Superconducting magnets: at the heart of NMR

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In 2002, scientists at the William R. Wiley Environmental Molecular Sciences Laboratory (EMSL) in Washington, USA, took delivery of a 900 MHz magnet, the world's largest wide bore magnet. EMSL is part of the Pacific Northwest National Laboratory (PNNL) in Richland, which already had the western hemisphere's most comprehensive collection of NMR magnets. So why did PNNL feel the need for a bigger magnet still, and why have subsequent orders been placed for commercial 900 MHz systems worldwide? How does the size and quality of magnet benefit spectroscopists and how is this achieved?

NMR at 900 MHz: why is bigger better?

Several features essential to high-quality NMR are dependent on the field strength of the magnet. Resolution is proportional to the magnetic field strength (B_0), with spectra becoming increasingly dispersed as the field strength increases (see Figure 1). Sensitivity is also improved by approximately the 3/2 power of the field strength. This results in the signal-to-noise (S/N) ratio improving by almost 20% in a 900 MHz instrument when compared to an 800 MHz system, or 84% compared to a 600 MHz. In addition, alignment is proportional to the square of the central field (B_0^2).

As larger and larger molecules are analysed, the interpretation of results is hampered not only by more complex spectra with more overlap, but also by broader resonance lines due to the nuclei of interest relaxing more quickly. Interference between different relaxation mechanisms results in different relaxation rates for the two components of an N–H doublet, producing an effect known as differential line broadening. This effect is increased in larger molecules. However, Transverse Relaxation Optimised Spectroscopy (TROSY) improves this situation, resulting in relatively narrow lines even for proteins of around 100 kDa.[1] TROSY provides some benefits at lower magnetic field strengths, but the effects are seen most between 900 MHz and 1 GHz and should be maximised at around 1.14 GHz (see Figure 2).

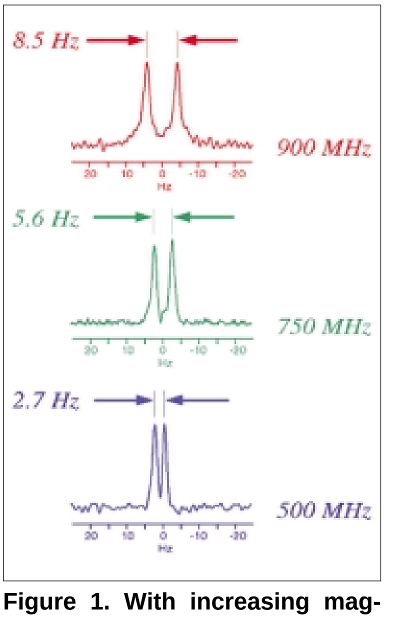

Figure 1. With increasing magnetic field strength, NMR spectra become increasingly dispersed.

What is achievable?

At 900 MHz, molecules of up to 100 kDa have been successfully analysed. The S/N ratio can also be increased by a factor of three using cryogenic probes, significantly improving data collection time. The noise level is dependent on temperature, and hence can be reduced by cooling the detection coils of the magnet.

Although the first commercial 900 MHz magnet systems are still being installed, data examples are already available as an applications laboratory was opened last year as a joint venture between Oxford Instruments and Varian Inc. The two companies produced the first 900 MHz spectra in the world, using the Varian Unity INOVA 900 based around the Oxford Instruments 900 MHz magnet. The applications lab enabled researchers to develop new test protocols with assistance from the 900 MHz magnet development team.

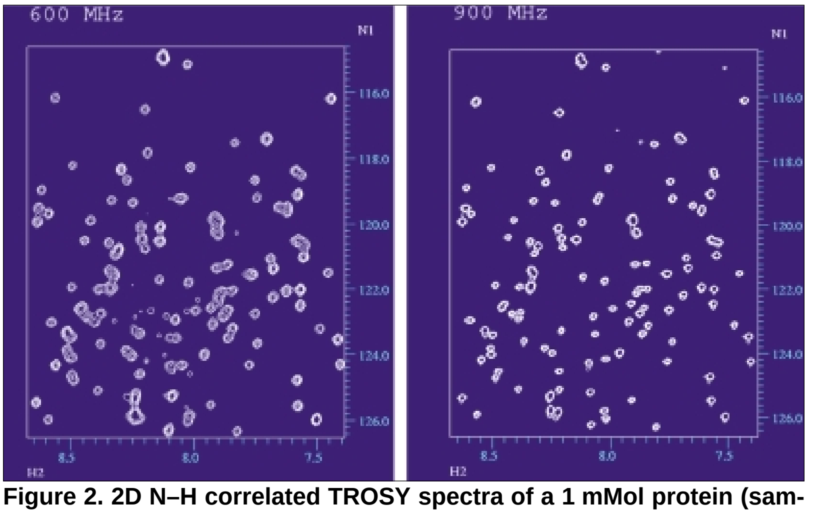

Figure 2. 2D N–H correlated TROSY spectra of a 1 mMol protein (sample courtesy of Dr L. Mueller) in H_2O/D_2O (9 : 1) recorded at 600 MHz and 900 MHz on a Varian INOVA spectrometer (courtesy of Varian).

