Portable NMR Spectrometers

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Towards Portable High-Resolution NMR Spectroscopy**

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The sensitivity and resolution of modern high-resolution NMR spectrometers are closely interlinked with ever-higher magnetic field strengths. The recent installation of the first 1 GHz spectrometer in Lyon impressively demonstrates the effort and profound technological development made in this area. However, the majority of applications in classical chemistry do not need this kind of resolution. In contrast, the high costs and intensive maintenance of modern high-resolution NMR spectrometers with superconducting magnets prevent the employment of NMR spectroscopy in chemical research and related fields, such as quality control and chemical engineering. There are also many applications where the sample cannot be moved to or into the spectrometer. As today's state-of-the-art high-resolution NMR spectrometers are extremely heavy and fragile with respect to their environmental conditions, the analysis in such cases cannot be performed. Thus, in light of these considerations, there is a strong application-driven need for small, relatively inexpensive, easy to maintain, and portable high-resolution NMR spectrometers.

The first portable NMR spectrometer was developed in 1996 by the group of Blümich at the RWTH Aachen: the NMR-MOUSE was a giant breakthrough, with a small permanent magnet used for the polarization of nuclear spins, a heavy box containing the radio-frequency (RF) amplifiers, and a laptop for control.[1] This development was followed by a number of different tabletop NMR instruments, for example, several configurations were constructed by ACT/Magritek, the Bruker Minispec series, the Oxford Instruments MQC, and clinically oriented systems from T2 Biosystems and nanoMR.

However, all the systems that are readily available today are designed to measure the relative relaxation rates of bulk samples, and allow, for example, the acquisition of 3D images or the determination of the overall fat content of food products. The spectrometers with their small, unshimmed magnets generally do not allow the resolution of different chemical shifts, which means they are of no use for classical NMR spectroscopic applications. A number of fundamental issues concerning the design of the magnets and the electronics needed for spectrum acquisition have to be overcome to achieve a portable high-resolution NMR spectrometer.

The three major concerns that have to be solved to obtain a useful portable high-resolution NMR spectrometer are:

1) the design of a magnet with sufficient homogeneity for the acquisition of spectra with chemical-shift resolution,
2) the stabilization of the magnet under real-life conditions,
3) the development of acquisition techniques that allow the use of lightweight electronics.

Recently, considerable progress has been made in all three areas, thus opening up the possibility of portable high-resolution NMR spectrometers within the next decade.

The most crucial factor for portable NMR spectroscopy is the design of a small magnet with sufficient homogeneity to allow sub-ppm resolution of the chemical shift. As helium-cooled superconducting magnets and heavy copper-wired conventional electromagnets are very difficult to transport, all serious designs are based on permanent magnets. Several groups have recently reported on such permanent magnets (see, for example, Ref. [2]); however, one design with outstanding performance deserves special attention: Danieli et al. have designed and built a magnet smaller than a tea mug that can be shimmed mechanically and has a proton resonance frequency of 30 MHz.[3] The basic design follows that of the Halbach magnet but with additional adjustments for mechanical shimming (Figure 1). The total weight of the magnet is only about 3 kg and the line width achieved with a conventional 5 mm NMR tube is approximately 0.15 ppm. This is an incredible homogeneous field if one considers that no electrical shims are applied. The magnet design will probably form the basis of future portable NMR spectroscopy. The reported research magnet is not yet sufficiently stabilized for use in real applications, but this issue is currently

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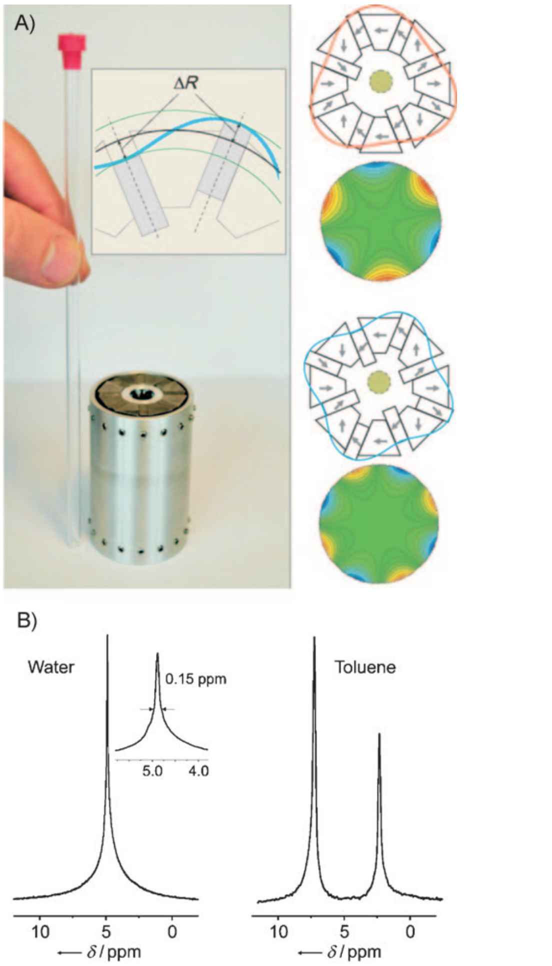

