As promising as the method is, detecting carbon cluster ions as proxies for the carbon nanomaterials means that the method does not directly indicate whether the carbon nanomaterials have been transformed *in vivo*. Any reactions (for example oxidation) undergone by the nanomaterials might be apparent in any new cluster ions that appear, but knowing the extent to which the nanomaterials are degraded would seem beyond the capabilities of the current imaging method.

Nonetheless, imaging mass spectrometry has a bright future when it comes to studying nanomaterials *in vivo*. One particularly exciting advance would be to extend the reported approach to enable the simultaneous detection of nanomaterials and nearby proteins or other biomolecules. Images that reveal what biological molecules orient themselves around nanomaterials would provide an even deeper understanding of the biochemical effects of such materials. One would think that

pictures such as this might then be worth ten thousand words or more. ❐

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NITROGEN–VACANCY CENTRES

Nanoscale MRI

Sensitive measurement of nitrogen–vacancy centres close to the surface of diamond enables magnetic resonance imaging with a resolution of a few nanometres in ambient conditions.

Vidya Praveen Bhallamudi and P. Chris Hammel

Magnetic resonance uses the spins of electrons and nuclei present in matter as precise *in situ* probes for imaging, chemical fingerprinting and structural analysis. The ability to measure the frequency of the oscillation of these spins underlies these applications. Because of the exquisite sensitivity of the spin resonance frequency to the local effective magnetic fields generated by the

surrounding atoms and molecules, magnetic resonance spectroscopy provides a unique fingerprint for a particular molecule or atomic arrangement and their interaction with the local environment. Magnetic resonance imaging has revolutionized medical imaging because it provides three-dimensional images of objects and is non-destructive. In medical MRI a number of spins on the order of 10^{15} are typically

used, however extending the technique to the molecular scale will require significant improvements in sensitivity because of the intrinsic weakness of the interaction of the spins with their surroundings.

Now, writing in *Nature Nanotechnology* three independent groups describe[1–3] how they have pushed the limits of magnetic resonance spectroscopy and imaging far into the nanoscale regime. They all employed sensitive optical detection techniques and microwave manipulation of spins to measure the magnetic resonance from a nanoscale group of nuclear spins, and all achieved an imaging resolution of 10–20 nm in ambient conditions. Such extreme sensitivity is needed to understand processes at the single-atom and molecular levels that are important for biological functions and also for developing the next generation of electronic devices. The common thread through all three experiments is the use of the unique combination of the properties of a defect in diamond known as a nitrogen–vacancy (NV) centre[4].

Nanoscale MRI was first achieved by using a sensitive cantilever whose swinging action was subtly modified by the forces exerted by the nuclear spins, an approach known as magnetic resonance force microscopy[5]. This approach enabled a resolution of a few nanometres, albeit at cryogenic temperatures (below 1 K) and with measurements lasting days to reduce the noise to a reasonable level. In an alternative approach, considerable progress has recently been made using negatively charged NV centres (NV$^-$).
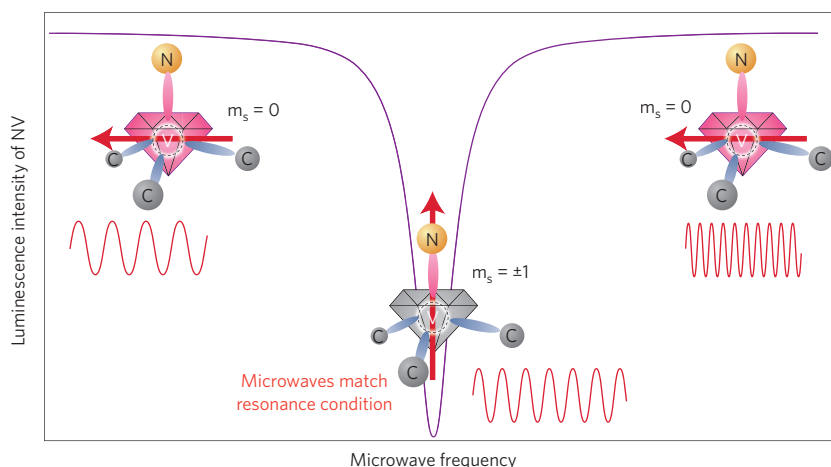

