Spin Dynamics Meta Meta Review PhL 4.3.08

Now that I have finished this book, and have written my raw notes *and* my meta review notes, I want to go back and ponder once again what I have read. Ignoring the extra older m-m Chap 15/16 notes at the end of this section, I have encapsulated the book in 9 pages. The point here is to see the forest and to ignore all the details of the trees.

Chap 1 and **Chap 2** are very basic, Matter and Magnetism. Definitions of FID and "chemical shift" δ. Main idea will be that $H = -\boldsymbol{\mu}\bullet\mathbf{B}$ and $\boldsymbol{\mu} = \gamma\mathbf{I}$ and γ varies for different nuclei. Classical precession of this $\boldsymbol{\mu}$.

Chap 3 (NMR) show the FID, writes it as $f(t) = \cos(\omega^0 t)\exp(-\lambda t)$, but a later chap shows this makes a pole in ω space such that $F(\omega) = 1/[\omega - (\omega^0 - i\lambda)]$ and the real and imaginary parts of this are the Absorption and the Dispersion. We get the idea of isotopomers, and the basic notion of the splitting **multiplets** caused by adjacent spins, usually H's. In iso liquids, this is J coupling at work. Mention of NOE as reason to "pre-blast" when doing decoupling blasts. Main idea: the location of NMR spectral peaks and their widths is *the* information you get from NMR, use to ID chemical under test (CUT) or to learn about its detailed properties if known.

Chap 4 talks about **NMR hardware**. Page 586 is about the quadrature receiver. This accepts the (real) $s_{\mathbf{FID}}(t) = k\cos(\omega^0 t)\exp(-\lambda t)$, uses local reference $\omega_{\mathbf{ref}}$ and generates two real signals $s_{\mathbf{A}}(t)$ and $s_{\mathbf{B}}(t)$ which add up to a complex signal s(t) given by [ϕ = a hardware phase]

$$s(t) = 2i\rho_-(t)\, e^{-i\boldsymbol{\phi}} = 2i\,[\rho_-(0)\, e^{(i\Omega_0-\lambda)t}]\; e^{i\boldsymbol{\phi}} = \{2i\rho_-(0)\, e^{-i\boldsymbol{\phi}}\}\, e^{(i\Omega_0-\lambda)t} = \{a\}\, e^{(i\Omega_0-\lambda)t}$$

$$S(\Omega) = a\, L(\Omega;\Omega_0;\lambda) \qquad \text{where } \Omega = (\omega-\omega_{\mathbf{ref}}) \qquad a = \{2i\rho_-(0)\, e^{-i\boldsymbol{\phi}}\}$$

where the actual (real) received signal is $s_{\mathbf{FID}}(t) = -k'\, 2\omega^0\, \mathrm{Im}[\rho_-(t)] = k\cos(\omega^0 t)\exp(-\lambda t)$. Malcolm spreads all this out in multiple places in the text which I found a little confusing, but I know his reasons. What the FT + hardware gives you is this: The Fourier Transform of the FID signal *expressed in* the "offset frequency" Ω. The factor $2i\rho_-(t)$ comes from fact that coil signal = $dM_{\mathbf{x}}/dt$ and $M_{\mathbf{x}} = \mathrm{tr}(\rho I_{\mathbf{x}})$ which in turn is $2\mathrm{Re}(\rho_-)$. Early in the book, the reader did not know what ρ_- meant, so the full picture could not be given at the time the peak shapes were studied.

Chap 5 is about **Fourier transform**, but I have given the results above. It talks about 2D arrayed experiments which we see plenty of later in the book, and explains the States Method for clean peaks. Passing mention of phase cycling and blasting.

Chap 6 is the review of **quantum mechanics**, with a spin emphasis.

