Magnetic resonance imaging studies of the behavior of fluids in gelatin and other porous materials

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MAGNETIC RESONANCE IMAGING STUDIES
OF THE BEHAVIOR OF FLUIDS
IN GELATIN AND OTHER POROUS MATERIALS

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Statement of Authorization

Title of thesis: Magnetic Resonance Imaging Studies of the Behavior of Water in Gelatin and other Materials

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Date: 3/7/71
to Deirdre,
my wife
MAGNETIC RESONANCE IMAGING STUDIES
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Abstract

by
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An application of magnetic resonance imaging to the study of the diffusion of water in gelatin and other materials is described. Gelatin was studied in great detail while plaster, balsa wood, and cement were studied to a lesser degree. Images of the materials at various stages of the diffusion process were recorded and analyzed. In order to properly interpret the imaging signal, the relationships between two intrinsic system parameters, $T_1$ and $T_2$, with the experimental parameters of the study need to be established. In the case of gelatin studies, $T_1$ and $T_2$ times were measured for gelatin samples varying in gelatin concentration and degree of D$_2$O dilution. $T_1$ and $T_2$ were found to decrease with increasing gelatin concentration and increase with increasing D$_2$O dilution. $T_1$ relationships were modeled successfully with the cross-relaxation theory while $T_2$ relationships were established empirically. Two gelatin studies were performed, one involving the counter-diffusion of H$_2$O and D$_2$O in a cross-linked gelatin matrix of a given gelatin concentration, and one involving the drying of a water containing gelatin matrix. In the counter-diffusion study, the self-diffusion coefficient for H$_2$O was found to be $2.0 \times 10^{-5}$ cm$^2$/s. The diffusion coefficients of H$_2$O in gelatin matrices of 1.5, 5, and 11% wt. gelatin were found to be 2.0, 1.8, and $1.5 \times 10^{-5}$ cm$^2$/s, respectfully. In the drying study, it was found that a good first approximation for the modeling of the drying process is provided by Fick's second equation solved with a diffusion coefficient depending linearly with gelatin concentration. The shrinking character of the drying gelatin sample needs to be included in a more precise model.
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List of Symbols and Abbreviations

\(a,b\) factors used to accommodate viscosity differences
\(b_i\) microscopic magnetic field
\(b(t)\) microscopic magnetic field changing as a function of time
\(b_x,b_y,b_z\) \(x, y, \text{ and } z\) components of the microscopic magnetic field
\(B_0\) external magnetic field
\(B_1\) RF magnetic field
\(D_i\) diffusion coefficient of \(i\)
\(f\) fraction of \(H_2O\) in \(H_2O-D_2O\) mixture
\(g\) gravitational constant
\(h\) mass transfer coefficient
\(^1H\) hydrogen nucleus, proton
\(^2H\) deuterium nucleus, deuteron
\(\hbar\) Plank's constant divided by \(2\pi\)
\(K\) proportionality constant in spin echo equation
\(k_b\) Boltzmann constant
\(k_{\text{ex}}\) exchange constant between water and protein proton populations
\(M\) net magnetization vector
\(M_0\) net equilibrium magnetization vector
\(M_s\) mass of dry protein
\(M_{x,y,z}\) \(x, y, \text{ and } z\) components of the net magnetization
\(M_{xy}\) transverse component of the net magnetization
\(M_w,M_p\) net magnetization resulting from water protons and protein protons
\(M_{wo},M_{po}\) net equilibrium magnetization from water and protein protons
\(MR\) magnetic resonance
\(MRI\) magnetic resonance imaging
\(n\) total moles of water
\(n_i\) difference in the number of spins in each energy level for a given population at a given time
\(N^+\) number of spins in the high energy level
\(N^-\) number of spins in the low energy state
\(R\) radius
\(RF\) radio frequency
\(S\) signal strength, arbitrary units
\([S_i]\) molar spin concentration of \(S_i\)
\(T\) Kelven temperature
\(TE\) echo time
\(TR\) repetition time
\(T_{1w},T_{1p}\) relaxation times of water protons and protein protons
\(T_{1b},T_{1s},T_{1bd}\) relaxation times of bulk, structured, and bound water
\(v_{b},v_{s},v_{bd}\) volume fractions of bulk, structured, and bound water regions
\(\gamma\) gyromagnetic ratio
\(\zeta\) factor to account for the protein proton magnetization gained by the perturbation signal
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<td>$\kappa$</td>
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<td>$\mu$</td>
<td>nuclear magnetic moment</td>
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<td>$\rho$</td>
<td>spin density</td>
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<tr>
<td>$\tau_c$</td>
<td>correlation time</td>
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<tr>
<td>$\phi$</td>
<td>gelatin concentration (g dry gelatin protein/mol water)</td>
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1. Introduction

Magnetic resonance imaging (MRI) is a nondestructive, diagnostic tool that has been used primarily in the clinical setting. It provides the researcher with an in-vivo image of the human body in much the same way as the well established computer assisted tomography (CAT) scanner but without the harmful ionizing radiation. In recent years, however, MRI has been applied to a number of non-clinical areas including that of materials investigation.

In this thesis MRI was utilized to record a signal from hydrogen nuclei of water molecules contained within various experimental systems. Molecular processes in four materials, gelatin, plaster, cement, and balsa wood, were investigated. Specifically, the diffusion process of water in gelatin, plaster, and balsa wood and the curing process in cement were studied. The diffusion studies were executed in a manner similar to that described by Hornak. The investigation of gelatin was carried out in detail and comprises the body of the thesis, while the studies of the other three materials were carried out in lesser detail and are contained in appendices A–C. The modeling of the diffusion of water in a gelatin matrix serves as the primary objective in this thesis and the establishment of the viability of MRI in the study of materials a secondary objective.

The study of the diffusion of certain species in a gelatin matrix is of particular interest to both photographic and pharmaceutical companies. Gelatin serves as the medium for most film chemistry and is used as a vehicle for time-release drug delivery. Modeling the diffusion of water in gelatin is an important venture in these areas. MRI also provides a sensitive, noninvasive technique to find concentration profiles and pore-size distributions within porous materials. This is of particular interest to those involved with
oil recovery from porous rock. Pore-size distributions are important in developing models for the prediction of such parameters as permeability and capillary pressure curves of rock samples from oil reservoirs.\textsuperscript{4,5} Using water under high pressure has long been used as a means to recover oil from porous rock. Understanding in detail the diffusion of water within the porous matrix will substantially aid in this endeavor.

Two gelatin systems were viewed: the counter diffusion of water, H\textsubscript{2}O, and heavy water, D\textsubscript{2}O, in a gelatin matrix and the drying of a water containing gelatin matrix. MRI was used to provide signal profiles, which are plots of the signal originating from the system that the imager records versus some spatial parameter in the system. These signal profiles can be converted to concentration profiles which represent the concentration of a diffusing species versus some spatial parameter of the system. This enables the researcher to make a direct comparison to a diffusion model and acquire information such as the diffusivity of H\textsubscript{2}O in gelatin and its relationship to gelatin concentration. The conversion from a signal value to a value proportional to the concentration of the diffusing species, however, requires knowledge of two intrinsic system parameters, T\textsubscript{1} and T\textsubscript{2}, which link the signal with the microscopic dynamics of the system. Once these quantities are understood not only can the conversion be made, but further information regarding the system such as viscosity effects or perturbed molecular motion due to a confined geometry can be acquired.

MRI serves as a powerful research tool in this area of study for several reasons. It is a noninvasive, nondestructive technique that can accommodate rather large sample sizes. Systems can be studied in their natural state as the various processes unfold. They need not be broken down to study only aspects of the whole, such as techniques that only examine boundary conditions to infer internal processes, or taken apart as destructive techniques demand. This allows for a more accurate and credible description of the system. It has obvious advantages over optical techniques which correlate transmittance with the concentration of a diffusing species as these techniques won't work for opaque or near opaque materials. Furthermore, there is an abundance of theoretical work done in the area
of magnetic resonance that is available to the scientist. Much of the theory is well established. There are limitations, however, that must be observed when employing MRI. The materials studied must not be ferromagnetic as this will cause large artifacts in the image (Appendix B). The time scale of the processes must be significantly longer than the image acquisition time in order for the image to represent accurately the state of the system at a given time. Image acquisition times are typically on the order of a few minutes. Also, for some materials there are conditions that may render a small signal or even no signal. These are described later in the background section.

The remainder of this thesis is divided into three sections. A background section provides information necessary to understand the magnetic resonance phenomenon and the process of diffusion. A results section describes the work done with the diffusion of water in a gelatin matrix. This is further divided into three subsections, the first of which describes the theory of the formulation of the relaxation times, $T_1$ and $T_2$, for the ternary $\text{H}_2\text{O}-\text{D}_2\text{O}$-gelatin system. The other two subsections describe two diffusion studies performed with MRI. Each subsection contains a discussion pertinent to that subsection. Finally, a summary section contains concluding comments regarding the thesis as a whole and discusses future endeavors in this line of study.
2. Background

2.1 Magnetic Resonance Phenomenon

MRI utilizes the magnetic resonance (MR) phenomenon which was first discovered in bulk materials by Purcell, et. al.\(^6\) and Bloch, et. al.\(^7\) in 1946. Many nuclei possess a property called spin. That is, they have an intrinsic angular momentum component which creates a magnetic moment, \(\mu\), which is able to interact magnetically with the environment. If no external magnetic field is present then the individual magnetic moments of the nuclei are randomly oriented in a non-magnetic material; however, when immersed in a strong, uniform magnetic field \(B_0\) the magnetic moments will respond in two ways. First, the magnetic moments of the nuclei will adopt a time dependent spatial configuration about \(B_0\). Since the hydrogen nucleus, \(^1\)H, has a spin of 1/2 it acquires one of two configurations (or spin states), a low energy orientation with a component parallel to \(B_0\) or a high energy orientation with a component anti-parallel to \(B_0\).\(^8\) The second response is that the nucleus will precess about \(B_0\) in much the same way the moment of inertia about the axis of symmetry of a spinning top precesses due to the force of gravity. This is called the Larmor precession. The rate of this precession, the Larmor frequency \((\omega_1)\), can be expressed (in rad/s) in the equation,

\[
\omega_1 = \frac{\gamma_n B_0}{\mu},
\]

where \(\gamma_n\) is called the gyromagnetic ratio and is specific for each nucleus.\(^8\) The precession leads to a resonance effect; energy can be imparted to the nucleus most efficiently at \(\omega_1\). Furthermore, it is necessary for this energy to be electromagnetic in origin in order for the
magnetic moment of the nucleus to interact with it. Introduction of this energy into the spin system may flip a nucleus to a higher energy level or provide a pathway for it to relax to a lower one.

The MR signal comes from an ensemble of spins as opposed to one spin alone. The magnetic moments of the nuclei assume an equilibrium configuration about $B_0$. In other words, there is a steady difference in the number of nuclei occupying the high energy state with that occupying the low energy state. At equilibrium there are more magnetic moments oriented in the low energy spin state as described by the Boltzmann distribution,

$$N^+/N^- = e^{-\gamma \hbar B_0 / k_b T},$$  \hspace{1cm} (2)

where
- $N^+$ = number of spins in high energy state
- $N^-$ = number of spins in low energy state
- $k_b$ = Boltzmann constant
- $T$ = temperature
- $\hbar$ = Plank's constant divided by $2\pi$.

The sum of all the magnetic moments in the system creates a net magnetization $M$ in the direction of $B_0$. This is depicted in Figure 1. We can define $M = M_0$ at equilibrium MRI is an extremely sensitive technique since the quantity $(1 - N^+/N^-)$ is on the order of $1 \times 10^{-6}$.

Under the influence of an applied radio frequency (RF) field $B_1$ at or near $\omega_1$, the configuration of $M$ will be perturbed. Two processes occur. First, some spins will flip to a higher energy level which changes the populations in each energy level. Secondly, the RF field will constrict the spins to precess in unison (phase coherence). The perturbed $M$ forms two components, the longitudinal magnetization $M_z$ and the transverse
Figure 1. The net magnetization vector at thermal equilibrium. An excess number of spins in the lower energy level creates a net magnetization, \( M \), for the system parallel with \( B_0 \). As is shown by equation (2) the magnitude of \( M \) depends upon the temperature, the strength of the magnetic field, and the properties of the nucleus.
magnetization $M_{xy}$ as is shown in Figure 2. $M_z$ is the sum of the $z$ component of the magnetic moments of all the individual spins, and $M_{xy}$ is the sum of all the $x$ and $y$ components. $M_{xy}$ results from a phase coherence of the spins and rotates about $B_0$ at the Larmor frequency. Due to the presence of molecular motion in the system which will create microscopic time-dependent magnetic field fluctuations, $b(t)_i$, which may interact with the individual spins, $M$ will in time return (relax) to $M_0$ after the perturbation. Each component of $M$ relaxes exponentially with its own characteristic time constant, $T_1$ for $M_z$ and $T_2$ for $M_{xy}$ (Figure 3). The processes which cause $M_{xy}$ and $M_z$ to decay are different in nature, in fact $M_{xy}$ usually disappears long before $M_z$ returns to $M_0$.$^{10}$

$T_1$, called the longitudinal or spin–lattice relaxation time, is a measure of how fast energy is returned from the perturbed nuclei to its environment, the lattice.$^{10,11}$ Another way of defining $T_1$ is the following. If $n_0$ represents the difference in populations of the two energy levels at equilibrium and $n$ after perturbation, then $T_1$ is the time it takes for $|n-n_0|$ to be reduced by a factor of $1/e$. $T_2$, called the transverse or spin–spin relaxation time, is a measure of how fast the individual spins dephase as a result of local magnetic field fluctuations.$^{10,11}$ $T_2$ is the time it takes for $M_{xy}$ to be reduced by a factor of $1/e$. The signal is recorded from $dM_x/dt$ or $dM_y/dt$ or both with a coil of wire oriented perpendicular to $B_0$.

