Nuclear magnetic resonance (NMR) is an analytical technique used in chemistry to help identify chemical compounds, obtain information on the geometry and orientation of molecules, as well as to study chemical equilibrium of species undergoing physical changes of composition, among many others. Capitalizing on the ability to manipulate the magnetization through different pulse programs in NMR, allows for the study and understanding of the kinetics of a system. The exchange rates between two sites can be evaluated through dynamic nuclear magnetic resonance experiments (DNMR). $^{17}\text{O}$ is a common, NMR active nucleus that is used in the study of kinetics.

**Introduction**

NMR uses radio frequency radiation to change the direction of nuclear spins that have been placed in a static magnetic field, and measures the change of magnetization as a function of time. Since its discovery, NMR has gone through many advancements that have enabled it to become a very useful analytical technique. The Fourier Transform NMR has enabled more complicated studies through the ability to create pulse programs that can manipulate the spectra, like saturate one species magnetization so no peak is produced. These pulse programs can also be used to tip the spin of certain nuclei, while keeping others along the z-axis. This is useful for many applications, including being able to quench signals, change the direction (positive or negative) of the signal, and track relaxation, to name a few examples. Using different pulse programs allows for the study of exchange rates between species. This is done by monitoring the changes in the environment of the NMR active nuclei as a result exchange between the sites. Because of the exchange, spins (magnetization) will be transferred, leading to changes in the bulk magnetization at both sites. Any NMR active nuclei can be used to study exchange rates, such as $^{13}\text{C}$, $^1\text{H}$, $^{17}\text{O}$, but $^{17}\text{O}$ kinetic studies are often performed. This is done because $^{17}\text{O}$ enriched water can be used as one of the exchange sites, normally the bulk solvent site.

$^{17}\text{O}$ NMR for Kinetics Studies

**Background and Equations**

Oxygen seventeen nuclei have a spin state of 5/2, making them susceptible to nuclear magnetic resonance. This isotope of oxygen is only 0.0373% naturally abundant, but using isotopically labeled oxygen compounds can result in useful information. Studying these nuclei in the presence of a magnetic field will provide information about the structure and environment of the oxygens in the molecule. Using dynamic NMR or DNMR, $^{17}\text{O}$ NMR experiments can be performed to understand chemical reactivity and kinetics of compounds. DNMR studies the effect of a chemical exchange between two sites that have either a different chemical shift or coupling constant. These studies are done by obtaining NMR spectra over time and analyzing the increase and/or decrease of the signals. Unlike other methods that are used to study kinetics, NMR studies can acquire information about the effects of the exchange on the molecules.

To utilize NMR spectra to establish kinetic information, the Bloch equations must be adapted to include terms that take into account relaxation as a result of chemical reactivity. While investigating exchange reaction of $^{17}\text{O}$ water between two sites, the bulk water and water bound to a metal, it is assumed that the kinetics are 1st order, such that:
\[
\begin{align*}
\frac{du_M}{dt} &= -\overrightarrow{k}_M u_M + \overleftarrow{k}_W u_W \\
\frac{du_W}{dt} &= -\overleftarrow{k}_W u_W + \overrightarrow{k}_M u_M
\end{align*}
\]

Where \(\vec{k}_M\) & \(\vec{k}_W\) represent the rate of exchange between the bulk water and the bound water. These two sites can be said to be coupled because the isotopically enriched oxygen is exchanging between the metal site and bulk water site. As exchange occurs, the magnetization of the \(^{17}\text{O}\) metal ensemble and \(^{17}\text{O}\) water ensemble will change, not only due to magnetization relaxation, but also due to the exchange. The exchange rate terms can be added into the Bloch equations to take into account the relaxation. With the addition of this term, the equations are known as the Bloch-McConnell equations. Since there are two sites and three Bloch equations per site, there is a total of six equations for the change in magnetization of the system. **Equations 1-3** are for the metal site, while **Equations 4-6** are for the bulk water site.

