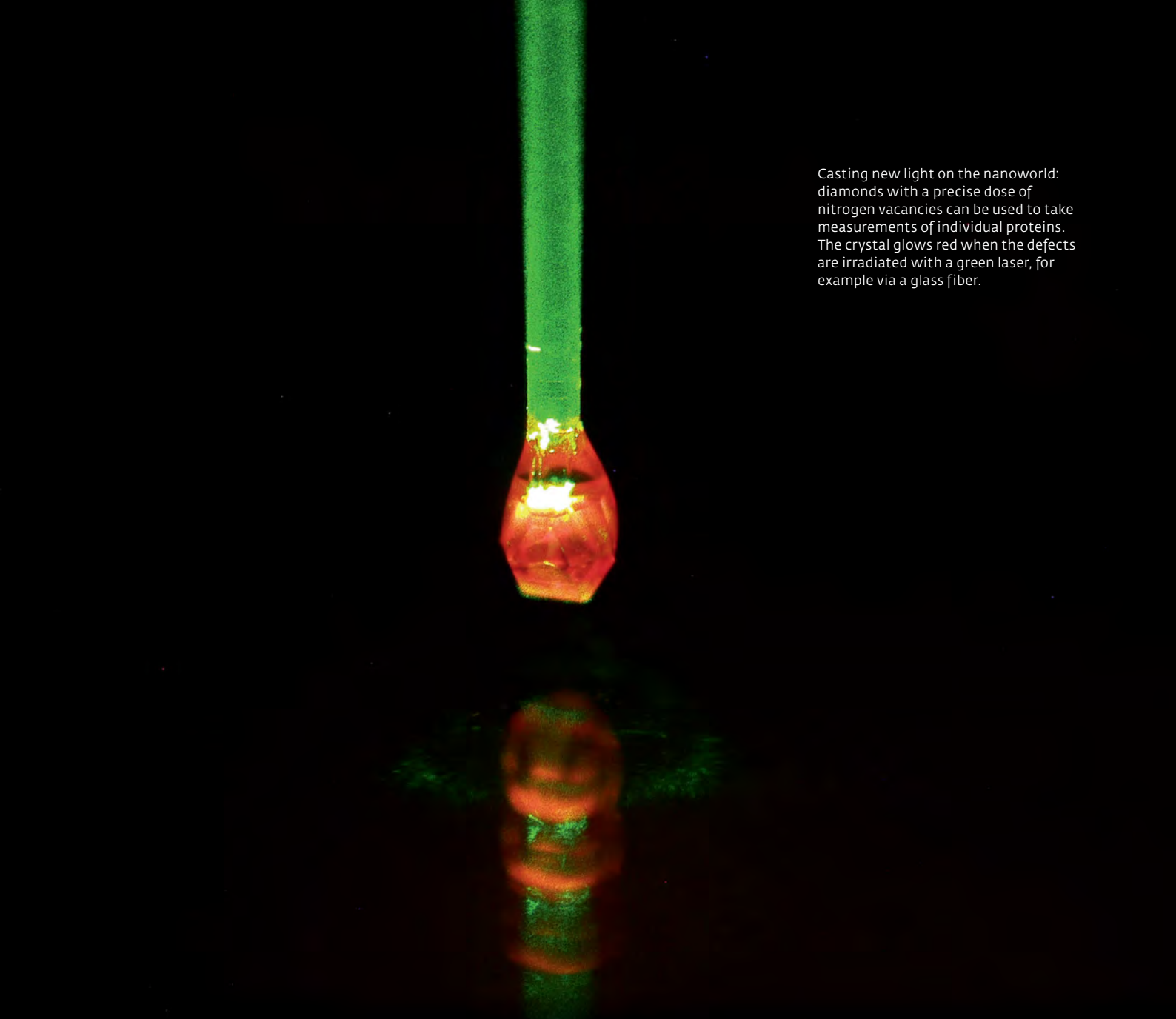


Diamond – a flawless sensor

Brilliant-cut diamonds can emit a dazzling array of light, but that is not what attracts **Joerg Wrachtrup** to these precious stones. The Professor of Physics at the University of Stuttgart and Fellow at Stuttgart's **Max Planck Institute for Solid State Research** works with less conspicuous diamonds. His team uses these to develop sensors that are intended to allow live observation of the molecular machinery in a living cell. These insights into the nanoworld could also be of benefit in medicine.