Chap 7 then applies this quantum mechanics and talks about the **Hamiltonians** for various kinds of spin interactions. For each case, we see the "full form" and the simplified "secular form". In addition, we have to worry about the nature of the NMR sample, so we know how much spatial averaging to perform. The simplest case is isotropic liquid. The electric quadrupole is mentioned with some quoted results, but the only cases that are used later in the book are these:

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
secular homo	$H = d_{12}(\theta)\ (\ 3\ I_{1z}\ I_{2z} - \mathbf{I_1 \bullet\ I_2})$ where $d_{12}(\theta) = b_{12}(3\cos^2\theta - 1)/2$, p 206
secular hetero	$H = d_{12}(\theta)\ (\ 2\ I_{1z}\ I_{2z}\ )$
J coupling	$H = 2\pi\ \mathbf{I_1 \bullet\ J \bullet\ I_2}$ p 212;
iso	$H = 2\pi\ J_{12}\ \mathbf{I_1 \bullet\ I_2}$
secular hetero iso	$H = 2\pi\ J_{12} I_{1z} I_{2z}$ // also applies to homo iso if "weak coupling", p 233

The d-d is also called "through space" while the J coupling is "through bond".

This chapter mentions the pulse effect which is $\mathcal{H}_{\mathbf{RF}} = -\omega_{\mathbf{nut}}[\ \cos I_{\mathbf{x}} + \sin I_{\mathbf{y}}]$ and $\omega_{\mathbf{nut}} = \gamma B_{\mathbf{RF}}/2$, where the 1/2 comes from RWA idea and we think of this applied only in the x direction. Nothing is said at this point about what the pulse does to spins. Nor do we yet know that "nutation" means.

The simplest case one can study is isotropic liquids because only the chemical shift and the J coupling survive your spatial averaging.

Chap 8 is therefore a study of spin in **isotropic liquids**, and is then mostly a study of **J coupling** in the background of chemical shift. Spins have the same chemical shift if they are **chem equiv**, an obvious matter of spatial symmetry modified by averaging certain motions. If two homo chem equiv spins have the same J coupling to all other spins, they are **mag equiv** and in this case you can ignore the J coupling between them, a fact proved in an appendix. Molecules are represented by little **graphs**.

Chap 9 focuses on the simplest possible spin system: a **single spin-1/2 spin**.

The first order of business here is (should have been) to define the **polarization vector** as $\mathbf{P} = \langle\psi|\mathbf{I}|\psi\rangle$. We then learn in what direction this vector points for different spin states $|\psi\rangle$. We solve the SE (in the S Picture) to see what $|\psi(t)\rangle$ does in the presence of the B_0 field. The answer is that it does this: $|\psi(t)\rangle = R_{\mathbf{z}}(\omega_0 t)\ |\psi(0)\rangle$ by "expo Ham". This implies that **P** "**precesses**" at **Larmor** $\omega_0 = \gamma B_0$. We know (notes) that the same result obtains in a classical analysis of a mag moment in a B field.

The second order of business is to define the "**rotating frame**" going at $\omega_{\mathbf{ref}}$, $\phi_{\mathbf{ref}}$ and rewrite the Ham in this frame, allowing for the "**Coriolis**" effects. The net effect is that ω_0 gets replaced by $\mathbf{\Omega}_0$, and the effect of the RF pulse (at $\omega_{\mathbf{ref}}$, $\phi_{\mathbf{p}}$) is simple, so we get $\mathcal{H}_{\mathbf{rot}} = \Omega_0 I_{\mathbf{z}} + \omega_{\mathbf{nut}}(I_{\mathbf{x}}\cos\phi_{\mathbf{p}} + I_{\mathbf{y}}\sin\phi_{\mathbf{p}})$ when an RF pulse is active. This Ham is simple because it is **time-independent**

This leads us to study the effect (in the rotating frame) of a lab **RF pulse** of some $\phi_{\mathbf{p}}$ lasting time t. For $\Omega_0 = 0$ and $\phi_{\mathbf{p}} = 0$ we get $\mathcal{H}_{\mathbf{rot}} = \omega_{\mathbf{nut}} I_{\mathbf{x}}$, and expo Ham tells us that $|\psi(t)\rangle = R_{\mathbf{x}}(\omega_{\mathbf{nut}}\ t)\ |\psi(0)\rangle$. We can then deduce that the polarization vector **P**(t) is rotating around the x axis at this "**nutation frequency**". Many times later in the book we shall consider the case where $\omega_{\mathbf{nut}}\ t = \pi/2$ and this is the $(\pi/2)_{\mathbf{x}}$ knockdown pulse. In the lab frame the tip of the **P**(t) arrow does the dense spiral implied by the

