ASPECTS OF NMR IMAGING
AND IN VIVO SPECTROSCOPY

by

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We accept this thesis as conforming
to the required standard

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The work described in this thesis deals mainly with aspects related to two- and three-dimensional NMR imaging.

A detailed discussion on frequency-selective excitation using amplitude modulated rf pulses in relation to slice selection in NMR imaging has been presented. This includes the analysis and implementation of the method as well as illustrative experimental results.

Several radiofrequency probe designs suitable for high field NMR imaging have been experimentally evaluated and their modification and construction are also described. The comparative results obtained indicate the merits and demerits of different designs and provide necessary guidelines for selecting the most suitable design depending on the application.

Practical aspects of two- and three-dimensional imaging have been discussed and NMR images of several intact systems have been presented.

Experimental methods which enable slice selection in the presence of chemically shifted species and two-dimensional chemical shift resolved imaging have been described and illustrated using phantoms. The use of three-dimensional chemical shift resolved imaging as a potential method to map the pH and temperature distribution within an object has also been demonstrated.

A preliminary investigation of the application of $^{31}$P NMR spectroscopy to study the biochemical transformations of the rat kidney during periods of ischemia and reperfusion has been presented.
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CHAPTER I

INTRODUCTION
I. INTRODUCTION

1.1 Background

Since the first measurements in 1946 by Bloch, Hansen and Packard [1] and Purcell, Torrey and Pound [2], Nuclear Magnetic Resonance (NMR) has developed into a sophisticated technique with applications in a wide variety of disciplines which now include physics, chemistry, biology and medicine. Over the years it has proved to be an invaluable spectroscopic tool for chemical analysis, molecular structure determination and investigation of molecular motion in solids and liquids. This rapid progress of NMR spectroscopy into diverse research areas can be attributed to a number of innovations, of which the development of pulse Fourier transform (FT) techniques by Ernst and Anderson [3] is probably the single most important example. Use of pulse FT techniques considerably alleviates the problem of low sensitivity of the continuous wave (CW) method thereby enabling less sensitive nuclei (nuclei with low magnetogyratic ratio), and time dependent phenomena, to be studied. Additional impetus for the development of the technique was provided by both the advent of high-field superconducting magnets and advances in computer technology. More recently, new experimental concepts such as two-dimensional (2D) NMR spectroscopy [4,5] have led to methods for studying molecules of extremely high structural complexity, which only a few years ago would have been regarded as essentially impossible.

In its latest development, application of NMR to studies of living systems has attracted considerable attention from the biochemist and the
clinician alike. These studies have progressed along two parallel and perhaps complementary paths. Firstly, NMR can be used as a spectroscopic method to provide chemical shift information from selected regions within an object; such spectra from localized areas of living tissue provide valuable metabolic information which is directly related to the state of health of the tissue and can, in principle, be used to monitor its response to therapy. In the second area of application, NMR is used as an imaging method to map the spatial distribution of substances within an object; in the clinical context, this can provide anatomical information and also discriminate between some pathological tissues.

The use of NMR as an imaging technique, first demonstrated by Lauterbur in 1973 [6], has opened a completely new area of science. To describe the technique, Lauterbur coined the term "zeugmatography" from the Greek word 'zeugma', meaning 'that which joins together'. The term refers to the coupling of the radiofrequency (rf) magnetic field and the spatially defined magnetic fields by the object being imaged.

Similarly to that of any other imaging technique, the goal of NMR imaging is to generate a map of a heterogeneous object showing its three-dimensional structure. Towards this end, NMR imaging exploits the spatial variation of the NMR signal intensity or any other NMR parameter in the sample of interest. Since the nuclear magnetic resonance phenomenon depends on the interaction of nuclei placed in a polarizing magnetic field ($B_0$) with radiofrequency (rf) radiation, the spatial information can be encoded into the NMR signal by suitable manipulation of either the $B_0$ field or the rf field. This is accomplished by the use of spatially varying $B_0$ or rf fields i.e. field gradients. The use of
polarizing magnetic field gradients is straightforward and also is more easily implemented while the use of rf gradients is more complicated. Since the Larmor frequency of nuclei is a function of the polarizing magnetic field, application of a magnetic field gradient causes nuclei at different positions along the gradient direction to have different resonance frequencies. The encoding of spatial information in this manner was recognized as early as in 1951 by Gabillard, who investigated one dimensional distributions of the NMR signal \[7,8\]. Thus all imaging methods depend on the use of field gradients, in one form or another, to yield spatial information. This is in contrast to high resolution spectroscopic measurements, where a polarizing magnetic field of high homogeneity (at least 1 part in \(10^8\)) is essential.

Prior to Lauterbur's report of the first imaging experiment, the discovery by Damadian that the spin-lattice relaxation times (T1's) of cancerous tissue are longer than those of analogous healthy tissue \[9\] provided an early basis for hope that NMR might provide information of medical and biological value. Thus, immediately after the contribution by Lauterbur, several alternative imaging schemes were devised and demonstrated by other investigators. Many of these initial studies were conducted either on water filled phantoms (phantom = a sample fabricated with a specific spatial structure designed to test an imaging scheme or device) or small vegetable samples using modified conventional NMR spectrometers with restricted sample access of about 1-3 cm. The encouraging results provided by the early experiments prompted the development of large scale systems by several groups, and the first well resolved NMR images of the human head were published in 1980 \[10,11\].
Even though the quality of these images was poor compared to the current standards, these outstanding technical achievements generated widespread scientific and commercial interest. As a result, more recently, extremely high quality NMR images of clinical value have been obtained from all parts of the human body.

The current interest in the use of NMR as a spectroscopic tool to probe biological systems was stimulated by a study reported by Hoult et al. in 1974 [12]. This study demonstrated that high-resolution $^{31}$P NMR spectra could be recorded from freshly excised intact rat muscle. The predominant resonances in the spectrum were identified as due to the major phosphorus-containing metabolites adenosine triphosphate (ATP), phosphocreatine (PCr) and inorganic phosphate (Pi). Although experiments on a variety of organs and tissues soon followed, studies on intact animals or humans were hindered by the lack of both the experimental techniques to obtain NMR signals from a specific region (as opposed to the whole specimen), and magnets with large enough bore to accommodate the specimen. The former problem was solved by using a single loop of wire as the NMR coil. When such a coil (surface coil) is placed close to the object under study, only the signal from the region in the vicinity of the coil is detected. This technology was innovated and successfully applied by Ackerman et al. in 1980 to produce $^{31}$P spectra from the leg muscle and the brain of an intact rat [13]. This study signalled the dawn of "in vivo NMR spectroscopy" and is now widely employed to study the metabolic and physiological status of various organs and tissues both in small animals and in man.

Even though other methods to obtain spectroscopic information from
a specific region within a sample (localized spectroscopy) have been developed, surface coils are still most frequently employed because of their simplicity and ease of operation.

Early NMR imaging methods ignored the possible effects of different chemically shifted species on the imaging process. Since one chemical shift was not discriminated from another, these imaging methods produced 'composite' images of all chemical shift species present in the object; for example, $^1$H NMR images of human tissue reflect the spatial distribution of both the major $^1$H containing chemical species, water and fat. Since most of the early NMR imaging experiments were performed at a low field strength (~0.2T), presence of chemically shifted species did not pose a problem. However, it was soon obvious that the chemical shift effects would become important in $^1$H imaging at high fields (>1.5T), as well as in imaging of nuclei such as $^{31}$P and $^{13}$C. In addition to the complications of image distortion due to chemical shifts, the growing interest in in vivo spectroscopic information independently prompted the modification of existing imaging techniques to incorporate chemical shift as an additional dimension. With these modified techniques, in principle, it is possible to image each chemically shifted species separately or, conversely, to obtain spectroscopic information from a given spatial location. It has already been shown recently that images of single chemical shift species can be very useful clinically in certain situations [14]. These experiments, generically known as "chemical shift resolved" methods, bring together the separate themes of in vivo NMR imaging and spectroscopy to a common focus. A more detailed discussion of these techniques will be given in the subsequent chapters.
The noninvasive and apparently hazard-free nature of NMR inevitably led to its application in the study of many biological systems and man. Especially in clinical studies, NMR appears to combine the advantages of other clinical imaging modalities (X-ray, Ultrasound and Nuclear Medicine) without sharing their disadvantages [15,16]. Advantages of NMR imaging derive from the fact that it does not use ionizing radiation and that the observed signal is a function of many parameters such as, spin density, spin-lattice ($T_1$) and spin-spin ($T_2$) relaxation times, and flow. Parenthetically, it is worth noting that the measurement of blood flow rates by NMR was initiated by Singer [17] as early as in 1959. This gives the ability to obtain images having different contributions from the intrinsic tissue parameters such as $T_1$, $T_2$, diffusion and flow. As a result, excellent soft tissue contrast and pathological discrimination can be obtained by manipulation of experimental parameters without the need for administration of contrast media. A further desirable feature is the ability to obtain NMR images in any desired plane without reformatting the patient or equipment. This greatly facilitates the perception of three-dimensional anatomy over that obtainable from other imaging techniques.

Recent NMR imaging investigations have demonstrated favorable comparison with the existing imaging techniques, both in terms of data acquisition time requirements and spatial resolution [18]. Clinical studies using NMR scanners in 0.3-0.5T range and 0.8 x 0.8 mm spatial resolution, have demonstrated that NMR imaging is superior to X-ray computed tomography (CT) in imaging many pathological conditions in the brain and thorax [19]. Most imaging efforts to date have been concen-
trated mainly on imaging the proton (\(^1\text{H}\)) distribution (from water and fat) because of its high natural abundance in living tissues. However, the present trend toward higher magnetic fields will enable other nuclei to be studied in the future.

Comprehensive accounts on various aspects of NMR imaging and in vivo spectroscopy can be found in Refs. 20-22.

1.2 Goals and Format of This Thesis

Most of the original advances in NMR imaging technology were accomplished by a small number of specialized research groups using prototype systems. The subsequent interest generated in the commercial sector has, more recently, led to the availability of NMR imaging systems suitable for many different applications, and capable of producing high quality images.

In contrast to the present technology, at the time of the commencement of the studies described in this thesis, an integrated system suitable for imaging as well as for spectroscopy was not available. However, the high field superconducting magnet technology was sufficiently advanced that large bore magnets suitable for imaging of small animals and human extremities were being developed. The studies described in this thesis were prompted by the acquisition of one such magnet with 31 cm diameter horizontal room temperature bore and operating at a magnetic field of 1.89 T (80 MHz for \(^1\text{H}\)), together with a high resolution NMR console. Further contributing factors were the growing interest in this laboratory in NMR "chemical microscopy" [23], guided
by the initial experiences from a 270 MHz high resolution spectrometer, coupled with the possible implications for future applications of NMR methods which integrate spectroscopy with imaging.

This thesis concentrates on the areas of study undertaken by the author to implement various imaging and in vivo spectroscopic techniques using the above magnet and the high resolution spectrometer console.

Within this general framework, two particular aspects of imaging have been examined in detail and are described in Chapters III and V. These studies provided the necessary basic insight and also generated previously unreported experimental data. Further, this thesis also demonstrates novel experimental concepts and applications related to NMR imaging and in vivo spectroscopy.

The format of the thesis is as follows: Chapter II introduces the reader to the basic concepts of NMR imaging and currently used experimental schemes. Chapter III is devoted to frequency selective excitation in the context of slice selection. The demonstration of various imaging techniques and the applications of chemical shift resolved imaging forms the basis of Chapter IV. A detailed discussion and experimental evaluation of probes suitable for NMR imaging is presented in Chapter V. Finally, preliminary results of $^{31}$P spectroscopic studies of rat kidney in vivo are reported in Chapter VI. The reader will note that the necessary background material, where appropriate, is included at the beginning of each chapter.

Since this work was initiated, numerous academic and commercial groups have become active in these areas, and therefore, appropriate citations are included throughout this thesis.
References: Chapter I


17. J.R. Singer, Science 130, 1652 (1959); see also Ref. 16, Chapter 7.


CHAPTER II

NMR IMAGING TECHNIQUES
II. NMR IMAGING TECHNIQUES

In this Chapter, the reader is introduced to the different experimental methods that have been developed to perform NMR imaging. The different techniques vary in their approach to determine the NMR signal intensity from each volume element in a three dimensional object. Of these techniques, emphasis is placed upon the Fourier imaging methods due to their generality, widespread use and particular relevance to this study. In order to lay the foundation for the discussion to follow, some basic concepts are initially reviewed.

2.1 Basic Concepts

2.1.1 Pulse NMR

In this Section, a brief introduction to pulse Fourier transform NMR [1-3] is given to ensure that the reader has access to the relevant concepts.

Consider an ensemble of identical spin 1/2 nuclei placed in a static magnetic field $B_0$. From quantum mechanical considerations it is known that the spin 1/2 nuclei can exist in one of two energy states which differ in energy by $\Delta E$;

$$\Delta E = \frac{\gamma h B_0}{2\pi}$$  \hspace{1cm} 2.1
where, $\gamma$ is the magnetogyric ratio and $h$ is the Planck's constant. At thermal equilibrium, the nuclei are distributed between the two energy levels according to the Boltzmann distribution which ensures that a slight excess of nuclei are present in the lower energy state.

Although many features of NMR can be understood only by the quantum mechanical approach, most of the experiments referred to in this thesis can be adequately described by the semi-classical vector model.

In the semi-classical vector model, nuclei are represented by the nuclear magnetic moment vector $\mu$. In the presence of an external magnetic field $B_0$, the magnetic moment vectors of spin 1/2 nuclei take up one of two possible orientations with respect to the field (parallel or anti-parallel) corresponding to the different energy states. The individual magnetic vectors precess about $B_0$ with random phase, and at equilibrium, spins oriented parallel to the field $B_0$ are in slight excess over those opposing it (Fig. 2.1a). Therefore, if $B_0$ is considered oriented along the z-axis, it can be seen that the net magnetization $M_0$ due to all the spins at equilibrium, is aligned along the z-axis. The x and y components of the magnetization are individually averaged to zero due to random phase of the magnetic moment vectors. If this net magnetization is displaced from its alignment along the z-axis, it exhibits a precessional motion about $B_0$ due to the torque exerted by the external field (Fig. 2.1b). The angular frequency of precession $\omega_0$ is given by

$$\omega_0 = \gamma B_0$$  \hspace{2cm} (2.2)

and is known as the Larmor frequency.
Fig. 2.1: (a) Precession of individual magnetic vectors about $B_0$ at equilibrium. (b) Precession of nonequilibrium magnetization $M$ about $B_0$ in the laboratory frame. (c) Motion of $M$ in the rotating frame in the presence of $B_1$. (d) Precession of $M$ in the rotating frame following a $90^\circ$ pulse.
In an NMR experiment, the nonequilibrium magnetization $M$ (Fig. 2.1b) is created by the application of a rotating magnetic field $B_1$ in the transverse x-y plane. The frequency of rotation of $B_1$, $\omega_r$, is chosen to be near the Larmor frequency of spins in the radio frequency range. The maximum effect on the magnetization is achieved when the frequency of $B_1$ matches the Larmor frequency, corresponding to the resonance condition (i.e. $\omega_r = \omega_0$). In practice, the rotating $B_1$ field is obtained by applying an oscillating magnetic field (rf field) directed along a certain direction in the x-y plane. The oscillating field can be decomposed into two counter rotating components, and the field component with the same sense of rotation as the precessional magnetization is responsible for the creation of the nonequilibrium magnetization. The field component with the opposite sense of rotation has negligible effect, and therefore, is ignored [4].

The motion of the macroscopic magnetization $M$ in the presence of an applied magnetic field is most conveniently described by the Bloch equations [1,5] in a frame rotating at the same frequency $\omega_r$ as the $B_1$ field (see also Chapter III). In such a frame of reference, at resonance ($\omega_r = \omega_0$), the motion of $M$ is seen as a precession about $B_1$, and the angle of precession $\theta$ (flip angle) is given by

$$\theta = \gamma B_1 t_w$$  \hspace{1cm} 2.3

where, $t_w$ is the duration of $B_1$ (pulse length). Thus, if the rotating frame axes, denoted as $x'y'z$, are chosen such that $B_1$ lies along the $x'$ axis, the motion of $M$ is then in the $zy'$ plane (Fig. 2.1c). If the
pulse length $t_w$ is such that the flip angle $\theta$ is equal to $\pi/2$ (90° pulse), at the end of the pulse the magnetization will be aligned along the $y'$ axis.

The decay of the nonequilibrium magnetization to the equilibrium value is governed by the spin-lattice and spin-spin relaxation processes [1,2]. The first order time constants for these processes are referred to as $T_1$ and $T_2$ respectively. In the vector model, $T_1$ characterizes the exponential growth of the longitudinal magnetization $M_z$ to its equilibrium value $M_0$, while, $T_2$ denotes the decay constant of the transverse magnetization components $M_x$ and $M_y$ to their equilibrium values (zero).

Once the rf pulse is terminated, $M$ continues to precess about $B_0$ in the laboratory frame with an angular frequency equal to the Larmor frequency $\omega_0$. In the rotating frame, this precession is viewed as of frequency $\Omega_0 = \omega_0 - \omega_r$ (Fig. 2.1d). The frequency $\Omega_0$ is commonly referred to as the offset frequency or the resonance offset.

The transverse magnetization components, $M_x$ and $M_y$, in the rotating frame after the pulse can be expressed as,

$$M_x(t) = M_0 \sin \theta \sin \Omega_0 t \exp(-t/T_2)$$  \hspace{1cm} (2.4)

and

$$M_y(t) = M_0 \sin \theta \cos \Omega_0 t \exp(-t/T_2)$$  \hspace{1cm} (2.5)

Here, it should be noted that even though the rotating frame axes were denoted as $x'$ and $y'$, the magnetization components along these axes are expressed without the prime notation.
In pulse NMR, the signal is detected as a time variation of the voltage induced in a coil due to the precessing transverse magnetization [6,7]. This initial signal which is in the rf frequency range, is converted to a low frequency signal by phase sensitive detection with respect to the frequency of the rf pulse [6,7]. The signal after phase sensitive detection (free induction decay), except for a constant factor, corresponds to the time evolution of the transverse magnetization components in the rotating frame. In quadrature detection, both magnetization components $M_x$ and $M_y$ are detected, and therefore the complex output signal following a 90° rf pulse can be written as

$$S(t) = M_y + iM_x$$  \hspace{1cm} 2.6

and hence,

$$S(t) = M_0 \exp(i\Omega_0 t) \exp(-t/T_2)$$  \hspace{1cm} 2.7

where $i = \sqrt{-1}$.

Fourier transformation of the time domain signal $S(t)$ yields the frequency domain spectrum $S(\omega)$ given by

$$S(\omega) = M_0 (A(\omega) + iD(\omega))$$  \hspace{1cm} 2.8

where

$$A(\omega) = \frac{T_2}{1 + T_2^2(\Omega_0 - \omega)^2} \quad \text{and} \quad D(\omega) = \frac{T_2^2(\Omega_0 - \omega)}{1 + T_2^2(\Omega_0 - \omega)^2}.$$  

The real part of $S(\omega)$, $A(\omega)$, corresponds to a Lorentzian absorption line centered at frequency $\omega = \Omega_0$ while the imaginary part, $D(\omega)$,
corresponds to a dispersion line centered at $\omega = \Omega_0$.

In general, an organic molecule exhibits a range of resonance frequencies (different $\Omega_0$ values) due to chemical shift effects [2]. Thus the free induction decay consists of a superposition of a series of signals of different frequencies. These different frequencies are recovered by Fourier transformation.

2.1.2 Linear Magnetic Field Gradient

In NMR spectroscopy, the static magnetic field $B_0$ is homogeneous, corresponding to a single Larmor frequency defined by Eq. 2.2. Thus, conventional NMR techniques are inherently one dimensional in the sense that the signal absorption is measured as a function of angular frequency. As mentioned in Chapter I, spatial variation of the NMR signal can be induced by the use of static field gradients.

A magnetic field gradient represents a variation of the field with the spatial coordinate. A linear gradient [8] imposes a linear variation of the field with the spatial coordinate and can be represented as

$$\frac{dB}{de} = \text{constant} = G_e$$

where $e$ represents the spatial coordinates $x$, $y$ or $z$, and $B$ is the magnetic field. $G_e$ denotes the magnitude of the gradient along $e$. In practice, a gradient field (generated by the 'gradient coil') is superimposed on the static field $B_0$ which is along the z-axis. The magnetic
field components along the x and y axes generated by the gradient coils can be neglected since these are much smaller than the static field. Thus the magnetic field directed along the z-axis ($B_z$) in the presence of a gradient field $G_x$ is represented by

$$B_z(x) = B_0 + G_x \cdot x$$  \hspace{1cm} 2.10

and this is illustrated in Fig. 2.2a.

It should be noted that the field variation within a plane perpendicular to $G_x$ is zero and the magnitude of the field in that plane depends on the x-coordinate. Therefore in the presence of a gradient, planes of constant field strength are created perpendicular to the gradient direction.

Since the resonance frequency depends on the magnetic field, application of a magnetic field gradient causes the resonance frequencies to be dependent on the position according to

$$\omega_x = \omega_0 + \gamma G_x \cdot x$$  \hspace{1cm} 2.11

and the planes of constant field also become planes of constant resonance frequency. This fundamental relationship between the spatial domain and the frequency domain in the presence of a gradient forms the basis for NMR imaging.

It follows that the NMR spectrum obtained in the presence of a magnetic field gradient will show a distribution of resonance frequencies as given by Eq. 2.11. The spectral amplitude at each frequency
Fig. 2.2: (a) The variation of the magnetic field $B_z$ with the spatial coordinate in the presence of a linear field gradient $G_x$.
(b) The relationship between the spin density distribution of an object and the NMR spectrum in the presence of a gradient. (i) a single tube of water, (ii) two tubes.
will be proportional to the spin density in the corresponding constant frequency plane. Therefore the NMR spectrum of an object placed in a magnetic field gradient corresponds to the projection of the spin density within the object onto the gradient direction (Fig. 2.2b).

From Eq. 2.7, the total signal observed in the presence of a single gradient \( G_x \) after phase sensitive detection can be written as,

\[
S(t) = \int K \rho(x) \exp[i(\Omega_0 + \gamma G_x x) t] \exp(-t/T_2) dx \tag{2.12}
\]

where \( \Omega_0 \) is the offset frequency, \( \rho(x) \) is the projection of the spin density onto the x-axis, \( K\rho(x).dx \) is the magnetization in length dx and \( K \) is a constant. If the phase sensitive detection is performed with the Larmor frequency \( \omega_0 \) as the reference (i.e. \( \Omega_0 = 0 \)), and \( t << T_2 \), which allows the second exponential term to be neglected, then the right hand side of the Eq. 2.12 corresponds to the inverse Fourier transform of \( \rho(x) \). Thus the Fourier transformation of \( S(t) \) yields the spin density projection. More precisely, from Eq. 2.12 it can be shown that the spectrum obtained in the presence of a gradient corresponds to the convolution of the spectrum in the absence of the gradient with the scaled spin density projection according to the gradient strength employed.

Use of magnetic field gradients to produce projections of the object under investigation is a key concept in NMR imaging and, as will be seen later, manipulation of gradients in all three directions can provide the three dimensional spatial spin density of the object.
2.1.3 Evolution of Magnetization in the Presence of Gradients

The evolution of magnetization in the presence of a gradient can be readily visualized in the rotating frame. Consider the excitation of a sample by a 90° rf pulse followed by the application of a magnetic field gradient. The total magnetization from the sample immediately after a 90° pulse, directed along the x'-axis, will be aligned along the y'-axis (Fig. 2.3a). Under the influence of a gradient, the individual components of the magnetization corresponding to different positions in the sample will precess at different frequencies as given by Eq. 2.11. Thus, in the rotating frame, the magnetization will be seen to lose phase coherence (dephase) about the offset frequency $\omega_0$ (Fig. 2.3b). In practice, the dephasing of the magnetization will be due to the combined effects of both the gradient and the inhomogeneity of the static magnetic field $B_0$.

