NMR Spectrometer Experiment

This experiment deals with liquid-phase proton nuclear magnetic resonance of organic molecules. For most students in Physics 4430 and 5430, it should be done after the Pulsed NMR Experiment, which is based on the 20 MHz TeachSpin PS1-A. That experiment covers magnetic resonance of *independent* nuclear spins, a subject that can be understood with the classical Bloch equation. The equipment nicely exposes the inner workings of pulsed NMR. This experiment uses a higher resolution spectrometer (the picoSpin/Thermo Scientific pS-45) operating at 45 MHz. Because of the higher resolution, you can explore the quantum mechanics of *interacting* nuclear spins, and learn why NMR is such a powerful analytical technique. However, the picoSpin is more of a "closed box" than the PS1-A, so you will understand what is going on better if you do the Pulsed NMR Experiment first. We also have the Earth's Field NMR Experiment, but it is not necessary to do that before either of these.

In the notes below, we will assume that you are already familiar with the basic ideas of pulsed NMR, including Larmor precession, 90° RF pulses, and the free-induction-decay. If you are doing this experiment without that background, you should first read Chapters 1–3 in Ref. 1.

1. Density Operator

Most introductory quantum mechanics courses only discuss exactly known or "pure" quantum states. However, in quantum statistical mechanics we have to consider averages over ensembles that may contain many different pure states. The density operator is a description of a quantum system that allows us to do this in a convenient way. It is widely used in condensed matter physics, quantum optics, molecular physics, and quantum information. It also plays a crucial role in the theory of quantum measurements.

Consider a pure state specified by the ket $|\psi\rangle$. The expectation value of an observable $\boldsymbol{O}$ in this state is $\langle \boldsymbol{O} \rangle = \langle \psi | \boldsymbol{O} | \psi \rangle$. A completely equivalent way to represent the state is in terms of its projection operator

$$\boldsymbol{\mathcal{P}} = |\psi\rangle\langle\psi|.$$

Using the projection operator, we can write the expectation value of $\boldsymbol{O}$ as

$$\langle \boldsymbol{O} \rangle = tr(\boldsymbol{O}\boldsymbol{\mathcal{P}}),$$

where *tr* stands for trace. This means we represent the operator $\boldsymbol{O}\boldsymbol{\mathcal{P}}$ as a matrix in some complete and orthonormal basis $|i\rangle$ and then sum the diagonal elements. We can show that doing this is equivalent to computing the usual expectation value:

$$\langle O \rangle = tr(O\mathcal{P}) = \sum_i \langle i|O|\psi\rangle\langle\psi|i\rangle = \sum_i \langle\psi|i\rangle\langle i|O|\psi\rangle = \langle\psi|O|\psi\rangle.$$

Suppose we have an ensemble containing many different states $|\psi_j\rangle$, each appearing with probability p_j. The density operator is defined as the average projection operator:

$$\rho \equiv \sum_j p_j \, |\psi_j\rangle\langle\psi_j|. \tag{1}$$

If we compute the trace of the operator product $O\rho$ we get the quantum expectation value averaged over the ensemble:

$$\langle O \rangle = tr(O\rho) = \sum_j p_j \langle\psi_j|O|\psi_j\rangle. \tag{2}$$

Thus, the density operator gives us a way to express the quantum aspects of an expectation value that include coherence and interference effects, and the ordinary averaging associated with any statistical ensemble.

To describe an NMR experiment, we need to know how the density operator evolves in time. For a time-independent Hamiltonian, we know that the Schrodinger equation causes pure states to evolve as

$$|\psi(t)\rangle = e^{-iHt/\hbar}|\psi(0)\rangle.$$

Substituting this into Eqn. 1 implies

$$\rho(t) = e^{-iHt/\hbar}\rho(0)e^{+iHt/\hbar}. \tag{3}$$

This looks like the motion of an operator in Heisenberg representation, but it is not. We are still in the Schrodinger representation where states evolve in time and operators (other than the density operator) are time-independent.

