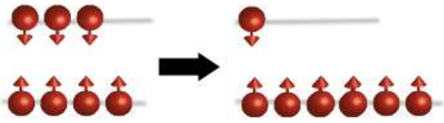
Branca Lab

Enhancing NMR sensitivity through nuclear hyperpolarization

By Tamara Branca

For the past 10 years, my work has focused on nuclear spin hyperpolarization techniques used to overcome the inherent sensitivity limitations of Nuclear Magnetic Resonance (NMR) and Magnetic Resonance Imaging (MRI). Almost 99% of MRI and NMR techniques are based on the detection of the nuclear spin of ^{1}H atoms, which are present at a very high concentration in tissues (tens of molar) in form of water.

When we **hyperpolarize** nuclear spins, we essentially increase the net magnetic field they produce by increasing their polarization, i.e. the difference in population between their energy levels.



With modern hyperpolarization techniques, the increase in nuclear spin polarization can be several orders of magnitude greater than what can be achieved at room temperature in clinical MR systems, enabling the detection of atoms and molecules other than ^{1}H that are present at a much lower concentration (milli-or micro-molar).

These techniques have greatly enhanced the potential of MRI over the past decade as a diagnostic tool, enabling new applications ranging from monitoring cancer metabolism to mapping lung function at the millimeter scale. In collaboration with the Center for Cystic fibrosis at UNC, our lab is currently using hyperpolarized Xe gas as a contrast agent for MRI to assess lung ventilation function in patients with cystic fibrosis (CF) (see images on next page). Considering that most CF patients are young and often need several x-ray scans over their lifetime, the lack of ionizing radiation of MRI coupled with the high sensitivity of hyperpolarization techniques is ideal to reduce radiation exposure.

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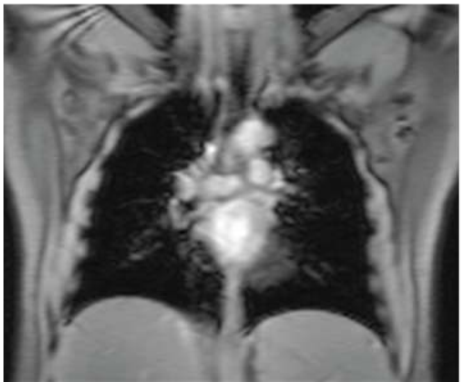
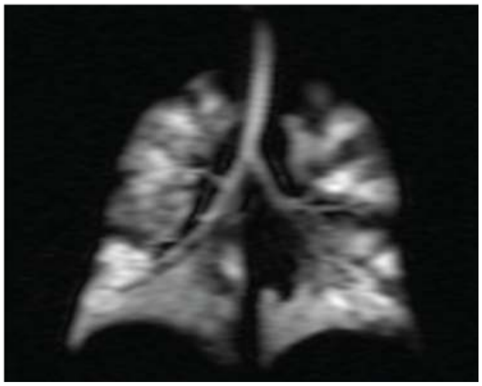
However, each hyperpolarization technique comes with its own unique challenges. For gas hyperpolarization, for example, one of the major challenges has been the low performance of currently available continuous-flow Spin Exchange Optical Pumping (SEOP) systems used to produce high quantities of highly polarized Xe gas needed for biomedical imaging applications. Experimental xenon polarization values have been notoriously much lower than what the standard theory predicts.