page 263 picture. This section finally considers the general case where $\Omega_0 \neq 0$ and $\phi_p \neq 0$. In this case, we find θ_p from $\tan\theta_p = \omega_{nut}/\Omega_0$ and the conclusion is that **P** rotates around an axis of polar angles (θ_p, ϕ_p) at rate $\omega_{eff} = \sqrt{\omega_{nut}^2 + \Omega_0^2}$. As you move away from $\Omega_0 = 0$ your θ_p slides down from $\pi/2$ to 0, and your "knock down" of **P** is less effective, so you lose FID signal and this sets a limit to your NMR machine bandwidth.

Chap 10 then adds the complexity of **statistical mechanics** to our single spin-1/2 system. What happens when we have an *ensemble* of such spins at some temperature T? Here I quote the meta meta paragraph I already wrote for this chapter:

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.

A coherence is simply a *name* given to an off-diagonal density matrix element ρ_{rs}. The polarization vector I called **P** above is finally introduced as $\mathbf{P} = (B/2)\mathbf{M}$ where **M** is a unit vector *if* you are at TE. We know B/2 is very small, so in the real world an ensemble of spins is mostly unpolarized. We write $\rho = 1/2 + (B/2)\mathbf{M} \bullet \mathbf{I}$ in general (not just at TE) . This derives simply from $\mathbf{P} = \mathrm{tr}(\rho \mathbf{I})$ which is the statistical generalization of our earlier $\mathbf{P} = \langle \psi | \mathbf{I} | \psi \rangle$.

In this chapter we ask for the first time ask what RF pulses *do* to the density matrix ρ. We learn about populations and "inversions" and about "free propagation" between pulses. The effect of T_1 and T_2 relaxation is added manually, but we see later in the book justifications for doing it this way.

We then do our very first "pulse sequence" which is just a $\pi/2$ knockdown which makes a FID starting with TE. We get $\rho_-(0) = B/4i$ and $a = B/2$ so the spectrum is $(B/2)\,\mathcal{L}(\Omega, \Omega_0, \lambda)$. If we do this same knockdown as $(\pi/2)_y$ we get $\rho_-(0) = B/4$ and $a = iB/2$ and $(iB/2)\,\mathcal{L}(\Omega, \Omega_0, \lambda)$ which swaps the D and A parts of the spectrum.

The density matrix gives "the **most complete description** that is possible" of your ensemble, since from it you can compute all observable quantities.

In this chapter, nothing is said about the interaction between the spin-1/2 spins in the ensemble, so the notion of a density matrix is fully general and can handle such interactions.

Comment: At this point, I have summarized the first half of the book (~300p) in 2.7 pages of text. Apart from the QM and the basic $\mu \bullet B$ and Fourier Transforms, everything I read was "new" to me.

Chap 11 talks about simple experiments you might try on your spin-1/2 ensemble where for now we ignore possible interactions between spins. Malcolm highlights *three basic experiments* here. Since MRI involves only H spins, all these experiments are very relevant to MRI.

We have already done the "zeroth" NMR experiment which is just a knockdown to make a FID which decays at T_2.

The first experiment is the "**inversion recovery**". The fundamental idea is to do a π pulse first to generate an inversion, let some time go by where it decays with T_1 , then do a knockdown to make a FID. This method lets you measure T_1 even it you have a mixture of spin-1/2 types with different T_1's. Fancy versions of this are called FLAIR and STIR in the MRI world.

The second experiment (called "**spin echo**") is a knockdown *followed by* a π pulse followed by a delay. The FID is "taken" at a time after the π pulse equal to the time before it from the knockdown. By varying the pulse gaps $\tau/2$, you can measure T_2 since this is the main decay rate for transverse signal. In later experiments in the book we "tune" $\tau/2$ for some purpose, and then the gap-π-gap combination is called a spin-echo sandwich or SES. A major feature of this sequence is the fact that the π pulse allows the T_2 dephasing due to B inhomogeneities to be undone, causing the "echo", and giving a mechanism for detecting diffusion of the sample, among other things.

