Spin Dynamics Meta Review PhL 1.16.08

Appendices are reviewed separately from the main body text at the end of this document.

********** Part 1: Nuclear Magnetism **********

----------Chapter 1: Matter (5) ---------- 18 p---------- ###

Nuclear spins provide a **probe point**. **Angular momentum**: quantized rotating dumbbell has $L = \sqrt{j(j+1)}$, spin is same idea but no macro world analog, **combining J's** and hence spins, **Pauli Principle**.

Statement that most nuclei have spins, **table page 14** shows spin value, γ from $\boxed{\boldsymbol{\mu} = \gamma \mathbf{S}}$, abundance and Larmor frequency at 11.74T where ^{1}H is 500 MHz. Spin values are 1/2, 1, 3/2, 5/2 and 3. Some **rules** for how to "compute" what a nucleus's ground state spin value is. Passing mention of atomic physics and L and S, then mention of molecular physics for diatomic molecules and a few others. Notion of **isotopomers** vs isotopes vs isomers.

Discussion of **gases, liquids and solids** and how they differ and are defined. Xenon, liquid crystal and its director, shear force response, volume filling.

---------- Chapter 2: Magnetism (23) ---------- 20 p ------ ###

Can induce as in $\mathbf{M} = \chi \mathbf{B}$. Nuclear spins are para/ferromagnetic situation so $\chi > 0$. *But*, $\boldsymbol{\mu} = \gamma \mathbf{S}$ and γ can have either sign. Spins in B that are not purely up or down will precess at Larmor frequency $\omega = -\gamma B$ where the – is because γ>0 gives CW or anti-RHR rotation. Comment that as you turn on a B, spins do Larmor, but relaxation processes T_1 cause them to move toward the purely aligned state, meaning the Larmor cone narrows over time. Otherwise could not polarize anything. If you flip spins z to y, then T_2 is the dephasing relaxation time constant. Picture of the NMR **pickup coil** aligned along x which sees the M_x until if fades with T_2, so the "NMR signal" is thus introduced, also known as the **Free Induction Decay** or **FID**. Mention of **chemical shift idea** as a modification of the local B by local molecule details.

---------- Chapter 3: NMR Spectroscopy (43) ---------- 28 p --------- ###

The simple FID decaying sinusoid produces, via FT, the **Lorentzian line shape** centered at the Larmor freq which recall is $\omega = -\gamma B$ and can have either sign. **Width is $1/(\pi T_2)$.** The game of NMR is in the height and location of all the Lorentzian peaks! Only the absorption peak is mentioned at this point.

Example: **TMS** has three spin types -- ^{1}H, ^{13}C and ^{29}Si -- averaged over isotopomers, so has a 3 line spectrum, two at ω<0, one at ω>0 (Si). Line widths are super narrow, about 50 milliHz. Big H line used as reference.

Notion of the relative frequency $\boxed{\Omega = \omega - \omega_{ref}}$ where ω_{ref} is what the NMR RF pulse runs at and which is close to lines (Larmors) of interest. Comment that, for γ<0 work, the Ω axis is conventionally pointed to the left. Notion of a channel as a small window around a peak.

If you add a **B field gradient**, line gets broadened. With a linear z gradient, line shape traces object outline, making a simple **1D MRI function**. Each axial slice through the sample has a different Larmor.

Example: Ethanol spectrum p60, both peaks are ^{13}C but *chemically shifted* apart, two isotopomers called II and III. Notion of dimensionless δ referenced to the TMS line. P62 has table showing δ for various situations.

The ethanol fine ***multiplet*** **structure** is determined by nuclear spin combinations of directly connect H atoms, so CH_2 gives the 1:2:1 while CH_3 gives 1:3:3:1. Just count the ways, binomial ratios. For liquid **these are J-couplings** and are in this case $^1J_{CH}$. In this example, two H's on CH_2 don't split each other due to mag equiv, later. Also, OH does nothing due to hopping around. Ultra fine ^3J splittings can also be extracted from spectrum. You can wash out the multiplets by doing "**RF blasting"** (hetero-nuclear de-coupling) to get cleaner spectra if you don't care about the multiplets.

********** Part 2: The NMR Experiment **********

---------- Chapter 4: The NMR spectrometer (71) ---------- 18 p ------ ###

This short chapter describes the parts of an actual NMR spectrometer. Need liquid N and He to run the magnet which could be up to 21 T, corresponding to Larmor $\gamma_H B \sim 900$ MHz. **Shims** provide super uniform B field over the sample (you could auto-adjust them using TMS as sample). Same coil used for transmit and receive, duplexer switch, tuning capacitors. Receiver is a quadrature design described in an appendix to put out Re and Im part signals to the digital electronics package. Need frequency synthesizer, analog phase shifter ϕ_{rec}, pulse & gap timing controls, digital phase shifter ϕ_{dig}, digital FFTs, displays, printer. Block diagram on page 85. Much later we learn how the two phase shifts are used in experiments.

NMR is hard to do for many reasons: nuclear moments are tiny, room temperature washes out most spin action, there is noise, need frequency high precision, magnet is messy and expensive.

---------- Chapter 5: The Fourier Transform in NMR (89) -------- 38 p ------- ###

To remove **noise**, we have to average (or add) lots of "shots" as shown in the p 93 figure. A single "shot" might contain several RF pulses, and **phase cycling** gets its first mention here, used to select/reject desired signals and to reduce systemic errors. A "blasting" example is given p96.

The idea of an **"arrayed experiment**". P 96 bottom shows t_1 and t_2 variables in the pulse sequence, the last just being the FID variable. This allows a **2D Fourier spectrum**; we see examples later in the book of such "experiments". Page 98 shows a very fancy multi-nuclei pulse orchestra score taken from an NMR journal article.

We shall later see that the general form of the **FID is $a_\ell \exp[(i\Omega_\ell - \lambda_\ell)t]$ for each spin**, which is of course complex so has a Re and Im part, examples of which appear p 99. Then p 100 shows how you can tell "not much" by looking at the time domain signal for multiple peaks, but the spectrum is useful. P 102 has details on the Re and Im parts of the Lorentzian, called A and D for absorption and dispersion. Note that D has "long tails".

We skip the FT-revealed section.

Frequency-dependent system errors and their fixes are shown top p 110.

We then start into the 2D FT. The FT is the product of the 1D FT's so looks like $(A_1 + iD_1)(A_2 + iD_2)$. However, the Re and Im parts of this are messy, Re p 113, Im p 114, both have "long tails" due to admixing of the D part. We then have a long discussion of the **"States Method**" which produces Re = A_1A_2 and so gives clean isolated peaks as shown on page 118. However, at this point it is very unobvious to the reader how to create the separate "cos and sin" terms needed to make States work. In other words, here we are just "doing the math" to get it into the record.

The 3D FT gets passing mention.

********** Part 3: Nuclear Spin Interactions **********

---------- **Chapter 6: Review of Quantum Mechanics (127) ---------- 40p --------- ###**

A very nice and broad review of QM with which I am very familiar. There are a few sections that are very important and that I find myself referring to over and over again, so I will comment on them.

P 143 shows a nice generic **"angular momentum like"** cyclic set of operators A,B,C with the main sandwich rotation result shown top of p 144. In the commutation relations, we have $\hbar = 1$.This is useful, because we need to stick lots of different things in for A,B,C later in the book. The simple pictures let you see exactly what the sandwich rotation does. For true rotations, the reason for this is obvious -- the sandwich really is rotating the operator, and this notion carries over to any A,B,C.

The SE appears on page 146. Then p 153 shows the three Lie rotations and the generators are called **I. Sandwich idea on page 154** shows how to do Euler-like rotation combinations. The pictures let you understand the effect of a series of rotations on a rigid object.

The **shift operator** equations appear on p 158, inversions on page 159.

Finally on page 163 we specialize to spin-1/2 and on **p 164 are the Pauli matrices** converted to I matrices as used in this book. Right below are the 2D representations of all three rotations. Page 165 gives the projection operators as matrices and in ket-bra usual notation. He does not here state combined rotation matrices.

---------- **Chapter 7: The Nuclear Spin Hamiltonian (170) -------- 52 p ---------- ###**

This is a monstrous chapter of stuff all new to me, so notes here will be a longer than above.

We are going here to talk about ALL of the significant **"interaction Hamiltonians"** a nuclear spin can have with other things in a molecule or with other molecules (electron clouds and other spins) or with externally applied B fields like B_0 or B_{RF}. For each interaction, we write a Hamiltonian then try to simplify it for motional averaging, or secular approximation, or both. Results are usually much simpler for an isotropic liquid than for other matter types. These Hamiltonians are the basis which allows you to compute what you expect to see in an NMR spectrum; then, when you do your experiment, you perhaps can learn the value of certain sample parameters. Without a **model**, the spectrum would be meaningless.

The chapter starts with a discussion of the **multipole moments** expansion of the *electric* charge and potential of the nucleus. Our first conclusion is that the nuclear ground state has a definite **parity**, and this means that the ground state cannot have any non-zero matrix element for an ℓ=odd tensor operator, so this means that $\rho_{\ell m} = 0$ for $\ell = 1,3,5...$ just because of parity. Hence, no electric dipole moment, for example. Here is a proof for ℓ=1: $\langle g|\mathbf{p}|g\rangle = p_g^2 \langle g|PpP^{-1}|g\rangle = 1 \langle g|-\mathbf{p}|g\rangle$ hence $\langle g|\mathbf{p}|g\rangle = 0$.

Our second conclusion is that, if the nuclear ground state has spin I, then those same matrix elements also vanish for any tensor operator with $\ell > 2I$, and this is trivial from Wigner-Eckart. A corollary to this second conclusion is that if I=1/2, then $\rho_{\ell m} = 0$ for $\ell = 2,3,4...$ But we already know $\rho_{\ell m} = 0$ for $\ell = 1$, so the only existing term in the electric multiple charge expansion is $\rho_{\ell m}$ for $\ell = 0$ for spin-1/2, so such a nucleus looks like a **simple point electric charge**. For I > 1/2 there can be (and is) an ℓ=2 quadrupole moment of the charge distribution ρ_{2m} and this interacts with potential moment Φ_{2m} which arises from an electric field if it has some gradient. This electric field could come from the electron cloud distribution and is then evaluated at $\mathbf{r} = 0$. Or it could come from an external source.

So the only electric Hamiltonian we will ever worry about is the lowest one (**quadrupole**) when nucleus has $I \geq 1$, and then $H' = \Sigma_m \int r^2 dr \ \rho_{2m}(r) \Phi_{2m}(r)$.

Everything else in this chapter will be magnetic stuff (except where it comes back to the electric quadrupole again). Because $\mathbf{P m P^{-1}} = +\mathbf{m}$ for the (pseudovector) magnetic dipole moment (and all other mag moments I suspect), the argument used above fails and you *can* have $\langle \mathbf{m} \rangle \neq 0$ for a nucleus, as we well know. And we know that $\boxed{H' = -\boldsymbol{\mu}\bullet\mathbf{B} = -\gamma \mathbf{I}\bullet\mathbf{B} = -\gamma I_z B}$ in our usual situation.

Page 179 shows B_{RF} where we make the rotating wave approximation (**RWA**) and replace B_x with a rotating B field (near resonance). But often later in the book we really do use just the I_x-only form.

Next, we classify the various **kinds of spin interactions**: chemical shift, quadrupole electric, direct dipole-dipole ("through-space"), J-couplings (indirect dipole-dipole), and spin-rotation.

Methods of doing motional **averaging** are described next: **rotations**, translation of **flow** and **diffusion** type, notion of a **diffusion sphere** (limited by NMR pulse sequence duration). Then we have the **inter** (**long** and **short** range) versus **intra** molecular distinction for interactions. Then we have to think about **gas** versus **liquid** versus **solid**. We get little charts showing which things vanish in which cases. The rest of the chapter then looks at each type of interaction in more detail.

(1) **Chemical Shift**. In general $\mathbf{B_{induced}} = \boldsymbol{\delta}\bullet\mathbf{B_0}$ (most general linear form) where δ is a 3x3 matrix like strain, so $\mathbf{B_{ind}}$ has three terms for B_z. Keep only the $\delta_{zz}(\theta)$ term if doing secular since H' has I_z, where θ is "angle" of molecule. Then do isotropic average to get δ^{iso}. Arm wave explains the result of this average, I found a better way. In any event, the shifted Larmor is $\boxed{\omega_0 = -\gamma B(1+\delta_{iso}).}$ Book then discusses how molecule local structure affects the size of the chemical shift δ. Chemical shift summarized in picture page 201, and recall page 62 table of δ's. For each spin, δ=0 is assigned to a line in some reference chemical like TMS or H_2O.

(2) **Electric quadrupole**. Vanishes in isotropic liquid because molecule (making Φ_{2m}) tumbles and nuclear spin (having ρ_{2m}) stays aligned in its direction. Summary p 203. Another reason for EQ = 0 in iso is given in the next chapter.

(3) **Direct dipole-dipole**. I derived the basic form on page 204, but I never learned how the secular approx works to give the page 206 results which allows for the **magic angle** of no interaction at all. This secular thing vanishes for isotropic liquids. [Later I did learn how it works, see raw notes.]

(4) **J-coupling**. This starts as $\mathbf{I_1} \bullet J \bullet \mathbf{I_2}$ but for isotropic becomes $2\pi J\, \mathbf{I}_1 \bullet \mathbf{I}_2$ and in the heteronuclear case further simplifies to secular $2\pi J\, I_{1z} I_{2z}$ which we use a lot later in the book. You can use J-coupling spectra to figure out local bond angles and structure of a molecule. Summary page 216.

(5) **spin-rotation**, but nothing really said, perhaps part of relaxation.

Page 217 then has a picture which summarizes the relative sizes of the various interactions.

Summary of the results of this chapter: (taken directly from raw notes)

External E and B fields:

- Magnetic: $H^{mag} = -\boldsymbol{\mu}\bullet\mathbf{B} = -\gamma \mathbf{I}\bullet\mathbf{B} = -\gamma\, B^0 I_z$ from static external field
  $H' = -\gamma B_{RF} I_x \approx -\tfrac{1}{2}\gamma B_{RF} [\, \cos(\omega_{ref} t + \phi_p)\, I_x + \sin(\omega_{ref} t + \phi_p)\, I_y \,]$ from pulse, p 179

- Electric: $H^{elec} = 0$ unless spin ≥ 1, then $H^{elec} = -\tfrac{1}{2}\, q_{ij} \nabla_i E_j$ from quadrupole

Comment: The book implies that even for I ≥ 1, $q_{ij}\nabla_i E_j \sim 0$ so we never worry about this interaction with an *external* electric field, whether static or part of the RF pulse. However, the quadrupole can be

large due to *internal* electric fields created by the electron clouds. Hard to make a strong E field gradient with a distant external apparatus, but local electron cloud could do it easily.