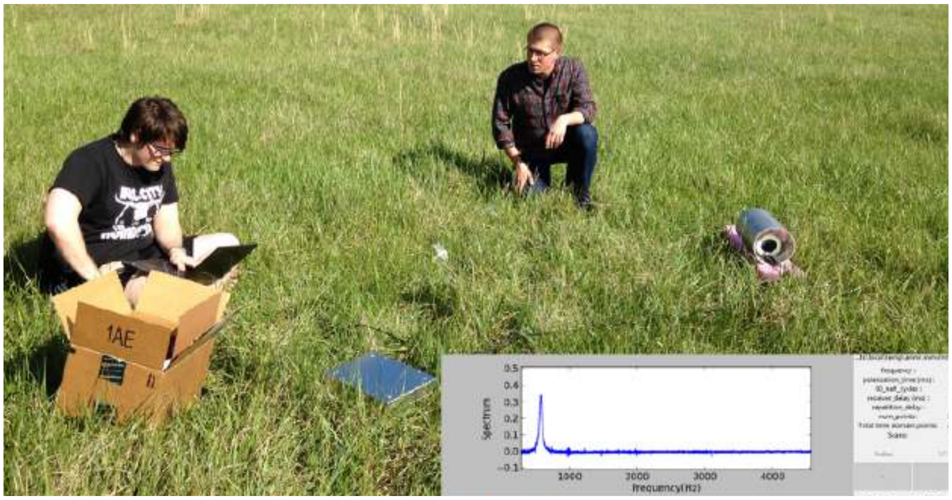
In the past, both our group and others have focused on depolarization mechanisms to understand the discrepancy between theoretical and experimental polarization values, but without much success. More recently, our group has taken a different approach. We have begun to question and evaluate the validity of the many assumptions made to adapt the general theory of SEOP (developed by UNC alumnus William Happer) to continuous flow SEOP setups. This work, led by Michele Kelley (see "student profiles" below), a fourth-year graduate student in my lab, is finally providing a better understanding of the discrepancy.

As in any other field, only when we have a good theoretical model, that is able to correctly reproduce experimental results, can we hope to make some progress.

My lab is also involved in studying the properties of hyperpolarized spin systems at low and ultra-low magnetic fields. Low-field NMR and MRI systems are becoming more and more popular as they are cheaper, portable, and often safer. For hyperpolarized nuclei, low field systems may even be more sensitive than high field systems,







***Top left**: A standard ^{1}H MRI image of the chest of a young CF patient acquired at UNC-CH. The lungs cannot be seen because of their low water content and because of the many air tissues interfaces, which lead to the rapid decay of the small MR signal. **Top right**: Hyperpolarized Xe gas MRI of the lungs of the same subject. Areas of the lungs that are poorly ventilated (dark regions) are clearly displayed. As opposed to standard pulmonary function tests that provide only a global measure of airflow obstruction and restriction, MRI with hyperpolarized xenon gas is more sensitive to early lung disease as it provides regional information about lung function and structure. **Bottom**: Christian Browning (left), a former Physics undergraduate, with Michael Antonacci (right), a former graduate student in the Branca lab, and now a faculty member in the Physics Department at San Vincent College, testing the portable Earth field NMR spectrometer built by Christian in an open field just outside campus.*

but the opportunities of MRI with hyperpolarized nuclei at low field are largely unexplored.

One of the research projects in my lab, led by Nick Bryden (see "student profiles" below) is focused on studying the magnetic properties of hyperpolarized Xe dissolved in biological tissues at low magnetic field strengths. Longer relaxation times of xenon at ultralow fields could open the doors to what we call "dissolved-phase" imaging, i.e. imaging of Xe atoms that, upon inhalation, dissolve in blood and tissues, changing their resonance frequency based on the chemical environment they probe. Nick took over the work started by Michael Antonacci, a former graduate student in my lab, and now a faculty member in the Physics Department at San Vincent College. Michael built, from scratch, an NMR spectrometer operating in the micro-Tesla to milli-Tesla range, a field that is several orders of magnitude smaller than that produced by superconducting magnets in typical clinical MRI systems. This is something that students working in an NMR lab rarely get to do, as these spectrometers are often treated as black boxes. It took a few months to build and debug a working spectrometer that could be used to detect the extremely small signal produced by the nuclear spins of hydrogen atoms at such low field. Anything from the power line in the nearby walls to a running laptop will produce noise that is orders of magnitude greater than the signal of interest.