At this point it is appropriate to consider the possible ways of bringing the dephased magnetization back into focus (refocussing). These refocussing methods are commonly employed in imaging pulse sequences as a means of delaying the signal and observation of the same as an echo (see discussion on spin-warp imaging, Sec. 2.2.3). The refocussing of the dephased magnetization can be accomplished either by applying a 180° pulse (Fig. 2.4a) or by reversing the gradient (Fig. 2.4b) at a time $\tau_d$ after the 90° pulse. The former method is the familiar spin-echo technique, and is illustrated in Figs. 2.3a-d. Application of a 180° pulse along the y' axis rotates the magnetization components about the y' axis to their mirror image positions
Fig. 2.3: Evolution of magnetization in the rotating frame in the presence of a gradient. $\Omega_0 = \text{offset frequency}$, $\Omega_0 \pm \Delta \Omega = \text{frequency in the presence of a gradient}$ ($\Delta \Omega = \gamma G_x x$).
Fig. 2.4: Signal refocussing methods. (a) Creation of a spin-echo in the presence of a gradient. (b) Creation of a gradient-echo by the application of a negative gradient.
(Fig. 2.3c). At a time $\tau_r = \tau_d$ later, all magnetization components are refocussed along the $y'$ axis, leading to a signal in the form of an echo (Fig. 2.3d). It should be noted that, during this time, the dephasing due to the inhomogeneities of static magnetic field as well as the off-resonance effects (due to chemical shift) are also refocussed. In the second method, reversing the gradient has the effect of interchanging the precessional frequencies about the offset frequency $\Omega_0$ (Fig. 2.3e). Therefore, provided that the magnitude of the reversed gradient is the same as before, dephasing due to the gradient is refocussed at a time $\tau_r = \tau_d$. In the more general case the echo time ($\tau_e$) after the initial $90^\circ$ excitation is given by [9],

$$\int_0^{\tau_e} G(t) \, dt = 0 .$$

2.13

In the gradient reversal method, the static field inhomogeneities and the chemical shift effects are not refocussed (Fig. 2.3f) and thus the amplitude and the phase of the echo signal will be different from that obtained with the $180^\circ$ pulse. The echo signal obtained by gradient reversal is referred to as a gradient-echo in order to distinguish from the usual spin-echo.

2.1.4 Slice Selection Methods

An essential step in any imaging technique is to define an imaging
plane or a slice in a three dimensional object. In NMR imaging, this is accomplished by restricting the NMR response to a particular slice of the object. The underlying concepts of different slice selection methods are described in this section.

2.1.4.1 Selective Excitation

Slice selection using the selective excitation technique is achieved by applying a frequency-selective rf pulse in the presence of a linear magnetic field gradient [10]. As already discussed in Section 2.1.2, application of a field gradient causes the resonance frequency of the spins to be dependent upon the position according to Eq. 2.11. Uniform excitation of all these frequencies produces a continuous spectrum of resonance frequencies, and each frequency in the spectrum represents a plane of spins perpendicular to the gradient direction.

If the spins are subjected to an rf pulse with a narrow frequency spectrum, (frequency-selective pulse) instead of one with a broad range of frequencies (nonselective pulse), then only the spins with resonance frequencies within the narrow range of the rf spectrum will be stimulated. (Such an rf pulse consists of a low power amplitude modulated pulse.) This effectively excites a spatial plane (slice) of spins perpendicular to the direction of the gradient and the subsequent NMR signal is received exclusively from this plane.

The particular slice selected is determined by the direction of the applied field gradient and the frequency band excited by the pulse.
Different planes corresponding to a particular slice orientation can be excited simply by changing the rf pulse spectrum to encompass a different frequency range. The spatial thickness of the selected slice ($\Delta x$) is given by the equation

$$\Delta x = \frac{2\pi \Delta f}{\gamma G_x}$$

where $\Delta f$ is the frequency band-width of the pulse. For accurate selection of a spatial plane, uniform excitation of spins within the slice and negligible (zero) excitation outside the slice is needed. This requires an rf pulse which has a rectangular profile in the frequency domain.

Theoretical and practical aspects of frequency-selective excitation in the presence of a gradient are examined in Chapter III.

2.1.4.2 Other Methods

The oscillating field gradient method [11,12] of slice selection relies upon the application of a time-dependent linear field gradient. If an alternating gradient field of the form $(x-x_0)G_x \cos(\Omega_xt)$ is used, where $x_0$, $G_x$ and $\Omega_x$ are constants denoting position, gradient amplitude and frequency respectively, an alternating magnetic field is created everywhere in the sample except in the plane at $x = x_0$ (zero field plane or sensitive plane). Therefore, the resonance signals derived from
nuclei outside the sensitive plane are frequency modulated due to the time variation in the field while the signals from within the sensitive plane are time invariant. Signal averaging over the gradient time dependence removes the signal from everywhere except that from the sensitive plane [12].

Another approach involves the use of spatially dependent rf fields to selectively saturate all but a slice of spins in the sample [13]. Application of an rf field $B_1$, which has a cubic dependence upon the distance, saturates the magnetization as the sixth power of the distance [13]. This allows the selection of a plane of spins perpendicular to the spatial variation of the $B_1$ field and centered about the origin. The width of the selected slice is controlled by altering the functional dependence of $B_1$.

2.2 Imaging Methods

Since the inception of NMR imaging, several different imaging methods have been proposed. In the early developmental stages, the sequential-point and -line methods (see classification below) were prominently used due to their simplicity. But currently, these methods have been replaced by the superior Fourier imaging method which offers several advantages. Therefore for a description of the sequential-point and -line methods, the reader is referred to the early reviews on the subject [8,14]. In this section, a classification of the available methods as well as a detailed description of the Fourier imaging method
will be presented. The projection-reconstruction method is also described briefly due to its historical importance.

2.2.1 Classification and Sensitivity of Imaging Methods

2.2.1.1 Classification

NMR imaging techniques can be classified [15] into four groups depending on the type of the volume that is chosen for observation at any instant; i.e. a point, a line, a plane or a volume (Fig. 2.5). Consider that the sample volume to be imaged is divided into $n$ volume elements (voxels) along each axis. Thus $n^3$ independent values are required to fully characterize the sample volume and to construct a complete image. These values may be obtained from $N$ experiments where $N \leq n^3$. The number of experiments, $N$, necessary to obtain sufficient information for construction of the complete image depends on the technique used.

In the simplest type of imaging methods, each volume element is observed selectively by one of the $N$ experiments (Fig. 2.5a). Thus $N = n^3$, and these methods are termed as "sequential-point" techniques. Imaging methods known as the sensitive-point method [11] and the field focussing nuclear magnetic resonance (FORNAR) [16,17] belong to this category. These two methods differ in the procedure by which a particular volume element is defined for observation.

Alternatively, if all the volume elements along a selected line are
observed and resolved simultaneously (Fig. 2.5b), then $N = n^2$, and the technique is referred to as a "sequential-line" measurement. The multiple-sensitive-point [18] method, the line-scan method [19] and its variants [20,21] fall into this class.

In a 'sequential-plane' measurement, an entire plane of volume elements is observed simultaneously (Fig. 2.5c). In this case $N = n$. Simultaneous observation and resolution of all volume elements in a plane in a single experiment can be achieved by either the planar imaging method [22,23] or the echo-planar imaging method [24]. These
methods call for stringent demands on instrumentation. More familiar sequential-plane measurements require, for example, \( n \) experiments to resolve all the volume elements in a plane while observing the signal from the entire plane in all the experiments. Thus the total number of experiments \( N = n^2 \). Experimental techniques such as projection-reconstruction [25], Fourier imaging [26] and rotating frame zeugmatography [27] fall into this category.

In 'simultaneous (volume)' methods the NMR signal from the whole three-dimensional object is observed in every measurement (Fig. 2.5d). These methods are derived from the extension of the sequential-plane methods into three dimensions. Even though the three-dimensional version of the echo-planar method is theoretically possible, it has so far not been demonstrated. In this case, the total number of experiments required to completely characterize the entire object would be reduced to one. On the other hand, the three-dimensional versions of the projection-reconstruction and Fourier imaging methods have been implemented, but require \( n^2 \) separate experiments, while observing the signal from all the volume elements in all experiments.

2.2.1.2 Sensitivity

At this juncture, it is appropriate to discuss qualitatively the sensitivity of different techniques; i.e. this discussion ignores the differences in the data acquisition procedure in each method. A more rigorous analysis is given in Ref. 15. The relevant quantity for
comparison of sensitivities is the signal-to-noise ratio (S/N) achievable from a single volume element in a given time. Let the S/N obtained from a single volume element in a single acquisition be arbitrarily assigned to unity. Thus, if the signal from a particular volume element is accumulated by only one of the N experiments needed to fully characterize the image, the S/N in the final image will also be unity. This applies to sequential point and line methods as well as the planar (PI) and echo planar (EPI) imaging methods. The above case should be contrasted to the projection-reconstruction (PR) and Fourier imaging (FI) methods in which, each volume element is observed by n or n² experiments depending on the type of the experiment (sequential-plane or simultaneous) performed. Thus with PR and FI methods, the S/N in the final image will be proportional to \( \sqrt{n} \) or \( n \) \([28,29]\). The S/N and the total experimental time (\( T_{\text{tot}} \) of each method are tabulated in Table 2.1. The relative S/N when all the methods are performed for an equal duration \( n^3 T \), \( (S/N)^3 \), is given in the last row of Table 2.1. From this analysis it can be seen that the maximum sensitivity is produced by the simultaneous methods, and the decreasing dimensionality of the method produces progressively lower S/N. It should be emphasized that the sensitivity ratios given by this qualitative picture is altered significantly by the experimental procedure used \([15]\). This is especially true in PI which produces markedly lower S/N than other sequential plane and simultaneous methods \([15]\). But the general trend predicted by the above analysis is observed.

It is of interest to examine the relationship between the parameters such as resolution (the number of voxels in each dimension),
Table 2.1: Relative sensitivities of NMR Imaging Methods

<table>
<thead>
<tr>
<th></th>
<th>Sequential Point</th>
<th>Sequential line (1D)</th>
<th>Sequential Plans (2D)</th>
<th>Simultaneous (3D)</th>
</tr>
</thead>
<tbody>
<tr>
<td>S/N</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>$S/N \sqrt{n}$</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$T_{tot}$</td>
<td>$n^3T$</td>
<td>$n^2T$</td>
<td>$nT$</td>
<td>$n.(n.T)=n^2T$</td>
</tr>
<tr>
<td>$(S/N) \sqrt{n}$</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**PI** - Planar Imaging  
**EPI** - Echo Planar Imaging  
**PR** - Projection Reconstruction  
**FI** - Fourier Imaging  

$n$ - # of pixels in each dimension  
$T$ - average time for a single experiment (scan)  
1D, 2D, 3D - Dimensionality of the experiment
imaging time and S/N of the image. Consider that it is desired to improve the resolution by a factor of 2 in all dimensions, i.e. an object previously represented by \( n \times n \times n \) voxels is now defined by \( 2n \times 2n \times 2n \) voxels. The volume of each voxel in the high resolution image is reduced by a factor of 8 and hence the S/N obtained is also reduced by the same amount. Thus the time required to obtain the high resolution image with same S/N as in the low resolution image is increased by a factor of 64. In fact the imaging time increases as \( a^6 \) where, \('a'\) is the factor by which the resolution is increased. If it is merely desired to improve the resolution in the image plane while the same slice thickness is retained, the imaging time increases as \( a^4 \). In either case, the image acquisition time and the S/N are drastically affected by the increase in resolution.

2.2.2 Projection-Reconstruction Imaging [25]

As already seen in the beginning of this Chapter, the NMR absorption line shape in a magnetic field gradient corresponds to the spin density projection of the three-dimensional object in a direction normal to the gradient. In the projection-reconstruction method, a series of such projections of the object is obtained at different angles by changing the gradient direction with respect to the object (Fig. 2.6). These projections, taken together, uniquely define the shape of the object, and therefore an image of the object can be reconstructed by a suitable procedure. The problem of reconstruction of the shape of the
Fig. 2.6: Projection-Reconstruction method. The image is constructed by obtaining several one-dimensional projections of the object at different directions (indicated by arrows) defined by the field gradient (from Ref. 25).

Object from its projections is a general one, and a review of reconstruction methods can be found in Ref. 30. This method also forms the basis of the highly successful X-ray computed tomography pioneered by Hounsfield [31].

In Lauterbur's original experiment [25], projections of the object (2 tubes of water) at different angles were recorded by the CW NMR method by rotating the object with respect to the gradient direction. These projections were then subjected to a standard reconstruction
algorithm to generate the image. However, use of FT methods to record the projections offer significant advantages, and are generally used. In addition to the well known improvement in sensitivity, many of the analytic reconstruction methods require Fourier transforms of the projections to be calculated, and these are directly available as free inductions decays in the case of FT techniques. The Fourier projection-reconstruction imaging method represents the best method for attaining the maximum signal-to-noise ratio [15]. Moreover, reorientation of the gradient direction is preferred over object rotation and can be easily accomplished by changing the magnitudes of the gradient vector components. For a n x n pixel image, a number of projections of order n in π radians is required with each projection containing n points. Extension of this method into all three dimensions has also been demonstrated [32,33], but has the drawback of requiring powerful computing facilities to attain reasonable efficiency.

2.2.3 Fourier Imaging [26]

The Fourier imaging method represents an extension of the concept of two-dimensional NMR spectroscopy to provide spatial information. This method utilizes multi-dimensional Fourier transformations to construct the entire image without resorting to reconstruction algorithms. It offers considerable computational and experimental simplicity over the projection-reconstruction method. Further, the Fourier imaging method is less susceptible to magnetic field inhomogeneity and motional
artifacts [34], and also can be easily adapted in a variety of ways. These advantages outweigh the decrease in sensitivity compared to the projection-reconstruction method due to the fact that the signal is not observed during the entire available time [26], and thus has become the imaging method of choice.

In general, the Fourier imaging experiment consists of three time periods; preparation, evolution and detection (see Fig. 2.7). The preparation period consists of a delay time, during which the spin system is allowed to reach the equilibrium condition, followed by excitation of the magnetization in a suitable manner. During the evolution period, the nonequilibrium magnetization created during the preparation period is allowed to evolve in the presence of magnetic field gradients to encode spatial information. Finally, the detection period represents the acquisition of the signal under suitable conditions.

The basic experimental sequence proposed by Kumar et al. [26] for two-dimensional imaging (encoding of two spatial axes) is shown in Fig. 2.7. The sequence consists of a 90° pulse which excites all the spins in the plane, followed by the application of the $G_x$ gradient for a time $t_x$. At the end of this period, the $G_x$ gradient is switched off and the $G_y$ gradient is applied. The free induction signal is observed during $t_y$ in the presence of the $G_y$ gradient. The observed signal is then a function of both time periods, $t_x$ and $t_y$. The experiment is repeated for a series of $t_x$ values by incrementing $t_x$ by a constant amount. This generates a data matrix $S(t_x,t_y)$, which upon double Fourier transformation gives a frequency domain data matrix $S(\omega_x,\omega_y)$, corresponding to the
Fig. 2.7: The basic two-dimensional Fourier imaging sequence.

spatial distribution of the spins within the plane.

In order to understand the above sequence, consider the signal from a volume element located at spatial coordinates \( x,y \). In the presence of \( G_x \), the angular precessional frequency of the magnetization in the rotating frame is given by \( \Omega_x = \Omega_0 + \gamma G_x x \), where \( \Omega_0 \) is the offset frequency in the absence of the gradient. Thus, during \( t_x \), the transverse magnetization from the volume element at \( x,y \) acquires a phase
angle $\phi_x$ given by

$$\phi_x = (\Omega_o + \gamma G_{x\cdot x}) t_x .$$  \hspace{1cm} 2.15

Therefore the phase of the signal detected during $t_y$ reflects the position of the volume element along $x$.

During $t_y$, the precessional frequency is changed to $\Omega_y = \Omega_o + \gamma G_{y\cdot y}$, and the signal observed is therefore given by

$$S(t_x, t_y) = K \rho(x,y) \exp i \left\{ (\Omega_o + \gamma G_{x\cdot x}) t_x + (\Omega_o + \gamma G_{y\cdot y}) t_y \right\} \exp \left\{ -\frac{(t_x + t_y)}{T_2} \right\}$$  \hspace{1cm} 2.16

where $\rho(x,y)$ is the spin density at point $x,y$. The Fourier transformation of the data matrix $S(t_x,t_y)$ with respect to $t_y$ produces the data matrix $S(t_x,\omega_y)$, in which the resonance line is centered at $\omega_y = \Omega_o + \gamma G_{y\cdot y}$. The phase of this resonance line will be modulated depending on $t_x$ according to the Eq. 2.15. The frequency of this modulation is determined by Fourier transformation of $S(t_x,\omega_y)$ with respect to $t_x$. A cross-section parallel to the $t_x$ axis in the data matrix $S(t_x,\omega_y)$ at $\omega_y = \Omega_o + \gamma G_{y\cdot y}$ is described by

$$S(t_x,\Omega_o + \gamma G_{y\cdot y}) = K T_2 \rho(x,y) \exp i(\Omega_o + \gamma G_{x\cdot x}) t_x \exp (-t_x/T_2)$$  \hspace{1cm} 2.17

The Fourier transformation of this cross-section with respect to $t_x$ yields a resonance line at $\omega_x = \Omega_o + \gamma G_{x\cdot x}$. Thus, Fourier transformation of all the cross-sections through $S(t_x,\omega_y)$ yields the data matrix $S(\omega_x,\omega_y)$, in which the resonance line is centered at coordinates
\[ \Omega_0 + \gamma G_{x}x, \Omega_0 + \gamma G_{y}y. \]

From the above discussion it is clear that the position and the amplitude of the resonance line in the two-dimensional spectrum \( S(\omega_x, \omega_y) \) is directly related respectively to the spatial coordinates and the spin density of the volume element. Thus the data matrix \( S(\omega_x, \omega_y) \), derived from all the volume elements within the plane corresponds to an image of the plane. It should be noted that the spatial coordinates \( x \) and \( y \) were encoded into \( S(t_x, t_y) \) by making the phase and the frequency of the signal dependent upon the respective coordinates. Consequently, the respective gradients used for these functions are referred to as the phase-encoding and frequency-encoding gradients.

Several noteworthy aspects of this experiment with regard to the image obtained should be mentioned. First, the spatially encoded frequencies are dependent upon the offset frequency \( \Omega_0 \) in both dimensions. The consequence of this is that the images of different chemical shift species (i.e. different offset frequencies) are shifted with respect to each other by the corresponding chemical shift difference. Second, in a similar manner, the inhomogeneity of the static magnetic field \( B_0 \) also causes the resonance frequencies to be distorted in both dimensions over that imposed by the gradients [35]. Both these problems can be alleviated by the use of large enough gradient magnitudes so that the frequency dispersion due to the gradient \( \gamma G_{x}x \) and \( \gamma G_{y}y \) dominates over the chemical shift difference and the magnetic field inhomogeneity.
Spin-Warp Imaging [36]

A variation on the Fourier imaging procedure of Kumar et al. [26] is the spin-warp method [36]. In the method of Kumar et al., the phase-encoding of the signal was achieved by the application of a constant gradient over an incremented time period; i.e. the phase angle $\phi_x$ in Eq. 2.15 was varied by incrementing $t_x$. Alternatively, the same effect can be realized by the variation of the magnitude of the field gradient ($G_x$) while keeping the phase-encoding time $t_x$ constant. This forms the basis of the spin-warp method. Therefore, the basic spin-warp imaging sequence for a two-dimensional case consists of the same sequence shown in Fig. 2.7, except that the amplitude of $G_x$ is varied linearly in successive experiments while keeping the phase-encoding time period constant.

The basic spin-warp sequence can be analyzed in a similar manner as described previously for the method of Kumar et al. Assuming $G_x$ is used as the phase-encoding gradient, the initial data matrix, now represented by $S(G_x, t_y)$, is given by Eq. 2.16, and a cross-section parallel to the $G_x$ axis is given by Eq. 2.17, in which $t_x$ is a constant. Fourier transformation of Eq. 2.17 with respect to $G_x$ yields a resonance line centered at $\gamma x t_x$, reflecting the x-axis position of the volume element. This is independent of the resonance offset $\Omega_0$, and hence, the chemical shift. Thus, as a consequence of keeping the phase-encoding time period constant, in spin-warp imaging, the effects of chemical shift as well as of static magnetic field inhomogeneity are eliminated from the phase-encoding dimension. Distortions due to the static magnetic field
inhomogeneities will still be observed along the frequency-encoding dimension \( y \), but can be overcome by increasing the strength of \( G_y \). Furthermore, the sensitivity of the spin-warp method is significantly different from the method of Kumar et al. [26] since the signal is sampled during a fixed time period. This sensitivity factor can be derived in combination with the analysis presented elsewhere [28,29,37], and can also be seen by inspection of Eq. 2.17. When \( t_x \) is constant (\( G_x \) variable, spin warp method), Eq. 2.17 represents a constant amplitude sinusoidal wave, whilst when \( t_x \) is the variable (method of Kumar et al. [26]) it represents an exponentially damped sine function. Since the peak intensity of a frequency domain signal is proportional to the area under the corresponding time domain signal [37], Fourier transformation of Eq. 2.17 in the spin-warp case produces a signal of higher amplitude. In practice, the sensitivity achieved will be lower than the maximum due to apodization\(^1\) of the signal to avoid undesirable line shapes [29] and the finite value of the phase-encoding period. A more subtle sensitivity loss mechanism which is present in both methods has been analyzed recently [38]. Further, the variation of the amplitude of \( G_x \) allows the maximum use of the available gradient strength, since both the positive and negative gradient magnitudes can be used to sample the Eq. 2.17.

The complete spin-warp sequence used in practice for two-dimensional slice imaging derives from that shown in Fig. 2.8 [36]. In Fig. 2.8, the gradients and the different time periods have been named according to their functions during the sequence, and the rf pulse is drawn so as to indicate that it is amplitude modulated. During the

\(^1\) Multiplication of the signal by a weighting function [2].
Fig. 2.8: The complete spin-warp imaging sequence for two-dimensional slice imaging.
slice selection period, a slice in a three-dimensional object is excited by applying a frequency-selective rf pulse in the presence of a gradient (G-slice). In the phase-encoding period, all three gradients are applied to accomplish specific functions. The application of the negative G-slice gradient refocusses the magnetization which dephased during the rf pulse (see Chapter III). The negative read-gradient (G-read) dephases the magnetization along the frequency-encoding direction which is subsequently refocussed by the application of a positive read-gradient during the detection period. This enables the signal to be observed as an echo after the read-gradient has stabilized, and avoids the possible signal distortion due to the finite gradient rise time if it was observed as a free induction decay. The G-phase gradient, which is incremented in successive experiments, encodes the spatial distribution of spins along the phase-encoding direction.

During the phase-encoding period, time-dependent gradients are normally used to avoid both the distortions due to eddy current effects and the technical difficulties involved in generating constant amplitude gradient pulses. For obvious reasons, the time dependence of the gradients usually takes the form of a half-sine-wave. It should be noted that profiling the gradient magnitudes in this manner demands considerable additional hardware and software controls.

Since the acquired data matrix $S(G_x, t_y)$ is sampled at specific values of $G_x$ and $t_x$, the maximum spatial distance (field-of-view) represented in the final image is determined by the sampling rate [2]. In order to prevent fold-over\(^1\) [2], the field-of-view should be slightly greater than the dimensions of the object. The field-of-view (FOV) in

\(^1\) Misrepresentation of frequencies due to inadequate sampling.
the phase-encoding (PE) and frequency-encoding (FE) dimensions are related to the experimental parameters via,

\[
(\text{FOV})_{\text{PE}} = \frac{2\pi}{\gamma(\Delta G_p)t_p} \quad \text{and} \quad (\text{FOV})_{\text{FE}} = \frac{2\pi}{\gamma G_r(\Delta t)}
\]

where \(\Delta G_p\) is the phase-encoding gradient increment, \(t_p\) is the phase-encoding period, \(G_r\) is the magnitude of the read-gradient, and \(\Delta t\) is the time between two sampled points in the digitized signal (dwell time).

In the case where the phase-encoding gradient is time-dependent, the \((\text{FOV})_{\text{PE}}\) is given by

\[
(\text{FOV})_{\text{PE}} = \frac{2\pi}{\gamma G_0}
\]

where \(\int_0^{t_p} G_p(t) \, dt = G_0 \cdot n\), and \(n\) is an integer. The phase-encoding gradient magnitude is determined by the value of \(n\) which is varied as \(-N/2, -N/2 + 1, \ldots, -1, 0, +1, \ldots, N/2 - 1\), where \(N\) defines the total number of gradient increments. The value of \(N\) is important for two reasons. It determines the spatial resolution obtained in the phase-encoding dimension given by \((\text{FOV})_{\text{PE}}/N\), and also the total imaging time given by \(TR \cdot N\), where \(TR\) (repetition time) is the time duration between individual experiments. Therefore, higher spatial resolution [smaller \((\text{FOV})_{\text{PE}}/N\)] along the phase-encoding dimension calls for proportionate increase in imaging time. Similarly, the spatial resolution along the frequency-encoding dimension is given by \((\text{FOV})_{\text{FE}}/N_1\), where \(N_1\) is half the number
of sampled points in the digitized signal.

