Benchtop NMR – Bringing New Access to Technology to the Next Generation of Scientists

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The discovery of Nuclear Magnetic Resonance (NMR) spectroscopy was published independently in 1946 by Felix Bloch and Edward Purcell. Their pioneering work showed that NMR can be used to analyse the molecular structure of material in condensed matter and was the catalyst for further NMR studies. Bloch and Purcell were jointly awarded the 1952 Nobel Prize in Physics for their work on NMR and chemical shifts.

The rapid development of NMR followed the commercial production of NMR systems with homogeneous (uniform electric field) electromagnets. In the 1950s-60s, improvements in magnet design and construction allowed an increase in field strength, raising the frequency of 1H NMR spectroscopy from 40 MHz to up to 100 MHz. However, to achieve these frequencies, the size of electromagnets became substantial – often well over 1 m^3 and 1 metric ton. Permanent magnets developed in the mid-1970s, often 60-90 MHz, were also of considerable size. Often known as 'Alnico' magnets, comprising the magnetic materials aluminium, nickel, and cobalt, some remain magnetised some 60 years later, and several are still in use thanks to updated electronics.

In the 1970s, firms began commercially manufacturing NMR spectrometers and from 1990, researchers, academics and businesses were able to purchase these commercial instruments. Since then, improvements in magnet technology have allowed increases in 1H NMR frequency, reaching 750 MHz in the 1990s to beyond 1.2 GHz in modern instruments.

Why education has missed out on NMR

High-field NMR spectrometers have typically been used in scientific laboratories for decades but, although very powerful, such instruments are not commonplace in educational institutions, due to their size and scalability, and the practicalities of housing such large-scale equipment. There is an argument that this must change as technology advances further, to allow those in education access to NMR technology to gain valuable experimental experience in analytical techniques.

There are several reasons why academia has previously missed out on NMR. First and foremost, NMR systems are expensive and universities, schools and colleges facing a lack of funding for investment in science, technology, engineering, mathematics subjects (STEM) has made NMR unaffordable for many educational institutions.

The practicality of housing an NMR system is another challenge, with NMR instruments relying on being installed in their own air-conditioned room which needs constant attention and maintenance to provide best performance. Their size also means they cannot be transported easily to other environments.

With universities and schools closed for weeks at a time, it is difficult to maintain instruments correctly. Superconducting magnets must always remain on and liquid helium and nitrogen must be regularly re-filled. Educational institutions are also faced with the issue that in order to use an NMR spectrometer, users have to be trained in how to use it – a complex and time consuming process that is often out of reach for universities and schools.

Skills shortage

The general lack of access to technology has led to a global shortage of students graduating in the field of scientific research. According to The Guardian, to become a scientist, students need to have practical awareness of experimentations - but gaining lab experience as an undergraduate is difficult. The Guardian further states that, in the UK, bioscience students participate in around three to nine hours of lab time per week, which falls far below the level of training needed to proceed into a job role post-university [1]. This makes on-the-job training inevitable which is time-consuming and costly.

Access to scientific equipment for undergraduates encourages individuals to pursue STEM subjects, which, in turn, will address the current skills shortage. According to the Economic Times, just two years ago there were around four million vacancies in STEM jobs in the US and just 40,000 graduates with STEM degrees [2]. This huge gap highlights the need to encourage people from a young age to pursue a career in STEM and industry and academia can work together to support this goal.

Given the valuable learning opportunities available through NMR spectroscopy, many educational institutions have so far significantly missed out on the potential that the technology has to offer.

The solution is benchtop NMR

A benchtop NMR spectrometer offers a compact and portable solution. It does not require dedicated infrastructure, extensive maintenance, or an installation process and can simply be placed on a benchtop and plugged in. Benchtop spectrometers offer improved workflows, particularly for novice users, as they are intuitive in use and do not require extensive training.

The advantages of benchtop NMR systems are paving the way for the introduction of this technology in education:

- Specialist NMR expertise is not required
- Same direct quantification and deep structural information as high-field NMR
- Compact benchtop size
- No additional infrastructure needed
- Cryogen-free permanent magnets – no need to re-fill liquid helium or nitrogen
- Operates from a single standard power socket
- Easy maintenance and optimum cost of ownership.

Some benchtop systems can be operated with the same, industry-standard software that is used on high-field NMR systems (e.g. Bruker's Fourier 80 can be operated with TopSpin software). This allows the students to become familiar with NMR in general, as well as the operation of high-field NMR instruments at the same time.

Similar to high-field NMR systems, the compact benchtop instrument can be brought into many different fields of application, such as food and beverage analysis and forensics. This means that as well as teaching students about a range of different analytical techniques, academics can also continue to observe high-accuracy data and experiments directly from the benchtop.