In order to properly interpret the MR signal, complete knowledge of the perturbation of $M$ needs to be maintained. In a pulse experiment the perturbing RF field is introduced in specific pulse sequences. The particular pulse sequence used in the study is called the spin–echo sequence which is diagramed in Figure 4. First, an RF pulse at the Larmor frequency of the nuclei of study is applied to rotate $M$ $90^\circ$. $M_z$ and $M_{xy}$ will immediately begin to relax upon the termination of the pulse; however, no signal is recorded at this time. Due to local field inhomogeneities the spins will begin to dephase quickly, however, this is recoverable. After some chosen time ($\tau$ in Figure 4) another $180^\circ$ RF pulse is applied. This will flip $M_{xy}$ $180^\circ$ and instead of the spins dephasing they are
Figure 2. The net magnetization perturbed by an RF signal $B_1$. When perturbed by an RF signal at the Larmor frequency, the net magnetization vector possesses two components, a longitudinal component, $M_z$, in the $z$–direction and a transverse component, $M_{xy}$, in the $xy$–plane. It is $M_{xy}$ that provides the signal for the instrument.
Figure 3. The behavior of the longitudinal and transverse magnetization as a function of time after perturbation from its equilibrium position. $M_z$ and $M_{xy}$ relax exponentially with their own characteristic time constants, $T_1$ and $T_2$ respectively.
Figure 4. Time diagram of the spin–echo pulse sequence. The first RF pulse creates a $B_1$ field which rotates $\mathbf{M}$ $90^\circ$ clockwise about $B_1$ (1–2). Time elapses as the spins dephase due to local field inhomogeneities (2–3). After time, $\tau$, a second RF pulse rotates the spins $180^\circ$ (3–4). As time elapses the spins now converge (rephase) and a signal is recorded. The maximum signal intensity is reached at (5) at a time $TE = 2\tau$. Due to $T_2$ processes some of the original transverse magnetization is lost, and as a consequence the magnitude of $\mathbf{M}_1$, at (5), is described by $\mathbf{M}_1 = \mathbf{M}_0 e^{-2\tau/T_2}$. 
put in an orientation where they will start to rephase again. This "echo", as it is called, is recorded as a signal which starts out small but grows as the spins rephase and then diminishes as the spins start to dephase again. The maximum height of the echo signal is reached at a time, $TE = 2\tau$, after the $90^\circ$ pulse. Due to $T_2$ processes, the magnitude of the transverse magnetization vector at position (5) in Figure 4 will have diminished exponentially so that $M_1 = M_0 e^{-2\tau/T_2}$. The shape of the RF pulses in Figure 4 represent the envelope of an RF waveform created by an apodised sinc function. This special shape helps to create a narrow, square distribution of frequencies with which to irradiate the sample thereby allowing for good spatial resolution.\textsuperscript{12} Two characteristic times are experimentally chosen to construct the sequence, the echo time $TE$ and the repetition time $TR$. $TE$ is defined as the time interval between the $90^\circ$ pulse and the midpoint of the sampling interval, or the time required to collect the signal. $TE$ is double the time between the $90^\circ$ pulse and $180^\circ$ pulse. $TR$ is the time interval between two succeeding $90^\circ$ pulses. Both are chosen to maximize the recorded signal in most cases but may also be chosen to highlight a particular spin characteristic.\textsuperscript{13} The signal strength, $S$, for the $TR >> TE$ case is an exponential function of these characteristic times:\textsuperscript{14,15}

$$S = K \rho (1-e^{-TR/T_1})e^{-TE/T_2},$$  \hspace{1cm} (3)

where $\rho$ is the spin density and $K$ is a proportionality constant. The relaxation times are essential in determining $S$.

The spin–echo sequence was chosen for this research because it gives information on both $T_1$ and $T_2$ so a dependence of both $T_1$ and $T_2$ on certain experimental parameters could be found. This is helpful because knowing the relaxation times provides a link to the microscopic motions and processes within the system.

In MRI the signal information is portrayed in an image.\textsuperscript{16} Figure 5 outlines this procedure. The imager first selects a volume slice through the sample which is
Figure 5. Outline of the image acquisition process. With use of magnetic field gradients, the imager isolates a tiny volume element, voxel, and records a $^1H$ signal from the water molecules within. The signal strength, given by equation (3), depends upon the density of $^1H$, $\rho$, and the relaxation times, $T_1$ and $T_2$. An image is then created by assigning to a picture element, pixel, a grey level value based on the signal strength value and displaying them correspondingly on a screen.
accomplished with the use of magnetic field gradients. Only hydrogen nuclei within a thin volume slice through the sample will experience a resonance with the excitation RF pulse. The outline within the volume slice in Figure 5 a sample in the shape of a small bottle. The imager then divides this volume slice into a 256 x 256 array of volume elements, or voxels. The dimensions of the voxel in Figure 5 represent what was used for the research done in this thesis. The signal from the hydrogen nuclei within the voxel is then recorded. Equation (3) dictates that the signal is a function of ρ, T₁, and T₂. The signal strength is assigned a value which is stored for later analysis or may be displayed as corresponding picture elements, or pixels, which are represented as certain intensities, or grey levels, on a screen.

2.2 Relaxation Theory

The relaxation of M arises from the interactions of the magnetic moments of the nuclear spins. The frequencies of the motions of the molecules in a sample cover a wide range, wider in liquids than in solids. The motions of the μi create varying fluctuating microscopic magnetic fields, b(t)i. For example, as a H₂O molecule tumbles in space, one ¹H experiences the b(t) of the other. If b(t) has frequency components of ω₁ a spontaneous transition between spin states may occur. This changes Mz and adds to the loss of coherence of the x and y components which reduces Mxy. We can consider one of these microscopic b fields interacting with the macroscopic M. If both vectors, b and M, have components in the three directions in Cartesian coordinates then the torque on M by b may be represented by,

\[ b \times M = i(b_yM_z - b_zM_y) + j(b_zM_x - b_xM_z) + k(b_xM_y - b_yM_x). \]  (4)
From this it is clear that $b_x$ fields provide relaxation mechanisms for $M_y$ and $M_z$, $b_y$ fields produce relaxation mechanisms for $M_x$ and $M_z$, and $b_z$ fields provide relaxation mechanisms for $M_x$ and $M_y$. In other words $b_x$ and $b_y$ cause $T_1$ and $T_2$ relaxation while $b_z$ causes only $T_2$ relaxation. This is not to say that $b_x$, for instance, affects $T_1$ and $T_2$ relaxation to the same extent as there are cases where this isn’t true. All of the components of $b$ are dynamic, however, since $\mu$ rotates about $B_0$ (directed in the $z$–direction), the motions of $b_x$ and $b_y$ possess high frequency components which are markedly higher than that of $b_z$. It is found that high frequency processes affect $T_1$ and $T_2$ while low frequency processes affect $T_2$ only. This is key in understanding relaxation mechanisms as we find quite often that $T_1 \neq T_2$.

The intricate process of relaxation is more easily understood if we introduce an important parameter called the correlation time, $\tau_c$. The correlation time has been described as the minimum time required for a molecule, in our case $H_2O$, to rotate one radian. It also can be described more generally for our system as the average time a $^1H$ resides at a given site. The word 'site' describes the proton's position in space and the magnetic field it experiences. The $^1H$ site may be changed as it moves from place to place in the system or as its magnetic environment changes when molecules around it occupy different sites. The correlation time is inversely related to temperature, $T$ and viscosity, $\eta$. A mathematical relationship between $\tau_c$ and the relaxation times, $T_1$ and $T_2$, is proved by the Blombergen, Percell, and Pound (BPP) theory and is shown graphically in Figure 6. If $\tau_c$ is on the order of the $1/\omega_1$ then energy may be exchanged with the lattice most efficiently. This is revealed in Figure 6 where the $T_1$ curve shows a minimum which depends on the field strength of $B_0$. The left side of figure 6 demonstrates the situation where we have low $\eta$. The molecular motions are rapid and high frequency processes are present, consequently $T_1$ and $T_2$ relaxation is affected. On the right side, however, highly viscous or solid characteristics are represented where low frequency processes are predominant and only $T_2$ is affected.
Figure 6. The effect of the correlation time, $\tau_c$, on the relaxation times $T_1$ and $T_2$ for a magnetic field strength of 1.5 Teslas (or a resonance frequency of $\omega_1 \leq 63$ MHz). These curves are calculated from the BPP relations. $\tau_c$ is indirectly proportional to $\eta T$. 

$B_0 = 1.5$ Tesla
There are many important relaxation mechanisms that are present in systems described in this thesis. The most significant of these in a system where water is present are the intramolecular and intermolecular interactions of two $^1$H in water. In the intramolecular case two $^1$H within a H$_2$O molecule interact. One $^1$H experiences the $b(t)$ of the other as the two tumble about one another in space. The frequency of the tumble depends upon both $\eta$ and $T$. In the case of the intermolecular interaction, one $^1$H in a water molecule interacts with another $^1$H in a different water molecule. The strength of the intramolecular interaction is inversely proportional to the distance between the two interacting nuclei to the sixth power, and the strength of the intermolecular interaction is inversely proportional to the distance of closest approach. The nucleus of the deuterium atom, $^2$H, has a magnetic moment as well and can interact with $^1$H in the same manner as described above, however, these interactions are approximately 20 times weaker.

Generally speaking, any nuclear or molecular species possessing a magnetic moment has the potential to interact with the $^1$H and provide a relaxation pathway. The oxygen molecule, O$_2$, has a magnetic moment caused by the electron spin of two unpaired electron and its presence will create a relaxation pathway. The presence of additional $b(t)_i$ from the O$_2$ molecules not only will induce more transitions of spin states but will cause increase loss of phase coherence of $M_{xy}$. Both $T_1$ and $T_2$ will decrease with increasing [O$_2$]. Other relaxation pathways may be provided by small concentrations of paramagnetic ions. Ions such as Cu$^{2+}$, Fe$^{3+}$, Mn$^{2+}$, and Cr$^{3+}$ in concentrations as low as $10^{-5}$ mol/kg will cause noticeable effects in the relaxation times.

The presence of macromolecules such as gelatin protein in an aqueous solution will affect the relaxation of the $^1$H in water. $^1$H within the protein will act as relaxation sites for the water $^1$H. Increasing the protein concentration will introduce more sites and inevitably $T_1$ and $T_2$ will decrease. Furthermore, the molecular motion of the water molecules will be perturbed in close proximity of the protein molecules. This will cause the average viscosity of the water within the solution to increase with increasing protein
concentration.\textsuperscript{11, 20, 21} This is also true of water within a confined geometry such as a pore within a material.\textsuperscript{4, 5} The motional characteristics of the water bound to the walls of the confined space is markedly different than of the bulk liquid and consequently raises the average viscosity of the liquid.

Two models of relaxation within a protein–water system were used to describe the gelatin systems studied in this thesis. The first of which, called the three-fraction hydration model was used in an attempt to model spin–lattice and spin–spin relaxation as a function of gelatin concentration and degree of D\textsubscript{2}O dilution. Described by Zimmerman and Brittin in 1957\textsuperscript{21}, the theory involves modeling aqueous protein solutions with three regions of water: 1) the bound water, described as a single layer of water directly hydrogen bonded to the protein, 2) the bulk water, the water that experiences no interactions with the protein, and 3) the structured water which experiences a perturbed motion due to the presence of the protein but is not directly bonded to it. Since the water within these three regions have different molecular motion characteristics their correlation times are different. Fullerton has reported these correlation times in a lysozyme solution for bound, structured, and bulk as $2 \times 10^{-9}$ s, $5 \times 10^{-11}$ s, and $6 \times 10^{-12}$ s, respectively.\textsuperscript{20} The observed $T_1$ is then found by adding volume fractions of each water region multiplied by its characteristic relaxation rate, and is demonstrated as follows:

$$\frac{1}{T_1} = \frac{v_b}{T_{1b}} + \frac{v_s}{T_{1s}} + \frac{v_{bd}}{T_{1bd}},$$

(5)

where $v_b$, $v_s$, and $v_{bd}$ are the volume fractions of the bulk, structured, and bound waters, respectively, and $T_{1b}$, $T_{1s}$, and $T_{1bd}$ are the relaxation rates of the bulk, structured and bound waters, respectively. As the gelatin concentration increases, the amount of hydrated water, bound and structured, increases and consequently the relaxation rate increases. The volume fractions are found with use of kinetic theory, and the relaxation rates for each of the three regions are found upon consideration of the significant relaxation pathways
germane to our system.

