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Hyperpolarized ^{129}Xe Nuclear Magnetic Resonance at 1.89 T and 85 G: A Signal-to-Noise Ratio Comparison

by

Mark McDonald, B.Sc.

A thesis submitted to
the Faculty of Graduate Studies and Research
in partial fulfillment of
the requirements for the degree of
Master of Science

Department of Physics

Carleton University
Ottawa, Ontario, Canada

January 2001

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submitted by **Mark McDonald, B.Sc.**
in partial fulfillment of the requirements for
the degree of Master of Science

Chair, Department of Physics

Thesis Supervisor

Carleton University

Date 19 Jan 2001

Abstract

Nuclear polarization of ^{129}Xe can be enhanced by up to five orders of magnitude by optical pumping and spin exchange. The resulting magnetization can be used as a powerful probe for magnetic resonance imaging. Because the magnetization is largely independent of the magnetic field strength, field strengths up to three orders of magnitude lower than conventional field strengths (1.5 T) can be used to image hyperpolarized ^{129}Xe . This, among other things, may drastically reduce the cost of the magnet used.

Nuclear magnetic resonance of hyperpolarized ^{129}Xe gas is investigated at 85 G and the signal-to-noise ratio compared to that of signals acquired at 1.89 T. A dedicated 85 G resistive magnet was constructed and used to acquire the signals. T_1 relaxation time measurements were made and radiation damping effects checked for. The SNR at 85 G was measured to be ~ 500 while the SNR at 1.89 T was measured to be ~ 10000 . This work suggests that Magnetic Resonance (MR) imaging at 85 G should be feasible using hyperpolarized ^{129}Xe gas.

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List of Abbreviations

CFA	Constant flip angle
CP	Carr-Purcell
CPMG	Carr-Purcell-Meiboom-Gill
EPI	Echo-planar imaging
FLASH	Fast low-angle shot
FID	Free induction decay
FOV	Field of view
FWHM	Full width half maximum
GE	Gradient echo
HF	High-field (1.89 T)
HP	Hyperpolarized
LF	Low-field (85 G)
MR	Magnetic resonance
NMR	Nuclear magnetic resonance
PFOB	Perfluorooctyl bromide
RF	Radiofrequency
SNR	Signal-to-noise ratio
T_1	Longitudinal relaxation time
T_2	Transverse relaxation time

TE	Echo time
TH	Thermally polarized
T_R	Repetition time
VFA	Variable flip angle

Chapter 1

Introduction

Traditionally, physiological and anatomical understanding of the human body has been acquired through either direct observation or more invasive techniques such as postmortem examination. Modern imaging techniques allow non-invasive observations that not only help the understanding of the human form but also aid in the detection and planned treatment of diseases early in their development. Among the variety of available modalities, Magnetic Resonance (MR) imaging is a non-invasive, non-ionizing technique well known for its minimal patient risk, excellent soft tissue contrast, and multi-planar cross-sectional views.

While clinical MR imagers use hydrogen nuclei, or protons (^1H), as the nucleus of interest for the anatomical imaging of proton-rich regions, noble gases such as helium (^3He) and xenon (^{129}Xe) can be used to image proton-deficient gas spaces, such as the lungs, and for dynamic or functional imaging, such as measuring blood flow to the brain. This provides an excellent complement to proton MR imaging. Furthermore, noble gas MR imaging can be performed at much lower magnetic field strength, therefore providing a more economical alternative to MR imaging by replacing high field ($> 1 \text{ T} = 10000 \text{ G}$) superconducting magnet technology with low-field (< 100

G) resistive or permanent magnets, while still maintaining the signal-to-noise ratio and image resolution of a high-field system. The implications of low magnetic field strength MR imaging are the development of low-cost, accessible imagers designed with specific geometries and dedicated to specific imaging tasks. This chapter will introduce the relevant concepts required to understand low-field MR imaging with ^{129}Xe gas.

1.1 Magnetic Resonance Imaging

MR imaging is an extension of nuclear magnetic resonance (NMR) spectroscopy, a technique first realized by Bloch[1] and Purcell[2] in 1946. In the presence of a static magnetic field, a nucleus will have a precessional frequency dependent upon the nuclear species and the strength of the field. This is the basic tenet of nuclear magnetic resonance. MR imaging exploits this field dependence of the frequency by altering the magnetic field strength spatially, through the use of magnetic field gradients, thus creating a spatial frequency map which can be used to generate an image.

Developments in MR imaging, based largely on the detection of hydrogen atoms in water, began in the 1970's. Damadian (1971)[3] reported that certain malignant tumours of rats differed from normal tissues in their proton NMR properties, and suggested that proton NMR might therefore have diagnostic value. The first linear-gradient images were formed by Lauterbur[4] and by Mansfield and Grannell[5], both in 1973. An image of a finger was reported in 1976 by Mansfield and Maudsley[6], studies of the hand by Andrew[7] and wrist by Hinshaw[8] both followed in 1977, and before long whole-body images were being obtained. Image quality continually improved, partly through engineering and technological developments, and partly through increasing skills and experience in the manipulation of field gradients and

radiofrequency (RF) pulse sequences. By 1980, the clinical evaluation of magnetic resonance imaging had begun, and since that time there have been continuing developments in instrumentation and application which have led to the present situation in which over 6000 whole-body imagers are installed world-wide.

The most wide-spread medical use of magnetic resonance is in diagnostic radiology; it is the imaging method of choice for examination of disorders of the central nervous system, and is increasingly used for the investigation of diseases in other organ systems[9][10] and for tumour detection. The technique provides excellent spatial resolution and a rich soft tissue contrast particularly for the limbs and head, which are least susceptible to motion artifacts.

Together with the diagnostic applications of MRI, there is increasing awareness of the role of MRI in the investigation of tissue physiology and function. To a large extent these more research-oriented studies exploit the dependence of MRI signals on hemodynamic effects, including blood flow and the oxygenation state of hemoglobin. In addition, there are further MRI approaches such as diffusion-weighted imaging, which are proving particularly sensitive to pathophysiology, and which promise to add significantly to our understanding of a number of disease states, as well as extending the scope of diagnostic MRI. A more extensive review of these topics and their references can be found in the work by Gadian[11].

1.2 Hyperpolarized Noble Gases

Although, in principle, any nucleus with an odd number of nucleons (protons or neutrons) has a net magnetic moment and thus can contribute an MR signal, hydrogen nuclei are the primary nuclei under investigation in MR imaging. The magnetic moment of a nucleus is determined by its gyromagnetic ratio, γ . Therefore, because hydrogen nuclei have the highest gyromagnetic ratio, resulting in a high magnetic

moment, and because 60-80% of biological tissue is composed of water, proton imaging yields a large signal. MR imaging with nuclei other than protons is not as successful due to the small magnetic moment and low density of these nuclei *in vivo*. ^{31}P and ^{23}Na are the best candidates for MR imaging other than protons. While the natural abundance of both isotopes is 100%, their respective densities in the human body are approximately 10 mM/cm³ and 80 mM/cm³ compared to a typical proton density of 100 M. As well, their magnetic moments are about 6.63% and 9.25% that of protons, respectively. The low magnetic moment and low density of these nuclei can only be compensated for by increasing the acquisition time from seconds to hours thereby making them impractical to work with.

While proton imaging is successful in the areas of anatomical MR imaging of the brain and internal organs, it cannot be used to view proton-deficient regions, such as the gas space of the lungs. Therefore, since no other organic nuclear species provides the necessary signal intensity, a suitable, biologically compatible, external species is desirable.

In the presence of a static magnetic field a nucleus with a spin of $1/2$ will be in one of two possible states, the ratio of the population density of which is close to one. This ratio is the polarization factor and is proportional to the signal obtained. While proton imaging does provide the most MR signal of any of the nuclei available in the human body, the polarization of protons is only on the order of 10^{-6} . Therefore, considerable effort has been put into higher field systems (1-9 T), improved RF coil design, and low-noise receiver systems to raise the signal-to-noise ratio (SNR) permitting increased spatial, temporal, or spectral resolution. In terms of the SNR, any substantial increase of the polarization will result in a significant improvement in image quality. Such a prospect has been realized with the advent of laser polarization techniques using spin $1/2$ noble gases, specifically ^3He and ^{129}Xe . Noble gases are used because they are biologically inert and while any non-zero spin nuclei can be

used to perform an NMR experiment, spin 1/2 nuclei are preferred as they yield the highest detectable NMR signal. Laser polarization, or hyperpolarization, of these gases forces the nuclei into one of the two possible energy states, therefore increasing the polarization and hence the signal by a factor of up to 10^5 . This will be discussed in greater detail in Chapter 2.

The techniques involved in laser polarization were first developed in 1950, when increasing nuclear polarization was of interest to nuclear physics. Kastler[16] first described how nuclear spins could selectively populate their ground state via optical pumping, where a circularly polarized light in the presence of a magnetic field will selectively excite one of the two ground state energy levels of an alkali metal electron created by the magnetic field. These excited nuclei will relax back to both ground state energy levels thus increasing the population of the energy level not being excited. In the 1960's, Colegrove *et al*[17] reported on the polarization of ^3He by metastability exchange (a technique whereby the nuclear polarization results from the strong hyperfine coupling between the electronic and nuclear spins of the metastable atom), while Bouchiat[18] was measuring the nuclear polarization of ^3He obtained by spin exchange from optically pumped rubidium atoms (where nuclear polarization results from the transfer of the alkali metal electronic polarization to the noble gas nucleus). This work focuses on the spin exchange method using ^{129}Xe . Metastable exchange using ^{129}Xe is not an option as ^{129}Xe does not have a metastable state.

^3He and ^{129}Xe are the only nonradioactive spin 1/2 noble gases that can be laser polarized. An excellent comparison of these two gases can be found in a review article by Mugler[12]. Table 1.1 lists the physical characteristics of these two isotopes.

^3He is produced cheaply from tritium (^3H) decay at $\sim \$100$ US per litre-atm, while natural abundance ^{129}Xe is collected as a byproduct of the liquid air industry and priced at $\sim \$10$ US per litre-atm. 80% enriched ^{129}Xe is more expensive at $\sim \$1000$

Nucleus	^3He	^{129}Xe
Gyromagnetic Ratio (rad/T/s)	20.378×10^7	7.4003×10^7
Natural Abundance (%)	10^{-4}	26
Self-Diffusion Coeff. (cm^2/s)	1.8	0.06
Ostwald Solubility Coeff.		
- Water	0.0098	0.083
- Blood	0.0099	0.14
- Oil	0.018	1.7

Table 1.1: Properties of ^3He and ^{129}Xe . Self-diffusion coefficients are measured at 1 atm and 20°C [12].

US per litre-atm. While xenon and its isotopes are readily available, tritium is a strategic material used in the manufacturing of nuclear arms and is therefore not easily accessible to the public. This may limit the use of ^3He for imaging purposes.

Both nuclei are good for gas space imaging (cracks, voids, lungs, sinus cavities) [62][22]. As the SNR is directly proportional to γ , ^3He will have a SNR 2.8 times better than that of ^{129}Xe [12]. The low diffusion constant of ^{129}Xe reduces signal attenuation while the smaller γ results in a lower signal decay rate. To counter this, the high diffusion constant of ^3He is ideal for characterizing the microstructure of complex gas spaces such as the lung. As well, helium won't dissolve into the bloodstream as readily as xenon would, as xenon has a greater affinity for fatty molecules, such as are found in red blood cell membranes, than helium. Also, signal decay rates of ^3He are larger than those of ^{129}Xe *in vivo* therefore allowing measurements of smaller voids.

Initially, hyperpolarized noble gases found application in the MR imaging of animal lungs. Albert *et al*[22] imaged the excised lungs of a mouse with ^{129}Xe where the nuclear polarization was increased by a factor of $\sim 10^5$ via optical pumping

and spin exchange (1994). Wagshul *et al*[23] obtained 2D lung images from live mice using the same setup as Albert. The dynamics and lineshapes of gas-phase spectra from mice thorax were also investigated (1996). These results suggested that a temporal variance in the amounts of gas in various structural compartments could be determined from the gas spectra based on the associated bulk magnetic susceptibility environments. Sakai[24] also obtained lung images from live rats.

The first human lung studies using ^{129}Xe were performed by a team of researchers from the University of Virginia, Princeton University and the State University of New York at Stony Brook[25] in 1997, where lung images were obtained from two healthy volunteers during suspended respiration. Human oral and nasal cavities and the paranasal sinuses have also been imaged[26][27].

As indicated in Table 1.1, ^{129}Xe is soluble in a variety of substances while ^3He is highly insoluble. ^{129}Xe is lipophilic, dissolving readily in oils and lipid-rich materials. ^{129}Xe is extremely sensitive to its environment, with a huge range in its relative resonant frequency, or chemical shift, upon adsorption and solution. Chemical shift is due to a nucleus' sensitivity to its electronic environment. Therefore, it is possible that xenon is more sensitive than helium due to the greater polarizability of its more complicated electronic structure. The result is that ^{129}Xe is both an excellent materials science and biological probe.

In its dissolved phase ^{129}Xe can be used for perfusion imaging of the brain, lung and other organs. When inhaled, it rapidly dissolves in the bloodstream and is subsequently transported throughout the body with preferential distribution to lipid-rich regions. However, in humans, ^{129}Xe is an anesthetic at concentrations $>70\%$ and so must be inhaled at concentrations of 30% at most[13], or the patient will fall asleep (possibly reducing cerebral blood flow making functional imaging more difficult). As an alternative to inhalation delivery, site specific injections of ^{129}Xe dissolved in a biologically-compatible carrier[14] (e.g.: perfluorocarbon emulsions.

lipid suspensions) may have several advantages: an increase in local concentration providing increased SNR, decreased transit time and therefore less signal degradation due to relaxation, targetability to specific organs or discrete sites, and a decreased systemic concentration compared to inhalation, potentially avoiding the anesthetic effects of the gas. In contrast, ^3He , with its low solubility, provides the opportunity to encapsulate the gas in the form of microbubbles, thereby using the gas along with its intrinsically greater γ for visualizing the structure and dynamics of fluidic systems[15].

The high solubility of ^{129}Xe in lipids and its enormous range of chemical shifts upon solution or adsorption are fundamental to the wide range of potential applications for ^{129}Xe . Both Wagshul *et al*[23] and Sakai *et al*[24] focussed on the temporal dynamics of dissolved-phase ^{129}Xe in the chests of animals. Both groups found three dissolved-phase resonances in mouse and rat thorax, with a range in chemical shift of 190-200 ppm. Wagshul assigned these to the blood (199 ppm), lung parenchyma (195 ppm) and other well-vascularized tissues in the thorax such as the heart (190 ppm). Both groups also measured apparent T_1 relaxation times (a time constant characterizing the exponential decay of the ^{129}Xe polarization lifetime) between 10 and 50 seconds. The long apparent T_1 times found in these two studies indicated that the lifetime of hyperpolarized ^{129}Xe in the bloodstream should be sufficient to allow for transport to organs distant from the lungs, such as the brain. Considering the range of chemical shifts, these results also suggested the possibility for dissolved-phase imaging of individual tissue components. Wilson *et al*[80] measured T_1 in homogenates of rat brain, kidney, and lung at varying oxygenation levels to be as low as 4.4 s in deoxygenated lung homogenate and as high as 22 s in deoxygenated brain homogenate, indicating that ^{129}Xe will make a unique and effective physiologic tracer for MR imaging with high tissue contrast.

In the first human studies using hyperpolarized ^{129}Xe , conducted by Mugler

et al[25], dissolved-phase signals were detected from both the chest and the head. The overall lineshapes of the dissolved-phase spectra in the human chest were very similar to those found by Sakai in the rat[24], while other resonances found in the head matched with signals found in rat brain[28]. Subsequent studies performed by Maier[29] using higher polarization levels, revealed four separate dissolved-phase resonances in the human brain. The specific compartments corresponding to these multiple resonances have not been determined.

The first dissolved-phase ^{129}Xe images were made by researchers at the University of Michigan[28]. Here, Swanson *et al* acquired dissolved-phase images of the rat brain and, more recently, have extended their work to investigate the dynamics and tissue distribution of ^{129}Xe in the lung, heart, brain and kidneys of the rat. Duhamel *et al*[81] also acquired dissolved-phase images of rat brain tissue and intravascular tissue via lipid-emulsified ^{129}Xe injected into the carotid artery. These results show the potential of ^{129}Xe for measuring cerebral blood flow, cardiac perfusion, kidney perfusion and lung function[30]. Utilization of these techniques in humans will probably require relatively large volumes of hyperpolarized ^{129}Xe and polarization levels higher than those currently achieved ($> 5\%$).

Another novel possibility with hyperpolarized noble gases is the potential to transfer the polarization from the gas to other nuclei such as protons[40]. Here, the spin polarization-induced nuclear Overhauser enhancement (SPINOE) can be used to transfer polarization from ^{129}Xe to protons and be detected in both proton spectra and images.

1.3 Low-Field MR Imaging

Whereas the nuclear polarization of conventional, thermally polarized nuclei is a linear function of magnetic field strength, the polarization of hyperpolarized nuclei

is not strongly dependent upon field strength, instead relying on other independent properties such as laser power and gas mixture. As a result, hyperpolarized MR experiments can be performed at considerably lower (~ 10 mT) magnetic field strengths than the average clinical MR imagers, which typically operate at 1.5 T.