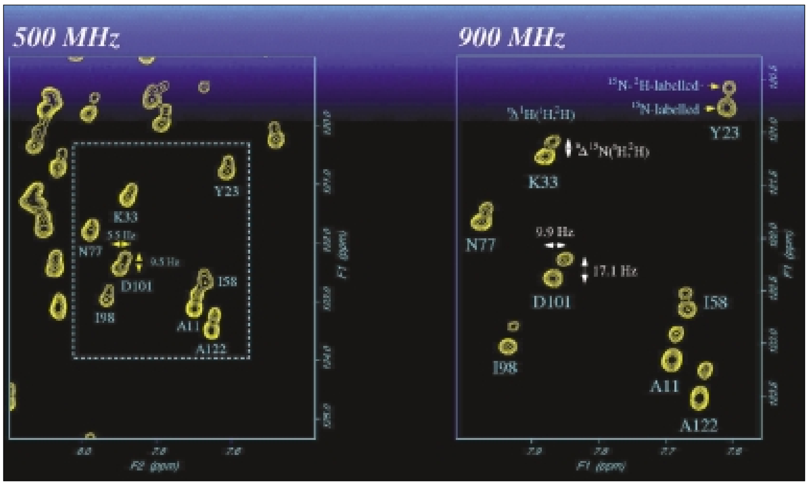

Figure 3. N–H correlated TROSY spectra of a mixture of H- and D-Lysozyme (sample courtesy of Dr C. Redfield) in H_2O/D_2O (9 : 1) recorded at 500 MHz and 900 MHz on a Varian INOVA spectrometer (courtesy of Varian).

Figure 3 shows data on H/D isotope effects in lysozyme obtained by Professor Iain Campbell's Oxford University group using the 900 MHz NMR applications lab.[2] The increased resolution of the 900 MHz magnet means that changes will have to be made to NMR protocols, not just to accommodate experiments such as TROSY. For example, the $CHCl_3$ lineshape test previously exhibited a single line but now forms a split peak due to the resolution of the $^{37/35}$Cl isotope shift.

How is this done?

To achieve this high level of NMR performance, the drift rate for the magnetic field has to be strictly controlled to within 1.5 Hz in 900 million per hour. The field also needs a high level of homogeneity and to be exceptionally stable with a good S/N ratio. For all these parameters to be possible, the magnet design and construction needs to consider: superconductor performance; forces and stress; energy management issues and the magnet's cryogenic environment.

Conductor performance

First, a conductor has to be chosen that can provide a stable field at 900 MHz in order to keep the field drift rate within 1 in 10^8 for high-resolution NMR experiments. Niobium titanium is used in the lower field regions of the magnet coil, but this cannot carry sufficient current in the higher field section. A unique Niobium tin wire, made up of thousands of filaments, was used to achieve this. The filament structure improves the stability of the magnet by preventing "flux jumping" that dissipates energy in the superconductor. The manufacture of this wire has to include stringent quality control procedures, to ensure first that short samples of wire perform at field, and also that a constant diameter is maintained. Any fluctuation in the wire diameter will result in detrimental effects on magnet stability.

However, it is practically impossible to manufacture a single length of wire to this standard when the solenoid for a 900 MHz magnet uses in the order of 180 miles of wire. Therefore, low resistance jointing techniques were developed to join lengths of both niobium titanium and niobium tin wire together.

Composite structures to withstand stress

The PNNL magnet contains 27 MJ of stored energy when at field. The 900 MHz magnets currently being produced commercially have 17 MJ—although this may sound like a lot less, it still equates to 4 kg of TNT exploding.

In order for the superconducting material to operate, it must be kept in a bath of liquid helium at 2.2 K. A few µJ of energy, equivalent to a pin dropping from the height of a few centimetres, would be enough to raise the temperature sufficiently to cause the magnet to become resistive, or "quench". Here, the helium boils off and 17 MJ of stored energy is released very quickly, risking damage to the magnet structure.

In addition to the amount of stored energy, the stresses experienced by the magnet are huge. Mechanical stress increases quadratically with the field strength for a given magnet. At 900 MHz, these stresses are greater than 2000 kNewtons, with a magnetic pressure of more than 250 MPa.