The second model, called the cross–relaxation model and described by Edzes and Samulski in 1977\textsuperscript{22}, is based upon the existence of a magnetic coupling between two populations of hydrogen nuclei, water $^1$H and macromolecular $^1$H. This was used to develop a spin–lattice relaxation relationship with the gelatin concentration and the degree of D$_2$O dilution. The theory states that sites on the macromolecule, namely $^1$H, will induce spin flips in water $^1$H in close proximity to the macromolecular relaxation sites and in doing so create a viable relaxation pathway for the water $^1$H. Increasing the gelatin concentration will increase the number of relaxation sites and consequently the observed $T_1$ will decrease. Quantifying this entails use of the Bloch equations\textsuperscript{23} which describe the rate of magnetization change within the system. It is convenient to represent the components by a rotating frame of reference rotating at an angular frequency of $\omega$. The Bloch equations may then be written as:

\[
\frac{dM_x}{dt} = -\gamma B_1 v - (M_z - M_0)/T_1 \tag{6}
\]
\[
\frac{du}{dt} = (\omega_1 - \omega) v - u/T_2 \tag{7}
\]
\[
\frac{dv}{dt} = -(\omega_1 - \omega) u + \gamma B_1 M_z - v/T_2 \tag{8}
\]

where

\[
u = M_x \cos \omega t - M_y \cos \omega t
\]
\[
v = M_x \cos \omega t + M_y \cos \omega t
\]
\[
B_1 = \text{field strength of the perturbation field}
\]
\[
B_0 = \text{field strength of the static field in the z direction}
\]
\[
\omega_1 = \gamma B_0
\]

Modified for cross–relaxation, the equations for the $z$ component for both the water and protein proton populations are:\textsuperscript{22–24}
\[
\frac{dM_w}{dt} = -(M_w - M_{wo})/T_{1w} + k_{ex}\{[H_2O](M_p - M_{po}) - [P](M_w - M_{wo})\} \\
\frac{dM_p}{dt} = -(M_p - M_{po})/T_{1p} + k_{ex}\{[P](M_w - M_{wo}) - [H_2O](M_p - M_{po})\}
\]

where the subscripts w, p, and o refer to the water population, the protein population, and the equilibrium state, respectively. The molar concentration of spins in water and protein are represented as \([H_2O]\) and \([P]\), respectively. The term, \(k_{ex}\), is the exchange constant, therefore the terms \(k_{ex}[H_2O]\) and \(k_{ex}[P]\) are the respective cross–relaxation rates. The term \(k_{ex}[P]\) describes the transfer of \(z\) magnetization from the water protons to the protein protons and the converse is true for \(k_{ex}[H_2O]\). The term, \(-\gamma B_1 v\), from equation (6) is eliminated because it describes a contribution due to the perturbation signal and were interested in the system after the signal has been turned off. The exchange between \(^2\text{H}\) of the water and \(^1\text{H}\) of the protein is not considered to contribute significantly.

The model may best be understood with use of the following analogy. Figure 7 represents the system as a coupled reservoir. Two reservoirs of magnetization energy will drain into a larger reservoir, the lattice, as the magnetization of the system resumes the equilibrium state. After perturbation the \(H_2O\) reservoir is filled with magnetization energy and has two outlets to the lattice reservoir: a direct pathway restricted by the spin–lattice relaxation rate of water alone and an indirect pathway restricted by both \(k_{ex}[P]\), the cross–relaxation rate for water and protein, and the spin–lattice relaxation rate of the protein \(^1\text{H}\). Since the correlation times of the immobilized protein \(^1\text{H}\) are so different than that of the water \(^1\text{H}\) only a small fraction will be affected by the perturbation, and as a consequence the protein reservoir is very close to its equilibrium magnetization state upon termination of the perturbation. For this reason, the \(k_{ex}[H_2O]\) "valve" has been left out of the diagram and the \(k_{ex}[P]\) valve may be thought of a one–way valve. In this scenario \(1/T_{1p}\) changes very little with changes in gelatin concentration and degree of \(D_2O\) dilution, \(1/T_{1w}\) decreases slightly as the concentration of \(D_2O\) increases, and \(k_{ex}[P]\)
Figure 7. An analogy for the cross-relaxation theory for the spin-lattice relaxation phenomenon. The analogy compares the situation where two reservoirs of thermal energy are draining into a larger reservoir. There are two populations of \(^1\)H, water protons and macromolecular protons. In the model the water reservoir contains excess magnetization energy after the perturbation. There are two possible routes for this magnetization energy to drain to the lattice: 1) directly to the lattice regulated by the rate \(1/T_{1w}\), and 2) indirectly, by exchanging energy to the protein protons which will in turn exchange with the lattice. The latter is regulated by the rates \(k_{ex}[P]\) and \(1/T_{1p}\).
increases substantially as the gelatin concentration increases.

2.3 Diffusion Theory

Diffusion is a process whereby mass is transported from one part of a system to another as a result of random molecular motion. A concentration gradient at points within the system acts as a driving force for the process. The diffusion process is bound by the second law of thermodynamics which states that within a closed system if the entropy of the environment remains unchanged then the entropy of the system can only increase. Fick derived an expression for diffusion from an analogy to heat conduction. His expression stated that the rate of transfer of a substance per unit area of a section in the system is proportional to the concentration gradient measured normal to that section, or

\[ J = -D \frac{\partial C}{\partial s}, \]  

(11)

where,  

- \( J \) = rate of mass transfer per unit area of section  
- \( C \) = mass concentration of the diffusing substance  
- \( D \) = diffusion coefficient  
- \( s \) = space coordinate measured normal to the section.

Equation (11) represents the steady-state case where \( \frac{\partial C}{\partial s} \) is constant. This is generally not the case. A more fundamental differential equation can be derived from equation (11) and is given below as the nonsteady-state diffusion equation, or Fick’s second equation:

\[ \frac{\partial C}{\partial t} = D \frac{\partial^2 C}{\partial s^2}. \]  

(12)
In many systems D is a function of space dimensions or concentration. Equation (12) may then be rewritten as,

\[ \frac{\partial C}{\partial t} = \frac{\partial}{\partial x}(D \frac{\partial C}{\partial x}) + \frac{\partial}{\partial y}(D \frac{\partial C}{\partial y}) + \frac{\partial}{\partial z}(D \frac{\partial C}{\partial z}), \] (13)

in three dimensions. By letting \( x = r \cos \theta \) and \( y = r \sin \theta \), equation (13) can be transformed into cylindrical coordinates:\(^{26,28}\)

\[ \frac{\partial C}{\partial t} = \frac{1}{r} \left\{ \frac{\partial}{\partial r}(rD \frac{\partial C}{\partial r}) + \frac{\partial}{\partial \theta}(D \frac{\partial C}{\partial \theta}) + \frac{\partial}{\partial z}(D \frac{\partial C}{\partial z}) \right\}, \] (14)

considering an element of volume of a cylinder of sides \( r \), \( dr \), \( d\theta \), and \( dz \).

Equations (13) and (14) are used to model the two gelatin systems studied in this thesis.
3. The Ternary H₂O–D₂O–Gelatin System

3.1 Relaxation Rate Theory

3.1.1 Introduction

In performing research with MRI it is important to know information concerning the relaxation times of the species being investigated (in our case water) for two reasons: 1) T₁ and T₂ times affect the detected signal and interpretation thereof, and 2) T₁ and T₂ times and processes reveal information regarding microscopic features of the system. Two models were used to calculate the relaxation times for water at a given gelatin concentration and degree of D₂O dilution. T₁ and T₂ times were measured for various values of gelatin concentration and degrees of D₂O dilution. The sample preparation and the measurement procedure are described below in the experimental section. These values were used to compare with that predicted by the models. Following the experimental section, a section is devoted for each model that describes in detail how the model was implemented into our system and the results of the implementation. The first model described, the three-fraction hydration model, was used to successfully model 1/T₁ and 1/T₂ for low gelatin concentrations only. The second, the cross-relaxation model, successfully modeled 1/T₁ for the range of gelatin concentrations and degrees of D₂O dilution experienced in the systems studied. A successful 1/T₂ relationship was not accomplished, however, the empirical results from the T₂ measurements were implemented into the studies.
3.1.2 Experimental

For the T₁, T₂ measurement study a Signa, 1.5 Tesla, superconducting magnetic resonance imager (General Electric, Milwaukee), located at the University of Rochester Medical Center, was used to collect data. The imager was employed to record images representing the hydrogen NMR signal intensity. The probe that was used with the imager to recover the MR signal is a standard GE quadrature, birdcage style head coil. Table 1 summarizes the imaging parameters used for the study.

Table 1. Imaging parameters for various studies.

<table>
<thead>
<tr>
<th>Study</th>
<th>T₁, T₂ Measurements</th>
<th>Counter Diffusion</th>
<th>Drying</th>
</tr>
</thead>
<tbody>
<tr>
<td>Instrument B₀ Strength (Tesla)</td>
<td>GE Signa MRI</td>
<td>GE Signa MRI</td>
<td>GE CSI*</td>
</tr>
<tr>
<td>Probe</td>
<td>GE Birdcage†</td>
<td>GE Birdcage</td>
<td>STS†</td>
</tr>
<tr>
<td>Slice Thickness (mm)</td>
<td>20.0</td>
<td>5.0</td>
<td>2.0</td>
</tr>
<tr>
<td>TR (ms)</td>
<td>varied</td>
<td>1000</td>
<td>2000</td>
</tr>
<tr>
<td>TE (ms)</td>
<td>varied</td>
<td>20</td>
<td>30</td>
</tr>
<tr>
<td>Sample Window (min)</td>
<td>varied</td>
<td>4.5</td>
<td>8.7</td>
</tr>
<tr>
<td>Z Resolution (mm)</td>
<td>—</td>
<td>0.47</td>
<td>0.11</td>
</tr>
</tbody>
</table>

* General Electric Chemical Shift Imager
† General Electric birdcage–style head coil
‡ Homemade single–turn solenoid

Gelatin samples varying in gelatin concentration and H₂O/D₂O content were prepared with FDA approved gelatin (Knox Gelatine, Inc., Englewood Cliffs, NJ), 18 MΩ cm deionized water, and 99.9 atom % D deuterium oxide (Aldrich Chemical). Through thermogravimetric analysis it was found that the gelatin contained 12% wt. H₂O as it is fully equilibrated with the surroundings. If we let Mₛ = the mass of the "dry" gelatin (or
the mass of the gelatin as it came from the manufacturer times 0.88) then we can define the concentration of gelatin as,

\[
\phi = \frac{M_s}{n},
\]

(15)

where \(n\) represents the total moles of water (\(H_2O\) and \(D_2O\)) in the gelatin matrix, including that introduced by the gelatin protein. We will use the variable, \(f\), to represent the degree of \(D_2O\) dilution. The variable, \(f\), is defined as the fraction of \(^1\)H contributed from the water that is found in the system compared with the total \(^1\)H and \(^2\)H contributed from the water. This is also shown as,

\[
f = \frac{\text{moles } ^1\text{H}}{2n}.
\]

(16)

Across the samples, \(\phi\) ranged from 0.24 to 7.5 g/mol and \(f\) ranged from 0.20 to 1.0. After preparation, the samples were poured into 20 ml high density polyethylene (HDPE) bottles, sealed to prevent evaporation, and cooled at 10°C.

The samples were placed in the imager in groups of twelve and an imaging plane was oriented perpendicularly with respect to the symmetry axes of the samples so that a single image revealed the cross sections of all twelve samples. The slice thickness was chosen to be large so that a single pixel value represented signal over a large volume. This was done to improve the signal-to-noise. \(T_1\) values were calculated from eight single echo, spin echo images with a fixed echo time, \(TE\), of 20 ms and varying repetition times, \(TR\), of 250, 500, 1000, 1500, 2000, 3000, 4000, and 6000 ms. For each sample in each image the signal intensity was averaged over a square area covering the majority of the sample's image. Using a weighted standard least squares algorithm on the imager, a fit to the equation,
was made and $T_1$ was acquired for each sample.

$T_2$ values were acquired from six single echo, spin echo images with a fixed TR of 1000 ms and varying TE of 20, 50, 75, 100, 150, and 200 ms. An analysis similar to the one described above was performed on the images using the equation,

$$S = k_2 e^{-\frac{TE}{T_2}}, \quad (18)$$

to acquire the $T_2$ values.

Provisions were not made to record a number of values at each given $f$ and $\phi$ to establish repeatability of the data points; however, the data for the low values of $\phi$ were recorded on two separate occasions to establish any uncertainty in the instrument. This is documented in section 3.1.3.2.

3.1.3 The Three-Fraction Hydration Model

3.1.3.1 Theoretical

It is known that the relaxation rates of water in the ternary system of $H_2O$, $D_2O$, and gelatin are dependent upon the degree of dilution of $H_2O$ by $D_2O$ as well as the increasing of the correlation time, $\tau_c$, by the presence of gelatin.

Equation (5) was used to model observed $T_1$ and $T_2$ values for the ternary system. The following describes the procedure for finding $T_1$. The formulation for $T_2$ follows similarly. $T_1$ relaxation times were formulated for each of the three regions. We can simplify the task by describing the three dominant relaxation pathways native to our system. They are dipole–dipole (dd) interactions and are described as follows:\footnote{1) the intramolecular case where a pair of $^1H$ nuclei or a $^1H$ and a $^2H$ nucleus of the same molecule}
interact, 2) the intermolecular case where two \(^1\)H nuclei or a \(^1\)H and a \(^2\)H nucleus of different molecules interact, and 3) intermolecular case where the \(^1\)H nucleus of a water molecule interacts with the dipole moment of the two unpaired electrons (ue) of a dissolved oxygen molecule. The distance dependence of \(T_1\) times for each are as follows:

\[
\begin{align*}
\text{dd(intra)}: & \quad (1/T_1)_1 \propto 1/r^6 \\
\text{dd(inter)}: & \quad (1/T_1)_2 \propto 1/a \\
\text{ue(inter)}: & \quad (1/T_1)_3 \propto 1/a,
\end{align*}
\]

where \(r\) is the distance between two \(^1\)H in a water molecule \((r \approx 1.6\) Angstroms\), and \(a\) represents the average distance between a \(^1\)H of a water molecule and the species containing the dipole moment on the molecule providing the relaxation pathway \((a \approx 3.2\) Angstroms\).

The interaction between the \(^1\)H and the \(^2\)H is approximately twenty times weaker than the interaction between two \(^1\)H, consequently the homonuclear case contributes most to the observed relaxation.

An equation taking into account all three interactions needs to be developed for each region of water present in the system. Let \(f\) represent the fraction of \(H_2O\) present and \((1-f)\) the fraction of \(D_2O\) present. We assume the condition that the fast exchange of \(^2\)H and \(^1\)H occurs and an equilibrium configuration is reached. Given a \(^1\)H, the probability of finding another relaxing species that will provide a relaxation pathway needs to be considered.