Hyperpolarized noble gases provide exciting possibilities for performing MR imaging at low (< 100 G) fields. The benefits of low-field MR imaging are potentially numerous[60]. A low-field magnet would not require superconducting technology to maintain its field strength and could instead rely upon more conventional, inexpensive and feasible resistive or permanent magnet technology. Superconducting magnets are expensive, require regular maintenance, and cryogenic cooling for their operation. A low-field resistive magnet could be inexpensive, portable and not require the special accommodations of a high-field magnet. As well, the low-field strength results in a reduced operating, or Larmor, frequency (kHz) which would simplify the RF electronics and reduce power consumption. These lower frequencies also have large skin depths, allowing gas space imaging inside conductive materials. Finally, at low magnetic fields there is a reduced effect of magnetic susceptibility heterogeneity, resulting in reduced image distortion, line broadening, and longer T_2^* thereby improving noble gas image resolution.

Low-field MR imaging began with Packard and Varian[43] in 1954 with prepolarized MR imaging in the Earth's magnetic field (~ 0.5 G), a technique that starts with a sample of nuclei with a high polarization in a high-field strength which is then transferred to a receiver coil aligned with the Earth's field and sampled before the relaxation effects can take place. They applied a polarization pulse in a NMR experiment using a pulsed field of 100 G and, after turning off the polarizing field nonadiabatically, were able to record the received signal in the Earth's magnetic field, obtaining an SNR of 20. This allowed them to estimate the signal's frequency accurately enough to compute the local magnetic field to 1 part in 15000.

Also in 1954, Bloom and Mansir devised an experiment for measuring T_1 relaxation times at very low-fields[44]. After prepolarizing at 100 G, they depolarized the sample for a variable time τ at a field of about 2 G, and detected the received signal varying as $e^{-\tau/T_1}$. The freedom to customize polarization waveforms introduced the possibility to create images weighted with a rich spectrum of T_1 dispersion contrast.

Since Packard and Varian, considerable basic research has been done using the Earth's magnetic field. Béné[45] has been working in this area since 1949 and in 1977 published *in situ* T_1 dispersion results that discriminated between normal and pathological amniotic fluid. In 1980 he published an exhaustive overview paper[46]. Borcard has continued the T_1 dispersion investigation using an experiment similar to the one proposed by Bloom and Mansir. Koenig *et al* have used a similar experimental setup to measure protein and tissue T_1 dispersion curves[47][48]. In 1985, the biophysics group at Lyon made the first phantom NMR images[49][50] using the Earth's field. A similar approach was used to obtain images of pears and apples by Stepišnik *et al* at Ljubljana[51][52].

Other techniques move away from the use of the Earth's field as the static imaging field. Sepponen of Instrumentarium Corporation has patented an MRI system in which spins are left parallel to the z field after a polarizing field ramps down. The imaging process for this configuration proceeds as usual with RF pulses and gradients. Le Roux has also proposed a pulse-polarized MR system. Macovski proposed a perpendicular configuration that eliminates the need for an RF amplifier for volumetric imaging. Recently, Carlson *et al*[53] built a prepolarized MR imaging (PMRI) system by adding a 1200 G polarizing field to a Toshiba ACCESS 640 G imager. Carlson has also used this system to investigate T_1 dispersion behaviour in an imaging format using several shots with a stepped prepolarizing pulse[54][55].

Since Albert's[22] introduction of hyperpolarized noble gases to MR imaging, improvements at low-field have been made using these gases to circumvent the pre-

polarizing step described above. For example, Darasse *et al* recently demonstrated laser-polarized ^3He human lung imaging at 1000 G[56], while Saam and coworkers obtained one-dimensional profiles of cells filled with laser-polarized ^3He at 31 G[57]. In addition, using superconductive quantum interference devices (SQUIDS), Augustine *et al* imaged laser-polarized ^3He and solid ^{129}Xe at liquid helium temperatures (4K) and 5.4 G[58]. Most recently, Wong *et al* demonstrated fast, single-scan 2D imaging at 20.6 G of laser-polarized ^3He in sealed glass phantoms[59] and excised rat lungs[60]. Radiation damping measurements and the low-field imaging system used for these experiments were also described[60]. Finally, a low-field hyperpolarized ^{129}Xe image of a live rat lung was obtained by Yang *et al*[87] by lowering the field strength of a superconducting magnet to 0.015 T (150 G).

The development of a low-field MR imaging system based on hyperpolarized noble gases opens the door to a wide variety of new applications. Examples in the biomedical field include portable systems for diagnostic lung imaging for humans, and tabletop MR instruments for research in animals. Dissolved phase imaging studies, like those performed at high-field strengths, could also be investigated assuming a sufficient SNR is obtained. Furthermore, a low-field MR imager would be compatible with operation in restricted environments, such as on board a space station, and may permit lung imaging of patients with artificial transplants such as pacemakers[61].

In the physical sciences, low-field hyperpolarized noble gas MR imaging will be effective in imaging voids in two classes of materials that are problematic for high-field MR: (i) heterogeneous systems, such as porous and granular media, which distort high-field images because of large, solid-gas magnetic susceptibility gradients; and (ii) electrical conductors, which prevent high-field MR imaging by RF shielding. Also, low-field NMR measurements of the restricted diffusion of noble gas imbibed in porous media may provide an effective and practical study of fluid permeability in such media[62].

The result should be a smaller, more portable, and more cost-efficient imager which could become commonplace in hospitals and clinics where the more expensive superconducting systems could not be sited.

1.4 Overview

The purpose of the research described in this thesis was to compare SNR at 1.89 T with 85 G as a step towards the imaging of hyperpolarized ^{129}Xe at low-field. The thesis describes the design and construction details of a prototype NMR system for hyperpolarized ^{129}Xe as well as the experimental methodology for acquiring hyperpolarized ^{129}Xe gas signals. A sample ^{129}Xe cell was analyzed and its parameters (T_1 relaxation time, polarization level, flip angle calibration) determined. A theoretical and experimentally validated SNR comparison of the low-field system with a high-field superconducting system was performed.

Chapter 2

Theory

The theoretical background necessary for the understanding of the topics discussed in this thesis is presented in this chapter. The core topics include the fundamental theory of NMR, MR imaging, the laser polarization theory behind hyperpolarized noble gases, and specific modifications in the case of low-field hyperpolarized noble gas imaging.

2.1 Nuclear Magnetic Resonance

Fundamental nuclear magnetic resonance theory begins with a single nucleus and its behaviour in a static magnetic field. From here, large populations of nuclei are considered and the effects of RF pulses applied to those populations. Combined with the relaxation mechanisms of the nuclei, equations governing the behaviour of the net nuclear magnetic moment are formed and the signals received by a spectrometer are explained. NMR spectroscopy is also discussed in this section.

While NMR is a quantum mechanical phenomena, the classical description is sufficient for the purposes of the research involved in this thesis. Quantum mechanical concepts will be introduced only when necessary or when deemed helpful in the understanding of the material. For a rigorous quantum mechanical explanation of

NMR, see Slichter[63].

2.1.1 Nuclear Properties in a Static Magnetic Field

Nuclei possess the quantum mechanical property of nuclear spin, I , the value of which is dependent upon the intrinsic spin of the protons and neutrons that the nucleus is composed of. Nuclei with unpaired protons or neutrons have a net spin which is non-zero and can give rise to NMR. This property determines the different possible values of the total angular momentum, $\vec{J}$, by quantizing the z axial component and fixing the magnitude of the vector. The relationships are:

$$J = |\vec{J}| = \hbar \sqrt{I(I+1)} \quad (2.1)$$

$$J_z = \hbar m. \quad (2.2)$$

where J is the magnitude of the vector, J_z is the z component and $\hbar = h/2\pi$ where h is Planck's constant. The possible values of m are:

$$m = -I, -I+1, \dots, I-1, I. \quad (2.3)$$

where: $\Delta m = 1$.

Nuclei with $I \neq 0$ also possess a magnetic moment, $\vec{\mu}$, which is the result of the moving nuclear charge about the nucleus as well as the intrinsic magnetic moments of the nucleons. $\vec{\mu}$ can be expressed in terms of the angular momentum, $\vec{J}$, by:

$$\vec{\mu} = \gamma \vec{J}, \quad (2.4)$$

where: γ is the gyromagnetic ratio, defined as the ratio of the magnetic moment to the angular momentum and given as $e/2m$, the ratio of the electronic charge, e , to nuclear mass, m , and therefore is a constant specific to the nuclear species under investigation. Therefore, because of this proportionality and the discrete nature of

$\vec{J}$, $\vec{\mu}$ is quantized. For ^1H , $\gamma = 26.7510 \times 10^7 \text{ radT}^{-1}\text{s}^{-1}$ and for ^{129}Xe , $\gamma = 7.4003 \times 10^7 \text{ radT}^{-1}\text{s}^{-1}$.

In the presence of a static magnetic field, $\vec{B}_0$, the magnetic moment experiences a torque, $\vec{\tau}$:

$$\vec{\tau} = \frac{d\vec{J}}{dt} = \vec{\mu} \times \vec{B}_0. \quad (2.5)$$

Substituting from Eq. 2.4 this becomes:

$$\frac{d\vec{\mu}}{dt} = \gamma \vec{\mu} \times \vec{B}_0, \quad (2.6)$$

which is the equation of motion of $\vec{\mu}$ about $\vec{B}_0$ with solution:

$$\mu = \mu_0 e^{-i\omega_0 t}, \quad (2.7)$$

where:

$$\omega_0 = \gamma B_0. \quad (2.8)$$

Equation 2.8 is the well known Larmor equation and describes the precession of $\vec{\mu}$ about $\vec{B}_0$ as shown in Figure 2.1. When defined in units of cycles per second (Hz), ω_0 is referred to as the Larmor frequency, ν_0 :

$$\nu_0 = \frac{\omega_0}{2\pi} = \frac{\gamma}{2\pi} B_0; \quad (2.9)$$

e.g. for ^{129}Xe $\nu_0 = 22.16 \text{ MHz}$ at 1.89 T .

The interaction of $\vec{\mu}$ with $\vec{B}$ can be described by a Hamiltonian, $\mathcal{H}$:

$$\mathcal{H} = -\vec{\mu} \cdot \vec{B} = -\gamma \vec{J} \cdot \vec{B} \quad (2.10)$$

The dot product can also be represented as a scalar product of two components, one representing the total magnitude and the other representing a projected value. The allowed energies of the system with $\vec{B} = B_0 \hat{z}$ are therefore:

$$\mathcal{H} = -\gamma J_z B = E = -\gamma \hbar B_0 m. \quad (2.11)$$

Figure 2.1: A single nucleus in the presence of a static magnetic field, $\vec{B}_0$, has a magnetic moment, $\vec{\mu}$, that precess about $\vec{B}_0$ with frequency ω .

For $I = 1/2$ (the only case to be examined in this thesis), m can have only two possible values, referred to as spin-up ($m = +1/2$) and spin-down ($m = -1/2$), resulting in:

$$E = \pm \frac{\gamma \hbar B_0}{2}, \quad (2.12)$$

commonly referred to as a Zeeman splitting, illustrated in Figure 2.2. Electromagnetic radiation of frequency:

$$\nu_0 = \frac{\Delta E}{h} = \frac{\gamma}{2\pi} B_0 \quad (2.13)$$

is sufficient to induce a transition from the lower energy state to the higher one. On examination, Eq. 2.13 is the Larmor equation (Eq. 2.8), indicating that a resonance condition exists: nuclear magnetic resonance.

2.1.2 Bulk Magnetization

In the presence of $\vec{B}_0$, thermal energy provided to the nuclei by the lattice at a temperature, T (i.e. T_1 or spin lattice relaxation mechanisms), causes an excess of nuclei in the spin-up state ($n_{\uparrow}$), $m = +1/2$, compared to the spin-down state ($n_{\downarrow}$), $m = -1/2$. This sets up a population ratio of the spin-up to the spin-down nuclear

Figure 2.2: A Zeeman splitting of the nuclear energy levels.

states described by the Boltzman distribution and given by:

$$\frac{n_{\downarrow}}{n_{\uparrow}} = e^{-\Delta E/k_B T} = e^{-\hbar\omega_0/kT}, \quad (2.14)$$

where k is Boltzman's constant. This excess fraction of nuclei in the spin-up state, which can contribute to an NMR signal, is given by the polarization factor, P :

$$P = \frac{n_{\uparrow} - n_{\downarrow}}{n_{\uparrow} + n_{\downarrow}} = \frac{1 - e^{-\hbar\omega_0/kT}}{1 + e^{-\hbar\omega_0/kT}}. \quad (2.15)$$

The bulk magnetization, $\vec{M}$, is defined as the net dipole moment per unit volume and is proportional to the polarization factor and is illustrated in Figure 2.3. Classically, this can be described as the sum of the dipole moment vectors, both parallel and anti-parallel to $\vec{B}_0$. Each dipole moment, $\vec{\mu}$, will rotate about $\vec{B}_0$ at an angle θ . As the dipoles are out of phase with each other, only the net magnetic moment will give rise to $\vec{M}$, parallel to $\vec{B}_0$. The relationship between the two is:

$$\vec{M} = \chi \vec{B}_0, \quad (2.16)$$

where χ is the magnetic susceptibility of the sample.

Classically, the magnetization, $\vec{M}$, will experience a torque and precess about $\vec{B}_0$ in the same fashion as the individual dipoles (Eqs. 2.5-2.7). Its equation of motion

Figure 2.3: The net dipole moment, or bulk magnetization, $\vec{M}$, is parallel to the z axis because the individual dipoles are out of phase, reducing M_{xy} to zero.

is expressed similar to Eq. 2.6:

$$\frac{d\vec{M}}{dt} = \gamma \vec{M} \times \vec{B}_0. \quad (2.17)$$

At equilibrium, the magnitude of the magnetization, $\vec{M}_0$, for a sample containing $N = n_+ + n_-$ nuclei is expressed as[66]:

$$M_0 = \mu N P, \quad (2.18)$$

and is parallel to the static field, $\vec{B}_0$.

2.1.3 RF Pulses

As seen in Eq. 2.13, the resonant condition is met when the nuclei absorb energy at the Larmor frequency. For typical MR imaging, these frequencies are in the radiofrequency (RF) band (e.g.: 80.15 MHz at 1.89 T). In NMR, an RF pulse at the Larmor frequency is applied to a population of spins such that an electromagnetic

field, $\vec{B}_1$, with frequency, ω , is applied perpendicular to the static field, $\vec{B}_0$, and $\vec{M}$. The net magnetic field then becomes:

$$\vec{B}_{tot} = B_0 \hat{k} + B_1 (\sin(\omega t) \hat{i} + \cos(\omega t) \hat{j}). \quad (2.19)$$

$\vec{M}$ will now precess about $\vec{B}_{tot}$ rather than $\vec{B}_0$. This can be seen in the equation of motion:

$$\frac{d\vec{M}}{dt} = \gamma \vec{M} \times \vec{B}_{tot}. \quad (2.20)$$

Choosing a frame of reference rotating with the applied RF frequency, ω , simplifies the analysis of the behaviour of the magnetization. In this so-called rotating frame of reference, indicated by the primed axes in Fig. 2.4, the effective field strength becomes[66]:

$$\vec{B}_{eff} = \left(B_0 - \frac{\omega}{\gamma} \right) \hat{k} + B_1 \hat{i}. \quad (2.21)$$

For the case of on-resonance radiation ($\omega = \omega_0$), $\vec{B}_{eff} = \vec{B}_1$ and $\vec{M}$ will tip away from the z axis at a precessional frequency $\omega_1 = \gamma B_1$ in the rotating frame and will do so as long as the RF pulse is applied in a process called nutation. The tip angle that $\vec{M}$ nutates through, α , is a function of the amplitude, B_1 , and pulse duration, t_p . α is defined in radians by:

$$\alpha = \int_0^{t_p} \omega_1 dt = \gamma B_1 t_p \quad (2.22)$$

for a rectangular pulse.

M_z and M_{xy} can be expressed in terms of α simply by[66]:

$$M_z^+ = M_z^- \cos \alpha \quad (2.23)$$

$$M_{xy}^+ = M_{xy}^- \sin \alpha, \quad (2.24)$$

where $-$ and $+$ indicate before and after the RF pulse, respectively. Because the NMR receiver is situated in the xy plane, the received signal will be proportional to M_{xy} , the maximum value of which is obtained when $\alpha = 90^\circ$, as shown in Figure 2.4(a). For $\alpha = 180^\circ$, the magnetization is inverted, as shown in Figure 2.4(b).

Figure 2.4: A rotating frame representation of (a) a 90° pulse completely tipping the magnetization into the xy plane and (b) a 180° pulse inverting the magnetization.