Casting new light on the nanoworld: diamonds with a precise dose of nitrogen vacancies can be used to take measurements of individual proteins. The crystal glows red when the defects are irradiated with a green laser, for example via a glass fiber.

TEXT **ROLAND WENGENMAYR**

Diamonds can also look like this – a tiny, rectangular block of jet-black material in a small box that Matthias Pfender has taken out of a drawer. Pfender is a doctoral student working under Joerg Wrachtrup, and we are in a laboratory at the University of Stuttgart, where Wrachtrup is Professor of Physics. Wrachtrup also carries out research as a Fellow at the neighboring Max Planck Institute for Solid State Research, of which he has a good view from his office window at the university.

Matthias Pfender then shows us a tiny yellow plate of diamond, whose

laser-cut shape is reminiscent of a small plastic building block in a child's bedroom. "We don't exactly give our diamonds a brilliant-cut finish," Wrachtrup smiles when he sees the astonished look on his guest's face. On the contrary, his research involves deliberately incorporating defects into diamond crystals, and these defects manifest themselves as discoloration. "Bling" is definitely not the word – and burglars would be disappointed with these tiny stones, which are barely recognizable as diamonds.

Here in Stuttgart, the physicists are more interested in the crystals' inner qualities, so to speak, because the de-

fects that give the diamonds their color also have special quantum properties. They can be used as extremely small, ultrasensitive quantum sensors for magnetic fields – or as components for the quantum information technology of the future. Both areas are the subject of research by teams working under Joerg Wrachtrup, who has spearheaded a veritable diamond fever among the scientific community. The number of research teams working in the field is growing steadily, and many of them are being set up and led by Wrachtrup's former students.

The purpose of the visit to Stuttgart is to see the smallest magnetic sensors

» A technique that allows the direct observation of biomolecules, atom for atom and in the living environment, could mark a breakthrough in biomedical research.

in the world. One day, these are expected to be capable of deciphering chemical structures, such as those of biomolecules. “The dream is to be able to study small or large molecules in living cells or their membranes using a quantum sensor of this kind,” says Wrachtrup, outlining the long-term aim of his research.

There are a variety of tricks that allow existing optical microscopy techniques to track the movements of proteins, for example, but optical microscopes are unable to resolve how atoms arrange themselves in biomolecules while they perform their functions. However, this is often a crucial part of understanding the biochemical processes of life. In many cases, such processes are driven by tiny movements in specific sections of large, coiled molecules. A precise view of proteins at work could also help re-

searchers develop starting points for new medical agents.

Until now, the techniques for resolving a molecular structure on the atomic scale required the molecules to be placed in hostile environments for life – that is, in a vacuum and in the cold. However, a molecular structure recorded using X-rays can deviate significantly from the structure operating in the living cell. Therefore, a technique that allows the direct observation of biomolecules, atom for atom and in the living environment, could mark a breakthrough in biomedical research.

DEFECTS WITH SPECIAL QUANTUM PROPERTIES

Over a coffee, Joerg Wrachtrup offers a lively explanation of why he and his colleagues need diamonds for measurements of this kind: they are the only

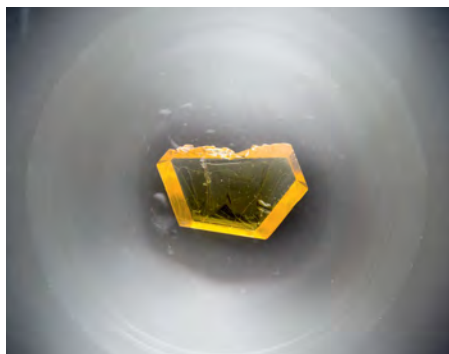
materials into which the scientists can incorporate defects with special quantum properties.