Considering all the possible interactions of the first two types of relaxation phenomenon leads to the following relaxation rate expressions,

\[
\begin{align*}
(1/T_1)_i &= f (1/T_1)_{H-H_i} + (1-f) (1/T_1)_{D-H_i} \\
(1/T_1)_{ii} &= 2f (1/T_1)_{H-H_{ii}} + 2(1-f) (1/T_1)_{D-H_{ii}},
\end{align*}
\]
where $i$ indicates intramolecular and $ii$ indicates intermolecular; the term, \((1/T_i)_{H-H_i}'\), then represents the average value for the relaxation rate of a \(^1\!H\) undergoing the intramolecular relaxation process with another \(^1\!H\), etc.

These expressions lead to a single equation for each of the three regions of water ($j=1-3$),

\[
(1/T_i)_j = [(f(1+C)(1/T_i)_{H-H_i} + (1-f)(1+2C')(1/T_i)_{H-D_{i}} + (1/T_i)_{H-O})(\sigma)_j, (24)
\]

where $C$ and $C'$ are constants that relate the intermolecular relaxation rate with the intramolecular relaxation rate, \((1/T_i)_{H-O}\) is the intermolecular relaxation rate due to the interaction of dissolved oxygen and the \(^1\!H\) of the water, and $\sigma$ is a factor that depends on $f$ and incorporates the viscosity (and hence, the correlation times) of the water due to a mixing of $D_2O$ and $H_2O$. The viscosity of a water mixture will increase as more $D_2O$ is added. The relationship between $f$ and $\sigma$ is given as a linear relationship:

\[
\sigma = \frac{\eta_d}{\eta_h} - (\frac{\eta_d}{\eta_h} - 1)f, \tag{25}
\]

where $\eta_d$ and $\eta_h$ are the viscosities of $D_2O$ and $H_2O$, respectively, at 20° C. The values used were 1.2514 cp for $\eta_d$ and 1.0050 cp for $\eta_h$.

Since the gelatin concentration will affect the amount water in the three different regions it is important to consider. We utilize a kinetic theory to find the relative volume fractions of the three regions of water. We let $b = \text{moles bound water}/M_s$ and $h = \text{moles hydrated water}/M_s$ (the word "hydrated" refers to bound and structured water). The value, $b$, is found by considering the water content of the gelatin protein at equilibrium. We assume $b = 0.007576 \text{ mol/gm}$ and is constant since the forces holding the bound water to the gelatin are much stronger than any other interacting phenomenon available in our system.
This will lead to the following equations for the fractions of water in the system,

\[ v_{bd} = b\phi \]  \hspace{1cm} (26)
\[ v_s = (h-b)\phi \]  \hspace{1cm} (27)
\[ v_b = 1 - h\phi \]  \hspace{1cm} (28)

where \( v_{bd} + v_s + v_b = 1 \). Equation (5) can then be recast in the form,

\[ 1/T_1 = [1 - (h-b)\phi]/(T_1)_b + (h-b)\phi/(T_1)_s + b\phi/(T_1)_{bd} \]  \hspace{1cm} (29)

Here \( h \) must depend on \( \phi \) since \( h = b = 0.007576 \text{ mol/gm} \) for packaged gelatin.

In establishing the values for \( h \) in terms of \( \phi \) the following kinetic model was considered. The volume of bound water for a given \( \phi \) is assumed to be constant. An equilibrium between the bulk and structured water is assumed and given by the constant, \( k_b \), which is equal to \( v_b/v_s \). This leads to the expression

\[ h\phi = (1+k_b b\phi)/(1+k_b) \]  \hspace{1cm} (30)

which in turn can be put into equation (29) to obtain,

\[ 1/T_1 = k_b (1-\phi b)/[(1+k_b)(T_1)_b] + (1-b\phi)/[(1+k_b)(T_1)_s] + b\phi/(T_1)_{bd} \]  \hspace{1cm} (31)

\( k_b \) is defined by the Gibbs free energy change resulting from a change from the structured region to the bulk region,

\[ \Delta G = \Delta H - T\Delta S = -RT \ln(k_b) \]  \hspace{1cm} (32)

This relation can be recast in the form,
\[ \Delta G = (h_b + \epsilon_s \phi) M_s / \phi - T \psi M_s / \phi, \]  

(33)

where \( \psi \) and \( \epsilon_s \) are positive. \( \Delta G \) will be positive for large \( \phi \), the first term in equation 33 will dominate, and negative for small \( \phi \), the second term will dominate. The reaction rate \( k_b \) can written as,

\[ k_b = e^{-A_b e^{B_b / \phi}}, \]  

(34)

where \( A_b \) and \( B_b \) are constants and are determined from the theoretical fit.

3.1.3.2 Results and Discussion

The theoretical fit for the spin-lattice relaxation rate was fairly good for small \( \phi \), but poor for large \( \phi \). Figure 8 demonstrates the \( \phi = 0 \) case. The theoretical curve (smooth) compares well to the data for an assumed \( \tau_c \) of \( 6 \times 10^{-12} \) s. In formulating the theoretical equation in \( f \) for \( \phi = 0 \) it was noted that the \( ^1\text{H}-^2\text{H} \) interactions offered a negligible contribution to the observed \( T_1 \). The increase in the spin-lattice relaxation rate as \( f \) increases is due primarily to the increases in the inter- and intramolecular \( ^1\text{H}-^1\text{H} \) interactions. As expected the oxygen contribution to the relaxation rate was constant in \( f \); the spin-lattice relaxation rate of the water protons at low \( f \) is dictated primarily by the amount of oxygen in the system. The slight concave down curvature is due to the effect of the viscosity of the mixture as \( f \) changes; D\(_2\)O adds to the viscosity of the mixture which will enhance the observed relaxation rate by increasing \( \tau_c \).

As gelatin is introduced into the system the three regions of water begin to develop and contribute to the observed relaxation rate. The results for three relatively low gelatin concentrations are shown in Figure 9. Data was recorded for each of the samples at two separate times in order to reveal any uncertainty the instrument might contribute. This is
Figure 8. The spin–lattice relaxation rate, $1/T_1$, as a function of $f$ for a mixture of H$_2$O and D$_2$O where $\phi = 0$. The quantity $f$ represents the molar fraction of H$_2$O in the mixture. The theoretical result of the three fraction hydration model is represented by a smooth curve. $1/T_1$ increases almost linearly in $f$. The slight curvature can be attributed to viscosity effects.
Figure 9. The spin–lattice relaxation rate, $1/T_1$, for the ternary system of H$_2$O–D$_2$O–gelatin as a function of $f$ for three relatively low values of $\phi$. The theoretical results of the three–fraction hydration model are represented by smooth curves. The gelatin samples were imaged at two separate times in order to establish any systematic errors introduced by the instrument. It is on the order of 5%. The data suggests a near linear relationship for $1/T_1$ in $f$ for small $\phi$. 
shown to be on the order of 5%. The values substituted for the terms $A_b$ and $B_b$ from equation (34) that provided the best fit were 3 and 5, respectively. The data reveals the trend expected in that the spin–lattice relaxation increases with increasing gelatin concentration because there is a greater volume fraction of hydrated water. Since this water has correlation times in the area where the $T_1$ curve in Figure 6, page 15 is at a minimum, the relaxation is most efficient. The theoretical curves match well with the data for the relatively low $\phi$. The correlation times for the three regions of water were found by using Figure 6, page 15, and are compared with that of Fullerton\textsuperscript{20} in Table 2, page 37. The bulk and structured water values for $\tau_c$ compare well, however, there is slight discrepancy in the bound water findings. Furthermore, it was found that the $^1$H–$^2$H interactions played an important role when gelatin was introduced into the system, as these interactions were accounted for in the bound and bulk regions to produce a good fit. This result is inconsistent with the intuitive notion that the $^1$H–$^2$H interactions have equal significance in all three regions. The fact that we need not consider these interactions for $\phi = 0$ but we do for $\phi > 0$ suggests that the relaxation rate is being enhanced by some mechanism unaccounted for. The data for higher gelatin concentrations provided for a poorer theoretical fit. This is represented in Figure 10. The data suggests that there should exist a slight upturn in the curves at lower $f$. This behavior cannot be explained by the three–fraction hydration model.

The same trends exist for the spin–spin relaxation rates as with the spin–lattice relaxation rates, however, the spin–spin relaxation rate proved even more difficult to model at high gelatin concentrations. The theoretical fits for the lower gelatin concentrations are demonstrated in Figure 11. The theoretical curves fit quite well for low $\phi$ as the correlation times found for the bound region compared well to those of Fullerton\textsuperscript{20} in Table 2, page 37. Again, however, the $^1$H–$^2$H interactions played an integral role in creating good theoretical comparison to data. Figure 12 shows the data and theoretical result for higher $\phi$. As with the spin–lattice relaxation behavior, there is
Figure 10. The spin-lattice relaxation rate, $1/T_1$, for the ternary system of $\text{H}_2\text{O}$-$\text{D}_2\text{O}$-gelatin as a function of $f$ for three relatively high values of $\phi$. The theoretical results of the three-fraction hydration model are represented by smooth curves. The behavior of the relaxation times at low $f$ suggest an upturn in the curves. This is not provided by the model.
Figure 11. The spin–spin relaxation rate, $1/T_2$, for the ternary system of H$_2$O–D$_2$O–gelatin as a function of $f$ for three relatively low values of $\phi$. The theoretical results of the three–fraction hydration model are represented by smooth curves. The gelatin samples were imaged at two separate times in order to establish any systematic errors introduced by the instrument. It is on the order of 5%. The data suggests a near linear relationship for $1/T_2$ in $f$ for small $\phi$. 

- $\Delta$ $\phi = 0.24$ (g/mol)
- $\times$ $\phi = 0.789$
- $\times$ $\phi = 1.57$
Figure 12. The spin–spin relaxation rate, \(1/T_2\), for the ternary system of \(\text{H}_2\text{O}–\text{D}_2\text{O}–\text{gelatin}\) as a function of \(f\) for three relatively high values of \(\phi\). The theoretical results of the three–fraction hydration model are represented by smooth curves. The behavior of the relaxation times at low \(f\) suggest an upturn in the curves. This is not provided by the model. The theoretical fit is poorer for \(1/T_2\) as compared with \(1/T_1\).
suggested here an upturn in the curves at low f. Not only is this upturn unaccounted for but the fit in \( \phi \) is even poorer than that of \( 1/T_1 \).

Table 2  Correlation times (in sec.) for the three regions of water

<table>
<thead>
<tr>
<th>Region of water</th>
<th>( \tau_c^\dagger )</th>
<th>( \tau_c^\ddagger )</th>
<th>( \tau_c^* )</th>
</tr>
</thead>
<tbody>
<tr>
<td>bulk</td>
<td>( 6 \times 10^{-12} )</td>
<td>( 6 \times 10^{-12} )</td>
<td>( 6 \times 10^{-12} )</td>
</tr>
<tr>
<td>structured</td>
<td>( 1 \times 10^{-11} )</td>
<td>( 1 \times 10^{-11} )</td>
<td>( 5 \times 10^{-11} )</td>
</tr>
<tr>
<td>bound</td>
<td>( 0.5 \times 10^{-9} )</td>
<td>( 7 \times 10^{-9} )</td>
<td>( 2 \times 10^{-9} )</td>
</tr>
</tbody>
</table>

\( \dagger \) for \( 1/T_1 \) data  
\( \ddagger \) for \( 1/T_2 \) data  
* Fullerton

Although the three-fraction hydration model can provide for a good comparison to \( T_1 \) and \( T_2 \) data for low \( \phi \), it fails to explain the fact that we needed to include the \( ^1\text{H} - ^2\text{H} \) interactions for \( \phi > 0 \) but not for \( \phi = 0 \). Furthermore, it seems to fail for high \( \phi \) and low f in \( T_1 \) and high \( \phi \) for \( T_2 \). In order to explain the behavior of the relaxation times in f and \( \phi \) it appears as though a new model needs to be considered.

3.1.4. The Cross-Relaxation Model

3.1.4.1. Theoretical

The temporal behavior of the magnetization in the ternary \( \text{H}_2\text{O}-\text{D}_2\text{O}-\text{gelatin} \) system undergoing magnetic exchange may be described by the Bloch equations modified for the exchange.\(^{22-24,33} \) Equations (9) and (10) can be recast into a simpler form for solving. For a given proton population, i, if we let \( n_i \) be the difference in the number of protons occupying the two spin states at a given time and \( n_{i0} \) at equilibrium then the
magnetization for that population may be given as \( M_1 = K_1 n_i [S_i] \), where \([S_i]\) is the molar concentration of either the protein or water population and \( K_i \) is a proportionality constant. This is substituted into equations (9) and (10) to acquire normalized relations. If we let

\[
\begin{align*}
\alpha &= n_{wo} - n_w \\
\beta &= n_{po} - n_p \\
k_1 &= k_{ex}[H_2O] \\
k_2 &= k_{ex}[P]
\end{align*}
\]

and then

\[
\begin{align*}
R_1 &= \frac{1}{T_{1w}} + k_2 \\
R_2 &= \frac{1}{T_{1p}} + k_1
\end{align*}
\]

equations (9) and (10) can be rewritten more simply as

\[
\begin{align*}
\frac{d\alpha}{dt} &= -R_1 \alpha + k_2 \beta \\
\frac{d\beta}{dt} &= -R_2 \beta + k_1 \alpha
\end{align*}
\]

Any system of single order, coupled differential equations can be given as a single, second order ordinary differential equation \(^{34}\) (Appendix D). The solution is

\[
\alpha = Ae^{-t/\tau_1} + Be^{-t/\tau_2}
\]

The spin–lattice relaxation time of the water protons can be described as a sum of two exponential decays. If we assume the following boundary conditions

\[
\begin{align*}
\alpha &= 1 \\
\frac{d\alpha}{dt} &= -R_1 + k_2 \zeta, \text{ for } t = 0
\end{align*}
\]
where $\zeta$ is $\beta/n_{p0}$ immediately after the 90° RF pulse, we then have

$$A + B = 1$$

$$-R_1 + \zeta K_2 = -A/\tau_1 - B/\tau_2$$

The factor $\zeta$ was chosen to be small, namely 0.1, and is rationalized by the following observations. The frequency width of the 90° RF pulse, $10^3$ Hz, is small compared to the protein $^1$H homogeneously broadened line of width $10^5$ Hz. A large perturbation ($M_z = 0$) to a small portion of the protein line is instantaneously on the NMR time scale transferred across the line. The resultant $\zeta$ for the ensemble of protein spins is $\zeta = 0.1$.