### Bloch-McConnell Equations for Metal Site (Equations 1-3)

\[
\begin{align*}
\frac{du_M}{dt} &= v_M(\omega_{rf} - \omega_o) - \frac{u_M}{T_{2M}} - \overrightarrow{k}_M u_M + \overleftarrow{k}_W u_W \\
\frac{dv_M}{dt} &= -u_M(\omega_{rf} - \omega_o) - \frac{v_M}{T_{2M}} - \overrightarrow{k}_M v_M + \overleftarrow{k}_W v_W \\
\frac{dm_{zM}}{dt} &= v_M \omega_1 - \frac{(m_{zM} - m_o)}{T_{1M}} - \overrightarrow{k}_M m_{zM} + \overleftarrow{k}_W m_{zW}
\end{align*}
\]

### Bloch-McConnell Equations for Bulk Water Site (Equations 4-6)

\[
\begin{align*}
\frac{du_W}{dt} &= v_W(\omega_{rf} - \omega_o) - \frac{u_W}{T_{2W}} - \overleftarrow{k}_W u_W + \overrightarrow{k}_M u_M \\
\frac{dv_W}{dt} &= -u_W(\omega_{rf} - \omega_o) - \frac{v_W}{T_{2W}} - \overleftarrow{k}_W v_W + \overrightarrow{k}_M v_M \\
\frac{dm_{zW}}{dt} &= v_W \omega_1 - \frac{(m_{zM} - m_o)}{T_{1W}} - \overleftarrow{k}_W m_{zW} + \overrightarrow{k}_M m_{zM}
\end{align*}
\]

To analyze the NMR spectra, which is obtained by measuring the magnetization in the x-y plane, requires an equation that explains the magnetization change in the x-y plane as a function of time. In the rotating frame, the total magnetization in the x-y plane is comprised of two components the “real” and “imaginary” parts. Therefore, the total magnetization in the x-y plane can be expressed \(m_{xy} = u + iv\), or \(u=m_{x}\) and \(v=m_{y}\). Taking the derivative of this equation with respect to time leads to \(\frac{dm_{xy}}{dt} = \frac{du}{dt} + i\frac{dv}{dt}\). Using the previous relationships, the Bloch equations for the two sites can be simplified and rearranged to give the magnetization in the x-y plane as a function of time.
time. Invoking the law of detailed balance, which states that the exchange rate of the metal site times the amount of $^{17}\text{O}$ at this site is equal to the exchange rate of the bulk water site times the amount of $^{17}\text{O}$ at this site, will eliminate one of the rate coefficients, simplifying the equations even further gives **Equation 7**.

**Equation 7:**

\[
\begin{bmatrix} m_{xy,W} \\ m_{xy,M} \end{bmatrix} = e^{-\begin{bmatrix} \bar{L} + \bar{R} + \bar{k} \end{bmatrix} t} \begin{bmatrix} m^0_{xy,W} \\ m^0_{xy,M} \end{bmatrix}
\]

where,

\[
\begin{align*}
\bar{L} &= \begin{bmatrix} i_W(\omega_{rf} - \omega_o) & 0 \\ 0 & i_M(\omega_{rf} - \omega_o) \end{bmatrix} \\
\bar{R} &= \begin{bmatrix} \frac{1}{T_{2W}} & 0 \\ 0 & \frac{1}{T_{2M}} \end{bmatrix} \\
\bar{k} &= \begin{bmatrix} \overrightarrow{k} & -\overleftarrow{k} \\ -\overrightarrow{k} & \overleftarrow{k} \end{bmatrix}
\end{align*}
\]

\(\bar{L}\) is the difference in the chemical shifts of the two sites signals, \(\bar{R}\) is the relaxation in magnetization at each site without exchange, and \(\bar{k}\) is the rate coefficients for the exchange. Taking the derivative of the equation, the magnetization of the bulk water signal and the magnetization of the metal site as a function of time results in **Equation 8**.

**Equation 8:**

\[
\begin{bmatrix} m_{xy,W}(t) \\ m_{xy,M}(t) \end{bmatrix} = e^{-\begin{bmatrix} \bar{L} + \bar{R} + \bar{k} \end{bmatrix} t} \begin{bmatrix} m^0_{xy,W} \\ m^0_{xy,M} \end{bmatrix}
\]

The \(m^0\) is the initial magnetization along the x-y plane before relaxation.

Using the Bloch-McConnell equation, the width and intensities of the peaks in the spectra become a function of the chemical exchange. By studying the change in the two peaks, the rate coefficients can be determined, which can be used to calculate other thermodynamic properties like entropy and enthalpy.