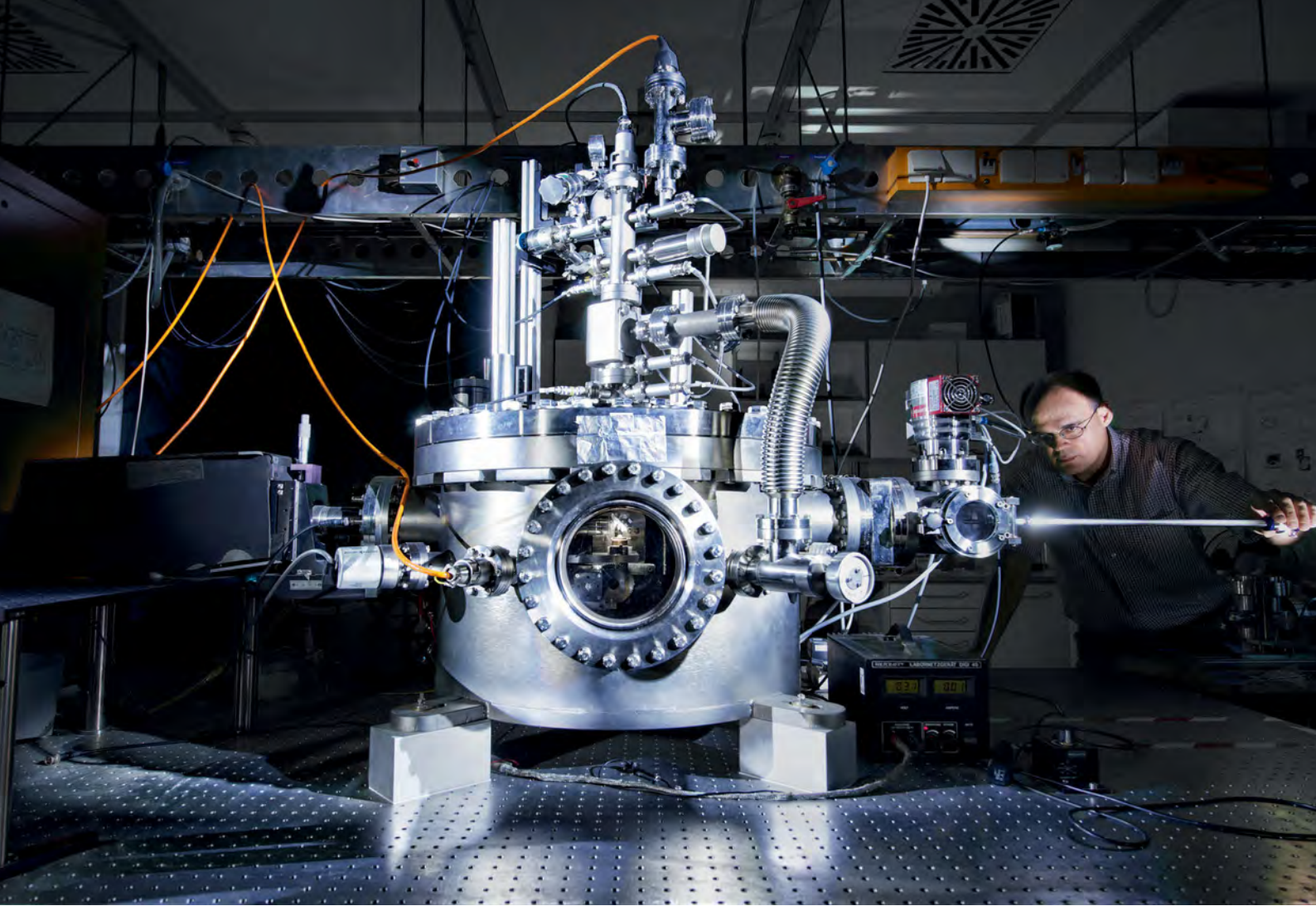
The artificial crystals are manufactured using two processes. One of these is the established industrial process, in which carbon is compacted under enormous pressure and at high temperatures to form diamond, the hardest and most precious form of carbon that exists. “This produces particularly perfect, stress-free diamonds,” says Wrachtrup. The other method is known as chemical vapor deposition. Here, the diamond grows on a substrate, depositing one layer of atoms at a time. This method can be used to produce extensive, flat samples of diamond that can be readily cut into various shapes using lasers. Such diamonds have a characteristic platelet shape, like that of the yellow sample we saw in the lab.

Producing ideal diamonds for use as quantum sensors is one objective of the collaboration between the Max Planck Institute for Solid State Research and the Fraunhofer Institute for Applied Solid State Physics (IAF) in Freiburg. This also involves incorporating a precise dose of nitrogen atoms into one of the artificial gemstones. Nitrogen atoms are a similar size to carbon atoms and therefore fit well into the crystal lattice. In large numbers, nitrogen atoms also produce a yellow discoloration because, unlike the pure carbon lattice, they can absorb or emit visible light. Defects of this kind are therefore also known as color centers.