The values for $1/\tau_1$ can be found from the secular equation,

$$1/\tau^2 - (R_1 + R_2)/2 + (R_1R_2 - k_1k_2) = 0$$

and are given as

$$1/\tau_{1,2} = (R_1 + R_2)/2 + /- \frac{1}{2} \sqrt{(R_1 - R_2)^2 + 4k_1k_2}$$

therefore

$$A = \frac{(R_1 + R_2)/2 + \frac{1}{2} \sqrt{(R_1 - R_2)^2 + 4k_1k_2}}{\sqrt{(R_1 - R_2)^2 + 4k_1k_2}}$$

The terms $A$ and $B$ are the normalized intensities of the two relaxation components in the relaxation curve of the water protons. The terms $1/\tau_1$ and $1/\tau_2$ represent the apparent relaxation rates for the two possible relaxation pathways demonstrated in Figure 7, page 20. The term, $1/\tau_2$, is the slower rate and corresponds to the rate dictated by the direct pathway from the water $^1$H reservoir to the lattice, and $1/\tau_1$ corresponds to the effective
rate determined by the two processes in the indirect pathway of the model.\textsuperscript{22}

The effects due to viscosity, O\textsubscript{2} concentration, and intra- and intermolecular H--H interactions need also be considered. As \( \phi \) increases so will the viscosity of the liquid within the gelatin matrix, therefore a viscosity factor of the form, \((1 + a \phi)\), is multiplied to \(1/T_{1w}\) to compensate. Here \( a \) represents some number that changes as a function of \( \phi \). Since viscosity and diffusion are both aspects of the same phenomenon the quantity, \((1 + a \phi)\), is inversely proportional to the average self diffusion coefficient of the water. In this sense the self diffusion coefficient for the water within the gelatin matrix may be found at any \( \phi \) given the known value of \(2.2 \times 10^{-5}\) cm\(^2\)/s in water alone.\textsuperscript{31} The relaxation time for water in a gelatin matrix is given as

\[
1/T_{1w} = f/T_{1h} + (1-f)/T_{1d} + 1/T_{O2}
\] (50)

where \( T_{1h} \) and \( T_{1d} \) are the relaxation rates of \(^1\text{H}\) in pure H\textsubscript{2}O and \(^1\text{H}\) in highly D\textsubscript{2}O diluted H\textsubscript{2}O, respectively, and \( T_{O2} \) is the paramagnetic contribution of dissolved O\textsubscript{2} in water equilibrated with air at STP.

The observed spin–lattice relaxation rate is then predicted by evaluating \(-\ln\{\alpha(3)\}/3\) for a given \( \phi \) and \( f \). The time, 3 s, was chosen because the longest TR used in the relaxation time measurements was 6 s, and a value midway between 0 and 6 s provided for the best fit.

3.4.1.2. Results and Discussion

Spin–lattice relaxation curves were constructed from the model as a function of \( f \) for given values of \( \phi \) and compared with the data recorded from the imager. The values used for \(1/T_h\), \(1/T_d\), and \(1/T_{O2}\) were 3.6, 50, and 25 s, respectively; these compared well with others.\textsuperscript{11,20,31} The results are demonstrated in Figures 13 and 14 where the theoretical
Figure 13. The spin-lattice relaxation rate, $1/T_1$, for the ternary system of $\text{H}_2\text{O}-\text{D}_2\text{O}$-gelatin as a function of $f$ for low $\phi$. The smooth curves are derived from the cross-relaxation theory. $1/T_1$ increases with both $\phi$ and $f$. The slight concave down curvature in the curves is attributed to viscosity effects. The theory provides a good fit to the data.
Figure 14. The spin–lattice relaxation rate, $1/T_1$, for the ternary system of H$_2$O–D$_2$O–gelatin as a function of $f$ for high $\phi$. The smooth curves are derived using the cross–relaxation theory. The scatter in the data is most likely caused by batch inconsistencies.
curves are represented as smooth lines. The lowermost curve in Figure 13 is the $\phi = 0$ case and compares well with Anderson.\textsuperscript{31} The increase in $1/T_1$ as $f$ increases results from the more efficient magnetization exchange between two $^1$H nuclei as compared to a $^1$H and a $^2$H nucleus. As the concentration of $^1$H nuclei increases the occurrence of $^1$H-$^1$H interactions increases and consequently the magnetization of the system relaxes to equilibrium much more quickly. As was demonstrated in section 3.1.3 the slight curvature results from the a viscosity effect; D$_2$O, being the more massive molecule, will slightly raise the viscosity of a water mixture and raise slightly the spin–lattice relaxation rate. In raising the viscosity, $\tau_c$ is raised to a value more conducive for this relaxation. In regards to Figure 6, page 15, the system is moving from left to right on the downward slope of the left side of the $T_1$ curve. The effect is to create a downward concavity in the data. This effect is overshadowed by the effects due to the presence of macromolecular protein as $\phi$ increases; one such effect is due to viscosity changes and is discussed. Generally speaking, the relationship between $1/T_1$ and $f$ found in this work demonstrates the well established premise that the primary mechanism for relaxation in water is a nuclear dipole interaction.

The influence of the protein on the spin–lattice relaxation rates is shown by the other two curves in Figure 13 and the two curves in Figure 14. These curves demonstrate the cross–relaxation mechanism in that the spin–lattice relaxation becomes more efficient at higher gelatin concentrations. As $\phi$ increases, the number of relaxation sites on the protein increases. In terms of the analogy discussed previously, the valve between the two upper thermal reservoirs opens wider to let the magnetization of the water proton population equilibrate at a faster rate. The rate constant for cross–relaxation, $k_{ex}$, was found to be 0.018 l/mol·s. An interesting feature is the upturn of the curves for high $\phi$ as the dilution of H$_2$O by D$_2$O increases. This is especially noticeable in the $\phi = 4.6$, and 7.5 g/mol curves. This can be explained by the fact that the reservoir of water spins will be less full due to the presence of the D$_2$O. The ratio of protein spins to water spins is increased with decreasing $f$ which results in a situation where the relaxation of water spins
becomes dominated by the cross-relaxation with protein protons at high $\phi$. The observed relaxation (i.e. the recorded $1/T_1$) does not, however, take into account the amount of water spins present as does the rate for magnetization decay. If the concentration of spins were accounted for in the $\frac{dM}{dt}$ relations then the curves would continuously decrease as $f$ decreases in high $\phi$.

The average viscosity of the water within the gelatin matrix will inevitably increase with an increasing $\phi$. As the amount of protein in the matrix increases so will the fraction of water immobilized by the protein. This is primarily what will lower the self-diffusion coefficient of water, $D_w$, in the gel phase. The factor $(1 + a\phi)$ was appropriately integrated into the theoretical equations to account for this effect. The spin-lattice relaxation time will change as a function of the changing $\tau_c$. The factor $(1 - a\phi)$ will then be inversely proportional to $D_w$. The values for $a$ and, consequently, $D_w$ were found for various $\phi$ values based on $D_w = 2.2 \times 10^{-5} \text{ cm}^2/\text{s}$ and found in Table 3. These values suggest that $D_w$ decreases more quickly in $\phi$ for lower $\phi$ values than for higher $\phi$ values. The fact that $D_w$ only decreases by a factor of two for $\phi = 7.5 \text{ g/mol}$ reveals that even for high gelatin concentrations where the matrix is physically very solid-like, the water molecules within act very much like a they are in a liquid state.

<table>
<thead>
<tr>
<th>$\phi$ (g/mol)</th>
<th>$a$</th>
<th>$D$ (x10^{-5} cm²/s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.23</td>
<td>0.49</td>
<td>2.0 +/- 0.1</td>
</tr>
<tr>
<td>0.79</td>
<td>0.41</td>
<td>1.7</td>
</tr>
<tr>
<td>1.57</td>
<td>0.38</td>
<td>1.4</td>
</tr>
<tr>
<td>3.09</td>
<td>0.26</td>
<td>1.2</td>
</tr>
<tr>
<td>4.59</td>
<td>0.19</td>
<td>1.15</td>
</tr>
<tr>
<td>6.05</td>
<td>0.18</td>
<td>1.1</td>
</tr>
<tr>
<td>7.47</td>
<td>0.15</td>
<td>1.0</td>
</tr>
</tbody>
</table>

$D_w = 2.2 \times 10^{-5} \text{ cm}^2/\text{s}$
The discussion of the three-fraction hydration model pointed out that there is good reliability in the values recorded from the imager as there is only a 5% uncertainty in the values. The results for the higher gelatin concentrations, however, reveal another factor affecting the reliability of the data. The values recorded for $T_1$ in figure 14 represent a large spread, on the order of 20% in places. This is an important concern because although the trends may be represented accurately, the specific values for the relaxation times need to be known for correct interpretation of the signal. An explanation for this spread in data may be provided by a consideration of the purity of the gelatin itself. Some of the points were recorded from samples made with gelatin of different batches. The $\phi = 4.6$ g/mol sample demonstrates the problem well. The filled triangles were points recorded from a different batch than that of the hourglasses. There is a consistent decrease in one set of values compared to the other. This may be caused by the inconsistency of the contents of various batches. As mentioned previously, certain impurities such as paramagnetic species within the gelatin may affect the relaxation of the magnetization and result in different observed relaxation rate values. If this is the case, the $T_1$ and $T_2$ times would be shortened with increasing impurity concentration. Samples made from a gelatin batch with little paramagnetic impurities would reveal relaxation rate curves that are shifted upward in comparison to those made from a batch with higher impurity concentrations. Of the three grades of gelatin, photographic, pharmaceutical, and edible-consumer, the edible-consumer grade is the least reliable in terms of purity and batch-to-batch consistency. Ideally, high batch-to-batch invariability is best for this type of study. This may best be achieved with the photographic grade gelatin as strict requirements are imposed for lot consistency. Results from a DC plasma analysis of gelatin performed by Dr. Thomas R. Keenan of Kind & Knox, a division of Knox Gelatine, Inc., however, do not substantiate this presumption. Table 4 summarizes the results for paramagnetic suspects. Since significant paramagnetic contribution to relaxation requires concentrations of impurities (i.e. paramagnetic ions) on the order of $100 - 1000$ ppm$^{18}$ the results will not
account for the observed spread in the $T_1$ data.

<table>
<thead>
<tr>
<th>Table 4</th>
<th>Paramagnetic impurity content as found through DC plasma analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>element</td>
<td>ppm</td>
</tr>
<tr>
<td>Fe</td>
<td>3.83</td>
</tr>
<tr>
<td>Cu</td>
<td>0.08</td>
</tr>
<tr>
<td>Cr</td>
<td>0.17</td>
</tr>
<tr>
<td>Ni</td>
<td>0.20</td>
</tr>
<tr>
<td>Mn</td>
<td>0.29</td>
</tr>
</tbody>
</table>

A more plausible explanation may lie in the consideration of the sample preparation. It was noted that in making gelatin of high concentrations tiny air bubbles became trapped within the matrix. Inconsistencies surrounding the concentration of bubbles from sample to sample may account result in inconsistencies in the observed $T_1$ values. In future experiments it would be prudent to remove these air bubbles, by means of centrifuging, perhaps, in order to acquire good batch consistency.

An attempt to model $T_2$ using the cross-relaxation theory was made, however, unsuccessfully. It was found that the $T_2$ theoretical curves fit poorly to the data especially at high $\phi$. The effects due to paramagnetic species within the gelatin or water cannot account for the discrepancy as $T_1$ would be affected as well. In private conversations with Bryant it was pointed out to me that $T_2$ is extremely difficult to model. There are an increased number of relaxation processes for $T_2$ as compared with $T_1$. Some of these processes are not yet understood.
3.2 The Diffusion of Water in Two Gelatin Systems

3.2.1 Introduction

MRI was utilized to study the diffusion of water in two systems: 1) a two phase system comprised of a liquid water phase and a gelatin phase, and 2) a cylindrically shaped gelatin sample exposed to drying conditions. The first study was performed to investigate the behavior of the diffusion coefficient of water as a function of gelatin concentration and to compare a theoretical model of the system with results from the imager. The purpose of the second study was to compare the diffusion model derived for the system with the results from the imager.

3.2.2 The Counter-Diffusion of H₂O/D₂O in Gelatin

3.2.2.1 Experimental

The imager used in this study is described in the T₁, T₂ relaxation times study. Table 1, page 24 summarizes the imaging parameters used in the study. The analysis for this study was performed with use of a Digital Equipment Corporation (DEC) VAX-8650 computer (Maynard, MA) located at the RIT campus. Programs for analysis specific to each study were written in FORTRAN.

For the counter-diffusion study three gelatin concentrations, \( \phi = 0.24, 0.79, \) and 1.6 mol/ml, were prepared in the same manner as described in section 3.1.2 with the exception that the samples were made with 100% D₂O. These samples were then poured into 60 ml HDPE bottles to about the half-way point, sealed, and cooled. D₂O was used in making the gelatin because the signal from \(^2\text{H}\) is not picked up by the instrument when it is tuned for \(^1\text{H}\). In a 1.5 Tesla field the resonant frequency of \(^1\text{H}\) is 63.87 MHz and that of \(^2\text{H}\) is 9.80 MHz. The difference between the two is substantially larger than the bandwidth of the instrument. This allows us to trace only the H₂O molecules in the system.
Three bottles containing the three gelatin concentrations were placed abreast in the imager with the symmetry axis of each bottle parallel with the direction of the force due to gravity. Immediately prior to the acquisition of the first image, 30 ml of deionized H₂O was introduced to the top of the sample. Figure 15 illustrates the sample. An imaging plane was oriented parallel to the symmetry axes of the samples so that a single image revealed all three samples. A TR of 1000 ms was chosen to keep the sample time down to just a few minutes which would be negligible in comparison to the diffusivity of the water in gelatin. The slice thickness was chosen small so any effects due to the curvature of the bottle were negligible. Images were recorded at approximately 30 minute intervals.