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**Experiments**

**T2 Studies**

The most common way of studying chemical kinetics in NMR has been through the bandshape technique, which studies the change in the signals of the spectra as a result of exchange kinetics. Before any exchange occurs, two sharp signals are present, one for each of the two $^{17}\text{O}$ sites. As the exchange rate speeds up, the two peaks will begin to broaden and overlap. At an extremely fast exchange rate, the peaks will coalesce and be centered at the weighted average of the Larmor frequency of the bulk water and the bound water. This occurs because the two exchange sites will have two distinct peaks at slow exchange rates because the NMR active exchange species will be at each site for long enough time that detection of two separate sites will occur. As the exchange rate increases, the nucleus will be exchanging so quickly that the detection of the nucleus on either site becomes averaged out, creating one signal in the spectra.
Figure 1: Coalescing Peaks

This figure shows the two peaks moving closer together and then coalescing as the exchange rate increases.

The figure above shows peaks from a two-site exchange. The top spectrum depicts a slow exchange rate. As they move down, the rate constants are getting increasingly larger until the peaks coalesce.

The width of the band at half height, or the full width at half max (FWHM) is used to track the rate coefficients of the exchange because it is proportional to both $T_2$ relaxation and the rate coefficient. During exchange rate experiments, Equation 9 can be used to calculate the exchange rate ($k$), which can then be used to determine other activation parameters such as Gibb’s free energy, entropy, and enthalpy.

Equation 9:

$$k = \frac{\pi \delta v^2}{2(\omega^* - \omega^o)}$$

Swift and Connick used bandshape experiments to study the exchange of water from the bulk to a paramagnetic metal. They developed an equation that relates the band width of the signal to the mole fraction of each water site, the bulk $P_W$ and the metal $P_M$. Equation 10 is the simplified Swift-Connick equation for the change in the paramagnetic water signal. ($\Delta w$ is the change in the full width measured at half height)

Equation 10:

$$\frac{1}{P_M} (\Delta w) = \frac{\Delta w}{1 + \frac{1}{k_M \dot{T}_{2M}}} + \frac{\Delta w^2}{k_{M}^2}$$

By obtaining the NMR spectra and measuring the signal width, the exchange rate can be calculated. It can be seen that the peak broadness is a function of the $T_{2M}$ relaxation, or the transverse relaxation. It can be evaluated from the
free-induction decay (FID). The FID is the time-domain signal of each frequency component. Each component results in a sine wave, which are then added together for the FID signal. At time zero, all the components are aligned, and over time they spread out and combine in a deconstructive manner, resulting in a decay of the total FID signal. This is an exponential decay and can be used to calculate the transverse relaxation with Equation 11.

\[ M_{xy}(t) = M_{0}e^{-\frac{t}{T_{2}}} \]

The FID is obtained by using a simple \( \frac{\pi}{2} \) pulse directed along the x-axis to tip the magnetization into the y-axis so it is processing in the x-y plane. The magnetization in the x-y plane is detected over time as the different frequency components process at different rates. This will result in the FID so \( T_{2M} \) can be found.

\textbf{T}_{1} \textit{Studies}

A second method of observing the magnetization exchange between bulk solvent and the metal is by studying the \( T_{1} \) relaxation. This method is completed by observing the intensity of one site’s signal, while the other signal is saturated by the applied radio frequency pulse program. As the saturated site’s spin is transferred to the second exchange site, the second site’s magnetization intensity increases as result of the additional spin, while the saturated site’s magnetization decreases. From the Bloch equations, the relaxation of magnetization in the z-axis is proportional to \( \frac{1}{T_{1M}} \). Studying the \( T_{2} \) relaxation tracks the magnetization change between the metal and bulk site through an inversion-recovery NMR experiment. This experiment is done using a two-pulse pulse sequence. A \( 180^\circ \) shape pulse with a radio frequency close to the bulk solvent’s Larmor frequency is directed at the sample. Since a shape pulse is a selective pulse, it will only flip the magnetization of the bulk solvent. The solvent’s magnetization, having been flipped 180 degrees, will be aligned opposed to the applied magnetic field. Once probed, the magnetization will begin to relax along the z-axis until it reaches it equilibrium position. After some time (t), a \( 90^\circ \) square pulse is applied. A square pulse is not selective and excites a broader range of frequencies, resulting in both the metal and solvent magnetizations to be tipped into the x-y plane to be detected. At time zero, the magnetization signal for the solvent will be large and negative because it will tipped into the x-y plane in the negative direction.

