Agilent 101: An Introduction to NMR

By Regina Schuck

Chances are that you or someone you know has had an MRI, a medical test in which you lie in an enclosed cylinder while a part of your body is scanned. The procedure results in a very clear, digital image that your doctor can use to diagnose a problem.

Agilent offers a full range of NMR measurement solutions.

What you may not know is that MRI is based on an analytical measurement technique called NMR. NMR is one of the original measurement technologies developed more than 60 years ago by Varian, which was acquired by Agilent in 2010.

MR stands for "nuclear magnetic resonance." MRI, the more familiar version used in clinical applications, stands for "magnetic resonance imaging."

You'll notice that MRI dropped the word "nuclear." That's because people don't like to hear the word "nuclear" when they're undergoing a medical procedure. However, NMR has nothing to do with nuclear weapons or radioactivity. It's called "nuclear" because it deals with the nucleus of the atom.

NMR allows us to obtain physical and chemical information about a sample based on the resonant frequencies of atomic nuclei in that sample.

With NMR we can observe molecules and substances in just about any form. They can be liquids, crystals or powders. They don't have to be soluble. Most important, we can observe them in a non-destructive fashion. It's a very flexible technology.

A noteworthy technology

In 1948, Varian was founded in California's Silicon Valley with six employees and $22,000 in capital. One of Varian's first two products was an instrument that measured the gyro-magnetic ratio of certain atoms. This effect later became known as nuclear magnetic resonance.

In 2010, Varian was acquired by Agilent. Its NMR solutions are now part of Agilent's Research Products Division in the Life Sciences Group.

Over the years, six Nobel Prizes have been awarded to scientists for their work in NMR and MRI:

1. 1943 Physics: Otto Stern (USA)
2. 1944 Physics: Isidor Rabi (USA)
3. 1952 Physics: Felix Bloch and Edward Purcell (USA)
4. 1991 Chemistry: Richard Ernst (Switzerland)
5. 2002 Chemistry: Kurt Wüthrich (Switzerland)
6. 2003 Physiology/Medicine: Paul Lauterbur (USA) and Peter Mansfield (UK)

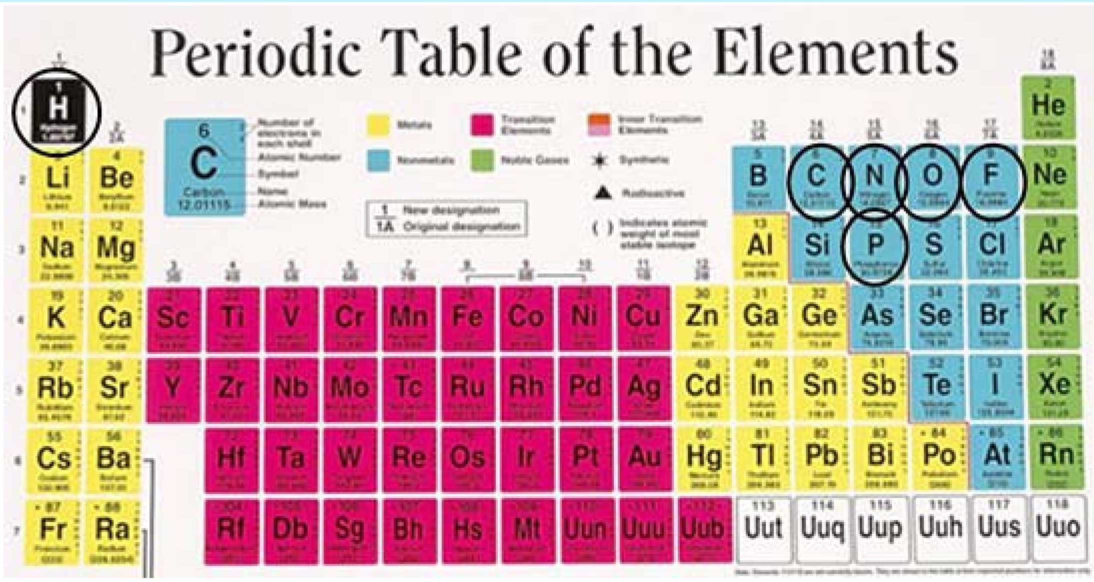
It's elementary!

More than 100 elements have nuclei with magnetically active isotopes. They will react measurably when exposed to magnet fields.

