of the US National Institutes of Health, and his colleagues developed a liposome-based encapsulation process to coat the nanodiamonds in a silica shell that can be easily modified (Bumb *et al.*, 2013). The procedure has the added benefit of selecting particles smaller than 100 nanometers in diameter to produce a monodisperse mixture in solution.

The researchers tested their ability to functionalize the particles by attaching a biotin tag, and they verified the performance of the functionalized nanodiamonds by tethering a single particle to a surface with a DNA molecule and then tracking the particle's movement. The stability of the nanodiamond fluorescence conveniently allowed them to eliminate background fluorescence by bleaching and to obtain strong and stable signals with a single nanodiamond.

These probes should be useful not only for single-molecule tethered-particle assays but also potentially for *in vivo* imaging applications in large organisms that would benefit from the near-infrared fluorescence emission of the probes. As with quantum dots, however, delivery of the probes will often not be as convenient as with genetically encoded proteins. But the performance qualities of nanodiamonds appear impressive enough that they should become an important class of probes for numerous biological applications, and one with the ability to interrogate magnetic fields in a way no other probe can.

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RESEARCH PAPERS

Bumb, A. *et al.* Silica encapsulation of fluorescent nanodiamonds for colloidal stability and facile surface functionalization. *J. Am. Chem. Soc.* doi:10.1021/ja4016815 (12 April 2013).

Le Sage, D. *et al.* Optical magnetic imaging of living cells. *Nature* **496**, 486–489 (2013).

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