With benchtop NMR spectrometers offering the reproducibility and stability of high-field NMR technology in a more accessible, smaller instrument that can be installed on the lab bench, it is a good fit for educational settings, such as universities, colleges, or even schools.

Benchtop NMR allows students to learn about NMR as a method and explore concepts such as chemical shift, coupling constants, relaxation, and pulses, as well as learning about advanced techniques such as selective excitation and solvent suppression. In an organic chemistry lab, students can check reactions, determine the yield and check the purity of reagents and products, as well as perform structure elucidation of organic molecules.

Applications in education

• Selective excitation

There is the opportunity with benchtop NMR to explore advanced techniques, such as selective excitation of a single resonance in a spectrum *(Figure 1)*. This can then be used further in more advanced experiments such as the one-dimensional total correlation spectroscopy (1D TOCSY), which only shows all the signals coupled with each other for further data insights. *(See Figure 2)*

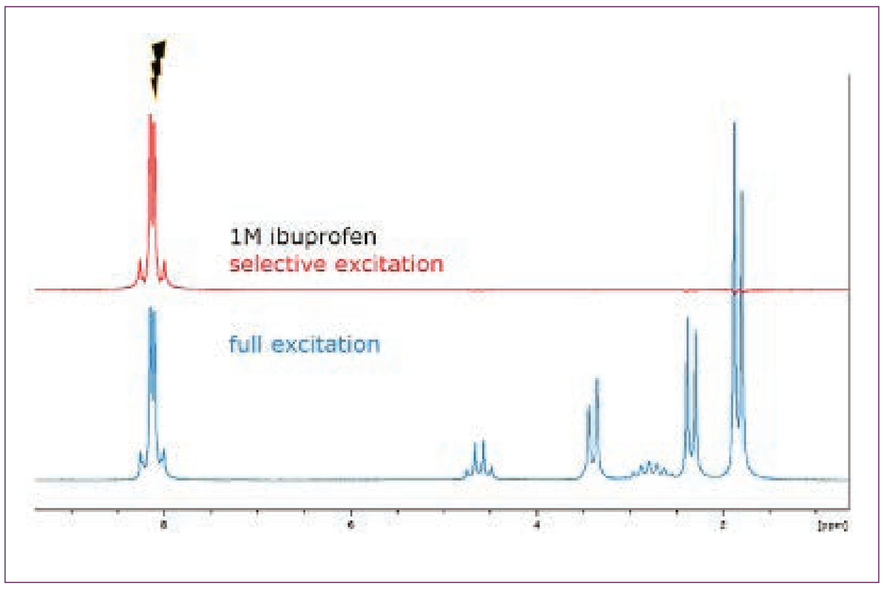

Figure 1. Comparison of 1-dimensional 1H NMR spectra recorded on a 1 M ibuprofen sample at 80 MHz (Fourier 80, Bruker BioSpin) to demonstrate the effect of selective excitation. While the fully selected spectrum (blue) shows all proton signals of the sample, in the selectively excited spectrum (red, region of selective excitation indicated by the black arrow) only the selected signals can be observed.

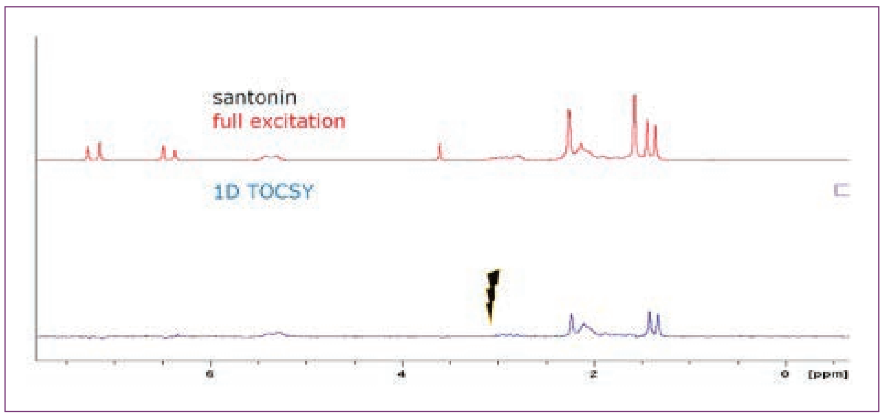

Figure 2. Comparison of 1-dimensional 1H NMR spectra recorded on a santonin sample at 80 MHz (Fourier 80, Bruker BioSpin). While the fully selected spectrum (red) shows all proton signals of the sample, in the 1D TOCSY spectrum (blue, region of selective excitation indicated by the black arrow) only signals deriving from spins coupled to the excited one can be observed.