Extension of Fourier imaging methods into three dimensions involves the use of two phase-encoding gradients and a frequency-encoding gradient [26, 39-41]. Since all combinations of the two phase-encoding gradient magnitudes need to be sampled, the total experimental time increases to $TR.N_x.N_y$ where $N_x$ and $N_y$ are the number of phase-encoding gradient increments in the respective dimensions. In the spin-warp method both phase-encoding gradients can be applied simultaneously and therefore the total duration of a single sequence is unaltered. This is not possible with the method of Kumar et al. [26]. Further details of the three-dimensional spin-warp sequence are presented in Chapter IV.

2.2.4 Chemical Shift Resolved Imaging

Imaging techniques discussed in the preceding sections ignore the presence of chemically shifted species, and pertain only to the encoding of the spatial spin distribution into the frequency domain. This, apart from the degradation of the image quality, causes the loss of chemical shift information present within the object under investigation. Chemical shift resolved imaging methods preserve this information by enabling each chemically shifted species to be imaged separately.

The original methods proposed for chemical shift resolved imaging were based on the projection-reconstruction method [42-44]. These approaches [43,44] require the magnitude of the field gradient to be sufficiently low so that the frequency spread of the resonances caused
by the gradient is smaller than the chemical shift separation. This represents a serious limitation, since the decreased gradient magnitudes also limit the achievable spatial resolution and hence preclude the general applicability of the technique. More recently, a method in which the intrinsic chemical shift can be used as a component of the magnetic field gradient in conjunction with the projection-reconstruction method has been proposed [45,46].

A chemical shift imaging method which employs rf field gradients instead of static magnetic field gradients has also been suggested [47]. This method, which is based on the principle of rotating frame zeugmatography [27], has been demonstrated using the inherent rf field gradients produced by a surface coil [48].

The most generally applicable method developed for chemical shift resolved imaging [49-54] derives from the spin-warp imaging technique. The basic sequence which enables one-dimensional mapping of chemically shifted species is shown in Fig. 2.9. The important feature of this experiment is that the signal is acquired in the absence of magnetic field gradients. This enables the chemical shift spectrum to be directly observed. The spatial distribution of the chemical shifts is encoded into the observed signal by the application of the phase-encoding gradients prior to signal acquisition. In practice, the sequence shown in Fig. 2.9 is modified so that the signal is observed as an echo by the application of a 180° pulse at the end of the phase-encoding period.

The initial data matrix $S_k(G_x, t_2)$, obtained from a volume element containing a chemical shift species $k$ defined by the angular frequency
Fig. 2.9: The basic chemical shift resolved imaging sequence.

\[ \Omega_k \text{ is given by} \]

\[ S_k(G_x,t_2) = K \rho_k(x) \exp \left\{ i \left( \Omega_k + \gamma G_x . x t_x + \Omega_k t_2 \right) \exp \left\{ -\frac{(t + t_2)}{T_{2k}} \right\} \right\} \]

where \( t_2 \) represents the signal acquisition time in the absence of any gradients.
Fourier transformation of the data matrix $S_k(G_x, t_2)$ with respect to $t_2$ and $G_x$ yields the two-dimensional spectrum $S(\omega_x, \omega_2)$, where $\omega_x$ and $\omega_2$ correspond purely to the spatial axis and the chemical shift respectively.

At this point it is appropriate to note that the chemical shift resolved experiment also provides a convenient means of mapping the distribution of the static magnetic field [55-57].

Extension of the experiment to incorporate all spatial dimensions involves simultaneous application of three phase-encoding gradients. This corresponds to a four-dimensional experiment. The total imaging time for such an experiment is given by $TR.N_xN_yN_z$ and is not affected in first order by the signal acquisition time. Therefore in situations where low spectral resolution along the chemical shift dimension can be tolerated, the total imaging time can be decreased by phase-encoding the chemical shift prior to signal detection [58,59]. In this case the imaging time is given by $TR.N_xN_yN_\delta$, where $N_\delta$ governs the spectral resolution along the chemical shift dimension leading to a reduction in the imaging time by a factor of $N_z/N_\delta$.

Another approach to chemical shift resolved imaging is via selective excitation or suppression of specific resonances. This offers a considerable saving in experimental time since the dimensionality of the experiment is reduced by one. A detailed discussion of this technique is presented in Chapter IV.
References: Chapter II


CHAPTER III

FREQUENCY-SELECTIVE EXCITATION IN NMR IMAGING
III. FREQUENCY-SELECTIVE EXCITATION IN NMR IMAGING

Several possible techniques that can be employed to define the spatial plane (slice) to be imaged were introduced in Chapter II, Section 2.1.4. Of these, the most widely used method is that of selective excitation in the presence of a magnetic field gradient [1-6]. This method has the advantage that it can be implemented more conveniently than the other techniques and the definition of the slice selected is also superior. In this Chapter, the theoretical and experimental considerations as well as the implementation of this technique is described. Further, a novel method to eliminate problems associated with slice selection in the presence of chemically shifted species is proposed, and its feasibility is also demonstrated.

3.1 Technique of Slice Selection

3.1.1 Theory of Selective Excitation

Selective excitation of a narrow frequency band in the context of slice selection in NMR imaging is equivalent to a similar problem encountered in NMR spectroscopy, where the excitation of a group of chemically shifted resonances, while not perturbing others, is desired for various purposes. These include solvent suppression for improved dynamic range, reducing complexity of crowded spectra by spin decoupling
and selective excitation in population transfer, chemical exchange, and relaxation experiments [7]. Thus, early studies done in relation to spectroscopy [8-11] provide the necessary background to the methodology that can be employed.

The exact spin magnetization excitation pattern due to an rf pulse in general can be determined by considering the Bloch equations [12,13] which describe the motion of magnetization under the influence of a magnetic field. However, the form of the time domain rf excitation needed to achieve a certain frequency domain excitation pattern is not immediately obvious via the Bloch equations. Therefore, initially it is helpful to consider the problem in terms of the linear systems approach [14,15] in the frequency domain.

3.1.1.1 Linear Systems Approach [14,15]

Consider the response of a linear system subjected to a driving function (input) \( I(t) \) (Fig. 3.1). The response from the system \( R(t) \) is given by the convolution of the driving function, with the system impulse response function \( H(t) \).

\[
R(t) = H(t) \ast I(t) \tag{3.1}
\]

Using the convolution theorem [16] Eq. 3.1 can be written in the frequency domain as,

\[
R(f) = H(f).I(f) \tag{3.2}
\]
Fig. 3.1: Relationship between the input and output of a linear system characterized by \( H(t) \) and \( H(f) \).

where \( I(f) \) and \( R(f) \) are the frequency domain driving function and the response respectively, and \( H(f) \) is the transfer function of the system. \( H(f) \) completely describes the system in the frequency domain just as \( H(t) \) does in the time domain. If the driving function \( I(t) \) is an impulse (a delta function), then \( I(f) \) is a constant, since \( I(f) \) is the Fourier transform of \( I(t) \). In this case, the time and frequency domain response functions, \( R(t) \) and \( R(f) \) correspond to the system impulse response function and the transfer function, \( H(t) \) and \( H(f) \) respectively. Thus the measurement of the system response to an impulse gives all the necessary information to completely characterize the system. Further, from Eq. 3.2, it can be seen that the response of a linear system in the frequency domain is proportional to the Fourier transform of the driving function.
If the response of a spin system to an NMR experiment is considered linear, the system transfer function corresponds to the "NMR spectrum", and the impulse response function corresponds to the free induction decay signal observed following a narrow rf pulse. With a narrow rf pulse, the frequency domain driving function $I(f)$ is essentially flat over the transfer function $H(f)$ and therefore the frequency domain response $R(f)$ corresponds directly to the NMR spectrum. This situation, shown in Fig. 3.2, represents the conditions normally encountered in NMR spectroscopy.

Fig. 3.2: Normal NMR experiment viewed in terms of the transfer function of the spin system.
It has been shown that, subjected to certain restrictions (see Section 3.1.1.2), the transverse magnetization ('response' of the spin system) created by an rf pulse of arbitrary shape (in the time domain) is directly proportional to the Fourier transform of the pulse [7] i.e. that Eq. 3.2 is valid. The inverse of this relationship can be used to produce the pulse sequence (or pulse modulation) necessary for a desired excitation pattern. The method based on this concept is known as the "synthesized (tailored) excitation" technique [10,17]. The ready conceptual link provided by the Fourier transform relationship between the excitation spectrum and the pulse modulation can be used in qualitative analysis and design of frequency-selective excitation schemes.

From the above discussion it is clear that frequency-selective excitation of the magnetization can be obtained most simply by making the frequency spectrum of the driving function narrower than the transfer function. In the case of a uniform distribution of spins along a magnetic field gradient in the context of slice selection, the transfer function is essentially a constant. Thus the frequency response of the spin system corresponds directly to the frequency spectrum (Fourier transform) of the pulse (Fig. 3.3). As a result, any desired frequency excitation pattern can be obtained by changing the shape of the rf pulse.

At this juncture it is appropriate to note an interesting aspect of this selective excitation scheme that has been discussed in the literature [18,19]. The direct correspondence between the frequency domain driving function and the system response in the case of a constant transfer function implies that the respective time domain functions also
have the same relationship; i.e. the response $R(t)$, is the same as the driving function $I(t)$. Therefore, since the NMR receiver is normally gated off during the application of the pulse, the primary response of the spin system cannot be observed and negligible signal will be detected after the pulse [18,19]. The physical interpretation of the

Fig. 3.3: Selective excitation experiment viewed in terms of the transfer function of the spin system.
above argument is that the different frequency components of the magnetization acquire different phase angles during the pulse. Thus, if the frequency components are completely dephased at the end of the pulse, no net signal can be detected. The dephased magnetization can be refocused either by reversing the gradient direction or by applying a nonselective 180° pulse immediately following the selective pulse [18,19]. Further, the shape of the echo formed after the gradient reversal (or 180° pulse) closely resembles the applied pulse [19], and at the maximum of the echo all magnetization components have approximately the same phase [21,23].

A driving function with a narrow frequency distribution is most conveniently obtained by a long weak rf pulse ('soft pulse'). This corresponds to a rectangular modulation of the pulse. Since the resonance signal resulting from an rf excitation pulse is detected with a phase sensitive detector using the rf carrier frequency as the reference, the rf carrier frequency may therefore be ignored in the analysis: i.e. the signal observed represents the behaviour of the spin system in a frame rotating at the rf carrier frequency. The rectangular modulation function and its Fourier transform are shown in Fig. 3.4a.

The principal frequency band-width of a rectangular modulation is given by $2/\tau$, where $\tau$ is the time duration of the modulation (pulse width). The amplitude of the pulse ($B_1$) is adjusted to obtain a 90° flip angle according to the relationship $\pi/2 = \gamma B_1 t_w$, where $t_w$ is the pulse length. Soft rf pulses are commonly used in NMR spectroscopy [20] but are not suitable for slice selection in NMR imaging because of the secondary excitation lobes on either side of the primary frequency band.
Fig. 3.4: Rf modulation functions and their Fourier transforms.

(see Fig. 3.4a). These side lobes result in excitation of magnetization in regions other than the desired plane.

An rf modulation function more suitable for NMR imaging applications takes the form of \((\sin \omega t)/\omega t\) [or sinc \(\omega t\)] which, together with
its Fourier transform, is shown in Fig. 3.4b. A sinc function extending for an infinite time has a well defined rectangular frequency spectrum but cannot be realized in practice. Therefore, a sinc function truncated over a finite time interval is commonly used; the effect of this truncation on the excitation spectrum is shown in Fig. 3.5. Abrupt termination of the function causes high frequency components on either side of the principal excitation band as well as uneven intensity within the principal excitation. The trend towards the theoretical limit with increasing width of the sinc function is clearly shown in Fig. 3.5.

The excitation spectra shown in Fig. 3.5 can be improved by apodizing the truncated sinc envelope with either a Gaussian or a triangular function [21]. The effect of any apodization function is to decrease the intensity outside the main excitation band and to produce a more uniform intensity within it. An example of this when using a triangular apodization function is shown in Fig. 3.6. It has been shown that the triangular apodization performs better than the Gaussian apodization [21]. A necessary consequence of apodization is the decrease in the sharpness of the edge definition of the principal band compared to unapodized case.

The phase of the frequency components in the excitation spectrum has not been addressed in this discussion. This is easily incorporated by considering both the real and imaginary parts of the Fourier transformed function when the time origin is taken at the beginning of the pulse (see Section 3.1.1.3, Eq. 3.16 and 3.17).
Fig. 3.5: Effect of truncation of the sinc modulating function on the excitation spectrum. Plots were obtained by Fourier transforming a sinc function (period = 1.8 ms) of varying length. The number of secondary lobes in the sinc function is indicated in the Figure.
Fig. 3.6: Effect of triangular apodization of the sinc function (period 1.8 ms) on the excitation spectrum. Plots were obtained by Fourier transforming the time domain function shown alongside each excitation spectrum. The triangular function was defined by the amplitude and the length of the sinc function. (a) unapodized case, (b) sinc x (triangle), and (c) sinc x (triangle)^2.
3.1.1.2 Effects of Nonlinear Behaviour of Spins

From the discussion in the preceding section it is clear that considerable insight to the problem of selective excitation can be obtained by considering the linear response methodology. However, the arguments presented are strictly valid only when applied to linear systems. The response of a spin system to an rf pulse as governed by Bloch equations, is nonlinear, and hence, the results from linear systems theory are not always applicable. Nevertheless, linear approximation can be used to predict the frequency response of the spins to an rf pulse, provided that the excitation time is short compared to the spin-lattice and spin-spin relaxation times, and also that the net perturbation at any frequency is small (i.e. small flip angles) [7,22]. It has been shown that the prediction of transverse magnetization (frequency response) via linear approximation is valid for rf pulses up to flip angles of 30°, and the departure from linearity becomes most apparent at flip angles close to 180° [18,22,23]. In the latter situation, analysis of the Bloch equations should be considered for accurate results.

An obvious modification to the linear approximation theory is to consider the flip angle, rather than the transverse magnetization, as being proportional to the Fourier transform of the pulse [5,22]. This enables the flip angle as a function of frequency, $\theta(\omega)$, to be expressed as

$$\theta(\omega) = \gamma B_1(\omega)$$ 3.3
where $\hat{B}_1(\omega)$ is the Fourier transform of the pulse $B_1(t)$. Then the transverse and longitudinal magnetization components ($M_{xy}$ and $M_z$ respectively) after the pulse are given by

$$M_{xy}(\omega) = M_0 \sin(\gamma \hat{B}_1(\omega))$$

and

$$M_z(\omega) = M_0 \cos(\gamma \hat{B}_1(\omega))$$

where $M_0$ is the equilibrium magnetization. This has been studied [22] in detail for the case of 180° sinc pulse, and it has been shown that the deviation of the spin response from linear approximation becomes apparent when the flip angle is large and the spins are not on resonance.

It has been shown [19] that in the presence of a gradient, an NMR signal can be observed immediately after a selective pulse only when the spin system is driven into the nonlinear region (i.e. flip angle $>30^\circ$). This response is a direct manifestation of the nonlinearity of the spin system and bears only a distant relationship to the primary response which occurs during the pulse. Both responses can be visualized by echo formation as mentioned earlier. A detailed account of this is given in Ref. 19.

3.1.1.3 Analysis of Bloch Equations

Since NMR experiments are routinely performed in the nonlinear
region, it is mandatory that solution of Bloch equations be considered to determine the exact excitation pattern. In order to lay the foundation for the discussion to follow, the motion of magnetization under the influence of a magnetic field will be briefly discussed [12,13].

Consider the net macroscopic magnetization $M$ of an ensemble of nuclear spins in a static magnetic field $B_0$ aligned along the $z$-axis in the laboratory frame. At equilibrium, the magnetization ($M_0$) is oriented along $B_0$. From classical considerations [24,25], the motion of magnetization $M$ in a magnetic field $B$ can be written as,

$$\frac{dM}{dt} = \gamma M \times B \quad \text{3.6}$$

In general, $B$ in Eq. 3.6 consists of both the static magnetic field $B_0$ aligned along the $z$-axis, and the rotating magnetic vector of the rf field $B_1$ in the $x$-$y$ plane. If the motion of the magnetization is viewed from a frame rotating about the $z$-axis at the same frequency ($\omega_r$) and sense as the $B_1$ field, the equation of motion becomes

$$\left( \frac{\partial M}{\partial t} \right)_{\text{rot}} = \gamma M \times B_{\text{eff}} \quad \text{3.7}$$

where

$$B_{\text{eff}} = (B_0 - \frac{\omega_r}{\gamma})k + B_1i \quad \text{3.8}$$
The rotating frame axes \((x',y',z)\) has been chosen so that the \(B_1\) lies along the \(x'\)-axis of the rotating frame, and \(\mathbf{i}\) and \(\mathbf{k}\) are the unit vectors in that frame.

\[
B_{\text{eff}} = bk + B_1i \tag{3.9}
\]

where

\[
\gamma b = \omega_0 - \omega_r \tag{3.10}
\]

in which

\[
\omega_0 = \gamma B_0. \tag{3.11}
\]

Thus, from Eq. 3.7, the motion of the magnetization \(M\) in the rotating frame follows a cone of precession about \(B_{\text{eff}}\). This is sketched in Fig. 3.7. It can be easily seen that when the frequency of the rf field \(\omega_r\) equals the Larmor frequency of spins \(\omega_0\) ("on-resonance" condition), the motion is in the \(z-y'\) plane of the rotating frame whilst the motion of the off-resonance magnetization \((\omega_0 \neq \omega_r)\) is in a tilted plane determined by \(B_{\text{eff}}\). This approach is useful when considering a rf pulse of constant amplitude \(B_1\). When \(B_1\) is time dependent this elementary picture may not be employed to advantage since the angle \(B_{\text{eff}}\) makes with the \(x\)-axis varies in time, and it is therefore difficult to see how the magnetization precesses about such a field.

From Eqs. 3.7 to 3.11, the Bloch equations [25] in the rotating frame including relaxation terms can be derived as
Fig. 3.7: Precession of spin magnetization about $B_{\text{eff}}$ determined by the offset $b$ and $B_1$.

$$
\frac{dM_x}{dt} = \Delta \omega \cdot M_y - \frac{M_x}{T_2} \quad 3.12a
$$

$$
\frac{dM_y}{dt} = -\Delta \omega \cdot M_x + \gamma B_1(t) \cdot M_z - \frac{M_y}{T_2} \quad 3.12b
$$

$$
\frac{dM_z}{dt} = -\gamma B_1(t) \cdot M_y + \frac{M_0 - M_z}{T_1} \quad 3.12c
$$
where

\[ \Delta \omega = \omega_0 - \omega_r \]  \hspace{1cm} 3.13

\( M_x, M_y \) and \( M_z \) refer to the components of the magnetization in the rotating frame, and \( T_1 \) and \( T_2 \) are the spin-lattice and spin-spin relaxation times respectively. The amplitude of the rf magnetic field \( B_1 \) is shown as a time dependent function.

If the rf magnetic field \( B_1 \) is constant, Eq. 3.12 can be solved analytically or by geometric analysis \([6,23,26]\). The magnetization components \( M_x \) and \( M_y \) existing at the end of a rectangular pulse of length \( t_p \) derived from Bloch equations can be expressed as

\[ M_y = M_0 \alpha_0 \text{sinc}(\gamma t_p \sqrt{B_1^2 + b^2}) \]  \hspace{1cm} 3.14

and

\[ M_x = M_0 \alpha_0 b \left\{ \frac{1 - \cos(\gamma t_p \sqrt{B_1^2 + b^2})}{\gamma t_p \sqrt{B_1^2 + b^2}} \right\} \]  \hspace{1cm} 3.15

where \( \alpha_0 \) is the nominal flip angle for on-resonance magnetization (i.e. \( \alpha_0 = \gamma B_1 t_p \)).

For comparison, \( M_y \) and \( M_x \) predicted by the Fourier transform relationship between the excitation pattern and the pulse modulation function is given below.

\[ M_y = M_0 \alpha_0 \text{sinc}(\gamma b t_p) \]  \hspace{1cm} 3.16
\[ M_x = M_0 \alpha_0 \left\{ \frac{1 - \cos(\gamma B t_p)}{\gamma B t_p} \right\} \] 3.17

Solution of Bloch equations in the presence of a varying $B_1$ field has been considered [19]. However, in general, Eq. 3.12 cannot be solved analytically when $B_1$ is time dependent [27]. Therefore in this Section, the excitation pattern due to amplitude modulated rf pulses has been determined by numerical integration of Bloch equations, and the results are compared with that of the linear approximation theory. Similar studies have been reported in the literature [21,23].

Numerical integration of Bloch equations was performed by dividing the time domain rf envelope into $n$ time steps. For each step, the change in each magnetization component ($\Delta M_x$, $\Delta M_y$ and $\Delta M_z$) was calculated and added to the existing value. When using a rectangular rf pulse, the number of times steps $n$, necessary for an accuracy of about 0.01% in the computed on-resonance magnetization was of the order of 5,000. In these calculations, relaxation during the pulse was assumed to be negligible. The example of the rectangular rf pulse was taken as one of the tests of the computer program. The details of the program are given in the Appendix. For each rf profile considered, the magnetization components $M_x$ and $M_y$ were calculated and plotted as a function of the offset frequency $\Delta f$ ($= \Delta \omega/2\pi$, see Eq. 3.13). In addition, the total transverse magnetization in the $x$-$y$ plane is also given by means of the polar coordinates $M_{xy}$ and $\phi$, where $M_y = M_{xy} \cos \phi$ and $M_x = M_{xy} \sin \phi$. It should be mentioned that because of the numerical error present in the calculations, some irregular points can be seen in the plots of $\phi$ vs $\Delta f$ at $\Delta f$.
values corresponding to very small $M_{xy}$ values. Thus in order to retain the clarity of the plots, in some cases only a selected region of the $\phi$ vs $\Delta f$ is shown.

Figure 3.8 shows the excitation pattern ($M_x, M_y, M_{xy}$ and $\phi$), at the end of a rectangular rf pulse of 10 ms duration and a nominal on-resonance flip angle of 90°, obtained by numerical solution of Bloch equations (solid curve). The broken curve shows the results obtained by assuming the Fourier relationship between the excitation pattern and the pulse modulation function (Eqs. 3.16 and 3.17). The two curves differ significantly near resonance, while at larger offset frequencies they tend to coincide. When the flip angle is reduced to 30° the curves show very good agreement (Fig. 3.9), implying that the response of a spin system to an rf pulse can be considered linear as long as the flip angle is small (<30°).

At this point it is worthwhile to compare the two curves where the Fourier relationship is assumed to hold between the flip angle (rather than magnetization components) and the pulse modulation. This modification is equivalent to taking the trigonometric sine of the broken curve in Fig. 3.8c, and the result is shown in Fig. 3.10. It can be seen that the modified linear approximation curve agrees well with that given by Bloch equations even at 90° flip angle, and the calculation for 30° flip angle produced identical curves (not shown). Nevertheless, the modified linear approximation curve for the 180° flip angle case shows (Fig. 3.11) considerable departure from Bloch equations' prediction.
Fig. 3.8: (a)-(c) Normalized plots of $M_x$, $M_y$, and $M_{xy}$ vs $\Delta f$ (offset), at the end of a rectangular rf pulse of 10 ms duration and an on-resonance flip angle of 90°. Solid curve: obtained by numerical solution of Bloch equations. Broken curve: obtained by linear approximation (Eqs. 3.16 and 3.17).
Fig. 3.8 continued: (d), the phase diagram corresponding to the solid curve in (c).
Fig. 3.9: Corresponding plots to that given in Fig. 3.8, for a rectangular pulse of 10 ms duration and an on-resonance flip angle of 30°.
Fig. 3.9 continued
Figure 3.10: Comparison of modified linear approximation (broken curve) and Bloch equations (solid curve) prediction for a rectangular rf pulse of 10 ms duration and a flip angle of 90°.

