ELECTRONICS MECHANICAL INDUSTRIAL

One out of the Lab

Writer Matt Philp

"Our strength," Professor Sir Paul Callaghan argued in a 2011 exposé, "lies in the weird stuff". The late, great physicist was making a case that New Zealand excels in niche industries, and that the country's future prosperity lay with exploiting "little pieces of technology where the big players can't be bothered".

He might have been predicting the rise of the firm that he co-founded, Magritek, and its revolutionary product, Spinsolve.

Developed by a team that includes several of Sir Paul's former students, Spinsolve is an analytical instrument that for the first time enables the power of nuclear magnetic resonance (NMR) spectroscopy to be used in a regular chemistry laboratory. Where previously, NMR analysis of chemical samples has been done by large, very expensive high-field spectrometers operated by specialists in dedicated rooms - often, a climate controlled university basement - Spinsolve has essentially democratised the technology by putting it into a benchtop box.

"It's a bit like what happened with the mainframe computer," Chief Technology Officer Robin Dykstra, says. Dr Dykstra, who was one of the co-founders of Magritek with Sir Paul back in 2004, adds "Desktop computing arrived and suddenly everybody could have access to computing facilities. We've come out with an instrument that significantly lowers cost, that is portable and easy-to-use, and now everyone has access to this measurement capability."

The Spinsolve development represents a "gamechanger" for the Wellington-based exporter, which has been "chipping away" with a succession of NMR and magnetic resonance imaging (MRI) products for academia, the oil and gas industry and others. "Spinsolve has allowed us to shift gears and grow our company quicker, generating significant revenue."

It was this dream of successfully commercialising science that inspired Dr Dykstra and Sir Paul to establish Magritek. The scientists met at Massey University, where they collaborated on developing instrumentation. "We'd had government research funding for years and thought, 'Maybe it's time to take a look at commercialising some of our activity and give the country some return on its investment.' It grew from there." Founding Chief Executive Andrew Coy has led Magritek through the transition from a spinout of Victoria and Massey universities to a high-tech exporter. Dr Coy, who completed his PhD in Physics under Sir Paul at Massey, says that from the beginning Magritek focused on making smaller and more portable NMR and MRI systems.

"Our technology originally arose from New Zealand scientists going down to Antarctica every year, trying to build NMR instruments to measure the sea ice. They took some commercial equipment in the first year and it all broke on the first day, so there was a clear need for instruments to be made more robust and compact. When we started Magritek in 2004, the vision

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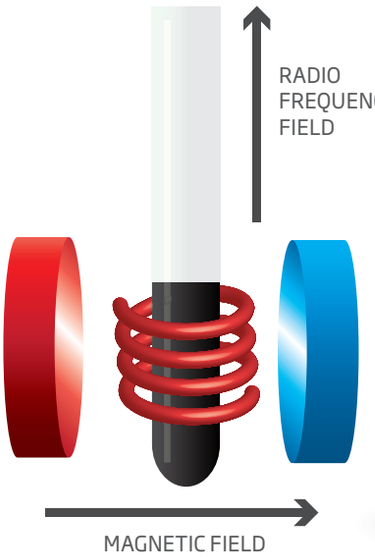
Robin Dykstra, Ronald van Maarseveen and Andrew Coy with the three "flavours" of Spinsolve. Each model is tuned to detect different types of nuclei.