2.1.4 Signal Acquisition

Detecting the occurrence of a magnetic resonance condition relies upon the principle of induction, i.e. that a changing magnetic field induces an electromotive force (EMF) in a loop of electrical conductor through which the field passes. Following the perturbation of the magnetization from its equilibrium state, $\vec{M}_{xy}$ will precess about $\vec{B}_0$ with angular frequency ω_0 producing an alternating magnetic field in a loop of wire, S , as in Figure 2.5(a). Intuitively, if $\vec{M}$ is close to S , the induced EMF will be large, whereas if the $\vec{M}$ is far away from S , the EMF will be small. Conversely, if a current is passed through S , as in Figure 2.5(b), it will generate a magnetic field, $\vec{B}_1$, that will be large close to the loop and smaller further away from the loop. There is a direct relationship between the EMF induced in loop S by a rotating moment, $\vec{M}\delta V_S$, where δV_S is the sample volume, at point P and the field $\vec{B}_1$ created by current flowing through loop S . Beginning with Faraday's Law of Induction[77]:

$$\xi_S = -\frac{\partial \Phi}{\partial t}, \quad (2.25)$$

where ξ_S is the induced EMF and defining the flux as: $\Phi = \vec{B}_1 \cdot \vec{M}$, where M is the magnetization per unit current, we can express quantitatively the above relationship

Figure 2.5: (a) The rotating magnetization $\vec{M}$ induces an EMF in loop S . (b) The signal from point P is proportional to the field $\vec{B}_1$ at that point. This is the Principle of Reciprocity.

using the Principle of Reciprocity:

$$\delta\xi_S = -\frac{\partial}{\partial t}\{\vec{B}_1 \cdot \vec{M}\}\delta V_S, \quad (2.26)$$

where $\delta\xi_S$ is the signal from a single dipole moment. Defining $\vec{M}$ as a vector with axial and planar components, we have from Eq. 2.7:

$$\vec{M} = \vec{M}_{xy}e^{-i(\omega_0 t + \sigma)} + \vec{M}_z, \quad (2.27)$$

where σ is the phase of the magnetization. It therefore follows that:

$$\delta\xi_S = -\frac{\partial}{\partial t}\{[\vec{B}_{1xy}e^{i\phi}] \cdot [\vec{M}_{xy}e^{-i(\omega_0 t + \sigma)} + \vec{M}_z]\}\delta V_S, \quad (2.28)$$

where ϕ is the phase of $\vec{B}_1$ with respect to $\vec{M}$. When evaluated and integrated over the sample, it can be shown[77] that:

$$\xi_S = \omega_0 B_{1xy} M_{xy} V_S e^{-i\omega_0 t}. \quad (2.29)$$

It should be noted that in the more general case, B_{1xy} , M_{xy} , σ and ϕ will all be functions of position. Taking $\vec{M}_{xy} = \vec{M}_0 \sin \alpha$ and recalling Eq. 2.18 and the Larmor relation (Eq. 2.8) we have:

$$\xi_S = \gamma B_0 B_{1xy} \mu N P \sin \alpha V_S e^{-i\omega_0 t} e^{-t/T_2^*}. \quad (2.30)$$

The last term in Eq. 2.30 describes the exponential decay of the signal due to transverse decay mechanisms (T_2^*), to be discussed in the following section. The signal equation has the form of an exponentially decaying sinusoid and is commonly referred to as a free induction decay, or FID. An example is provided in Figure 2.6.

Figure 2.6: A free induction decay, or FID, characterized by a sinusoidal offset frequency, $\nu = 500$ Hz, and an exponential decay constant, T_2^* .

The loop S is a simplified version of the RF coils used to induce $\vec{B}_1$ and detect $\vec{M}$. In practice, these coils may have varying geometry (solenoids, saddle-shape,

Helmholtz sets) and essentially act as tuned circuits that resonate at a specific frequency. Two variable capacitors, one in parallel and one in series with the circuit, control the resonant frequency of the tuned circuit. As the NMR signal voltage is on the order of a microvolt, any increase in signal amplitude is welcome. This can be done by using a high-power transmitter, thereby increasing B_1 , a high-gain and low-noise preamplifier, and a large sample volume.

Because the detector may not be exactly aligned with the magnetization in the xy plane, two orthogonal detectors (real and imaginary channels) are used to detect the M_x and M_y components of the magnetization, $\vec{M}$. The magnitude of this complex signal is then used as the signal amplitude. Detection in this manner is referred to as detection in quadrature.

The Signal-to-Noise Ratio

The signal-to-noise ratio (SNR) is a more meaningful figure of measurement than simply the signal strength. The SNR considers both the magnitude of the noise as well as the NMR signal. In order to quantify the SNR, noise must first be considered. While random noise resulting from spins undergoing Brownian motion is always present and important for large samples at high fields ($B_0 > 1$ T), the dominant noise source for sufficiently small samples at high fields and for nearly any sized sample at low fields is Johnson, or thermal noise from the receiver coils[77]. At temperature T [77]:

$$\xi_N = \sqrt{4kTR\Delta f}, \quad (2.31)$$

where ξ_N is the noise amplitude, R is the coil resistance and Δf is the noise bandwidth of the system, defined as the inverse of the sampling time ($1/T_s$), the time delay between data acquisitions. Taking the ratio of the signal (Eq. 2.30) and noise equations (Eq. 2.31) and looking at the maximum amplitude ($\alpha = 90^\circ$) we have for

the SNR at $t = 0$:

$$SNR = \frac{\gamma B_0 B_{1xy} \mu N P V_S}{\sqrt{4kTR\Delta f}}. \quad (2.32)$$

Here, the nucleus dependent parameters are γ and μ . The RF coil will determine both B_1 and R , while the data acquisition time (DAQ) will determine Δf . If we assume a specific number of spins, N , at a set volume, V_S , at a temperature T , the only remaining variable is the static field strength, B_0 , determined by the magnet coil windings and current.

By analyzing the relationship between the energy stored in the B_1 field, which is a measure of the coil inductance, and introducing the noise figure, F , to account for the noise introduced by the receiver, it can be shown[77] that, for a solenoid, the above expression is equivalent to:

$$SNR = K\eta M_0 \sqrt{\frac{\mu_0 Q \omega_0 V_c}{4FkT\Delta f}}, \quad (2.33)$$

where K is a numerical factor depending on the receiving coil geometry; η is the filling factor, i.e., the fraction of the coil volume occupied by the sample; μ_0 is the permeability of free space; and V_c is the volume of the coil. SNR improvements can therefore be made by using low noise, high gain preamplifiers to reduce the noise figure, and by improving the RF coil Q factor to increase signal amplitude. The use of RF shielding also improves SNR, as discussed in the next section.

The ratio of SNR between two experiments at two different field strengths can be calculated using the expression:

$$\frac{SNR_1}{SNR_2} = \frac{\eta_1 P_1}{\eta_2 P_2} \sqrt{\frac{(Q f_0 V_c / FT \Delta f)_1}{(Q f_0 V_c / FT \Delta f)_2}}, \quad (2.34)$$

where $K \sim 1$ in both cases and the ratio of M_0 's is reduced to a ratio of P factors.

RF Shielding

SNR can also be increased by reducing the extraneous noise from surrounding radiation sources (e.g.: computer monitors, powers supplies, etc.) through the use of RF shielding. The effect of encasing the RF coil in an electrically conductive material of thickness t , such as Al, Sn, or Cu, is the exponential attenuation of the RF signals passing through the shield by a factor $e^{-t/d}$. The coefficient d is the skin depth of the shielding material, that is the distance required to attenuate the signal by a factor e^{-1} . The skin depth will depend upon the frequency, ω , of the signals as well as the permeability, μ , and conductivity, σ , of the shielding material. For a good conductor ($\sigma \gg \omega\mu$), the relation is[65]:

$$d = \frac{2}{\sqrt{\omega\sigma\mu}}. \quad (2.35)$$

For aluminum at 22 MHz, $\sigma = 2.8 \times 10^{-8} \Omega^{-1}\text{m}^{-1}$ and $\mu = 1.3 \times 10^{-6} \text{ N/A}^2$ resulting in a skin depth of $1.8 \times 10^{-5} \text{ m}$.

From Eq. 2.35 we see that at lower frequencies noise will be harder to attenuate and will have larger skin depths (e.g. $d = 2.7 \times 10^{-4} \text{ m}$ at 100 kHz). Conversely, penetration of RF will be much better at lower frequencies perhaps allowing imaging of conductive objects (e.g.: metals) not possible at high frequencies.

2.1.5 Other Factors Affecting NMR Signal

After the nuclear system has been disturbed from its equilibrium by an RF pulse, the system will begin to relax to its equilibrium state (i.e. $M_z = M_0$ and $M_{xy} = 0$) via certain relaxation mechanisms specific to the nucleus under investigation. Two variables characterizing these relaxation mechanisms are the spin-lattice, or longitudinal relaxation time, T_1 , and the spin-spin, or transverse relaxation time, T_2 . T_1 governs the axial component of the magnetization, M_z , returning to thermal equilibrium, while T_2 deals with the dephasing of the spins in the transverse plane

and the exponential decay of M_{xy} as it precesses about B_0 . For a rigorous treatise on relaxation effects see Abragam[86] or Slichter[63].

Spin-Lattice Relaxation Time, T_1

Generally speaking, a spin relaxes by a component of local magnetic field within the relaxing frame. A nucleus experiences a fluctuating local magnetic field created by its own motion and that of neighboring magnetic moments, usually dipole moments from electrons and nuclei. This local field, $\vec{B}_{loc}$, has components parallel to and perpendicular to $\vec{B}_0$. The perpendicular component, when oscillating at the Larmor frequency, induces transitions between energy states, relaxing M_z at a rate:

$$\frac{1}{T_1} \approx B_{loc}^2 J(\omega), \quad (2.36)$$

where $J(\omega)$ is the spectral density function, a frequency distribution of the possible frequencies that B_{loc} may have.

The probability of inducing transitions is dependent upon the amplitude of $J(\omega)$ at the resonant frequency of the nucleus in question. The spectral density function is the Fourier transform of the autocorrelation function, $G(t)$, approximated by:

$$G(t) \approx e^{-t/\tau_c}, \quad (2.37)$$

where τ_c is the correlation time constant for reorientation of the neighboring dipole moments, typically determined by inertial and viscosity effects. $G(t)$ expresses the probability that a magnetic dipole source will have the same magnitude that it had at $t = 0$ at some later time t , at the position of the relaxing nucleus. $J(\omega)$ can therefore be expressed as a Lorentzian function:

$$J(\omega) = \mathcal{F}\{G(t)\} \approx \frac{\tau_c}{1 + \omega^2 \tau_c^2}. \quad (2.38)$$

The shape of $J(\omega)$ depends on nuclear and molecular tumbling rates. An example is provided in Figure 2.7.

Figure 2.7: Hypothetical spectral density function for different τ_c . Different correlation times, τ_c , corresponding to the nature of the sample (solid, liquid, gas) influence the shape of the curve.

From Eqs. 2.36 and 2.38 it can be seen that T_1 is dependent on ω . This results in a dependence on B_0 , due to the Larmor relation, and on temperature, T , as molecular and atomic frequencies are dependent on the thermal contribution to their kinetic energy, $\frac{3}{2}kT$.

The dominant T_1 relaxation mechanisms include: dipole-dipole interactions, generally the most important mechanism for spin 1/2 nuclei, where the nucleus experiences a fluctuating field due to the motion of neighboring magnetic dipoles, from other nuclei or unpaired electrons; chemical shift anisotropy, where the chemical shielding of the nucleus depends on the orientation of the molecule with respect to the direction of $\vec{B}_0$; and spin-rotation interaction, where local fields are induced as

a result of the moving charges of electrons and nuclei which arise from a rotating molecule.

A large B_{loc} combined with $\omega_0 \approx \tau_c^{-1}$ are conditions for efficient T_1 relaxation. Its time dependence can be expressed as[66]:

$$\frac{dM_z}{dt} = \frac{M_0 - M_z}{T_1}, \quad (2.39)$$

with solution:

$$M_z = M_0(1 - e^{-t/T_1}), \quad (2.40)$$

where it can be shown that with increasing time, M_z approaches the thermal equilibrium value M_0 .

Spin-Spin Relaxation Time, T_2

Following an RF pulse, the magnetization is either partially or wholly tipped into the transverse plane depending on the tip angle, α (Eq. 2.24), creating a transverse magnetization component, M_{xy} . This component precesses about the z axis at the Larmor frequency. However, because of the slightly differing local magnetic field strengths about each of the spins, each spin will precess at a slightly different frequency than the rest. These local variations in the field are the result of the same fluctuating magnetic field that gives rise to T_1 relaxation. The component of $\vec{B}_{loc}$ parallel to $\vec{B}_0$ alters the field strength that a nucleus experiences and therefore alters its precessional frequency. This results in a gradual dephasing of the individual nuclei and a decay of M_{xy} characterized by the relaxation constant T_2 :

$$\frac{1}{T_2} \approx \frac{1}{2T_1} + B_{loc}^2 J(0) + \text{other}, \quad (2.41)$$

where it can be seen that T_2 also depends on the spectral density function at zero frequency since the components of B_{loc} parallel to $\vec{B}_0$, and not rotating in the laboratory frame of reference, can affect M_{xy} . As it includes T_1 , T_2 will also be susceptible

to T_1 mechanisms and the temperature and field strength dependence that characterize T_1 , as described previously. The T_1 term indicates that half of the local field available for relaxation can affect the transverse component, compared to the longitudinal component. In addition, the second term in Eq. 2.41 is quite large (Fig. 2.7) for solids ($T_2 \ll T_1$) and typically dominates, but is small for viscous liquids and quite small for non-viscous liquids as B_{loc} decreases resulting in $T_2 \approx T_1$. The third term in Eq. 2.41 includes time dependent effects such as diffusion and chemical exchange.

The equation of motion of M_{xy} is given by[66]:

$$\frac{dM_{xy}}{dt} = -\frac{M_{xy}}{T_2} \quad (2.42)$$

in the rotating frame of reference with solution:

$$M_{xy}(t) = M_{xy}(0)e^{-t/T_2}. \quad (2.43)$$

Further transverse relaxation mechanisms include dephasing due to inhomogeneities in the static magnetic field, ΔB_0 , magnetic susceptibility, χ , and chemical shift, δ . This results in a faster decay rate with an effective decay constant, $T_2^* < T_2$, where:

$$\frac{1}{T_2^*} = \frac{1}{T_2} + \left(\frac{1}{T_2^{\Delta B}} + \frac{1}{T_2^{\chi}} + \frac{1}{T_2^{\delta}} \right). \quad (2.44)$$

As these additional dephasing contributions to T_2 are not time dependent, they can be refocused with a spin echo. An example of T_2^* vs. T_2 decay is shown in Figure 2.6.

Spin Echoes

Spin echoes are created when the dephasing of the transverse magnetization is partially refocused, as shown in Figure 2.8. As previously discussed, M_{xy} decays according to an effective relaxation constant, T_2^* , rather than T_2 (Fig. 2.6). A spin

echo utilizes a 180° pulse applied after the spins have been tipped into the transverse plane via a 90° pulse. The 180° pulse is typically applied along the transverse axis orthogonal to the 90° pulse so that the dephased spins will rephase. The echo time occurs at time TE , where $TE/2$ is the time between the initial 180° and the 90° pulse. In this case, the e^{-t/T_2} term in Eq. 2.30 can be replaced by:

$$\xi_S(0 < t < TE/2) \propto M_{xy} \sin \alpha e^{-t/T_2} e^{-t/T_{2f}}, \quad (2.45)$$

where $1/T_{2f}$ is the sum of the refocused terms in Eq. 2.44. At $t = TE/2$, the spins are flipped within the xy plane and begin to rephase:

$$\xi_S(TE/2 < t < TE) \propto M_{xy} \sin \alpha e^{-t/T_2} e^{-|t-TE|/T_{2f}}, \quad (2.46)$$

and at $t = TE$ we find that:

$$\xi_S(t = TE) \propto M_{xy} \sin \alpha e^{-TE/T_2}. \quad (2.47)$$

Note that in Eq. 2.47 the signal decay is governed only by T_2 .

Radiation Damping

As previously discussed, the transverse component of magnetization, M_{xy} , will precess about the z axis inducing a current into the receiver coil which is detected as the free induction decay. However, if this current is sufficiently large (i.e. M_{xy} is large) it will create its own magnetic field which will interact with the surrounding spin system, producing a torque on the magnetization which will cause $\vec{M}$ to rotate back towards the z axis and hence reduce signal (a consequence of the Principle of Reciprocity). This rotation is referred to as radiation damping. It is a dynamic process resulting from the interaction between $\vec{M}$ and the FID current. For a more descriptive discussion, see Mao and Ye[64].

Figure 2.8: Effect of a spin echo on the magnetization in the transverse plane: (a) the dipoles are tipped into the xy plane all pointing in the same direction; (b) the dipoles begin to dephase with T_2^* ; (c) further dephasing of the spins; (d) a transverse 180° pulse is applied at $t = TE/2$ flipping the spins 180° out of phase; (e) the spins continue to precess resulting in a rephasing; (f) complete T_2^* rephasing at $t = TE$. M_{xy} has decayed by e^{-TE/T_2} at $t = TE$.

Radiation damping resembles nutation. Both are rotations of the magnetization induced by the coil-magnetization interaction. However, there are differences. Nutation is induced by an external RF pulse and is described as a uniform rotation by:

$$\gamma B_1 = \omega_1, \quad (2.48)$$

whereas radiation damping is a nonuniform rotation expressed as:

$$\gamma B_{rd} = -\frac{\sin \alpha}{T_{rd}}, \quad (2.49)$$

where T_{rd} is the radiation damping constant given by[64]:

$$T_{rd} = \frac{1}{2\pi\eta\gamma QM}, \quad (2.50)$$

where η is the filling factor and Q is the quality factor of the RF coil. Because radiation damping is inversely proportional to the magnetization, it is generally not important in most NMR applications except at high fields where liquid-phase thermal magnetization is large. However, it may also be observed when hyperpolarized magnetizations are used[60], as will be discussed further in this thesis. Radiation damping is characterized by a time dependence which is a hyperbolic secant function of the form[64]:

$$M_{xy} = M_0 \text{sech} \left[\frac{t}{T_{rd}} - \ln \left(\tan \frac{\alpha}{2} \right) \right] e^{-i\Delta\omega t}, \quad (2.51)$$

where M_0 is the initial value of the magnetization and $\Delta\omega$ is the offset frequency from resonance. For $\alpha > 90^\circ$ this model of the signal will show an initially increasing FID amplitude before it decays. For large T_{rd} , this relation reduces to:

$$M_{xy} = M_0 \sin \alpha e^{-i\Delta\omega t}. \quad (2.52)$$

Therefore, radiation damping will be present depending on the relative values of T_{rd} and T_2^* , and can be detected by the presence of an initially increasing FID. Figure 2.9 models Eq. 2.51 (without the exponential offset term) and illustrates how, for increasing T_{rd} , this function simplifies to a sinusoidal function.