That is just the beginning, however. The key ingredient for the perfect defect is a hole, a missing atom in the

Variants of diamonds: an industrial process at high pressure and high temperature produces particularly perfect gemstones, which take on a yellow color due to the large number of nitrogen atoms that are incorporated (left). Chemical vapor deposition, on the other hand, leads to the growth of flat crystals that can be cut into various shapes (right).





Physically refined: in order to convert an artificially manufactured diamond into a quantum sensor, Andrej Denisenko pulls it into the chamber of an implanter using a telescopic rod. There, nitrogen atoms are added to the crystal, giving it special quantum properties.

three-dimensional network of the crystal lattice. The holes produced during the diamond's preparation migrate through the diamond lattice until they become attached to nitrogen atoms, because defects often tend to stick together. In a stroke of luck for researchers, this effect produces what are known as nitrogen-vacancy centers, or NV centers for short.

The special thing about these double defects is that they connect several individual electrons together into a tiny bar magnet. Electrons themselves are not elementary magnets; the origin of the magnetism is their spin, a sort of quantum mechanical pirouette. The very special environment in the NV center causes them to combine to form a tiny bar magnet, which is able to rotate. On entering a magnetic field, however, this bar magnet acts like an old-fashioned electrical rotary switch

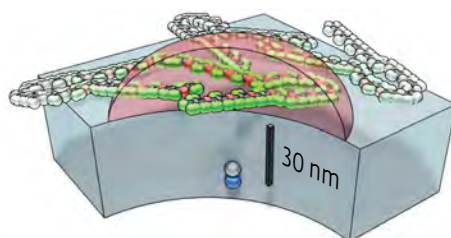
and can only click into place in two positions: parallel or antiparallel to the field. This behavior is determined by the laws of quantum physics. Since these two states can store the information zero and one, they turn the magnet into a perfect quantum bit – the smallest processing unit of a quantum computer, which may one day be many times faster than conventional computers at solving certain tasks. In addition, an NV center in a diamond can also be used as an ultrasensitive quantum sensor for magnetic fields.

Such quantum sensors for magnetic fields are suitable not only for examining the structures of individual proteins or other biomolecules, but also for analyzing irregularities in the structure of solids in nanoscopic detail. For this, Joerg Wrachtrup is working with Klaus Kern, Director at the Max Planck Institute for Solid State Research. As a result,

quantum sensors in diamonds could help to accurately analyze the structure of superconductors, which can already conduct electricity losslessly at relatively high, but not yet practicable, temperatures. Such analyses could help scientists to understand this effect better and to develop practical everyday materials for the resistance-free transmission of electricity.

DIAMOND'S STRUCTURE PROTECTS THE QUANTUM STATE

The reason why the double defect – consisting of a nitrogen atom and a vacancy in the diamond's crystal lattice – is so well suited to gaining insights into the nanoworld is that this structure provides exceptionally good protection for the sensitive quantum state in which these spins exist. This means that even at room temperature, the NV



Magnetic resonance imaging in the nanoworld: a nitrogen-vacancy center (the blue and white spheres) in a diamond can detect tiny magnetic signals, and can be used to determine the structure of an individual protein.

centers retain a quantum state stored in the electron spin for several thousandths of a second – an eternity in the quantum world.

INFORMATION FROM THE NV CENTERS READ USING LIGHT

In conventional materials, the spin state would be destroyed approximately a billion times faster, unless colossal efforts were made to insulate it and cool it down to temperatures well below freezing point. This is because artificially prepared quantum states are usually extremely sensitive, especially to the thermal vibration of neighboring atoms. Room temperature is therefore essentially forbidden territory for many quantum technologies. The fact that NV centers retain their special quantum state even at room temperature makes them ideal for researching biological systems, which cease to operate at very low temperatures.

However, NV centers also have another important property: they can translate the quantum states of the tiny magnets directly into information that can be read using light. This is where the properties of the color center come into play. In simple terms, if you shine the right color of laser light at the diamond, the NV centers will

glow, and the intensity of this glow depends on the quantum state of the respective tiny magnets. With the help of a microscope lens, the light can then be captured and analyzed with a camera sensor.

Accordingly, anyone who can manipulate the NV centers in the diamond skilfully has an extremely useful system at their disposal. Because it is microscopically small and therefore part of the molecular world itself, it can approach the molecules in question directly in order to act as a magnetic superlens. The spatial resolution can be enhanced to the size of a single NV center. “If we trace the samples with this, we can detect magnetic fields at a resolution of one ångstroem,” says Joerg Wrachtrup. An ångstroem is a tenth of a nanometer, which is in turn equal to a billionth of a meter. For example, a carbon atom – the building block of the diamond lattice – has a covalent radius of slightly less than one ångstroem.