Figure 1. A) The magnet with a conventional NMR tube for size comparison (left) and the principle of mechanical shimming (top and right) are shown. B) The design allows the acquisition of high-resolution spectra with 0.15 ppm resolution at 30 MHz by using a conventional 5 mm NMR tube.[3]

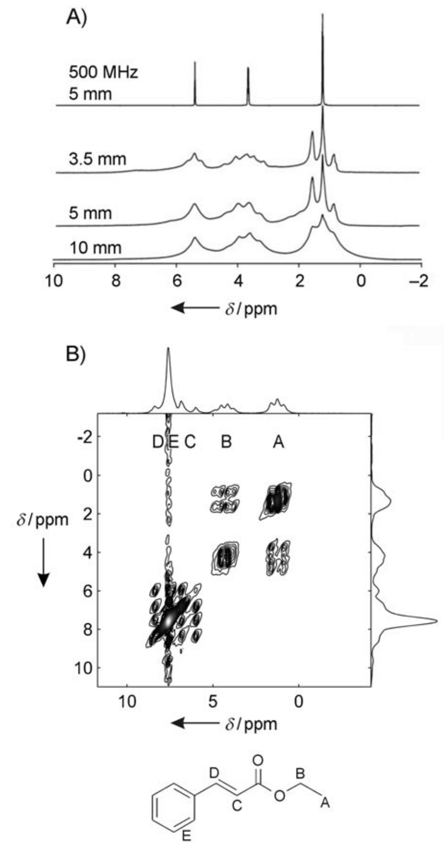

Figure 2. A) Example spectra of ethanol acquired with a prototype 20 MHz spectrometer with NMR tubes of different diameters; a 500 MHz spectrum is shown at the top for comparison. B) A 2D COSY experiment acquired on the same spectrometer.[6]

being addressed and can usually be solved with corresponding electronic measures.

The field stability needed for 1D and especially 2D experiments is very high. The magnetic properties of most alloys for permanent magnets show a small but distinct temperature dependence. While this property can be neglected for most conventional applications, an NMR spectrometer with chemical-shift resolution requires the magnetic field to have a stability of about 1 Hz. With typical magnetic fields, which correspond to a Larmor frequency of tens of MHz, the stability of the field must be kept around 10^{-7} or 0.1 ppm. A report on a prototype low-field NMR spectrometer that fulfills this prerequisite is currently being published by Cudaj et al.[4] and is based on a 20 MHz Bruker Minispec system. The enormous stability and homogeneity of the 80 kg permanent magnet is achieved in this case by controlling its temperature to within $\pm 0.001\,°C$ by the use of an additional electrical shim with 12 shim coils and by an external ^{19}F lock for correcting field fluctuations. This setup allows the possibility to measure proton spectra with resolved J couplings and even for 2D experiments (Figure 2). The system appears to be a fully operational low-field, high-resolution tabletop NMR spectrometer. Its use for portable NMR spectroscopy, however, is limited due to the relatively heavy magnet and the classical Fourier transform (FT) acquisition scheme, which requires relatively bulky and heavy electronics.

The heaviest and also most power consuming electronic devices in a modern NMR spectrometer are the high-power RF amplifiers used for the generation of short RF pulses that form the basis of FT-NMR spectroscopy. Although the RF energy needed for the excitation of a given bandwidth can be reduced significantly by the use of shaped pulses,[5] high-power amplifiers are still mandatory. However, the Blümich research group again invented an acquisition scheme that was based on the application of a phase-modulated train of very low power RF pulses in so-called Frank sequences.[6] The signal, out of which the NMR spectrum will be constructed, is acquired during the delay between the small flip-angle pulses. The overall applied RF power is so small that the energy of a coin cell is sufficient to run the spectrometer, and the whole future electronics to operate the NMR spectrometer might fit into a small case with a size somewhere between a cell phone and a small laptop.

In summary, low-field, high-resolution NMR spectroscopy is advancing fast, with several decisive breakthroughs having been reported in 2010. Novel, mechanically shimmable, and very lightweight magnets, such as a 30 MHz magnet with a weight of 3 kg and the size of a tea mug, have been constructed, and a prototype of an operational 20 MHz tabletop NMR spectrometer with electronic stabilization has been built. Together with an acquisition scheme that requires very low usage of RF power, this will provide the basis for future portable spectrometers. With such affordable and portable NMR spectrometers available, the number of potential future applications seems almost unlimited. One area of application, for example, would be quality control, which can make use of the simple quantification possible by NMR spectroscopy; low-field NMR spectrometers might also be used as a standard, chemically sensitive detector in liquid chromatography, and in engineering and other sciences it will be routinely possible to examine all kinds of products in depth through the generation of spectroscopic information. Last but not least, as a personal remark, the availability of low-cost NMR spectrometers should allow an adequate, hands-on education for students at all levels and in all universities. In this way, future generations will know more about the wide range of applications that are possible with NMR spectroscopy and how to make use of this outstanding technique to solve their specific scientific problems.

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