For $T_{rd} \gg T_2^*$, it can be shown[64] that the intensity of the signal, here defined as the time integral of the FID for $0 < t < \infty$, will be a sinusoidal function of the flip angle:

$$I = \int_0^\infty M_0 \sin \alpha e^{-t/T_2^*} dt = M_0 T_2^* \sin \alpha. \quad (2.53)$$

But for $T_2^* \gg T_{rd}$, this relation breaks down and is replaced by a linear one, derived in the same manner as Eq. 2.52 but integrating instead Eq. 2.51. The calculation

Figure 2.9: Eq. 2.52 for increasing T_{rd} as a function of (a) flip angle, α , using a fixed time, $t=1$ s, and (b) time, t , using a fixed flip angle, $\alpha = 130^\circ$. As T_{rd} increases, and radiation damping decreases, the sech function simplifies to a sinusoidal one, as indicated by the sine wave (solid line), $\sin \alpha$, in (a) and the constant value, $\sin(130^\circ) = 0.766$, in (b).

is straightforward by letting $x = t/T_{rd} - \ln[\tan(\alpha/2)]$:

$$I = \int_0^\infty M_0 \text{sech} \left[\frac{t}{T_{rd}} - \ln \left(\tan \frac{\alpha}{2} \right) \right] dt = M_0 T_{rd} \int_{-\ln[\tan(\alpha/2)]}^\infty \text{sech} x dx = M_0 T_{rd} \alpha. \quad (2.54)$$

Since Eq. 2.54 is fundamentally different from Eq. 2.53, radiation damping is important to consider when calibrating α and measuring SNR. The final expression for the signal in a NMR experiment involving radiation damping is:

$$SNR = K \eta M_0 \sqrt{\frac{\mu_0 Q \omega_0 V_c}{4 F k T \Delta f}} \text{sech} \left[\frac{t}{T_{rd}} - \ln \left(\tan \frac{\alpha}{2} \right) \right] e^{-i \Delta \omega t} e^{-t/T_2^*}. \quad (2.55)$$

NMR Spectroscopy

NMR spectroscopy exploits the change in local magnetic field seen by a nucleus due to its environment[84]. In the presence of a static magnetic field, B , a substance with no unpaired electrons (e.g. water, ^{129}Xe , etc.) exhibits diamagnetism, where currents in the electron clouds induced by the application of the magnetic field oppose that field. The electronic shielding characteristic of diamagnetism results in a nucleus seeing an effective magnetic field strength $B(1 - \sigma)$ where σ is the shielding constant, dependent on the electron cloud. Therefore, two identical nuclei placed in different electron clouds (e.g. molecules) will have two different resonant frequencies. NMR provides a precise measure of these resonant frequencies, or chemical shifts, δ , of a sample, giving information about the molecular environment.

In an NMR spectroscopy experiment, a pulse is applied with a carrier frequency ω for a duration t_p . This is referred to as a “hard” or square pulse. The bandwidth of the frequencies irradiated is $1/t_p$ and the frequency resolution of the received signal is defined as the sampling rate of the analog-digital converter (ADC) acquiring the data, S_R . Typical values for t_p and S_R are $50 \mu\text{s}$ and 10000 Hz , respectively. The received signals are then Fourier transformed to separate the complex superimposed frequencies that the FID is comprised of. For each δ the Fourier transform shows a series of typically Lorentzian-shaped peaks as a function of frequency, expressed as:

$$F(\omega) = \frac{T_2^{*2}}{1 + (\omega - \omega_0)^2 T_2^{*2}}. \quad (2.56)$$

where the relationship between the full spectral width at half the maximum signal intensity (FWHM) and T_2^* is:

$$FWHM = \frac{1}{\pi T_2^*}. \quad (2.57)$$

Typically, spectral intensity is plotted against chemical shift, not frequency. The chemical shift, δ , is defined as the relative deviation in frequency from a reference

frequency, ω_{ref} , provided by a known standard (e.g. a gas phase xenon signal).

$$\delta = \frac{\omega - \omega_{ref}}{\omega_{ref}} \times 10^6 = \frac{\sigma_{ref} - \sigma}{1 - \sigma_{ref}} \times 10^6. \quad (2.58)$$

The units of chemical shift are parts per million (ppm). The advantage of using δ over frequency for the abscissa is that δ is independent of field strength, allowing comparisons of experiments from different spectrometers and magnets. Chemical shift can also be defined according to the shielding factor, σ , using a reference shielding factor, σ_{ref} .

2.2 Laser Polarization of Noble Gases

As discussed, the nuclear spin may be polarized by spin lattice relaxation at room temperature giving $P \sim 10^{-6}$ (Eq. 2.15). Laser polarization techniques can be used to increase P by up to five orders of magnitude, with respect to the thermal polarization. While a number of laser polarization techniques exist, the one used throughout this project was spin-exchange with optically pumped alkali vapour, in this case rubidium (Rb). A more rigorous, quantum mechanical treatment of spin exchange with optical pumping can be found in papers by Happer[20] and Walker[67].

2.2.1 Optical Pumping

The first step in the polarization process is the optical pumping of the sample cell. Sample cells typically contain an alkali metal vapour (Rb, 88°C), a noble gas (^{129}Xe), and a quenching gas (typically N_2). Optical pumping is a technique used to repopulate a distribution of electronic spins, favouring one of the two possible spin states for the 2S orbital electron of Rb as shown in Figure 2.10. The two spin states are a result of the Zeeman splitting induced by a static magnetic field, B_0 . Laser light is applied at the transitional frequency, 794.8 nm, to excite electrons from the 2S to the 2P state. As photons carry one quantum of angular momentum, $\hbar$, the

Figure 2.10: Energy level diagram for Rb illustrating the optical pumping of electron transitions in accordance with the selection rule $\Delta m = 1$.

change in the energy states will be from the $^2S_{1/2}$ ($m = -1/2$) state to the $^2P_{1/2}$ ($m = +1/2$) state, obeying the $\Delta m = 1$ selection rule. Collisions with the noble gas in the sample will redistribute the spin states between the $^2P_{1/2}$ ($m = +1/2$) state and the $^2P_{1/2}$ ($m = -1/2$) state. Further collisions with the N_2 gas will relax the alkali electrons to their $^2S_{1/2}$ ground state. This results in a net increase in the $^2S_{1/2}$ ($m = +1/2$) population relative to the ($m = -1/2$) population. Some of the mechanisms involved in the destruction of the optically pumped spin distribution include Rb-Rb collisions, radiation trapping, and wall relaxation.

Radiation trapping occurs as a result of the de-excitation of the Rb spins. When light is emitted from a $^2P_{1/2}$ spin, it will interact with several other spins in the sample before exiting the cell. This results in the fluorescence of $^2S_{1/2}$ ($m = +1/2$) spins thereby reducing the population of the optically pumped spins. This effect is eliminated by the presence of a quenching gas, such as N_2 . Collisions with N_2 result in the de-excitation of Rb without the emission of light thus maintaining the highly

polarized state of the Rb vapour.

Wall relaxation occurs when Rb spins diffuse towards the sample cell walls before interacting with ^{129}Xe . Upon contact, the spins completely depolarize. Diffusion towards the laser beam window of the cell, and subsequent depolarization of the spins, effectively reduces the penetration depth of the beam. Therefore the beam requires a penetration depth greater than the mean diffusion length of the gas. This can be accomplished by reducing the Rb vapour pressure, slightly detuning the laser, or using a beam with a broader bandwidth.

The Rb polarization rate, defined as $\Gamma/2$, depends on beam power, Rb vapour pressure and temperature. Typical polarization times for Rb are on the order of milliseconds. N_2 has a third role: pressure broadening. This increases the Rb linewidth so that it more closely matches that of the laser. This can also be accomplished using helium, as in this thesis.

2.2.2 Spin Exchange

The next step involves exchange of spin (or angular momentum) between the Rb electrons and the ^{129}Xe nuclei, as illustrated in Figure 2.11. Spin exchange occurs as a result of the collisions between excited Rb atoms and ^{129}Xe gas atoms. The interaction is an interatomic hyperfine scalar coupling that results in the temporary formation of a Van der Waals molecule. During the lifetime of the molecule, the electronic Rb spin is transferred to the nuclear ^{129}Xe gas spin. The creation of these molecules is partially dependent on the presence of N_2 , which acts as a third body to provide a greater probability of formation.

2.2.3 Polarization Factor

Once polarized, the ^{129}Xe gas will reach an optimum polarization value, P , dependent on the optical pumping rate, $1/T_p$, and the relaxation rate, $1/T_1$. The pumping rate

Figure 2.11: Van der Waals molecule formation through ^{129}Xe -Rb collisions. Spin exchange occurs when the molecule separates back into Rb and ^{129}Xe . N_2 is used to increase the exchange efficiency.

is expressed as a function of the number of polarized Rb atoms, and the spin exchange probability:

$$\frac{1}{T_p} = \frac{\Gamma}{2} [\text{Rb}] \bar{v} \sigma_{\text{Xe}}, \quad (2.59)$$

where $[\text{Rb}]$ is the Rb concentration, $\bar{v}$ is the mean relative velocity between the xenon and the Rb and σ_{Xe} is the xenon gas spin exchange cross-section[68]. The overall time dependence of the polarization is given by:

$$\frac{dP}{dt} = \frac{1}{T_p} - \frac{P}{T_1}, \quad (2.60)$$

with solution:

$$P = \frac{T_1}{T_p} (1 - e^{-t_{HP}/T_1}), \quad (2.61)$$

where t_{HP} is the polarization time of the laser. Taking the limit with $t_{HP} \rightarrow \infty$ the maximum achievable polarization is[69]:

$$P = \frac{T_1}{T_p}. \quad (2.62)$$

Typical values are in the range of a few percent (as opposed to $\sim 10^{-4}\%$ for thermally polarized nuclei) and are as high as 70%[83].

2.2.4 Relaxation Mechanisms

Relaxation mechanisms have already been described in Section 2.1.5. They are described as originating with couplings between magnetic dipoles. Because ^{129}Xe is a monatomic inert gas, couplings of this nature are very weak except during collisions with other atoms and the sample cell wall. As a result, care must be taken in the cleaning of sample cells so as not to contaminate the ^{129}Xe with impurities, such as oxygen, and the inside of the cells are coated with Surfrasil, an organosilicon compound used to negate the effects of the ^{129}Xe colliding with the cell walls. Also of particular importance is relaxation due to collisions with paramagnetic nuclei, such as molecular oxygen. The coupling with the unpaired electronic dipole moment of paramagnetic oxygen, which is three orders of magnitude greater than the nuclear moment, will greatly enhance the relaxation of the nuclei. Therefore, cells need to be free of O_2 , which will also react with the rubidium vapour to form a rubidium oxide. Typical T_1 values are in the range of 30-60 minutes for gaseous ^{129}Xe in glass sample cells and in the range of 2-3 minutes in the dissolved phase[79]. This is due to the presence of additional dipole moments in the dissolved state (i.e. water, dissolved O_2 , etc.).

T_1 Estimation

Following laser polarization, ^{129}Xe nuclei will collectively form a magnetization, M'_0 , due to the increased polarization, P , up to five orders of magnitude greater than the thermal value, M_0 :

$$M'_0 \gg M_0. \quad (2.63)$$

As a result of the polarization level not being in an equilibrium state, two important differences between thermally and hyperpolarized MR arise. First, the axial component of M'_0 will immediately begin to decay exponentially to M_0 with relaxation time, T_1 . Therefore there is a time constraint regarding the use of the gas and experiments must be carried out within a time short relative to T_1 ($T_R \leq 3T_1$). Second, as the magnetization will be decaying, it will also be non-replenishable after an RF pulse. A pulse with tip angle α will reduce M_0 by a factor $(1 - \cos \alpha)$. Therefore, small tip angles ($\alpha \sim 5^\circ$) must be used in order to conserve the magnetization. Figure 2.12 illustrates the differences between thermal and hyperpolarized T_1 relaxation behaviours.

Look and Locker proposed a one shot method of estimating T_1 using a train of RF pulses at a constant, small tip angle, α , separated by a constant repetition time, T_R [70], ideal for hyperpolarized ^{129}Xe . Following their notation, M_n^+ and M_n^- are the longitudinal magnetization just before and after the n th RF pulse of tip angle α_n , respectively. Taking into account the magnetization decay of ^{129}Xe :

$$M_n^+ = M_n^- \cos \alpha_n \quad (2.64)$$

$$M_{n+1}^- = M_n^+ e^{-T_R/T_1}, \quad (2.65)$$

which, when combined, yield:

$$M_{n+1}^- = M_n^- \cos \alpha_n e^{-T_R/T_1}. \quad (2.66)$$

Figure 2.12: (a) Conventional T_1 recovery for thermally polarized nuclei. The nuclei will recover to the M_0 value. (b) T_1 relaxation for hyperpolarized nuclei. The nuclei will decay exponentially to $M_0 \sim 0$ from the initial value M'_0 .

The recursive relation will thus be:

$$M_{n+1}^- = M'_0 \prod_{i=0}^n (\cos \alpha_i) e^{-(n+1)T_R/T_1}, \quad (2.67)$$

where, again, M'_0 is the initial value of the hyperpolarized magnetization. If all of the tip angles are the same then this simplifies to:

$$M_{n+1}^- = M'_0 (\cos \alpha)^{n+1} e^{-(n+1)T_R/T_1}. \quad (2.68)$$

This relation can be further compacted for purposes of modeling by realizing that the $(n+1)$ th pulse takes place at a time $t = (n+1)T_R$. Therefore, the relation can

be written as:

$$M_{n+1}^- = M_0' (\cos \alpha)^{t/T_R} e^{-t/T_1}, \quad (2.69)$$

or:

$$M_{n+1}^- = M_0' e^{-t/T_{1eff}}, \quad (2.70)$$

where:

$$\frac{1}{T_{1eff}} = \frac{1}{T_1} - \frac{\ln(\cos \alpha)}{T_R}. \quad (2.71)$$

In the limit $T_R \ll T_1$, α may be estimated, whereas in the limit $T_R \gg T_1$, T_1 may be estimated.

Patyal[75] proposed a technique for measuring hyperpolarized ^{129}Xe T_1 based on the Look-Locker method. The ratio of successive signal intensities, S , from a train of RF pulses separated by a constant repetition time, T_R , can be given by:

$$\frac{S_n}{S_{n-1}} = \cos \alpha e^{-T_R/T_1}. \quad (2.72)$$

As T_R is constant, the signal ratios will be equal. Taking the mean of these ratios and by setting the repetition time $T_R \ll T_1$, thereby approximating the exponential in Eq. 2.72 to unity, the flip angle can be calculated according to:

$$\alpha = \cos^{-1} \left(\frac{1}{N} \sum_{n=1}^N \frac{S_n}{S_{n-1}} \right). \quad (2.73)$$

Variable Flip Angle Sequences

Based upon Eqs. 2.67 and 2.68, the signal equations for constant (CFA) and variable (VFA) flip angles can be written as:

$$(S_{n+1})_{VFA} = M_0' \sin \alpha_{n+1} \prod_{i=0}^n (\cos \alpha_i) e^{-(n+1)T_R/T_1} \quad (2.74)$$

$$(S_{n+1})_{CFA} = M_0' \sin \alpha (\cos \alpha)^{n+1} e^{-(n+1)T_R/T_1}. \quad (2.75)$$

Due to the non-replenishable nature of hyperpolarized ^{129}Xe , a series of constant flip angles leads to a diminishing signal over time. A sequence of variable flip angles can be designed such that the measured signal remains a constant over the time, which will allow for signal averaging. By forcing the measured signals to be constant for a total of N RF pulses, and using a 90° pulse at the end of the sequence to employ all of the remaining magnetization, the VFA sequence will be[79]:

$$\alpha_n = \tan^{-1} \left(\frac{e^{-(N-n)T_R/T_1}}{\sqrt{N-n}} \right). \quad (2.76)$$

T_2 Estimation

T_2 relaxation is measured using a Carr-Purcell (CP) pulse sequence for both thermally and hyperpolarized nuclei. Spin echos, introduced in Section 2.1.5, described the refocusing of T_2^* dependent variables to obtain an echo which has decayed only with T_2 . CP employs the same principles as the spin echo sequence (Fig. 2.8) where a train of 180° pulses are applied following the initial 90° pulse. The sequence can be represented by:

$$90 - \tau - 180 - \tau - \text{echo} - \tau - 180 - \tau - \text{echo} \dots$$

where: $TE = 2\tau + t_p(180^\circ)$, $t_p(180^\circ)$ being the pulse duration. This is illustrated in Figure 2.13.

The diffusion contribution to measured T_2 via CP is given by[66]:

$$\frac{1}{T_{2diff}} = \frac{D\gamma^2 G^2 \tau^2}{3}, \quad (2.77)$$

where D is the diffusion coefficient, G is the average static field gradient, τ is one half the echo time for CP and γ is the gyromagnetic ratio. The diffusion contribution introduces a dependence on magnetic field strength which arises from the G^2 term:

$$\frac{1}{T_{2diff}} \propto G^2 \approx (\Delta B_0)^2 \approx (B_0 \Delta\chi)^2, \quad (2.78)$$

Figure 2.13: A spin echo sequence. The signal decays and grows again with relaxation time T_2^* due to the refocusing 180° pulse. The refocussed echo has decayed according to T_2 .

where $\Delta\chi$ is the magnetic susceptibility inhomogeneity. Defining the calculated value as an effective value, T_{2eff} we have:

$$\frac{1}{T_{2eff}} = \frac{1}{T_2} + \frac{D\gamma^2 G^2 \tau^2}{3}. \quad (2.79)$$

Therefore, by measuring T_{2eff} twice, using the same settings and varying only the echo time, TE ($\tau=TE/2$), the actual T_2 can be calculated by solving for T_2 from the two equations.

