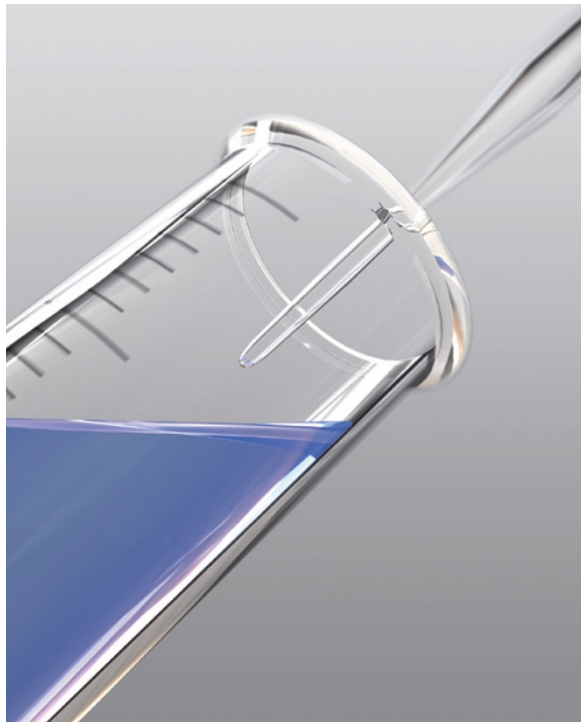


DOI:
10.1038/nphys865

 MILESTONE 10

A shift in expectations



Paolotoscani | Dreamstime.com

Nuclear magnetic resonance (NMR) spectroscopy (Milestone 8) is one of the most powerful analytical techniques in modern chemistry — a window into the world of molecules that can provide information about their structures, dynamic behaviour and how they interact with one another.

Prior to the 1950s, the study of NMR was rooted firmly in the physics community. It was assumed that the frequency at which a given nucleus resonated depended only on the strength of the magnetic field in which it was placed. Physicists therefore anticipated that they could use the technique to measure — with unprecedented precision — the magnetic moments of different nuclei.

When, in 1950, Warren Proctor and Fu Chun Yu set out to do this for ^{14}N , something unexpected happened.

For their experiments, they chose the compound ammonium nitrate (NH_4NO_3), which is highly soluble in water and contains two nitrogen nuclei per molecule — factors that were expected to improve the NMR signal. In what they described as a “surprising observation”, however, not one but two resonance frequencies were detected — one for the nitrogen nuclei in the ammonium (NH_4^+) ions and the other for those in the nitrate (NO_3^-) ions.

This was the first reported observation of the phenomenon that soon became known as ‘chemical shift’, in which the local chemical environment surrounding a nucleus influences the frequency at which it resonates. The implications of NMR for the structural analysis of organic compounds became apparent soon afterwards, when, in 1951, a group of researchers from Stanford University showed that different ^1H nuclei in the same molecule resonate at different frequencies.

James Arnold, Srinivas Dharmatti and Martin Packard demonstrated the huge potential of NMR spectroscopy by applying the technique to ethanol ($\text{CH}_3\text{CH}_2\text{OH}$), a compound in which each molecule comprises three sets of non-equivalent ^1H nuclei. Using tiny sample volumes and placing them in the most uniform region within a magnetic field, they obtained a spectrum displaying three separate lines, corresponding to the resonant frequencies of the ^1H nuclei in the CH_3 , CH_2 and OH groups, respectively. Moreover, the relative

intensities of the three signals corresponded with the number of protons in each different chemical environment. So it was possible not only to identify different molecular fragments but also to glean quantitative information about the number of equivalent nuclei in each.

Later in 1951, Herbert Gutowsky and David McCall showed that different spin-active nuclei in the same molecule interact with one another, giving rise to fine structure in the NMR signals that encodes a wealth of information regarding molecular connectivity and structure.

It did not take the chemistry community long to embrace the technique for the spectroscopic analysis of compounds. Techniques using radio-frequency pulses — rather than a continuous source — broadened the scope of NMR spectroscopy, and Fourier-transform methods of data processing notably improved the sensitivity of the method. The combination of these advances allowed the development of sophisticated multi-dimensional NMR experiments that revolutionized the field (Milestone 16).

Stuart Cantrill, Chief Editor,
Nature Chemistry

ORIGINAL RESEARCH PAPERS Proctor, W. C. & Yu, F. C. The dependence of a nuclear magnetic resonance frequency upon chemical compound. *Phys. Rev.* **77**, 717 (1950) | Hahn, E. L. Spin echoes. *Phys. Rev.* **80**, 580–594 (1950) | Arnold, J. T., Dharmatti, S. S. & Packard, M. E. Chemical effects on nuclear induction signals from organic compounds. *J. Chem. Phys.* **19**, 507 (1951) | Gutowsky, H. S. & McCall, D. W. Nuclear magnetic resonance fine structure in liquids. *Phys. Rev.* **82**, 748–749 (1951) | Carr, H. Y. & Purcell, E. M. Effects of diffusion on free precession in nuclear magnetic resonance experiments. *Phys. Rev.* **94**, 630–638 (1954) | Ernst, R. R. & Anderson, W. A. Application of Fourier transform spectroscopy to magnetic resonance. *Rev. Sci. Instrum.* **37**, 93–102 (1966) | Aue, W. P., Bartholdi, E. & Ernst, R. R. Two dimensional spectroscopy: Application to nuclear magnetic resonance. *J. Chem. Phys.* **64**, 2229–2246 (1976)

FURTHER READING

Becker, E. D. Magnetic resonance: an account of some key discoveries and their consequences. *Appl. Spectrosc.* **50**, 16A–28A (1996)