The "spin" of a charged nucleus causes it to behave like a tiny magnet. The energy level of the nucleus will change in proportion to the strength of the magnetic field. With a suitable apparatus, we can observe the transition from one energy level to another.

Figure 1 shows the periodic table of the elements. Some elements have nuclei that are easily accessible and observable using NMR. Fortunately for researchers, these elements include hydrogen, carbon, nitrogen, oxygen, fluorine and phosphorous – the building blocks of any kind of life. They constitute 99 percent of what makes up all humans, animals and plants.

Figure 1: Periodic table of the elements

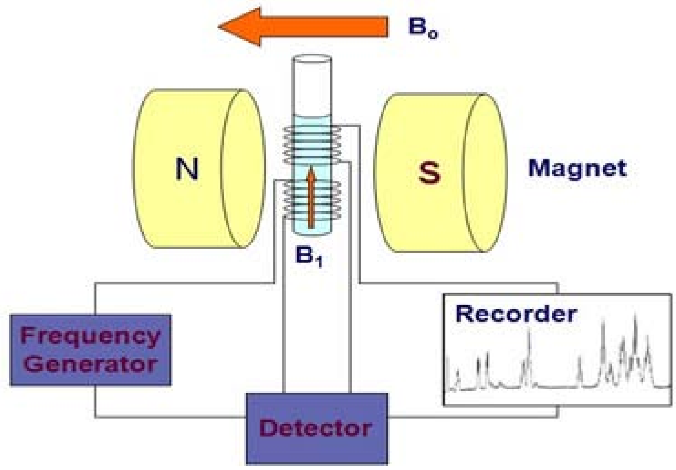


More than 100 nuclei are NMR active. The most commonly measured include hydrogen, carbon, nitrogen, oxygen, fluorine and phosphorous.

NMR spectrometry

Figure 2 shows a simplified schematic of an NMR system. You have a very large magnet, represented by the two yellow discs with north and south poles. You insert a test sample into that magnet. Then you create a smaller magnetic field that's perpendicular to the big magnet. You control the smaller magnetic field through a computer and console. Finally, you record what happens to your sample.

Figure 2: NMR schematic

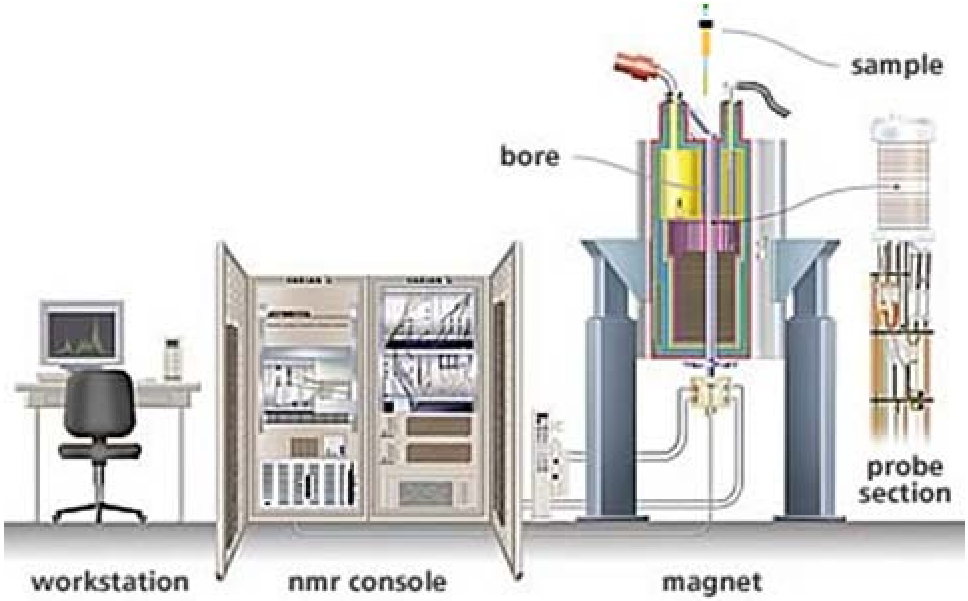


Nuclear magnetic resonance occurs when the nuclei of certain atoms are immersed in a static magnetic field and exposed to a second oscillating magnetic field.