2.3 Magnetic Resonance Imaging of Hyperpolarized ^{129}Xe

Magnetic resonance imaging is a spatially-localised version of NMR used to obtain 2D images of objects through the use of magnetic gradient coils. By varying the magnetic field strength in all three spatial dimensions, the density of spins (and T_1 and T_2) of an object can be mapped as a function of position. This section will describe the most popular MR method, the 2D spin-echo imaging sequence, as an example, and is shown in Figure 2.14. A more in-depth discussion of MR imaging principles can be found in Haacke[66].

2.3.1 Slice Selection

The first step in the spatial localization of a three dimensional sample of spins is the slice selection of the sample. Through the use of a gradient magnetic field coil, which alters the field strength as a function of position within the magnet, the field strength along the z axis varies linearly with z . This can be seen with the relation:

$$B(z)\hat{z} = B_0\hat{z} + G_z z\hat{z}. \quad (2.80)$$

where G_z is the axial gradient magnetic field strength in G/cm expressed as:

$$G_z = \frac{\Delta B}{\Delta z}. \quad (2.81)$$

Typically $G_z \sim 1$ G/cm.

In order to induce a resonance condition in the spins in a slice of thickness Δz the transmitted RF pulse must have a bandwidth $\Delta\omega$, where:

$$\Delta\omega = \gamma\Delta B = \gamma G_z \Delta z. \quad (2.82)$$

Such a bandwidth can be excited by applying a “soft” RF pulse with frequency ω and duration $1/\Delta\omega$. In MR terminology, a soft pulse usually means a sinc-modulated

RF pulse with a Fourier transform clearly showing a frequency range $\omega \pm \Delta\omega/2$. By applying a soft pulse with this bandwidth, the spins in a slice of the sample of thickness Δz are tipped and the resultant signals analyzed. By changing the frequency of interest, ω , different slices can be selected to form a 3D map of the sample. This is called multislice MR imaging.

2.3.2 Frequency Encoding

The second step in the spatial localization of the sample is the frequency encoding of spins along the x axis in the xy plane containing the selected slice. This encoding is accomplished by using a gradient field, G_x , aligned along the z axis but varying in magnitude as a function of x , that alters the magnitude of B but not its direction:

$$B(x)\hat{z} = B_0\hat{z} + G_x x\hat{z}. \quad (2.83)$$

This gradient is applied during the read-out of the signal, coincident with the formation of a spin echo ($t = TE$), as shown in Figure 2.14. The gradient alters the resonant frequencies of the spins as a function of x so that the signal is a superposition of all the frequencies. When Fourier transformed, this provides a spatial distribution of the spins along the x axis. The field of view, FOV , provided along the x axis is:

$$(FOV)_x = \frac{2\pi}{\gamma G_x \Delta t}, \quad (2.84)$$

where Δt is the sampling or dwell time. The read-out time, T_x , is given by:

$$T_x = N_x \Delta t, \quad (2.85)$$

where N_x is the number of sample points.

2.3.3 Phase Encoding

The third and final step in the spatial localization of the sample is the phase encoding of the spins. This gradient, G_y , is applied along the y axis for a duration τ , between

the end of the excitation RF pulse and the beginning of the read-out, as shown in Figure 2.14. While this gradient is active, nuclei located at different y locations will have different precessional frequencies and will acquire a phase that is dependent upon their y position. When the gradient is deactivated, the spins will all precess with the same frequency but will retain their y -dependent phase. This takes the encoding one step further, making the detected signal a superposition of frequencies with different phases along the y direction. For a given G_y this signal corresponds to a single line in the Fourier space of the sample.

Obtaining a two-dimensional image of the sample requires that the process of slice selection, phase-encoding, and reading-out with a frequency-encoding gradient repeated N_y times with an incremental ΔG_y and a repetition time, T_R , to yield an $N_x \times N_y$ data set which is subsequently Fourier transformed in 2D to give an image. The resultant field of view along the y axis is:

$$(FOV)_y = \frac{2\pi}{\gamma \Delta G_y T_y}. \quad (2.86)$$

Gradient Echoes

When a magnetic field gradient is applied during an imaging sequence, the transverse magnetization is dephased by an amount⁴ dependent on the strength, G , and the duration, τ , of the gradient. For phase-encoding purposes this is desirable, but in the case of slice-selection and frequency-encode gradients this dephasing must be compensated for. The application of the negative gradient at the same amplitude and for one half of the duration, $\tau/2$, will rephase the spins dephased by the slice-selective and frequency-encoding gradients. This is a gradient echo and is necessary in order to acquire a proper MR image. In fact, an entire image can be obtained this way, without the need for a 180° refocusing pulse. This is called gradient echo (GE) imaging. GE imaging allows very rapid scan times (~ 1 s) usually by using a

Figure 2.14: Spin-echo imaging pulse sequence timing diagram.

very short T_R ($\sim 2\text{-}10$ ms) and a small flip angle ($\alpha < 30^\circ$). This is also a preferable method for imaging hyperpolarized ^{129}Xe since the magnetization is non-renewable. That is, once laser polarized, the magnetization can only be used once since it relaxes to a very small value of M_0 .

Chapter 3

Methods

The experimental procedures and apparatus used in this study are described in this chapter. The primary topics include the design and construction of the low-field resistive electromagnet, laser polarization techniques and materials, the NMR spectrometer specifications, and pulse sequences used for relaxation time measurements. A block diagram of the complete apparatus is shown in Figure 3.1. This diagram shows the three main sections of the apparatus: the resistive electromagnet (dark grey), the laser polarization (light grey), and the NMR spectrometer (white).

3.1 Resistive Electromagnet

The low-field electromagnet constructed was a split-solenoid coil designed by Magnex Scientific Ltd. (Abington, Oxfordshire, UK). The split-solenoid design was chosen in order to optimize power and field homogeneity, as this design provides a reasonable region of homogeneity (~ 10 cm) with $\sim 20\%$ less windings and power than a single solenoid. The coil was designed using Garrett's theory of axially symmetric magnetic fields[71] which describes the spatial variation of a magnetic field produced by a coil configuration as an expansion of spherical harmonics. A more detailed analysis can be found in Hanson[72], Franzen[73], and Garrett[71].

Figure 3.1: A block diagram of the experimental setup used. The greyscale is used to indicate the three main sections of the apparatus: the resistive electromagnet (dark grey), the laser polarization (light grey), and the NMR spectrometer (white). A sample cell (black) is laser polarized inside the magnet and kept at a constant temperature (88 °C) using an oven and temperature controller. The magnet is cooled using an antifreeze bath and chiller. The transmitter sends an RF pulse to the sample and the received MR signals are detected and processed through a preamplifier, mixer, phase detector and amplifier. Data is analyzed at a computer terminal.

The coordinate system used to describe the system involves the use of both cylindrical (ρ, ϕ, z) coordinates and spherical (r, θ, ϕ) coordinates. Figure 3.2 illustrates both the axis and plane of symmetry that characterize the coordinate system.

It has been shown[72] that the axial component of the magnetic field strength of a solenoid can be written as:

$$H_z(r, \theta) = \sum_{n=0}^{\infty} H_n r^n P_n(\cos \theta), \quad (3.1)$$

where $P_n(\cos \theta)$ is a Legendre polynomial. Since $r = z$ when $\theta = 0$ and $P_n(1) = 1$, it follows that the field strength along the symmetry axis is given by:

$$H_z(z, 0) = \sum_{n=0}^{\infty} H_n z^n, \quad (3.2)$$

Figure 3.2: The two coordinate systems used to describe the magnetic field in an axially symmetric system. Because of the cylindrical symmetry of the coil, the ϕ coordinate in each coordinate system can be ignored.

where:

$$H_n = \frac{1}{n} \left[\left(\frac{d^n}{dz^n} \right) H_z(z, 0) \right]_{z=0} \quad (3.3)$$

are the coefficients. This can be simplified to[71]:

$$H_z(z, 0) = \frac{4\pi N_s I}{10 \cdot 2r_s} \left\{ 1 - \left[\frac{1 - u_s^2}{u_s} \right] \sum_{n=1}^{\infty} \frac{1}{2n} \left(\frac{z}{r_s} \right)^{2n} P'_{2n}(u_s) \right\}. \quad (3.4)$$

Here, N_s is the total number of turns of wire on the coil, I is the current through the coil in amperes, r_s is the distance from the origin to the coil edge in centimeters, θ_s is the angle between r_s and the axis of symmetry, $u_s = \cos \theta_s$ (see Fig. 3.3), and:

$$P'_{2n}(u_s) = \left(\frac{d}{du_s} \right) P_{2n}(u_s). \quad (3.5)$$

Eq. 3.4 was used to model the field strength along the axis of symmetry of the magnet, the most sensitive region of the coil in terms of the field homogeneity[72]. A more detailed explanation of Garrett's theory is provided in Appendix B.

In considering the construction of the coil, the following design criteria were used: a 10 cm diameter sphere imaging volume was to be the region of homogeneity with a field homogeneity $\Delta B_0 \leq 1\%$; the inner diameter of the coil was fixed at 30.48 cm (1 ft) due to the outer diameter of the gradient coils to be placed inside the magnet for future imaging purposes; and the field strength was to be 84.9 G in accordance with the 100 kHz RF coil already constructed.

A split-solenoid resistive electromagnet was constructed as shown in Figure 3.3. Based on Eq. 3.4, a split-solenoid can be treated as a solenoid with end turns at θ_{s1} minus a solenoid with end turns at θ_{s2} , as shown in Fig. 3.3. Figure 3.4 shows the theoretical field strength as a function of z for the split-solenoid based on Eq. 3.4. Also, shown, for comparison, is the field plot for a conventional single layer solenoid. The magnet was designed for a 10 cm region of homogeneity at 84.9 Gauss, the field strength corresponding to the ^{129}Xe resonant frequency (100 kHz). This choice of field/frequency was dictated by the frequency of the spectrometer, as discussed in the next section. This region of homogeneity was chosen as a space large enough to enclose a large gas sample or small animal, such as a rat. At ± 5 cm from the center of the coil the homogeneity of the coil was estimated to be 0.75% (0.6 G or 750 Hz). This design predicts 428 turns of wire and approximately 430 W of power for 84.9 G. The model shows that a single solenoid coil would require 518 turns, which corresponds to 100 W more than the split-solenoid design due to the increase in the resistance of the coil.

The coil was wound on a 1 ft diameter piece of cardboard concrete former reinforced with fibreglass cloth. It was wound on a lathe with number 18 AWG wire and simultaneously treated with marine strength epoxy resin to prevent thermal expansion of the wire.

Physical and electrical operating characteristics are provided in Table 3.1. Two power supplies, a Sorenson SRL 40-50 and a Harrison Laboratories Model 814A were used to provide the necessary power (430 W). This resulted in some heating of the magnet. The magnet was cooled using chilled antifreeze circulated through 3/16" copper tubing wound around the layered windings.

The magnetic field of the coil was mapped using a FW Bell 640 Gaussmeter with an axial magnitude probe. The temperature correction coefficient for the probe was calibrated at 0.0013 K^{-1} by measuring the variation in field strength at a set

Figure 3.3: (a) A longitudinal cross-sectional view of the low-field resistive electromagnet. The split-solenoid design is characterized by two bands of windings, each 6 cm wide and 4 layers of wire deep. The bands are spaced 10 cm apart. Specifications are provided in Table 3.1. The inset shows the winding configuration of the coil. (b) A 3D schematic of the cylindrical coil.

distance from a magnetic field while varying only the temperature of the probe. The field was also mapped along both the z axis and in the xy plane of symmetry at $z = 0$. A frame was constructed to hold the gaussmeter probe at a variable position, both axially and radially, within the bore of the coil. The axial position of the probe was calibrated using one end of the coil (touching the tabletop when the coil is mounted vertically) as a reference, while the radial position was predetermined by holes drilled into the frame at set 1 cm intervals. The azimuthal position within the bore was measured using a protractor mounted on the frame set to a marked reference position on the coil. Axial magnetic field accuracy was within ~ 5 mm, radial accuracy within ~ 1 mm, and azimuthal accuracy within $\sim 2^\circ$. Note that the axial position of the probe was offset by 0.5 cm due to the location of the Hall sensor within the probe. This was compensated for in the magnetic field maps.

Figure 3.4: A modelled homogeneity comparison between a single layer solenoid electromagnet (dashed line) and a split-solenoid electromagnet (solid line). Both designs have an inhomogeneity of $\leq 0.75\%$ at 5 cm. The split-solenoid uses 428 turns of wire while the single layer solenoid uses 518 turns. The difference in turns is equivalent to ~ 12 V and ~ 100 W. These results were calculated using Eq. 3.4.

Current fluctuations were on the order of 1.0 mA, or equivalently 0.01 G or 15 Hz in the NMR signal frequency. Typically, the magnet was allowed to warmup for 1 hour before any measurements were taken so that the coolant and the windings could reach a steady state.

3.2 NMR Spectrometer

The NMR spectrometer is based on a 85 G polarimeter design proposed by Saam[74] and built by a previous post-doctoral fellow in our laboratory. Modifications to this

Mechanical Characteristics	Measured Value
a_1	5.00 ± 0.05 cm
a_2	11.00 ± 0.05 cm
b_1	13.56 ± 0.05 cm
b_2	14.16 ± 0.05 cm
N	8.29 turns/cm
No. layers	4
Tot. turns	428 ± 4
Wire Gauge (AWG)	18
Electrical Characteristics	Measured Value
R	$9.1 \pm 0.1 \Omega$
B_z	12.34 G/A
I	6.880 ± 0.001 A
P	430 ± 5 W

Table 3.1: Physical and electrical specifications of the resistive electromagnet.

design that were implemented for this study included isolating the preamplifier, increasing shielding for the RF coil, quadrature phase detecting, and interfacing the system to an MRRS (formerly SMIS, Surrey Medical Imaging Systems, Surrey, UK) MR5000 console by changing the output impedance to 50Ω . Circuit diagrams for the modifications are provided in Appendix A.

The preamplifier was isolated by removing it from the casing in which the NMR electronics were contained and placing it in a separate casing to decrease the level of electronic noise being amplified.

The RF coil used was a Helmholtz design tuned to 100 kHz with a bore diameter of 1 cm and a length of 2.7 cm. The coil was encased in an aluminum box 3 mm thick to shield the coil from any extraneous electromagnetic interference (e.g. computer

monitors, power supplies, etc.). The RF coil was tuned to 100 kHz by placing it in parallel with two capacitors for a total of ~ 570 pF.

The quadrature phase detector constructed was optimized by adjusting the variable resistor which balances the amplitude of the received signals in each of the two orthogonal channels. A Lissajous plot was first used to balance the signals (i.e. adjusting the variable resistor until the elliptical shape of the Lissajous plot changed to that of a circle), followed by a superposition of the two signals while adjusting the resistance to remove any differences in their amplitudes.

3.3 Laser Polarization

Figure 3.5 shows a simplified schematic of the setup used. Figures 3.6 and 3.7 are photographs of the setup. The ^{129}Xe gas was polarized inside the low-field magnet to ensure that experimental conditions are reproducible and to optimize SNR (we have shown that considerable loss of magnetization can occur while moving the sample from a fringe polarizing field to the low-field NMR system). A 30 W Al-Ga-As diode array laser was used emitting at 794.8 nm and operating at 25.6 °C and 23 W (Opto-Power, Tucson, AZ). The beam was directed parallel to $\vec{B}_0$ and circularly polarized using a $\lambda/4$ filter to ensure an angular momentum transfer of one unit ($\hbar$) to the Rb vapour. The laser was focussed on a glass polarization sample cell internally coated with SurfraSil (Pierce Chemical Laboratories), containing 730 mbar natural abundance Xe gas (26% ^{129}Xe), 102 mbar N_2 and a few mg of Rb metal. SurfraSil is an organosilicon compound used to reduce the relaxation of the ^{129}Xe gas due to wall collisions. The cell was kept at 88°C in order to vapourize the Rb and to maintain an optimum vapour pressure. Polarization time remained constant at 20 minutes. Optimization of both temperature and polarization time are described in more detail elsewhere[79]. To ensure a maximum number of Xe-Rb interactions, the

Figure 3.5: Polarization setup used for our experiments. The laser is aligned with the z component of the field and polarizes the sample located in an oven inside the magnet.

sample cell was made with a diameter no larger than the width of the laser beam ($\sim 1''$).

The sample cell polarization level will decrease over long periods of time ($\sim$ months) if the cell is polarized regularly. This is due to a degradation of the Rb in the cell which oxidizes readily in the presence of trace amounts of oxygen. This can be partially compensated for by shaking the cell vigorously after the Rb has melted to coat the inside of the cell in fresh, not-yet oxidized Rb. Changes in the Rb quality were checked for by looking for differences in the received signal intensities. No such changes were detected.

3.4 SNR Measurements

A comparison of the SNR at 1.89 T and 85 G was also made using Eq. 2.34, repeated here:

$$\frac{SNR_{HF}}{SNR_{LF}} = \frac{\eta_{HF} P_{HF}}{\eta_{LF} P_{LF}} \sqrt{\frac{(Q f_0 V_c / FT \Delta f)_{HF}}{(Q f_0 V_c / FT \Delta f)_{LF}}}, \quad (3.6)$$

Figure 3.6: The bore of the 85 G magnetic coil. The sample cell and RF coil are placed inside of the RF shielding box at the center of the coil. Heating tape is wound about the box and acts as an oven for polarization purposes.

Figure 3.7: The 85 G resistive magnet. Copper tubing is wound about the windings to cool the coil with antifreeze. The power supplies are situated in the background.

where the HF and LF subscripts represent the high and low-field strengths of 1.89 T and 85 G, respectively. Using this expression, the ratio of SNR's was calculated and compared to the measured quantities for both the hyperpolarized and thermally polarized scenarios.