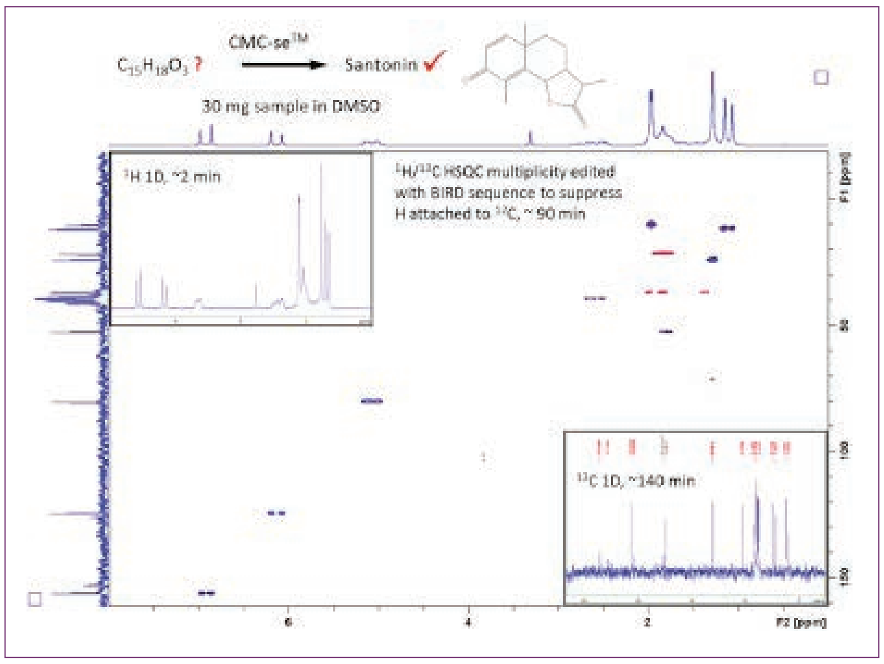

Figure 3. The structure of santonin (30 mg in DMSO) has been elucidated automatically by TopSpin CMC-se software (Bruker BioSpin) using a pre-defined set of spectra recorded at 80 MHz (Fourier 80, Bruker BioSpin) only. The 1D 1H (top left), 1D 13C (bottom right) and 2D HSQC-me (multiplicity-edited Heteronuclear Single Quantum Coherence) spectra are shown.

• Structure elucidation

Within its limits, even structure elucidation is possible with benchtop NMR, which determines the structure of unknown molecules. It is often presumed that only high-field instruments can elucidate the structure of a molecule and that low-field NMR spectroscopy is restricted to the structure verification of small and simple molecules. Modern benchtop NMR systems are proving that it is possible to use this technique in academia and that the elucidation of small molecular structures is no longer the sole province of the commercial laboratory. Students can determine the structure of unknown molecules with extensive experimental libraries and dedicated software tools such as Bruker CMC-se *(see Figure 3)*.

• Monitoring reactions

Benchtop NMR allows for the precise monitoring of reactions in the lab. For example, the majority of undergraduate chemistry labs have synthesised aspirin from the simple starting materials of salicyclic acid and acetic anhydride. This reaction can be followed on a benchtop spectrometer, checking the starting materials to make sure they are pure, monitoring the reaction over time and verifying the final product purity *(Figure 4)*.

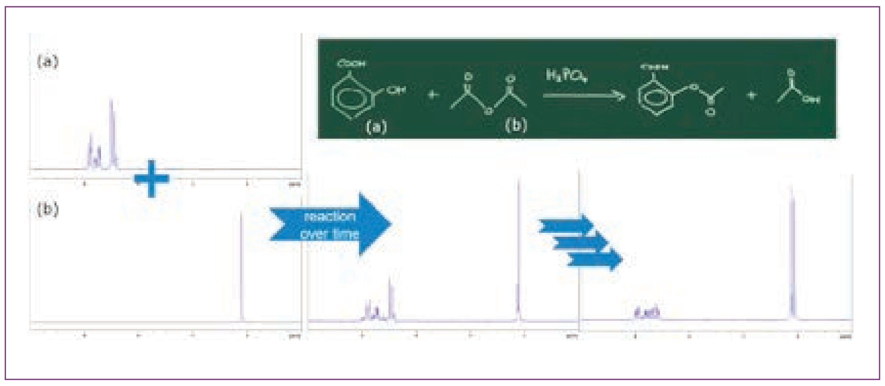

Figure 4. The synthesis of aspirin using salicylic acid (a) and acetic anhydride (b) as educts observed over time using 80 MHz 1D 1H NMR spectra (Fourier 80, Bruker BioSpin).