The excitation patterns computed for sinc shaped rf pulses using Bloch equations are shown in Figs. 3.12-3.14. The rf modulating function used is given by

\[ B_1(t) = A \text{sinc} \left( \frac{\pi}{\tau}(t-t_0) \right) \quad \text{for} \quad 0 \leq t \leq t_0 \]  \hspace{1cm} 3.18

and

\[ B_1(t) = 0, \quad \text{for} \quad 0 > t > t_0 \]  \hspace{1cm} 3.19
Fig. 3.11: Plot of $M_{xy}$ vs $\Delta f$ for a rectangular rf pulse of 10 ms duration and a flip angle of $180^\circ$. Solid curve: Bloch equations prediction. Broken line: Modified linear prediction. (b), the phase diagram of the solid curve in (a).
where $2\tau$ is the period of the sinc function, $2t_o$ is the duration of the pulse and $A$ is the amplitude. The plots shown in Figs. 3.12-3.14 were calculated with $\tau = 1$ ms and $2t_o = 8$ ms (or 4 ms) to conform to the experimental results given in the next Section. The pulse amplitude $A$ was calculated to give the desired on-resonance flip angle $\theta$ according to the relationship

$$\theta = \gamma A \int_0^{2t_o} \frac{\pi}{\tau} \sin\left[\frac{\pi}{\tau}(t-t_o)\right] dt.$$  

Figure 3.12 shows the excitation profile for a 90° rf pulse amplitude modulated according to Eq. 3.18 with $t_o = 4\tau$; i.e. the pulse consists of 3 side lobes on either side of the principal lobe. The profile of the transverse magnetization $M_{xy}$ (Fig. 3.12a) shows that a high degree of selective excitation can be achieved. Nevertheless, the presence of smaller excitation lobes on either side of the principal excitation band is evident as a consequence of the abrupt truncation of the sinc function. The phase of $M_{xy}$, shown in Fig. 3.12b suggests that the transverse magnetization is completely dephased, and as a result, at the end of the pulse almost no signal will be observed. However, it can be seen that the phase angle is approximately a linear function of the frequency at least within the principal excitation band. This enables refocussing of the excited magnetization by the gradient reversal method or by application of a nonselective 180° pulse [18,19]. Individual magnetization components $M_x$ and $M_y$ are also shown in Figs. 3.12c and 3.12d.
Fig. 3.12: Magnetization components existing after a 90° sinc modulated rf pulse. Pulse length = 8 ms; period of the sinc function = 2 ms.
Fig. 3.12 continued
Fig. 3.13: Transverse magnetization ($M_{xy}$) and phase ($\phi$), existing after a 90° sinc modulated rf pulse of length 4 ms. Period of the sinc function = 2 ms.
Fig. 3.14: Transverse magnetization ($M_{xy}$) and phase ($\phi$) existing after a $180^\circ$ sinc modulated rf pulse of length 8 ms. Period of the sinc function = 2 ms.
The effect of further truncation of the sinc function is shown in Fig. 3.13 where $t_o = 2\tau$, i.e. one side lobe. On comparison with Fig. 3.12a it can be seen that the principal magnetization profile is broadened, along with less sharper edge definition. The extension of the secondary excitation lobe to higher frequencies and uneven intensity distribution within the principal excitation band are also evident with the pulse of shorter duration.

The excitation profile corresponding to a flip angle of $180^\circ$ and $t_o = 4\tau$ is shown in Fig. 3.14. It can be seen that frequency selectivity is not realized and complete inversion of the magnetization is achieved only at resonance. When the Larmor frequency is offset from the frequency of the rf pulse, the magnetization is rotated by angles greater or less than $180^\circ$, thus leaving a considerable amount of magnetization in the transverse plane leading to poor selectivity. It is hardly surprising that a sinc shaped selective $180^\circ$ pulse performs poorly. It is a manifestation of the spin system being driven into a region where the response is highly nonlinear. Thus, a pulse modulation function derived from considerations based upon the linearity of system cannot be expected to produce the desired result. A discussion of the potential problems involved in using selective $180^\circ$ pulses (in relation to $T_1$ experiments) in NMR imaging has appeared in the literature recently [22].

From the preceding examples presented it is clear that, while $90^\circ$ pulses with acceptable selectivity can be obtained by using modulating functions derived from the Fourier relationship, selective $180^\circ$ pulses warrant considerable improvement. In both cases, improved performance
can be achieved by taking into account the nonlinearity effects when designing the pulse modulation function. Two approaches can be used to solve this problem. First, given the desired excitation profile, Bloch equations may be solved in reverse to yield the correct modulation function. This method has been used to generate a 90° selective excitation function by employing a numerical procedure [28]. The pulse modulating waveform obtained by this approach shows a small time shift compared to the waveform produced by the Fourier transform approach. The effect of the time shift is reflected in the reduction in the phase error of the magnetization after a non-selective 180° refocussing pulse [28]. An efficient selective 180° inversion pulse has also been developed recently by using a pulse modulated in the form of a complex hyperbolic secant [27-29]. The second approach depends on the use of an error minimization procedure [30]. In this method, the deviation from ideality of the magnetization response to a multi-parameter modulating function is calculated, and a range of parameter values are explored to find the best envelope shape. A selective 180° pulse of comparable efficiency to the hyperbolic secant pulse has been developed by this method. This modulation function, a modified truncated sinc function, has the distinct advantage over the hyperbolic secant pulse of not requiring simultaneous amplitude and phase modulation.
3.1.2 Implementation of the Technique and Experimental Results

When the present work was initiated, few practical details of the technique or experimental results such as those documented here were available in the literature. Two relevant reports which describe several useful practical aspects have been published only recently [31,32]. Therefore the following discussion is devoted to a description of the actual implementation of the technique used in this study, along with some experimental results.

The technique of selective excitation discussed above requires amplitude modulation of the rf carrier frequency with a suitable function (i.e. generally a modified sinc function). This method differs from the earlier synthesized excitation technique [10,17] in that the spectral excitation characteristics are contained in a single pulse rather than in a series of pulses.

A block diagram of the experimental setup used here to generate amplitude modulated rf pulses is shown in Fig. 3.15.

The component central to the assembly is the double balanced mixer (Hewlett-Packard model 10514A) which, used as a balanced modulator, combines the rf carrier frequency and the modulating waveform. The output of the mixer consists of the product of the carrier and the modulating waveforms in the time domain, corresponding to the double-side band suppressed carrier [33] spectrum. The rf carrier signal was obtained from the spectrometer frequency synthesizer unit and was gated by a gating pulse from the pulse programmer. The modulating waveform was generated by using an arbitrary waveform generator (Wavetek model
Fig. 3.15: Block diagram of the experimental setup used to generate amplitude modulated rf pulses.
75) capable of generating waveforms with a vertical resolution of 4096 points (12 bits) and a horizontal resolution adjustable from 2 to 8192 points. Typically, each complete cycle of the waveform was defined by 361 horizontal points and the maximum possible vertical resolution. Upon receiving a trigger signal, the waveform generator produces an analog voltage signal proportional to the values stored in the waveform memory between predefined start and stop locations. The time resolution for each memory location and the amplitude of the analog signal can be externally programmed into the waveform generator anywhere in the range from 500 ns to 50 s, and 0.01 to 10 Vp-p into a 50 Ω load respectively.

The waveform generator was interfaced to the Nicolet-1280 computer via a RS-232-C serial data transfer channel. The desired modulating waveform was initially generated in the computer and subsequently transferred to the waveform generator memory. The waveform generation and communication software necessary to accomplish this procedure was written in 1280 assembly language by the author. The trigger pulse necessary to initiate the waveform generator was obtained from the pulse programmer. In the experimental configuration used, the output of the waveform generator was first fed into a digitally controlled analog switch and the output of the switch was connected to the control port (X) of the mixer. This configuration provides the capability to generate high amplitude rectangular rf pulses and low amplitude modulated pulses in the same pulse sequence. The input to the control port (X) of the mixer is connected either to a constant voltage source (+5V) or to the low voltage (typically 750 mV) modulating signal from the waveform generator depending on the position of the switch. The position of the switch
is controlled by the same control pulse which triggers the waveform generator.

The modulated rf output from the mixer was amplified by a linear rf power amplifier (100 W ENI) and was fed into the probe via the transmitter/receiver coupler (Tx/Rx coupler) unit of the spectrometer. In addition to the assembly of components shown in Fig. 3.15, resistors and attenuators of appropriate values were suitably inserted into the setup to limit the maximum current or voltage applied to a particular component according to its specifications.

The presence of nonlinear devices (e.g. mixer and Tx/Rx coupler) in the experimental setup significantly alter the shape of the modulated rf waveform supplied to the probe as compared to that of the original modulating waveform. Thus it is imperative that the rf profile be observed at different stages using an oscilloscope. In this study, the rf profile was optimized by observing the voltage induced in a small pickup coil (3.0 mm diameter) placed at the center of the probe. The most prominent distortion to the rf shape was found to be caused by the Tx/Rx coupler due to the cross-diodes present in the device. The oscillograms of the actual waveforms observed, shown in Fig. 3.16, illustrate the problem. In each case the original modulating waveform has been superimposed on the rf waveform for ready comparison. Figure 3.16a shows the voltage induced in the pickup coil when the output from the amplifier was connected directly to the probe (Fig. 3.15, dotted line connection (a)). This situation was realized when a sinc shaped modulating waveform of peak amplitude 150 mV was applied as the input to the mixer via a 490 Ω current limiting resistor. At this input level
Fig. 3.16: Oscillograms of the rf pulse waveforms. The modulating waveform is superimposed on the rf waveform for comparison.
the mixer and the amplifier response is approximately linear, and hence, the rf waveform detected by the pickup coil follows closely the applied modulating function. The waveform detected by the pickup coil when the output from the amplifier was connected to the probe via the $T_x/R_x$ coupler is shown in Fig. 3.16b. In this case, gross distortion of the rf shape is apparent and this is ascribed to the nonlinear response of the Tx/Rx coupler. The nonlinearity of the Tx/Rx coupler was overcome by increasing the input level of the modulating function to a peak amplitude of 750 mV, as shown in Fig. 3.16c. After correcting for the nonlinearities in the system, the rf power level applied to the probe was found to be too large compared to the desired power level for a 90° pulse. At this stage, the rf power level was adjusted by using an attenuator of appropriate value after the Tx/Rx coupler.

Although the method adopted above to overcome the nonlinearity of the system was found to be convenient and suitable for preliminary implementation of the technique, it is appropriate to discuss some possible improvements. The control of rf power after the Tx/Rx coupler is undesirable in practice since this also attenuates the received signal; furthermore it also limits the power available for the non-selective pulses. These difficulties can be eliminated by modifying the shape of the modulating waveform to account for the nonlinear nature of the system via an experimentally determined calibration curve; this solution was not pursued here due to its demands on software. Therefore, the experimental excitation profiles given in the next section have been obtained with optimized rf profiles according to the procedure described earlier. In the case of the images presented in Chapter IV,
the rf profile was optimized by varying the modulating waveform input level (without using attenuation after the Tx/Rx coupler unit) while observing the shape of the selected slice.

Experimental evaluation of several amplitude modulated rf waveforms with regard to their excitation profiles was carried out using this configuration. The experimental results were then compared to the excitation profiles calculated using the Bloch equations in Section 3.1.1.3.

These experiments were performed on a 1 cm diameter spherical phantom containing water, placed at the center of a NMR probe. In order to determine the excitation pattern of an amplitude modulated rf pulse, a series of spectra were obtained in a homogeneous magnetic field by varying the frequency of the rf pulse with respect to the Larmor frequency of the water resonance. For a particular series of spectra, the rf pulse amplitude was adjusted so that the required flip angle was obtained for the on-resonance condition.

The signal was observed as a free induction decay by initiating the acquisition immediately after the rf pulse. Signal echo formation, as mentioned in the previous Sections, was not necessary due to the fact that only a single resonance was being observed. The absolute-value Fourier transformed data are displayed as a series of spectra plotted on the same horizontal axis, showing the relative amplitude of the excitation (transverse magnetization $M_{xy}$) as a function of frequency relative to the carrier. While the actual excitation profile is symmetrical with respect to the carrier frequency, only the low frequency side with respect to the carrier is shown in the experimental plots.
Several series of experimental excitation profiles are shown in Fig. 3.17. The excitation pattern due to a 2 ms constant amplitude 90° rf pulse (Fig. 3.17a) shows that the excitation of the magnetization extends far beyond the principal band (± 500 Hz) to an extent that cannot be neglected. This is compatible with the discussion presented earlier (see Fig. 3.8). Figures 3.17b, c and d show the excitation patterns corresponding to rf pulses modulated according to the Eq. 3.18 with a period of 2 ms, and pulse lengths 2, 4 and 8 ms respectively. In each case the amplitude of the rf pulse has been adjusted to give a 90° flip angle. The general trend of increasing selectivity with increasing pulse length is clearly demonstrated. Further, on comparison with Figs. 3.12 and 3.13, it can be seen that excellent correspondence has been achieved between the experimental and calculated profiles for offset frequencies below 1000 Hz. In Figs. 3.17c and d, spurious excitation not predicted by Bloch equations, can be seen at offset frequencies close to 1500 Hz. This is attributed to the third intermodulation harmonic generated by the mixer [34]. Intermodulation suppression is a function of many parameters and generally can be minimized by lower input levels to the mixer.

Experimental determination of the effect of triangular apodization of the sinc function is shown in Fig. 3.18. Suppression of the secondary excitation lobes as well as the decrease in sharpness of the principal excitation lobes can be clearly seen from these plots. The poor selectivity obtained by using a 180° modulated rf pulse, which shows close correspondence to the calculated curve (Fig. 3.13), is shown in Fig. 3.19.
Fig. 3.17: Spectral series showing the excitation patterns of modulated 90° rf pulses. (a) Rectangular modulation of length 2 ms. (b) Sinc modulation of period 2 ms and a pulse length of 2 ms.
Fig. 3.17 continued: (c), Sinc modulation of period 2 ms and length 4 ms. (d), Same as (c) with length 8 ms.
Fig. 3.18: Effect of triangular apodization of the sinc rf modulating function. (a) Sinc modulation of period 1.55 ms, pulse length 8.53 ms, 90° pulse. (b) Apodization of the sinc function in (a) with a symmetrical triangular function of length 8.53 ms.
3.2 Slice Selection in the Presence of Chemical Shifts

3.2.1 Limitations of the Current Technique

The frequency-selective excitation method of slice selection relies upon the direct correspondence between the frequency dispersion of a resonance caused by the applied gradient and the spatial distribution of the spins. Such a scheme provides excitation of well defined spatial planes in the presence of a single chemical shift species. However, when many chemical shift species are present, the frequency dispersion
observed in the presence of a gradient represents the combination of the spatial spin distribution and the corresponding chemical shift dispersion. In these circumstances, frequency-selective slice selection gives rise to improper selection of the spatial planes. Figure 3.20 illustrates the case for two chemically shifted species.

The frequency spread of a resonance in the presence of a gradient as given by Eq. 2.11 in Chapter II can be rewritten to include the chemical shift as,

\[ \Omega_x = \Omega_k + \gamma \Delta \nu \cdot x \]

where \( \Omega_k \) defines the frequency of the chemically shifted species \( k \) in the rotating frame. According to Eq. 3.21, in the presence of a gradient, each chemically shifted resonance will be broadened about its own chemical shift frequency (Fig. 3.20a). As a consequence, for different chemical species, a particular frequency \( \Omega_x \) corresponds to a slightly different spatial coordinate. Therefore a band-limited excitation pulse (Fig. 3.20b) stimulates each chemical species in slightly different spatial planes (Fig. 3.20c). Any subsequent imaging process thus produces a composite image of the two chemical species with each "chemical image" originating from a different location. The spatial separation between the selected planes is given by \( \Delta S = 2\pi \Delta \nu / \gamma G \), where \( \Delta \nu \) (Hz) is the chemical shift separation and \( G \) is the magnetic field gradient. This limitation is also present in the spatial localization techniques such as depth-resolved surface-coil spectroscopy (DRESS) [35] and volume-selective-excitation (VSE) [36].
Fig. 3.20: Illustration of frequency-selective excitation and its corresponding spatial selection for two chemically shifted species, $W$ and $L$, in the presence of a gradient. $\omega_A$ and $\omega_B$ are the respective chemical shifts. (a) Frequency spectrum in the absence (solid line) and presence (broken line) of a gradient. (b) and (c), Frequency domain rf excitation profile of a conventional slice selection pulse and its spatial selection. (d) and (e), Frequency domain rf profile needed to excite both chemical shifts at the center of the object and its spatial selection.
The misregistration of chemical shift planes can be minimized by increasing the magnitude of the gradient; however, it is important to note that it is impossible to achieve perfect registration of these planes in this manner. At low operating fields, sufficient gradient magnitudes can be employed so that $\Delta S$ is smaller than the slice thickness. In this situation, effectively overlapping spatial planes of each chemical species are excited. But at higher fields, the problem is accentuated by the increased chemical shift separation, and the experimental conditions (gradient strength and slice thickness) may be such that completely different planes are excited giving rise to a noticeable image degradation. For example, the chemical shift separation between water and lipid signals of human tissue at 200 MHz is approximately 700 Hz. Under these conditions, use of a slice selection gradient of 0.5 G/cm would give rise to a separation of approximately 3 mm between the selected spatial planes. If the slice thickness is assumed to be in the order of 1-2 mm, the spatial planes selected will be completely separated from each other by at least 1-2 mm. Such separations which are comparable to the slice thickness are clearly undesirable and cannot be ignored. This problem has already been encountered in high resolution imaging of small animals at 200 MHz [37].

3.2.2 Possible Solutions

The problem of slice selection in the presence of chemically shifted species has been mentioned briefly by several authors [39,42].
But a solution to this drawback has not been suggested previously.

Several two-dimensional Fourier imaging techniques have been reported [38-46] to separately image different chemical shift species. The majority of these methods [38,40-45] depend on either frequency-selective excitation or suppression of specific resonances, while the others depend on combination of images obtained under different experimental conditions [39,46]. Thus it is appropriate to consider possible modification of these techniques in order to obtain 'composite' images of chemically shifted species originating from the same spatial plane. With all above techniques, this requires combination of separate images corresponding to different species and originating from the same spatial plane. This can be accomplished more easily with some techniques than others. For example, with methods which depend on selective excitation and suppression [38,40-45], it would be necessary to change the rf carrier frequency within a pulse sequence (especially for slices which are off-center). This technical sophistication is available only in highly flexible imaging devices. On the other hand, methods which depend on image combination [39,46] would require proper combination of at least four separate images in the case of two chemically shifted species. A more convenient technique which enables two chemically shifted species to be imaged in the same spatial plane is described below.

Consider two chemically shifted species (hereafter referred to as water (W) and lipid (L)) to be imaged at the same spatial plane; for example, at the center of the object. If the object is centered with respect to the gradient null position in the magnet, this requires a
frequency domain rf excitation profile consisting of two bands positioned at the respective chemical shift frequencies (Fig. 3.20d). Excitation of slices other than the center can be achieved by shifting the rf excitation profile away from the chemical shift frequencies while maintaining the frequency separation (equal to the chemical shift difference) between the bands.

However, in practice, since the gradient imposed frequency dispersion of the resonances will be greater than the chemical shift separation, each rf excitation band will stimulate both chemical shift species giving rise to additional undesired spatial excitation as shown in Fig. 3.20e. The strategy suggested here to eliminate the contribution from the unwanted components in the final image is based on the acquisition of two data sets with proper phase relationship between the desired and undesired magnetization components. If the data acquisition conditions are such that in one data set all magnetization components are in phase, whilst in the other the magnetization from desired and undesired planes are of opposite phase, suitable combination of these data sets will result exclusively in the desired image.

The frequency domain rf excitation profile shown in Fig. 3.20d can be generated by amplitude modulation of the rf pulse in the time domain. By inverse Fourier transformation of the desired excitation profile, it can be shown that the required amplitude modulation function, $A_m(t)$, is given by

$$A_m(t) = \cos \omega_1 t \frac{\sin(\omega_2/2)t}{(\omega_2/2)t}.$$ 

3.22
This modulating function generates two frequency bands on either side of the carrier frequency, offset by a frequency equal to the frequency of the cosine function ($\omega_1$). The width ($\omega_2$) and the frequency profile of each band is determined by the frequency and the duration of the sinc function.

The way in which the required in-phase and out-of-phase relationship of the magnetization components can be achieved is discussed with reference to the pulse sequence and the rotating frame diagrams shown in Figs. 3.21 and 3.22 respectively. The (cos x sinc) amplitude modulated (Eq. 3.22) rf pulse excites a total of four magnetization components;

Fig. 3.21: Rf and gradient sequence used to demonstrate the technique described in the text. The dotted portion of the gradient applies only when the data collection is initiated at point C, otherwise, the gradient is kept constant during A-C.
Fig. 3.22: Evolution of magnetization components in the rotating frame during the pulse sequence shown in Fig. 3.21.
two desired components and two undesired components (see Fig. 3.20e). These components, in the presence of the gradient, are denoted as \( W(\omega_A) \), \( L(\omega_B) \) (desired components) and \( W(\omega_B) \), \( L(\omega_A) \) (undesired components). \( W(\omega_A) \) and \( W(\omega_B) \) refer to water magnetization excited at the frequency bands centered at the chemical shift frequencies \( \omega_A \) and \( \omega_B \) respectively and likewise for the lipid magnetization. In the rotating frame diagrams, the desired magnetization components are indicated by longer vectors and their symbols are underlined. The rotating frame frequency is assumed to be equal to the chemical shift frequency of water (\( \omega_A \)). The nonselective 180° pulse refocusses all four magnetization components after a time \( t_w/2 \) (Fig. 3.21, point A and Fig. 3.22A), where \( t_w \) is the duration of the amplitude modulated pulse. Evolution of the magnetization components for a time \( t = \pi/(\omega_A - \omega_B) \) causes \( \omega_B \) frequency components to acquire a phase angle of 180° relative to the \( \omega_A \) components (Fig. 3.21 point B and Fig. 3.22B⁺). In order to minimize the dephasing of the magnetization within each frequency band during the period A-B, the width of the frequency bands should be narrow compared to their separation. At point B, if the gradient is switched off, all magnetization components will begin to precess at their respective chemical shift frequencies; i.e. the unwanted components \( W(\omega_B) \) and \( L(\omega_A) \) will change their frequencies to \( \omega_A \) and \( \omega_B \) respectively (Fig. 3.22B⁺). Consequent evolution of the magnetization for a further time \( t = \pi/(\omega_A - \omega_B) \) in the absence of a gradient causes the undesired components to acquire a 180° phase angle with respect to the desired components (Figs. 3.21, point C and Fig. 3.22C⁻). An intermediate time between points B and C is shown in Fig. 3.22B⁰. Therefore, a suitable combina-
tion of the two data sets, acquired with phase relationships shown in Figs. 3.22A and 3.22C, will result in cancellation of the contribution from the unwanted spatial planes.

3.2.3 Experimental Demonstration of the Proposed Method

Figure 3.23 shows the selective excitation of two frequency bands using an rf pulse amplitude modulated according to Eq. 3.22; the pulse sequence used is that shown in Fig. 3.21, except for the modification that the gradient was kept constant after the 180° pulse. For the spectrum shown in Fig. 3.23b, the time domain data were acquired as a full echo by initiating the acquisition immediately after the 180° pulse, and the spectrum is displayed in the magnitude mode. By acquisition of the second half of the echo in a separate experiment, it was observed that minimal frequency dependent phase correction is needed to properly phase both frequency bands. This implies that the magnetization components of both frequency bands are approximately in-phase at the echo maximum.

Experimental verification of the proposed method was performed using a phantom containing a single chemical shift species (4 cm diameter bulb containing water) and 15 cm diameter home-built gradient coils [47] with rise time less than 300 µs. The data were acquired in the presence of the slice selection gradient so that the relative phase of the magnetization components can be determined. The data collection was initiated at either point A, B or C (Fig. 3.21). Since one chemical
shift species was used, the effect of different chemical shifts (water and lipid) was simulated by having the chemical shift frequency coincide with one or the other rf excitation bands in separate experiments.