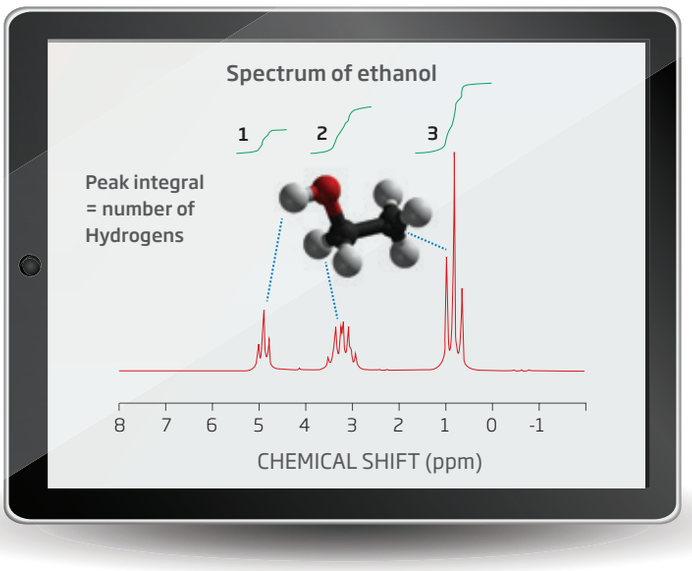
was always about getting NMR out of the dedicated lab and into non-specialist hands."

In the area of portable NMR spectroscopy, Sir Paul and his team were acknowledged to be one of the top two leading research groups in the world. The other was in Germany, headed by Bernhard Blümich, a Professor of macromolecular chemistry at Aachen University. Coincidentally, both groups decided to pursue commercialisation at the same time, albeit playing to quite different strengths. The New Zealanders were adept at the electronics and software; the Germans' expertise was with magnets.

"Almost immediately we started to look at whether we could combine some of the things they were doing with what we were working on, to create products that customers would find exciting and appealing," Dr Coy says. "We ran as two separate companies for the first five years. It reached a natural point where we thought, 'We complement each other really well, but we could be so much more effective if we operated as one company'."

Before the merger, Magritek had enjoyed some success with its early products, including a rock core analyser that it sold to the petrochemical industry and smaller NMR devices for industries such as food processing and medicine. In 2010, the founding scientists were awarded the $500,000 Prime Minister's Science Prize, partly in recognition of the team's achievements





Far left: NMR measures the electromagnetic impulse response of a sample exposed to a polarising magnetic field. Image: Magritek.

Left: The spectrum of the impulse response gives molecular structural information. Image: Magritek.

Right: Chemical samples are prepared in standard five millimetre NMR tubes and are easily inserted into the Spinsolve.

Far right: An intuitive interface enables measurements to be performed quickly by non-NMR experts.

in commercialising their research. The partnership with the Germans, however, signalled a new level of growth, and brought some serious scientific horsepower to the development of Spinsolve.

It was an idea well overdue. Other instruments used for analytical chemistry techniques such as chromatography and mass spectrometry had been revolutionised over the years, Dr Coy notes.

"Mass spectrometry used to involve very large instruments that filled a room, required specialist operators and cost a million dollars. About 20 years ago there was a big push to make them smaller and when benchtop mass spectrometers arrived the market suddenly exploded. Mass spectrometry today is 10 times larger than the NMR market."

Magritek believed a benchtop NMR could have a similar impact - but there were some tricky problems to solve. Critically, NMR requires a strong, stable and uniform magnetic field, which is why superconducting magnets are traditionally used. In turn, that requires the use of cooling liquid helium and a temperature-controlled facility, as well as a dedicated operator.

For the team, the question was how you could maintain that vital uniform field while using smaller permanent magnets.

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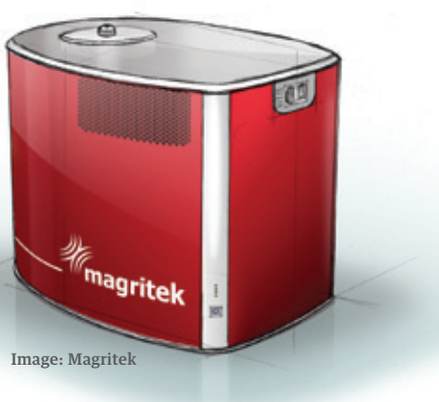

Image: Magritek

"People had made NMR systems that way in the past but they've been notoriously unstable," Dr Coy says. "It is very hard to create a magnetic field that is uniform and very difficult to make that uniform field stable, because permanent magnets are so sensitive to temperature."

The answer was to deploy the magnets in what's known as a Halbach array, a circular arrangement that augments the field on one side while cancelling it to near zero on the other.