A ¹H signal profile for each sample was established from the average signal value for horizontal pixels in a 2 cm wide band passing vertically down the center of the sample. The position of the interface, \( z = 0 \), was found from the \( t \approx 0 \) image.

### 3.2.2.2 Diffusion Theory

The diffusion of the H₂O molecule in the system was modeled using Fick's second diffusion equation, equation (12),

\[
\frac{\partial [^1H]}{\partial t} = D \frac{\partial^2 [^1H]}{\partial z^2}
\]

where \([^1H]\) is the molar concentration of \(^1H\) in the water including that brought in by the hygroscopic gelatin protein.

This is solved for the liquid phase and the gel phase with the matching of boundary conditions at the interface. The solution to the coupled diffusion equations in the liquid (l) and gel (g) slabs respectively are\(^{28}\)
Figure 15. Schematic representation of the sample configuration in the counter diffusion studies. Each sample was made with the bottom-half of a 60 ml HDPE bottle filled with various concentrations of gelatin mixed with 100% D$_2$O. Deionized H$_2$O was introduced on top of the set gelatin. A distance value of 0 is assigned to the interface. Positive values of distance are assigned to points within the liquid phase and negative values to points within the gelatin matrix.
\[
\frac{[\text{H}^1] - [\text{H}^1]_0}{[\text{H}^1]_1 - [\text{H}^1]_0} = p_l \quad \frac{[\text{H}^1]_0 - [\text{H}^1]}{[\text{H}^1]_0} = p_g
\]  

(52)

where

\[
p_j = 2 \sum_{n=0}^{\infty} \frac{(-1)^n}{(n+1/2)!} \pi \cos[(n+1/2)\pi(d_i - |z|)] e^{-(n+1/2)^2 \pi^2 D_j t/d_j^2}
\]  

(53)

To assure mass continuity across the sample the following boundary conditions are observed:

\[
([\text{H}^1]_0)_{1} = ([\text{H}^1]_0)_{g}
\]

and

\[
\int_{-d_g}^{d_1} [\text{H}^1] dz + \int_{0}^{d_1} [\text{H}^1] dz = [\text{H}^1]_1 d_1
\]

(54)

where \([\text{H}^1]_0\) and \([\text{H}^1]_1\) represent the interface and initial \(\text{H}^1\) molar concentrations, respectively.

3.2.2.3 Results and Discussion

Theoretical relationships for the \(T_1\) times as a function of \(\phi\) and \(f\) reported in the section 3.1.4.2 and empirical relationships for \(T_2\) times were used concurrently with the results of the diffusion equation in constructing signal profiles for the three samples at various times. In the liquid phase, the value for \(\phi\) is 0. The specific relations used for the best fit were within experimental uncertainty. The value for the \(\text{H}^1\) concentration was directly substituted in for the spin density, \(\rho\), for points in the liquid phase, and multiplied by a factor of 0.97 for points in the gelatin phase to account for the volume the gelatin
protein occupies. The factor, 0.97, was found through density studies of gelatin; the density of the three gelatin concentrations were measured and compared to that of water, and it was found all three had the same density of 0.97 times that of water. Finally, an arbitrary value for the proportionality constant, $K$, in equation (3) was found. In this manner, signal profiles are constructed directly from the $T_1$, $T_2$ data and the solutions to the diffusion equation.

These theoretical signal profiles are, in Figure 16, compared with the signal profiles acquired from the instrument, which are adjusted for the signal baseline. This figure represents three different times for the $\phi = 0.24$ g/mol gelatin sample. The derived curves are smooth. The fit provided is very good. The enhanced signal in the gelatin phase is not readily apparent in this low gelatin concentration, but it becomes a more dominant feature in higher concentrated gelatin phases as is illustrated in Figure 17. The small dip in the acquired signal curve close to the gelatin–water interface where it goes below the fitted curves is due to the presence of small air bubbles on the surface of the gelatin. The fitted curves for the other gelatin concentration well resemble the acquired curves.

Table 5. Diffusivities of water in the liquid mixture and in gelatin.

<table>
<thead>
<tr>
<th>$\phi$</th>
<th>$D_1$ ($\times 10^{-5}$ cm$^2$/s)</th>
<th>$D_g$ ($\times 10^{-5}$ cm$^2$/s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.24</td>
<td>2.0 $\pm$ 0.05</td>
<td>2.0 $\pm$ 0.05</td>
</tr>
<tr>
<td>0.79</td>
<td>1.9</td>
<td>1.8</td>
</tr>
<tr>
<td>1.57</td>
<td>1.9</td>
<td>1.5</td>
</tr>
</tbody>
</table>

Table 5 gives values of the diffusion coefficients of H$_2$O in gelatin, $D_g$, and the self–diffusion coefficient of H$_2$O in water, $D_1$. The value for $D_1$, 2.0$\times 10^{-5}$ cm$^2$/s, compares well with values from previous works.$^{36}$ The uncertainty listed in Table 5 is derived from the tolerance of the theoretical fit to the data. A value that is slightly lower than what
Figure 16. Signal profiles of the $\phi = 0.24$ g/mol sample at three separate times. The theoretical curves, derived from results of the $T_1$ and $T_2$ studies and Fick's second equation, are represented as smooth lines. These signal profiles bear a close resemblance to concentration profiles, concentration of a diffusing species versus distance. The theoretical curves provide a good fit with $D_1 = D_g = 2.0 \times 10^{-5}$ cm$^2$/s.
Figure 17. A signal profile for a sample of $\phi = 1.57$ g/mol at $t = 117960$ s. The signal enhancement of the signal in the gel phase is caused by the protein providing additional relaxation pathways. The theoretical curve, derived from the $T_1$ and $T_2$ studies and Fick's second equation, provides a good fit with $D_1 = 1.9 \times 10^{-5}$ cm$^2$/s and $D_g = 1.5 \times 10^{-5}$ cm$^2$/s.
was reported by Franks is expected because the $\text{H}_2\text{O}$ molecule is diffusing through a mixture of both $\text{D}_2\text{O}$ and $\text{H}_2\text{O}$. The $\text{D}_2\text{O}$ has a lower zero point energy and will tend to make the system slightly more rigid thereby hindering the diffusion of the $\text{H}_2\text{O}$ molecule slightly. The results for $\text{D}_1$ compare very well with those found in Table 3, page 44. This result provides a good experimental verification of theory.

The results reveal that the gelatin at low concentrations hinders the diffusion of water only slightly. Although the gelatin matrix demonstrates solid-like behavior at room temperature, the water within behaves like a liquid.

3.2.3 The Bulk Drying Process in Gelatin

3.2.3.1 Experimental

Six cylindrical gelatin samples of dimensions, diameter = 2 cm and height = 4 cm, were prepared with gelatin provided by the Eastman Kodak Company (Rochester, NY) and deionized $\text{H}_2\text{O}$ (18 MΩ cm) to a concentration of $\phi = 3.85$ g/mol. Each of five samples were allowed to air-dry at time intervals of 24 hours with the conditions of approximately 60% relative humidity, $20^\circ\text{C}$, and minimal convection. Significant shrinkage occurred with the samples as they dried. Approximately 18 hours after the last sample was exposed to the drying conditions each sample was imaged individually with a 2.0 Tesla, superconducting, chemical shift imager (General Electric, Freemont, CA). A simple, single turn, solenoidal probe of dimensions, diameter = 3.5 cm and height = 6.0 cm, was used with the imager to acquire a $^1\text{H}$, single echo, spin echo image of each sample. Table 1, page 24, summarizes the imaging parameters used for the study. The remaining sample was not exposed to the drying conditions and was imaged to see what signal value the minimum gelatin concentration should have. The signal values recorded were normalized to this value. The images were transferred to a DEC VAX–8650 computer (Maynard, MA) located at the RIT campus for post processing.
The imaging plane was oriented perpendicularly with respect to the symmetry axis of each sample to reveal the entire diameter of the sample so the H$_2$O concentration as a function of radius could be analyzed. Programs for analysis were written in FORTRAN for use with the VAX-8650 computer referred to above. The field of view (FOV) was chosen to reveal the best resolution, and the slice thickness was chosen to be small in order to reduce the effects caused by uneven drying. A single profile of normalized $^1$H signal strength versus radius was made by averaging the pixel values in four radial directions.

3.2.3.2 Diffusion Theory

The diffusion of the H$_2$O molecule in the system was modeled using Fick's second diffusion equation in cylindrical coordinates, equation (14),

$$\frac{\partial [^1H]}{\partial t} = \frac{1}{r} \frac{\partial}{\partial r} \left( r D \frac{\partial [^1H]}{\partial r} \right),$$

(55)

where $[^1H]$ is the time and distance dependent molar concentration of water. The coefficient, $D$, is the diffusion coefficient of the water molecule in the system which is modeled as linearly dependent on the concentration and is given by, $D = D_0(1+b[^1H])$. The change in $D$ with concentration is therefore represented as, $\frac{\partial D}{\partial C} = D_0 b$. Equation (55) can thus be rewritten as,

$$\frac{\partial [^1H]}{\partial t} = \frac{D_0(1+b[^1H])}{r} \frac{\partial [^1H]}{\partial r} + D_0 b \left( \frac{\partial [^1H]}{\partial r} \right)^2 + D_0(1+b[^1H]) \frac{\partial^2 [^1H]}{\partial r^2}$$

(56)

If we introduce the reduced variables, $\theta = [^1H]/[^1H]_0$, $\tau = \frac{D_0 t}{R^2}$, $\varphi = r/R$, and $\epsilon = b[^1H]_0$, where $[^1H]$ is the initial concentration and $R$ is the radius, then equation (56) can be recast as,
\[
\frac{\partial \theta}{\partial \tau} = (1 + \epsilon \theta) \left( \frac{1}{\varphi} \frac{\partial \theta}{\partial \varphi} + \frac{\partial^2 \theta}{\partial \varphi^2} \right) + \epsilon \left( \frac{\partial \theta}{\partial \varphi} \right)^2 .
\] (57)

Equation (57) was then solved for \( \theta \) using a Crank–Nicolson method (outlined in Appendix E) with the following conditions:

1) boundary,
\[
N_a|_{\varphi=0} = 0
\]
\[
N_a|_{\varphi=1} = h([{^1H}]_i - [{^1H}]_g)
\]

2) initial
\[
\theta = 1, \text{ for } \tau = 0
\]

where \( N_a \) is the molar flux at \( \varphi \), \( h \) is the mass transfer coefficient with units moles \( \text{H}_2\text{O}/\text{cm}^2 \cdot \text{s} \), and \([{^1H}]_i\) and \([{^1H}]_g\) are the concentration values at the surface and within the ambient gas, respectively. These conditions are imposed to insure proper mass balance. The gelatin system was modeled so that the density and radius, \( R \), were constant in time.

3.2.3.2 Results and Discussion

The signal recorded by the imager is affected by the relaxation processes of the \(^1\text{H}\) in the system so we seek a relationship between the relaxation times of the \(^1\text{H}\) and the system parameter, \( \phi \). A theoretical relationship of \( T_1 \) with \( \phi \) was acquired from results discussed in section 3.1.4.2 and an empirical relationship for \( T_2 \) was derived from results in section 3.1.2. These are featured in Figure 18. Both relaxation rates increase as \( \phi \) increases with the \( \phi \) values used in the studies, although \( T_2 \) is clearly more sensitive in \( \phi \). The effect of these relationships on the signal strength are shown in Figure 19 as an exponentially decaying function. In this Figure, a signal strength of one has been assigned to a gelatin concentration of \( \phi = 3.85 \text{ g/mol} \), the starting gelatin concentration. This dependence
Figure 18. The spin-lattice and spin-spin relaxation rates, $1/T_1$ and $1/T_2$, respectively, as a function of $\phi$. The smooth curve for the $1/T_1$ data is derived from the cross-relaxation theory, and the smooth curve for the $1/T_2$ data is derived empirically from the $T_2$ measurements. The latter is specifically derived from a second-order polynomial least squares fit. Both curves display an increase in $\phi$, however, $1/T_2$ is more sensitive.
Figure 19. The MRI \(^1\text{H}\) signal as a function of \(\phi\). The curve, derived from the relations demonstrated in Figure 18 and equation (3), indicates the sensitivity of the instrument. Signal loss is experienced in the vicinity of \(\phi \geq 27 \text{ g/mol}\). A signal value of 1 corresponds to \(\phi = 3.85\), the gelatin concentration before drying.
between \( \phi \) and the signal strength and the solution to equation (57) were implemented into equation (3) to construct theoretical signal profile curves which are depicted in Figure 20 as solid lines. The theoretical curves matched well with the data up to a point at approximately 0.85 on the abcissa. Inhomogeneous shrinkage in the sample upon drying resulting in a non-uniform radial distance for each sample creates unavoidable experimental uncertainty in the data beyond 0.85.