The series of spectra in Fig. 3.24A show the phase relationship of $W(\omega_A)$ and $W(\omega_B)$ magnetization components at points A, B, and C (Fig. 3.21) in the pulse sequence. At point A, both magnetization components
are in phase (Fig. 3.24A(i)). Figures 3.24A(ii) and (iii) show the spectra obtained when the data collection is initiated at points B and C respectively. These spectra have been subjected to the same phase correction that applied to Fig. 3.24A(i). The 90° phase relationship of Figs. 3.24A(i) and (ii) is due to the fact that the data are shown with respect to a rotating frame frequency of \((\omega_A + \omega_B)/2\) (i.e. carrier frequency) rather than \(\omega_A\) as assumed in Fig. 3.22. Since the series of spectra shown in Fig. 3.24A was obtained with the chemical shift frequency centered at the \(\omega_A\) band, the unwanted magnetization component corresponds to the band of frequencies centered at \(\omega_B\). Taking the difference of data shown in Figures 3.24A(i) and (iii) will cancel this component while retaining the required magnetization centered at \(\omega_A\); this is shown in Fig. 3.24A(iv). Figures 3.24B(i)-(iv) show the series of spectra obtained when the chemical shift frequency is coincident with the frequency band at \(\omega_B\), simulating the phase relationship of \(L(\omega_B)\) and \(L(\omega_A)\) magnetization components. Taking the difference of Figs. 3.24B(i) and (iii) cancels the unwanted component, now at \(\omega_A\), as shown in Fig. 3.24B(iv). The data shown in Fig. 3.24 confirm that the proper phase relationship between the desired and undesired magnetization components can be achieved by commencing the acquisition of data at point A and point C.
80.3 MHz $^1$H NMR spectra obtained from a single chemical shift using the sequence in Fig. 3.21. A(i)-(iv), chemical shift centered at the high frequency ($\omega_A$) excitation band and B(i)-(iv), chemical shift centered at the low frequency ($\omega_B$) band. (i), Acquisition of data at point A (Fig. 3.21). (ii) and (iii), Acquisition of data at points B and C respectively and phase correction same as that applied to (i). (iv), the difference of the data shown in (i) and (iii). Cosine function frequency ($\omega_1$) = 7450 Hz, the principal lobe of the sinc modulation (8 ms duration) was employed. Echo time after 180° pulse = 4.3 ms. Time delay between acquisition points A and B, and, B and C = 337 $\mu$s.
3.2.4 Incorporation of Imaging and Further Extension

The scheme discussed above can be easily incorporated into an imaging sequence as shown in Fig. 3.25. The desired phase relationship of the magnetization components will be obtained at the maximum of the echo created by the read (frequency-encoding) gradient. The complete experiment involves acquisition of two imaging data sets with $\Delta t = 0$ and $\Delta t = 2\pi/(\omega_A - \omega_B)$. Combination of these data sets will generate an image showing the distribution of the two chemical species in an identical spatial plane. The complete two-dimensional experiment to illustrate this technique (i.e. obtain experimental images similar to Fig. 3.20(d) and (e)) involves the use of the slice selection gradient also

![Diagram](image)

**Fig. 3.25:** Proposed imaging sequence which enables two chemically shifted species to be imaged in the same spatial plane. $\Delta t$ refers to the time duration denoted A-C in Fig. 3.21. The phase-encoding gradient (not shown) is applied during the time interval between the rf pulses.
as the phase-encoding gradient during the imaging experiment. This could not be accomplished due to software limitations but the one dimensional version described here corroborates the feasibility of the method.

Proper cancellation of unwanted magnetization ideally requires phase-sensitive two-dimensional data and good magnetic field homogeneity in the imaging plane so that phase distortions that can occur during time $\Delta t$ (Fig. 3.25) are minimized. But when there is overlapping of the frequency distribution of the desired and undesired magnetization components in the presence of the read gradient, above problems can be partially overcome by addition of the magnitude mode data [39]. With the method described here, the cancellation of the unwanted components will occur even when the imaging plane is moved away from the center.

In this discussion, the well-known effect of chemical shift along the frequency-encoding dimension [48,49] has not been addressed. The three-dimensional version of the recently proposed refocussed gradient method [50] eliminates the chemical shift and static field inhomogeneity effects from all spatial dimensions. However, combination of the method described here with the refocussed gradient method will remove chemical shift contribution from both the slice selection and frequency-encoding dimensions with consequent reduction in experimental time. Straightforward extension of this technique to multi-chemical shift systems will generally result in incomplete cancellation of the unwanted magnetization. Therefore the method described is best suited for high field NMR imaging whenever two well separated chemically shifted species are dominant.
References: Chapter III


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CHAPTER IV

IMAGING RESULTS
IV. IMAGING RESULTS

The introductory aspects of NMR imaging methods were discussed in Chapter II. This chapter serves to demonstrate the implementation of two-dimensional and three-dimensional imaging methods using phantoms and intact systems. Further, the concept of frequency-selective excitation and suppression of specific resonances as a means of chemical shift resolved imaging is also introduced. Demonstration of two possible applications of three-dimensional chemical shift resolved imaging are also presented in the final section.

4.1 Two Dimensional Imaging

4.1.1 The Method

The particular pulse and gradient sequence employed in this study for two-dimensional imaging is shown in Fig. 4.1. The operation of the sequence is most easily viewed by considering the action of each gradient separately. Firstly, the slice selection is performed in the usual manner by the application of a low-power amplitude modulated rf pulse in the presence of the slice selection gradient, G-Slice (Interval I). At the end of this interval, the spins within the selected slice are dephased considerably in the rotating frame. The refocussing of these spins is achieved during interval III, by the application of a
Fig. 4.1: Two-dimensional imaging sequence used in this study.
non-selective 180° pulse followed by G-Slice. With ideal gradient behavior, maximum refocussing of spins is achieved after the 180° pulse at a time equal to half the duration of the selective pulse \[1\]; at this point in the sequence, the slice selection gradient is turned off. The frequency encoding gradient (G-Read) is applied during the time intervals II and IV when the G-Slice is inactive. Application of G-Read during interval II initially dephases the selected plane of spins along the frequency-encoding direction. This dephasing is subsequently refocussed after the 180° pulse by the activation of G-Read during interval IV forming a spin-echo. Interval IV also constitutes the signal detection period. The phase-encoding gradient (G-Phase) is incorporated into interval II and provides the required spatial discrimination along the phase-encoding direction. The complete imaging experiment involves the accumulation of a series of echo signals with different magnitudes of G-Phase. This modified version of the spin-warp experiment was necessary to avoid the signal distortions observed when using the gradient inversion procedure with the available gradient coil system.

In practice, it is important that each aspect of the experiment be verified and optimized to obtain the best results. This also serves to identify any malfunctioning or inappropriate set-up of the instrumentation. The optimization procedure adopted by the author is described below.

The slice selection aspect of the experiment is best optimized by using a slightly different scheme from that shown in Fig. 4.1. The modification involves the signal be acquired immediately after the 180°
pulse in the presence of the slice selection gradient only. This requires the setting of G-Phase and G-Read to zero as well as the extension of G-Slice, after the 180° pulse, to match the acquisition time. The echo signal observed with this scheme represents the refocusing of spins within the selected slice, and this signal, when subjected to Fourier transformation and calculation of the magnitude spectrum, corresponds to the profile of the selected slice. This procedure allows the slice profile to be optimized by direct observation, and suitable changes to the rf power and/or shape of the selective pulse could thus be made. Such adjustments are necessary since they will be sample dependent.

In practice, the time at which the echo is formed following the nonselective 180° pulse is dependent not only on the length of the selective pulse, but also on the delay time between the two pulses, due to the finite rise- and fall-times of the gradient. The echo-time observed here gives a very approximate value for the time interval III in the imaging sequence (see Fig.4.1).

Once the slice selection is optimized, the imaging sequence shown in Fig. 4.1 should be initially performed without the phase-encoding gradient. This enables the projection of the spin density distribution of the selected slice onto the frequency-encoding direction to be observed. During this procedure, it will be noted that the intensity of the echo-signal obtained is determined by the duration of interval III. Non-ideal gradient switching causes this time duration to be less than that determined earlier, and thus should be optimized to give the maximum signal intensity. Improper setting of interval III results in
substantial degradation of the signal-to-noise ratio and also produces a distorted projection of the selected slice. Once this is accomplished, it was found that the phase-encoding gradient produces minimal errors and the final image produced is a good representation of the object.

4.1.2 Experimental Results

The procedure discussed in the previous section is illustrated with experimental data obtained from a 4 cm diameter spherical phantom containing water. These are shown in Figs. 4.2-4.4.

Figure 4.2a shows the $^1$H NMR spectrum of the phantom in the presence of a linear magnetic field gradient of ca. 0.23 G/cm using an rf pulse of 17.0 $\mu$sec. This corresponds to the projection of the entire volume of the sample perpendicular to the direction of the field gradient. Figure 4.2b shows the slice selection profile obtained by using an amplitude modulated rf pulse followed by a 180° nonselective pulse. This was obtained by using the experimental setup described in Chapter III, Section 3.1.2 without using rf attenuation after the $T_x/R_x$ coupler unit. A 1 kW linear amplifier (ENI model LPI-10) was used to provide a reasonably short pulse length for the nonselective pulse. The amplifier was actually driven at a much lower power (ca. 400W) than its capacity and provided a nonselective 180° pulse length of 100 $\mu$s. The rf modulating function consisted of a sinc function (period = 4 ms), and a modulated pulse length of 8.0 ms was employed. However, the rf waveform supplied to the probe resembled that of Fig. 3.16b in Chapter
Fig. 4.2:  (a) 80.3 MHz $^1$H NMR spectrum of a 4 cm diameter spherical water phantom in the presence of a gradient of magnitude 0.23 G/cm.  (b) The slice profile obtained by the use of a sinc modulated rf pulse in the presence of the gradient used in (a).  (c) Projection of the slice shown in (b) onto a direction parallel to the plane of the slice (see text for further details).
III due to the nonlinearities of the system components. The amplitude of the modulated pulse was optimized to provide the best selection profile. The slice selection profile shown in Fig. 4.2b, obtained with the same gradient strength as used in Fig. 4.2a and drawn to the same horizontal scale, corresponds to a slice thickness of ca. 5 mm.

The projection of the spin density within the selected slice, obtained by using the sequence given in Fig. 4.1 with the phase encoding gradient set to zero, is shown in Fig. 4.2c. The same slice selection parameters as used for Fig. 4.2b, and a read-gradient strength of ca. 0.23 G/cm were employed. The optimum duration of the interval III in the pulse sequence to produce a maximum echo signal was found to be 7.1 ms when the interval II was set at 12.0 ms. Thus the echo-time of the signal defined as the time duration between the center of the modulated rf pulse and echo maximum during the detection period, corresponded to 33.1 ms. Very good correspondence between the expected profile and that shown in Fig. 4.2c indicates the proper adjustment of the experimental scheme.

The data obtained during a complete imaging experiment is shown in Fig. 4.3. Fig. 4.3a shows a portion of the total time domain data set $S(G_x, t_y)$ obtained by incrementing the magnitude of the phase-encoding gradient in successive experiments. The gradient increment used corresponded to a value of $2.44 \times 10^{-3}$ G/cm as calculated from the 8 cm total field-of-view obtained along the phase-encoding dimension in the final image. Other experimental parameters were unchanged from that used to obtain Fig. 4.2c. A total of 128 phase-encoding gradient values $(N)$ consisting of both positive and negative magnitudes proportional to
Fig. 4.3: Processing of two-dimensional imaging data. (a) Original time domain data $S(G_x, t_y)$. (b) First Fourier transform (FT), $S(G_x, \omega_y)$. (c) Transposition (TD), $S(\omega_y, G_x)$. (d) Second Fourier transform, $S(\omega_y, \omega_x)$. In all cases only a selected set of traces from the real part of the complex data set is shown. Each trace represents the entire real part of the data containing 128 points. The block numbers of the traces are indicated on the right of each data set.
were used. In the ideal case, the maximum signal intensity in the two-dimensional data set should be observed when the phase-encoding gradient is zero. In Fig. 4.3a this occurs in block number 66 rather than 65 due to a small bias gradient generated when its magnitude is set to zero.

Figures 4.3b-c represent intermediate data sets obtained during data processing (double Fourier transformation) of $S(G_x,t_y)$. Fourier transformation of $S(G_x,t_y)$ with respect to $t_y$ produces the data set $S(G_x,\omega_y)$, of which selected spectral traces are shown in Fig. 4.3b. It should be noted that the oscillatory behavior of the spectra shown in Fig. 4.3b is a consequence of the Fourier transformation of a whole echo signal [2], and is unrelated to the imaging process. Prior to the second Fourier transformation with respect to $G_x$, the data matrix $S(G_x,\omega_y)$ is transposed to yield $S(\omega_y,G_x)$, which is shown in Fig. 4.3c. The traces of $S(\omega_y,G_x)$ result from a series of overlapping cosinusoidal signals (see Chapter 2, Eq. 2.17) of differing frequency and thus appear as a decaying signal. Fourier transformation of these traces yields the data matrix shown in Fig. 4.3d corresponding to $S(\omega_y,\omega_x)$.

The final image is obtained by calculating the absolute value of $S(\omega_y,\omega_x)$. The data obtained are shown in the form of a stacked plot and as well as a contour plot in Fig. 4.4. Images shown in Fig. 4.4 show a uniform signal intensity corresponding to the spin density distribution within the selected slice. The slight decrease in intensity on the right side of the images is due to the small volume of air trapped inside the water phantom.
Fig. 4.4: $^1$H NMR images (slice thickness 5 mm) taken using a 4 cm diameter sphere containing water.
Imaging of intact Systems

From the initial study with phantoms the experiment was extended to imaging of fruits, human forearm and a small laboratory animal. The images obtained are shown in Figs. 4.5-4.9.

At this point it should be recalled that the signal intensity in an NMR image is not only a function of the spatial spin density distribution but also of other parameters such as $T_1, T_2$ and flow. Therefore, the contrast between different structures depends heavily on the experimental parameters such as the pulse repetition time (TR) and total echo-time of the signal (TE). These correspond to the time between successive $90^\circ$ selective pulses and the sum of the intervals $I/2 + II + III + IV/2$ in Fig. 4.1 respectively.

All the images shown in Figs. 4.5-4.9 have been displayed with a color scale comprising ten different shades of blue ranging from white to dark blue. In all the images, the total intensity range is displayed, and white corresponds to high signal intensity and dark blue corresponds to low signal intensity. The relevant experimental parameters are given in the Figure captions. The gradient magnitudes quoted correspond to the values calculated according to the experimentally observed field-of-view assuming constant amplitude gradient pulses. Images were obtained with either a 12 cm (for arm and orange images) or a 7 cm (for lime and rat images) diameter of inductively coupled H-resonator probe (see Chapter V).

Figures 4.5 and 4.6 show $^1$H NMR images obtained from an orange and a lime respectively using the sequence shown in Fig. 4.1. In both
Fig. 4.5: $^1$H NMR image (80.3 MHz) of an intact orange (diameter 6.5 cm). Imaging parameters: Slice thickness 2.5 mm, Image digitization 256 x 256, Image resolution 0.32 x 0.32 mm/Pt, TE = 46 ms, Total imaging time 13 min, TR = 3.0s, Slice selection gradient 0.48 G/cm, Frequency-encoding gradient 0.3 G/cm, Phase-encoding gradient increment $2.8 \times 10^{-3}$ G/cm.
Fig. 4.6: $^1$H NMR image (80.3 MHz) of an intact lime (diameter 4.5 cm). Imaging parameters: Slice thickness 2.0 mm, Image digitization 256 x 256, Image resolution 0.2 x 0.23 mm/Pt, TE = 52 ms, Total imaging time 11 min, TR = 2.5s, Slice selection gradient 0.57 G/cm, Frequency-encoding gradient 0.24 G/cm, Phase-encoding gradient increment $2.1 \times 10^{-3}$ G/cm.
images very fine septa are clearly resolved. This indicates the spatial resolution obtained. The seed case and its interior are clearly visible in the orange image. Closer examination of the same reveals the outer layer of the skin distinct from the inner layer which contributes negligible signal. This is due to the difference in \(^1\text{H}\) relaxation times between the outer and the inner layer of the skin.

Cross-sectional \(^1\text{H}\) NMR image of a human forearm is shown in Fig. 4.7. In this image, the water as well as fat contributes to the signal intensity. Due to the short repetition time (TR = 500 ms) between the experiments, the regions of high signal intensity (represented by white) correspond mostly to fatty tissue because of its rapid \(T_1\) relaxation compared to water [3]. Therefore, the subcutaneous fat, the bone marrow (surrounded by the bone which contributes negligible intensity) and also other fatty deposits between the muscles can all be easily visualized in the image. The muscle structure is represented as a darker blue region and cannot be clearly differentiated in this image. It is also possible to see several veins which appear as dark regions within the fat layer.

Figure 4.8 shows a coronal view of the head of a live rat. In this image, the most intense is the brain which is surrounded by a dark outline due to the skull. The mandible also appears as dark and is well resolved. The muscles of the jaw and the tongue are of intermediate intensity. The air in the nasopharynx is also clearly seen as a dark region below the brain. The above interpretations of the image are based on that given in Ref. 3.

These results demonstrate that reasonably good quality images of small animals and human extremities can be obtained with adequate
Fig. 4.7: Cross-sectional $^1$H NMR image (80.3 MHz) of a human forearm. Imaging parameters: Slice thickness ~3 mm, Image digitization 256 x 256, Image resolution 0.45 x 0.34 mm/pt, TE = 30 ms, TR = 500 ms, Total imaging time 2.0 min, Slice selection gradient 0.38 G/cm, Frequency-encoding gradient 0.2 G/cm, Phase-encoding gradient increment $2.6 \times 10^{-3}$ G/cm.
Fig. 4.8: Coronal $^1$H NMR image (80.3 MHz) of a rat head. Imaging parameters: Slice thickness ~1.5 mm, Image digitization 256 x 256, Image resolution 0.2 x 0.2 mm/pt, TE = 29 ms, TR = 500 ms, Total imaging time 17.0 min, Number of scans = 8, Slice selection gradient 0.75 G/cm, Frequency-encoding gradient 0.5 G/cm, Phase-encoding gradient increment 5.2 x $10^{-3}$ G/cm.
spatial resolution using the currently available equipment in this laboratory. Initially, it was hoped that the internal structure of the rat brain may in fact be revealed through NMR imaging. But the poor discrimination obtained between the soft tissues in the brain (Fig. 4.8) was disappointing. However, a recent publication [4], has demonstrated improved contrast within the rat brain obtained through variation of imaging parameters.

4.2 Three-dimensional Imaging

Aspects of simultaneous three-dimensional imaging with regard to its sensitivity and experimental time were discussed in Chapter II. Further to these considerations, three-dimensional imaging enables investigation of very thin slices compared to two-dimensional imaging, and also allows the construction of images in any arbitrary direction. Elimination of the need for a separate slice selection scheme reduces the complexity of the experiment, but at the same time introduces a more demanding data processing procedure.

4.2.1 The Method

The pulse and gradient sequence for the three-dimensional imaging is shown in Fig. 4.9. The rf sequence consists of a nonselective 90° excitation pulse followed by a 180° pulse. The formation of the
spin-echo signal in the presence of G-Read, frequency encodes the spin along the direction of the gradient. The spatial discrimination in the other two dimensions is achieved by means of two perpendicular phase-encoding gradients (G-Phase 1 and G-Phase 2) which are applied simultaneously. A series of phase modulated spin-echo signals are acquired by systematic variation of the magnitude of both the phase-encoding gradients similar to that in a two-dimensional experiment. For the two phase-encoding gradients, the incremental gradient magnitude and the total number of increments can be different, and therefore, the field of view and the resolution of each dimension can be adjusted independently. It is necessary that all combinations of the two phase-encoding gradient magnitudes be sampled in order to extract the complete three-dimensional information. Assuming \( G_x \) and \( G_y \) are used as the phase-encoding gradients and \( t_z \) denotes the signal detection period, the initial data matrix can be represented as \( S(G_x,G_y,t_z) \). Three-dimensional Fourier transformation of \( S(G_x,G_y,t_z) \) yields the matrix \( S(\omega_x,\omega_y,\omega_z) \), which corresponds to the three-dimensional image of the object.

At this stage it is instructive to examine how the three-dimensional Fourier transformation is achieved in practice. The data format of the initial time domain data depends on how the two phase-encoding gradients \( G_x \) and \( G_y \) are incremented in order to provide all the combinations of their magnitudes. This is most easily done by keeping one of the gradients (say \( G_x \)) constant and varying the magnitude of the other (say \( G_y \)). The whole sequence is then repeated for all the values of \( G_x \). This generates the three-dimensional data set \( S(G_x,G_y,t_z) \) which can be considered as a series of two-dimensional \( G_y,t_z \) blocks of data.
Fig. 4.9: Pulse and gradient sequence used for three-dimensional imaging.
corresponding to different values of $G_x$. This is represented in Fig. 4.10a. With this original data format, the three-dimensional Fourier transformation can be achieved by a series of one-dimensional Fourier transforms and as indicated in Fig. 4.10b. The data transposition steps, TD1 and TD2, shown in Fig. 4.10b, require additional software capability to that available in standard commercial NMR software packages. From the final data matrix, $S(\omega_z, \omega_y, \omega_x)$, it is possible to extract the image corresponding to any desired plane. It should be noted that the complicated data transposition steps can be eliminated if only the images corresponding to different $x,y$ planes (i.e. spatial coordinates defined by the two phase-encoding gradients) are desired. In this case, the extraction of a single data trace corresponding to a particular $\omega_z$ through the data matrix $S(G_x, G_y, \omega_z)$ gives the two-dimensional data matrix, $S(G_x, G_y)_{\omega_z}$, in one-dimensional format. These data, upon conversion to the two-dimensional format and subsequent two-dimensional Fourier transformation produce the data set, $S(\omega_x, \omega_y)_{\omega_z}$, which corresponds to the $x$-$y$ image at a particular $z$ coordinate. This process can then be repeated to produce a series of $x$-$y$ images at different $z$ locations.

4.2.2 Experimental Results

Initial demonstration of the three-dimensional experiment was performed using a phantom comprising of an Erlenmeyer flask (5 ml) and a round bottom flask (5 ml) containing water. Figure 4.11 shows the
Fig. 4.10: (a) Data format of the three-dimensional imaging data matrix $S(G_x, G_y, t_z)$. (b) Flow chart of three-dimensional imaging data processing. FT-Fourier transform, TD1 and TD2 - Data transposition steps.
images corresponding to all three spatial planes obtained from a single three-dimensional data set. Images show good definition of the shape of the phantom used. The software necessary for data transposition during image processing was written by the author. The images were constructed from an original data matrix size of 64 x 64 x 128 and were subsequently zero-filled to 128 x 128 x 128 during data processing. The repetition time between experiments was 500 ms, corresponding to a total data acquisition time of 34 min. The image processing took approximately three hours. This data processing time can be reduced considerably by using fast data processors and automated software. In the attempts to reduce the experimental time by reducing the repetition time, it was found that the data transfer time (ca. 150 ms) between the computer memory and the disk was the limiting factor. This corresponds to a minimum data acquisition time of approximately 10 mins for 64 gradient increments in each phase-encoding dimension.

The three-dimensional imaging experiment was then extended to obtain a series of coronal images of a rat head and these are shown in Fig. 4.12. Each image corresponds to a slice thickness of 0.5 mm and a data matrix size of 64 x 64. In order to confirm the actual position of the image planes, a marker (two, 2 cm long capillary tubes containing water) was placed on the rat's head as shown in Fig. 4.12a; this marker can be seen in the images B, C and D. The images A and E correspond to slices taken just in front and back of the marker respectively. Out of the possible 40 image slices which encompass the 2 cm length of marker, only the images with distinct changes in the anatomy are shown.
Fig. 4.11: $^1$H NMR images of a phantom (5 ml Erlenmeyer flask and a round bottom flask containing water) obtained from a single three-dimensional imaging experiment. (a) Longitudinal YZ slice. (b) Cross-sectional XZ slice. (c) and (d) Transverse XY slices extracted from different positions along the longitudinal z-axis.
Fig. 4.12: $^1$H NMR images (80.3 MHz) of a rat head obtained from a three-dimensional experiment. (a) Photograph of the rat showing a marker consisting of two capillary tubes containing water. (A)-(E) Selected coronal sections (0.5 mm thick) taken from the front to the back end of the marker. Imaging parameters: Image digitization 64 x 64, Image resolution 0.8 x 0.8 mm, TE = 12 ms, TR = 250 ms. Total experimental time = 17.0 min.
In the image A, the most intense region corresponds to the brain, and its change in shape can be clearly seen in the successive slices. Other regions in image A can be identified on comparison with the high resolution image shown in Fig. 4.8. The two prominent dark regions with zero intensity in image B (Fig. 4.12) correspond to the sinuses while the smaller dark area in the center is assigned to the trachea. The dark intrusions in images C and D are probably due to a combination of the sinuses and the ear bones. The general anatomical change seen in these images compares well with the existing data [5], but requires further experimentation for unambiguous assignment. The interpretations given above were formulated in consultation with Dr. J. Andersen (Department of Anatomy, UBC) and Dr. P. Reiner (Department of Psychiatry, UBC).