Internal interactions:

Motional averaging:
intermolecular: gas = 0, iso liquid = long only, other = long + short
intramolecular: always something

Chemical shift: $H^{cs} = -\gamma\, \delta_{zz}(\theta) B^0 I_z$ // secular. For iso get δ^{iso} in there.
inter = 0 for gas, = long only for iso liquid, = tiny long for aniso liquid

Chemical shift + External Mag: $H = -\gamma B^0 I_z - \gamma\, \delta_{zz}(\theta) B^0 I_z = -\gamma B^0 (1 + \delta) I_z = -\gamma \omega^0 I_z$

Electric quadrupole: $= \omega^Q (3I_z^2 - I^2)$ secular, where $\omega^Q = Q\langle V_{zz}(\theta)\rangle/[4I(2I-1)]$ p 202, = 0 for iso

Dipole-dipole $H = b_{12} (3\, \mathbf{I_1 \bullet n\, I_2 \bullet n} - \mathbf{I_1 \bullet I_2})$ where $b_{12} = \gamma_1\gamma_2\hbar/[4\pi r_{12}^3]$ p 204
$= d_{12}(\theta) (3\, I_{1z} I_{2z} - \mathbf{I_1 \bullet I_2})$ where $d_{12}(\theta) = b_{12}(3\cos^2\theta - 1)/2$ secular, p 206
except the $\mathbf{I_1 \bullet I_2}$ term vanishes secular if nuclei are different
for iso in general, or at magic angle θ_{magic}, we get H = 0 intra.
inter = tiny long only in liquid

J coupling $H = 2\pi\, \mathbf{I_1 \bullet J \bullet I_2}$ p 212; for iso this is $H = 2\pi J_{12}\, \mathbf{I_1 \bullet I_2}$ with J_{12}= usual average
which then becomes $2\pi J_{12} I_{1z} I_{2z}$ for iso with different nuclei
inter = 0

So, for isotropic liquids, what do you get from the above? If we ignore the inter long part, then
chem shift = $-\gamma\, \delta_{iso} B^0 I_z$, dipole-dipole = 0, J coupling = $2\pi J_{12}\, \mathbf{I_1 \bullet I_2}$ for same nuclei.

---------- Chapter 8: NMR in Isotropic Liquids (223-237) -------- 14 p ---------- ###

Here, we have **only chemical shifts and J-couplings** to worry about, so we can use the **graphic method** shown page 224 to represent a molecule. Shapes are the chem shifts, lines are the J couplings. Of course this graphic is not showing the actual shape of the molecule! If you have 4 spins in general, you would have four shifts and 6 J-couplings to worry about, as shown on this page.

Next, it is noted that the OH-in-ethanol **fast chemical exchange** mechanism often removes certain J couplings from contributing. Secondly, it is noted that when there is an electric quadrupole moment, its interaction is so strong that you get T_1 = 1 μsec and such a nucleus relaxes so fast you cannot get a FID from it, so can ignore it.

Next is the notion of **"chemical equivalence"**. When two H's for example are in the same effective environment due to some molecular symmetry, they must have the same chemical shift. The sameness of the environment includes the possibility that some group like $-CH_3$ might rotate relative to the molecule rapidly and so make the three H's chemically equivalent even if there is no symmetry. Good examples.

If a set of spins are chemically equivalent, then they may also be **"magnetically equivalent"**. This is the case if they are the only spins in the molecule, *or* if this set of spins has identical J couplings to all other spins in the molecule. The graphic bottom page 230 and its caption given an example. In this case, you can throw out the $\mathbf{I}_i \bullet \mathbf{I}_j$ terms in the J-coupling Hamiltonian for all pairs within this set of spins. Graphically, this corresponds to deleting all lines connecting spins in the mag equiv set of spins. Examples are given on page 231. The appendix on page 583 proves why this is true.

If the chemical shift between a pair of J-coupled spins is much larger than the J coupling itself as shown top page 233, then you can replace $\mathbf{I}_i \bullet \mathbf{I}_j$ by $I_{iz}I_{jz}$ (a secular approx) and this is called **"weak J coupling"**. If you cannot do this, you have to read appendix on page 588 which I have not read at this point. A pair of heteronuclear spins always are weakly coupled in this sense.

It is noted that, if your "blast" on one set of spins during a shot, you can think of the remaining (different type) spins as being alone, so you can remove all blasted-spin spin terms from the Ham. Once you do this, you might find that some or all of your remaining spins are then mag equiv, so you can then also remove their J couplings. This method is called **RF decoupling**, but I have not proven to myself yet why it works this way. [I have now figured this out, see section in Chap 13 notes.]

The **alphabet notation** describes which spins are weakly coupled, chem equiv, or mag equiv. For example, AX means 2 spins not chem equiv, while AA' means two spins that are. If they are also mag equiv, then you write AA or A^2. Can extend to 3 or more spins in obvious fashion. Chapter 12 will talk about AX systems where A and X are the same spin *type* (homonuclear), but have largely different chem shifts. A different subject would be AX heteronuclear systems. I think AB is an approach to AA', the chemical shift is very small.

********** Part 4: Uncoupled Spins-1/2 **********

---------- **Chapter 9: Single Spin-1/2 (241-271) -------- 30 p ---------- ###**

Chapter Meta Overview: In the first section below, we "play" with the polarization vector $\langle\psi|\mathbf{I}|\psi\rangle$ and see how it can be pointed in various directions. This could have been presented in a better manner I think. Then we define the **rotating frame** going at ω_{ref} which "takes out" all of the Larmor rotation if $\omega_{ref} = \omega^0$, otherwise takes out most of it. We examine the effect of an **RF pulse** in this rotating frame, and we find that it causes the polarization vector to "**nutate**" at a strange frequency and about a strange axis. The nutation greatly simplifies if our transmitter frequency ω_{ref} exactly matches the Larmor frequency ω^0 (resonance) and we learn then about the general $(\beta)_\phi$ **RF pulse** idea and $(\pi/2)_x$ in particular. We then look at the penalty we have to pay for going off-resonance with $\Omega = \omega - \omega_{ref} \neq 0$ and we find that our spectrometer has a very limited **"bandwidth"** of operation which is roughly $\Delta\Omega = \Delta\omega \sim \omega_{nut} \leq 200$ kHz. This is maximized by maximizing B_{RF}. My notes are long here because, even with a trivial spin-1/2 system, there is much to be said, and my first pass through this chapter was a little foggy, so I try to clear things up here. Note that $\omega^0 = \gamma B^0$ but $\omega_{nut} = \gamma B_{RF}/2$ because we lose half our B_{RF} to RWA. The magnetic splitting of spin energy levels is called the Zeeman Effect so we have "Zeeman states".

The polarization vector. This chapter defines the (z-based) spin-1/2 Zeeman states as $|\alpha\rangle$ and $|\beta\rangle$ and defines $\boxed{\omega^0 = -\gamma B^0}$ as the **Larmor frequency** of a spin having γ, so of course then $\boxed{H' = +\omega^0 I_z}$. We learn

what linear combinations ψ of the two base states (with complex coefficients) cause the "**polarization vector**" $\langle\psi|\mathbf{I}|\psi\rangle$ to be in various directions, such as in direction $-\hat{\mathbf{y}}$ or $+\hat{\mathbf{x}}$ as on 247. For example, the state $|\psi\rangle$ that puts $\langle\psi|\mathbf{I}|\psi\rangle = (1/2)\hat{\mathbf{x}}$ we call $|+x\rangle$. The state shown as $|\theta,\phi\rangle$ has $\langle\mathbf{I}\rangle$ in the $+\theta,\phi$ direction. We know very generally that vector operator **I** will precess under the action of H', as described in **"density matrix transformations.doc"** where I made a little picture. We could then watch, for example, how $\langle+x|\mathbf{I}|+x\rangle$ **precesses**, if we start our spin in the +x state, and these are the pictures shown page 251. The answer we know is $\mathbf{I_T}(t) = U\,\mathbf{I_T}(0)\,U^{-1} = \mathbf{I_T}\cos\theta + [\mathbf{I_T} \times \hat{\mathbf{z}}]\sin\theta$, where $\theta = -\gamma B^0 t = +\omega^0 t$ and $\mathbf{I}_L$ stays constant.

Rotating frame and relative frequency Ω. If our NMR transmitter sends in RF at frequency ω_{ref}, it is convenient to define a "rotating frame of reference" that rotates at this frequency in the same direction as the Larmor precession, so that *in* this rotating frame, if you are right *at* the Larmor frequency $\omega_{ref} = \omega_0$, the precession will be frozen and $\langle\mathbf{I}\rangle$ will just sit there fixed in some direction. And if ω_{ref} is a bit off this resonance, then the spin vector will precess slowly one way or the other at frequency Ω^0, the "relative frequency", which is defined as $\boxed{\Omega^0 = \omega^0 - \omega_{ref}}$. Here ω^0 is our Larmor frequency. { More generally we can talk about an arbitrary frequency ω near ω^0 and then define relative frequency $\Omega = \omega - \omega_{ref}$. }

We can compute the Hamiltonian in this rotating frame, and we get the page 255 top result in which we rotate the lab frame Hamiltonian, and we also pick up a Coriolis term. If we jam $H' = +\omega^0 I_z$ into this formula, the first term gives $\omega^0 I_z$ and the Coriolis term gives $-\omega_{ref} I_z$, so get $H'_{rot} = (\omega^0 - \omega_{ref})I_z$ and this says $\boxed{H'_{rot} = \Omega^\circ\ I_z}$ which is of course a desirable result.

If there is a chemical shift, we write $\omega^0 = -\gamma B(1+\delta^0)$. If we define δ_{ref} by $\omega_{ref} = -\gamma B(1+\delta_{ref})$, then we find that $\Omega^0 = \omega^0 - \omega_{ref} = -\gamma B(\delta^0 - \delta_{ref})$, though not clear why useful. We could also define a relative sweep variable δ as $\omega = -\gamma B(1+\delta)$ and then $\Omega = -\gamma B(\delta - \delta_{ref})$. So can think of ω, Ω, or δ as a variable.

The RF Pulse and ω_{nut} nutation. The next task is to add in an RF pulse. The RWA is shown in (9.22) for this pulse where now we also have ϕ_p as the specific phase of the RF pulse. When we add this into our rotating frame Ham, we get the result top page 260 with $\boxed{\omega_{nut} = |\gamma B_{RF}/2|}$. This (9.26) is easy to understand. It says that the Ham rotator is going to be $U = \exp[\,-i(\Omega^0 I_z + \omega_{nut}(\cos\phi_p I_x + \sin\phi_p I_y))\,t]$. We can write this in our general form $\exp(-i\omega_{e0} t\ \hat{\mathbf{n}} \bullet \mathbf{I})$ where ω_{e0} is an effective frequency, where $\hat{\mathbf{n}} = [(\omega_{nut}/\omega_{e0})\cos\phi_p, (\omega_{nut}/\omega_{e0})\sin\phi_p, (\Omega^0/\omega_{e0})]$ and $\omega_{e0}^2 = (\omega_{nut})^2 + (\Omega^0)^2$. So basically this says the polarization vector is rotating about some weird fixed axis $\hat{\mathbf{n}}$ at a frequency ω_{e0} as shown. We could define a unit vector in the transverse plane $\hat{\boldsymbol{\phi}} = [\cos\phi_p, \sin\phi_p]$ so that $\hat{\mathbf{n}} = [\ (\omega_{nut}/\omega_{e0})\hat{\boldsymbol{\phi}}, (\Omega^0/\omega_{e0})]$. Later on page 266 we write $\hat{\mathbf{n}}$ as a (θ_p,ϕ_p) vector so now $\hat{\mathbf{n}} = [\sin\theta_p\,\hat{\boldsymbol{\phi}}, \cos\theta_p]$, and $\tan\theta_p = (\omega_{nut}/\Omega^0)$. In this case we can write $U = \exp(-i\omega_{e0} t\ \hat{\mathbf{n}} \bullet \mathbf{I}) = R(\theta,\phi)R_z(\omega_{e0}t)\,R(\theta,\phi)^{-1}$ as in 9.37.

If $\omega_{nut} << \Omega^0$, then $\hat{\mathbf{n}}$ is close to $\hat{\mathbf{z}}$. [$\hat{\mathbf{z}}$ would be the rotation axis if no RF pulse] In the other extreme, $\hat{\mathbf{n}}$ is close to $\hat{\boldsymbol{\phi}}$. The pictures on page 267 show $\hat{\mathbf{n}}$ as a white arrow for various ratios (Ω^0/ω_{nut}) where $\phi_p = 0$. In all these pictures, we assume that the spin started off in state $|\alpha\rangle$ which means $\langle\mathbf{I}\rangle_0 = \langle\mathbf{I}(0)\rangle = \langle\alpha|\mathbf{I}|\alpha\rangle = 1/2\ \hat{\mathbf{z}}$. Then later at time t, we have that $\langle\mathbf{I}(t)\rangle = \langle\alpha|\ U^{-1}\,\mathbf{I}(0)\,U\,|\alpha\rangle = \langle\alpha(t)|\,\mathbf{I}(0)\,|\alpha(t)\rangle = \langle\mathbf{I}\rangle_t$ where $U = \exp(-i\omega_{e0} t\ \hat{\mathbf{n}} \bullet \mathbf{I})$. It is this vector $\langle\mathbf{I}\rangle_t$ (the polarization) whose tip path is

shown in the drawings on page 267. This vector is what rotates about the axis $\hat{\mathbf{n}}$. All the paths start at $\langle \mathbf{I} \rangle_0 = 1/2\ \hat{\mathbf{z}}$ since assume start in the $|\alpha\rangle$ state. [We are shuffling between "pictures" here.] Notice that we don't at this point have a situation like that shown on page 263, we have rotation at ω about the fixed axis $\hat{\mathbf{n}}$ in our rotating frame.

On-resonance RF pulse. If we go exactly on resonance so $\Omega^0 = 0$, then we get $U = R_{\phi_p}(\omega_{nut} t) = R_{\phi_p}(\beta)$ where $\boxed{\beta = \omega_{nut} t.}$ This would apply as well if we are very close to resonance. So here we get our famous RF pulse which one writes as $(\beta)_{\phi_p}$ and an example is $(\pi/2)_x$ which rotates the spin polarization down from +z to -y, and we can correspondingly say $R_x(\pi/2)|+z\rangle = |-y\rangle$. It is shown p 264 that $R_{\phi_p}(\beta) = R_z(\phi_p) R_x(\beta) R_z(-\phi_p)$ = (9.33) using our sandwich formula, so here is an Euler-like representation of $R_{\phi_p}(\beta)$ except we have x in the middle instead of y. During an x-pulse, the **I** vector is rotating in the z-y plane, and if we transform back to the lab frame, we pick up the very fast rotation so we get the spiral shown page 263, with extremely fine threads on the order of B_{RF}/B^0.

