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Sabbatical Report
Fall 2001 - Spring 2002

Introduction

For my sabbatical leave during 2001-2002, I worked at the ENS Laboratory in Lyon, France with Dr. Lyndon Emsley, a leader in the field of solid-state nuclear magnetic resonance (NMR) spectroscopy from October 2001 until March 2002. From March 2002 until August 2002, I was in Seattle, WA doing some research while my wife had a stem-cell transplant at the Seattle Cancer Care Alliance. While working with Lyndon, my research focused primarily on three projects. The first was to build a working dynamic-angle spinning controller and probe to use in Lyon. The second was to develop new dipolar decoupling pulse sequences involving dipolar Hamiltonian reversal rather than nullification. The final project was to combine the magic-angle spinning technique with the stray-field imaging experiment to do high resolution three-dimensional imaging experiments. None of these three projects were completed as my return to USA occurred nearly 5 months earlier than hoped. For my time spent in Seattle while my wife had treatment, I worked on the departmental web pages (under the DuPont technology grant) as well as spent time learning about cancer care. Even though this time had little in the way of academic elements, I learned a great deal about life, death and the human spirit in my time in Seattle. Three months of Fulbright support remains and I hope to return to Lyon to work with Lyndon either the summer of 2003 or 2004. All of the projects will be continued in some form at Berea in the coming months. The impact this sabbatical has had on my teaching is primarily in the area of undergraduate research where I have brought back a new enthusiasm for some novel research topics. I return with the experience of living in a foreign country and have reflected on how this turned me back into a student again. It also has led me to continue my study of the French language at Berea College where I hope to pursue additional courses in the French department.

Project Narrative

The major goal of my sabbatical stay in Lyon, France was to develop my research skills and bring those back to enhance my own undergraduate research program at Berea College. Enhancing the research experience of undergraduates at Berea College will improve the overall chemistry program. In addition, I have made contacts with researchers in France with whom I will continue to collaborate and with whom students from Berea College might consider doing summer research or graduate studies. The three research projects that I will briefly summarize include magic-angle spinning stray-field imaging, decoupling through dipolar reversal, and dynamic-angle spinning experimental equipment construction.

Magic-Angle Spinning Stray-Field Imaging

The concept of doing stray-field imaging was developed many years ago when researchers realized that a large superconducting NMR magnet has massive field gradients along the z-axis (the B_0 direction). A modern superconducting magnet has a field strength of 117,000 G (11.7 T) or greater. This field rapidly drops as you descend from the field center over a distance of about 100 cm to the base of the magnet where the field will be 100 G or less. In the figure to the right, I indicate that there must be a location where the rate of change of the field (the field gradient) is largest and I would estimate this to be a gradient of about 10.0 T/m located halfway down the magnet from the field center. Thus the idea was born to use this gradient to do magnetic resonance imaging (MRI) which is normally called stray-field imaging (STRAFI).[1-9] This works very well on small samples for getting a one-dimensional z-axis image. Applications have focused primarily on looking at thin films and layered materials. Some work has been done to extend STRAFI to two and three-dimensions but the fundamental difficulty came in trying to determine a method to either reorient the sample or reorient the field gradient. Using another gradient coil is

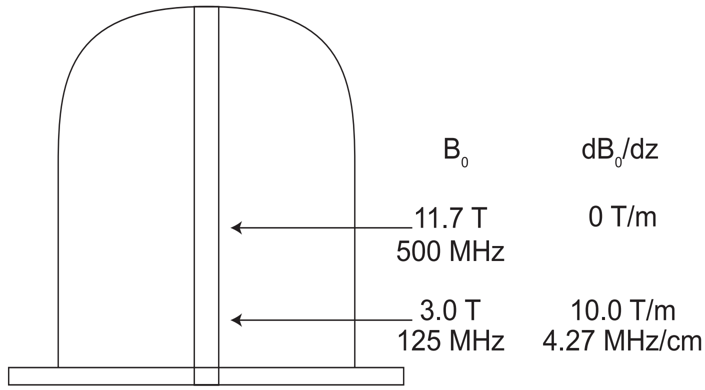

Figure 1. Origin of Stray Field Imaging. This diagram shows a superconducting NMR magnet with a narrow sample bore. As you descend down from the field center at 11.7T, the field gradient increases as the B_0 drops until it peaks (in this case 10 T/cm). At this location the NMR signal which is normally 1 Hz wide will be spread over 4.2 MHz/cm, giving a MRI resolution of about 3 nm!