2. Equilibrium State

In our NMR experiments the spin system will start in a thermal equilibrium state. Suppose the system Hamiltonian is H with exact energies and eigenstates E_j and $|j\rangle$. According to Boltzmann, the probabilities p_j to find the system in these states in thermal equilibrium will be proportional to

$$p_j \propto e^{-E_j/kT}.$$

Therefore, from Eqn. 1 above, the equilibrium density operator is

$$\rho_{eq} \propto \sum_j e^{-E_j/kT} |j\rangle\langle j| = \sum_j e^{-H/kT} |j\rangle\langle j| = e^{-H/kT}. \tag{4}$$

3. Spin Hamiltonian

In NMR spectroscopy the nuclear spins are placed in a strong and highly-uniform magnetic field B_0, conventionally oriented in the $\hat{z}$ direction. We will consider only NMR of spin-1/2 protons, the nucleus of the hydrogen atom. The Hamiltonian is a sum of two parts, one describing the Zeeman interaction of the spins with the applied field, and the other describing interactions between the spins. The Zeeman term for N spins can be written as:

$$H_Z = \sum_{i=1}^{N} (-\omega_0 + \omega_i) S_i^z. \tag{5}$$

This is just the energy of N spin-1/2 magnetic moments in an applied magnetic field. The subscript i on the spin operators S_i^z labels which spin they act on. The spin Larmor precession frequency ω_0 is

$$\omega_0 = \gamma B_0,$$

where the gyromagnetic ratio for protons is $\gamma = 2\pi \cdot 42.58\,\text{MHz/T}$. In our experiments, the magnetic field strength B_0 will be 1.06 T, giving a Larmor frequency of $\omega_0/2\pi = 45$ MHz. The Hamiltonian is expressed in angular frequency units. To convert to Joules, multiply it by $\hbar$, or to convert to Hz, divide by 2π.

We include in the Zeeman Hamiltonian a small frequency offset ω_i which can be different for each spin. This is called the "chemical shift," and it is due to diamagnetic screening of the applied field by the electrons surrounding the nucleus. Its value is usually expressed in parts-per-million (ppm) of the Larmor frequency. For protons in non-magnetic organic molecules (that is, without any electronic magnetism) chemical shifts are usually in the range 0–12 ppm. The resolution of the picoSpin spectrometer is about 50 ppb (parts-per-billion), or about 1 Hz, so this effect can be seen easily.

The equilibrium state can be determined to sufficient accuracy by considering only the largest term in the Hamiltonian, which is the first term in Eqn. 5. At room temperature we have

$$\hbar\omega_0/kT \approx 10^{-5}$$

so we can approximate the exponential in the equilibrium density matrix Eqn. 4 by the first two terms of its Taylor series

$$\rho_{eq} \propto e^{-\frac{H}{kT}} \approx \mathbb{I} - \frac{H}{kT} \approx \mathbb{I} + \frac{\hbar\omega_0}{kT}\sum_{i=1}^{N} S_i^z,$$

where $\mathbb{I}$ is the unit operator. The unit operator will not contribute to the expectation value for the observables we are interested in, and we do not care about overall normalization, so for our purposes we can simply use

$$\rho_{eq} = \sum_{i=1}^{N} S_i^z = M^z, \tag{6}$$

where M^z is the z-component of the magnetization operator, equal to the sum of the single-spin operators S_i^z.

The full Hamiltonian for liquid-phase NMR, including interactions between the spins, is best written in a frame of reference that rotates around the z-axis at the Larmor frequency ω_0. (If you are familiar with interaction representations in quantum mechanics, this corresponds to the interaction representation with respect to the first term in Eqn. 5 above.) The complete spin Hamiltonian is

$$H = \sum_{i=1}^{N} \omega_i S_i^z + \sum_{i>k} J_{ik} \vec{S}_i \cdot \vec{S}_k. \tag{7}$$

In the rotating frame, the term proportional to the Larmor frequency ω_0 does not appear, because the frame itself is already rotating at the Larmor frequency. The chemical shifts ω_i do appear, and they cause slow precession of spins at frequencies up to a few hundred Hz relative to the rotating frame. The interaction term is a double sum over all spins of the dot product of the spin operators for each spin pair. It is restricted to $i > k$ so that pairs are not double counted. It is called the scalar interaction, *J*-coupling, or indirect hyperfine interaction, and is due to slight polarization of the electrons by one spin, which then creates a small magnetic field at another nearby spin. The coupling constants J_{ik} can have either sign and their magnitude is usually in the range $J_{ik}/2\pi = 0$ - 20 Hz. The J_{ik} do not depend on the strength of the applied field, while the frequencies ω_i are proportional to the field strength. We express chemical shifts in ppm so their values will not depend on field strength.

The two terms in the spin Hamiltonian represent powerful analytical information about the spin system. Briefly, the chemical shift allows one to identify the chemical groups present in the molecule, while the *J*-coupling reveals the connectivity of the molecule. Together, these two effects make liquid-phase NMR the most important analytical tool in organic chemistry.