Off-resonance RF pulse. We can ask about the probability $|\langle \beta(0)|\alpha(t)\rangle|^2$ of being in state $|\beta\rangle$ after time t if we started in state $|\alpha\rangle$. We can compute $\langle \beta| U(t)|\alpha\rangle = \langle \beta| R(\theta,\phi) R_z(\omega t) R(\theta,\phi)^{-1}|\alpha\rangle$ and square the result. I got this answer, where now we use $\omega_e^2 = (\omega_{nut})^2 + (\Omega)^2$ so that as we vary Ω perhaps away from our spin resonance Ω^0, we vary ω_e correspondingly,

$$|\langle \beta|\ R_y(\theta)\ R_z(\omega_e t) R_y(-\theta)\ |\ \alpha\rangle|^2 = \sin^2\left(\sqrt{\omega_{nut}^2 + \Omega^2}\ \ t/2\ \right) /\ [\ 1 + (\Omega/\omega_{nut})^2\ ]$$

At resonance you get $\sin^2(\omega_{nut} t/2)$ so we get repeated equal peaks as time goes by. If we chose a pulse length such that this is 1 when the pulse ends, then such a pulse would put us in the $|\beta\rangle$ state. After such a pulse, we would have to emit a photon to get back to the $|\alpha\rangle$ state and that makes a strong FID signal. An example would be $\omega_{nut} t/2 = \pi/2$ so that $\beta = \omega_{nut} t = \pi$ which is of course the famous "π pulse".

If we are off resonance so $\Omega \neq 0$ and do a π pulse, the probability for being in the $|\beta\rangle$ state at the end of the pulse is $1/[\ 1 + (\Omega/\omega_{nut})^2\ ]$. Note that $\Omega/\omega_{nut} = 2\Omega/\gamma B_{RF}$ so for a given offset Ω, a large B_{RF} puts you closer to the bandwidth peak, with a resulting stronger signal. Roughly speaking, our spectrometer has an Ω **"bandwidth"** of about ω_{nut} in each direction away from $\Omega = 0$. This means it has this same bandwidth in ω away from ω_{ref}. You won't see any peaks outside this bandwidth very well. So if you want to increase your machine's bandwidth, you need to increase B_{RF}. Largest practical ω_{nut} is 200 kHz it is claimed which I think corresponds to $B_{RF} \sim .01T = 100$ G.

Wherever we happen to be operating under the bandwidth curve, the bandwidth of a spectral peak we might see is controlled by T_2, so the Lorentzian peak width and our bandwidth peak are different animals.

---------- Chapter 10: Ensemble of Spins-1/2 (273-312) -------- 39 p ---------- ###

Chapter Meta Overview. The **density matrix** ρ is introduced as a method to handle **thermal** effects, and our FID signal is going to be driven by $\langle \mathbf{M_T} \rangle \sim \mathrm{tr}(\rho \mathbf{I_T})$ where $\mathbf{I_T}$ is the total transverse spin of our system. For a set of M spin-I nuclei, a method is given for defining the indices of ρ_{mn}. The **single-quantum frequency** $\omega^0 = -\gamma B^0$ is what matches the various equal gaps between the levels before

interactions are added, which interactions split the levels slightly. The ρ_{nn} are called **populations**, while the $\rho_{n\neq m}$ are called **coherences**. The nature of the levels indicated by indices n and m on ρ_{mn} determines the **order of coherence** (eg, 2-quantum) of the elements $\rho_{m\neq n}$ and this order tends to increase as you move away from the diagonal. The **box notation** is defined. The creation of **the FID signal** is explained in both classical-field and quantized-field ways. The form of ρ in TE is given for spin-1/2 with methods for finding it generally; in TE ρ is diagonal and static. The effect on populations and coherences of some **simple RF pulses** is considered. A way to compute **M** for an arbitrary pulse is given, such pulse being known as $(\beta)_{\phi_P}$. The notion of **T1 and T2 relaxation** is introduced phenomenologically and added to the elements ρ_{mn}. The generation of the NMR signal using a special **quadrature receiver** is reviewed and we obtain exactly the form for the complex receiver output s(t) that was assumed earlier in the book, see Chapter 5 page 98.

The density matrix. The density *operator* (see Schiff) can be written $\rho = \Sigma_\alpha |\alpha> p_\alpha <\alpha|$ which is a state-probability-weighted projection operator sum over a statistical ensemble of states α. When you sandwich some Hamiltonian eigenstates around the above, you get the **density matrix**, such as $\rho_{nm} = \Sigma_\alpha <n|\alpha> p_\alpha <\alpha|m>$. A non-zero off-diagonal matrix element means that state α has a foot in both the n and m states and these matrix elements are called **coherences**. The diagonal elements are $\rho_{nn} = \Sigma_\alpha p_\alpha |<\alpha|n>|^2$ (hence real) and give the fractional population of state n. Notice that $\rho_{nm}^* = \rho_{mn}$ so ρ is a Hermitian matrix.

For spin-1/2, that means $\rho = 1/2 + k\mathbf{M}\bullet\mathbf{I}$ where **M** is a scaled magnetization and $\mathbf{I} = \boldsymbol{\sigma}/2$. That is to say, $tr(\rho\mathbf{I}) = kM_i tr(I_i\mathbf{I}). = kM_i (1/2)\hat{\mathbf{i}} = (k/2)\mathbf{M}$ showing that $\mathbf{M} = (2/k)<\mathbf{I}>$ so $\rho = 1/2 + 2 <\mathbf{I}>\bullet \mathbf{I}$.

The usefulness of ρ is that you can compute expectation values such as $<\mathbf{I}> = tr(\rho\mathbf{I})$. The density matrix gives "the **most complete description** that is possible" of your ensemble, since from it you can compute all observable quantities. Note that $tr(\rho I_z) = \Sigma \rho_{nn} (I_z)_{nn}$.

A spin-I spin has N = 2I+1 states |n>, so the density matrix will be (2I+1)x(2I+1).

In a system with M spins of spin I you have a direct product representation with $N = (2I+1)^M$ states and so its density matrix will be $(2I+1)^M$ x $(2I+1)^M$[three spin-1/2 means 8x8]. For such a system, the (no interactions) energy diagram has 2(MI)+1 distinct levels stepping MI, MI-1, MI-2, ...-MI. Since $(2I+1)^M > 2(MI)+1$, there will be lots of degenerate states in general (broken when interactions are considered). The energy gap between adjacent pairs of non-degenerate states (ignoring interactions) is going to be $\gamma \Delta I_z B^0$ with $\Delta I_z = 1$. The nominal photon absorption energy quantum (single photon) will be $\hbar\omega_0 = \gamma \Delta I_z B^0 = \gamma B^0 = \omega^0$. So the NMR machine is going to run near this frequency which we think of as **the single-quantum frequency**.

Suppose you draw an energy level diagram and *order* these N states by energy (to define indices n and m of ρ_{nm}). If you then examine a first off-diagonal [which contains matrix elements for $n = m\pm1$], you will find a mixture of single-quantum terms and, where the adjacent pair of states is degenerate, zero-quantum terms. A second off-diagonal will have then a mixture of 2,1 and 0 quantum terms, and so on. The upper right corner represents the maximal difference between n and m, and this will be the gap between MI and -MI which is 2MI, so this ρ element will represent a "2MI-quantum" coherence. In our AX system with I=1/2 and N=2 this would be a 2-quantum coherence. The number of nominal $\hbar\omega^0$ quanta linking the states n and m is called the **"order of the coherence"** (recall that the off-diagonal ρ_{nm} is itself called "a coherence"). When degenerate levels get split, the implied transition requires one

approximate $\hbar\omega^0$ photon in, and another (slightly different ω) out, so remains a "zero quantum coherence".

Levitt uses a **"box notation"** to replace the indices on ρ_{mn} where, for each of the M spins, you get a label. If, between the two states n and m of ρ_{nm}, a given spin does not change state, the label is that spin state α or β [or 1,0,-1 perhaps for spin 1, etc] . If it does change state, then the label is either + or – depending on which way it changes (I suppose more generally a label could be $+^k$) . So with four spin-1/2's, you might have a coherence of the form $\rho_{\alpha+++}$ which would have order of coherence 3, or $\rho_{\alpha+-+}$ or order 1. Page 344 (12.6) shows this matrix for the case N=2 and I=1/2.

For N=1 and I=1/2, it's easy to show that $\langle \mathbf{I}_T \rangle = \mathrm{tr}(\rho \mathbf{I}_T) \neq 0$ if $\rho_- \neq 0$. There are two ways to think of the FID being non-zero due to such an off-diagonal ρ element.

The **field-classical way** is that $\langle \mathbf{M}_T \rangle = \gamma \langle \mathbf{I}_T \rangle = \mathrm{tr}(\rho \mathbf{M}_T) \neq 0$, so you have a time-varying $\mathbf{B}_{FID} = \mu_0 \langle \mathbf{M}_T \rangle$ which induces a Faraday's Law voltage in the x-oriented pick-up coil which is the FID signal.

The **field-quantum way** is that the coherence links two energy levels and, during the FID period, some number of RF photons linking these levels are emitted by spontaneous emission. First, we know that $d\rho_{mn}(t)/dt = -i H'_{mn} \{ \rho(t)_{nn} - \rho(t)_{mm} \}$ which says that a population difference between our two levels m and n *creates* off-diagonal ρ element values when the RF pulse is active ($H' = -\gamma B_{RF}/2\ I_x$). Thus, photons got absorbed. During the FID they get emitted and our same equation shows the transition rate driven by the population difference between the transition levels, weighted by the corresponding H' matrix element. These emitted photons are then absorbed in the pickup coil, and the photon polarizations are just right so as to induce a voltage in the coil.

Thermal Equilibrium (TE). In TE the matrix ρ is diagonal and those diagonal elements are determined by **Boltzmann** statistics as shown on page 282 (10.15). For 2 states, the numerators are $1 \pm B/2$ where $B = -\hbar\omega^0/kT$, and the denominator sum is 2, so we get values $1/2 \pm B/4$, and this is shown in 10.17. Since ρ is diagonal, it is the same in lab or rotating frame, which are related by a z-rotation. $B \sim 10^{-4}$ according to page 282 at room temperature for H spins, so populations are very close to being equal in all states.

In general, $M_x + iM_y = (4/B)\ \rho_-$ showing how, in our classical way above, the coherence drives the transverse mag. We can even write $\rho = 1/2 + (B/2)\mathbf{M} \bullet \mathbf{I}$ which fits our general form $\rho = 1/2 + \mathbf{a} \bullet \mathrm{I}$ where **M** is the magnetization *unit vector*. Notice that the true magnetization here is $\mathbf{M}_{true} = (B/2)\mathbf{M}$ so is very small.

RF Pulses. When you apply the RF pulse on resonance, ρ transforms by $R_{\phi p}(\beta)$ as in 10.27, so our game is to see what happens to ρ from a given kind of pulse. We work in the rotating frame as usual. The $(\pi/2)_x$ pulse is taken as an example. It equalizes the two populations and produces an off-diagonal element $\rho_- = B/4i$ which is very small, top page 289. At this point, we would then have $M_x + iM_y = (4/B)\ \rho_- = -i$, meaning $M_y = -1$ as we expect. Levitt always refers to a "**strong RF pulse**" meaning it is strong enough to offset a small distance off resonance we might be working at. Next, we find that the $(\pi)_x$ pulse reverses the populations and makes no off-diagonal ρ. On page 292 we are reminded that the FID in the quantum view comes from spontaneous emission, though you might get stimulated emission during an RF pulse. I think Malcolm has could be clearer on this.

Free propagation between RF pulses. As time goes by, ρ moves according to $R_z(\Omega_0 t)$ in the rotating frame, and this causes coherence ρ_- to pick up a phase $\exp(i\Omega_0 t)$ as in 10.30. This corresponds to **M**

rotating at the Larmor Ω_0, as shown top p 294. Page 295 then summarizes the single $(\pi/2)_x$ experiment. On top page 297 middle we see this Larmor Ω_0 free-precession action on I "written out". Above it is a similar z rotation ϕ_p which plays a part in the most general $(\beta)_{\phi_p}$ rotation shown in Euler form there.

Written out pulse aids: Page 296 shows the "written out" forms for pulses $(\beta)_x$, $(\beta)_y$, $(\beta)_{-x}$, $(\beta)_{-y}$. The *meaning* of these equations is as follows: if you have $\rho = 1/2 + k\mathbf{M}\bullet\mathbf{I}$, you know that $\rho' = 1/2 + \mathbf{M}\bullet R\mathbf{I}R^{-1} = 1/2 + \mathbf{M}\bullet R^{-1}\mathbf{I}$. So to get from ρ to ρ', you replace $\mathbf{I} \rightarrow R^{-1}\mathbf{I}$, and that is what all the equations in the boxes are showing. I find it easier to think of $\rho' = 1/2 + R\mathbf{M}\bullet\mathbf{I}$ and then you replace $\mathbf{M} \rightarrow R\mathbf{M}$. If $\mathbf{M} = M_z\hat{z}$, then for a $(\pi/2)_x$ pulse you replace $\mathbf{M} = M_z\hat{z} \rightarrow M_z R\,\hat{z} = -M_z\hat{y}$.

Adding Relaxation with T1 and T2. For a coherence, we just add $e^{-t/T2}$. For a population, we do (10.42) page 300 using T1. Book then shows plots of the populations for $(\pi)_x$ on p 301 and then for $(\pi/2)_x$ on p 302. The theory limit which says $T_2 \leq 2T_1$ is given (which I proved in a simple way and sent to Malcolm). We then see some "relaxation spirals" in the rotating frame for various T1 and T2.

The NMR Signal. Appendix 17.7 page 586 shows the design of the **quadrature receiver** which fits into the larger diagram on page 85. Basically this is a super-heterodyne receiver which downshifts the incoming signal from ω^0 to Ω^0 which you could think of as the IF frequency. It does this using a multiplier called a **mixer** which we know generates sum and difference frequencies, and a low pass filter dumps the sum. It does this in two separate channels, one where the reference oscillator phase is shifted $\pi/2$, hence "quadrature" and hence two outputs which, it turns out, form the real and imaginary part of a signal called s(t). The appendix derives the fact that $s(t) \sim 2i\rho_- \exp(-i(\phi_{rec} + \phi_{dig})$, where ϕ_{rec} is an analog delay in the reference input, and ϕ_{dig} comes later. [constant is missing].