"By using the Halbach method we were able to make the instrument very small and also ensure that there was no magnetic field outside the system - the 'stray field' is completely inside the box, making it safe to deploy in a regular chemistry lab next to other analytical instruments."

Crucially, the innovation also removed any need for liquid cryogens or the alternative of "cryo coolers", which require large amounts of power and space.

"We had to develop a temperature control system and mechanical structure that would support the magnet and keep its temperature stable to within 1/100th of a degree," Dr Dykstra says. Any slight changes to the magnet temperature or stresses will cause the magnetic field to drift or distort and so distort the measurement.

"The thermal control system uses a two stage approach to thermally decouple the magnet from the room temperature. The first stage uses a thermoelectric unit to provide a 0.1 degree stable environment that contains the electronics and the magnet assembly.

A second stage controls the magnet temperature to within that 1/100th of a degree."

Even such precise temperature control, however, is not adequate for long term NMR measurements. Consequently, the Magritek scientists developed a novel system that uses an electromagnetic coil to compensate for small changes in magnet temperature and which additionally cancels out the effects of people moving metallic objects around the unit.

While the German team solved the puzzle of magnet design, Magritek's New Zealand arm went to work on the electronics and software.

"We had to put electronics around it to allow the system to set itself up automatically," Dr Dykstra says, adding that it wasn't an easy task. "The thing about NMR is that you have to have quite a high power radio frequency transmitter to excite the sample, and then an ultra-sensitive receiver to pick up the signal that comes back. When you try to start squeezing all of that into a little box, you require methods to stop interference from different sections bleeding into each other. That's the challenge: to squeeze these things together while making them less susceptible to interference."

How did they do it? One of Magritek's key strengths even prior to Spinsolve has been the use of modern digital signal processing technology and methods. "Basically, we borrow from the developments made by the cellphone industry and apply it to our needs. With Spinsolve, we used a lot of digital signal RF [radio frequency] processing within field programmable gate array (FPGA) devices. [For the uninitiated, an FPGA is an integrated circuit designed to be configured after manufacturing.] It has allowed us to shrink things down significantly."

Size and cost were one target; ease of use was another. From the beginning, the Magritek team used the analogy of a photocopy machine. A person using Spinsolve to analyse a chemical sample ought to be able to push a button marked "start" and let the software figure out the rest.

Software engineer Ronald van Maarseveen was charged with making the product as streamlined and simple to use as any iPhone. He took an "agile" approach to the software development for Spinsolve, starting off with some very basic functionality and prototyping potential features as he went. (An "agile" approach is one where the developer is open to the software requirements evolving during the development process.)

"It grew in capabilities, evolving until it met the need.

"We started by creating a long checklist of questions the system

Left: The robustness and small footprint permits the Spinsolve to be placed on an ordinary laboratory bench. Photo: Magritek.

Above: The Spinsolve Carbon-13 version can provide information about the carbon "backbone" of organic molecules such as pharmaceuticals and fuels. Photo: Magritek.

needed to ask itself," he says. "So, 'Am I set up correctly? Are the magnets shimmed correctly? Are they at temperature?' When the system has concluded that all these criteria have been met it proceeds to do the experiment."

Rather than burden the end user with too many decisions, Mr van Maarseveen kept the options to a minimum. However, if someone wants more latitude - to change the parameters of their experiment, say - the software has been designed to allow that, too. "With the latest version we have added something called scripting which can expose more features for those people who want to do more sophisticated measurements."

The Spinsolve project was a learning experience, he says. For the first time Mr van Maarseveen used an architectural pattern called Model-View-ViewModel (MVVM), which was developed by Microsoft to simplify event-driven programming of user interfaces. "Spinsolve is like an empty shell," he says. "When you start it up, it will collect whatever protocols are available and then they are used to dynamically create the whole user interface. We also got a graphic designer involved early on because we wanted to make it as visually appealing and as intuitive to use as we could."