A full justification of Eqn. 7 requires a longer story than we want to give here. For a molecule fixed in space, the chemical shift screening has to be described by a tensor, and the indirect hyperfine interaction is also a tensor interaction. Fast tumbling of molecules in liquids averages the anisotropies away, and also averages away direct magnetic dipole interactions between the proton spins. Eqn. 7 is a time-independent Hamiltonian, but the rotating frame transformation creates some interaction terms that oscillate at the Larmor frequency. These can be neglected according to a "secular approximation." Our result for the equilibrium density matrix Eqn. 6 is unchanged in the rotating frame. See Refs. 2 and 3 for more details.

4. Spin Simulations

At the beginning of a pulsed NMR experiment, we disturb the equilibrium state M^z by applying a 90° RF magnetic field pulse. If the pulse duration and frequency are correct, the magnetization will tip into the x-y plane, and we can suppose that it is initially equal to M^x in the rotating frame.

(The rotating frame frequency is conventionally set equal to the transmitter frequency, which must be tuned close to the proton Larmor frequency. The rotating frame phase, or equivalently, the RF pulse phase, determines how the initial magnetization is oriented in the x-y plane. This phase can be adjusted when the data is collected, or later during analysis.) The density matrix will then evolve according to

$$\boldsymbol{\rho}(t) = e^{-iHt} \boldsymbol{M}^x e^{+iHt}, \tag{8}$$

where $\boldsymbol{H}$ is given by Eqn. 7. A coil with its axis in the x-y plane detects the precessing transverse magnetization by Faraday induction. The signal is amplified, digitized, and then frequency-translated by mixers and low-pass filters. The net result is that the instrument records the free-induction-decay, or FID, a complex time-series who's real and imaginary parts are proportional to the x- and y-components of the magnetization in the rotating frame. Our observable is thus $\boldsymbol{M}^x + i\boldsymbol{M}^y$, and the free-induction-decay $F(t)$ is computed from the density matrix using

$$F(t) = tr\big((\boldsymbol{M}^x + i\boldsymbol{M}^y)\boldsymbol{\rho}(t)\big). \tag{9}$$

The FID can be examined directly, but it is more informative to look at the NMR spectrum, which is the Fourier-transform of the FID.

Equations 7, 8 and 9 express our theory for liquid-phase NMR spectroscopy of spin-1/2 nuclei. We have only included unitary evolution (Eqn. 8), so the oscillations in the FID will not decay away over time as they will in experiments. This can be corrected by including and averaging over "environmental" degrees-of freedom, such as molecular motions and other spins. Instead of doing this, we can simulate the effects of relaxation simply by multiplying the predicted FID by an decaying exponential function. With this adjustment, our theory gives a very good account of most proton NMR spectra.

Many features of NMR spectra can be understood through analytical calculations, but, because this is a laboratory course and we want to focus on experiments, we will rely on numerical analysis of Eqns. 7, 8 and 9. We provide the MATLAB program **liquid_NMR.m**, a simple NMR spectrum simulator. The code is brief and heavily commented. You should be able to understand exactly how it works. A Mathematica version is also available, but MATLAB is a better choice for problems like this that do not involve symbolic manipulation.

5. Theory Exercises

1. Derive Eqn. 2 from Eqn. 1. Make every step as explicit as possible.

2. Justify every step needed to get from the left side of Eqn. 4 to the right side.

3. To construct matrix representations of spin operators such as $\boldsymbol{S}_i^x$ for a multi-spin system, we use matrix direct products (also called Kronecker products). This is best explained by example.

Suppose we have a two-spin system and we want to represent S_2^x, which acts on the second spin. This is given by the matrix direct product

$$\mathbb{I} \otimes S^x,$$

where $\mathbb{I}$ is the 2x2 unit operator and the spin matrices are

$$S^z = \frac{1}{2}\begin{pmatrix} 1 & 0 \\ 0 & -1 \end{pmatrix}, \quad S^x = \frac{1}{2}\begin{pmatrix} 0 & 1 \\ 1 & 0 \end{pmatrix}, \quad S^y = \frac{1}{2}\begin{pmatrix} 0 & -i \\ i & 0 \end{pmatrix} \tag{10}$$