3.4.1 Predictions

Polarization Factors

The thermal polarization, P_{TH} , of a sample of spins was calculated using Eq. 2.15. repeated here:

$$P_{TH} = \frac{1 - e^{-\hbar\omega_0/kT}}{1 + e^{-\hbar\omega_0/kT}}. \quad (3.7)$$

Hyperpolarized P measurements required the measurement of both a hyperpolarized and a thermally polarized signal. For the same nucleus/sample at the same field strength, the ratio of polarizations is equivalent to the ratio of the measured signal amplitudes, S , according to Eq. 2.30. The hyperpolarized polarization, P_{HP} , can therefore be calculated by:

$$P_{HP} = P_{TH} \left(\frac{S_{HP}}{S_{TH}} \right). \quad (3.8)$$

Acquisition of S_{TH} and S_{HP} will be discussed below.

Electronic Factors

As the Q values of the RF coils were not known, they were determined by measuring the bandwidth of the coil, Δf_c , and calculating the Q values from the equation:

$$Q = \frac{f_0}{\Delta f_c}, \quad (3.9)$$

where f_0 is the resonance frequency of the coil. The coil bandwidth was measured by injecting a signal from a frequency generator centered on f_0 into the coil and measuring the signal received as the frequency was varied by adjusting the output of

the frequency generator. The bandwidth was calculated for the frequency range at the FWHM mark and estimated as twice the standard deviation in a fit to a Gaussian distribution. The error was taken from the error in the fit, using a Levenberg-Marquardt fitting routine.

The noise figures, F , of the two receivers were also measured. The noise figure of a receiver is given as:

$$F = 20 \log \left(\frac{SNR_{out}}{SNR_{in}} \right). \quad (3.10)$$

The noise figure of the receiver was measured by placing a $50 \, \Omega$ shielded resistor at the input of the receiver and recording the receiver output using an oscilloscope. Next, the shielded resistor, attached to a small cable, was placed in a liquid nitrogen bath and, after being allowed to cool to the bath temperature ($77 \, \text{K}$), the receiver output was again measured. If the receiver is perfect the noise would almost halve, as $77 \, \text{K}$ is almost one quarter of room temperature, and would require an attenuation factor of $\alpha = 2$ (6 dB) to match the room temperature measurement. In practice, $\alpha < 2$ and the noise figure is given as[82]:

$$F = 10 \log \left(1 - \frac{77}{T} \right) - 10 \log \left(1 - \frac{1}{\alpha^2} \right). \quad (3.11)$$

where T is the room temperature in Kelvin (K). The noise was taken as the standard deviation of the signals recorded. The error in the noise figure was estimated from the standard deviation of 10 consecutive measurements of the noise.

Other Factors

The filling factor, η , is given as the ratio of sample volume to coil volume, V_s/V_c , which reduces to the squared ratio of sample and coil radii, $(r_s/r_c)^2$. Assuming the sample is the same, a ratio of filling factors therefore reduces to $(r_c^{LF}/r_c^{HF})^2$. The coil radius of each coil was taken as the mean radius from the outer to inner windings.

The volume of a coil is given by $\pi r_c^2 l_c$, where l_c is the coil length. Coil radius and volume were measured using Vernier calipers.

The coil temperatures were taken to be room temperature (298 K) in all cases except the low-field hyperpolarized signals, where $T = 361$ K (88 °C), the temperature that the sample cell was polarized at. The polarization temperature was measured using a thermocouple wire attached to the heating oven used to keep the Rb at a constant vapour pressure. The receiver bandwidth, Δf , was taken as the smaller of the sampling rate or the coil bandwidth.

3.4.2 Measurements

NMR signals were first obtained by recording a free induction decay at the predicted field strength of 85 G. From there, finding the exact resonant condition (i.e. reducing the offset frequency to ~ 0) involved optimizing the magnetic field strength by adjusting the power supply output. The reproducibility of the acquired signals was measured by repeating a given experiment five times and checking for fluctuations in the spectral intensity and frequency. Consideration was given to the frequency resolution as a larger resolution would make checking for stability difficult. All signals were acquired via quadrature detection. To avoid any DC offset artifacts in the spectrometer, signals were acquired off-resonance by up to 700 Hz.

Signal amplitudes were measured as the integrated area under the Fourier transformed FID over the receiver bandwidth of the signal, subtracting the integration of the Fourier transformed empty coil signal. Noise was measured as the standard deviation of the empty coil signal over the receiver bandwidth. The area was calculated using a trapezoidal integration algorithm. The error in the SNR was taken as the statistical error in the integrated areas for multiple (3-5) signal acquisitions.

B_1 Calibration

The pulse flip angle, α , was determined so that a maximum signal intensity corresponding to $\alpha = 90^\circ$ could be obtained. The method for flip angle calibration suggested by Patyal[75] and discussed in Section 2.2.4 was used in this study. However, because signals were acquired off-resonance, and B_1 was small, the flip angle calibration must be modified to account for the nutation of the magnetization about an effective magnetic field, $\vec{B}_{eff}$, as described in Eq. 2.21. The effective flip angle, α_{eff} , is given by:

$$\alpha_{eff} = \gamma B_{eff} t_p, \quad (3.12)$$

similar to Eq. 2.22. B_{eff} is given as the magnitude of Eq. 2.21:

$$B_{eff} = \sqrt{B_1^2 + (\Delta\omega/\gamma)^2}, \quad (3.13)$$

which is a function of the resonant offset frequency, $\Delta\omega$, and B_1 . Therefore, to calculate α_{eff} , B_1 must be determined.

The off-resonance components of the magnetization $\vec{M}$ can be given by[84]:

$$M_x = M_0 \sin \alpha_{eff} \sin \theta \quad (3.14)$$

$$M_y = M_0 (1 - \cos \alpha_{eff}) \sin \theta \cos \theta \quad (3.15)$$

$$M_z = M_0 [\cos^2 \theta + \cos \alpha_{eff} \sin^2 \theta], \quad (3.16)$$

where θ is the angle between $\vec{B}_{eff}$ and the z axis and is given as:

$$\theta = \tan^{-1} \left(\frac{B_1}{\Delta\omega/\gamma} \right). \quad (3.17)$$

Applying these off-resonant conditions to the Look-Locker method of flip angle and T_1 estimation as described by Patyal[75], we have:

$$\frac{S_n}{S_{n-1}} = [\cos^2 \theta + \cos \alpha_{eff} \sin^2 \theta] e^{-T_R/T_1}. \quad (3.18)$$

Patyal's method was used to calibrate B_1 by repeating the experiment six times, for pulse widths ranging from 50-100 μs in 10 μs intervals, and plotting pulse width, t_p , vs. the slope of the signal decay, S_n/S_{n-1} . The number of signals acquired for each t_p was $N = 16$. Once B_1 was calibrated, α_{eff} could be calculated for any offset frequency.

A result of Eq. 3.16 was that the maximum off-resonance signal will not be obtained using a tip angle of 90° . The maximum signal is obtained when the magnetization is entirely in the xy plane, i.e. when $M_z = 0$. Solving Eq. 3.16 for $M_z = 0$, the effective 90° flip angle, $\alpha_{eff}(90^\circ)$, is:

$$\alpha_{eff}(90^\circ) = \cos^{-1} \left[- \left(\frac{\Delta B}{B_1} \right)^2 \right]. \quad (3.19)$$

For example, an offset frequency of 300 Hz combined with a B_1 of 1 G results was an optimal flip angle of 93.7° (rather than 90°) for ^{129}Xe . As a result of off-resonance effects, Eqs. 3.6 and 3.8, both of which assume a constant flip angle, must now include an additional term:

$$\frac{S.N.R_{HF}}{S.N.R_{LF}} = \frac{\eta_{HF} P_{HF}}{\eta_{LF} P_{LF}} \sqrt{\frac{(Q f_0 V_c / FT \Delta f)_{HF} A_{HF}}{(Q f_0 V_c / FT \Delta f)_{LF} A_{LF}}} \quad (3.20)$$

$$P_{HP} = P_{TH} \left(\frac{S_{HP}}{S_{TH}} \right) \frac{A_{TH}}{A_{HP}}, \quad (3.21)$$

where:

$$A = \sin \theta \sqrt{\sin^2 \alpha_{eff} + (1 - \cos \alpha_{eff})^2 \cos^2 \theta}. \quad (3.22)$$

The repetition time (T_R) for these experiments must be short enough to approximate the exponential decay of the signal between pulses to unity ($e^{-T_R/T_1} \sim 1$). Therefore, some knowledge of the value of T_1 must be known beforehand. T_1 was predicted to be on the order of 100 s, based on observations made in the fringe field at 85 G. Therefore, T_R was chosen to be 100 ms with a sampling time of 20 μs .

Signal Acquisition, 1.89 T

SNR measurements at 1.89 T were acquired on the aforementioned MRRS MR5000 console using an Oxford 30 superconducting magnet (30 cm bore), with a sampling time of 120 μ s and a pulse width of 54 μ s. For thermally polarized ^{129}Xe signal acquisition a separate sample was used: 5140 mbar of Xe and 1519 mbar O_2 . The high pressure of the cell increases the low thermal ^{129}Xe signal amplitude, while the presence of oxygen relaxes the ^{129}Xe quickly enough so that short repetition times can be used to shorten acquisition time between consecutive acquisitions. This high pressure sample cell had the same filling factor as the lower pressure cell and, while the xenon density was relatively higher, the loading characteristics of the the coil did not change the Q since the sample was still in a gaseous state and had an overall low density (as opposed to a liquid or a solid). 128 signal averages were used to acquire the signals.

Hyperpolarized signals at 1.89 T were measured in the same manner as the thermal signals but with a sampling time of 20 μ s, without the use of signal averaging and using the sample cell described in Section 3.3.

Signal Acquisition, 85 G

Even with the aid of a high pressure sample cell, detection of a thermally polarized ^{129}Xe signal at 85 G is extremely difficult and beyond the capacity of the low-field imager constructed. However, estimation of a signal strength was made based on the signal strength of a different nucleus with a higher magnetic moment (i.e. protons) detected from the same spectrometer. Beginning with a ratio of signal equations (Eq. 2.30) and eliminating the exponentials we have for ^{129}Xe and hydrogen nuclei (protons):

$$\frac{S_{Xe}}{S_H} = \frac{\omega_{Xe} B_{Xe} \mu_{Xe} N_{Xe} P_{Xe} V_{Xe} A_{Xe}}{\omega_H B_H \mu_H N_H P_H V_H A_H}, \quad (3.23)$$

where ω is the resonant frequency, B is the applied (RF) magnetic field strength, μ is the magnetic moment, N is the number of nuclei per unit volume, P is the thermal polarization, V is the sample volume, and A is the off-resonance correction factor. As the spectrometer has a fixed resonant frequency and transmitter power, reflected in the B term, both ω and B will be independent of the nucleus and therefore cancel. The polarization, as a function of both ω and T will also cancel as T is constant. Finally, recalling that $\mu \propto \gamma$ (Eq. 2.4) and assuming the sample volumes to be equal we have:

$$S_{Xe} = S_H \frac{\gamma_{Xe} N_{Xe} A_{Xe}}{\gamma_H N_H A_H}, \quad (3.24)$$

where $N_{Xe} = 4.6172 \times 10^{24}$ atoms/m⁻³ and $N_H = 6.6875 \times 10^{28}$ atoms/m⁻³. N_{Xe} was calculated from the known pressure (730 mbar) according to the ideal gas law and N_H was calculated based on the molecular weight (18 g/mol) and density (1 g/cm³) of water. The off-resonance terms, A , will, for a given off-resonance frequency, differ only in the gyromagnetic ratios of the nuclei. In this manner a thermally polarized ¹²⁹Xe signal was measured from a proton signal at the same resonant frequency (100 kHz), where the field strength is changed for the proton signal acquisition, from 85 G to 23 G, in accordance to the Larmor relation. Thermal proton signals were acquired with a sampling time of 20 μ s and a pulse width of 114 μ s. 1000 signal averages were used for a total acquisition time of 15 minutes.

Hyperpolarized signals at 85 G were obtained using the sample cell discussed in Section 3.3, but with only a single acquisition. Signals were acquired using a sampling time of 20 μ s and a pulse width of 411 μ s.

T_1 Measurement

The T_1 relaxation time of the sample at 85 G was measured using the same sample as described in Section 3.3 and the same technique as the flip angle calibration discussed above except using $T_R = 20$ s $\sim T_1$. Since α_{eff} was calculated (above).

T_1 was estimated according to Eq. 3.18. The data were fitted using a Levenberg-Marquardt nonlinear least squares fitting technique to extract T_1 .

Radiation Damping

Radiation damping was investigated using two different techniques. First, the signal intensity was plotted against flip angle ($0^\circ < \alpha < 120^\circ$) and fit to both linear and sinusoidal functions, as described in Section 2.1.5. A linear fit indicates that damping is present, while a sinusoidal fit indicates that no damping is present.

Secondly, tip angle calibrations for a series of 16 FIDs were compared at different acquisition times along the FIDs. Different calibrated values of α would indicate that the relaxation rate of the signals was changing as a function of time along the FID. This is the case for radiation damped signals as $T_{rd} \propto M_0$, where M_0 is decreasing with time along a FID and also with each successive FID. If damping is not present, no change in the flip angle calibrations will be observed, as T_2^* is independent of M_0 .

Chapter 4

Results

Experimental results are provided in this chapter for the SNR at 85 G in comparison with the SNR at 1.89 T. Test results of the resistive electromagnet's field uniformity and stability are provided: measurements of SNR dependent parameters (P , Q , F , r_s , r_c , V_c , and Δf) are given: flip angle calibration results and T_1 measurements of the sample cell are provided: and radiation damping test results are presented.

4.1 Resistive Electromagnet

4.1.1 Field Uniformity

Magnetic field plots for the 85 G resistive electromagnet are provided in Figures 4.1 and 4.2. Fig. 4.1 shows a plot of B_z for $\theta = 0$ along the z axis of symmetry. Fig. 4.2 shows B_z at $z = 0$ in the xy plane of symmetry. As discussed in Section 3.1, the resistive electromagnet was designed to have a 10 cm region of homogeneity at the coil centre. This is also shown in the modelled curve of Fig. 4.1, predicting a field inhomogeneity of 1.25% at ± 5 cm. The experimental measurements meet that prediction, within the experimental error.

Figure 4.1: The axial magnetic field strength along the z axis of symmetry. Error bars are due to gaussmeter fluctuations (~ 0.2 G). As predicted, the field is homogeneous within a 10 cm region at the center, with an inhomogeneity of 1.25%. The field map was corrected for the positional displacement of the Hall probe by 0.5 cm.

Figure 4.2: The axial magnetic field strength in the xy plane of symmetry. The greyscale indicates field strength. Inhomogeneities near the rim of the surface (near the windings of the coil) are likely due to interference from the power supplies located adjacent to the low-field coil. As predicted, the field is homogeneous within a 10 cm radius at the center, as designed.

Figure 4.3: Repeatability data for the low-field resistive electromagnet. The received signals have a frequency error or fluctuation of 1.5% and an intensity error of 2.2%. Here, $t_p = 411 \mu\text{s}$, with an offset frequency of 700 Hz and a sampling time of $20 \mu\text{s}$. A small DC offset artifact can be seen near the zero frequency mark.

4.1.2 Field Stability

Figures 4.3 and 4.4 show the fluctuations in magnetic field stability as a function of spectral intensity and frequency at 85 G using the sample described in Section 3.3. Signal fluctuations were tested for over a time period of 3 hours, with spectra fluctuating within a frequency range of 50 Hz (1.5%) and a spectral intensity of 2.2%.

Figure 4.4: Repeatability data for the low-field resistive electromagnet. The received signals have a frequency error or fluctuation of 1.5% and an intensity error of 2.2%. Here, $t_p = 411 \mu s$, with an offset frequency of 700 Hz and a sampling time of $20 \mu s$. A small DC offset artifact can be seen near the zero frequency mark.

Figure 4.5: Tip angle calibration data. The slope of the data sets changes according to the pulse width, t_p .

4.2 B_1 Calibration

B_1 calibration data is provided in Figure 4.5 and shows the change in the signal decay rate for different pulse widths. t_p . S_n/S_{n-1} vs. t_p is plotted in Figure 4.6 and is fit to Eq. 3.18, giving an estimate of $B_1 = 0.77 \pm 0.72$ G. These signals were recorded with an offset frequency of 440 Hz.

4.3 Polarization Measurements

Polarization factors, P_{HP} , for both high and low-field strengths are presented in Table 4.1 along with the calculated thermal polarizations, P_{TH} . A water FID, used to calculate P at 85 G is shown in Figure 4.7. Signals for all four cases are presented

Figure 4.6: B_1 calibration plot. $B_1 = 0.77 \pm 0.72$ G and the $\chi^2 = 0.7928$ per degree of freedom.

in Figure 4.8.

	1.89 T	85 G
Thermal	1.7852×10^{-6}	8.0561×10^{-9}
Laser	0.0148 ± 0.0005	0.0231 ± 0.0016

Table 4.1: Polarization values, P , for the hyperpolarized and thermally polarized gas experiments. The thermal (or Boltzman) polarizations are provided for comparison. The errors in the laser polarizations were determined from the statistical repeatability of the hyperpolarized experiment SNR, as described in Section 3.4.2.

Figure 4.7: ^1H free induction decay from a water sample at 23 G. Sampling time = 20 μs , $t_p = 114 \mu\text{s}$ (90°), 1000 signal averages.

4.4 Electronic Factors

Figure 4.9 shows the bandwidth estimates used to calculate the Q 's with Eq. 3.9. The high-field bandwidth was estimated to be 111.8 ± 6.4 kHz with a Q of 198.2 ± 11.2 while the low-field bandwidth was measured to be 3.400 ± 0.355 kHz with a Q of 29.41 ± 3.07 . The Q was also measured for the water-filled low-field coil to check for differences in the loading of the coil when acquiring the proton signal for the 85 G polarization measurement.