In the derivation, we start with $s_{FID}(t) \sim d/dt\ (2\ Re\ \rho_-)$ because $2\ Re\ \rho_- \sim \langle M_x \rangle$ in the coil, and we are using Faraday's Law that a changing magnetic field flux through the pickup coil induces a voltage (Purcell p 243). But we know that $\mathbf{B} = \mu_o\mathbf{M}$ if $\mathbf{H}=0$ as on page 139 B&B. The flux of interest is $B_x(t) = \mu_o M_x(t)$. So pretty clear that the lab-frame Larmoring $\mathbf{M}_T$ makes a changing flux and hence $s_{FID}(t)$.

Now back to $s(t) \sim 2i\rho_- \exp(-i(\phi_{rec} + \phi_{dig})$. During the FID time, ρ is in free-run (no pulse) and we know it then has the form $\rho_-(t) = \rho_-(0) \exp[\ (i\Omega_0 - \lambda)t\ ]$ { in rotating frame } and

$$s(t) = a \exp[\ (i\Omega_0 - \lambda)t\ ]$$
$$a = \text{constant} * 2i\rho_-(0) \exp[-i(\phi_{rec} + \phi_{dig})]$$

Finally then we see why this was the form *assumed* way back on page 98 which caused the Lorentzian peak. On page 98 a subscript is added for each "spin" that might be in your sample, $s(t) = a_\ell \exp[\ (i\Omega_\ell - \lambda_\ell)t\ ]$. Two protons at different chemical shifts would cause two peaks as was shown page 100.

The point of the quadrature receiver is to output a signal at a nice low frequency like Ω_0 which goes to A/D converters. This is the difference frequency and we don't have to apply a digital FT directly to an ω^0 rate signal.

In the first experiment now considered, we do a $(\pi/2)_x$ and this creates some $M_x(t)$ and this makes a FID which begins at t=0. It is shown that $\rho_-(0) = B/(4i)$ and so a = B/2 and we get the prototypical

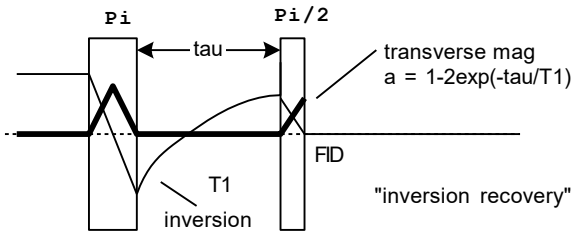
Lorentzian at Ω_0. For the $(\pi/2)_y$ we get $\rho_{-}(0) = B/(4)$ and so a = iB/2 so here the two parts of the peak are swapped.

In the case of M direct product spins, I think one could show it is the sum of all the single-quantum terms in ρ that replace ρ_{-}. An example appears top of page 353 for M=2 and I=1/2. This is very clearly true when viewed in the field-quantized manner.

---------- Chapter 11: Experiments on non-interacting spins (315-335) ------- 20 p ---------- ###

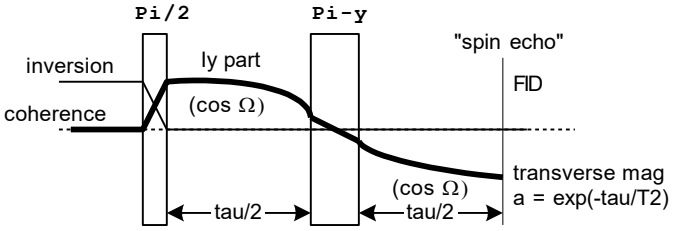
Example 1: (inversion recovery and T_1) seq = $\pi_x,\tau,\pi/2_x,t$. You create an inversion, let it decay at T_1 for time τ, then flip it 90 to make a signal ("knockdown"). So the amplitude at t=0 will be a = [1-2exp(-τ/T_1)]. Do FT only in the FID t and get p318 picture. Along the τ direction you see "inversion recovery" with a T_1 for each of the three peaks in this example. Computer could read this data and report out your $(T_1)_\ell$ for each peak ℓ. For MRI, we are looking at the H peaks from water molecules, so probably only one peak to worry about. Then a(0) = 1-2exp(-τ/T_1) is a measure of T_1 for each sample, so you could then get a(t=0,x,y) = 1-2exp(-τ/T_1(x,y)). If you choose τ to be on the order of brain T_1 times, this would be a "T_1-weighted image". **FLAIR** is *fluid attenuation* inversion recovery. You tune the pulse sequence to remove a certain small range of T_2 from the image, you match that to the **fluid** which normally covers lesions, and then you can see the lesions more clearly because the fluid is "attenuated".

STIR is *short TI* (= like τ/2) inversion recovery and it is tuned to remove the **fat** signal by hitting the null of the exponential shown on page 317.



Note: When pulse sequence is repeated at T_R which does not allow TE to fully recover, formulas are slightly different for inversion recovery, see **"mri notes and sources.doc"**. You get a mixture of T_1 and T_2 which lets you tune what you want to filter out, be it CSF liquid, or be it fat (FLAIR and STIR).

Example 2: (spin echo and T_2) seq = π/2, τ/2, π_y, τ/2, t. This sequence produces a = [exp(-τ/T_2)] so you get a direct measure of T_2.



Run this at several τ to determine T_2, or select τ in medical range to map out T_2(x,y) and then you have a "T_2 weighted image." In this case, the I_y strength grows after the π_y pulse, reaches a peak, and then decays down with T_2 during the FID. So your I_y component sort of peaks out in free space to the right of

the second pulse. There is a second effect having to do with **inhomogeneities** which cause dephasing. During the first $\tau/2$ pulse they dephase the signal and it expo decays, but after the π_y we get **rephasing** and this brings up the pulse amplitude to the right, so this is the actual **"echo"** you see bottom page 323 and also page 325 bottom. If there is motion in the sample, rephasing will be incomplete, so this lets you measure the water speed field s(x,y), perhaps that is **diffusion MRI** letting you display tracts in the brain.

Note: Again, with the practicality of a rep rate $T_R < \infty$, you get some effect of T_1 on your T_2 image.

Example 3: (**2D imaging**) By putting **gradients** in two perp directions and pulsing one on during a t1 period and the other on during a t2 period and doing a full **2D FT**, you can with a simple single-pulse $\pi/2$ sequence (p330) create a 2D FT whose intensity reflects that of a 2D object sample. Something like this is no doubt done in a **MRI** machine, but then they have to have some method to select a slice. That method is not explained here. You could imagine a 3D FT and then you get the whole 3D object in "spin density". Maybe the machines really work that way, I don't know. By fiddling the pulses as discussed earlier, you could do this same thing with T_1 or T_2 weighting, or just stay with "proton density".

Note: See " **MRI Notes and web sources"** for how MRI machines do spatial localization.

********** Part 5: Coupled Spins 1/2 **********

---------- Chapter 12: Homonuclear AX systems (339-383) ------- 44 p ---------- ###

Chapter Overview: From the sample AX molecule shown p339, we expect two chemically shifted C peaks and each will be fine-split in two by the local H, so there will be four peaks. Analyzing this situation is the subject of this long chapter. In the first section below, we just repeat all the things we did in the single spin-1/2 case. In the second section we get all involved with writing things as 4x4 matrices, and we learn to interpret various "terms in ρ" as correlations if they are like $I_{1x}I_{2y}$ and we write out ρ for TE. In the third section, we learn the messy rules for how $\exp(-i2\pi J I_{1z}I_{2z}t)$ acts on various product terms. It all pretty mechanical, you just "do it" with the formulas I provide. Finally, the last section describes the Spin Echo Sandwich SES and shows the idea of sliding the π pulse to the left with the remaining propagation by τ being driven only by $\exp(-i2\pi J I_{1z}I_{2z}t)$. And finally if we tune so that $\pi J\tau = \pi/2$, we find that the SES causes the swapping of double and single product terms in ρ, but we don't know why that is useful.

(339-355) We know the Ham with its (secular) J-coupling term $2\pi J\, I_{1z}I_{2z}$ and we set up our **base states** like $|\alpha\alpha\rangle$ = up, up. We obtain the **energy level diagram** and the four energies, and we assume the **"weak-coupling"** case so J << the chemical shift energy split which itself is very small, so we use the **secular** Ham. Even with J=0 we still get split of the middle two energy levels by the chemical shift. We write the **4x4 density matrix** using box notation. We go into the usual **rotating frame** and that changes Ham so ω replaced by Ω as in eq (12.9), no surprise there, and we have then $H = \Omega_1 I_{1z} + \Omega_2 I_{2z} + 2\pi J\, I_{1z}I_{2z}$. We then study **free evolution of ρ_{mn}** and as expected find that $\rho_{mn}(t) = \rho_{mn}(0)\exp[-i(\Omega_m-\Omega_n)t]$ and define $\Omega_{mn} = \Omega_m-\Omega_n$ as the energy level differences, but **box notation** is used in place of m and n as on page 352 where all the energy differences are written out. Then we add the expected $\mathbf{T}_2$ **decay factor**. We then draw the **energy level diagrams** in various cases where I think Malcolm has a small graphical

error, and we see also the spectrum with its four peaks. If we had J=0, we still have 4 distinct levels, but only two distinct photon energies, so it really is J that causes the fine splitting. That split is $\Delta\Omega = 2\pi J$. We were told page 340 that J = 2.9 Hz and this appears correctly in the picture page 340 where $\Delta\Omega/2\pi = J =$ 3 Hz.

Footnote: $\rho' = U\rho U^{-1}$ where $U = e^{-itH}$ = diagonal. Thus $\rho'_{mn} = U_{mm}U_{nn}^{*}\,\rho_{mn}$ and this is where those phases come from, $\rho_{mn}(t) = \rho_{mn}(0)\exp[-i\,(\Omega_m-\Omega_n)t]$.

(357-366) Here we use idea that $[A\otimes B]_{ai,bj} = (A)_{ab}\,(B)_{ij}$ for our **direct product representation** and he does this without explanation using a graphical method which works fine. Note eg that $2I_{1x}I_{2y}$ means 2 $I_{1x}\otimes I_{2y}$ and I_{2x} means $1\otimes I_{2x}$. On page 359 he comments on the matrix $-I_{1y} = -I_{1y}\otimes 1$. I know just from **the raise/lower argument** that this will involve box-labeled coherences with index $\pm\alpha$ and $\pm\beta$, I don't need to see the actual matrix. Next example is $-2I_{1y}I_{2z}$ which I know involves the same. Suppose $-2I_{1y}I_{2z}$ shows up in your ρ, what can you say? $\langle\gamma_1\gamma_2|\,-2I_{1y}I_{2z}|\gamma_1',\gamma_2'\rangle = -2\langle\gamma_1|I_{1y}|\gamma_1'\rangle\langle\gamma_2|I_{2z}|\gamma_2'\rangle$. The sign of $\rho_{-\beta}$ and $\rho_{-\alpha}$ are opposite because $\langle\gamma_2|I_{2z}|\gamma_2\rangle$ has opposite signs for $\gamma_2 = \beta$ vs α, so "this kind of term in ρ" causes an **antiphase multiplet**, recall that $\rho_{mn}(0)$ controls the NMR signal. You can associate **ensemble pictures** with a "term in ρ". For example a term $+5I_{1z}$ means $\langle I_{1z}\rangle = \mathrm{tr}(\rho I_{1z}) \sim +5$, so most 1-spins point in the + z direction. Another example is a $-2\,I_{1z}I_{2z}$ term meaning $\langle I_{1z}I_{2z}\rangle = \mathrm{tr}(\rho I_{1z}I_{2z}) \sim -2$ so we have spins **anti-correlated** in the z direction. Here we have used the idea that $I_i^2 \sim 1$. So the sign of each ρ term suggests a picture. Next, in **TE** we find that the two center states, being so close, have the same population to high accuracy, and $\rho = (1/4)\,\mathrm{diag}(1+B, 1, 1, 1-B)$ meaning $\rho \sim (B/4)\,[\,I_{1z}\,1 + 1\,I_{2z}]$.

(366-381) Malcolm keeps using 4x4 matrices, but I prefer to use the direct product. I know that $\rho \sim I_{1z} + I_{2z}$ will become $\rho = -I_{1y} - I_{2y}$ under a $(\pi/2)_x$ without drawing 4x4 matrices. And $\rho \sim I_{1x}I_{2y}$ will become $\rho = I_{1x}I_{2z}$.

We know that free-evolution means putting $\Omega_1 I_{1z} + \Omega_2 I_{2z} + 2\pi J\, I_{1z}I_{2z}$ into an expo as on p 374, and we can think of this as three separate rotations done in any order. The hardest **rotation involves the last J-coupling term**, but luckily I know that [set $\phi = \pi J\tau$]

$$\exp(-i\,\phi\,2I_{1z}I_{2z})\;I_{1k}\;\exp(+i\,\phi\,2I_{1z}I_{2z}) = I_{1k}\cos\phi + \varepsilon_{kmz}\,2I_{1m}I_{2z}\sin\phi + \delta_{kz}\,I_{1z}\,(1-\cos\phi)$$

so we then know that

$$\exp(-i\,\phi\,2I_{1z}I_{2z})\;I_{1x}\;\exp(+i\,\phi\,2I_{1z}I_{2z}) = I_{1x}\cos\phi + 2I_{1y}I_{2z}\sin\phi$$
$$\exp(-i\,\phi\,2I_{1z}I_{2z})\;I_{1y}\;\exp(+i\,\phi\,2I_{1z}I_{2z}) = I_{1y}\cos\phi - 2I_{1x}I_{2z}\sin\phi$$

and similarly acting on I_{2x} or I_{2y}. The other rule of course is this: [and here $\phi' = \Omega_1\tau$]

$$\exp(-i\,\phi' I_{1z})\;I_{1x}\;\exp(+i\,\phi'\,2I_{1z}) = I_{1x}\cos\phi' + I_{1y}\sin\phi'$$
$$\exp(-i\,\phi' I_{1z})\;I_{1y}\;\exp(+i\,\phi'\,2I_{1z}) = I_{1y}\cos\phi' - I_{1x}\sin\phi'$$

and using these formulas, we can compute how any "term in ρ" changes under free evolution.

Spin Echo Sandwich. [See Appendix 17.9 for more on SES]. Sequence is $U(\tau/2) * \pi_x * U(\tau/2); t$. In the appendix one can rewrite this exactly by sliding the π pulse to the right (meaning it acts first), to get $U(\tau/2) * U'(\tau/2) * \pi_x$ where $U'(\tau/2) = \pi_x U(\tau/2) \pi_{-x}$ where U is the full expo of H. The pair of $\pi_{x's}$ changes the sign of the linear I_{kz} terms in H, but not that of $I_{1z}I_{2z}$ term, so $U'(\tau/2)$ is the same as $U(\tau/2)$ but with the linear terms negated. If it were true that [$U'(\tau/2)$, $U(\tau/2)$] = 0, meaning that [H(linears negated), H] = 0, then get $U(\tau)_{J\text{-only}} \pi_x$ which is the desired result. The commutator vanishes if τ is very small, then to order τ the H's do commute, and this is the **short duration limit**. If we can use the secular H, then they commute for any τ, but elsewhere we see that secular H is not justified for tiny τ, so this is the **large duration limit**. The point is that in these cases, the spin echo sandwich **SES [$U(\tau/2) * \pi_x * U(\tau/2)$] is replaced by [$U(\tau)_{J\text{-only}} \pi_x$]**and this is shown graphically on page 382.