To form the direct product, write the first matrix and then place the second matrix at each element of the first matrix, multiplied by the first matrix element:

$$\mathbb{I} \otimes S^x = \begin{pmatrix} 1 & 0 \\ 0 & 1 \end{pmatrix} \otimes \begin{pmatrix} 0 & 1/2 \\ 1/2 & 0 \end{pmatrix} = \begin{pmatrix} 1\begin{pmatrix} 0 & 1/2 \\ 1/2 & 0 \end{pmatrix} & 0\begin{pmatrix} 0 & 1/2 \\ 1/2 & 0 \end{pmatrix} \\ 0\begin{pmatrix} 0 & 1/2 \\ 1/2 & 0 \end{pmatrix} & 1\begin{pmatrix} 0 & 1/2 \\ 1/2 & 0 \end{pmatrix} \end{pmatrix} = \begin{pmatrix} 0 & 1/2 & 0 & 0 \\ 1/2 & 0 & 0 & 0 \\ 0 & 0 & 0 & 1/2 \\ 0 & 0 & 1/2 & 0 \end{pmatrix}$$

a) Write the matrix $S^y \otimes \mathbb{I}$. To check your result, read the comments in **liquid_NMR.m** and set it up for a two-spin system (with any values of the chemical shifts and J-coupling). Then run it. (Set your current directory to the folder containing the **liquid_NMR.m** file and type 'liquid_NMR' at the command prompt.) Now use the MATLAB workspace browser to examine Sy{1}, which is the program's notation for the matrix $S^y \otimes \mathbb{I}$ that represents the operator S_1^y. (The same quantity in the Mathematica version is Sy[[1]].)

b) Write the matrix $\mathbb{I} \otimes S^x \otimes \mathbb{I}$. Start at the left and first form the 4x4 direct product $\mathbb{I} \otimes S^x$, then form the direct product of the result with $\mathbb{I}$ to get an 8x8 matrix. Set **liquid_NMR.m** up for a three-spin system, run it, and check your result. (If you need to clear the workspace, type 'clear all' at the command prompt.)

c) So far, we have only considered matrices that operate on one spin at a time. Construct the 4x4 matrix $S^x \otimes S^x$ for a two-spin system. To do it the way the program does it, construct the matrices $S^x \otimes \mathbb{I}$ and $\mathbb{I} \otimes S^x$, and then matrix-multiply them together. To check your result, set **liquid_NMR.m** up for a two-spin system, run it, and then type 'test= Sx{1}* Sx{2}' at the command prompt and examine the variable 'test' in the workspace browser. You can get the same result by forming the matrix direct product of S^x with S^x. Type 'test=kron(sigma_x,sigma_x)' to do it this way using MATLAB's Kronecker product function. (In Mathematica use: MatrixForm[Sx[[1]].Sx[[2]]] and MatrixForm[KroneckerProduct[sigmaX,sigmaX]]).

Look closely at the lines in **liquid_NMR.m** where the spin matrices are built, and see if you can understand what is happening. Look at the lines where the Hamiltonian is built to see how the interaction operator $\vec{S}_i \cdot \vec{S}_k$ is formed for each pair of spins. Can you see how Eqns. 8 and 9 are implemented in the code?

4. Two-spin spectrum. Set **liquid_NMR.m** up for a two-spin system. Set the chemical shift of the first spin to 1.0 ppm and the second spin to 5.0 ppm. (This corresponds to 45 Hz and 225 Hz at a

45 MHz Larmor frequency.) Set the J-coupling to zero and leave all other parameters at their default values. Run the program and examine the FID and the spectrum. You should see two single lines ("singlets"), one at 1.0 ppm and one at 5.0 ppm. This is the spectrum of two independent spins precessing at slightly different frequencies. Now set the *J*-coupling to 10 Hz and run the program. You should see two doublets. How is the doublet splitting in Hz related to the J-coupling? Set the J-coupling to 300 Hz and run again. Things are more complicated now—the two middle lines are close together and much stronger than the two outer lines. It is a general rule in NMR that simple, well-separated, multiplets appear when the J-coupling is much smaller than the chemical shift difference, but not otherwise.

6. Experiment

1. Work through the picoSpin-45 Installation and Setup document (see Ref. 4 below). You can probably skip the first three pages if the instrument is already setup and connected to a computer.

Turn the instrument on as soon as you get to the lab and then leave it on. The magnet is temperature controlled for field stability and it takes about 20 minutes to reach equilibrium. Read and understand the precautions about injecting samples. Your samples should be clean, clear, low-viscosity liquids. The cartridge contains an 0.4 mm ID capillary that can be clogged by a dirty sample. Always use a filter when injecting samples, and use only gentle pressure.

Inject a water sample, and follow the instructions for finding the signal and shimming the magnet. You will want to shim the magnet every time you use the spectrometer. Otherwise your spectral lines will be broad and you will not be able to extract much information from them.

Once you have shimmed the system, inject a sample of ethyl acetate and make a spectrum, following the instructions. Your results should look similar to Figure 19.