The noise figure, F , was calculated for both systems for the preamplifiers and the receivers as discussed in Section 3.4.1, using Eq. 3.11. The results are tabulated in Table 4.2. Noise figures of the receiver are used in further calculations.

Figure 4.8: A comparison of thermally (TH) and hyperpolarized (HP-Xe) signals at 1.89 T and 85 G. (a) Hyperpolarized ^{129}Xe at 85 G, $t_p = 411 \mu\text{s}$, 634 Hz frequency offset; (b) thermally polarized ^1H (water) at 23 G, $t_p = 114 \mu\text{s}$, 488 Hz frequency offset, 1000 signal averages, $T_R = 1.5$ s, total acquisition time was 25 minutes; (c) hyperpolarized ^{129}Xe at 1.89 T, $t_p = 54 \mu\text{s}$, 49 Hz frequency offset. The dip in the spectrum near the middle is an artifact of the quadrature phase detector; (d) thermally polarized ^{129}Xe at 1.89 T, $t_p = 54 \mu\text{s}$, 378 Hz frequency offset, 128 signal averages, $T_R = 2$ s, total acquisition time was 256 s. All intensities are in arbitrary units corrected for the number of acquisitions.

Figure 4.9: (a) High-field (1.89 T) RF coil bandwidth is estimated to be 111.8 ± 6.4 kHz. The Q is therefore calculated to be 198.2 ± 11.2 . (b) Low-field (85 G) RF coil bandwidth is estimated to be 3.400 ± 0.355 kHz. The Q is therefore calculated to be 29.41 ± 3.07 . Error bars are not displayed on either plot as they are not visible.

4.5 Experimental Confirmation of the SNR Dependence on Field Strength

The measured SNR's are presented below in Table 4.3. All four values are normalized to the 730 mbar xenon sample used for the laser polarization experiments.

The ratio of SNRs (high-field divided by low-field) for the hyperpolarized and thermally polarized measurements is provided in Table 4.4. These values are then compared to the theoretical calculation according to Eq. 3.6. Table 4.5 includes a listing of the variables and their values used in this calculation. A ratio of measured

	1.89 T	85 G
Receiver	4.26 ± 0.11	16.73 ± 5.28
Preamplifier	3.31 ± 0.01	13.14 ± 0.30

Table 4.2: Noise figure measurements for both 1.89 T and 85 G receivers and preamplifiers. Most of the noise from both receivers appears to originate with the preamplifiers.

	1.89 T	85 G
Thermal	$(4.40 \pm 0.68) \times 10^2$	$(1.830 \pm 0.016) \times 10^{-2}$
Laser	$(2.708 \pm 0.069) \times 10^6$	$(8.26 \pm 0.15) \times 10^4$

Table 4.3: Measured SNR's for high and low-field hyperpolarized and thermally polarized ^{129}Xe . While not all of the signals were acquired using the same sample cell, the numbers here are all scaled relative to the 730 mbar xenon sample used for laser polarization experiments.

to calculated values is also provided in Table 4.4.

	Thermally Polarized	Laser Polarized
Measured	$(2.42 \pm 0.49) \times 10^4$	32.8 ± 1.5
Calculated	$(2.21 \pm 0.38) \times 10^4$	28.8 ± 5.2
Ratio (Calc./Meas.)	1.09 ± 0.25	1.14 ± 0.21

Table 4.4: Comparison of the measured SNR ratios to the calculated values.

4.6 Relaxation Time Measurements

T_1 relaxation time data are provided in Figure 4.10. T_1 was estimated to be 189.9 ± 41.1 s.

	1.89 T	85 G
τ_c (cm)	0.7363 ± 0.0087	0.7025 ± 0.0087
P_{HP}	0.0148 ± 0.0005	0.0231 ± 0.0016
P_{TH}	1.7852×10^{-6}	8.0561×10^{-9}
Q	198.2 ± 11.2	29.41 ± 3.07
V_c (cm ²)	9.3321 ± 0.0900	1.8450 ± 0.0201
F (dB)	4.26 ± 0.11	16.73 ± 5.28
T_{HP} (K)	298 ± 1	361 ± 1
T_{TH} (K)	298 ± 1	298 ± 1
Δf_{HP} (Hz)	50000	3400 ± 355
Δf_{TH} (Hz)	8333	3400 ± 355

Table 4.5: Parameters used to estimate the ratio of SNR using two different spectrometers at two different static field strengths.

4.7 Radiation Damping

A plot of the signal intensity versus flip angle is provided in Figure 4.11. The sinusoidal fit ($\chi^2 = 0.6604$) is better than the linear fit ($\chi^2 = 1.0388$). No radiation damping was therefore indicated.

As a further check, signal decay was analyzed at different acquisition times along a series of FIDs. Because the data all decayed at the same rate, radiation damping does not appear to be present, as shown in Table 4.6.

Based upon this experimental evidence, radiation damping does not appear to be an issue with our experiments. Therefore, the hyperbolic secant radiation damping term in the signal equation can be ignored and signal decay according to exponential T_2^* can be assumed.

Figure 4.10: T_1 relaxation time decay: $t_p = 42 \mu\text{s}$. 20 pulses. T_1 was estimated at 189.9 ± 41.1 s, with a $\chi^2 = 1.0012$.

Acquisition Time (ms)	Flip Angle α ($^\circ$)
0.30	26.60 ± 0.35
0.60	26.73 ± 0.35
2.00	27.03 ± 0.36
4.00	26.25 ± 0.34

Table 4.6: Comparison of flip angle calibrations at different acquisition times along the FID. The results show that there is no statistically significant change in α along the FID. Therefore, no radiation damping is present.

Figure 4.11: Signal intensity vs. flip angle, α . The linear fit (solid line) has a χ^2 of 1.0388 per degree of freedom, while the sinusoidal model (dashed line) has a χ^2 of 0.6604 per degree of freedom.

Chapter 5

Discussion

The results of our experiments indicate that the resistive magnet constructed is operating within the predicted parameters (i.e. 10 cm region of homogeneity at 85 G) and that the received signals are stable (i.e. fluctuate within 2.2%) for both frequency and amplitude and do not appear to be affected by radiation damping. The hyperpolarized ^{129}Xe NMR signals obtained using this magnet and the low-field spectrometer match the predicted signal strengths to within 20%. The B_1 applied RF field was calibrated at 0.58 ± 0.05 G, the T_1 relaxation time was measured to be 189.9 ± 0.3 s, and the T_2^* relaxation time was measured to be 13.5 ± 0.4 ms. These results, their sources of error, and a comparison with Wong *et al*[60] are discussed below. This is followed by a discussion of the SNR requirements of MR imaging, how our results compare to those requirements, what can be done to improve them, and some future considerations of this research project.

The xy plane of symmetry map of the magnetic field strength of the resistive coil provided in Fig. 4.2 indicates that the field outside the region of homogeneity, near the windings, is higher on one side of the magnet than the other. This asymmetry is also present to a lesser degree in the axial z map of the field in Fig. 4.1. Garrett's theory does not predict this asymmetry and states that the field strength should decrease radially from the axis of symmetry in a symmetric fashion (see Appendix

B). This is most likely due to the influence of the power supplies located near one side of the magnetic coil, the electrical activity and ferromagnetic components of the power supplies producing a distortion in the field. The power supplies have since been moved further away from the coil to reduce this asymmetry.

The homogeneity at 5 cm from the centre of the 85 G coil is 1.25%, as opposed to a few parts per million (1 ppm = 0.0001%) for the 1.89 T superconducting magnet. However, these values are relative to their static field strengths, i.e.: a $\Delta B = 1G$ will have a relatively higher homogeneity at 85 G than at 1.89 T. As it is the behaviour in the rotating frame that is important to MR (i.e. after the resonant frequency has been removed), the ΔB will cause the same dephasing of the spins at low field as at high. Increased field homogeneity is still desirable, however, as it lengthens the T_2^* relaxation time, allowing for longer read out times and better spatial resolution. Field homogeneity can be improved by shimming the magnetic field. Shimming is the process of removing the spherical harmonics (see Appendix 1) that comprise the field inhomogeneity through the strategic placement of ferromagnetic materials around the magnet and the use of harmonic-cancelling magnetic field coils, or shim coils.

The fringe field of the 1.89 T superconducting magnet changed the T_2^* relaxation time of the received signals from 6.9 ms to 13.5 ms, allowing for longer signal durations in the presence of the high-field and essentially acting as a shimming source. This indicates that a more thorough shimming of the magnet will improve signal duration. Shimming can be more properly provided by adjusting the field homogeneity over the volume of a shimming phantom, typically a sphere of water with a diameter matching the desired region of homogeneity. A simple shimming technique involves placing plates of ferromagnetic materials (e.g. iron) near both ends of the cylindrical coil and adjusting their relative positions to the coil until the contrast of the phantom image (or the signal amplitude) is uniform.

the imaging field strength is usually a relatively much stronger field. For low-field imagers, this is not always the case. Here, the presence of the 1.89 T superconducting magnet is beneficial to our results, but this may not always be the case. Magnetically shielding the coil from external static fields might therefore be considered. Such shielding techniques involve encasing the resistive coil in μ -metal to attenuate the static fields.

Fitting for the T_1 relaxation time was very sensitive to the B_1 calibration, as any error in the flip angle will present a large relative error ($\sim 50\%$) in the T_1 . Also, the confounding effects of varying T_R and α can be difficult for the measurement of T_1 . The larger the flip angle, the more it dominates the decay but the better the received signals are, therefore the better the fit. However, a longer T_R increases the T_R/T_1 weight in the fit but also reduces the number of pulses (i.e. the number of points) used for the fit due to the increase in the decay between pulses, decreasing the accuracy of the fit. Different combinations were tried but the combination used ($T_R = 20$ s, $\alpha = 11.7^\circ$, and $N = 20$) presented the best combination of weighting distribution and number of data points.

T_1 of ^3He was measured by Wong[60] to be on the order of 100 hrs in a glass sample cell. This differs from our result by three orders of magnitude and is primarily due to the differences in the nature of the atoms being observed. Xenon has a much larger electronic structure, and therefore more electronic shells, than helium. As a result, the binding energies of the outer shell electrons of xenon will be weaker than those of the outer shell electrons of helium, a result of the inverse-square law governing those binding energies. This indicates that, while both are noble gases, and do not chemically react with their environments, a trait that makes them excellent candidates when working with biological substances, the xenon atoms are, in fact, more susceptible to external electronic environments. This elasticity or stickiness of the xenon atoms is one explanation for their interaction with the sample cell walls.

Helium does not suffer from this limitation and will therefore have a considerably longer longitudinal relaxation time, as indicated by the above results.

The data provided in Fig. 4.11 and Table 4.6 indicate that if radiation damping is present it is playing a very small role. The signals acquired from the spectrometer do not completely conform to either a damped or non-damped signal model probably due to non-ideal shimming of the magnetic field. However, while the free induction decay, shown in Figure 5.1, did increase in amplitude before decaying, it was not nearly as severe an increase as that of a damped signal, given the FID's flip angle (130°). Even though T_{rd} was not estimated, as the fit to the data failed, we can still infer that radiation damping was not present because the amount by which the FID increases is indicative of the flip angle (Fig. 2.9). Therefore, no matter what the value of T_{rd} is, the FID will increase by a fixed amount: T_{rd} is a measure of the decay of the signal, much the same way T_2^* is. Figure 5.1 qualitatively illustrates this idea. While radiation damping was present in work done by Wong[60], that group used ^3He rather than ^{129}Xe as the nucleus of interest, which has a gyromagnetic ratio ~ 3 times greater than that of ^{129}Xe , and with which Wong had higher polarization levels (10% rather than our own 3.4%). These differences increased their magnetization levels by a factor of ~ 20 , compared to ours, which in turn shortens the damping time. $T_{rd} \propto 1/(\gamma^2 P)$, by a similar amount, making radiation damping a problem. They recorded $T_{rd} \sim T_2^* \sim 100$ ms, which implies that our $T_{rd} \sim 2000$ ms, 200 times greater than our T_2^* of ~ 10 ms. Radiation damping was checked for at 1.89 T, as well, and not found to be a factor. As the magnetization is much higher at this field strength (~ 10 times greater), and damping was not indicated, then at 85 G damping would not be expected.

Radiation damping will become a problem with increasing magnetization, i.e. increased polarization or spin density (Eq. 2.50). It will also be a problem for longer T_2^* . As T_2^* increases and the ratio of T_2^*/T_{rd} approaches unity, damping effects

Figure 5.1: Models of the conventional T_2^* exponential decay envelope and the radiation damping T_{rd} hyperbolic function envelope compared to the FID ($\alpha = 130^\circ$). Qualitatively, the T_2^* fit is the better of the two.

will begin to manifest. As both increased M_0 and T_2^* is desirable in every other aspect of MR imaging, radiation damping may be an inevitable problem. It may be corrected for by estimating the damping time, T_{rd} , and correcting the acquired images accordingly.

The aim of this research project was to demonstrate that the constructed low-field imager has an SNR that is sufficient for imaging in accordance with the theory proposed in Section 2.1.4. The SNR measurements recorded in Table 4.3 indicate that the measured results and the calculated predictions are within each others experimental uncertainty, thus validating this theory. Discrepancies in the results can, however, be accounted for in a number of ways.

In modeling the noise, traditionally a difficult task, a number of different sources need to be taken into account. Here, as is standard practice[77], only the thermal noise is accounted for in the Hoult SNR model. Other sources of noise are typically ruled out as they have a negligible effect on signal strength at high-field strengths. At low field strengths, however, these same effects, such as $1/f$ noise and sample noise, may be stronger (or conversely, the thermal noise may have less of an effect), thereby influencing the SNR results to a more noticeable extent.

Another assumption made when modelling the SNR in these experiments has been that the K factor in the SNR equation, a factor related to the geometry of the RF coil, is typically taken to be ~ 1 and therefore ignored. However, because the ratio of SNR between the two field strengths uses two different RF coils with different geometries (solenoid vs. Helmholtz) the K factors may be different for the two coils, thus influencing the SNR results. The K factor can be more closely studied by looking at ratios of SNR at the same resonance frequency using the same spectrometer and sample but with two different RF coil geometries. Eq. 3.6 then becomes:

$$\frac{SNR_1}{SNR_2} = \frac{K_1}{K_2} \sqrt{\frac{Q_1 F_2}{Q_2 F_1}}. \quad (5.1)$$

Measuring both Q and F in the same fashion as described in Section 3.4.1, the K factors can be measured.

A third source of error in our results is the hyperpolarization factor, P , at 1.89 T. While all low field polarizations and experiments were performed inside the 85 G resistive magnet, high-field polarizations were performed in the fringe of the 1.89 T magnet and the samples then transferred to the bore of the superconducting magnet. Polarizations were not made inside the bore of the superconducting magnet as the geometry of the sample cell oven and the 1.89 T RF coil were not compatible. The time delay in transferring the sample and beginning signal acquisition allows for T_1

relaxation to occur, reducing the amplitude of the received signal by a factor e^{-t/T_1} , where t is the time delay. The time delay is small (no longer than 20 s) and the decay therefore on the order of $e^{-20/189} \sim 0.9$, i.e. a 10% reduction in signal. This is indicated by the different values of P in Table 4.1. While this potential correction to the SNR should, in theory, improve our results, it appears to worsen them. This could be accounted for in the previous arguments with regard to noise and the K factor, or simply the experimental uncertainty of our results.

As can be seen in the above discussion, the number of correction factors involved in comparing SNR between different samples, RF coils, field strengths, etc. does not allow for any immediate recognition of the matching of the theory to the SNR measurements. A quick check of any preliminary results can be made using the following argument.

Eq. 2.33 describes the signal-to-noise ratio for an NMR signal. It is given as:

$$SNR = K\eta M_0 \sqrt{\frac{\mu_0 Q \omega_0 V_c}{4FkT\Delta f}}. \quad (5.2)$$

Consider the ratio of SNR between the hyperpolarized and thermally polarized signals at a given field strength using a given sample. Assuming that the imaging system used for both the thermal and hyperpolarized experiments is the same, this ratio would reduce to a ratio of P factors:

$$\frac{SNR_{HP}}{SNR_{TH}} = \frac{P_{HP}}{P_{TH}}, \quad (5.3)$$

where P_{TH} is given by Eq. 2.15 and is linearly dependent on B_0 , while P_{HP} is independent of the field strength and is dependent on parameters related to the optical pumping and spin exchange of the nuclei in the polarization process (Eq. 2.61). From Eq. 2.33 we see that the field dependencies come from the M_0 , Q and ω_0 terms, as $M_0 \propto P$ and $Q \propto f_0 \propto B_0$. Since P_{TH} is proportional to B_0 we have:

$$SNR_{TH} \propto M_0 \sqrt{Q\omega_0} \propto B_0 \sqrt{B_0^2} = B_0^2. \quad (5.4)$$

Therefore the SNR of the thermal signal will be proportional to B_0^2 while the hyperpolarized system will have an SNR proportional to B_0 . This relationship can now be further simplified to:

$$\frac{SNR_{HP}}{SNR_{TH}} \propto \frac{1}{B_0}. \quad (5.5)$$

So for two different field strengths, $B_0^{(1)}$ and $B_0^{(2)}$:

$$\left(\frac{SNR_{HP}}{SNR_{TH}}\right)_{B_0^{(1)}} \left(\frac{SNR_{TH}}{SNR_{HP}}\right)_{B_0^{(2)}} = \frac{B_0^{(2)}}{B_0^{(1)}}. \quad (5.6)$$

We can therefore check the feasibility of our results by using the four SNR measurements from Table 4.3 in Eq. 5.6 and comparing to the ratio of field strengths. Using our results, the left-hand side of the equation is equal to 0.0014 ± 0.0003 , while the ratio of field strengths is equal to 0.0045. While these numbers are not the same, they are within an order of magnitude, providing further validation that the acquired signals are following the established theory.