Wide range of applications

Despite their lower field strength compared with modern high-field systems, the advanced electronics and methodology of modern benchtop NMR spectrometers make these instruments ideally suited to high-throughput chemical analysis, far superior to that of early low-field spectrometers.

NMR in its benchtop form does not only become broadly accessible to chemistry students but reaches beyond. A prosperous application area is dealing with the analysis of food and beverages, highly interesting for biochemists and nutritional science students who might be yet to experience the power that NMR can provide. For example, the quantification of the fat content in milk, the differentiation of arabica versus robusta coffee beans *(Figure 5)* and the detection of fraudulent low-quality sunflower oil mixed in high-quality olive oil are interesting applications.

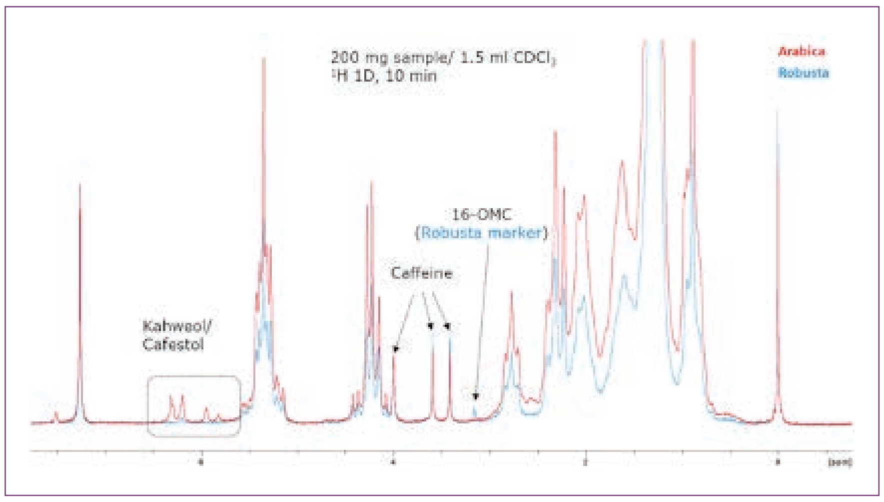

Figure 5. Students can analyse extracts from coffee beans to find out whether it is arabica or robusta and determine whether their coffee sample contains any caffeine using 1D 1H spectra recorded at 80 MHz (Fourier 80, Bruker BioSpin).

Simple interface

Software designed for the operation of modern benchtop NMR systems is user-friendly and some may provide easy access to vast experiment libraries and functionalities known from high-field NMR systems. This is well-suited for students and encouraging for those interested in using NMR as a technique when choosing a career path, taking confidence and knowledge from early NMR studies into a professional laboratory.

Students can acquire both qualitative and quantitative data and those in educational institutions can analyse NMR spectra through industry-standard software. This supports access for training purposes, as licenses are often free for academic, governmental, and non-profit institutions.

Conclusion

The past 50 years of NMR spectroscopy innovation have, until recently, been centred around steadily increasing the field strength of analytical instruments. While high-field systems can provide unparalleled insights into the structure and dynamics of complex molecules, low-field benchtop NMR spectrometers offer the reproducibility and stability of NMR in a simpler, smaller instrument.

As analytical technologies continue to evolve, so too does the potential for students to experience formerly specialised techniques such as NMR early in their scientific careers. While high-field NMR spectroscopy is playing an increasingly important role in numerous fields such as analytical chemistry and drug discovery, the accessibility of benchtop NMR is facilitating the emergence of this technology in a wide range of settings.

Benchtop NMR can support undergraduates to utilise the equipment and experimental data, while gaining significant lab experience to support and encourage students into a career in science. The use of benchtop NMR in educational institutions allows students to observe experiments that historically would only have been possible on high-field NMR spectrometers. Removing these barriers can offer further advantages to academics in various fields of application by transferring experiments to a low-cost, conveniently sized instrument that reports with a high degree of accuracy.

Benchtop NMR is seeing great success in applications such as food analysis, quality control, forensics and education. These solutions are only a starting point. There is vast potential for this technology in an almost unlimited range of applications.

For more information about benchtop NMR for education,
please visit: https://www.bruker.com/products/mr/nmr/benchtop-nmr.html

About the author:

Dr Venita Decker studied Biochemistry and Neuroscience, but did her dissertation in the field of solid-state NMR (Max Planck Institute for Biophysical Chemistry, Goettingen, Germany). In 2012, she joined the Bruker solid-state NMR application. As a NMR-late entrant she since then actively supported Bruker solutions that simplify the complexity of NMR (TopSolids, the minispec FormCheck, Fourier 80). Meanwhile, she became the Product Manager for Compact NMR (TD/FT) solutions, bringing her mission to the next level.

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