For the theoretical curves in Figure 20, \( \epsilon \) was found to be 1.1. The density of gelatin at \( \phi = 3.85 \text{ g/mol} \) was found to be 1.07 \( \text{g/ml} \) which leads to the relationship, \( [^1\text{H}] = 53.9/(1+\phi) \). This results in a value of 0.090 \( \text{l/mol} \) for \( b \). The diffusion coefficient changes only slightly in \( \phi \) over the range of \( \phi \) encountered in this study. Table 6 gives the values for the quantity \( \kappa = h/\text{RD}_{0} \) needed to properly fit the theoretical curves in figure 20 for various times. The uncertainty in \( \kappa \) represents the tolerance of \( \kappa \) to the theoretical fit. This change in \( \kappa \) with time most likely is caused by a change in \( R \). In documenting the mass loss in the samples in time it was found that within the first 18 hours of drying approximately 20\% wt. loss occurred. For each of the following 24 hour intervals the mass loss averaged approximately 5\%. During this time the radius of the sample decreased by approximately 12\% and consequently the surface area decreased. One of the assumptions made in using this diffusion theory is that the system maintains a constant radius and surface area. The consequent effect is the lowering of \( \kappa \).

<table>
<thead>
<tr>
<th>( t(\text{h}) )</th>
<th>( \kappa )</th>
</tr>
</thead>
<tbody>
<tr>
<td>18</td>
<td>0.35</td>
</tr>
<tr>
<td>42</td>
<td>0.29</td>
</tr>
<tr>
<td>66</td>
<td>0.23</td>
</tr>
<tr>
<td>90</td>
<td>0.23</td>
</tr>
<tr>
<td>114</td>
<td>0.23</td>
</tr>
</tbody>
</table>
Figure 20. Signal profiles for the drying gelatin at several times. The smooth curves are derived from the results of the $T_1$ and $T_2$ studies and Fick's second equation in cylindrical coordinates. These curves bear a close resemblance to concentration profiles. The theoretical curves fit well under 0.85 cm and with a slightly changing $\kappa$. The uncertainty in the region above 0.85 cm can be attributed to nonuniform drying.
Our results have shown that for the early to middle stages of the drying of gelatin a good first approximation for the qualitative analysis of the diffusion of water out of the system can be accomplished using Fick's second equation with the assumptions of constant radius and a diffusion coefficient that is linearly dependent upon the gelatin concentration. For thorough quantitative analysis, the shrinking radius needs to be dealt with. Some limits exist in drawing conclusions about the system during later stages in drying. Since data was only acquired for $\phi < 7.5$ g/mol, $T_1$ and $T_2$ values beyond that are only speculative. Furthermore, the $\phi$ dependence of the diffusion coefficient, $D$, may show a non-linear feature at gelatin concentrations higher than that studied.

Continued investigation of higher gelatin concentrations is also somewhat limited by this method. It was found that the imager was only able to pick up a signal from gelatin of $\phi < 27$ g/ml (40% wt H$_2$O) and is shown in Figure 19. Small gelatin samples taken at the point where the signal quickly drops off into the noise were analyzed using thermogravimetry. At the point of $\phi \approx 27$, the shrinking $T_2$ plays a large part in decreasing the signal.
4. Summary

The main material studied in this thesis is gelatin. MRI provided a useful means to investigate the diffusion of water within two gelatin systems: 1) the counter diffusion of water and heavy water in a gelatin matrix of a given gelatin concentration, and 2) the drying of a gelatin sample originally at a given concentration. MRI provided the author with images consisting of an array of pixels that have been assigned a signal value relating to the amount of \(^1\)H nuclei present in the corresponding voxel in the sample. In order to interpret the signal, however, the relationship between the relaxation rates, 1/T\(_1\) and 1/T\(_2\), and the water and gelatin concentrations needed to be established. The formulation of 1/T\(_1\) was attempted with use of two different models, the three–fraction hydration model and the cross–relaxation model. Both proved adequate in formulating 1/T\(_1\) for low gelatin concentrations although some discrepancies exist with the former in terms of physical interpretation. For example, the heteronuclear \(^1\)H–\(^2\)H interactions proved to be significant for the hydrated water but not for the bulk in creating a good theoretical fit. Furthermore, there is no accommodation in the model to describe the upturn of data at low H\(_2\)O concentrations, high gelatin concentrations. Through the analysis of the failure of the three–fraction hydration theory to model the higher gelatin concentrations successfully, there is indication of the existence of relaxation pathways not taken into account by this theory.

The spin–lattice relaxation rate for the ternary system was formulated successfully with the cross–relaxation model. It provided a good theoretical fit, within experimental uncertainty, for the various gelatin concentrations studied. Magnetization energy can be transferred from the population of water \(^1\)H to the population of protein \(^4\)H. This
mechanism plays an integral part in explaining the observed relaxation phenomenon. The observed spin–lattice relaxation rate can be described by the sum of two exponential terms.

The $1/T_2$ formulation based upon the three–fraction hydration model proved to be more difficult to achieve. Although the theory fits fairly well for low gelatin concentrations, the same problems exist with the higher gelatin concentrations as with the $1/T_1$ formulation (i.e. poor fit for high $\phi$). The introduction of more gelatin highly complicates the mechanism of spin–spin relaxation. A formulation of $1/T_2$ based upon the cross–relaxation model was not attempted unsuccessfully. The spin–spin relaxation time in this ternary system is not clearly understood.

The results from the cross–relaxation modeling of $1/T_1$ and the empirical relationships for $1/T_2$ with $f$ and $\phi$ were used to interpret the images from the two gelatin systems studied. The diffusion theory for the counter diffusion system compared well to that interpreted from signal profiles acquired directly from image data. The uneven drying of the gelatin sample in the other system created some difficulty in interpreting data close to the edge of the sample, but the nature of the diffusion of water in the bulk of the sample is recognized. An adjusted diffusion theory taking into account the shrinking radius may prove to deliver curves that fit better in the time domain, however, the one used in the study provides a good first approximation. The diffusion coefficients for water molecules within gelatin at a given concentration were easily extracted once the $1/T_1$ and $1/T_2$ relationships were obtained.

The self diffusion coefficient of water obtained in the study matched very well with established values and supports the validity of the MRI technique. The values obtained for the diffusion coefficient of water within a gelatin matrix at different gelatin concentrations are very close to the self–diffusion coefficient of water which indicates that the diffusion of water is only hindered slightly by the presence of the gelatin. The close comparison of these values suggests that the translational diffusion processes of water within a gelatin matrix are similar to that within a liquid, even though the matrix can be
characterized as a solid.

In summary, magnetic resonance imaging is a convenient and powerful technique to investigate diffusion processes in materials especially polymers. It allows the researcher to noninvasively obtain a large amount of information regarding moisture content within a system and provides for a number of applications in the many fields of polymer study. The potential of this exciting technique is only beginning to be realized in the field of materials science.
Appendix A

A Magnetic Resonance Imaging Study of the Diffusion of Water in Plaster

Introduction

The study of diffusion in porous media is very important in numerous fields including that of oil recovery. Plaster provides a good model for a porous medium, as it is readily available and easy to work with. A study of the diffusion of water in modified plaster of Paris samples was undertaken using MRI. The samples were modified such that the voids within the plaster matrix were filled with a specific gas. The interaction of the gas present within the voids with the water provides a marked effect on the diffusing characteristics of the water and the signal obtained by the imager.

The relaxation behavior of the water protons in the fluid within the voids of the porous matrix is sensitive to the size and geometry of the vacancies and the constituents of the porous solid. MRI provides a viable means to study these effects.

Experimental

Three plaster samples were prepared with calcined plaster of paris (United Gilsonite Laboratories, Scranton, PA), CaSO$_4$-H$_2$O, in accordance with the manufacturer's specifications. Approximately 125 ml of the plaster mixture was poured into each of three 250 ml HDPE bottles and then dried under mild heat for 24 hours.

The plaster samples were then prepared for the introduction of a specific dominant gas. Each sample was individually pumped under a vacuum of approximately $10^{-4}$ torr for
eight hours, in order to minimize the air and water vapor content, then sealed. Three gasses, carbon tetrachloride, carbon dioxide, and air, were introduced into the pores of the respective samples under a pressure of 1 atm and were allowed to equilibrate for eight hours. The air sample was allowed to equilibrate in air at STP. To minimize diffusion of materials in or out of the porous media before imaging the samples were carefully sealed before removal from the respective atmospheres.

Approximately 125 ml of deionized H$_2$O (18 MΩ cm) was introduced to the top of each sample container just prior to imaging. Figure A.1 illustrates the sample configuration and Table 1 lists the experimental imaging parameters. The imager used in this study was the same as that described in section 3.1.2. Furthermore, the analysis of the data was performed similarly to that described in that section. A $^1$H signal profile for each sample was established from the average signal value for horizontal pixels in a 3 cm band passing vertically down the center of the sample.

Results and Discussion

Signal profiles for each sample were recorded at time intervals of approximately five minutes. Signal profiles for the CO$_2$ sample at three times are displayed in Figure A.2. The plaster–water interface is located at $z=0$, where the signal drops sharply. The water above the plaster is represented by the large plateau in the signal for $0 < z < 2.5$ cm at $t = 180$ s. As time increases, the level of the water drops and the front of the diffusing water in the plaster progresses towards the bottom of the container located at $z = -5.5$ cm. Figure A.2 also demonstrates an increase of the proton signal of the water in the plaster with time.

Some conclusions can be drawn from this preliminary work. The drop in the signal at the plaster–water interface can in part be explained by a porosity effect. That portion of the signal proportional to the water content in a voxel should decrease proportionally
Figure A1. Schematic representation of the sample configuration in the plaster study. Each sample was made with the bottom-half of a 250 ml HDPE bottle filled with plaster mixed with deionized H$_2$O to manufacturer’s specifications. Deionized H$_2$O was introduced on top of the set plaster just prior to imaging. A distance value of 0 is assigned to the interface. Positive values of distance are assigned to points within the liquid phase and negative values to points within the solid plaster matrix.
Figure A2. Signal profiles of the CO$_2$ plaster sample recorded at three times. The profiles reveal the progression of the diffusing water with time. The signal was normalized to that recorded in the water above $z = 0$. Note the change in the scale of the y-axis at the break.
with the reduced volume. Comparing mass measurements of water saturated plaster and dry plaster, it was found that approximately 40% of the volume of the plaster matrix is occupied by solid \( \text{CaSO}_4 \cdot \frac{1}{2} \text{H}_2\text{O} \). Spin relaxation times of the bulk water in the plaster being equal, the signal would be approximately 0.6 times the signal of water alone. This, however, is not the case as it was found that the signal of the water in the plaster finally tops out at less than 30%.

The relaxation times of the protons in water will affect the MRI signal and play an important role in this system. The presence of the solid \( \text{CaSO}_4 \cdot \frac{1}{2} \text{H}_2\text{O} \) may affect the molecular motion of the water molecules nearby which would affect the observed relaxation rates of \(^1\text{H} \) in the water. The more surface area the plaster pores expose to the water the greater the volume of the bound water. The correlation times can only be speculated at this point as well as the percentage of water actually perturbed by the walls of the pores. A \( T_1, T_2 \) study of the plaster matrix needs to be performed in order to begin to gain insight on the effects of the relaxation times on the MRI signal. No such study was performed. In order to describe, in part, the fact that the signal of the water in plaster lies somewhere near 0.3 instead of 0.6, it is speculated that the observed \( T_2 \) has decreased due to the perturbed motion of the water molecules near the surface of the plaster.

Another interesting feature of Figure A.2 is revealed by the study of the shapes of the signal curves within the matrix. The features of the curves remain constant in time. Attention is drawn to \( z = -1.1 \) cm where a peak is recorded in the \( t = 180 \) s curve and remains in the same position for later times. This peak may indicate that within the 3cm wide path of pixels that were averaged there were on the average more voids or a relatively large void in the path. In this capacity this method may be used to find slight imperfections in homogeneous media.

The effect of the various gases within the plaster matrix is demonstrated in Figure A.3. Signal profiles for the three samples at a given time are revealed. The diffusion occurs at a faster rate in the \( \text{CO}_2 \) filled plaster matrix than the others. This can be
Figure A3. Signal profiles of the three plaster samples recorded at $t \approx 800$ s. The profiles reveal the extent to which the diffusing water progressed in each of the samples. The difference in this progression in each sample is attributed to the difference in the water solubility of the specific gas that occupies the pores of each sample. The increased signal in the $\text{CO}_2$ sample may, in part, be attributed to the effects resulting from the formation of carbonic acid. Note the change in the scale of the $y$-axis at the break.
attributed to the fact that the solubility of CO₂ in water is much greater than that of the other gases. Listed in Table A.1 are the solubilities of the respective gasses in water. The solubilities of N₂ and O₂ are greater than that of CCl₄ which explains why water in the air sample has progressed slightly further than that of CCl₄. As the water fills a void within the plaster matrix a certain amount of gas is dissolved which creates a low pressure region in the void that draws the water further in. This process occurs to a large extent with the CO₂ sample, a much smaller extent with the air sample, and an even smaller extent (if not at all) in the CCl₄ sample.

<table>
<thead>
<tr>
<th>gas</th>
<th>solubility (cm³/100 ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CCl₄</td>
<td>very slight</td>
</tr>
<tr>
<td>N₂</td>
<td>2.33</td>
</tr>
<tr>
<td>O₂</td>
<td>4.89</td>
</tr>
<tr>
<td>CO₂</td>
<td>171.3</td>
</tr>
</tbody>
</table>


Another feature of Figure A.3 needs to be addressed as well, the large relative increase in signal of the water in the CO₂ sample below z = 0. As CO₂ dissolves in water carbonic acid is formed. The pH of a water sample in which several chunks of dry ice were immersed was found to be 3.7 while a sample exposed to N₂ had a pH value close to 7.0. T₁ and T₂ effects were considered to play a role in this marked increase in signal and a T₁, T₂ study was consequently performed on the aforementioned samples. Since O₂ affects the relaxation times significantly, the N₂ sample was compared with the CO₂ sample to isolate the CO₂ effect. T₁ varied little between the samples and T₂ decreased by approximately 0.1 s in the acidic sample. This is in good comparison with other work done on the
subject, however, this effect does not explain the results.