Now, suppose you adjust τ such that $\phi = \pi J\tau = \pi/2$ so $\sin\phi = 1$ and $\cos\phi = 0$. Then we know the effects of $U(\tau)_{J\text{-only}}$ from above, such as $I_{1x} \rightarrow 2I_{1y}I_{2z}$. Then we can compute $U(\tau)_{J\text{-only}} \pi_x$ acting on any ρ term as shown p 383. The results show that **all double terms (implying correlation) become single terms (uncorrelated), and vice versa**. This conversion is really being done by $U(\tau)_{J\text{-only}}$ and not by the π_x. Why we are interested in doing these correlation conversions is not clear at this point.

Footnote: We know from earlier that $\rho_{mn}(t) = \rho_{mn}(0) \exp[-i (\Omega_m-\Omega_n)t]$. So consider $\rho_{mn}' = [I_{1x}]_{mn} \exp[-i (\Omega_m-\Omega_n)t]$. This tells us exactly what happens to each matrix *element*, but it is **not very obvious** how you would write out the result as a linear combination of the matrix products! For example, if $\Omega_1 = \Omega_2 = 0$ and $\pi J\tau = \pi/2$, we know that $\rho_{mn}' = [I_{1x}]_{mn} \exp[-i (\Omega_m-\Omega_n)\tau] = [2I_{1y}I_{2z}]_{mn}$ exactly. As another example, if J=0, we know that $\rho_{mn}' = [2I_{1x} I_{2y}]_{mn} \exp[-i (\Omega_m-\Omega_n)\tau]$ = 4 terms on page 376 which are a linear combination of $2I_{1x} I_{2y}$, $2I_{1x} I_{2x}$, $2I_{1y} I_{2y}$ and $2I_{1y} I_{2x}$ with coefficients depending on $\Omega_1\tau$ and $\Omega_2\tau$.

---------- Chapter 13: Homonuclear AX Experiments (387-432) ------- 45 p ---------- ###

This chapter describes four kinds of experiments people have done with AX spin systems in which we know that J-couplings between the A and X spins are active. The first three experiments have mnemonic names COSY(2D), INADEQUATE(1D and 2D) and INEPT(1D) and are examples of what one can do with interesting pulse sequences. The States method with its separate "sin" and "cos" sequences is used routinely to make clean 2D peaks. The latter two experiments use spin echo sandwich sequences, and the last demonstrates the concept of magnetization transfer.

The fourth experiment uses "bicelles" to force a solution of AX molecules into an anisotropic liquid state which activates the dipole-dipole interaction in addition to the J coupling, allowing the measurement of the angles of bonds inside the AX molecule. These are all excellent examples for Levitt to use.

COSY. " correlation spectroscopy"

COSY is an application of **2D spectroscopy** to AX molecules, and we get to use the work we did earlier in Chapter 5 on 2D Fourier Transforms. We start with pulse sequence is $(\pi/2)_x$, $\tau = t_1$, $(\pi/2)_x$, t_2 . We find that the peaks occur in two kinds of quartets called diagonal and cross-peak. The edge of the square of each quartet is $2\pi J$ where J is the coefficient of the J-coupling in the AX molecule, so this experiment can measure J pretty well. The four antiphase cross-peaks can be made very clean using the States procedure and this is routinely done. One use is to solve "the assignment problem" which arises if you

only do 1D spectroscopy with two AX molecule types where you get 8 peaks. Page 389 shows that the three possible assignments can be distinguished in COSY.

I have written this section up in a separate document which contains my own explanation of COSY. There I first trace the TE **density matrix** through the first pulse, free period, and second pulse to the start of the FID. This is all done for the "COS" pulse sequence shown at the top of page 390. The result is this:

$$\rho = -I_{1z}C_\phi C_{\theta 1} - 2I_{1x}I_{2y}S_\phi C_{\theta 1} + I_{1x}C_\phi S_{\theta 1} - 2I_{1z}I_{2y}S_\phi S_{\theta 1} + (1\leftrightarrow 2)$$

which shows coherence orders of 0,1 and 2. We have $\theta 1 = \Omega^0_1\tau$, $\theta 2 = \Omega^0_2\tau$ and $\phi = \pi J\tau$, where τ is the inter-pulse interval which we maintain as τ instead of t_1 so our $(1\leftrightarrow 2)$ operation works properly. Keeping only the order 1 terms we have

$$\begin{aligned}\rho &= I_{1x}C_\phi S_{\theta 1} - 2I_{1z}I_{2y}S_\phi S_{\theta 1} + (1\leftrightarrow 2)\\ &= I_{1x}(S_{\theta 1-\phi} + S_{\theta 1+\phi})/2 - 2I_{1z}I_{2y}(C_{\theta 1-\phi} - C_{\theta 1+\phi})/2 + (1\leftrightarrow 2)\end{aligned}$$

Using the convenient operator method [for example, $I_{1y}I_{2z} = (1/2i)(I_1^+ - I_1^-)(I_2^\alpha - I_2^\beta)$] I extract:

$$\rho_{-\alpha}(t_1, t_2) = [\ (1/2)(S_{\theta 1-\phi} + S_{\theta 1+\phi})/2 + (1/2i)(C_{\theta 2-\phi} - C_{\theta 2+\phi})\ ]\ \exp(+i[\Omega^0_1 + \pi J]\, t_2)$$
(1) (2) (3) (4)

where I have added the last factor to account for the FID period and changed $\tau \rightarrow t_1$. I then show where these peaks appear in the page 397 2D spectrum as 1,2,3,4. I do similarly for peaks 5,6,7,8 and then analyze the two quartets to confirm their **location and phasing** as indicated in the picture.

I then show that the cosine terms (only) satisfy the **"States criteria"**. The implication is that if you can find a second "experiment" that generates the same $\rho_{-\alpha}(t_1, t_2)$ as that above, but $C_{\theta 2-\phi} - C_{\theta 2+\phi}$ becomes $S_{\theta 2-\phi} - S_{\theta 2+\phi}$, then you can do the States processing and you will get sharp peaks for the cross-peak quartet peaks (see page 397 grid), although the diagonal peaks become a mess (page 398 grid). I guess Malcolm has nice programs to model and compute these things. [So do I now! See below]

Finally, I analyze the **matching SIN experiment** Fig 13.7 p 390 and show that it is a proper States partner for the first COS experiment (for the cos terms only). Here are the two results compared:

$$\begin{aligned}\rho^{COS} &= +I_{1x}(S_{\theta 1-\phi} + S_{\theta 1+\phi})/2 - 2I_{1z}I_{2y}(C_{\theta 1-\phi} - C_{\theta 1+\phi})/2 + (1\leftrightarrow 2)\\ \rho^{SIN} &= -I_{1x}(C_{\theta 1-\phi} + C_{\theta 1+\phi})/2 - 2I_{1z}I_{2y}(S_{\theta 1-\phi} - S_{\theta 1+\phi})/2 + (1\leftrightarrow 2)\end{aligned}$$

In all of the above I ignore the relaxation factors because I know how to add them in the end: just replace each $i\Omega$ with $i\Omega - \lambda$. I shows that the "other terms" which make the diagonal peak really do come out as D_1D_2 with States, and they are a real mess.

Author comments that with an even fancier cycled pulse sequence, you can get all peaks to be clean, this is called "double quantum filtered COSY" or 2QF-COSY and hints are given in problem 13.2 [and I did the details of this eventually.]

INADEQUATE. "Incredible Natural Abundance Double QUantum TEchnique"

Motivation. This method solves a problem which occurs in molecules like CH_3CH_2OH = ethanol. Most molecules with *any* ^{13}C spins will be ones with *one* such spin. Such single-spin molecules will show two large lines which are just the $\hbar\omega$ lines for the two ^{13}C chemical shift locations existing in ethanol. If you blast on the H protons you can wash out the fine structure they cause and you get two large single lines.

Now suppose you want to study those very few ethanol molecules that have *two* ^{13}C and which are therefore AX systems? We know that a double-spin spectrum will produce four lines, but each pair will be sandwiching the huge single-^{13}C molecular peaks, so you won't be able to even see the four lines. The four peaks are small because the double-^{13}C molecules are so rare in the sample (1 in 10,000).

So INADEQUATE is a pulse sequence which passes these small AX lines, but blocks the big peak lines! It happens that when you use this method, the four peaks show up as two anti-phase peaks as shown page 410, whereas normally they show up as a two pairs of in-phase peaks as shown page 354.

Method. We use a standard SES followed by a phase-cycled finisher pulse, as shown page 405. We use the SES result of Appendix 17.9 which says you can replace the upper with the lower picture on page 405. The order flow diagram is shown page 410 where the back-end cycled pulse acts as a "double quantum filter", only accepting ρ terms like $I_{1+}I_{2+}$ and mapping them to the -1 output order.

What happens to the single-^{13}C ethanol molecules when this pulse sequence is used? We use the lower p405 picture with J=0. We go $I_z \rightarrow +I_y \rightarrow +I_z$ and we are at point 4. If the last pulse were a static $(\pi/2)_x$ pulse, it would flip this I_z to $-I_y$ and we have order -1 output which we don't want. The filter removes this. On page 407 we see how things cancel explicitly, but in Appendix 17.10 we learn more generally why this works and we then don't have to compute it.

What happens to the double-^{13}C molecules with the J coupling? It is easy to show that, at the input to the last (cycled) pulse, we have $\rho = 2I_{1x}I_{2y} + 2I_{2x}I_{1y} = -i\, I_{1+}I_{2+} + iI_{1-}I_{2-}$ which has only order ± 2. This of course gets through the final "double quantum filter". We can compute one phase and then all other phases do the same thing. Author shows this explicitly, but we know it from Appendix 17.10. So the last pulse turns this into $\rho(\text{FID start}) = -2I_{1x}I_{2z} - 2I_{2x}I_{1z}$ and this gives us the pair of antiphase peaks. [It takes some knowledge to understand why that is so. You first take all matrix elements like $\rho_{-\alpha}$ and you tack on each one's unique FID phasor. The $-\alpha$ and $-\beta$ frequencies differ by $2\pi J$, and the I_{2z} factor changes the sign of the β peak making it an antiphase-doublet. The other two signals α- and β- involve the other chemically shifted location, so they make another pair, but a distance away. Hence top of 410.]

Two dimensional INADEQUATE adds another time parameter t_1 as shown page 413. The math is non-trivial (at least the way I did it), but you end up with a States pair (13.13,14) which is the same as 1D INADEQUATE in the τ variable, but has an extra "sum of frequencies" factor in the new $t_1$variable. The result is that the 4 usual spectral points of the 1D spectrum are elevated to the sum height in the 2D spectrum as shown page 415. If you study a molecule with lots of AX systems shifted differently, you get a 2D spectrum as on page 416, and the 2D benefit is that you can "see the groupings" of four, whereas they would all be on a line together in the 1D INADEQUATE. COSY had this same benefit, though the groupings were different in COSY. 2D INADEQUATE of course also filters out the unwanted strong isotopomer peaks, just as the 1D did.

INEPT "**I**nsensitive **N**uclei **E**nhanced by **P**olarization **T**ransfer"

This is the first appearance of "magnetization transfer" in this book. You imagine that you have a hetero AX system with spins we call I and S, and we assume that I has a large γ (like H) and S has a small γ (like

^{15}N). You apply separate pulse sequences as shown p 418, SES-like, and you "take your FID" from the S system with the small γ. The main idea is that the large γ which lies inside the B_I TE Boltzmann factor (making $B_I >> B_S$) *gets transferred* from the I_T spin to the S_T spin by this pulse sequence, and it is the J coupling that does this. You end up as shown page 421 which says $\rho = B_I I_{Iz} I_{Sy}$ and $B_S I_{Sy}$. This causes a large amplitude antiphase doublet from the first term, and a small in-phase doublet from the second term, and these are illustrated on page 421, and what you "get" is the sum of the two (which is mostly the first term). In the QM world of ρ, I see this all happening, but I don't see a simple classical mechanism to explain it, but I am sure there is one. It must be like a pair of coupled pendulums with different mass, and you transfer energy and amplitude from one to the other. I should redo this problem tracking the M_z and the M_T of each spin species and draw some plots. The reason we might want to "take our FID" from the weak species is that the other strong species might have lots of extra lines that confuse the spectrum, though this is not discussed much. For me, the main idea is that magnetization transfer is possible and meaningful.

In a little "coda" section, they talk about a slightly fancier version of INEPT where we sort of "do it again". I am now used to this idea from the MRI spin-echo stuff. In this case, the result can be understood from the final $\rho = B_S I_{Iz} I_{Sy} + B_I I_{Sy}$. Now the strong term is an in-phase doublet (second term), and the weak term is an antiphase doublet (see page 424 graphs). The merging of the two in-phase peaks here results from blasting the I spin during the S FID, and I discuss this in detail in the raw notes.

A key point Malcolm makes early on is that FID ~ $\gamma^{2.5}$ so having a 10X stronger γ can yield a FID that is 300X larger.

BICELLES

Imagine you have an asymmetric molecule, perhaps an ellipsoid. Imagine a C-H bond in this molecule. This method is going to tell us something about the *orientation* of that bond relative to the ellipsoid major axis. It is amazing that you could extract such information doing *anything* in NMR! The trick is to dissolve your molecule of interest in a solute containing Oreo-cookie like **bicelles** which cause the ellipse molecules to line up a small amount in one direction. The bicelles put the test molecules into the state of an **anisotropic liquid**, and this means that, in our AX system, we have our original J coupling, but now we also have a dipole-dipole coupling with its "d-function" which is a function of the angle of our bond relative to the major ellipse axis. [Everything is secular.] So that is how this angle gets into the picture. As shown page 426, you get a J-coupling-like Hamiltonian term, but it contains the J and d-d pieces in the coefficient. So the upshot is that the amount of "J" splitting is going to depend on that angle, in an average over orientations sense. It is good to take this section in general terms, with the point being that the J-splitting-cum-bicelles (with the d-d added into the J, so to speak), can tell you "something about" the angle of a bond in the molecule under test (MUT). [On first reading, I was unable to derive the d(θ) factor, but in secular dipole-dipole.doc I did the derivation, summary comments are in the raw notes for the Ham chapter 7.]