By 2012, the team had a product to take to the world. Weighing just 55 kilogrammes in a sleekly curved package, and running off a standard 240-volt wall socket, the Magritek Spinsolve is as far removed from the conventional NMR spectrometer as the old mainframe computer and the personal computer. For a callow chemistry undergraduate, analysing a sample becomes a simple matter of loading a standard five-millimetre-NMR tube, then tapping start on an external tablet computer.

"They will screen a sample, check whether their reaction has worked or not, and if it looks successful they may go on and submit it to the high field."

What's traded off for this simplicity and size? Physicist Bertram Manz, who was part of the Wellington-based team, says benchtop NMR spectrometers can't offer the same resolution as a high-field instrument.

"You're at a lower field, so you are trading off sensitivity. You don't get as much signal, so you need more of your sample. It's harder to read, but the information is still there. The way Spinsolve is being used now in teaching labs, the amount of sample is never a problem."

Dr Dykstra calls it a "disruptive" technology, and says it promises to change the way people use NMR. "Anyone can walk up to one of these machines, put in their sample and get a result."

The company has identified three main markets for Spinsolve, starting with chemistry education. "What tends to happen when universities teach NMR spectroscopy methods is that students don't get to actually run their sample. Now we can put a machine in the lab and students will be able to measure their real sample - and there's nothing like upfront validation."

Another use is as a time saver in the laboratory. Instead of researchers having to run a sample through a basement NMR spectrometer, a time consuming exercise at the end of which they might learn their experiment has been a wasted effort, they can use the benchtop Spinsolve for a quick check.

Dr Manz remarks that some graduate students are already using Spinsolve in that way. "They will screen a sample, check whether their reaction has worked or not, and if it looks successful they may go on and submit it to the high field."

Outside academia, the company also sees big opportunities for selling

Spinsolve to industry, particularly pharmaceuticals and industrial processing. “We’re looking at bringing NMR out of the lab and putting it into production processes,” Dr Dykstra says. “That’s a game-changer. Traditionally it has always been too difficult for pharmaceutical or chemical processing companies, who haven’t been interested in these big expensive systems that require liquid helium. Now they can bring NMR systems into their labs without all those risks and complexities. They are already evaluating it.”

In fact, since the original Spinsolve product was released two years ago, industry has become as important a customer as academia, Dr Coy says. “We think benchtop NMR isn’t just about capturing some of the current NMR segment; there’s a whole new market out there of people who have never had access to NMR before. Just as with mass spectrometry, a benchtop solution is the only way they’re going to be able to use this very powerful analytical technology in their industries and processes. So we see a huge opportunity ahead of us.”

Not surprisingly, so does the competition. There are now a handful of companies offering benchtop NMR, including two that are Nasdaq-listed and a third that is listed on the London stock exchange. These are large, deep-pocketed organisations, with well-established channels to market. How can Magritek win?

“We have by far the best product on the market,” Dr Coy answers. “Even our competitors admit it. We have a big technical head start on them – but we do realise that’s only part of the answer. We are going up against very large-scale marketing engines, and we are learning how to compete with them. So far I think we have exactly the right strategy. We differentiate ourselves at the premium end of the market, while most of our competitors are competing aggressively at the budget end.”

The company is also innovating furiously to create new markets. Recently it released Spinsolve Carbon, a world-first carbon-13 capable benchtop spectrometer, opening up NMR for organic chemists. It is also working on creating an option for online reaction monitoring, allowing users to watch as a reaction progresses and tweak the parameters.

“The goal is to build an enduring and sustainable business,” Dr Coy says, noting that Magritek’s success has had spin-off benefits for several other local companies, with the machining and electronics done in Lower Hutt. “We’re not just trying to build the cheapest possible product. We aim to be the best in our particular market segment.”

Smart design, world-leading science, an innovative niche product – it’s the high-tech exporting holy grail, really, and exactly the formula Sir Paul promoted so passionately. Dr Coy says the company’s co-founder would be thrilled at progress.

“Every time we hit a milestone we all sit down and say, ‘If Paul was here today how proud he would be’. He’d be singing from the rooftops.” «