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Introduction to compact NMR: A review of methods

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ABSTRACT

Recent progress in magnet design has led to compact permanent magnets capable of resolving the chemical shift, so that small NMR spectrometers are now available, which can measure multi-nuclear and multi-dimensional NMR spectra on the workbench of the chemical laboratory. Although not as powerful as today's high-field spectrometers, their performance by far exceeds that of spectrometers from former times when high-field instruments were not available. Moreover, they are compact and robust, enabling the use of NMR in studies currently constrained by the demands posed by operating large cryogenically cooled magnets. The current state-of-the-art of compact low-field NMR instruments is reviewed from a methodological point of view making reference to basic NMR theory where needed to characterize their performance.

Contents

1. Introduction

The aim of this review is to introduce the NMR layman to NMR with compact, low-field instruments, which in very recent years have become available commercially also for NMR spectroscopy [1–4]. Compact NMR spectrometers open up new possibilities for chemical analysis on the spot and at the site such as for product control and reaction monitoring on the workbench of the chemistry laboratory. Depending on the manufacturer, their emphasis is placed on compact instruments, which may use superconducting magnets and medium to high magnetic field [5,6] or low-field instruments with permanent magnets, which require little to no maintenance [1–4,7]. This review sets the focus on the intersection of compact instruments and low-field instruments [1–4]. It describes the state-of-the-art of NMR experiments that can be conducted with compact low-field NMR instruments. Their use is reviewed in further contributions in this special issue among others with attention to spectroscopy for chemical analysis, reaction monitoring, teaching, process control, and ultrafast 2D spectroscopy [8–11].

NMR is popular among chemists for molecular analysis by NMR spectroscopy, among radiologists for diagnostic imaging, and among engineers for materials testing and oil well logging. Each discipline has developed its own language to explain the use of the technique to its community. Examples are terms like free induction decay (FID), pulse, and linear gradient, which are well understood within the NMR community, despite of being highly special, imprecise, and wrong, respectively, in the context in which they are usually being mentioned. On the other hand impulse response, impulse and constant gradient are perceived as awkward

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Abbreviations: 1D, one-dimensional; 2D, two-dimensional; CPMG, Carr, Purcell, Meiboom, Gill; DEPT, distortion-less enhancement by polarization transfer; DNP, dynamic nuclear polarization; DOSY, diffusion-ordered spectroscopy; FID, free induction decay; HMBC, hetero-nuclear multiple bond correlation; NMR, nuclear magnetic resonance; MRI, magnetic resonance imaging; MOUSE, mobile universal surface explorer; rf, radio frequency; S/N, signal-to-noise ratio.

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to many NMR scholars. Because compact NMR is seen by the author as an uprising branch of NMR, which reaches out beyond the classical NMR community, the more general terminology is used in the following, which refers to the principles of systems analysis and resonance phenomena, as the branches of science to which many types of spectroscopy including NMR belong from a methodological point of view. Along with some basic NMR theory, this language is helpful in connecting and characterizing the different branches of NMR, i.e. spectroscopy, imaging, and relaxometry, which are all served today by compact low-field NMR instruments.

Since the first experiments in condensed matter [12,13] the nuclear magnetic resonance (NMR) phenomenon [14–18] has found its use in a multitude of applications ranging from chemical analysis [19–23] and bio-molecular studies [24,25] to medical imaging [26,27], materials testing [28–30] and geophysical well logging [31,32]. The major issue driving instrumental developments is the inherently low sensitivity of the method due to the small nuclear magnetic polarization, which by common arguments rests on the small population difference of nuclear spin states in thermodynamic equilibrium. For protons, the most sensitive stable NMR nucleus, this number is determined at the typical operating conditions of most NMR instruments by

$$(n_- - n_+)/(n_- + n_+) \approx h\gamma B/(4\pi k_B T), \tag{1}$$

where the left hand side expresses the relative population difference of the lower and upper energy states of spins ½ in terms of the populations n_- and n_+ in the limit of high magnetic field, and h is Planck's constant, γ the gyromagnetic ratio, B the magnetic field, k_B the Boltzmann constant, and T the temperature. At room temperature and a 1 T strong magnetic field this number is as small as 0.000007. The obvious way to increase this number, is to increase the magnetic field strength B, whereby the NMR frequency is

$$\nu = \gamma B/(2\pi). \tag{2}$$

Taken population difference and NMR frequency together, the sensitivity approximately scales with the square of the magnetic field strength. Moreover, with increasing field strength the frequency dispersion

$$\nu_{\max} - \nu_{\min} = (\delta_{\max} - \delta_{\min})\gamma B/(2\pi). \tag{3}$$

of the chemical shift range $\delta_{\max} - \delta_{\min}$ increases, so that at given resolution in terms of line-width the dispersion improves to differentiate more and more complex chemical structures. These observations have guided the development of NMR spectrometers in the last seven decades towards higher and higher field strengths to improve the analytical power of NMR spectroscopy while the common trend towards miniaturization has largely bypassed the NMR world due to the instrument-determining size of the magnet [33].