4.3 Chemical Shift Resolved Imaging

4.3.1 Frequency-Selective Excitation and Suppression of Specific Resonances

Chemical shift resolved imaging methods which incorporate the intrinsic chemical shift as an additional dimension into the basic two-dimensional spin-warp technique demand excessively long measuring times due to the increase in dimensionality of the experiment (see Chapter II). Therefore, it is of considerable interest to develop alternative techniques to overcome this disadvantage. The method
proposed and demonstrated here utilizes the techniques of frequency-selective excitation or suppression of specific chemical resonances coupled with conventional two-dimensional imaging. Frequency-selective excitation allows direct observation of the image corresponding to a particular chemical shift component, while the selective saturation method eliminates a preselected chemical species from the image. These methods enable the acquisition of chemical shift images with experimental times comparable to that of conventional imaging. Further, this approach to chemical shift resolved imaging alleviates the dynamic range problems when observing species of low concentration (or intensity) in the presence of more abundant species.

The pulse sequence used to demonstrate the technique is shown in Fig. 4.13. For selective suppression of resonances, a low power rf pulse is used to selectively saturate an unwanted resonance [6-8] prior to the application of the nonselective 90° pulse. In the case of selective excitation, the saturating pulse and the nonselective 90° pulse are replaced by a frequency-selective pulse which acts as a 90° pulse for the resonance of interest. Both the resonance selection methods are performed in the absence of magnetic field gradients and prior to the application of the imaging sequence. Therefore the bandwidth required during selective excitation or saturation is governed by the high-resolution conditions. In this particular study, selective excitation was achieved either via a long weak rf pulse (soft pulse) [9] or a DANTE pulse [10]. The DANTE pulse consists of a train of short, strong, equally spaced rf pulses, each with flip angle \( \theta \ll \pi/2 \). Only those resonances that are offset from the transmitter by \( n/r \) Hz, where \( r \)
is the pulse spacing and $n$ is an integer, are excited to a significant extent by the pulse train.

The experimental demonstration of the method was performed using a phantom comprising four glass capillary tubes (1.2 mm i.d.) located inside a 5 mm NMR tube. Two of the capillary tubes were filled with water while the other two contained ethanol. The experiments were conducted using a high resolution, narrow bore 270 MHz spectrometer and the selective saturation and excitation pulses were obtained from the decoupler.
A series of spectra of the phantom obtained under different excitation conditions are shown in Fig. 4.14. These spectra were obtained by initiating the signal acquisition immediately following the signal excitation without recourse to echo formation. Figures 4.14A and B show respectively the high resolution spectrum of the phantom and the spin density projection spectrum in the presence of the G_x gradient. Selective saturation of water (Fig. 4.14C) and selective excitation of the ethanol resonances (Figs. 4.14D-F) are all seen to produce the desired discrimination between the water and ethanol resonances. Due to the parallel orientation of the ethanol tubes (see Inset Fig. 4.14) with respect to the applied gradient (G_x), the ethanol resonances appear as two distinct peaks in Figs. 4.14B-F.

Figure 4.15 shows the images of the phantom obtained using the pulse sequence shown in Fig. 4.13. The normal image (Fig. 4.15B) obtained with a 90° nonselective pulse excitation shows only the water tubes, and attempts to scale up the intensity to visualize the ethanol image resulted in gross distortion of the entire image. Selective saturation of water (Fig. 4.15C) produces a clear view of the ethanol images via the methyl resonance while the water and other ethanol resonances are absent. Selective-excitation images of the methyl resonance using either a long weak pulse (Fig. 4.15D) or a DANTE pulse (Fig. 4.15E) resulted in an almost exclusive image of ethanol. However, the selective-excitation image of ethanol via the methylene resonance was far less selective (Fig. 4.15F). This is attributed to the refocusing of the residual water magnetization excited during the DANTE pulse (not visible in Fig. 4.14F) by the 180° pulse.
Fig. 4.14: Inset - the orientation of the phantom; W, water, E, ethanol. [A] 270 MHz $^1$H spectrum of the phantom. [B] Spectrum in the presence of a static magnetic field gradient of strength ca. 446 Hz/cm directed along the x-axis. [C] Spectrum obtained by saturation of the water with a 1.0 sec continuous irradiation prior to data acquisition, with the gradient being applied only during the acquisition time. [D] Selective excitation of the ethanol -CH$_3$ peak with a weak pulse of 20 ms duration from the decoupler, and data acquisition in the presence of the gradient. [E] Selective excitation of the ethanol-CH$_3$ peak with a DANTE pulse train consisting of 36, 1 $\mu$s pulses and 3 db attenuation of the main transmitter. [F] Selective excitation of the ethanol-CH$_2$ peak with a DANTE sequence of 40, 1 $\mu$s pulses and 6 db attenuation.
Fig. 4.15: Inset—Orientation of the phantom (W, water, E, ethanol).
[A] $^1$H spectrum of the phantom in the presence of a gradient of 446 Hz/cm. [B] Reconstructed $^1$H image of the phantom. ($G_x$-Read = 446 Hz; $G_y$-Phase increment = 14 Hz/cm; Number of $G_y$-Phase increments = 64, Echo time = 100 ms, Relaxation delay 20 s). [C] Water saturated image (saturation 1.0s). [D] Image with a 90° selective pulse of 20 ms through the decoupler at the ethanol-CH$_3$ resonance, [E], [F] Images with selective 90° DANTE pulse trains on the ethanol-CH$_3$ and -CH$_2$ resonances respectively. DANTE pulses are as described for Fig. 4.14E and F.
The results presented above demonstrate the essential features of the technique. In this study, the slice thicknesses of the images were determined by the length of the receiver coil. But in a practical application of the technique, a slice selection process needs to be incorporated into the pulse sequence. This can be conveniently accomplished in the selective saturation method by replacing the nonselective 90° pulse in Fig. 4.13 with a slice-selective pulse (i.e. a frequency-selective pulse in the presence of a gradient). But for the selective excitation method it is more difficult, and it has been suggested [11,12] that the slice selection process be performed at the same time as the selective excitation of the chemical resonances. This procedure however, is only suitable when the chemical shift separation is larger than the frequency spread of the resonances in the presence of the slice selection gradient. Thus a more appropriate technique to incorporate slice-selection into the selective excitation method is to convert the nonselective 180° refocussing pulse into a slice-selective pulse. This approach, though not preferred due to the difficulty in obtaining such pulses, is commonly used in multi-section imaging [13] and in situations similar to that encountered here [14, 15]. Further, it has also been a subject of a recent publication [16].

It should be mentioned that the utility of selective saturation as a means of chemical shift resolved imaging has also been recognized by other workers [17,18]. Since the report of the concepts developed here [19], several variations of the selective excitation technique have been suggested and their application to human imaging has been demonstrated [11,14,20,21].
4.3.2 Applications of Three-dimensional Chemical Shift Resolved Imaging

So far, the studies involving chemical shift resolved imaging have been directed towards the generation and clinical assessment of images corresponding to a particular chemical shift species [22]. This study demonstrates the application of the technique to map the spatial distribution of parameters such as pH and temperature [23]. The approach pursued here for this purpose is to perform a three-dimensional chemical shift resolved experiment while observing a chemical shift species which is sensitive to the changes in pH or temperature. Though other methods using computed tomography [24] and spin-lattice relaxation variations of NMR images [25] have been considered for temperature mapping, determination of the pH distribution within an object has not been considered previously.

The three-dimensional chemical shift resolved experiment consists of a variation of the sequence shown in Fig. 4.9. The variation involves the elimination of the frequency-encoding gradient (G-Read) and observation of the signal under high resolution conditions. This creates a three-dimensional data set in which two of the coordinates represent the spatial axes determined by the phase-encoding gradients, while the third is assigned to the chemical-shift axis. Processing of this data set in a similar manner to that described in Section 4.2.1 allows the extraction of images corresponding to a particular chemical shift or of spectroscopic data corresponding to a particular position in the image plane. If slice selection is desired along the remaining spatial dimension, the initial 90° pulse (Fig. 4.9) is replaced by a
frequency-selective pulse in the presence of the appropriate gradient.

When the chemical shift of the observed signal is sensitive to changes in either the pH or temperature, the spatial distributions of these parameters are reflected in the line-width of the observed resonance. Thus depending on whether the distribution of pH or temperature is spatially continuous or is compartmentalized into separate zones, the observed resonance would be merely broadened or split into different peaks. For either situation it is possible to extract the spatial distribution corresponding to a certain pH/temperature range from the three-dimensional data set.

In the present study, the resonances of inorganic phosphate ($^{31}\text{P}$) and water ($^1\text{H}$) were used as the pH and temperature 'probes' respectively. These were chosen because of their well known chemical shift dependence on the pH and temperature [26,27] as well as their potential applicability to in vivo studies.

The experimental demonstration of the method was performed using phantoms containing appropriate solutions. The phantom used for the pH studies comprised three concentric compartments made of Plexiglas, each filled to a height of 1.5 cm with inorganic phosphate (0.1 M) adjusted to pH 12.0, 7.0 and 3.0 respectively. The transverse view of the phantom along with its dimensions is shown at the top of Fig. 4.16.

The temperature phantom consisted of two glass tubes of diameter 1.0 and 1.6 cm filled with water to a height of 3.0 cm. The smaller diameter tube was fitted with a condenser type jacket so that water inside the tube could be maintained at an elevated temperature by circulating hot air through the jacket. The equilibrated temperatures
of water inside the two tubes under the experimental conditions used were found to be ca. 75°C and 32°C. Both tubes were wrapped with fiberglass insulating material to keep the temperatures as steady as possible during the course of the experiment.

In both experiments the sample depth was used to define the slice thickness along the third spatial dimension thereby eliminating the need for slice selection. Each phase-encoding gradient (G_x and G_z) was incremented 32 times and 512 data points were acquired for each signal to produce an experimental data set of dimensions 32 x 32 x 512. The data matrix was zero-filled in the phase-encoding dimensions prior to Fourier transformation to produce final image data size of 128 x 128. In all the experiments, only the second half of the echo signal was collected by initiating the signal acquisition at a time 't' after the 180° pulse, set equal to the delay between the 90° and 180° pulses. This was done to avoid the acquisition of an unsymmetrical whole echo signal.

The pH- and temperature-distribution maps of the phantoms and their high resolution spectra are shown in Figs. 4.16 and 4.17, respectively. The assignments of the spectra are indicated in the figures. The images displayed were obtained by summing all the individual images corresponding to a particular frequency region of interest. In each case, the frequency region of interest was defined by the resonances corresponding to different pH/temperature compartments. In order to obtain complete separation between the images of each chemically shifted resonance, it is necessary that the frequency separation between the resonances be greater than the static magnetic field inhomogeneity in the imaging
Fig. 4.16: Mapping of pH distribution. Top; Transverse view of the three compartment (I, II, III) phantom used for pH mapping (dimensions in millimeters) and phosphate solution pH values. [A] 32.5 MHz $^{31}$P spectrum of the phantom filled with phosphate solutions of different pH. Peak labels correspond to compartments indicated. [B-D] $^{31}$P pH maps of the phantom produced by chemical shift resolved imaging. Maps were produced from a single data set by extracting data corresponding to frequency ranges defining each peak.
Fig. 4.17: Mapping of temperature distribution. [A] 80.3 MHz $^1$H spectrum of two tubes of water maintained at ca 75°C and 32°C respectively. Peak labels L and H correspond to low- and high-temperature tubes. [B and C] Separate low- and high-temperature $^1$H images of the tube assembly. [D] $^1$H image of the phantom with both tubes at room temperature. Image was obtained as a separate experiment with experimental parameters identical to that of [B] and [C].
plane. Thus, because the pH range studied was rather large, each region gave well separated peaks in the spectrum, and the individual pH maps could be obtained without any interference from the other regions of the phantom. In contrast, in the temperature experiment where the frequency separation between the resonances induced by the difference in temperature of the tubes was small (ca. 40 Hz), separate images could only be obtained by careful selection of the frequency region to extract each image. This in turn resulted in incomplete spatial definition of the images. The slightly lower signal-to-noise ratio of the high-temperature map is attributed to the longer $^1$H spin-lattice relaxation time of water at elevated temperature [28] and hence partial saturation of the signal under the rapid pulse repetition rates.

The results presented here demonstrate that either the pH or temperature distribution of a compartmentalized object can be conveniently mapped using chemical shift resolved imaging. Either of the probe nuclei used here are suitable for studies of systems where the system has a wide distribution of properties.

4.4 Experimental

The configuration of the imaging system used in the studies described in this Chapter (except for that given in Section 4.3.1) and the rest of the thesis is as follows. The system consists of an Oxford Instruments 1.89 T (80.3 MHz for $^1$H), 31 cm horizontal-bore magnet interfaced to a Nicolet NT-300 high resolution console controlled by a
Nicolet-1280 computer (256K) and a 293 C pulse programmer. Data acquisition and processing are based on the standard NMC-1280 programme. The magnet is equipped with a gradient coil system, supplied by Oxford Instruments, and capable of producing up to 1.3 G/cm. The gradients are controlled via the driving voltages generated by digital-to-analog converters in the pulse programmer and are amplified by Crown M-600 amplifiers operating at constant voltage. Data storage facilities include a high capacity disc (96 MByte, CDC-CMD 9448-96) and a Nicolet floppy disc drive. Images are displayed on a Ramtek color graphics terminal (Model 6211) capable of displaying 16 colors at a time out of a total of 64.

The spectrometer system now also include rf pulse tailoring capability (see Chapter III) and a variety of home-built rf probes suitable for imaging (see Chapter V).

The software necessary to control the gradients and to display images were earlier developed and written at UBC by Dr. S. Sukumar. Male Wistar rats (250-350 gm) were used for all rat imaging experiments. The rats were anaesthetized with 10% inactin injected intraperitoneally at 0.1 mL/100 gm body weight. This was performed by Dr. P. Reiner (Department of Psychiatry, UBC). Using this anaesthetic the rats could be experimented with for several hours. At the end of the experiments the rats were returned to their cage to be used for future experiments or were sacrificed depending on their condition.

The arm image (Fig. 4.5) was obtained by employing a male volunteer.
References: Chapter IV


CHAPTER V

EVALUATION OF RADIOFREQUENCY PROBE DESIGNS

SUITABLE FOR NMR IMAGING AT HIGH FIELDS
V. EVALUATION OF RADIOFREQUENCY PROBE DESIGNS

SUITABLE FOR NMR IMAGING AT HIGH FeldS

5.1 Introduction

The probe is one of the most important components in an NMR spectrometer since it represents the interface between the magnet, transmitter, receiver and the sample. The probe permits the excitation of the sample and detection of the NMR signal, and therefore improvements in its design can greatly increase the overall performance of the spectrometer.

By far the most common type of probe used in pulsed NMR is the "single coil" probe, where the same coil is used for both the transmission of radiofrequency (rf) energy into the sample (excitation) and the reception of the signal (detection) from the sample. A schematic diagram of a single coil probe is shown in Fig. 5.1. The radiofrequency coil, which is wrapped around the sample, is tuned to the desired frequency of operation using a parallel resonance circuit. This circuit is in turn connected to the transmitter and the receiver by suitable means.

In this Chapter, attention is focussed on probe designs suitable for high field NMR imaging. In order to provide the background to the subject, the probe requirements and associated problems are discussed initially. This is followed by a brief introduction to several alternative probe designs. The final Section describes the modification, construction and experimental evaluation of these designs.
Fig. 5.1: Schematic diagram of a single coil NMR probe. L represents the rf coil which acts as an inductor; \( C_T \) and \( C_M \) are the tuning and matching capacitors respectively.

5.2 Probe Requirements and Associated Problems

The general requirements of an NMR probe are essentially the same for either spectroscopy or imaging. However, one important difference is that for imaging, probes of much larger dimensions are generally required as compared to those used for conventional spectroscopy. This requirement in turn imposes several important considerations which are highlighted in this section.

The fundamental requirement of any NMR coil is that the magnetic field \((B_1)\) created by a current passing through it should predominantly
be in a plane perpendicular to the main magnetic field \( (B_o) \) produced by the magnet. The coil system used to produce the \( B_1 \) field is dependent upon the magnet employed. In an iron magnet, the \( B_o \) field is in an orthogonal plane to the access of the magnet, thus a solenoidal coil can be used (Fig. 5.2a). But in a superconducting solenoidal magnet, \( B_o \) is produced along the axis of the bore of the magnet. Therefore, a saddle shaped coil is preferable (Fig. 5.2b) since it does not restrict the sample access. However, any coil configuration can be used as long as it is oriented in the magnet such that the \( B_1 \) field is orthogonal to the \( B_o \) field, and as mentioned above, the most commonly used coil configurations are the solenoid and saddle shaped coils. The direction of the \( B_1 \) field created by these coils is shown in Fig. 5.2.

The NMR coil is tuned to the desired frequency of operation with the aid of a capacitor, and the resonance frequency \( (f_r) \) of the circuit is given by

\[
f_r = \frac{1}{2\pi\sqrt{LC}}
\]

where \( L \) is the inductance of the coil, and \( C \) is the total capacitance of the circuit. The total capacitance of the circuit comprises the external tuning capacitor \( (C_T) \) and the distributed capacitance of the circuit. The distributed capacitance of a circuit is the capacitance that exists between the turns of wire, between terminal leads, and between turns and electrical ground etc. [1]. The highest frequency to which a coil can be tuned (called the self-resonance frequency) is
determined by the distributed capacitance since the total circuit capacitance cannot be made smaller than this value. In general, radio-frequency coils are operated well below this limiting frequency to

![Diagram of B1 field in solenoidal (a) and saddle shaped (b) coils.]

Fig. 5.2: Orientation of the $B_1$ field in solenoidal (a) and saddle shaped (b) coils.
ensure that electrical losses occurring in the coil form, or any other
dielectric that may be present in the electric field associated with the
coil, are minimized [1]. Furthermore, close to the self-resonance
frequency, coil tuning becomes extremely sensitive to the changes in
temperature and the sample itself [2].

In NMR imaging, large diameter coils (ca. 50 cm for a whole body
coil) are required, and the traditional solenoidal or saddle shaped
coils of such diameter have a large inductance (for a single layer
solenoid, inductance is proportional to the diameter of the coil and the
square of the number of turns [3]). Therefore these coils have a low
self-resonance frequency and their usable frequency range is generally
limited to below 10 MHz. With the present day NMR imaging equipment
being manufactured to operate at high fields (>50 MHz), coils with lower
inductance and which can be easily tuned to the required frequency are
needed. This is a problem, even for somewhat smaller diameter coils,
such as those used for studies of human limbs.

A further concern when using large diameter coils is the generation
of electric fields inside the coil, which have the ramifications consid­
ered below. When the coil dimensions are such that the length of the
conductor becomes comparable to the rf wavelength, a substantial
electric potential difference is created along the coil; this generates
an electric field which penetrates the sample within the coil [4]. With
conducting samples, these electric fields can cause significant energy
dissipation leading to undesirable heating of the sample [5]. Further­
more, detuning of the coil can occur upon sample introduction [6]. More
importantly, these electric fields contribute to an additional noise
source when studying conducting samples [4].

From the preceding discussion it is evident that the solenoidal and saddle shaped coils become increasingly inefficient as NMR receiver coils at higher frequencies and large dimensions. This has prompted the current research interest in alternative radiofrequency probe designs. The aspects considered so far also apply to conventional spectroscopy, but become prominent only at much higher frequency (>400 MHz), since the coil dimensions used are comparatively small.

In addition to the above considerations, it is necessary that the probe parameters which govern the signal-to-noise ratio (S/N) also be optimized. The influence of the probe parameters on S/N can be expressed as (see Ref. 7, Eqs. 8, 21)

\[
\frac{S}{N} \propto \frac{B_{1u}}{R^{1/2}} \text{ or } (\eta Q)^{1/2}
\]

where \( R \) and \( Q \) are the resistance and the quality factor of the coil, \( \eta \) is the filling factor and \( B_{1u} \) is the magnetic field (perpendicular to the main field \( B_0 \)) produced by a unit current flowing in the receiving coil.

Therefore in general, an NMR probe should satisfy several different criteria; it should provide stable tuning with minimum effects due to sample introduction, have a high Q value, a good filling-factor, a high \( B_{1u} \) value, minimal electric fields, and a reasonable \( B_1 \) homogeneity over a large volume as possible.
5.3 Effects of Conducting Samples

The electrical conductivity of biological tissues (approximately equal to that of 100 mM NaCl solution) has profound effects on the signal-to-noise ratio of the NMR signal [8,9]. In essence, a conducting sample serves as an additional noise source which reduces the obtainable signal-to-noise ratio.

The principal source of the noise produced by conductive samples is the currents generated in the sample. These currents, produced either inductively by the changing magnetic field, or dielectrically by the electric fields (due to the distributed capacitance) passing through the sample, dissipate energy in an analogous manner to power loss in a resistance. Therefore each of these loss mechanisms, inductive [8] and dielectric [9], can be represented by resistances, \( R_m \) and \( R_e \) respectively, in series with the intrinsic resistance \( R_c \) of the coil [4]. This is shown in Fig. 5.3. Hence, the combined resistance of \( R_m, R_e \) and \( R_c \) contributes to the observed noise.

Since the inductive losses originate from the changes in rf magnetic field, they are closely allied to the reception of the NMR signal, and therefore, their contribution to noise cannot be avoided. However, the dielectric losses can be reduced by minimizing the electric field penetration into the sample [9,10]. The amount of electric field experienced by the sample is dependent upon the probe design; thus, probe designs with minimum stray electric fields are desirable.

Both the inductive and dielectric losses can be modelled by adding appropriate circuit elements to the basic parallel resonance circuit of
Fig. 5.3: Representation of different loss mechanisms. $R_m$ and $R_e$ represent the equivalent resistances due to inductive and dielectric losses respectively. $R_c$ and $L$ are respectively the intrinsic resistance and the inductance of the coil.
the receiving coil [9-11]. However, the contribution from different loss mechanisms to the observed noise can be estimated experimentally by determining the effects of the sample on the Q-factor of the circuit and on its resonance frequency.

The quality factor (Q-factor) of a circuit, expressed in terms of the intrinsic resistance $R_c$ of the coil is given by

$$Q = \frac{\omega_0 L}{R_c}$$

where $L$ is the coil inductance and $\omega_0$ is the resonance frequency. Therefore the Q of the circuit is a measure of the resistance of the coil.

If the sample losses due to inductive and dielectric effects are expressed as resistances $R_m$ and $R_e$ in series with coil, then,

$$Q_L = \frac{\omega_0 L}{(R_c + R_m + R_e)}$$

where $Q_L$ is the Q of the probe circuit in the presence of the sample (i.e. loaded Q). Therefore the effect of $R_m$ and $R_e$ is to reduce the probe Q, and the loaded Q is a measure of the total losses due to the coil resistance as well as the inductive and dielectric effects.
From Eqs. 5.3 and 5.4,

\[
\frac{1}{Q_L} = \frac{1}{Q_{UL}} + \frac{1}{Q_S}
\]

where \( Q_{UL} \) is the \( Q \) of the unloaded probe (without the sample) and \( Q_S \) takes \( R_m \) and \( R_e \) into account. Thus \( Q \) measurements of loaded and unloaded probes give an estimate of the total losses due to the sample. Since sample losses are unavoidable, the desired condition is \( Q_{UL} \gg Q_L \). In this situation, the sample losses dominate over the intrinsic coil losses due to its resistance, and the observed noise arises mainly due to the sample.

An estimate of the electric field penetration into the sample can be obtained by measuring the shift of the probe resonance frequency (\( \Delta f_0 \)) upon introduction of the sample [9,12]. The differing dielectric properties of the sample compared to air alter the distributed capacitance of the coil and hence its resonance frequency (see Eq. 5.1). This measurement is usually carried out with pure water as the sample since its high dielectric constant causes large shifts in the resonance frequency while having minimal effects on the coil \( Q \) factor due to its low conductivity [12].

5.4 Alternative Probe Designs

Several alternative probe designs have been suggested in recent
years to overcome the inadequacies of the conventional saddle and solenoidal shaped coils. Of these designs, the simplest are the elliptical coil [13] and spherical coils [14,15]. These coils are tailored to match the shape of the part of the body to be imaged and therefore provide an improvement in the filling factor over that which can be obtained with conventional coils. The reported frequency of operation of these coils is less than 10 MHz, and it is conceivable that they would also suffer from the same disadvantages as the conventional coils at high frequencies.