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Along the same lines, several undergraduate students in my lab have worked on cheap (less than $100) spectrometers that could detect the nuclear spin signal at the very weak magnetic field of the Earth. Undergraduate students working for my lab have been building these spectrometers essentially from the ground up.

Despite the many setbacks that they faced along the way, there is something empowering for students to build their own detector from scratch and then use it to perform scientific experiments.

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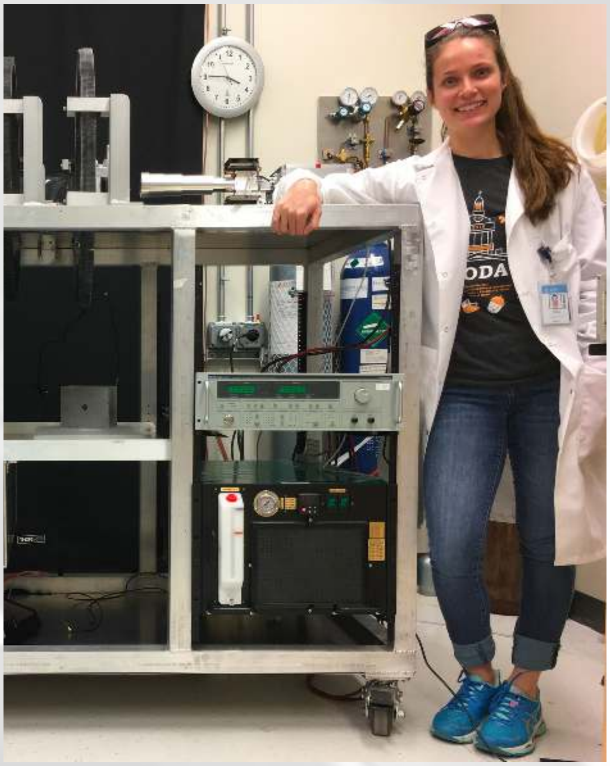
Two student profiles



Michele Kelley

I am a fourth-year graduate student in the Branca Lab, a Royster Fellow, and the recipient of an NSF Fellowship. My work focuses on the hyperpolarization of ^{129}Xe nuclear spins for nuclear magnetic resonance spectroscopy (NMR) and imaging (MRI). Specifically, I am interested in understanding why theoretical models of ^{129}Xe hyperpolarization, which is done through a process called Spin-Exchange Optical Pumping (SEOP), have historically predicted much higher Xe polarization values than what we achieve experimentally. This has been an open question in my field for over 20 years. To answer this question, I have used a combination of experimental and computational techniques, as well as reevaluating some of the assumptions made in these models and I believe that finally we have an answer to why our theoretical models were so poor. The next step in my research is to use the computational tools I developed to optimize the design of a more efficient ^{129}Xe polarizer. In addition to my research, I also serve on the Graduate Studies and Affairs Committee, as a department media co-chair, and mentor in the new GRAM program.

Nick Bryden

I am a third-year graduate student and the recipient of an NSF Fellowship. My research is on the magnetic properties of hyperpolarized nuclei at ultra-low field (ULF) strengths. The insensitivity of NMR has necessitated the use of large magnetic fields to produce detectable signals from samples like the water in our bodies. Using hyperpolarized nuclei, like ^{129}Xe, this requirement is far less stringent, allowing the use of more space and cost-effective equipment. We have constructed an NMR spectrometer which operates at field strengths up to 100,000 times weaker than those used in conventional MR scanners. In this regime, many of the relaxation properties of ^{129}Xe are under-explored or unknown. Many of these are linked to its performance as an agent for MR imaging, which has been well characterized in high-field studies. We hope to further develop our spectrometer by adding imaging capabilities to extend this characterization into the ULF regime. The combined used of hyperpolarized nuclei and ULF MR is expected to drastically reduce the cost of medical imaging and introduce a level of portability otherwise unknown to the practice.