---------- Chapter 14: Multiple Spin-1/2 Systems (435-474) ------- 39 p ---------- ###

This chapter *generalizes* the notion of J coupling between two spins to that involving N spins, with special attention to the 3-spin case which is called an AMX system, where M is the "third spin". Only spin-1/2 spins are considered in this chapter, and things are isotropic as before.

It is not hard to write down the Hamiltonian and compute the eigenenergies. When it comes to coherences, a new element arises when N>2, namely, you can have a -1 coherence of the form ρ_{--+} in which all three spins are active, called a "combination coherence" as opposed to a "simple" one like $\rho_{\alpha\beta-}$ with only one spin active.

As N increases, the number of coherences of any given order gets very large, as shown table page 440.

The "energy of a coherence" (Ω_r - Ω_s) can be calculated from our previous eigenenergies, or using a graphical method presented page 441-2.

In an isotropic system there is lots of degeneracy so the number of distinct spectral peaks is manageable. In non-isotropic systems for biomolecules, you might get a million peaks to worry about -- intractable.

Only the simple (one minus sign) coherences are directly observable in the FID (p 443). The spectrum for an N-spin system is therefore going to have N 2^{N-1} potentially distinct FID peaks (N places to put the – sign, and 2^{N-1} ways to arrange the remaining α's and β's). For N=2 we always had 4 peaks possible. For N=3, there are $3*2^2 = 12$ peaks as shown p 444. If the molecule is "linear" in its graph, meaning $J_{13} = 0$, you degenerate down to 8 peaks as middle page 445. For N=5, expect $5*2^4 = 5*16 = 80$ peaks. Magnetic equivalence can simplify this as shown page 446 where only the traditional 7 lines for A_2X_3 -- this was the fine splitting of an early chapter.

With general N, there are lots of fancy terms possible in ρ, such as $I_{1z}I_{2x}I_{3y}$. As we know, each term implies a certain position and polarity of spectral lines, and this is explored on page 448-9 for N=3. As usual, an I_z factor causes a polarity flip somewhere.

In TE, we have $\rho = 2^{-N}(1 + BI_z)$ where I_z is the sum of our N contributions. The leading factor was 1/4 in our N=2 work, here it is different.

We already know what a pulse does to any "term" in ρ.

When we consider "free precession" with N=3, we have 6 Ham terms to worry about, 3 are chemical shift, 3 are J couplings of $I_{iz}I_{jz}$ form. Page 453 lists certain "terms" which "don't evolve under J coupling", only under the "chemical shift" as shown page 452. Otherwise you have to do the computation, and an example is given of how a particular term moves under J couplings.

Spin echo sandwiches with N≥3 have a similar simplification to the N=2 case and by picking τ carefully, you can achieve desired "term conversions" as top page 457. The SES was used in the **INEPT** sequence which achieved **mag transfer** from I to S in a hetero IS system (N=2). Here that experiment is generalized to N > 2, and we find slight differences in "transfer enhancement factor" onto S between IS, I_2S and I_3S, which is not surprising. [The "refocused INEPT" is considered here, which has τ and τ' variables.]

We now ask "what happens in COSY for N > 2? " Recall that in COSY N=2 we got a set of 4 quartets which formed a larger square, as on page 394, with two diagonal quartets and two cross quartets. We learned how to do DQF COSY to make all the peaks look States-clean.

For N=3 we get 9 16-tets which form four large squares as on page 462 (instead of getting 4 quartets which formed one square for N=2). Each dimension of one of the "tets" will always have 2^{N-1} peaks so the "tet" will have 4^{N-1} peaks (4 for N=2, 16 for N=3). The number of tets will be NxN because in each dimension there are N different chemical shift values for the N spins. [Ignoring the tet groupings, each dimension will have N 2^{N-1} peaks (as noted 5 paragraphs above), so the 2D spectrum will have N^2 4^{N-1}

total peaks, in agreement with what we just said above. The peak groupings arise because usually the chemical shifts are large and the J couplings are small.]

Malcolm figures out the polarity pattern of the top center 16-tet shown page 462 (or 465).

We are then posed a problem. Suppose we do N=3 COSY on a system containing AMX and A'M'X' species (could be a single molecule containing both these situations). If the molecules are "nonlinear" (in their J coupling graph sense), even though the two box-like spectra appear in the same spectrum, we can disambiguate them. However, for linear molecules, the NW and SE corner 16-tets are missing because $J_{13} = 0$ in this case. Then we cannot disambiguate if it happens that M and M' have the same chemical shift!

The **TOCSY** pulse sequence (Total Correlation Spectroscopy) then *solves* this last problem by causing those two corner 16-tets to reappear! TOCSY does this by replacing the final COSY knockdown pulse with a set of several hundred closely spaced π_y pulses. As well described by Malcolm without math detail, this causes the transverse spins to equalize (more or less) between all three spin species, so an "effective" J_{13} coupling arises from these π pulses from the existence of the J_{12} and J_{23} existing couplings. It is this effective coupling which then restores the missing corner 16-tets and solves the ambiguity problem.

---------- Chapter 15: Motion (479-511) ------- 32 p ---------- ### 3.25-26.08

This chapter opens with a broad and quick survey of kinds of motions: **libration** p 479, rotation of groups about the bond connecting them to the main body of the molecule, chemical exchange is regarded as a "motion" -- two forms separated by some activation potential as in 480 bottom or 481 top. Free rotations of molecules themselves. Mention of "**magic angle spinning**" or **MAS** which causes the average angle for dipole-dipole interaction to be the magic angle (see separate doc), so the d-d relaxation mechanism goes away and spectral lines become resolved into finer lines (since less relaxation).

Malcolm talks on page 485 about various **timescales** for motions. On page 486 he shows how various processes fit into these timescales.

We then go off and do a fairly detailed treatment of **"two-site exchange"**, and we study several interesting situations where this model applies.

Application 1: Most of the work is done in Appendix 17.12 where we produce a matrix equation which describes the rate at which coherences (ρ_{A-}, ρ_{B-}) change in time, where A and B are two spin locations in a molecule (with different chemical shifts) and one spin (or more than one) moves back and forth between these two locations. When we solve this matrix equation, we find a certain spectrum shown on page 631. Depending on how fast the exchange takes place (rate k) relative to the chemical difference frequency (Ω_Δ), we either get two separate lines, or we get one line. All the math is here. For small k (or no k), you get your usual **two spectral lines** because there are two chemical shift positions A and B. As k increases, the lines **move closer and get broader** and they merge at a critical value of k where they become a broad peak. As k is increased beyond this point, this broad peak stays a single peak, but ***narrows***. The entire situation is shown page 495 on a time scale drawing, double peak on the left, single on the right.

Application 2: We will find in Chapter 16 that, for an IS two-spin system, the relaxation of I spins can *appear to be* an exchange situation where the I is either up or down, acting as A and B positions for the S spin; this produces two environments for the S spin and so we get the exchange effect described in the previous paragraph for the S spin. If the I spins flips fast due to fast relaxation, that is like large k and

we get a single narrow peak for our S spin (which is J-coupled to that I spin). But if the I spins flip very slowly due to long slow relaxation, then there is little effect on the S spin and we get the usual two peaks. So this subject here is how the relaxation of "the other spin" can affect the spectral line appearance of a spin under consideration.

Generalization: In the previous examples, we treated exchange where k was the rate for both directions of the chemical reaction, but we can also consider an **asymmetric** reaction where the two rates are **k and k'**, and these result in different molarities on the two sides of the reaction so get **K = k/k'.** This asymmetry results in the two peaks being ***different in height*** (because one environment is used by the spin most of the time). When the exchange rates increase, the peaks merge into one which is ***off-center*** due to the asymmetry, all as shown on page 498. So here the idea is that NMR experiments can measure chemical reaction K values in certain situations!

Application 3: The next topic is the **Knight Shift** in metals, and it is just an example of 2 paragraphs back. There we talked about the I spin having two states α and β due to relaxation and this affects the S spin. In the Knight shift, you are looking at some nuclear spin S in the solid, and the relaxation is in fact an *electron* spin that is going up and down α and β, not a nuclear spin. This electron spin is from an unpaired conduction electron in a metal. Since μ_e is huge compared to nuclear spins, this relaxation rate is very fast, so we are in the large k limit in our little exchange model. That means you get a single narrow line and it is shifted off the center point of the usual nuclear spin peaks *because* the α and β electron spin states have different energies so $k \neq k'$. This shift is the Knight shift, and here we are interpreting it as an exchange effect in which the nuclear spin is experiencing swapping environments A and B. The same math solves many problems.

The next subject is how to do **2D exchange spectroscopy** such that you can measure the value of k in a symmetric exchange process, especially when k is very small, where observation of peak broadenings is not really doable. One again, the math heavy lifting is done in an appendix, this time Appendix 17.12.4 page 631. We assume that we have some transition rate W between α and β states of a spin (one type now), and we *also* have a symmetric exchange process k which takes the spin between two environments. The rate W which connects to two populations represents **longitudinal relaxation**. As in the last appendix, we come up with a matrix equation describing the populations α and β in the A and B situations, so we have a 4-vector of populations as our variable, and a 4x4 matrix containing W and k to represent the time rate of change of the vector. By *converting* from the four populations to the two magnetizations $\langle I_z \rangle_{A,B}$ we end up with a 2x2 matrix equation which looks exactly like our previous exchange 2x2 matrix equation, but some values in the 2x2 matrix are substituted. We solve this matrix equation as before, and we come up with four "flow rates" such as a rate $a_{A \to B}$. At the end of the mix period, for $\langle I_z \rangle_A$ we have the amount that remained there from the start of the mix period $a_{A \to A}$, plus the amount of magnetization that transferred over from the $\langle I_z \rangle_B$ that existed at the start of the mix period. The variables $\langle I_z \rangle_A$ and $\langle I_z \rangle_B$ are cross coupled by the exchange rate k and so affect each other in a way that does not happen in free propagation. They "mix" during the mixing period τ_m. The four flow rates have the form diag = $\cosh(k\tau_m)$ $\exp(-(k+1/2W)\tau_m)$ and cross = sinh same thing, and these four flow rates *become* the heights of the four peaks that occur in the little 2D spectrum that emerges from our 2D spectroscopy pulse sequence (variables are t_1 and t_2 page 501). By looking at the relative size of the cross peaks for various values of τ_m (the duration of the mixing period), you can deduce the size of k, even if it is very small. This general method is called "exchange spectroscopy". The pulse sequence uses a phase cycle to remove certain undesired terms from the ρ matrix at time 4 in the sequence -- only order

0 is preserved by the little phase filter. There are 4 peaks because there are 2 peaks in each dimension because k is assumed small.

We shall see this subject appear again in Chapter 16.

---------- Chapter 16: Relaxation (513-568) ------- 55 p ---------- ### 3.26-31.08

(1) We start off with a list of relaxation mechanisms: tumbling vs dipole-dipole , tumbling vs chemical shift (called CSA), tumbling vs spin-rotation, tumbling vs electric quadrupole. The chapter later provides examples of the first two mechanism, but not of the last two.

We then do a "**noise** review" with an understanding that tumbling/banging-around of molecules causes fluctuations in B_x (a prototype variable). These fluctuations are characterized by an autocorrelation function $G(\tau)$ where $G(0)$ is the fluctuation total energy per unit volume ~ B_x^2. The FT of $G(\omega)$ is called $J(\omega)$ and is the **spectral density**, and I had some issues with now this is normalized. This last fact follows trivially from my old friend diagonalization.

Malcolm then asks how this fluctuating B_x^2 affects a spin system, and without mentioning it, he uses the **Fermi Golden Rule** to derive the rate W between the up and down levels. He than has to correct this rate W to account for the TE energy levels being a little different, so we get $W_{\pm}$.

With B_x^2 treated as a constant, from the calculation of $W = (1/2)\gamma^2 J(\omega_0) \langle B_x^2 \rangle$, we now have our first physical model for $T_1 = 1/(2W)$, this last relation being obtained from a simple relaxation equation he develops on page 524 based on rates $W_{\pm}$ and $d\rho_{pop}/dt$. The plot of T_1 versus τ_c shows a minimum at $\tau_c = \omega_o$, our spin α-β energy gap. We expect τ_c to decrease as temperature T increases , so we can predict how a system's T_1 might "move along the T_1 vs τ_c curve". I had my issue with possible temp dependence on B_x^2.

(2) We now delve into the large subject of **"longitudinal dipole-dipole relaxation"** which of course requires at least 2 spins, so we do it with exactly two spins. We draw the usual 2-spin energy level diagram and give names to the transition rates between levels such as W_{++}. All these rates are "adjusted versions" of the three basic rates W_0, W_1 and W_2. I summarize my calculation of each of these rates. Malcolm then writes down rate equations for the 4 populations using the same 4x4 matrix method just mentioned in the last chapter, but here we have 2 spins instead of 1 spin to worry about and now we have a variety of rates. Because the matrix equation is in block form, we can extract a subset 2x2 matrix equation, this time for $\langle I_{z1,2} \rangle$, whereas before it was $\langle I_z^{A,B} \rangle$. The coefficients of the 2x2 matrix are R_{cross} and R_{diag}, and each is a linear function of the various W_i rates. Malcolm then goes on to write a simple equation for the d/dt of the *total* I_z, and this leads to the conclusion that total I_z has $1/T_1 = R_{sum} = R_{auto} - R_{cross}$. He makes graphs on page 535 showing how R_{auto} and R_{cross} vary with τ_c. R_{cross} starts negative, has a minimum, then has a zero crossing and goes positive, which is not very useful we shall later learn. The new T_1 is plotted versus τ_c and has the same shape as our earlier general prototype case with $\langle B_x^2 \rangle$. This T_1 is caused specifically by the dipole-dipole relaxation mechanism!

The 2x2 equation has the same form as in the $\langle I_z^{A,B} \rangle$ of the last chapter, and therefore has the same solution and the same implications. In the current context, the 2x2 equation is given the fancy name **Solomon Equations**, page 534. The solutions imply that there is "mixing" between $\langle I_{z1} \rangle$ and $\langle I_{z2} \rangle$ during free propagation. He has not used the solution of these equations yet, but when he does we know

that the solution is going to involve mixing rates like $a_{1\to1} = \cosh(R_{cross}\tau_c)$ exp(...) and $a_{1\to2}$ = sinh, etc.

(3) Malcolm now states that there is also a theory of **"transverse dipole-dipole relaxation"**, but he skips the derivation here and just quotes the results. We have the same Solomon-like equations, but now the variables are presumably $\langle I_{T1,2}\rangle$ and the 2x2 matrix contains R^T_{auto} and R^T_{cross} which are similar linear combinations of the rates. I think this subject returns later.