The measured SNR for the low-field hyperpolarized ^{129}Xe experiments can be compared to similar experiments carried out by Wong *et al*[60] using ^3He . Wong reports an SNR of ~ 1700 . It is important to note that the definition of SNR for imaging purposes is typically taken as the spectral peak amplitude, not the integrated area as we have used, divided by the standard deviation of the noise. Area calculations are used to compensate for different T_2^* relaxation times for different signals which alter the shape and therefore the height of a spectral peak. Using this definition, our experiments yield a SNR of ~ 10000 at 1.89 T and ~ 500 at 85 G, within the same order of magnitude as Wong. As Wong was able to acquire an MR image with this SNR, such an agreement between results implies that imaging with our SNR results may be possible. In order to more properly determine the feasibility of hyperpolarized ^{129}Xe MR imaging, we must take a closer look at the minimum requirements for MR imaging. If we assume that the minimum signal-to-noise ratio

criteria for imaging is an SNR per voxel (typically a mm^3) of ~ 2 , then the SNR values recorded in Table 4.3 must be divided by a factor of $N^{3/2}$ for a two-dimensional image with an $N \times N$ field of view for each slice of the object imaged, where the N phase encodes act to signal average the image. Furthermore, because the signal is also non-replenishable and is depleted with each successive RF pulse, the SNR will usually be conserved through the use of a variable flip angle pulse sequence to produce a constant SNR per pulse. The SNR is thus decreased by a factor dependent on the number of RF pulses applied to the sample. Therefore, imaging sequences requiring few pulses or a single pulse should be the sequences of choice for hyperpolarized imaging. The best approach is to therefore decide upon a sequence that allows the least number of RF pulses and then to decide upon a spatial resolution necessary to obtain, at the very least, an SNR per pixel of ~ 2 .

Echo-planar imaging (EPI) is an imaging technique that uses a single 90° pulse to image a complete two-dimensional slice of an object. This sequence, while powerful, requires a long T_2^* in order to acquire the echos necessary for the image to form. As well, this sequence requires specialized NMR hardware designed for faster imaging. While still largely experimental, EPI shows much promise for the future of MR imaging, particularly in the area of real-time proton imaging. While real-time imaging would be considerably more difficult to perform with a non-replenishable magnetization, EPI, and sequences like it, offer a maximum use of the magnetization using only a single RF pulse. Assuming that T_2^* is long enough to implement EPI, a minimum spatial resolution, Δx , can be calculated based upon the minimum SNR desired per voxel. Consider that the region of homogeneity of the low-field magnet is $10 \text{ cm} = 100 \text{ mm}$. Therefore, the field of view may not exceed this limit without introducing significant image distortion. Assuming that a larger RF coil is built to accommodate a larger sample with similar electronic characteristics to produce a comparable, if not improved, SNR of ~ 500 , a spatial resolution of 1 mm^2 is selected

with 32 x 32 pixels (i.e. 32 mm x 32 mm FOV) and no slice selection we have an SNR of:

$$SNR = \frac{500}{32^{3/2}} = 2.76/\text{mm}^2, \quad (5.7)$$

which is very near to the minimum requirement for MR imaging. If a multiple pulse sequence is used this SNR must be further divided up by the number of pulses in the sequence, i.e. a ten pulse sequence will reduce the above SNR to 0.276. As the SNR estimate is already near the minimum required, any further reduction must be compensated for by decreasing the number of pixels used for the image or, if keeping a constant FOV is a concern, increasing the pixel size. Wong[60] uses the variable flip angle FLASH (Fast Low-Angle SHot) pulse sequence to measure the gas space of excised rat lungs. The FLASH sequence can utilize a flip angle between 0° and 90° but the selection of the angle and the repetition time, T_R , will alter the contrast of the image in connection with the T_1 relaxation time. Therefore, a greater flip angle than the one Wong uses, 12° , might not yield a better SNR. As with EPI, FLASH also requires a long T_2^* in order to acquire the number of echos necessary for an image to form.

Improvements in T_2^* are expected at low field strengths due to the interaction between the field and the magnetic susceptibility deviation, $\Delta\chi$. Assuming that the nonuniformity of χ is characterized by a Gaussian spatial distribution with mean χ_0 and standard deviation $\Delta\chi$, $\Delta\chi$ will cause decoherence for stationary nuclei precessing in the resultant varying fields, characterized as a contribution to T_2^* in the form:

$$\frac{1}{T_2^*} = \frac{1}{T_2} + \frac{\gamma\Delta\chi B_0}{2}. \quad (5.8)$$

Therefore, it can be seen that the decrease in B_0 leads to a decrease in the effects of magnetic susceptibility deviation, which include image distortion artifacts, thereby increasing the T_2^* to a value closer to T_2 . Further improvements to T_2^* can be obtained

by shimming the magnetic field as discussed above. This increase in T_2^* will also, for a given gradient strength, yield an increase in the optimum imaging resolution at low field strengths as described by Callaghan[78]:

$$\Delta x \propto \left(\frac{2}{\gamma G T_2^*} \right)^{3/2}. \quad (5.9)$$

Under the right conditions, as reported by Wong[60], this improvement in T_2^* can yield a resolution comparable to a high-field system. While increasing T_2^* is possible, it is ultimately limited by the T_2 relaxation time. T_2 is affected by diffusion and chemical exchange, which occurs when there is an exchange of the spin state between regions of different chemical shift resulting in no net loss of energy from the spin system, but a loss of phase information. As with the diffusion contribution to T_2 (Eq. 2.77), the chemical exchange contribution has a quadratic dependence on the static field:

$$\frac{1}{T_2^{CE}} \propto \gamma^2 B_0^2. \quad (5.10)$$

Therefore, T_2 will be longer at lower field strengths, thus providing further encouragement regarding the use of gradient echo pulse sequences such as EPI and FLASH.

Another imaging consideration is the construction of a larger RF coil to contain a larger sample. The increase in size of the coil will require a higher transmitter power (i.e. B_1) to drive the coil current and therefore will produce more noise in the signal. Also, due to the geometrical differences of the RF coil and the sample, such as a rat, the filling factor of the coil will be considerably lower than that of a glass cell. Therefore, while the larger sample will increase the SNR, the lower filling factor will contribute to a reduction in SNR. This will be countered by employing quadrature transmitting to reduce the amount of power necessary to excite the spins (i.e a lower B_1) and therefore increasing the SNR. The new coil should not be solenoidal, as loading larger samples would be clumsy and problematic, but instead a birdcage coil or saddle coil could be implemented. Both of these coil designs are commonly used

for larger sample MR imaging. The Q of the RF coil can also be increased (or the coil bandwidth decreased) to narrow the spectral linewidth to increase SNR (Eq. 2.57) up to the limit imposed by T_2^* . Our results show that the low-field RF coil had a much smaller Q than the high-field coil, a result of the high number of turns of wire used in the low-field coil which introduced a large resistance in the coil.

SNR can be increased by improving the noise figure of the preamplifier, possibly through the use of low-noise operational amplifiers or liquid nitrogen cooling. SNR improvements can also be produced through isotopic enrichment of the xenon and through increased gas pressures. However, these approaches to increasing SNR are problematic as xenon acts as an anesthetic at high concentrations and because biological systems such as lung spaces can only tolerate certain levels of gas pressure before becoming dangerous to the subject. While, logically, an increase in B_0 would improve the SNR, a factor of 2 improvement in the SNR would require an increase in the field strength by a factor of ~ 4 ($\text{SNR} \propto B_0^{1/2}$), which in turn requires a power increase of a factor of ~ 16 ($P \propto I^2 \propto B_0^2$), requiring a substantial upgrade in the power supply electronics. Improvements to the SNR can be made by increasing the polarization through optimization of the laser polarization time and cell temperature, and longer T_1 relaxation times (Eq. 2.61), i.e. by decreasing wall relaxation effects through the use of Surfrasil and the removal of impurities such as oxygen from the cell. Finally, acquiring on-resonance will ensure a maximum obtainable SNR as well as simplify flip angle calibrations. On-resonance signal acquisition will require the removal of the zero frequency artifact resulting from the DC offset in the transmitter. This can be corrected for electronically speaking, but fine-tuning the correction will involve post-processing. An algorithm must be developed to center the FID on the zero signal mark without having any set reference. Improvements such as these are currently being investigated.

Future work involving the low field system constructed will involve gas phase

imaging, as discussed above, starting with the sample cell used in these experiments. Imaging will require the use of gradient coils, a set of which have been provided but not yet implemented. Once the cell has successfully been imaged, larger, more complex samples will be considered, such as excised rat lungs and eventually a living rat. Beyond gas phase studies, dissolved phase MR imaging could be explored in blood plasma and suitable biologically compatible substitutes (such as PFOB) as described in Chapter 1. Such dissolved phase work is currently being carried out at 1.89 T in this laboratory. Relaxation studies for gas and dissolved phase imaging will be pursued in order to determine the amount of time available for xenon to diffuse into the bloodstream and to reach target organs (T_1), and to determine the allowable pulse sequences to be used (T_2). It is already known that T_1 is considerably shorter when dissolved in blood plasma, therefore severely limiting its targetability. However, the above arguments indicate that T_2 should be considerably longer at lower field strengths. A flow system for hyperpolarized ^{129}Xe is currently under construction for hyperpolarized experiments in our laboratory. Once finished, the system will be tailored towards maximizing its polarization factor through optimizing the polarization time, the cell Rb vapor temperature, and the gas flow rate. Such a flow system will also lead towards acquiring gas and dissolved phase images while employing signal averaging due to the constant replenishing of the hyperpolarized gas in the system of interest.

In closing, the SNR results obtained not only are a good match to the accepted theory but also, based on the discussion provided, indicate that a sufficient amount of SNR is available to generate a crude MR image. Image quality will only improve assuming that the recommended modifications to the low-field system are implemented, particularly the shimming of the magnetic coil and improved RF coil design. Transverse relaxation times promise to increase at lower field strengths offering the employment of gradient echo pulse sequences to minimize the loss of magnetization

through the use of sequences with few or a single RF pulse. Radiation damping, while not an issue in this work, will undoubtedly become one as the nuclear hyperpolarization increases and T_2^* lengthens. Based on these results and the vast amount of room available for their improvement, MR imaging of hyperpolarized ^{129}Xe at low magnetic field strengths (i.e. 85 G) is not only feasible, but highly likely to be successful.

Appendix A

Low-Field Polarimeter Modifications

The transmitter was modified from Saam's[74] to provide two carrier frequency reference signals for the quadrature phase detector. This can be seen in Figure A.1. An 8 MHz crystal oscillator is used here and divided by a factor of 4 using a 7473 flip-flop. Further division by a factor of 10 using 74HCT161 synchronous binary counters which output a 200 kHz signal to two separate 74HCT74 flip-flops results in the output of two separate orthogonal 100 kHz square wave signals, labeled Z1 and Z2. These signals are used as references for the quadrature phase detector shown in Figure A.2. The two signals trigger two separate MAX319 switches prior to the final amplification stage in the receiver. Note that the resistors on both output channels have been changed from Saam's values to accomodate the 50Ω input impedance of the SMIS.

Figure A.1: Modified transmitter circuit. An 8 MHz crystal is divided first using a 7473 divide by 4 circuit. Further division to 100 kHz is provided by 74HCT161 counters and 74HCT74 flip-flops, where two separate 100 kHz square wave signals are output (Z1 and Z2) 90° out of phase with each other for use as reference signals for the quadrature phase detector.

Figure A.2: Quadrature phase detection based on Saam phase detector[74]. The circuit is identical to Saam's with the exception of a second phase detection channel branching off from the first OP-27 amplifier. The reference frequencies used to signal the MAX319 switches are provided by the dual channel transmitter shown in Figure A.1.

Appendix B

Axial Symmetry in Magnetic Fields

Garrett[71] has given a complete discussion of the magnetic field produced by currents in a system of conductors with cylindrical symmetry. To describe the spatial variation of the field it is most convenient to use an expansion in spherical harmonics. The field is completely specified if the field along the axis of symmetry is known.

The coordinate system used to describe the system involves the use of both cylindrical (ρ, ϕ, z) coordinates and spherical (r, θ, ϕ) coordinates. Figure 3.2 illustrates both the axis and plane of symmetry that characterize the coordinate system. In certain situations there is also a plane of symmetry which is perpendicular to the axis of symmetry. In these cases it is convenient to take the intersection of the symmetry axis and the symmetry plane to be the origin of the coordinate system. To describe the magnetic field we shall use the components parallel to and perpendicular to the axis of symmetry. Thus we can write:

$$\vec{H} = H_z(r, \theta)\hat{k} + H_\rho(r, \theta)\hat{\rho}, \quad (\text{B.1})$$

where $\hat{k}$ and $\hat{\rho}$ are unit vectors parallel and perpendicular to the symmetry axis, respectively. Since the system of conductors is axially symmetric, the magnetic field will not be a function of the azimuthal angle ϕ .

It is convenient to use the scalar potential in expressing the fields due to axially symmetric systems. The potential inside a system of conductors with cylindrical symmetry is of the form:

$$V(r, \theta) = \sum_{n=1}^{\infty} \left(-\frac{H_{n-1}}{n} \right) r^n P_n(\cos \theta). \quad (\text{B.2})$$

It immediately follows from this potential function that the radial and axial fields are given by:

$$H_z(r, \theta) = \sum_{n=0}^{\infty} H_n r^n P_n(\cos \theta) \quad (\text{B.3})$$

$$H_\rho(r, \theta) = \sum_{n=0}^{\infty} \left(\frac{1}{n+1} \right) H_n r^n \frac{d}{d\theta} P_n(\cos \theta). \quad (\text{B.4})$$

As explained in Section 3.1, since $r = z$ when $\theta = 0$ and $P_n(1) = 1$, it follows that the field strength along the symmetry axis is given by:

$$H_z(z, 0) = \sum_{n=0}^{\infty} H_n z^n, \quad (\text{B.5})$$

where:

$$H_n = \frac{1}{n} \left[\left(\frac{d^n}{dz^n} \right) H_z(z, 0) \right]_{z=0} \quad (\text{B.6})$$

are the coefficients. This shows that the axial component and all of its derivatives at the origin define the field everywhere in the central region. This expansion is valid throughout a sphere centered at the origin with a radius extending from the origin to the nearest current-carrying conductor.

Inhomogeneity within the spherical region surrounding the solenoid center is best considered by examining the dependence of the field on θ . Since for any n the maximum value of $P_n(\cos \theta)$ is $P_n(1) = 1$, the variation of $H_z(r, \theta)$ as a function of r is greatest for $\theta = 0$, i.e. the components of the field parallel to the symmetry axis possess the greatest degree of nonuniformity along the axis. The maximum values of the various expansion terms of the radial field can be shown to be of the same order of magnitude as the axial components, but numerically smaller. As well, the radial

field will be of second order when considering only the magnitude of the field due to being added in quadrature to the axial component. Therefore, variations in the field along the symmetry axis are a good indication of the degree of homogeneity of the coil. Designing a coil for maximum homogeneity can therefore be accomplished using only Eq. B.5.

For the case of thin solenoids, as they are easier to accurately wind, Eq. B.5 can be written as Eq. 3.4, repeated here:

$$H_z(z, 0) = \frac{4\pi N_s I}{10 \cdot 2r_s} \left\{ 1 - \left[\frac{1 - u_s^2}{u_s} \right] \sum_{n=1}^{\infty} \frac{1}{2n} \left(\frac{z}{r_s} \right)^{2n} P'_{2n}(u_s) \right\}. \quad (\text{B.7})$$

Since there is a plane of symmetry passing through the origin perpendicular to the axis, there are no odd powers of z in this expansion. Eq. B.7 can therefore be rewritten as:

$$\begin{aligned} H_z(z, 0) = \frac{4\pi N I}{10} \cos \theta_s & \left[1 - \frac{3}{2} \sin^4 \theta_s \left(\frac{z}{a_s} \right)^2 \right. \\ & - \frac{5}{8} \sin^6 \theta_s (7 \cos^2 \theta_s - 3) \left(\frac{z}{a_s} \right)^4 - \frac{7}{16} \sin^8 \theta_s \\ & \left. \times (33 \cos^4 \theta_s - 30 \cos^2 \theta_s + 5) \left(\frac{z}{a_s} \right)^6 - \dots \right]. \end{aligned} \quad (\text{B.8})$$

where N is the number of turns per centimeter. The successive terms are referred to as zero order, second order, fourth order, etc. These terms can be removed by using correction windings, i.e. by winding additional coils with counter-rotating currents and angles θ_s such that higher order terms cancel. An example of a coil constructed with correction windings is given by Hanson[72]. Alternatively, if optimizing power consumption is an issue, as it was in our case, correction coils can be discarded (as they each require their own power supply) in favour of alternative coil designs. Split solenoid coils can be wound with less windings, less power and greater homogeneity than single solenoids. A split solenoid is considered as a solenoid with end turns at θ_{s1} minus a solenoid with end turns at θ_{s2} , as shown in Fig. 3.3. Therefore, by

selecting angles θ_{s1} and θ_{s2} such that $\cos\theta_{s1}\sin^4\theta_{s1} = \cos\theta_{s2}\sin^4\theta_{s2}$, second order terms can be reduced to zero. Calculations show that θ_{s1} must be less than 63° . In the limiting case when $\theta_{s1} = \theta_{s2} = 63^\circ$, the split solenoid becomes a Helmholtz pair. For the purposes of simplifying winding accuracy, a split solenoid design (not a Helmholtz set) was used. For optimum field homogeneity, Garrett's eight-order double Helmholtz coil arrangement should be used. For further information, see Garrett[71] and Franzen[73].

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