Figure 1 | Optical detection of the magnetic resonance of a NV diamond centre. The spin state of an electron (red arrow) associated with an NV centre, and hence its manipulation using magnetic resonance, is detected via its influence on the optical luminescence. The luminescence is bright when the spin state is in the quantum mechanical state $m_s = 0$ and darker when in the other two states: $m_s = +1$ or $m_s = –1$. Magnetic resonance induces transitions between the $m_s = 0$ and $m_s = ±1$ levels when microwaves (indicated by the sine waves) are applied. The laser light that causes luminescence also initializes spin(s) to the $m_s = 0$ state. Hence, when microwaves in resonance with the spin oscillations shift the spin to the $m_s = ±1$ state the luminescence changes and this can be picked up by a highly sensitive detector. Resonance of a single NV centre can be measured in ambient conditions.

An NV centre, which consists of a nitrogen impurity adjacent to an empty site in the lattice of carbon atoms, exhibits a strong luminescence that is dependent on its magnetic state resulting from its spin and orbital moments. By monitoring this luminescence, it is possible to measure the magnetic state of the NV centre[6] with high sensitivity (Fig. 1). Furthermore, other properties of the NV centre make it a powerful tool for magnetic resonance applications. First, the luminescence does not photobleach with increasing excitation power, which, in principle, allows the noise of the detected signal to be reduced by simply exciting with higher intensity. Second, the excitation laser can be used to orient the spin in the state that maximizes its sensitivity to fields from the surrounding nuclear spins. Finally, the NV spins can maintain their orientation for relatively long periods (approaching milliseconds), which is an important feature for some measurement protocols needed in MRI experiments.

This combination of properties has allowed the detection of the magnetic resonance of a single electron spin in ambient conditions[6] and has provided the basis for a promising quantum computing platform[7,8]. Although an impressive achievement, measuring an individual NV⁻ spin is only the first step towards measuring the resonance of a small number of nuclear spins. The next step is measuring the tiny changes in magnetic field, experienced by the NV⁻ centre, when nuclei close by are perturbed at their own resonance frequency. This nuclear magnetic field decreases as $1/x^3$, where x is the distance from a nucleus. In practice it is ~1 nT at only 10 nm away. An essential achievement for all three groups[1–3] was that the distance of the NV centre from the target nuclei was reduced by creating NV centres within a few nanometres of the diamond surface.

Another problem to be solved is that because of their high sensitivity, NV centres tend to pick up magnetic noise generated by sources other than the target nuclei. A technique developed in the past to solve this problem uses microwave pulses to detect nuclear spins within a 5 nm³ volume[9] (shown schematically in Fig. 2). The key point of the technique is that the experiment can be arranged so that all the spurious magnetic fields will average to zero, except for those of the target nuclei. It has been pointed out[10] that one must take caution to avoid contamination of the signal by harmonics of unwanted background nuclei.

Although the basic measurement protocol is similar for all three imaging experiments, there are some differences.
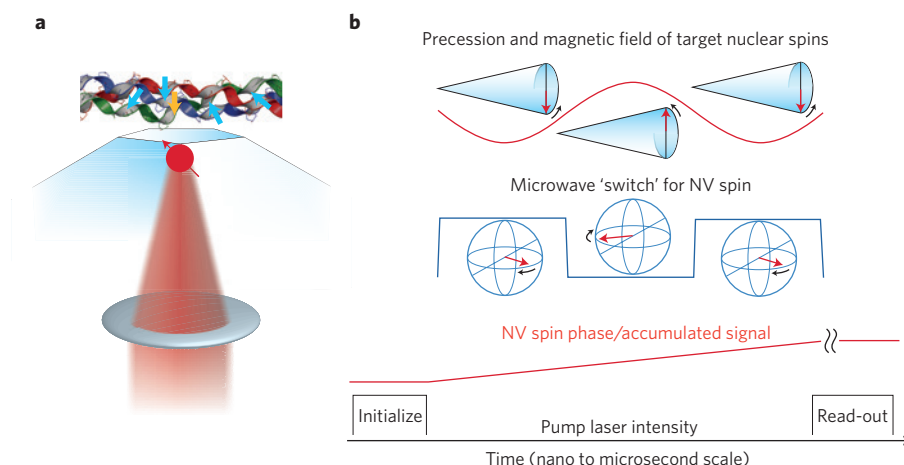