In practical terms, measurements with the quantum sensor follow the pattern of a long-established technique known as nuclear magnetic resonance (NMR) spectroscopy. The medical variant of this is magnetic resonance tomography, which is better known as magnetic resonance imaging (MRI).

Both techniques exploit the fact that the atomic nuclei of certain chemical elements act as tiny magnets. The most important of these is the omnipresent atom hydrogen, which is built into all biologically relevant molecules on a massive scale. Another example is ^{13}C . This naturally occurring stable isotope of the carbon atom plays an important role for the team in Stuttgart: it contains one more neutron than ^{12}C , which is almost a hundred times more common in nature.

THE ENVIRONMENT HAS AN IMPACT ON SPINNING NUCLEI

NMR and MRI measurements, including those with an NV center as a sensor, work by causing magnetic atomic nuclei to spin in a strong magnetic field. In the Stuttgart researchers’ laboratory, this field is generated by a superconducting magnet in a tank containing a coolant; this looks a lot like the hot water storage tank found in some homes. The researchers place the diamond quantum sensor in a tube that sits beneath the tank and encloses a cavity measuring about a hand’s width across. A whole host of optical instruments complete the experimental setup on the lab bench, which is approximately the size of a double bed.



Diamond in the pipeline: Nabeel Aslam (left) and Matthias Pfender adjust the optical instruments that they use to read the results of magnetic field measurements taken with a quantum sensor (top). They place the sensor in a cavity (left, partly obscured by a tank containing coolant) inside the field of a superconducting magnet, which operates at a temperature well below freezing point. To obtain the measurements, the researchers must fire microwave pulses at the diamond. They therefore clamp the crystal into a structure that generates pulses of this kind (below).

Photos: Wolfram Scheible (2)



Once the researchers have applied the sample to the diamond for analysis, they fire a radio signal at it to tilt the atomic gyroscope of the sample molecules. The rotating nuclear spins then gradually return to their original position. In the process, they emit a radio signal of their own, and this response is recorded by receiving coils. Medical MRI scanners use the response to generate images of the inside of the body.

NMR spectrometers, as well as the Stuttgart team's quantum sensors, deliver different information. The most important part of this, and the easiest to decipher, is the chemical element represented by the emitting nucleus. However, the signal also contains considerably more information because, like small compasses, the spinning nuclei are influenced by the atoms in their environment. As a result, NMR signals can be used to draw very accurate conclusions about the chemical structure of molecules. Like a fingerprint, certain parts of the signal indicate where the emitting atom is within the molecule and what chemical

bonds it has to neighboring atoms. NMR spectroscopy has therefore become one of the most powerful tools for elucidating chemical structures, although the technique would be even more powerful if it could also determine the structure of a single molecule. However, their relatively large coils mean that today's NMR instruments are not sensitive enough for the radio signals emitted by molecules.

MAGNETIC SENSOR TECHNOLOGY IN THE NANOWORLD

The quantum sensors from Joerg Wrachtrup's lab can transcend the boundaries of magnetic sensor technology in the nanoworld. This involves applying the sample to the surface of the tiny diamond. In the extreme case, a single NV center directly below it acts as a sensor. "It's then far smaller than the molecule it's being used to examine," Wrachtrup points out. This allows it to detect exactly how far away a specific atom is in the molecule. You can imagine it



The Stuttgart-based researchers use a diamond to measure the field of a cube-shaped magnet (left). The intensity of the glow from the quantum sensor when irradiated with green laser light depends on the strength of the magnetic field.

as like standing directly under an apple tree so that you can see exactly where the individual fruits are hanging above you. Of course, there are limits to the visibility: the signal strength of the spinning nuclei falls away quickly with distance, so the NV center can only cover a volume with a radius of a few nanometers. If the methods for analysing the chemical fingerprints in NMR spectroscopy are one day adapted to evaluating the light signals from NV centers, they will allow the precise chemical structure of a molecule to be deciphered.

A PROTEIN'S MOTION CAN BE OBSERVED

Initial experiments have shown that this works in principle. As part of an international scientific collaboration back in 2015, the Stuttgart-based researchers demonstrated that the technique can be

used to observe the movements of a protein. For this test, the team took a key protein for cell division and placed it in an environment that simulated the conditions in a living cell.