Yet with respect to permanent magnets the argument about sensitivity is a bit subtler especially when it comes to spectroscopy: The area of a multiplet at a particular chemical shift in the spectrum is given by the concentration of the chemical groups in the solution, and the peak width is determined by the field homogeneity. When the field is homogeneous, all nuclei resonate at the same frequency, and the resonance line is tall and narrow (Fig. 1a). But when the magnetic field varies across the sample volume, the nuclei in different volume elements resonate at different frequencies and the line is wide and small (Fig. 1b). Moreover, the benefit of better dispersion at higher field is lost due to lower resolution from larger line-widths. In the end, the signal-to noise ratio S/N determines if a peak can be recognized as a signal or a noise spike. The S/N is defined as the peak height divided by the standard deviation of the noise. Thus the more homogeneous the magnetic field, the better the S/N in NMR spectroscopy and the more lines can be resolved in the spectrum. Optimally one would like to have high field strength and high homogeneity for high sensitivity, narrow lines, and large spectral dispersion. But this is often hard to achieve with permanent magnets, so that a permanent magnet with lower field strength

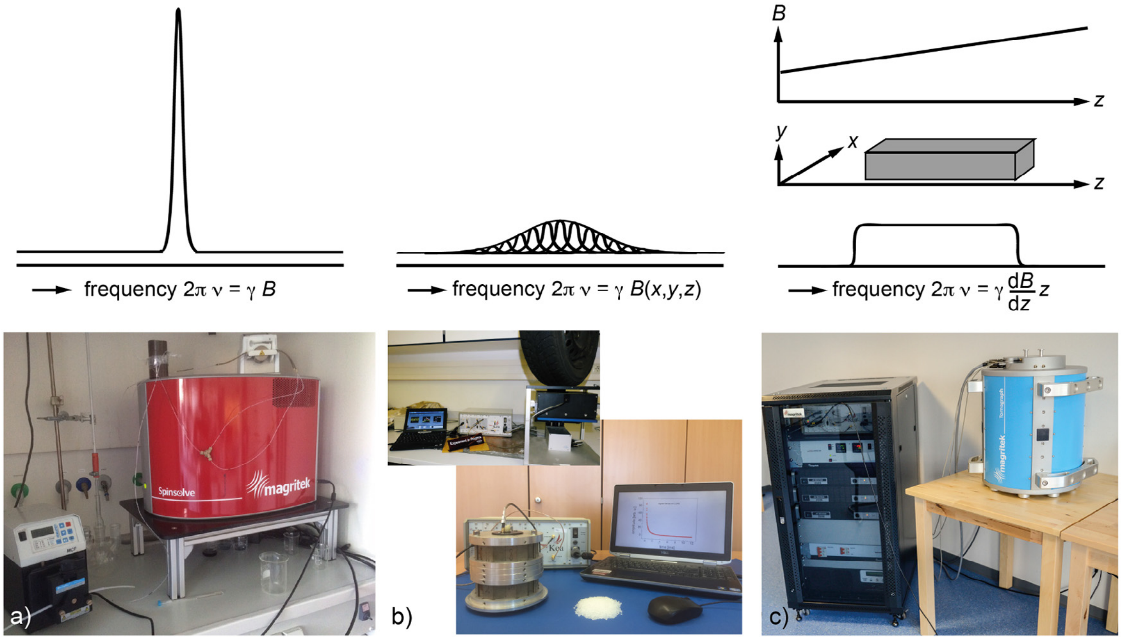

Fig. 1. Resonance lines and field homogeneity (top) along with compact NMR instruments (bottom). a) In a homogeneous field all spins resonate at the same frequency so that the resonance line is narrow and tall. This is the ideal situation for NMR spectroscopy. b) In an inhomogeneous field, the resonance line is broad and small, because nuclei at different positions in the sample resonate at different frequencies. The chemical shift cannot be resolved. Only relaxation times and diffusion can be measured for materials characterization with relaxometers employing simple magnets (bottom right) or stray-field sensors like the NMR-MOUSE (bottom left). c) The magnetic field varies linearly across the object and so does the NMR frequency. The NMR spectrum then provides a projection of the spin density of the object. This case is explored in NMR imaging.