Figure 3 is another view of an actual NMR system. On the right, you have the big magnet that dominates the picture. On the far right is a probe that will be inserted into the magnet. The probe contains a tiny sample. On the left you have the NMR console, which creates and controls the second, smaller magnetic field.

The sample is only about half a milliliter, so it's really small. The big magnet, on the other hand, can be quite large – even taller than an adult person.

Figure 3: Figure 3: NMR Spectrometer



In an NMR system, the test sample is inserted into the center of a superconducting magnet using a probe. A computer console generates RF pulses that excite the sample's nuclear spins away from their normal state of thermal equilibrium.

NMR applications

NMR is very widely used because its flexibility enables us to analyze solids, liquids, liquid crystals and even nano materials. We can even analyze "squishy" materials – such as gels, resins or tissue samples – which are very hard to analyze with any other technique. Again, these samples can be analyzed in a non-destructive fashion.

In **biological NMR**, the technology is used by pharmaceutical companies in drug discovery. NMR can determine the structure of proteins and nucleic acids in complex molecules.

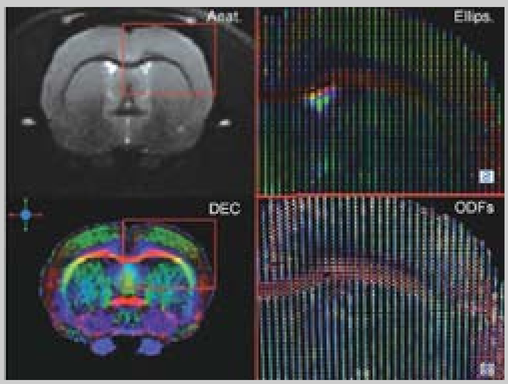
NMR is the only technique that allows you to perform this analysis in in-vivo conditions [within a living organism]. Consequently, it is used in academia as well as in pharmaceutical companies. Most, if not all, chemistry, bio-chemistry and medical schools have NMR and/or MRI spectrometry. It is very powerful.

An application that I believe will become prevalent in the future is the use of NMR in **biological solids**. Most of the proteins in the human body are membrane-bound proteins, which makes them very difficult to study, even with NMR.

Currently, the NMR applications in biological solids are mainly limited to academia. But I believe that this will become a more widespread application down the road, as we make it easier to use. And it is our job to make it easier to use.

NMR versus MRI

Nuclear magnetic resonance is the study of molecular structure by means of the interaction of radio-frequency (RF) electromagnetic radiation with a collection of nuclei immersed in a magnetic field. Magnetic resonance imaging is a branch of NMR that uses manipulations of the magnetic field to encode spatial information into the NMR signal. This enables an MRI experiment to produce an image.



MRI images of brain diffusion. Images courtesy of Laboratory of Functional and Metabolomic Imaging, Ecole Polytechnique Fédérale de Lausanne, Lausanne, Switzerland

NMR and Agilent

The total available market for NMR is just under $500 million. Academia and government comprise roughly a third of this market. Pharmaceutical and biotech are roughly 30 percent. Chemical applications account for roughly 11 percent. Oil and gas, food and a number of small niche applications account for the remainder.

In January 2010, Varian (now part of Agilent) successfully completed the world's first actively shielded 7-Tesla whole-body magnet for human MRI research.

Agilent solutions address more than half of this total available market. The nice thing is that this market is a bit anti-cyclical, because it is largely driven by academic and government funding. Whenever the economy slows down, the government tends to fund academia as a stimulus. This is what happened in the U.S. and Japan a couple of years ago.

So when the economy slows down, our NMR business tends to do well.

Are there any disadvantages of NMR? Yes, NMR is four to 10 orders of magnitude less sensitive than mass spectrometry.

If NMR had higher sensitivity, it would be much more broadly applied, and this $500 million market would be several billion dollars instead. As you can imagine, this is the primary research area that Agilent is focusing on. One of our biggest technological opportunities is to improve the sensitivity of NMR.

The integration of NMR into Agilent has been very positive and well received by customers. Our three-year plan is to expand the portfolio across all target segments and achieve technology leadership. NMR remains a valuable and compelling technology with a bright future.

Regina Schuck is vice president and general manager of Agilent's Research Products Division in the Life Sciences Group. Regina has more than 25 years of experience in NMR and research MRI. She holds a doctorate in natural sciences from the University of Frankfurt in Germany.

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