The third experiment shows how you can use B field gradients to reconstruct an **image** of the sample, and this of course is the basis of MRI. This tomography method is *completely different* from that used in the CT where you have X-ray scattering.

In **Chap 12** we now assume that our isotropic liquid contains molecules each of which has *two* spins 1/2 (identical in type = homonuclear), so we now have to consider the J coupling between these two spins. We of course don't worry about spins in different molecules interacting with each other since there is no J coupling between such spins. Also, we don't worry about spins in the same molecule which are very far apart, since J would be very tiny. We assume that our two spins are close to each other, probably just one bond separated, so that we have some significant coupling to examine. We assume these two spins have significantly different chemical shifts so that $J << \Delta\omega$ and we can do "secular" for the J coupling Hamiltonian, being in the "weak coupling" limit. Such a two spin system is called a **homonuclear AX system**, where the letters are "far apart" in the alphabet, implying a large chemical shift

So that is the problem we want to attack. A huge amount of new machinery must be powered up to handle it! The Ham here has three z-type terms: I_{1z} and I_{2z} and the J coupling combination $I_{1z}I_{2z}$. There are now four eigenstates of form $|\alpha\beta>$ and it is easy to find the eigenenergies and plot the four levels -- these involve both J and the two ω_0's. We know ahead of time that the spectrum will have two chemical shift peaks each split in two by "the other spin" for a total of 4 peaks, we saw that in Chap 3. Since we just wrote down the eigenenergies, we already know the locations of the four peaks, so we know the splittings as well. The split peaks are shifted $\pm\pi J/2$ from the unsplit location, so separation is πJ.

In the rotating frame, the Ham appears just as you would expect, page 349, and you can recompute the eigenenergies in that frame. The eigenstates just "phase along" in the usual expo Ham manner. The density matrix is now 4x4. The coherences "phase along" as usual, because (in S picture) the two states rs in $<r|\rho|s>$ "phase along", but of course now we have difference frequencies between r and s for the coherence phasing. These coherence phase energies are the same in the lab or rotating frame because they are energy level differences. There are now four -1 coherences and they each create one of the four spectral peaks.

What this all means is that our zeroth order FID experiment is completely solved, we have our four peaks, all done.

BUT, in other pulse sequences, we have much more to worry about. We have to be able to track the ρ matrix through pulses and free propagations, and this takes some work. Due to the J coupling, we cannot just "separate" the problem into its two spin-1/2 pieces in the direct product sense. We can of course write direct product spin matrices in our new 4-space.

Although the coherences just "phase along", the motion of the density matrix as a whole is not so simple (being as its matrix elements are all phasing along *differently*). If we just do a simple knockdown pulse, it does "separate" and our TE starting point ρ moves to $-I_{y1}-I_{y2}$ in the usual manner. However, once we go into free propagation after a pulse, we have to apply our full expo Ham to transform $\rho' = U^{-1}\rho U$ and it is not easy to simply expo a linear combination of I_{1z}, I_{2z} and $I_{1z}I_{2z}$ (but doable).

This is all worth repeating. We represent the ρ matrix as a sum of canonical basis matrix terms with coefficients, then we need to find out what happens to the individual terms in this sum. Even if ρ starts out very simple, it usually ends up not very simple. Each term has to be "processed" one at a time, in any order, by our three rotations as shown page 374. In general, it is quite a mess.

The chapter ends with the claim, proven in an appendix, that with suitable assumptions, the spin echo sandwich of gap-π-gap can be replaced by π-doublegap and during this double gap the chemical shift rotations can be set to zero.

Chap 13 then examines four relatively complex (for a beginner like me) experiments one does on AX systems, and this harnesses all of the very fancy machinery developed in Chapter 12 above. In many ways, these experiments are the climax of this book. See comments also in the meta review.