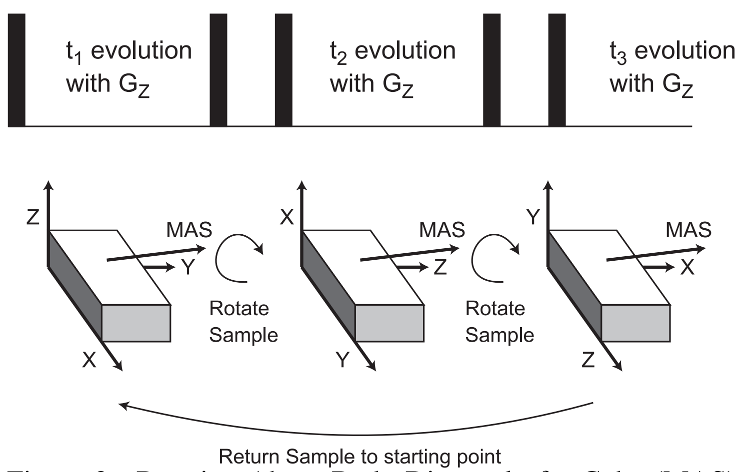

Figure 2. Rotation About Body Diagonal of a Cube (MAS) can produce effective gradients in three orthogonal directions (notice how x becomes z becomes y under 120˚ hops).

unsatisfactory since this will be a much smaller gradient and give much worse resolution in the direction of the pulsed field gradients.

While working at the ENS-Lyon on the dynamic-angle spinning (DAS) probe, we began thinking about using a DAS probe to do MRI. These thoughts led us to realize that by using rotation about a single direction (the magic-angle with respect to the z-axis) we could achieve three orthogonal gradients [10-14] (as seen from the sample frame of reference). The fundamental idea behind this technique comes in recognizing that rotation about the magic-angle can be represented as rotation about the body diagonal of a cube (see figure 2). As you rotate about such a diagonal, the x, y and z-axes will interchange in a cyclic fashion (x becomes y becomes z becomes x) as the rotor rotates in discreet 120˚ steps. Of course an actual MAS NMR probe does not hop in discreet steps but undergoes continuous rotation at rates ranging from 50 to 15,000 Hz. At the lower end, the rotation can be treated as discreet steps if the magnetization of the sample is stopped from undergoing evolution while the rotor moves between 120˚ steps. This very slow rotation will appear as static motion if one considers that the rotation period is approximate 20 ms and the evolution time at each of the three steps is less than 500 μs. Calculations were performed to determine the amount of error introduced in this approximation and the distortion of the image will be minimal.

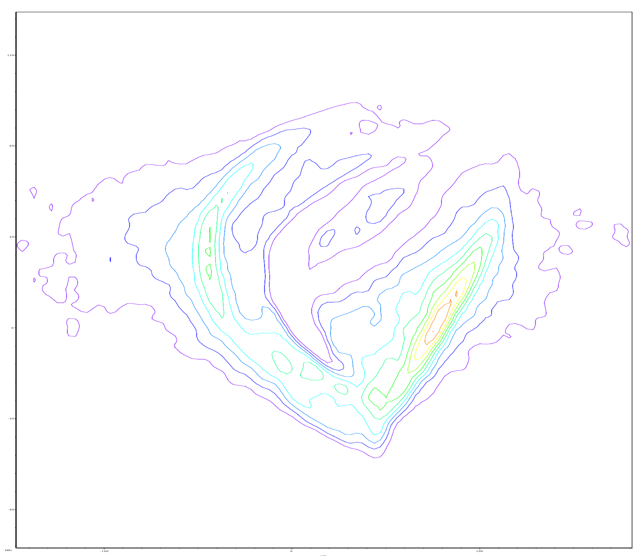

Figure 3. MAS-STRAFI image of a coffee bean. The ^{1}H signal arises from oils inside the bean. It is useful to note the manner in which the bean wraps around itself.