Traditional ways of reinforcing the coils (wax impregnation) were insufficient at these high fields. For the 900 MHz magnet project, the coil was evacuated in a special vacuum chamber and the chamber let back up to atmospheric pressure with epoxy resin to replace the air voids.

With a project of this size, the cost of failure is very high and repeated building and testing of full-size coils would push costs up considerably. Therefore, problems needed to be predicted rather than the scientists waiting for them to happen and then working out why. For this reason, coil performance studies and instrumentation for prediction and modelling of coil stresses were used to calculate stresses and to work out efficient ways of constraining and reducing them. These studies can also be used to explore design variables such as field strength versus bore size, factors that can make a huge difference to the stresses experienced by the magnet.

Managing stored energy

In the event of magnet failure, how can you manage the dissipation of 17 MJ energy without causing terminal damage to the magnet structure? The challenge is to develop ways of releasing the energy very quickly, in a manner that avoids magnet damage through thermal gradients or excessive voltages in the coil. To address this, an energy management system was developed to ensure that during failure mode all coil stresses and voltages are kept within design limits.

Cryogenics

High field NMR cryostats need to maintain 2.2 K whilst still allowing for refills at atmospheric pressure. This temperature has the effect of increasing the superconductor's critical current characteristics, thus increasing the upper critical field limit and enabling the magnet to reach 900 MHz. The most straightforward way of achieving this is to pump directly on the liquid helium reservoir.

The structure also needs to be able to support the magnet mass, even under changing levels of cryogen and evaporation rates, whilst minimising any heat leak into the system that could raise the temperature above 2.2 K. A series of support rods support the mass of the 900 MHz magnet, reducing inherent vibration that could affect the quality of results. These need to be capable of supporting 2G force in any direction whilst being light enough to minimise the heat leak to mWatts.

In addition, the cryostat needs to be strong enough to withstand the discharge of large volumes of helium gas if the magnet becomes resistive and "quenches", when the raise in temperature evaporates the liquid helium. Multiple venting devices and pressure relief discs are designed to rupture when the pressure rises above a certain threshold. However, these have to be designed in such a way that they do not increase the radiation and increase the heat leak, resulting in the liquid helium boiling off.

Magnet shielding

In addition to magnet performance, it is also important to take into account where the system is sited. Shielding can play a vital role here, not just in limiting stray field from the magnet and controlling the environment, but also in limiting external magnetic sources that may impact on experimental results.

Passive shielding works by placing a specially designed structure around the magnet. Systems such as Oxford Instruments' Vectorshield™ give 800/900 MHz NMR systems protection from the negative effects exerted by external electro-magnetic disturbances on NMR data quality. This helps maintain quality data as well as limiting the stray field. Shielding can also help with security and safety and enables magnets to be housed in, for example, built-up areas that would not otherwise be suitable.

Ergonomics

Lower field magnets are small enough for a person of average height to reach the top and insert samples or refill the liquid helium cryogen. However, the sheer size of magnets such as the 900 MHz magnet system makes this difficult. For this reason, the design of the 900 MHz system includes a user access platform that allows the spectroscopist to load/unload samples and refill cryogen levels. Samples are still loaded via the top of the magnet where an air column lowers it to the centre of the magnet field. The platform also helps to isolate vibrations that could detrimentally affect results.

Beyond 900 MHz?

As previously mentioned, the TROSY experiment probably needs 1.14 GHz for maximum effect. Increasing the magnet strength still further would also continue to increase resolution, sensitivity etc. However, increasing the size and strength of superconducting magnets, even by another 100 Hz, puts far more pressure on the conductor. Currently, there are none available that can give 100 A mm^{-2} (the critical current density needed for superconductivity) at 1 GHz/23.1 Tesla. Using new superconducting materials such as niobium aluminium may solve this problem. Alternatively, High Temperature Superconductors (HTS, these are largely ceramic materials that retain their superconducting properties up to temperatures of more than 90 K) may prove useful. However, it is difficult to achieve the necessary homogeneity of conductor performance with HTS, as they are brittle and very difficult to wind in the manner of a wire solenoid. For this reason, the most realistic option may be to try to push the limits of materials used in current designs.

Conclusions

More than 50 years after the phenomenon of NMR was first demonstrated, it remains an essential tool for researchers in structural biology, materials science and many other research fields. The area continues to evolve, with more powerful systems yielding more detailed information on larger molecules and allowing novel experimental techniques to optimise the data produced. With magnet technology continuing to improve sensitivity and resolution, NMR should continue to provide an invaluable research tool for years to come.

References

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