However, before they could resolve the signals from individual atoms in such a protein accurately, they had to crack another fundamental problem: the difference between the nuclei's magnetic transmission frequencies is so small that they are difficult to separate. They are like radio stations that are very close to each other on the tuning dial – only a good radio can receive them clearly.

This is precisely the problem with using NV centers as quantum sensors: although they are sensitive, they are unable to resolve the atomic transmission frequencies in a molecule because a single measurement only delivers a weak signal that is hard to distinguish from neighboring signals. You can imag-

ine the problem as two loosely coupled pendulums, the first of which is supposed to measure the frequency of the second. The measuring pendulum must swing for long enough so that it can accurately tune in to the frequency of the other pendulum. The quantum sensor is like a pendulum that cannot swing for long enough.

STORING MULTIPLE MEASUREMENT RESULTS

The researchers in Stuttgart therefore had the idea of storing the results of multiple individual measurements. They came up with this approach not least because they are also researching how quantum information can be processed using NV centers. This depends on being able to store a quantum bit for a prolonged period of time. It therefore seemed obvious to save the information from the magnetic quantum

»» This would allow researchers to watch life itself at work in a cell, so to speak.

sensors in the same way as they store, for example, intermediate results of quantum information processing from an NV center.

The scientists' trick is to transfer the frequency information from a short magnetic measurement with an NV center into a directly adjacent long-term memory. For this, they use the nuclear spin of a ^{13}C atom. This variant of carbon also occurs time and time again in the diamond lattice, and sometimes in the direct vicinity of an NV center. The researchers then repeat the measurement with their quantum sensor several times, using a complex sequence of radio waves and microwaves to store result after result. In this way, the frequency information stored in the ^{13}C nucleus becomes more and more precise. Thanks to this trick, the quantum sensor can now separate the closely neighboring frequencies transmitted by the sample molecule.

This step was the key to being able to use the quantum sensor for NMR examinations in the nanoworld. However, there is still a great deal of research to do. Together with their colleagues at the Fraunhofer Institute for Applied Solid State Physics (IAF), the Stuttgart researchers are developing a nano-NMR scanner, which is based on a diamond quantum sensor and may in future provide insights into the nanoworld in many laboratories or even in medical radiology.

"The grand vision is to take the technology and apply it to actual microscopic imaging," says Wrachtrup. His team is therefore working on combining the quantum sensor with ex-

remely high-resolution optical microscopes. The optical microscope image could show where a specific protein molecule is currently located in a cell, and the nano-NMR sensor would then record the chemical structure of the protein. This would allow researchers to watch life itself at work in a cell, so to speak. Moreover, such a technique

could open up completely new avenues for the early detection of diseases: clinical MRI scanners equipped with the diamond would be so sensitive that they could detect much smaller tumours than today's apparatus. Diamonds for nano-NMR could therefore usher in the next quantum leap in biology and medicine. ◀

SUMMARY

- To gain a better understanding of biological processes and to identify new approaches to medical treatments, researchers led by Joerg Wrachtrup are developing a quantum sensor that can analyze the structure of individual proteins and other biomolecules while these are actively operating in cells.
- An NV center in a diamond can be used as a quantum sensor in order to examine the atomic structure of individual biomolecules. This is possible because the vacancies in the crystal lattice detect NMR signals from atoms in their environment. The information can then be read optically.
- In order to resolve the NMR signals from different atoms using their quantum sensor, the Stuttgart-based researchers gather the results of individual measurements in a quantum memory so that the various signals are amplified and can be clearly distinguished from one another.

GLOSSARY

NMR spectroscopy: NMR stands for nuclear magnetic resonance. It provides information about the magnetic properties of individual atoms. As the magnetic signals are influenced by the atoms' position in a molecule or crystal, NMR spectroscopy can be used to analyze the chemical structure of a sample material. In its medical derivative, known as magnetic resonance imaging (MRI), it provides detailed insights into the human body.

NV center: A nitrogen atom that occurs in diamond, paired with a gap in the crystal lattice (NV stands for "nitrogen-vacancy"). Thanks to its special electronic configuration, a defect of this kind acts as a tiny bar magnet that detects very weak magnetic fields and converts them into optical information.

Superconductor: A material that conducts electricity without electrical resistance. At atmospheric pressure, the effect only occurs at temperatures significantly below -100°C . Coils made of such materials generate strong magnetic fields and are therefore used in NMR spectroscopy and magnetic resonance imaging.