One set of experiments was initially conducted on coffee beans in the sample compartment. Coffee beans contain a large amount of saturated oils that give rise to a moderately sharp single NMR peak. Using the slow spinning experimental apparatus, we were able to get a rough image show in figure 3. We believe you can see the fold of the bean as it wraps around itself like the cross section of a closing fist. We decided we really needed to get some better phantoms and turned to imaging water/plastic phantoms. These experiments were just begun in Lyon and the initial results are promising. These experiments will be continued in Berea once my MAS probe returns from repairs. The long term benefit of this work is the potential to doing three-dimensional imaging on very small samples. Given the large stray field gradients in magnets 7.0 T and larger, it is not unreasonable to calculate a resolution of better than 20 nm on a sample size of 0.5 mm in each dimension. At this resolution, one might consider doing living organisms in a stopped-flow probe. This might be a potential alternative to traditional microscopy where optical approaches become very limited below the μm scale. Assuming experiments progress as expected, I believe this new technique may develop some commercial value.

Decoupling Through Dipolar Reversal

The research the Lyndon's group in Lyon has been pursuing with greatest vigor in the last few years is improved methods of obtaining high resolution $^1H/^{13}C$ or $^1H/^{15}N$ correlation spectra analogous to the HSQC experiment in liquids. They have had a great deal of success using frequency-switched Lee-Goldberg (FSLG) decoupling in the indirectly detected 1H dimension of these experiments.[15-18] Other multiple-pulse decoupling schemes have been utilized as well (WHH[19], MREV8[20], etc.) and the FLSG family seems to be the most effective at this point. The overall performance of these kinds of sequences does not yet approach the liquid resolution that researchers need if they are to apply solid-state NMR techniques to biological samples. Recent work in the Emsley group has led to the discovery of certain continuous phase modulated decoupling schemes that are equal to or slightly better than the performance of the FSLG. Some theoretical calculations indicate that there are no solutions (short of random isotropic motion) which can exceed the performance of FSLG or DUMBO[21]. Yet most of these calculations operate under the assumption of continuous irradiation with the goal of continuous zero average dipolar Hamiltonian. If we relax this criterion to have an indirectly detected sequence where the overall average is zero but not the instantaneous average, it might be possible to have a higher performance sequence. The overall approach that we began was developing sequences which utilize diplolar Hamiltonian evolution periods followed by periods where the Hamiltonian is scaled by a –1/2 factor. By alternating between these positive and negative evolution periods in a 1:2 ratio in time, the overall average Hamiltonian can be made zero (see figure 4). Experiments

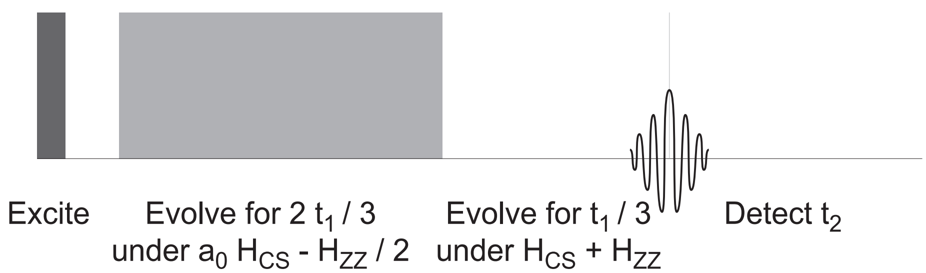

Figure 4. Dipolar Reversal 2D Indirect Detection. In this experiment, a series of pulses (the gray box) are applied to produce the reversed dipolar Hamiltonian, followed by a period of free evolution. The net result should be an isotropic evolution at the detection point (starting t_2).