The last part of the document talks about the NMR data analysis program MNova. We have a site license for it. It is not strictly necessary to use MNova for this experiment. You could instead capture your data by making a screenshot of the display, similar to the one shown in Figure 19. However, MNova has many useful features, including phasing, apodization (filtering), measurement cursors, and integration. You should definitely work with it if you are planning to do a project on NMR for the course.

2. Read the nice Wikipedia article about ethyl acetate. For a general Hamiltonian, a spin system with N spins-1/2 can have up to $N2^{N-1}$ spectral lines, or 1024 lines for 8 protons. That would be a very complex spectrum! However, you can see that the spectrum of ethyl acetate is actually quite simple, consisting of one triplet, one singlet, and one quartet. Why? As always in quantum mechanics, it has to do with symmetries, in this case permutation and reflection symmetries.

The two CH_3 groups in the molecule both rotate rapidly about the C-C bond direction. Because of this, each CH_3 group is a set of three "equivalent spins," spins that have equal chemical shifts and equal J-couplings to all other spins. The two protons in the CH_2 are also equivalent, because their positions are related by a reflection plane. Thus there are only three distinct chemical shifts, one for each CH_3 group and one for the CH_2 group. There is only one significant J-coupling, that between each of the CH_2 protons and each proton in the adjacent CH_3 group. The other CH_3 group is too far away from other spins to have any J-couplings that are significant, so it evolves independently of the other spins. You might think there should be J-couplings within a group of equivalent spins. There are, but such couplings do not have any effect on the spectrum.

When two sets of equivalent spins are coupled, and the J-coupling between them is small compared to the chemical shift difference, the multiplicities are given by the "N+1 rule." This states that the multiplicity of a given group will be equal to one more than the number of spins in the group is it coupled to. In ethyl acetate, this implies that the CH_2 group appears as a quartet, since it is coupled to three equivalent spins, and the adjacent CH_3 appears at a triplet, since it is coupled to two equivalent spins. The singlet in the spectrum is due to the other CH_3, which is not coupled to anything.

With this background, see if you can use **liquid_NMR.m** to construct a spin Hamiltonian for ethyl acetate that gives a good description of the spectrum. What values do you get for the J-coupling and the chemical shifts? If your computer is too slow to do eight spins, omit the uncoupled CH_3 group. (Only the chemical shift differences are significant. Absolute chemical shifts must be measured relative to a standard mixed into the sample. Tetramethysilane is usually used for proton NMR.)

If you search on the internet, you will be able to find proton NMR spectra for ethyl acetate and many other molecules. Usually they won't be at the same Larmor frequency as you have. However, the J-couplings expressed in Hz and the chemical shift (differences) expressed in ppm will still be the same. In **liquid_NMR.m** you can simulate spectra for a spectrometer with any Larmor frequency.

Chemists use proton NMR (and NMR of other nuclei) to analyze unknowns, of course. To get some appreciation for the enormous knowledge-base in this area, see Ref. 5.

7. Project Ideas

1. Mixtures of ethanol and water. The OH proton is "labile," meaning it moves back and forth from ethanol to water. Study how the spectrum changes versus water concentration. Can you see both the "fast exchange" and "slow exchange" limits? Can you measure the exchange rate? See this link: http://www.facstaff.bucknell.edu/drovnyak/Ethanol-Water_Exp.pdf

2. There are many examples of projects posted as application notes on the web sites of NMR vendors. Besides Ref. 4, see web sites of Anasazi Instruments, Nanalysis and Magritek.

3. Can you observe satellite peaks due to carbon-13? See examples in Ref. 4 below.

4. Spectra of simple unknowns. Commercial nail polish remover is usually a mixture of simple solvents such as water, acetone, isopropanol, ethanol, ethyl acetate and xylene.

5. NMR sample thermometry. See the application note in Ref. 4.

8. References

1. Josef P. Hornak. "The Basics of NMR," https://www.cis.rit.edu/htbooks/nmr/

2. Malcolm H. Levitt, "Spin Dynamics," Wiley (2007).

3. Lecture notes and YouTube lectures by Ilya Kuprov, http://spindynamics.org

4. Start at this link for documentation on the picoSpin-45 spectrometer: http://www.thermoscientific.com/en/products/nuclear-magnetic-resonance-nmr.html For basic operation click on "Operations and Maintenance" and then "Installation and Setup" and "User Guide". Click on "NMR Spectral Library" for example spectra, and see also the links under "NMR applications" and "Teach NMR".

5. Hans Reich's Chem 605 web site at the Univ. of Wisconsin: http://www.chem.wisc.edu/areas/reich/chem605/