(4) Now we move to an application called the **steady-state (SS) nuclear Overhauser effect** or **NOE**. This applies to a hetero I-S spin system where you irradiate the I system with strong resonant RF. This causes the population equalizations shown on page 540, and then a simple rate balance equation (16.26) leads to an amazing result. We find that the TE population equation has been altered and now has the form $\rho_{SS} = 1/4 + 1/4\ \varepsilon_{NOE}\ B_S S_z$ instead of $\rho_{TE} = 1/4 + 1/4\ B_I I_z + 1/4\ B_S S_z$. We certainly thought that the irradiation would remove the I_z term , but we are surprised to find that the residual S_z term is "enhanced" by the NOE factor. This factor is a function of γ_I and γ_S and the rates W_i, and can be as large as 4. If one is trying to do spectroscopy on the S spin system, one gets this "signal boost" by applying irradiation (blasting) to the I spin. All the math is done here and I checked it using Maple. Somehow we are getting a magnetization transfer effect here from the I spins to the S spins, somewhat as we saw in the INEPT situation. ε_{NOE} being a function of the W_i is therefore a function of τ_c (correlation time) and Malcolm plots $\varepsilon_{NOE}(\tau_c)$ on page 542. Assuming I = ^{1}H, in the case of S = ^{13}C, ε is always positive, but in the case of ^{15}N it changes sign, starting negative and ending positive.

The physicist Albert Overhauser in 1953 discovered this effect in a system where I = electron spin and S = nuclear spin. Since μ_e is 1000 times larger than $\mu_{nuclear}$, he found an enhancement of a factor of 1000, not 4. So what we have here is the "nuclear" Overhauser effect.

(5) At this point we start into the **NOESY** pulse sequence, and the reader is anxiously waiting to see how this applies the NOE I-S spin effect he just read about. But it turns out that NOESY just carries the NOE name, but does not apply the NOE effect. For example, there is no "irradiation", but it does apply to an I-S system and we are going to see some kind of spin magnetization transfer.

The NOESY pulse sequence is the same as the pulse sequence on page 501 used for exchange spectroscopy. It is a 2D sequence with times t_1 and t_2, and there is a mixing time of duration τ_m. Instead of mixing $\langle I_z^{A,B}\rangle$ during time τ_m, we are now going to mix $\langle I_{z1,2}\rangle$ where 1,2 = I, S. So now Malcolm finally uses the known solution I mentioned above a few paragraphs, with $\cosh(R_{cross}\tau_m)$, and we get the same mixing situation and the same 4 peak spectrum with two diagonal and two cross. We noted earlier that R_{cross} starts off negative for small τ_c, so this implies negative cross peaks in the NOESY spectrum. The main idea of NOESY should not be lost: by examining the relative heights of the cross and diagonal peaks, and doing this for several experimental values of τ_m , one can deduce the value of R_{cross} and can therefore deduce the size of the dipole coefficient b which is a scale factor (as b^2) for R_{cross}. Since we know that $b \sim 1/r^3$ where r is the dipole spacing (through space!), one can deduce the spacing of pairs of spins in a fancy molecule, and one can thereby determine its shape! This is of particular interest in finding the shape of proteins!! Page 549 shows an example of a NOESY spectrum for a protein and you see that there is lots of information in such a spectrum. They used this to nail down the shape of this protein, and it is shown in one of the Plates. This is a major victory for NMR I think, and the result was

quoted in Watson as well. The only other way to determine protein shape I think is crystallization and x-rays which is not easy.

(6) Next comes a similar pulse sequence called **ROESY**. The sequence is similar, but now there is irradiation during the entire τ_m mixing period, as shown page 554. In this experiment, we are going to have a mixing not of $\langle I_{z1,2} \rangle$ between the I and S spins, but a mixing of $\langle I_{x1,2} \rangle$. This mixing is going to happen due to the transverse dipole-dipole relaxation mechanism, not the longitudinal one. Malcolm quoted without proof the 2D Solomon equation, and he repeats that here giving expressions now for R^T_{auto} and R^T_{cross} as functions of the J(ω) functions evaluated at the usual points 0, ω_0 and $2\omega_0$. [this means he is thinking now of an I-I homo system, not an I-S hetero one, at least for his presentation.] We know that we are going to get the usual cosh formula for peak amplitudes here, but now it turns out that R^T_{cross} is always negative, which is helpful in spectral analysis. So sometimes ROESY is cleaner than NOESY in doing an analysis of a molecular shape. One major issue in ROESY is that you have to do spin-locking so that transverse magnetization transfer can actually happen and be maintained. This is the function of the irradiation used during the τ_m mixing period. A very strong RF field is needed to get the spins to lock, and Malcolm gives a good description of how the locking occurs, based on earlier work in the book.

(7) The subject now changes to a new one called **cross-correlation**. We have two noise-like parameters and we can write a cross-correlation function which is a generalization of the autocorrelation function for one noise variable. If there is a strong cross-correlation, it suggests that some underlying process is responsible for both noise variables. In our examples to follow, that underlying process is molecular spin, and the two variables are going to be the effects of multiple d-d interactions, or the effect of one d interaction and a CSA situation. In either case as a molecule spins, we get this "cross correlation" between different d-d pairs because the molecule is rigid and when it rotates, the pairs have a fixed geometric relationship to each other.

Case 1: correlation between two dipole systems, call it **DD/DD cross correlation.**

The first example is hard for me to embed in the framework just described. If we have two C-H bonds as shown page 560, we know that the angle between them stays fixed during rotation, it is a parameter of the problem. My question is: what are the two noise variables whose correlation we are interested in here? I think the answer might be they are the effects that these two C-H systems have on some as yet unmentioned third system. If we jump over to the molecular example on page 561, that third system would be the C-C dipole situation connecting the two C-H spin pairs.

So we now go study this molecular example (without math). The two C atoms of interest are somehow labeled as ^{13}C. We have a 4-spin system in the sense of Chapter 14. Somehow we have to imagine a pulse sequence which exposes the double-minus coherences (I am OK with that since we saw it on DQ COSY). So somehow we imagine resonance peaks for things like $\rho_{\alpha--\alpha}$. Here, the two C atoms are in the middle, so they are both making transitions from α to β at the same time. In general, for each such coherence, we expect a spectral peak (when the double quantum is somehow converted to a FID), so we expect four peaks in this double-quantum spectrum. The whole discussion here is going to be about the *widths* of these four peaks!

We start by drawing a geometric picture to associate with the $\rho_{\alpha--\beta}$ spectral peak, page 562. The claim is that the two H atoms lying as satellites to the two C atoms have subtractive effects in this picture.

That is to say, the B fields which the H atoms make for the C atoms are subtractive in some sense (which is not made clear because we have run out of book!) This means that the d-d relaxation effects on the C atoms from the H atoms are subtractive, and that means we will have a slow relaxation rate (small W, large T, small width λ), and we know that implies a narrow peak, as shown center top 562 for the two central peaks. Conversely, the $\rho_{\alpha--\alpha}$ geometry shown on page 563 implies an additive effect so we expect a fast relaxation, hence large W, small T, large λ, and indeed we see broad peaks on page 562 top. Similar comments are made about the other molecular "anomer" which has different geometry and therefore different conclusions.

So again, we have two C-H systems affecting a C-C system here, and the two C-H systems are "cross correlated" as indicated by the geometric pictures (which pictures and their conclusions are invariant under rotations of the molecule).

The implication here is that by studying widths of the spectral lines, one might be able to figure out the angles of the geometry of this H-C-C-H 4 spin system, and I think that really can be done, but the details are certainly not presented here!

Case 2: correlation between a dipole system and the CSA, call it **DD/CSA cross correlation.**

Here the rotation affects both the dipole system, and the B field generated by induction from the B_o field, so we expect cross correlation somehow between the DD and the CSA mechanisms. Again we use simple geometric pictures and we either get an additive or a subtractive situation, depending on whether the N-H dipole has the H proton in the α or the β state. These two cases then result in different rates of relaxation of the ^{15}N spin. The spectrum shown page 567 shows these different widths. You can select the B_o field size to get exact subtractive cancellation in the one case, and this makes an optimally narrow peak for that case. The application of **TROSY** is to heavy molecules like proteins which have large τ_c and therefore small T_2 [see page 538 graph] and therefore have unpleasantly broad spectral peaks. The TROSY cancellation mechanism makes these peaks narrow again, allowing you to "do spectroscopy" on heavier molecules that you would be able to do otherwise. TROSY = Transverse Relaxation Optimized Spectro.

APPENDICES

Appendix 17.1: Rotations and Cyclic Commutation p 573-4 2 pages

Gives a derivation of the basic sandwich formula. I did my own general derivation in "evaluate n dot J rotation of J.doc" and got this result

$$\exp(-i\theta\,\hat{\mathbf{n}}\bullet\mathbf{J})\;J_k\;\exp(+i\theta\,\hat{\mathbf{n}}\bullet\mathbf{J}) \;=\; J_k\cos\theta \;+\; \varepsilon_{kms}J_m n_s\sin\theta + n_k(\hat{\mathbf{n}}\bullet\mathbf{J})(1-\cos\theta) \qquad (1)$$

which I can specialize as needed (see "sandwich rules page.doc"). I did two derivations, one uses the CH formula, the other uses rotational arm-waving.

Appendix 17.2: Rotation Sandwiches p 575 1 page

The formula proved here says this:

$$R_x(\theta)R_y(\beta)R_x(-\theta) = \exp\left(-i\beta\, R_x(\theta)\, I_y\, R_x(-\theta)\right)] = \exp\left(-i\beta[\, I_x \cos\theta + Iy \sin\theta] \right)$$

For me, the proof is given in the above line along with the sandwich result of the previous appendix.

Appendix 17.3: Spin-1/2 Rotation Operators p 576-577 2 pages

The three 2x2 rotations are written down here. One is derived using the usual expansion of expo. I have these written on my tool-kit rotation matrix pages.

Appendix 17.4: Full Quadrupolar Interaction p 577-578 2 pages

This appendix simply quotes the Hamiltonian describing the interaction between the nuclear electric quadrupole moment and gradients of the electric field seen at the nucleus. A simplified secular approximation is also stated and this is what is quoted in the main-line text of Chapter 7 page 201. I went off and did my own derivation of the full result in Section 9 of "multipole expansions.doc", it was non trivial.

Appendix 17.5: The Secular Approximation p 578-582 6 pages

I was never happy with this appendix. I think you really need to do second-order perturbation theory to understand why and when you can throw out off-diagonal terms in a Hamiltonian. For example, you might have H' = $\mathbf{I}_1 \bullet \mathbf{I}_2$ and you reduce this to $I_{1z}I_{2z}$ with the idea that a term like $I_{1x}I_{2x}$ only has off-diagonal matrix elements. This appendix says what the approximation is, but not why it is valid. Maybe at some future time I will appreciate this appendix more.

Appendix 17.6: Magnetic equivalence with J-couplings p 583-585 2 pages

This excellent appendix first proves a general theorem about throwing out certain terms in a Hamiltonian, then it applies this theorem to J-coupling and all those $\mathbf{I}_1 \bullet \mathbf{I}_2$ terms. He shows that spins which are in the same mag equiv group don't interact with each other, so those J coupling Hamiltonian terms can be omitted. This is represented on his diagrams by throwing out the interaction lines connecting such equivalent spins. Remember that mag equiv means chem equiv *and* all J couplings to other spins are the same. This appendix is referenced from Section 8.5 page 229 which discusses magnetic equivalence. I provide my own complete proof of the theorem and its application in my notes for Chapter 8 Section 8.5.

Appendix 17.7: The Quadrature Receiver and coherences p 585-588 3 pages

Malcolm draws a picture of the NMR quadrature receiver and, starting with the notion that Voltage ~ B_x ~ M_x ~ ρ_- and he ends up with the result that [where s(t) is "the NMR signal"]

$$s(t) \sim 2i\omega_{Larmor}[\text{ sum of } \rho_- \text{ coherences }] \exp(-i(\phi_{rec} + \phi_{dig})]$$

The 2 comes from the fact that ρ_+ and ρ_- both contribute, and the $i\omega_{Larmor}$ comes from the time derivative of Faraday's law. Larger B^0 means larger ω_{Larmor} and so larger s(t), called "high field" situation.

A key idea is that $M_x \sim tr(\rho I_x)$ and this picks up the ρ_- terms in ρ. Actually, the appendix only shows this for the single spin-1/2 system. But for two spins, you would have $tr(\rho[I_{1x} + I_{2x}])$ and somehow you would get the result I claim. The receiver here is really a "detector" or perhaps a "demodulator". It makes use of the transmitting signal as a heterodyne reference signal, and it has mixers which multiply signals, and then bandpass filters. The output signal s(t) written above has a Re and Im part and these two real output signals are then sent to the first Fourier Transform. I suppose you could do this detection either in analog or digitally using L3 methods. The above result is first quoted in the spin-1/2 ensemble Chap 10 page 305, the chapter in which coherences are first introduced.

Appendix 17.8: Strong J Coupling p 588-593 5 pages // read this 4.1.08

This information was not needed in the book, but the problem is interesting. We know that the full J coupling has a dot product $\mathbf{I_1 \bullet I_2}$ but every time we compute something with it in the book, we make the "weak J coupling" approximation which says $J_{12} << \Delta\omega$ and then we write $I_{1z}I_{2z}$. In this appendix, he wants to see what we can do if we keep the full dot product. As part of this analysis, he throws in a secular d-d coupling, not attempting to "do it" also in the full sense. It is the strong J coupling we are really interested in here. SO, we start with the Ham shown page 588. Notice that part of the secular d-d coupling mimics the J coupling, so the true coefficient of the dot product is $[2\pi J - d]$.

It turns out that if you treat this as a 4x4 matrix system, you can diagonalize H if you properly mix the interior two states which we called $\alpha\beta$ and $\beta\alpha$. The mixing angle is called ζ and it is a function of 2πJ-d and the chemical split Ω_Δ . As $\zeta \rightarrow 0$, the interior states approach our usual states and we are back in the weak limit. Larger ζ means we are truly in the "strong" regime.

In this new 4-state basis, you do some work to compute the coherences which have names like $\rho_{32}(0)$, just after a standard knock-down pulse. We then let these propagate with their proper eigenenergies and thus we have $\rho_{32}(t)$. To compute what the FID will see, we need $M_x = tr(\rho I_x)$, and this then involves matrix elements of I_x between the true eigenstates. We compute these and get 17.27 which shows our FID term for each coherence, and these matrix elements now appear as weighting factors ("efficiencies"), not the same. We finally end up with a spectrum of 4 peaks with frequencies shown bottom p 591 such as Ω_{21} and with coefficients such as a_{21}. The problem is now solved, and everything is a function of the dimensionless parameter ζ.