\[ \text{Metal site magnetization} \]
\[ \text{Bulk solvent site magnetization} \]

\[ \text{Initial} \quad \text{After 180 pulse} \quad \text{After 90 pulse} \]

\textbf{Figure 2: Magnetization as a result of the pulse program}
The bulk solvent magnetization is tipped to be against the static magnetic field, while the metal site magnetization remains inline with the static magnetic field. Then the short 90° pulse is applied to tip both site's magnetizations into the x-y plane for detection. The bulk solvent magnetization will result in a negative signal, and the metal site magnetization will be positive.

As exchange occurs, the magnetization along the z-axis will become positive because of natural relaxation, and because the $^{17}$O from the metal will be positively in the z-direction, helping speed up the relaxation. This can be tracked by varying the time between the $180^\circ$ and $90^\circ$ pulse, since the direction (positive or negative) and intensity of the peaks will change.

Equation 12:

$$M_z(t) = M_o(1-e^{\frac{t}{T_1}})$$

Figure 3: Magnetization along z-axis

The magnetization of the bulk water site, directed against the static magnetic field, will begin to relax back towards the initial condition (all magnetization direct with the static magnetic field). The relaxation will cause the bulk water site's negative signal to decrease in size and then become positive as the oxygen on the metal site exchange.

The above image shows that at t=0 the solvent peak is large and negative, since no magnetization will have had time to relax. Between t=1 and t=2, the magnetization along the z-axis has inverted back, and will produce a positive peak.

The exponential line from the first negative peak to the last positive peak results in Equation 12.

Equation 12:

$$|M_z(t)| = M_o(1-e^{\frac{t}{T_1}})$$

Figure 4: $T_1$ equation representation

As the magnetization relaxes along the z-axis, it relaxes exponentially with Equation 12.
\( T_{\text{1}} \) can then be used to calculate the exchange rate through the Bloch-McConnell equations. A plot of the intensity of magnetization as a function of time would look like:

Figure 5: Plot of intensity versus time for the bulk solvent site magnetization

These are just two pulse sequences that can be used to study kinetics through NMR. More intricate pulse sequences can be used to perform kinetic studies on more complex systems.

**NMR Kinetic Studies**

NMR studies have been carried out to understand the kinetics water exchange with different compounds as a function of temperature and pressure. There also have been experiments that track the affects of pH on the exchange rates of chemical systems. Below is a list of some journal articles containing dynamic NMR experiments with \(^{17}\text{O}\). A quick search on DNMR experiments will produce many journal articles that have been published over the years.


References


Outside Links


Problems

1. Describe the difference between the $T_1$ and $T_2$ relaxation.
2. Why are the Bloch-McConnell equations needed for kinetic NMR studies?
3. Describe what would happen in an inversion-recovery experiment if the signals from the solvent and metal site occur at similar frequencies?
4. What problems can arise from using the Swift-Connick equation and the bandshape technique?
5. Draw the pulse sequence of the inversion-recovery experiment. (A schematic of the frequency versus time)

Solutions

1. The $T_1$ relaxation is relaxation of the magnetization in the z-axis and is known as longitudinal relaxation. The $T_2$ relaxation is relaxation in the x and y axis, or xy plane. It is known as transverse relaxation.
2. The Bloch-McConnell equations are the extension to the Bloch equation. They include an extra term that takes into account exchange between two species. Without this relationship, kinetic studies would not be able to be studied using NMR.
3. If the signals are too close together, the 180 degree shape pulse would flip both magnetizations, not separating the two to allow for analysis. More intricate pulse sequences can be used with more pulses to obtain the magnetizations in opposite directions along the xy plane.
4. NMR signals are often small since its a very insensitive technique. Peaks can not only be easily lost in the noise, but the bandwidth may be extremely difficult to determine, making the Swift-Connick equation hard to use.
5. Pulse sequence drawing for the inversion-recovery experiment
Contributors

- Adele Panasci