The best compromise at high frequencies is offered by "resonator" type probes [1,5,16-24]. Illustrations of the designs used in this work are given in Section 5.5. Of these designs, that of Alderman and Grant [5] (hereafter referred to as the "H-resonator" after its shape of the conductor) is most widely used for high frequency NMR imaging [20,25]. The success of this design is attributed partly to its flexibility in dimensions which can be varied to suit the space available in the magnet and, more importantly, to its ability to minimize the electric fields inside the probe. However, the homogeneity of the radiofrequency $B_1$ field of this design compares less favorably with the other designs (see Section 5.5).

A variation on the H-resonator theme is the "mortarboard" probe design [19], in which one end of the H-resonator is terminated by a conductive plane. In this configuration, the effective length of the structure is approximately doubled and the magnetic field is more homogeneous toward the terminating plane compared to the H-resonator [19].
The 'split-ring' resonator probe [18], which can be viewed as a low inductance single turn solenoid [1], was first used as a magnetic resonance probe for the frequency range 200-2000 MHz. The potential use of this design as an imaging probe at 80 MHz has since been demonstrated [21] and is presented as a part of this work later in the Chapter. The main advantages of this design are its excellent radiofrequency homogeneity (see Section 5.5) and very high Q. The split-ring resonator produces a magnetic field along the axis of the resonator and thus needs to be mounted transversely in a superconducting magnet. This restricts its use in in vivo applications using small bore magnets. Nevertheless, it is well suited for small scale inanimate imaging applications [21], and its easy adaptation as a surface coil probe has already been demonstrated [12].

A significant improvement in the transverse rf field of an axially mounted probe can be achieved by the "bird-cage" design [22]; the original work which led to this design is given in Refs. 23 and 24. It depends on the principle that a very homogeneous transverse magnetic field in an infinitely long cylinder can be generated by a surface current which runs along the length of the conductor and is proportional to Sinθ, where θ is the cylindrical azimuthal angle [22]. The conventional saddle coil approximates this ideal sinusoidal current distribution for six equally spaced values of θ (θ = 0, 60, 120, 180, 240, 300°). Of these six conductors, four carry equal currents whereas no conductors are needed at θ = 0 and 180° because the currents at these points are zero [22]. A further advantage of the bird-cage design is that it allows quadrature excitation and detection, and thus leads to a
decrease in rf power requirements by a factor of two and an increase in signal-to-noise ratio by a factor of \( \sqrt{2} \) [22, 26-28].

5.5 Experimental Evaluation of Resonator Probe Designs

Three resonator probe designs, the H-resonator, the split-ring resonator and the bird-cage resonator were chosen for evaluation of their performance compared to a conventional saddle coil. Illustrations of the resonator probes used are given in Figs. 5.4-5.6.

The resonator probes used in this study have several important features. First, they were coupled to the rf transmitter/receiver (Tx/Rx) using an inductive mechanism rather than via a capacitor. In the inductive coupling method, Tx/Rx is directly fed into a copper ring which couples magnetically with the main probe body (Figs. 5.4-5.6). The maximum coupling was achieved by changing the distance between the resonator and the coupling ring. Inductively coupled NMR probes have been used [12,18,21,26] and treated in detail [29,30] by several groups.

Secondly, the fine tuning of the H-resonator and the bird-cage designs was achieved by using an unattached copper ring on the opposite side of the probe with respect to the coupling ring (Figs. 5.5 and 5.6). The movement of the tuning ring with respect to the probe structure alters the resonance frequency by changing the total effective inductance of the structure [12]. The inductive coupling and tuning method as applied to the H-resonator and the bird-cage resonator has not been described previously.
Fig. 5.4: Split-ring resonator probe. A, copper foil; B, screw threaded holder housing the coupling ring. Inset shows five layers of material; Plexiglas, copper (0.25 mm), Teflon (0.9 mm), copper (0.25 mm), Plexiglas.
Fig. 5.5: H-Resonator probe. A, guard rings; B, H-shaped conductor; C, capacitance; D, coupling ring; E, tuning ring.
Fig. 5.6: Bird-cage resonator probe. A, copper strips; B, copper end rings; C, capacitance; D, coupling ring; E, tuning ring.
Finally, the capacitance needed for these structures was formed by overlapping copper foils separated by a dielectric (Teflon). These modifications completely eliminated the need for high-cost commercial capacitors and resulted in easily fabricated and low-cost probes.

### 5.5.1 Probe Construction

All the probe designs under evaluation were constructed with identical diameter (7.5 cm) to enable direct comparison and were mounted on a cylindrical Plexiglas former.

The saddle shaped coil (Fig. 5.2b) was fabricated of 2 mm diameter copper wire and consisted of a single turn. The length of the coil was equal to the diameter (7.5 cm) and the circular sections of the wire subtended an angle of 120° at the center. This corresponds to the most commonly used configuration of the saddle coils in spite of the fact that better rf homogeneity can be obtained when the coil length is twice its diameter [2].

The split-ring resonator probe (14 cm long, Fig. 5.4) was constructed of a single copper foil (0.25 mm thick, 101 grade, OFHC) wrapped around a Plexiglas former with two flaps which project normally from the circumference of the cylinder. These flaps, separated by a 0.7 mm thick sheet of Teflon and sandwiched between two Plexiglas plates, provided the capacitance required for tuning the probe. The capacitance was varied by fine adjustment of the distance across the Teflon dielectric with the aid of Teflon screws. The resonator was inductively
coupled to the transmitter via a single copper ring (diameter 7.5 cm) attached to the end of a coaxial cable and mounted inside a screw-threaded holder which fits around the cylindrical former. The whole probe body was fitted into a suitably shaped Plexiglas frame so that the probe can be accurately positioned inside the magnet. The probe fabricated with dimensions shown in Fig. 5.4 was found to have a tuning range of 78.0-200.0 MHz.

The H-resonator structure (Fig. 5.5) was fabricated of 3 layers of material. The innermost layer of guard rings was constructed of copper sheet (0.1 mm thick, OFHC) soldered into a ring shape. Directly above each guard ring a layer of Teflon dielectric (thickness 0.5 mm) was placed (this is not shown in Fig. 5.5). The outermost layer of two H-shaped halves of conductor was constructed of 0.1 mm thick copper sheet. The wings of each of the H-shaped halves were made slightly longer than necessary and the extra length was bent at the four positions above the guard rings. The bent portions from each half were separated by Teflon (thickness 0.5 mm) to provide the extra capacitance needed for tuning. Each of these capacitor sections were sandwiched between two small Plexiglas sections and were secured by Teflon screws. The overall dimensions of the probe were such that the relative dimensions of various sections were those given by the original authors [5]. This corresponded to a probe length of 14 cm, diameter of 7.5 cm and a guard ring width of 4 cm. The angle subtended at the center by the vertical sections of the H-shaped halves was 80°. The particular probe described above was inductively coupled and tuned using copper rings of diameter 7.0 cm and had a tuning range of 80-82 MHz. In addition to
this, for comparative purposes, a second probe was fabricated in which the H-shaped halves were joined by chip capacitors. This probe was capacitively coupled and tuned in the standard manner and corresponded to the originally proposed configuration of the structure [5].

The bird-cage resonator used in this study was constructed of sixteen, 5 mm wide copper (0.25 m thick) strips equally spaced around the circumference of a 7.5 cm diameter coil former (Fig. 5.6). The copper strips were soldered onto two circular copper end rings (width 8 mm) on either end. The capacitance needed for the structure was created by cutting the copper strips in the center and overlapping the corresponding strips by sliding the two individual halves inwards. A thin film of Teflon was then inserted between the overlapping areas of each pair of strips. The copper strips were held in place by a cord tied around the assembly. This configuration corresponds to the low pass version of the bird-cage resonator [22]. The coarse tuning of the probe was obtained by changing the area of overlap between the strips and by using Teflon film of appropriate thickness. The dimensions of the structure when tuned to ca. 80 MHz corresponded to a total length of approximately 14 cm, length of strip overlap 2 cm and a Teflon film thickness of 0.1 mm. The probe was inductively coupled and tuned (copper ring diameter 7.0 cm). It was found that the probe tuning was not stable over long periods due to the changes in the capacitance formed by the overlapping strips. This can be overcome by improving the mechanical stability of the probe. Improved versions of this probe are presently being investigated.

The mechanical construction and electronic details of the probes
were carried out by Messrs. C. Neale and T. Markus, respectively, of the UBC Chemistry Department.

5.5.2 Probe Evaluation

The probes constructed were experimentally evaluated by measuring several parameters which are directly related to the design of the probe. They are, the probe Q factor (loaded and unloaded), the effect of a water sample on the probe resonance frequency and the homogeneity of the rf magnetic field inside the probe. In addition, the signal-to-noise ratio and the 90° pulse-width for a 1 ml water sample placed at the center of probe were also determined.

The experimental data obtained for the probe Q-factor and the shift in probe resonance frequency are given in Table 5.1. The loaded Q values (Q_L) were measured when a 150 ml bottle containing 0.028M KH2PO4 solution was introduced into the probe. Such a solution mimics the effect of in vivo samples (e.g. rat) on the probe Q-factor [20]. The change in resonance frequency (∆f_0) of the probe was measured by placing a 150 ml bottle of water inside the probe.

In order to find the effect of a surrounding shield, the probe Q and ∆f_0 values were measured when the probes were unshielded and as well as when inserted into a 22.5 cm diameter copper tube. The upper and lower values given for the entries in Table 5.1 correspond to the values obtained when the probe was unshielded and shielded respectively. The Q_s values given in Table 5.1 were calculated using Eq. 5.5.
Table 5.1: Characteristics of different probe designs

<table>
<thead>
<tr>
<th>Probe Design</th>
<th>Q&lt;sub&gt;UL&lt;/sub&gt;&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Q&lt;sub&gt;L&lt;/sub&gt;&lt;sup&gt;b&lt;/sup&gt;</th>
<th>Δf&lt;sub&gt;o&lt;/sub&gt;&lt;sup&gt;c&lt;/sup&gt; (MHz)</th>
<th>Q&lt;sub&gt;s&lt;/sub&gt;&lt;sup&gt;d&lt;/sup&gt;</th>
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<td></td>
<td>1600</td>
<td>470</td>
<td>0.40</td>
<td>665</td>
</tr>
</tbody>
</table>

Probe designs: 1. Saddle coil  
2. Capacitively coupled/tuned H-resonator  
3. Inductively coupled/tuned H-resonator  
4. Inductively coupled/tuned bird-cage resonator  
5. Inductively coupled split-ring resonator

The upper and lower, Q and Δf<sub>o</sub> values given in each entry correspond to the measurements taken with an unshielded probe and a shielded probe respectively (see text).

- "Unloaded" Q.  
- Q, when the probes were loaded with 150 ml, 0.028M KH<sub>2</sub>PO<sub>4</sub>.  
- Resonance frequency shift caused by 150 ml of distilled water.  
- Calculated value using Eq. 5.5.
From Table 5.1, it can be seen that the shielded probe Q values are generally higher than the unshielded probe Q's; the most notable being the increase in the unloaded Q of the split-ring resonator. This is attributed to the reduction of radiation losses when the probes were placed inside the shield. The same effect was observed when the probes were inserted into the magnet, and hence, the shielded probe Q values give a better indication of the efficiency of the probe during an experiment.

On comparison of the Q values obtained with the two configurations of the H-resonator design, the inductively coupled and tuned version affords a slightly higher Q. This increase in efficiency is most likely due to the fact that the losses associated with the capacitive coupling/tuning network are avoided in the inductively coupled/tuned version.

Since $\Delta f_0$ values are an indication of the dielectric losses, Table 5.1 shows that the maximum dielectric losses are associated with the saddle coil. This is to be expected with a coil configuration in which the length of the conductor is a significant fraction (~1/6 in this case) of the rf wavelength [4]. Comparative $\Delta f_0$ values show the superior performance of the H-resonator with regard to the dielectric losses. This is due to the presence of guard rings in the structure which keeps the electric fields to a minimum and removed from the sample [4]. The bird-cage and the split-ring resonators offer intermediate performance compared to the saddle coil and the H-resonator.

The results given in Table 5.1 show that the loaded probe Q values ($Q_L$) are substantially lower than the unloaded probe Q's due to the
losses introduced by the KH$_2$PO$_4$ solution. In the case of the split-ring resonator probe, $Q_L \ll Q_{UL}$, indicating that the sample losses dominate over the losses due to the resistance of the probe. Further, the split-ring resonator probe affords the highest shielded $Q_L$ value and hence the best sensitivity under sample loaded conditions.

The calculated $Q_S$ values given in Table 5.1 indicate the sample losses due to both the inductive and dielectric mechanisms. The $Q_S$ values obtained for the saddle coil and the H-resonator designs indicate that the total sample losses for these two probes are similar. Since higher dielectric losses are encountered with the saddle coil, it implies that inductive losses are greater for the H-resonator probes. The $Q_S$ and $\Delta f_0$ values obtained for the bird-cage resonator probe possibly indicate slightly smaller inductive losses compared to the H-resonator. The comparatively higher $Q_S$ value obtained for the split-ring resonator probe suggests lower inductive losses compared to the H-resonator design.

The trend in the inductive losses encountered with different designs can be qualitatively rationalized by considering the factors determining the inductive losses. The inductive losses, represented by a resistance $R_m$ in series with the coil, for a cylindrical sample of diameter $d$, length $l$ and conductivity $\sigma$, immersed in a uniform alternating magnetic field (frequency $\omega$) parallel to the cylinder axis is given by [10]

$$(R_m)_l = \pi \omega B_1 \mu \sigma l d^4 / 128 \quad 5.6$$
where $B_{1u}$ is the magnetic field produced by the coil per unit current. Thus $R_m$ depends on the coil design via the parameter $B_{1u}$. Therefore the dependence of inductive losses on the probe design can be attributed to the changes in $B_{1u}$ as well as its distribution over the sample volume. Another contributing factor is the direction of $B_1$ with respect to the sample. Following an analysis similar to that given in Ref. 31 in which the $R_m$ for a rectangular sample block was calculated, it can be shown that the resistance $R_m$ when $B_1$ is oriented perpendicular to the axis of a conducting cylinder is given by

$$ (R_m)_\perp = \frac{1}{15} \omega^2 B_{1u}^2 \sigma \ell^2 d^3 $$

Comparison of $(R_m)_m$ and $(R_m)_\perp$ values for a $d/\ell$ ratio of 2/3 (corresponding to the sample dimensions $d = 5.0$ cm and $\ell = 7.5$ cm used in this study) and identical $B_{1u}$, $\sigma$ and $\omega$, shows that $(R_m)_\perp$ is greater than $(R_m)_m$ by a factor of 1.8. Therefore lower inductive losses are encountered when the cylinder axis is parallel to $B_1$. This corresponds to the orientation of the sample within the split-ring resonator, while with the other probe designs, the $B_1$ is directed perpendicular to the sample axis. Therefore it is postulated that the lower inductive losses for the split-ring resonator arise, at least in part from the difference in orientation of the sample.

The 90° pulse width and the S/N afforded by each design for a 1 ml of water sample placed at the center of the probe are given in Table 5.2. The desirable characteristics of smallest pulse width and highest
Table 5.2: 90° Pulse Width (t\textsubscript{90°}) and S/N data\textsuperscript{a}

<table>
<thead>
<tr>
<th>Probe\textsuperscript{b}</th>
<th>t\textsubscript{90°} (\mu s)</th>
<th>S/N\textsuperscript{c}</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>69</td>
<td>650</td>
</tr>
<tr>
<td>2</td>
<td>58</td>
<td>740</td>
</tr>
<tr>
<td>3</td>
<td>42</td>
<td>1030</td>
</tr>
<tr>
<td>4</td>
<td>55</td>
<td>825</td>
</tr>
<tr>
<td>5</td>
<td>34</td>
<td>1290</td>
</tr>
</tbody>
</table>

\textsuperscript{a} Data were obtained by using a 1 ml water sample placed at the center of the probe and 140 W of rf power.

\textsuperscript{b} Numbers indicating the probe design correspond to that given in Table 5.1.

\textsuperscript{c} Average of five measurements. Maximum deviation -1%. 
S/N are given by the split-ring resonator probe. The inductively coupled/tuned H-resonator also offers good performance, and the saddle coil produces the longest pulse width and the least S/N. The observed 90° pulse width and the S/N values are in good agreement with the expected inverse relationship [7] between the two parameters. Considering the shielded Q values (Table 5.1) and the S/N afforded by each design, calculations show that the S/N observed with the lower Q probes is progressively lower than that predicted by the square root relationship in Eq. 5.2. This is due to the changes in the filling factor (η) which depends on the distribution of $B_1$ and hence the probe design [7].

The rf magnetic field profiles ($B_1$-maps) for each design are shown in Figs. 5.7-5.10. Details of the experimental procedure adopted are given in Section 5.7. The figures show the magnitude of the $B_1$ field as a function of the spatial distance along the three axes. The z-axis defines the longitudinal axis of each probe; for the split-ring resonator, this corresponds to a perpendicular orientation compared to other probes when placed inside the magnet. Since the $B_1$-maps of the two H-resonator probes were similar, only the map corresponding to the inductively coupled design is shown. Due to the instability of the high power amplifier used here, no comparison is intended between the absolute values of $\gamma B_1$ (in Figs. 5.7-5.10) and the pulse widths quoted in Table 5.1. This does not present a difficulty since, only the change in $\gamma B_1$ within each map is of interest. Comparison between different probes was obtained by defining a $B_1$ inhomogeneity parameter $\Delta B_1/B_1(0)$, where $\Delta B_1$ refers to the field deviation at $r/2$ or $l/4$ and $B_1(0)$ to the field at the center; $r$ and $l$ are the radius and the total length of the
probe respectively. The approximate inhomogeneity parameters obtained from the $B_1$ maps are given in Table 5.3. It should be noted that in some cases it is difficult to measure the $\Delta B_1$ from the maps. In these instances the inhomogeneity parameter is given as less than the value calculated based on the digital resolution along the $\gamma B_1$ axis.

Figures 5.7-5.10 show that the $B_1$-maps are highly dependent upon the probe design. In general, the $B_1$ homogeneity in the transverse $xy$ plane is better than along the longitudinal axis. An interesting observation in Figs. 5.7-5.9 is the increase in $B_1$ along the $y$ axis at positions away from the center. The transverse rf homogeneity of the bird-cage resonator compares less favorably with other designs, while that of the H-resonator is comparable to the saddle coil. The decreased performance of the bird-cage resonator is probably due to the particular features of the design used in this study. The H-resonator affords poor $z$-axis homogeneity due to the presence of guard rings, and improved performance is offered by the saddle coil and the bird-cage resonator. The split-ring resonator provides excellent $B_1$ homogeneity along all three axes. The asymmetry of the $z$-axis $B_1$-map of this probe is due to the fact that the signal from the higher negative $z$-values is lost due to the inhomogeneity of the main $B_0$ field. (The phantom used to produce this map is 14 cm long and is oriented perpendicular to the $B_0$ field, and hence the difficulty in shimming). The decrease in $B_1$ at higher $z$-values shows the unavoidable roll-off of field intensity at the ends of the coil.
Fig. 5.7: $B_1$-homogeneity maps of the saddle coil. The probe orientation is shown by the end-view (right). A, circular conductor sections; B, straight conductor sections. $B_1$; direction of the $B_1$ field.
Fig. 5.8: $B_1^-$ homogeneity maps of the inductively coupled and tuned H-resonator. Probe orientation is shown by the end-view (right). Symbols refer to that given in Fig. 5.5
Fig. 5.9: $B_1$-homogeneity maps of the inductively coupled and tuned bird-cage resonator. The probe orientation is shown by the end-view (right). Symbols refer to that given in Fig. 5.6.
Fig. 5.10: $B_1$-homogeneity maps of the split-ring resonator. The probe orientation is shown by the end-view (right). A, copper foil.
Table 5.3: $B_1$ Inhomogeneity Parameters\textsuperscript{a} of Different Probe Designs\textsuperscript{b}

<table>
<thead>
<tr>
<th>Probe</th>
<th>$\left(\frac{\Delta B_1(x)}{B_1(0)}\right)_{r/2}$</th>
<th>$\left(\frac{\Delta B_1(y)}{B_1(0)}\right)_{r/2}$</th>
<th>$\left(\frac{\Delta B_1(z)}{B_1(0)}\right)_{l/4}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>&lt;8</td>
<td>&lt;8</td>
<td>11</td>
</tr>
<tr>
<td>2</td>
<td>&lt;5</td>
<td>&lt;5</td>
<td>30</td>
</tr>
<tr>
<td>3</td>
<td>&lt;5</td>
<td>&lt;6</td>
<td>33</td>
</tr>
<tr>
<td>4</td>
<td>&lt;10</td>
<td>13</td>
<td>20</td>
</tr>
<tr>
<td>5</td>
<td>&lt;4</td>
<td>&lt;4</td>
<td>&lt;4</td>
</tr>
</tbody>
</table>

\textsuperscript{a} Values are given as the percentage of the field at the center. (see also the text).

\textsuperscript{b} Numbers indicating the probe design correspond to that given in Table 5.1.
5.6 Concluding Remarks

The results presented in this Chapter indicate the relative merits and demerits of different rf probe designs.

In summary, it is seen that higher Q values are afforded by the resonator probe designs and that the split-ring resonator gives the best results. In general, the dielectric losses associated with the resonator probes are lower than that of the saddle coil, and the H-resonator provides the best performance with respect to this parameter. Qualitative estimates show that the resonators generate higher inductive losses compared to the saddle coil. The best rf homogeneity is provided by the split-ring resonator. The rf homogeneity of the saddle coil is comparable to that of the H-resonator in the transverse plane and the former offers better performance along the longitudinal axis.

The comparative results of different probe designs also indicate the difficulty in optimizing all the desirable features with a single design. Thus compromises are essential, and the choice of a probe is best done by giving particular attention to the desired criteria depending on the application. It can be stated that, of the designs investigated here, the split-ring resonator probe provides the best overall performance. But unfortunately its use is restricted because of the awkward orientation of the probe inside the magnet.

Under severe sample loaded conditions \((Q_{UL} \gg Q_L)\), and when the sample losses are mostly due to inductive losses, the S/N ratio is independent of any probe parameters [22a]. Hence, any further improvement of probe design will have little effect on the S/N. But with a
particular sample, the attainment of the above condition depends on the probe design used. The best indicator of this is the $Q_{UL}/Q_L$ ratio\(^1\) of the probe. From the values given in Table 5.1, this ratio is highest for the split-ring resonator ($Q_{UL}/Q_L = 3.4$) and lowest for the saddle coil ($Q_{UL}/Q_L = 2.3$). Considering also the fact that the dielectric contribution to the sample losses is small for the resonator designs, use of these probes should be preferred over the saddle coil.

Further, the independence of $S/N$ of probe parameters upon reaching the condition $Q_{UL} \gg Q_L$ does not imply that little attention should be directed towards the characteristics of the particular design used. For example, good $B_1$ homogeneity would still be required since it determines the uniformity of the image. The $B_1$ homogeneity maps show that H-resonator designs are poor candidates for imaging in the planes which include the longitudinal axis of the probe and that the split-ring resonator is most suitable choice for three-dimensional volume imaging.

5.7 Experimental

The probe $Q$ values were measured on the bench with the probe tuned and matched approximately to 80 MHz. The experimental setup [32] used was that available in the UBC Chemistry Department Electronic Shop. This included a signal generator (Wavetek 3001), a sweep generator

\(^1\) Note that these ratios cannot be taken as indicative of the total sample losses when comparing different probe designs.
(Wavetek 2002A), an rf reflexion bridge, an rf detector and an oscilloscope. The Q values reported for each probe are the average values of several independent measurements, taken as the ratio of the resonance frequency to the full-width at half-power point (70% of the voltage maximum) of the probe resonance.

S/N values were determined using standard software [33]. For each measurement the magnet was shimmed with a 1 ml water sample so that the typical line-width was approximately 3 Hz. The actual S/N ratio is higher than the values quoted because of the deviation of the signal from a true Lorentzian line shape.

5.7.1 Method of $B_1$-mapping

The $B_1$ magnetic field profiles were generated by using a variant of an existing method [34,35]. The pulse sequence used consisted of a spin-echo experiment performed in the presence of a gradient (see Chapter II, Fig. 2.4a), and in which the length of the first rf pulse ($t_1$) was made variable. A data matrix, $S(t_1, t_g)$, was acquired by incrementing $t_1$ by a constant amount while the second rf pulse was set to 180°; $t_g$ corresponds to the signal acquisition time, which is initiated after the 180° pulse, in the presence of a gradient. Double Fourier transformation of $S(t_1, t_g)$ produces $S(\omega_1, \omega_g)$, where $\omega_1$ and $\omega_g$ correspond, respectively, to the magnitude of $\gamma B_1$ and the spatial axis defined by the gradient. Thus the magnitude of the $B_1$ magnetic field and the lack of uniformity thereof are directly obtained from the pro-
cessed data set.