1. COSY. This is knockdown, gap, knockdown, FID. The first knockdown is simple, but the gap is complicated. During this gap time t_1, we pick up sinusoidal dependence on $\Omega_1{}^0t_1$ and $\Omega_2{}^0t_1$, with some J offsets. In a sense, the purpose of the *second* knockdown is simply to *start* the t_2 time period of the FID, so that we can have (t_1, t_2) for 2D Fourier analysis. At the end of the second knockdown, which is to say, at the start of the FID at $t_2 = 0$, we have

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

We then *evaluate* the ρ_- matrix elements, and then these just "phase along" during the t_2 FID with expo time dependence $\Omega_1{}^0t_2$ and $\Omega_2{}^0t_2$, again with J offsets (inside variable ϕ). The *result* then is we have a 2D symmetrical spectrum (t_1, t_2) →FT→ (Ω_1, Ω_2) where we have our known four AX peaks in each direction, so we get a set of 16 peaks in a square pattern, where the chemical shift is the edge of the square, and the πJ is the spacing in each corner quartet. We then do States on this whole thing to make all the peaks be clean (called DQF-COSY, which I derived in full detail).

Technically, the hard part of this problem is tracking the ρ matrix through the t_1 gap and keeping track of the ρ terms we know will make the FID signal. We could track ρ through the second gap (FID time), but that would be wasted computation because it is easy to see how the ρ_- elements just phase along there. In the first gap, we need to know how ALL of ρ propagates, because just knowing ρ_- in the gap is not enough information because the second knockdown pulse will link many coherences into the

final ρ_- ones. The other technical issue is working through the States clean-peaks analysis. I have done this in a separate document.

Practically, the purpose of COSY is to get a 2D "footprint" of each AX spin pair in a complex chemical. The footprint is a square of quartets. If you have a lot of these, it is impossible to see what is going on in 1D, but feasible to see what is going on in 2D. Book shows sample spectra on page 399 and 400. Here is my theory of the vertical line due to water: the first knockdown takes down the water, but it quickly gets back to TE during the gap due to fast T_1. The second knockdown hits it again, and then we just get a water line in the t_2 FID spectrum, and that corrupts the picture.

It may be that COSY was the first 2D spectral method, and it is probably the simplest.

2. INADEQUATE. This one is knockdown, tuned SES, knockdown. You have a ^{13}C at two sites for your AX, but you are swamped by isotopomers having only *one* ^{13}C. These molecules make huge lines which conceal the little AX split pairs you are looking for. So this pulse sequence with its phase cycle is used to filter out those unwanted large peaks. In 1D, the result is that you get your four peaks, but each is a dipole pair as on 410. There is a 2D version of inadequate where you sort of tack a COSY sequence onto the end of the SES to get your t_1 and t_2 variables. The result is that each AX double-tagged ^{13}C pair makes a horizontal line of 4 peaks, but the lines are pulled apart in the vertical dimension, again giving visibility on "what is going on", example on page 416.

Technically, there are various interesting issues involved in this example. We use the SES rule to get a period of "J coupling only" which makes it easier to track ρ. The "filter" is accomplished by a phase cycle that only lets "double quantum" coherences pass through a certain point, to achieve the goal. The 2D sequence includes blasting on H to prevent H from splitting the lines of this ^{13}C spectrum.

3. INEPT. This is for *hetero* AX, and the pulse orchestra has two scores, one for I, one for S. In this experiment (which again involves the SES sequences), we assume $\gamma_I >> \gamma_S$, and we want to look at the S spectrum. Normally the S signal would be small due to small γ_S (hence small B_S), but this experiment manages to "transfer the magnetization" from I over to S, so your FID shows up with $B_I I_z S_y$ and now you get a large S signal instead of a tiny one. I suspect classically it is like transferring energy from a heavy pendulum with small amplitude to a light one with large amplitude, something like that.

A slightly fancier version is called refocused INEPT. In regular inept, since you get dipole peaks, if you try to blast I during the S FID to remove H splittings of the S spectrum, you wipe out the entire FID. If you could get those dipoles to be untwisted so only one direction, they you could do the blasting and you get strong single peaks for the S spectrum. Page 422 shows comparison in bottom two graphs.