A feasible explanation lies within the fact that the carbonic acid will work to dissolve the plaster. As the acidic solution dissolves some of the solid, various elements found as impurities in the plaster will come out in solution as paramagnetic ions. These ions, perhaps Ni\(^{2+}\), Mn\(^{2+}\) and Cr\(^{3+}\) ions, would provide efficient relaxation pathways for the magnetization. If present T\(_1\) would become significantly smaller and the signal, with TR=1000 ms, would increase. Furthermore, only small traces of these ions, on the order of 10\(^{-5}\) mol/kg are needed to create a significant effect, therefore it their existence acts as a viable explanation for the enlarged CO\(_2\) signal.

The diffusion of water in plaster would provide a formidable problem for modeling. Since the MRI signal comes from an average of the gas filled pores and liquid pores in each voxel, a pore size distribution for the plaster matrix is needed to estimate the amount of water present within the voxel and the amount affected by the walls of the pores. An attempt was made to find the pore size distribution for a plaster sample by creating a saturation recovery curve. The technique is described by Davies and Packer. Essentially the size of a pore is related to the water \(^1\)H T\(_1\) within the pore. If the saturation recovery curve revealed a T\(_1\) distribution, a pore size distribution could be directly calculated. This attempt failed which seems to suggest that a T\(_1\) distribution is not present or, more likely, the technique is insensitive to the relatively large size of the plaster pores or their geometry.

A consideration of the connectivity of the voids in a porous matrix is important for a diffusion model. The large pores will inevitably be filled first forcing gas into the smaller voids. This progression will resist the filling of the small pores unless there are a large number of paths for the gas to escape. Surface analysis techniques may be of some use. In any case the model will have to simplify the very complex physical nature of the plaster system.
Appendix B

Investigating Cement Aggregates Using Magnetic Resonance Imaging

MRI has limited utility in the study of cement and cement products. Many cement aggregates contain appreciable amounts of ferromagnetic iron, measured to be approximately 2% wt. in a bag of Sacrete sand mix (Rochester Portland Cement Corp, Rochester, NY). Ferromagnetic iron creates a large artifact in the MR image which renders it uninformative. The MR technique is extremely sensitive to the presence of ferrous material as a single iron filing can disrupt an area of 4 cm³ in an image. Samples of cement aggregates must be free of any ferrous materials before imaging.

An attempt to image a cement sample was performed in order to gain insight into the curing process. A 250 ml sample was prepared with type I portland cement (Rochester Portland Cement Corp, Rochester, NY) in accordance with manufacturers specifications after ferrous material had been removed by magnetic extraction. An attempt was made to image the sample approximately five minutes after water was introduced to the dry portland. Using the same imager as described in section 3.1.2 no image was recorded due to lack of a NMR signal.

The failure to observe a MR image revealed information regarding the molecular motion of the water within the cement matrix as it is curing. During curing, water is involved in hydration reactions with calcium silicates and calcium aluminates. Water molecules are tightly bound in the hydrated compounds and have very restricted motional capability. It was postulated that no signal was observed because the correlation times of the bound water protons are relatively long and cause $T_2$ times to be too short for a signal to be observed, even at the shortest TE attained on the imager. This is supported by a
high resolution proton NMR spectrum of a cement sample. A proton spectrum of a very thin cement mixture was recorded on a 200MHz NMR spectrometer (Nicolet, Minneapolis, MN) minutes after it was mixed. The sample was made so that the amount of water required to completely react with the cement present was exceeded. The resultant spectrum revealed two peaks, a very narrow peak on resonance from the free water and a much broader peak approximately 3000Hz downfield from the chemisorbed water (Figure B.1). Assuming the free water peak represents the maximum limit of inhomogeneous broadening in the spectrum, the bound water peak must be homogeneously broadened. The $T_2$ of the broad peak is therefore no larger than 0.08 ms, two orders of magnitude smaller than the smallest TE value attainable on the imaging system.
Figure B1. A high resolution NMR proton spectrum of a wet, thin cement mixture. The thin peak on resonance is caused by the protons of the free water molecules in the sample, and the broader peak, approximately 3000 Hz downfield, is caused by the protons of the chemisorbed water molecules. Measuring the width of the peak reveals that the $T_2$ times of the chemisorbed water protons are much too short for imaging experiments.
Appendix C

Magnetic Resonance Imaging of Balsa Wood

Perhaps the most versatile of building materials is wood as man has found innumerable applications. Its major drawback, however, has been its rather poor durability on exposure to weathering. Much of this problem can be attributed to water-related deterioration. It is therefore prudent to study the diffusion of water in wood products in an attempt to understand and minimize water-related deterioration.

Wood is an extremely complex polymeric system and the diffusion of water within the system cannot be considered a simple process. MRI provides a viable macroscopic technique to investigate the presence of water within a wood system. MRI was therefore used to image various balsa wood samples in an effort to investigate the behavior of diffusing water.

Two experiments were performed with balsa wood blocks (2.5 cm x 5.0 cm x 10.0 cm) in order to study the diffusion of water into the media. Both were carried out using the imaging device described in section 3.1.2. Balsa wood was chosen because of its high porosity. In the first experiment, two blocks were placed in a pan of water one centimeter deep just prior to imaging. One block was placed in the pan with the wood grain perpendicular to the surface of the water and the other parallel. In the second experiment, five blocks were placed at 24 hour intervals into a pan of water, kept at a level of one centimeter. Two hours prior to imaging and 12 hours after the last block was placed in the water, all the blocks were wrapped separately in parafilm to insure no evaporation of surface water and imaged simultaneously.

The first experiment revealed a relatively fast surface wetting and a much slower
diffusion into the bulk media. The surface of each block was completely wet within 1.5 hrs, however, after a period of 2 hrs the image revealed that the water diffused into the bulk media of each block no farther than 2 mm regardless of grain orientation. The second experiment showed that no significant diffusion of water into the bulk media had occurred over a period of a week as revealed in images where the water only progressed to a maximum depth of 3 mm. An image of the edges of each block revealed the grain patterns. A sharper signal existed along the grain lines which outlined the pattern. These observations are consistent with theories that water supports the degradation of wood but is not the cause.41

MRI provides a viable technique to investigate the presence of water in a wood system although some applications may require an in—plane resolution finer than the 0.3 mm available in this study. The technique may be of use to those interested in studying wood sealant products. In order to model the diffusion of water into wood, however, factors such as grain patterns and the surface wetting phenomenon need to be examined in more detail.
Appendix D

Decoupling Differential Equations

Any $n$th-order differential equation may be written as a system of $n$ first-order differential equations by defining $n-1$ new variables. For example, we have the following first-order differential equations:

$$\frac{d\alpha}{dt} = -R_1\alpha + k_2\beta$$  \hspace{1cm} (D.1)

$$\frac{d\beta}{dt} = -R_2\beta + k_1\alpha$$  \hspace{1cm} (D.2)

These may be written as one second-order, linear differential equation through the following steps:

1) the second derivative with respect to time of equation D.1 is found,

$$\frac{d^2\alpha}{dt^2} = -R_1\frac{d\alpha}{dt} + k_2\frac{d\beta}{dt}$$  \hspace{1cm} (D.3)

2) from equation D.1 we have,

$$\beta = \frac{1}{k_2} \frac{d\alpha}{dt} + \frac{R_1}{k_2} \alpha$$  \hspace{1cm} (D.4)

3) which is substituted into equation D.2 to acquire,

$$\frac{d\beta}{dt} = -R_2\left(\frac{1}{k_2} \frac{d\alpha}{dt} + \frac{R_1}{k_2} \alpha\right) + k_1\alpha$$  \hspace{1cm} (D.5)
4) \( \frac{d\beta}{dt} \) of equation (D.5) is substituted into equation (D.3) to obtain a second-order, linear, homogeneous, ordinary differential equation,

\[
\frac{d^2\alpha}{dt^2} + (R_1 + R_2)\frac{d\alpha}{dt} + (R_1R_2 + k_1k_2)\alpha = 0 \tag{D.6}
\]

This type of differential equation has the following as a solution,

\[
\alpha = Ae^{-t/\tau_1} + be^{-t/\tau_2} \tag{D.7}
\]

Since \( e^{-t/\tau_1} \) or \( e^{-t/\tau_2} \) are never zero, the secular equation can be formed by substituting either one into equation (D.6).\(^{34,35} \) This is shown in the body of the thesis as equation (47).
Appendix E

An Application of a Crank–Nicolson Method

The solution to equation (57) is found with use of a finite difference method called the Crank–Nicolson method. The distance and time space is defined by the following grid,

\[
\begin{align*}
\Delta & = t_j - t_{j-1} \\
\delta & = x_i - x_{i-1}
\end{align*}
\]

where the old time step is represented by \( j-1 \) and the new time step by \( j \). The differential equation is evaluated at the half-way point \((i,j - \frac{1}{2})\) and is given in the explicit finite-difference form as,

\[
\frac{\theta_{i,j} - \theta_{i,j-1}}{\Delta} = (1 + \epsilon \theta_{i,j-1}) \left[ \frac{1}{\varphi} \left( \frac{\theta_{i+1,j-1} - \theta_{i-1,j-1}}{2\delta} \right) + \frac{\theta_{i+1,j-1} - 2\theta_{i,j-1} + \theta_{i-1,j-1}}{\delta^2} \right] + \epsilon \left( \frac{\theta_{i+1,j-1} - \theta_{i-1,j-1}}{2\delta} \right)^2,
\]

(E.1)

and in implicit finite-difference form as,

\[
\frac{\theta_{i,j} - \theta_{i,j-1}}{\Delta} = (1 + \epsilon \theta_{i,j-1}) \left[ \frac{1}{\varphi} \left( \frac{\theta_{i+1,j} - \theta_{i-1,j}}{2\delta} \right) + \frac{\theta_{i+1,j} - 2\theta_{i,j} + \theta_{i-1,j}}{\delta^2} \right] + \epsilon \left( \frac{\theta_{i+1,j} - \theta_{i-1,j}}{2\delta} \right) \left( \frac{\theta_{i+1,j-1} - \theta_{i-1,j-1}}{2\delta} \right).
\]

(E.2)
In order to linearize the differential equation, every non-linear term in the implicit form is partitioned into a factor taken at the new time step and one taken at the old. Using a weighting factor, \( \lambda \), the differential equation can be written as a combination of both the explicit and implicit forms,

\[
\frac{\theta_{i,j} - \theta_{i,j-1}}{\Delta t} = (1 - \lambda) \text{(explicit form)} + \lambda \text{(implicit form)}
\] (E.3)

where \( \lambda \) is between 0 and 1. It can be shown that if \( \lambda \geq 0.5 \), the solution is stable. We used a relatively high value, \( \lambda = 0.85 \), for our equation which ensures low discretization error. To solve, a system of equations can be formed in the following structure:

\[
\begin{align*}
\theta_{0,j} - \theta_{1,j} &= 0 \\
a_2 \theta_{0,j} + b_2 \theta_{1,j} + c_2 \theta_{2,j} &= d_2 \\
a_3 \theta_{1,j} + b_3 \theta_{2,j} + c_3 \theta_{3,j} &= d_3 \\
\vdots & \quad \vdots \\
a_n \theta_{n-1,j} + b_n \theta_{n,j} + c_n \theta_{n+1,j} &= d_n \\
\vdots & \quad \vdots \\
a_{m-1} \theta_{m-2,j} + b_{m-1} \theta_{m-1,j} + c_{m-1} \theta_{m,j} &= d_{m-1} \\
\theta_{m-1,j} + \theta_{m,j} &= d_m,
\end{align*}
\] (E.4)

where the coefficients for \( \theta_{i-1,j} \), \( \theta_{i,j} \), and \( \theta_{i+1,j} \) are found from equation (E.3) and are given respectively as,

\[
\begin{align*}
a_n &= \lambda(1 + \epsilon \theta_{i,j-1})(\frac{1}{2\varphi_0} - \frac{1}{\delta^2}) + \frac{\lambda \epsilon}{4\delta^2} (\theta_{i+1,j-1} - \theta_{i-1,j-1}) \\
b_n &= \frac{1}{\Delta} + 2\lambda(1 + \frac{\epsilon \theta_{i,j-1}}{\delta^2}) \\
c_n &= -\lambda(1 + \epsilon \theta_{i,j-1})(\frac{1}{2\varphi_0} + \frac{1}{\delta^2}) - \frac{\lambda \epsilon}{4\delta^2} (\theta_{i+1,j-1} - \theta_{i-1,j-1})
\end{align*}
\] (E.5, E.6, E.7)
and the \( d_n \) terms are found from the \( \theta \) values at the old time step. From the boundary conditions, listed as equations (58) and (59), we have,

\[
\theta_{0,j} - \theta_{1,j} = 0 \quad (E.8)
\]

and

\[
\theta_{m-1,j} - \theta_{m,j} = \kappa (1 + \epsilon \theta_{m-1,j}) \quad (E.9)
\]

where \( \kappa = \frac{h}{RD_0} \) and is described in the body of the thesis and \( m \) represents the total number of iterations. A matrix of the coefficients \( a, b, \) and \( c \) is called a tridiagonal matrix and is solved by the Thomas algorithm which is outlined as follows:

\[
\theta_{m,j} = \gamma_m
\]

\[
\theta_{n,j} = \gamma_n - \frac{c_n \theta_{n+1,j}}{\sigma_n}, \quad n = m-1, m-2, \ldots, 1 \quad (E.10)
\]

where the \( \sigma \)'s and \( \gamma \)'s are found from the following recursion formulas,

\[
\sigma_1 = b_1, \quad \gamma_1 = d_1/\sigma_1
\]

\[
\sigma_n = b_n - \frac{a_n c_{n-1}}{\sigma_{n-1}}, \quad n = 2, 3, \ldots, m
\]

\[
\gamma_n = \frac{d_n - a_n \gamma_{n-1}}{\sigma_n}, \quad n = 2, 3, \ldots, m \quad (E.11)
\]
References

7. F. Bloch, W. W. Hanson, and M. E. Packard. Phys. Rev. 69, 127 (1946)