It is conceivable that this experiment could be extended to incorporate all three spatial axes by introducing phase-encoding gradients between the two rf pulses. This would enable complete characterization of the rf magnetic field in the whole volume enclosed by the probe. However such an experiment would produce a large amount of accumulated data which would have to be subjected to a four-dimensional Fourier transformation.

The results reported in this Chapter were obtained by using a 5 mm NMR tube containing water as the phantom. The phantom was oriented along either one of the three principal axes x, y or z with the corresponding gradient being applied during the sequence of each experiment. The data matrices typically consisted of 64 pulse length values, a pulse length increment of 20 μsec and an acquisition block size of 256. The data were apodized with a sine-bell function [33] in both dimensions prior to Fourier transformation and zero-filled once along the $t_1$ dimension giving rise to a final real data matrix size of 128 x 128. The length of the water phantom was selected depending on whether the axial or the radial $B_1$ homogeneity was being investigated. For axial homogeneity measurements the phantom length was approximately equal to the length of the probe (14 cm), while for radial measurements the phantom length (6.5 cm) was dictated by the inner diameter of the probe (7.0 cm).

The use of a similar procedure for $B_1$ mapping has also been presented at a recent conference [36].
References: Chapter V


CHAPTER VI

$^{31}$P NMR SPECTROSCOPY IN VIVO
6.1 Introduction

Since the initial attempts to detect NMR signals from a living animal [1], in vivo $^{31}$P NMR spectroscopy has progressed to a stage where its clinical utility is beginning to emerge [2]. This rapid advancement has been mainly due to the introduction of the surface coil (a flat loop of wire) [3,4] as an NMR receiver coil. Surface coils provide a simple method of detecting signals from a localized region close to the surface of a sample. Thus, during the last few years skeletal muscle disorders have been extensively studied using this technology [5,6].

Unlike the skeletal muscle, noninvasive NMR study of the internal organs such as the kidney, liver and the heart present a formidable challenge. In these situations direct use of a surface coil or other coil types is not possible due to the unwanted signal contributed by the tissues around the organ of interest. Several signal localization methods have so far been proposed to circumvent this problem [4,7]. Most of these methods are either inconvenient to use in a practical situation or still under development [7]. Though in vivo $^{31}$P spectra from the liver [8] and the kidney [9] have been obtained noninvasively via the field profiling technique [8], this method is not routinely used due to its complexity and lack of flexibility. Therefore, in vivo spectroscopic studies of internal organs usually rely upon surgical intervention to position the organ in the NMR receiver coil, concur-
rently removing it from the surrounding tissue [10,11]. In order to reduce the possible adverse effects due to these surgical maneuvers a technique for implanting rf coils around the organ of interest has also been reported [12]. More recently, the use of two concentric surface coils to obtain rat liver spectra without the need for surgery has been described [13].

The application of $^{31}$P NMR to study the metabolic processes in the kidney has attracted wide attention in the past decade and a variety of kidney preparations have been investigated [14]. Due to the restriction of space in the NMR probe, initial studies were conducted on isolated kidneys, and advances in magnet design together with the developments noted earlier have recently enabled such studies to be conducted in vivo [15-19].

The work described here was initiated to examine by $^{31}$P NMR, the biochemical transformations of the rat kidney in vivo during (ischemia) and after (reperfusion) a period of inadequate blood flow into the organ. Of further interest was the influence of various agents (drugs) on the rate of recovery of renal adenosine triphosphate (ATP) levels following an ischemic period. The interest in these studies lies in the fact that warm renal ischemia is commonly encountered in a number of clinical situations, and is particularly important in transplant procedures [20]. Application of $^{31}$P NMR to study the metabolic changes in the rat kidney in vivo during ischemia and reperfusion has also been undertaken by other workers [17].

This work was performed in collaboration with, and following an initial suggestion by Dr. A.P. Autor (Department of Pathology, UBC), who
pointed out the importance of such studies. The author's efforts were concentrated on the aspects related to the NMR experiment. Accordingly the particular experimental protocol adopted and some preliminary results are discussed in the next section.

6.2 Experimental Protocol, Results and Discussion

Prior to performing any experiments, it was necessary to devise a suitable procedure to obtain $^{31}$P NMR spectra representative of the rat kidney. The method pursued here was based on the procedures reported earlier [15-17], and involved the use of a surface coil as the NMR coil. For this purpose a surface coil probe, consisting of a flat bed (31 x 18 cm) made of Plexiglas was constructed so that the animal could be laid in a horizontal posture. A schematic diagram of the probe and animal positioning is shown in Fig. 6.1. The coil itself (diameter 1.5 cm) was constructed of two turns of copper wire (diameter 1.25 mm) insulated with Teflon, and consisted of leads long enough to reach the area to be investigated. The coil was supported above the animal with the aid of Teflon bars attached to the side of the probe. This support was adjustable horizontally as well as vertically, and provided the required flexibility in positioning the coil. The capacitors required for coil tuning were mounted underneath the probe bed. The probe constructed in this manner, when tuned to ca. 32.5 MHz, was found to have a Q value of 150.
Fig. 6.1: Schematic diagram of the NMR surface coil probe and the animal orientation used for $^{31}$P NMR studies of the rat kidney.
Typically, the anesthetized animal with its abdominal cavity exposed was placed on the probe bed and the rf coil was suitably positioned. Subsequently, the whole NMR probe with the animal in position was inserted into the horizontal bore magnet.

In order to find the signal localizing ability of the surface coil, an initial experiment was performed by placing the surface coil directly above the left kidney. In this instance suitable care was exercised not to disturb the kidney from its natural position except to remove the surrounding fat to facilitate coil placement. The spectrum obtained with this arrangement is shown in Fig. 6.2a. The peak assignments are based on that given in Ref. 17. As the kidney does not contain phospho-creatine (PCr) [16,17], the significant amount the PCr seen in this spectrum indicates the contribution from the surrounding muscle to the observed signal. This situation was unacceptable, and further the improved signal localization afforded by the variations in pulse length (and hence the sample region detected by the coil) and displacement of surrounding tissue was judged to be inadequate.

Guided by this experience it was subsequently found that the PCr signal can be conveniently eliminated by partially closing the abdominal cavity and suspending the kidney in an orientation as indicated in Fig. 6.1. The spectrum obtained with this coil and organ positioning is shown in Fig. 6.2b. The essential features of this spectrum, except for the signal-to-noise ratio, is identical to that of the normal kidney reported in the literature [17]. The small amount of PCr seen in the spectrum is most probably from the abdominal muscle. It was found that this method was convenient and the spectrum could be reproduced without
Fig. 6.2: 32.5 MHz $^{31}$P NMR spectra of the rat kidney. (a) Surface coil placed directly above the kidney in its natural position. (b) The kidney is positioned as shown in Fig. 6.1. Experimental parameters: pulse width = 10 μs, relaxation delay = 500 ms, number of scans = 1000, acquisition time = 256 ms, line broadening = 20 Hz.
difficulty. Prior to adapting the above configuration, the method of flank incision and the use of a solenoidal coil was also tested [17], but was found to be less convenient due to a more subtle surgical procedure in these cases, spectra showed an increased inorganic phosphate content due to the partial ischemic nature of the organ immediately after the operative procedure.

The study was then extended to monitor the changes in phosphorus metabolite concentrations during ischemia and reperfusion. After the surgical procedure (see later), the viability of each preparation was confirmed by acquisition of one or two spectra under normal conditions. The left kidney was then made ischemic for 30 min by occluding the renal vessels with a small plastic clip, and "ischemic" spectra were collected during this period. After the ischemic period the clip was removed and "reperfusion" spectra were obtained. A series of spectra obtained under such conditions is shown in Fig. 6.3. Each spectrum in Fig. 6.3 represents the average of the metabolite concentrations during the 12 min observation period. During the period of ischemia ATP levels decreased rapidly with concomitant increase in inorganic phosphate. Following the release of the renal vessels the reverse process was observed. This trend was reproduced in all animals studied.

However, the interest is focussed on the recovery of the ATP levels to the control (preischemic) values since it indicates the possible renal damage due to ischemia and reperfusion [17]. On comparison of the $\beta$-ATP resonance in the spectra shown in Fig. 6.3(i) and (vii) it can be seen that the recovery of ATP is incomplete. In the limited number of animals studied the extent of ATP recovery was found to have a large
Fig. 6.3: 32.5 MHz $^{31}$P NMR spectra obtained from a rat kidney during periods of ischemia and reperfusion. Each spectrum represents 12 min accumulation time.
variation. It was subsequently evident that the changes in the body temperature of the animal during the experiment was a contributing factor to this observation. The preliminary results obtained by treating the animal with different drugs were encouraging but warrant further study.

Due to the preliminary nature of this study, definite conclusions could not be drawn. It is necessary that these experiments be repeated under more controlled conditions, in that the body temperature of the animal be maintained and monitored during the experiment. The facilities for these controls were not available at the time of this study. However, the experiments reported here indicate that the protocol adopted (NMR and surgical) can be used to study ischemia/reperfusion models in the rat kidney and thus provides the necessary foundation for the future work to be carried out in this laboratory.

6.3 Experimental

The NMR spectra were recorded using the spectrometer system described in Section 4.4. The magnet was initially shimmed using a phantom containing H₃PO₂ and constructed to the approximate dimensions of a rat kidney (2.0 x 1.5 x 1.0 cm). Subsequently, the magnet was further shimmed by observing the ¹H signal from the kidney while the coil was tuned to ³¹P [21]. ³¹P spectra were recorded by adjusting the pulse width to obtain the maximum signal intensity when using the surface coil [22].
Surgical procedure: Male Wistar rats weighing 300-350 g were used in all experiments. Anesthesia was induced by intraperitoneal injection of 3.6% chloral hydrate 1 ml/100 g body weight. A midline abdominal incision was made and the viscera were reflected to the left. The inferior vena cava was cannulated with polyethylene tubing (PE 50) for administration of drugs and fluids. The left kidney was then mobilized into the wound based on its vascular supply. The kidney was suspended in the wound by closing the latter with interrupted sutures of 3-0 silk. The kidney was oriented with its long axis in the same line as the incision and its lateral edge pointing anteriorly. The vessels were not kinked or twisted. The animals were given 2 ml of 0.9% NaCl intravenously every hour and supplemental anesthetic as needed.

After the acquisition of the normal kidney spectrum, the animals were given heparin (50 units) intravenously, and the renal vessels were occluded with a small plastic vascular clip. Following the acquisition of "ischemic" spectra the animals were treated intravenously with 1.5 ml 5% dextrose (D5W). Two minutes after the treatment, the vascular clip was removed and the "reperfusion" spectra were obtained. At the end of the experiment the animals were sacrificed by cervical cord dislocation.

The above surgical procedure was performed by Dr. N. Gurll.
References - Chapter VI


SUMMARY AND DISCUSSION
SUMMARY AND DISCUSSION

This Section serves to summarize briefly the studies described in the previous Chapters and to discuss future extension and applications.

At the commencement of this work (September 1982) NMR imaging was mostly being performed using the first generation of whole body imaging systems operating at low fields (<0.25T). But the availability of horizontal bore magnets designed for spectroscopic studies at high field (1.8T) prompted several groups including ours to incorporate imaging capabilities to such devices. One facet of the work described in this thesis was performed with this aim.

Chapter II dealt with the basic concepts of NMR imaging with special emphasis on Fourier imaging techniques. In the absence of an account in the literature which concentrates on important aspects of this widely used imaging method in detail, it is hoped that this Chapter would fill the void.

Chapters III and V focussed on two essential ingredients of NMR imaging. Specifically, a systematic study of the theory, implementation and the experiment of the tailored excitation procedure in relation to slice selection was presented in Section 3.1. Even though the essential concepts of this procedure were well known, the practical details of the use of continuous rf modulation scheme in NMR remained elusive. Therefore a detailed description of the procedure adopted here is included in Section 3.1. Experimental results which correspond closely with that predicted by theory were also obtained with the described scheme. It
should be mentioned that since initiation of this study, two reports which describe useful practical aspects of the method have been published.

A detailed account of rf probe designs suitable for high field imaging, describing their modification, construction and performance was presented in Chapter V. The subject was approached from an experimentalist's point-of-view. The probe designs investigated here (H-resonator, bird-cage resonator and split-ring resonator; see Section 5.4) were suitably modified to produce easily fabricated and low-cost probes. The modifications involved the incorporation of inductive coupling and tuning mechanisms into the originally proposed configurations together with efficient use of intrinsic features of each design to generate the capacitance (Section 5.5). The three resonator probe designs and a conventional saddle coil were then evaluated by measuring several parameters directly related to the performance of the probes (Section 5.5). The $B_1$ homogeneity of the probes was experimentally evaluated by employing the spin-echo version of the rotating frame zeugmatography experiment (Section 5.7). This method enables the determination of the magnitude of the $B_1$ field and the lack of uniformity thereof directly from the experimental plots and hence would be of considerable value for future studies. Comparative results of the probe designs investigated here show that the best overall performance is provided by the split-ring resonator probe and that it would be a more suitable choice for three-dimensional volume imaging. Though the perpendicular orientation of this probe inside the magnet creates some difficulties, it is nevertheless well suited for inanimate imaging applications. Previously
unavailable comparative results produced by this study indicate the merits and demerits of different probe designs and thus provide some guidelines for selecting the most suitable design depending on the application.

The capabilities afforded by the above studies were then used to image several intact systems. Good quality images with adequate spatial resolution were obtained (Section 4.1.2). Three-dimensional images of a rat were also presented in Section 4.2.2.

It is anticipated that further improvement in image quality can be realized by giving more careful attention to aspects such as the signal-to-noise ratio of the spectrometer system and optimization of gradient behavior. Further, a more versatile image display device would be an added asset in improved data display and hence in optimization of experimental parameters to obtain the best contrast between the structures of interest.

Two experiments which relate to chemical shift effects were described in Sections 3.2 and 4.3.1. In one, the problem of slice selection in the presence of chemically shifted species was addressed. A possible solution to this problem based on the use of a suitably modulated rf pulse followed by appropriate data acquisition and manipulation was illustrated with a simple phantom. This work is most pertinent to high field NMR imaging applications where images free from chemical shift artifacts and of very high spatial resolution are desired. However it remains to be established whether such artifacts are best eliminated by the increase in gradient strength or by other means.
Techniques which enable two-dimensional chemical shift resolved imaging were introduced in Section 4.3.1. The methods involve selective excitation and suppression of specific resonances prior to the application of conventional imaging sequences. This allows chemical shift selection to be carried out under high resolution conditions and also the image resolution, signal-to-noise ratio and the acquisition time to be maintained similar to that of conventional imaging. Since the report of this approach its utility has been recognized by other workers and several convenient adaptations of the technique have been suggested and demonstrated.

The application of three-dimensional chemical shift resolved imaging to map the spatial distribution of pH and temperature was demonstrated in Section 4.3.2. The importance of this demonstration lies in the fact that at present there is no reliable means of noninvasive in vivo pH and temperature mapping, and that such information would be extremely valuable in many occasions. For example, temperature maps would be of invaluable help when hyperthermia treatments for malignant tumors are considered and similarly pH maps could well provide greater insight to the bioenergetics of human muscle. However, the extension of the present study to in vivo systems would be met with more stringent demands, in that mapping of narrower pH/temperature ranges along with finer spatial resolution would be required for most applications. Nevertheless, the present work provides a foundation for such studies which may best be attempted at higher magnetic fields and therefore its full potential remains to be explored.
Finally, the preliminary results of $^{31}$P NMR spectroscopic studies of the rat kidney during periods of ischemia and reperfusion were presented in Chapter VI.
APPENDIX
A Computer Programme to Integrate BLOCH Equations for a rectangular pulse.

COMMON YDLRAY(2000)
DIMENSION DFREQ(210), AMX(210), AMY(210), AMZ(210), AMXY(210), PHI(210), IPAK(210), FTMX(210), FTMY(210).

C DEFINE VARIABLES
C
AMO = INITIAL VALUE OF MZ
TPULS = PULS LENGTH (MSEC)
ANGL = FLIP ANGLE (DEGREES)
N = NO. OF TIME STEPS
NM = PLOTTING PARAMETER

READ(5,10) AMO, TPULS, ANGL, N, NM
FORM(3F10.4, 2I6)
WRITE(6,20) AMO, TPULS, ANGL, N, NM
FORM(/, 2X, 'INITIAL VALUE OF MZ = ', F10.4,
/ , 2X, 'PULS LENGTH (MSEC) = ', F10.4,
/ , 2X, 'FLIP ANGLE (DEGREES) = ', F10.4,
/ , 2X, 'NO. OF TIME STEPS = ', I6,
/ , 2X, 'PLOTTING PARAMETER = ', I6)
PI = 4.0 * ATAN(1.0)
ANGLR = PI * ANGL / 180.
OMEGA1 = ANGLR * 1000. / TPULS
DT = TPULS / 1000. / FLOAT(N)
DF = 1000. / TPULS / 20.
DFREQ(1) = -5. * 1000. / TPULS
WRITE(6,30)

C Start DO LOOP to go through different DFREQ values
C
DO 500 I = 1, 201
AMX(I) = 0.0
AMY(I) = 0.0
AMZ(I) = AMO
TIME = 0.0
IJ = -1

C Start DO LOOP for the Time Integration
C
DO 400 J = 1, N
AMX1 = AMX(I)
AMY1 = AMY(I)
AMZ1 = AMZ(I)
AMX(I) = AMX1 + DT * AMY1 * 2. * PI * DFREQ(I)
AMY(I) = AMY1 + DT * OMEGA1 * AMZ1 - DT * AMX1 * 2. * PI * DFREQ(I)
AMZ(I) = AMZ1 - DT * OMEGA1 * AMY1 - DT * AMX1 * 2. * PI * DFREQ(I)
TIME = TIME + DT
CONTINUE

AMXY(I) = SORT((AMX(I) * AMX(I)) + (AMY(I) * AMY(I)))
PHIR = ATAN(AMX(I) / AMY(I))
PHI(I) = PHIR * 180. / PI
IF(AMX(I).GE.0.0) IJ = 1
IF(AMY(I).GE.0.0) GO TO 310
PHI(I) = PHI(I) + (IJ * 180.0)
C LINEAR APPROX. CALC.

310  FTDF = 2. * PI * TPULS * DFREQ(I) / 1000.
IF(ABS(FTDF).GT.0.0) GO TO 320
320  FT MX(I) = AMO * (1. - COS(FTDF)) * ANGLR / FTDF
FTMY(I) = AMO * ANGLR * SIN(FTDF) / FTDF
FTMXY(I) = SIN(SORT(FTMX(I)*FTMX(I)+FTMY(I)*FTMY(I)))
330  DFREQ(I+1) = DFREQ(I) + DF
500  CONTINUE
700  CONTINUE
950  STOP
END

C A COMPUTER PROGRAMME TO INTEGRATE BLOCH EQUATIONS
FOR A SINC PULSE

IMPLICIT REAL*8(A-H,O-Z)
REAL*4 DOME,AMXX,AMYY,BMXY,PHI I
DIMENSION W1(10),X1(10),DOME(410).AMXX(410),AMYY(410),BMXY(410),PHII(410)
DATA W1/ 0.066671344308688D0, 0.149451349150581D0,
1 0.219086362515982D0, 0.269266719309966D0,
2 0.295524224714753D0, 0.295524224714753D0,
3 0.269266719309966D0, 0.219086362515982D0,
4 0.149451349150581D0, 0.066671344308688D0/
DATA X1/ -0.973906528517172D0, -0.865063366688985D0,
1 -0.679409568299024D0, -0.433395394129247D0,
2 -0.148874338981631D0, 0.148874338981631D0,
3 0.433395394129247D0, 0.679409568299024D0,
4 0.865063366688985D0, 0.973906528517172D0/

C READ IN INPUT VARIABLES
C DEFINE VARIABLES
C AMO = INITIAL VALUE OF MZ
C TAU = 1ST NODE PT. OF SINC FUNCTION
C TPULS = TOTAL LENGTH OF SINC FUNCTION(MS)
C N = NUMBER OF TIME STEPS NECESSARY FOR THE TIME
C INTEGRATION
C ANGL = FLIP ANGLE ( DEGREES )

READ(5,10) AMO, TAU, TPULS, N, ANGL
10 FORMAT(3F10.4,16,F10.4)
WRITE(6,20) AMO, TAU, TPULS, N, ANGL
20 FORMAT(/,2X,'INITIAL VALUE OF MZ' = ',F10.4,
1 /,2X,'1ST NODE PT. OF SINC FUNCTION(MS) = ',F10.4,
2 /,2X,'TOTAL LENGTH OF SINC FUNCTION(MS) = ',F10.4,
3 /,2X,'NO. OF TIME STEPS = ',16,
4 /,2X,'FLIP ANGLE ( DEGREES ) = ',F10.4,/
PI = 4.DO * DATAN(1.DO)
ANGLR = PI * ANGL / 180.DO
SUM = 0.0
C NUMERICAL INTEGRATION OF THE SINC FUNCTION

DD 200 I = 1, 10
   ZETA = X1(I)
   X  = TPULS * ZETA / 2000.DO
   XX = PI * 1000.DO * X / TAU
   FX = DSIN(XX) / XX
   SUM = SUM + W1(I) * FX
200 CONTINUE
   SUM = SUM * TPULS / 2000.DO

C CALCULATE THE AMPLITUDE AND TIME AND FREQUENCY INTERVALS

AMPL = ANGLR / SUM
DT = TPULS / 1000.DO / FLOAT(N)
DF = 8.DO * 500.DO / TAU / 400.DO
DFREQ = -4.DO * 500.DO / TAU
NPTS = 401

WRITE(6,210) AMPL, DT, DF
210 FORMAT(/,2X,'AMPLITUDE OF THE SINC FUNCTION = ',4X,F10.4,1/,2X,'TIME STEP = ',F10.8,2/,2X,'FREQUENCY OFFSET STEP = ',4X,F10.4,/) WRITE(6,30)
30 FORMAT(/,10X.'DFREQ',8X,'AMX',12X,'AMY',12X,'AMXY',12X,'PHI',/)

C START DD LOOP TO GO THROUGH DIFFERENT DFREQ VALUES

DD 500 I = 1, NPTS
   AMX = 0.DO
   AMY = 0.DO
   AMZ = AMD
   TIME = 0.O
   IJ = -1

C START DD LOOP FOR THE TIME INTEGRATION

DO 400 J = 1, N
   TSHIFT = 1000.DO * (PI / TAU) * ( TIME-TPULS/2000.DO)
   IF(DABS(TSHIFT).GE.10.D-4) GO TO 310
   OMEGA1 = AMPL
   GO TO 320
310 OMEGA1 = AMPL * DSIN(TSHIFT) / TSHIFT
320 AMX1 = AMX
   AMY1 = AMY
   AMZ1 = AMZ
   AMX = AMX1 + DT * AMY1 * 2.DO * PI * DFREQ
   AMY = AMY1 + DT * OMEGA1 * AMZ1
   AMZ = AMZ1 - DT * AMX1 * 2.DO * PI * DFREQ
   AMX = AMX1 + DT * AMY1 * 2.DO * PI * DFREQ
   AMY = AMY1 + DT * OMEGA1 * AMZ1
   AMZ = AMZ1 - DT * OMEGA1 * AMY1
   TIME = TIME + DT
400 CONTINUE

C CALCULATE MXY AND THE PHASE ANGLE

AMXY = DSQRT((AMX * AMX) + (AMY * AMY))
PHIR = DATAN(AMX / AMY)
PHI = PHIR + 180.DO / PI
IF(AMX.GE.0.DO) IJ = 1
IF(AMY.GE.0.DO) GO TO 410
   PHI = PHI + (IJ * 180.DO)
410 DOME(I) = DFREQ
   AMXX(I) = AMX
   AMYY(I) = AMY
   BMXY(I) = AMXY
   PHII(I) = PHI
   DFREQ = DFREQ + DF
   WRITE(6,450) DOME(I), AMXX(I), AMYY(I), BMXY(I), PHII(I)
450 FORMAT(F15.4,3F15.9,F15.4)

CALL GRAPH(NPTS,DOME,AMXX,AMYY,BMXY,PHII)
STOP
END