Malcolm then does some "simulations". In these simulations instead of varying ζ, he varies Ω_Δ while keeping the numerator 2πJ-d fixed. Generally when this Ω_Δ denominator is large, ζ is small and you are in the weak limit and we get our traditional AX spectrum of 4 peaks: two large separated pairs from the chemical shift, and then each split in two by J. As ζ is increased, the peaks move together and converge into one peak group, and subtle things happen to peak heights in the middle ground where we have strong coupling called AB. In the *extreme* limit it is the same as if you set $\Omega_\Delta = 0$ which means same CS's which is the *magnetic equivalence limit* where we know we can ignore J coupling between our two spins, and we just get one strong peak. The three regions are called **AX** then **AB** (strong J coupling) and then $\mathbf{A}_2$ for the mag equiv limit. [in this example d=0 so there is no d-d splitting in this limit.]

He makes three sets of plots for various sizes of the J and d in the 2πJ-d factor. The first has d=0 and merges to that single line. The second has J=0 instead and the limit is a d-d doublet. The third case has J and d set to the same value (really d/2π).

Appendix 17.9: Spin Echo Sandwiches (SES) p 594-597 4 pages

This appendix is referenced from Chap 12 on AX systems, page 381. It proves that, in two limits (small τ and large τ), you can replace the SES shown page 381 with the equivalent (and easier to work with) pulse sequence shown top of page 382. In this equivalent sequence, only the J-coupling part of the Hamiltonian drives the free propagation. So we only have to rotate things by $I_{1z}I_{2z}$ instead of by this plus the chemical shift terms.

The SES is used in the INADEQUATE experiment page 405.

On page 598 the conclusion is generalized for a situation where you have multiple SES in series. You just slide all the π's to the left.

The last section talks about dealing with a heteronuclear pair of spins. If you apply separate overlapping π pulses to the I and S systems, you get the same result for the equivalent system shown, where we get only J coupling for both. Or you might just apply your π to the I system, and then only it is simplified.

Appendix 17.10. Phase Cycling. pp 600-626 26 pages

This is a very substantial appendix. It begins showing on page 601 the notion of coherence order flow in terms of dark lines moving along the "order staff" (in the sense of a musical staff). Another example is shown on page 602 that is a little fancier. This is all motivation.

A. Theory

Then on page 603 we have an excellent picture showing the idea that there is an quantum amplitude for any pre-pulse coherence to *be* some post-pulse coherence. This amplitude is denoted by quantity Z(ϕ,β) which is of course a function of the nature of the pulse $R_{\phi}(\beta)$. In my writeup "phil theory of coherence flow.doc" I show an explicit expression for Z for the 2-spin AX system which is this: [think for example ab = αβ = up, down]

$$Z_{ab\leftarrow cd,ef\leftarrow gh}(\phi,\beta) = [R_x(\beta)]_{ae}\,[R_x(\beta)]_{bf}[R_x(-\beta)]_{cg}\,[R_x(-\beta)]_{dh}\ \exp\{-i\phi\,\Delta p^{ab\leftarrow cd,ef\leftarrow gh}\}$$

This is the amplitude through a pulse where $_{ef\leftarrow gh}$ is an arbitrary input coherence and $_{ab\leftarrow cd}$ is an arbitrary output coherence. $\Delta p^{ab\leftarrow cd,ef\leftarrow gh}$ is equal to order($_{ab\leftarrow cd}$) - order($_{ef\leftarrow gh}$). It is the difference in the orders of the two arbitrary coherences that we are looking at on the two sides of the pulse. This coherence order difference controls completely the ϕ dependence of Z, while the various R_x 2x2 rotation matrices control the β dependence. In this same writeup, I define a coherence vector ρ, and then the effect of a pulse is expressed as $\rho' = Z\rho$.

We have a similar expression which describes coherences moving across a "gap" between pulses. We know that each coherence just phases according to its eigenenergy, so we can represent this as a diagonal matrix

$$(P(\tau_b))_{jk} = \exp(+i\,\Omega_j\,\tau_b)\,\delta_{jk}$$

where now we have switched to more compact indices like j which denote ρ vector components. For example, the index j might have the value αβ for our 2-spin system. The τ_b is the duration of the gap, and of course P is a diagonal matrix. P stands for free Propagation.

When we have a *sequence* of pulses, we can imagine a "coherence music staff" which has one line for each coherence. We can then draw paths from TE input coherences to final order -1 desired FID output coherences, and such a path rides along the staff and zigs through each Z pulse with an amplitude as shown above. I show in my writeup that the final NMR signal is a sum over all paths. For example, if there are three pulses and two gaps in a sequence, we have our output NMR signal equal to this:

$$s(\phi_3,\phi_2,\phi_1) = 2i\,\Sigma_{ikmn}\;\; p_{ikmn}(0,0,0)\,\exp(\,-i\;\;\Phi_{ikmn}) \;\; = \Sigma_{ikmn}\text{ "path" } = \text{"sum over paths"}$$

where

$$p_{ikmn}(0,0,0) = M_{-1,i}(Z_3(0))_{ik}(Z_2(0))_{km}(Z_1(0))_{mn}\,(\rho_{in})_n\,\exp\{+i\,[\,\Omega_k\,\tau_b + \Omega_m\,\tau_a]) = \text{"path"}$$

$$\Phi_{ikmn} = [\,\phi_3\,\Delta p^{ik} + \phi_2\,\Delta p^{km} + \phi_1\,\Delta p^{mn}\,]$$

The ϕ dependence of each pulse has been extracted and placed in the factor $\exp(\,-i\;\;\Phi_{ikmn})$ where Φ_{ikmn} is the total "path phase". The factor $\exp\{+i\,[\,\Omega_k\,\tau_b + \Omega_m\,\tau_a])$ contains a similar path phase describing phasing during the gaps, but this phase is not emphasized by Levitt. [You might do some kind of phase cycling by varying the τ's in a sequence, but this subject is never broached.]

The matrix M is my "order matrix" which projects coherences into their order class, and we apply it at the end of the line because we want to get the total -1 order signal. The matrix element $M_{J,i} = 1$ if coherence "i" is of order J, otherwise it is 0. In our 2-spin case, M is a 5x16 projection matrix. If we apply matrix M to a coherence vector **ρ** in any gap, we produce an "order vector" **O** and we can write **O** = M**ρ**. Wherever an order vector has non-zero components, we draw a dark line in our figures.

Of course (ρ_{in}) is the input coherence vector.

B. The Phase Cycling Idea.

Consider the path phase $\Phi_{ikmn} = [\,\phi_3\,\Delta p^{ik} + \phi_2\,\Delta p^{km} + \phi_1\,\Delta p^{mn}\,]$. If we decide to "cycle" for example phase ϕ_3 (the third pulse) through some periodic pattern of N steps, and if we represent this cycling as $\Sigma_K\, s(\phi_3(K),\phi_2,\phi_1)$, the K sum can be pushed all the way to the right in our expression for s, and at the far right we end up with this factor

$$\text{sum} = S = \Sigma_K\;\exp(\,-i\;\;[\,\phi_3(K)\,\Delta p^{ik}])$$

By an appropriate selection of the pattern sequence $\phi_3(K)$, one can cause the sum to vanish *except* when the order change Δp^{ik} is equal to a set of evenly spaced order values. When a pulse is phase-cycled in this manner, the pulse acts as a "coherence order filter", passing some coherence orders and not others. You can think of phase cycling as filtering the order vector **O** which emerges from the cycled pulse.

C. Application.

The idea is that you phase-cycle some pulse to create a filter which will zero out all coherence paths through the pulse sequence which are undesired. We saw above how this filtration happens in a very isolated way. For desirable paths that are *not* filtered away, we want to make sure their outputs reinforce each other at the output, and that is done by cycling the post-FID digital phase ϕ_{dig}. Notice that the pattern installed into ϕ_{dig} has no effect on the filtration characteristics of a phase-cycled pulse somewhere in the pulse sequence.

The appendix then gives quite a few examples and gives a set of instructions on page 611 for how you construct a phase-cycle filter to meet your needs. The order separation of allowed order paths is equal to N, the number of steps in the cycle, so larger N gives you better order "rejection". If N is large enough, you can select a single path between two pulses, where either one is the one cycled. Or you could perhaps select only two paths with a smaller N.

Due to the way things appear in the path phase Φ_{ikmn}, you can cycle a block of pulses in exactly the same way you cycle a pulse, and this is shown on page 616 and following. The requirement is that a block is treated as a phase-rigid object, so you have to cycle all the pulses in the block in the same way.

On page 617 the INADEQUATE method provides a phase-cycling example. At the start of pulse B, we want to pass (to -1 output) only the "double-quantum" order coherences and block all others. So we set up an N=4 filter and select -1 one of the pass channels. The filter will then select input orders +2, +6, ... -2, -6 ... . However, there are no ±6 coherences, so the filter acts as a perfect double-quantum-filter. This subject is treated in detail in Chapter 13, but here we see the "phase cycling" understanding of what is really happening at the back end of this pulse sequence.

On page 618 we see our first example of simultaneously applying phase-cycling to more than one pulse. In this case we use N=2 on the first pulse and N=4 on the last pulse. Whether or not you phase-cycle the first pulse, the cycled last pulse provides the same double-quantum filter just described above. It then turns out that this sequence provides a clean "sin" term for a COSY pair. For the "cos" sequence you set the first pulse to ϕ_{-y}. The cycling of the first pulse just complicates the understanding here a bit and perhaps assists in reducing error somehow, and in Problem 13.2 page 433 the first cycling is omitted. In my App 17.10 notes I computed the output of the cycled sequence on page 618 to be

$$\rho^{COS} \rightarrow +(1/2)(I_{1z}\, I_{2x} + I_{1x}\, I_{2z})\ [\ (S_{\theta 1-\phi} - S_{\theta 1+\phi})\ + (S_{\theta 2-\phi} - S_{\theta 2+\phi})\ ]\ = \text{really } \rho^{sin}$$

$$\rho^{SIN} \rightarrow +(1/2)(I_{1z}\, I_{2x} + I_{1x}\, I_{2z})\ [\ (C_{\theta 1-\phi} - C_{\theta 1+\phi})\ + (C_{\theta 2-\phi} - C_{\theta 2+\phi})\ ]\ = \text{really } \rho^{cos}$$

The first line is what emerges at FID start from the sequence shown, and the second line is the partner sequence. You can see that these meet the States Rules, so all peak quartets come out clean.

The final sections of this appendix claim that phase cycling can reduce system errors, and points out that certain NMR machines cannot phase-cycle odd multiples of $\pi/4$ for ϕ_{dig}, that gradients can be used along with phase cycling, and that as yet (2001) there is no "general theory of phase cycling". Maybe I can develop this general theory using some nice math tools.

Appendix 17.11. Bloch Equations pp 626-627 2 pages

See "Appendix 17.11: Block Equations.doc" for notes on this subject. Here we just summarize:

Malcolm presents the equations for d**M**/dt as a 3x3 matrix times **M**, which describes precession in the rotating frame, plus a vector which includes the relaxation effects. In the lab frame, the equation has an even simpler form as d**M**/dt = γ**M**x**B** - relaxation terms. These equations allow you to solve problems that involve precession and relaxation at the same time, but I don't think Malcolm ever calls upon them in that manner. The historical significance for NMR is that before 1970, NMR machines used the continuous wave steady-state method, and then the Bloch Equations told you the shape of the resonant peaks. This was before the pulsed FT method came into use, and now nobody does it the old way anymore for many reasons. Usually B_o was swept instead of ω_{ref} and that is where the terms low field and high field came from as terms referring to ends of the spectrum.

Appendix 17.12. Chemical Exchange pp 627-633 7 pages

See "xAppendix 17.12 Chemical Exchange.doc" for notes on this subject.

(1) What we have here is a little "matrix math problem". We have variables ρ_-^A and ρ_-^B . The first represents the coherence for molecules which have spins in the "A environment", the other for the B environment. Because of chemical exchange, a given spin moves back and forth between the A and B location in some random fashion and this is represented by a 2x2 matrix [-k, k, k, -k] where k is the rate of exchange. This is the "incoherent dynamics" for dρ/dt. The "coherent" is the usual free propagation with λ decay. So the upshot is that we have a matrix equation dρ/dt = Lρ where L is the 2x2 matrix shown page 630.

The math trick is how you solve this equation for ρ. Although L is not a Hermitian matrix, we can still bring it to diagonal form by a similarity X whose columns are the eigenvectors of L. Doing this process gives us a way to write down the solution which we otherwise only know in the formal form which says ρ(t) = exp(Lt)ρ(0). The problem here is that we don't know how to exponentiate the matrix Lt.

The eigenvalues are stated, and we come up with a general solution for ρ(t) where we start with a TE value for ρ(0). We then simply add the two components of our solution vector to get ρ_{NMR} and it has the time dependence shown on page 631. Depending on the size of parameter k, this either describes two peaks or it describes one broad peak, or it describes a narrowing peak for k > critical value. All these details are done in the main line in Chapter 15 Section 5.

(2) There is a completely separate matter addressed in this appendix, Section 17.12.4. In this problem, instead of worrying about things like ρ_-, we worry about the populations like ρ_α^A . There are four of these, so we have a 4x4 matrix equation which involves W and k where W is the $\alpha \leftrightarrow \beta$ transition rate and k is the same exchange rate as before. We convert from the 4-vector to the 2-vector containing the quantities $\langle I_z^A \rangle$ and $\langle I_z^B \rangle$ and we then have a 2x2 matrix "longitudinal" problem of exactly the same form as described in section (1) above, except the 2x2 matrix L is different here. We use the same method to solve the problem. This is then were we arrive at the four coefficients like $a_{A \to A} = a_{diag} = \cosh(k\tau_m)$ etc which then apply to the diagonal and cross peaks. Here, our time variable t is replaced with τ_m since this is the length of the mixing period in a pulse sequence.

Appendix 17.13 The Solomon Equations pp 633-635 3 pages

Here we have a matrix equation with a 4-vector P containing the 4 populations of a 2 spin system. The matrix W_P here is 4x4 and is just a tedious set of rate terms that I did in detail. We then convert from the P 4-vector to another called Z which contains $\langle I_{1z} \rangle$ and $\langle I_{2z} \rangle$ as the middle two components. We then rewrite our matrix equation in terms of Z, and we find that its matrix has 1+2+1 block form. We take only the middle block and end up with the famous 2x2 matrix involving R_{auto} and R_{cross} where each of these is a linear combination of the three rates W_i. So this equation is describing how two longitudinal spin components intermix with each other during the "mixing period" of an NMR experiment.

Appendix 17.14 Cross Relaxation Dynamics pp 635-636 2 pages

Here we solve the little 2x2 Solomon equation in the case where we drop the "equilibrium" constant terms. But then we have a math problem we have *already solved* in Appendix 17.12 but with different parameter names. So we just copy those results making the parameter changes for this new situation, and we things like get $a_{1\rightarrow 1} = \cosh(R_{cross}\tau_m)$ etc. These are used in the NOESY and ROESY experiments.