were attempted using some simple dipolar reversal sequences and the results were promising. We are continuing to explore the conditions under which this kind of averaging might be valid. One of the major benefits is that the free dipolar evolution windows would present time periods in which other pulses might be applied to do other experiments (such as magic-angle turning[22]). The research at this point is focused on developing computer simulations that can be used to create new pulse sequences. We will be doing these simulations using our LINUX workstations at Berea College running a program called SIMPSON (which is a free solid state NMR pulse sequence calculation application).

Dynamic-Angle Spinning (DAS) NMR

The DAS technique was first created in the late 80's and early 90's at UC Berkeley [23-32] to study quadrupolar nuclei in the solid state. This application is still being pursued as an active area of research by the Grandinetti (OSU), Stebbins (Stanford) and Zwanziger (IU) laboratories, but has fallen into disuse by other research teams as the multiple-quantum magic-angle spinning (MQMAS)[33-39] experiment has emerged as a technically easier experiment to accomplish a similar goal. There are a wide range of problems that DAS might be used to solve that have been avoided by other researchers due to the difficulty in setting up the experiment. In Lyon we began the process of building the probe and controller. Due to my early departure the only finished product was the controller itself. We had begun to develop drawings we might use for the probe and when I return in the summer of 2003 or 2004, one of the projects would be to finish building the probe.

Educational Projects

One of my major goals while in France will be to learn the language and experience the French culture. While I had to leave France early, what I learned was that language immersion requires true immersion. The people in the ENS unfortunately tended to revert to English language very quickly in my presence and so I never felt that I was learning the French language very quickly. Since returning from sabbatical I have begun taking French 101 here at Berea College and am finding that I do indeed know many words from my 5 months in France. I am optimistic that I will be a much more proficient speaker when I return in the summer of 2003 or 2004 to finish my Fulbright fellowship. As to learning about French culture, Lyon provided ample opportunity to see fine art, eat great food and see the French people living on a day to day basis. I think going to a place like Lyon is very different than the standard trip to Paris that many people participate in when doing studies in France. Most of the Fulbright students and faculty were living and working in Paris. I thought it was a very good experience to live outside of Paris (in Lyon) and then visit Paris only once in a while. Paris (at least in the old city) is very geared towards tourism whereas Lyon is distinctly not. In Lyon proper there are a few nice museums but nothing like Paris. For the most part you see the people living their lives and going to work. Now that I have been in France once, I really want to go back again and spend more time there in the future. The impact of this travel on my teaching is so far hard to qualify. My travels certainly thrust me back into the role of student and forced me to reexamine how I learn in that situation.

A second goal from my work in Lyon was to do some course development. I had hoped to do some development for our advanced laboratory program but ran out of time. Instead, my course development work primarily occurred when my family and I were living in Seattle. The primary course development came in the form of improving the chemistry department web pages. This was partially funded through a DuPont technology grant and complete report to that agency has already been filed. If this report is of interest, I can forward it. The short description of this work was adding PHP and MySQL language programming to the current HTML code of the chemistry department web site. This allowed us to create seminar speaker and past student databases that can be more easily updated and modified. The past student database in particular is set up to allow students to modify some information on their own and thereby keep us and themselves informed about current activities. Also I worked on developing some online portfolio and testing materials relevant to the new chemistry laboratory curriculum.

Conclusions

The overall goal of this project was to gain some research experience in some new MAS techniques and bring this research back to Berea College to help improve my research and teaching here. Three projects were started and none were completely finished due to circumstances beyond my control, but good progress was made. We are very optimistic that all of these projects will bear fruit in the form of publications and undergraduate research opportunities in the near future. I learned a great deal about the French culture and am continuing my studies of the French language. As I return to France again in the future, I anticipate that these travels can ultimately lead me to open the door for chemistry students at Berea College to do similar travels.

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