Figure 2 | Measuring the magnetic field of a nuclear spin oscillating at its resonance frequency. **a**, The nuclear spins of interest (yellow arrow), perhaps in a biomolecule (coloured ribbon structure), are brought within a few nanometres of a single NV centre or a collection of NV centres embedded in diamond and located close to the surface. The sample may contain other unwanted spins (blue arrows). The luminescence of the NV centre is monitored while manipulating it with pulsed microwave radiation. **b**, A schematic explaining the protocol for measuring the magnetic resonance of a nuclear spin. The top panel shows the precession (black arrows), that is, a spinning-top-like motion of the nuclear spins (red arrows) at their resonance frequency due to an applied magnetic field. This motion results in an oscillating magnetic field, represented by the red curve, that gets detected by the NV spin. The rotation frequency of the NV spins due to their precession in the applied field is slightly modified by the small additional fields from other spins, including the target nuclear spins. The middle panel shows how pulsed microwaves can be used to effectively switch that response by flipping the NV spins. The blue line shows the sign of the NV centre electron spin and its variation in time. Each time the spin is hit by a microwave pulse, denoted by the vertical lines, the spin changes its sign. Bottom panel: In general, the oscillating nuclear spin field will speed up the NV spins as much as it slows them down, so the NV spins will not accumulate any phase, that is, they will end up in the same place they started. However, if the precession rate of the target nuclear spins is set to be precisely half the flipping rate of the NV spins, the sign of the response of the NV spins reverses exactly as often as the nuclear field varies. As a consequence the nuclear field always has the same effect, thus causing the NV spins to accumulate a phase. This accumulation partially shifts the NV spins from the $m_s = 0$ to $m_s = \pm 1$ state, thus altering the measured luminescence. Image of collagen model protein, coloured ribbon, in panel **a**, © iStock/Thinkstock.

Dan Rugar and colleagues from IBM, Stanford University, University of California, Santa Barbara and University of Chicago[1] and Friedemann Reinhard and colleagues from the University of Stuttgart and the Max Planck Institute in Stuttgart[2] adopted an approach that involved scanning the sample, mounted at the end of a micrometre-scale cantilever, relative to the NV centre that serves as the detector. Rugar and colleagues spectroscopically analysed the nuclear moment of hydrogen, a key component of biomolecules, with 12-nm spatial resolution, limited by the stability of their scanning hardware. Reinhard and colleagues spectroscopically analysed both ¹H and ¹⁹F. Ronald Walsworth and colleagues from Harvard University and Hebrew University[3] added a third species, ³¹P. They also demonstrated the imaging capabilities using a collection of NV centres in a diamond chip and took a snapshot of the optically detected magnetic resonance

with a charge-coupled device camera. Although this camera approach coarsens the spatial resolution, it is fast and therefore potentially useful for rapidly assaying a sample.

The field of NV magnetometry-based magnetic resonance detection has been advancing systematically and holds substantial technological promise for commercialization. However, the spectral resolution attained in measuring the resonance frequency of the nuclei is still far from the sensitivity level achieved in conventional spectrometers using inductive detection. Also, the reliable fabrication of diamond detectors with near-surface NV spins that maintain the long spin lifetimes needed for high sensitivity measurements is still a challenge, despite some progress, particularly for lithographically fabricated nanoscale diamond probes that are needed for a more widely applicable scanning probe approach. The submicrometre spatial

resolution achieved for a large collection of NV centres, albeit having short spin lifetime, could enable rapid assaying of larger-scale samples as opposed to the structural imaging of small molecules that is likely to require scanning of individual NV centres. Perhaps more fundamental is the fact that the nuclear spin detection sensitivity degrades substantially for nuclei more than a few nanometres away from the NV centre. This could become an issue for fully three-dimensional imaging of a large molecule where some regions are far from the

detector. The key, of course, is continuing to improve detection sensitivity such as by increasing the light coupling efficiency by, for example, using solid immersion lenses, or alternatively, amplifying the signal at distances farther away from the nuclei by means of a ferromagnetic amplifier[11]. ❒

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PIEZOELECTRICITY

Now in two dimensions

Single layers of molybdenum disulphide can exhibit piezoelectric effects.

Evan J. Reed

Piezoelectric crystals exhibit an electrical polarization under an applied strain. This effect enables a wide variety of applications including resonators for clocks, stress sensors for aircraft, inkjet printers, and surface acoustic wave devices for radiofrequency signal processing. These applications all employ piezoelectric effects in three-dimensional crystals. Writing in *Nature*[1] and *Nature Nanotechnology*[2], two independent research groups now report the observation of piezoelectric effects in the atomically thin two-dimensional crystal, single-layer MoS_2.

For a crystal to be piezoelectric it must not have a centre of inversion symmetry: that is, there should be no point in the crystal whereby reflection of all atomic positions through that point leave the atomic positions unchanged (Fig. 1). The recent isolation of few-layer and single-layer materials such as graphene and MoS_2 provides crystals with symmetry properties that are distinct from those of bulk crystals. Bulk MoS_2 consists of stacked layers of MoS_2 monolayers bonded by van der Waals forces, and has a centre of symmetry located between the layers; it is therefore not piezoelectric. However, peeling a single layer of MoS_2 from the bulk crystal removes the centre of symmetry, potentially leading to piezoelectricity.

One might naively imagine that such a piezoelectric effect in a two-dimensional crystal might be rather small compared with the three-dimensional case. However, Xiang Zhang and colleagues at the University of California at Berkeley and

Lawrence Berkeley National Laboratory show[2] that monolayer MoS_2 exhibits a piezoelectric effect with a coefficient that is comparable to three-dimensional piezoelectric wurtzite structure materials, such as ZnO. The researchers apply an electric field across a suspended MoS_2 monolayer. The piezoelectric effect changes the tension in the monolayer, altering the deflection of a cantilever in contact with it, thus allowing the quantification of the piezoelectric coefficient.

In contrast to the use of suspended layers, Zhong Lin Wang, James Hone and colleagues at Georgia Institute of

Figure 1 | Crystal symmetry and piezoelectricity. **a**, A centrosymmetric crystal yields no electrical polarization, *P*, when strained uniaxially because there is no specific direction for a polarization to point. **b**, A non-centrosymmetric crystal instead exhibits a specific direction under uniaxial strain and therefore an electrical polarization. The triangular shape is non-centrosymmetric because there is no point about which an inversion leaves the orientation of the triangle unchanged.

Technology, the Chinese Academy of Sciences and Columbia University report piezoelectricity in monolayer MoS_2 using a flexible substrate[1]. Strain is applied to the monolayer by bending the substrate; piezoelectric effects are observed in the current and voltage measured across electrical contacts to the monolayer. This experimental approach is promising for use in flexible sensors and electronics.

The presence of inversion symmetry in bulk MoS_2 leads one to expect the piezoelectric coefficient to decrease to zero as the number of layers increases. However, both research groups report that the piezoelectric coefficient exhibits a non-monotonic decrease with an increasing number of layers[1,2]. The piezoelectric coefficient of a bilayer is found to be zero (within experimental uncertainty) due to the presence of an inversion centre between the two layers that does not exist for a single layer. The piezoelectric coefficient of a trilayer is found to be non-zero due to the lack of an inversion centre, but smaller in magnitude than that of a monolayer. These observations are consistent with a decay towards the bulk value of zero. Both groups also report that the piezoelectric effect changes sign on rotation of the monolayer by 90° (refs 1,2). The magnitude and symmetry-related properties of the piezoelectric coefficients of both these experiments are in agreement with earlier theoretical predictions[3–5].

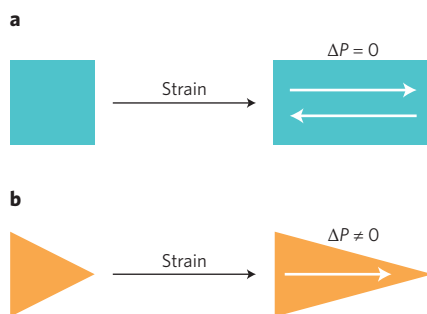There are likely to be a number of other two-dimensional piezoelectric materials, including boron nitride[6] and many of the