4. BICELLE Method. Here you add bicelles to the solvent to cause weak anisotropy of your species of interest, and this activates the dipole-dipole coupling as well as the J coupling. When you add the bicelles to the mixture, the J coupling splitting move slightly together or apart depending on the sign of the d coupling. This can then be used to discover the orientation of the AX bond relative to the molecule's bicelle alignment axis, since this orientation affects the sign of the d coupling, even when you do a full angular average of things. The point: this is a method of getting bond ANGLE information. Later in ROESY and NOESY we get some bond LENGTH information (or at least dipole separation distances).

In **Chap 14**, we take everything we did with N=2 in Chap 12, and we generalize it to N=3 or more spin-1/2 systems. The only interaction considered is again the secular J coupling, still isotropic liquid. This is all fairly mechanical stuff: what does TE look like? What does ρ look like? Etc.

The N=3 case is considered somewhat, called an **AMX system** of course (all J's are weak). If the AX J linkage is zero, we have a linear graph in the sense of Chap 8, called linear AMX. The COSY spectrum of AMX has a 3x3 squares pattern with 9 peak groups, each containing 4x4 peaks. The 3-ness is since there are three chemical shift values (AX had 2) and the 4-ness in the cluster is because each spin is split by two other spins. In the linear AMX case, if you have AMX and A'M'X' with M' = M in chemical shift and both linear, an ambiguity problem arises (p 468). This is resolved by using the **TOCSY** pulse sequence which is like COSY, but the second knockdown is replaced by a large number of dense π pulses which cause equilibration which causes the outer 2 of the 9 spectral peaks to reappear, allowing the ambiguity to be resolved.

COMMENT: I first wrote the Chapter 15 and 16 first-cut meta meta review notes you find now at the end of this document. I then reviewed them to come up with more appropriate meta meta review notes which follow right here.

Chapter 15

1. Opens discussing **libration**, **rotation** and gives dual-CH_3 **exchange** molecule example.

2. In **magic spinning** of a solid sample, you try to get all of it at the d-d magic angle so lines can be narrow because the d-d relaxation process is reduced.

3. Discussion of the **A, B chemical exchange problem**. Math is given for **k=k'** case, **motion of peaks** versus k is described, shown on p 493 + 495.

4. In a system of **two J-coupled spin-1/2 spins**, when one spin flips up and down due to **relaxation** W, it changes the effective chemical environment for the second spin and therefore creates an A,B exchange *analogy*. The math of item 3 above applies if you replace $k \rightarrow 1/2T_1 = W$, and $\Omega_\Delta \rightarrow 2\pi J$ (acting as the unperturbed chem shift), picture on page 497 shows peak motion versus T_1 change.

5. Without doing the math (but I have now done it) Levitt shows what the peaks do for an **A,B exchange when k ≠ k**, a generalization of item 3 above. Shows the asymmetric peak motion ending up with a single peak not exactly in between the weak k peaks. There is a shift at high k.

6. In metals, you have this same effect of item 5 above, but one spin is actually a conduction band electron spin, so effect is very strong and asymmetrical. Pictures shown page 500, this is called the **Knight Shift**. The reverse interaction where nucleus splits the electron energy level in hydrogen is called the **Lamb** Shift, the 21 cm stuff, both are **hyperfine** interactions.

7. When you think about a spin in an A,B exchange environment, the spin itself might be moving (page 481), or something else in the molecule might be moving, causing the effect (509). In the second case, it is easy to think of A and B species of molecules being in a sample.

8. The **A,B exchange problem with k = k'** is treated again, this time with independent **relaxation** of the A and B species spin at rate **W**. We obtain in the appendix a 2x2 matrix equation, and we solve it using our usual methods (see 2x2 matrix problem doc!). The solution is this:

$$\begin{pmatrix} \langle I_z \rangle^A(t) \\ \langle I_z \rangle^B(t) \end{pmatrix} = \begin{pmatrix} a_{A\to A}(t) & a_{B\to A}(t) \\ a_{A\to B}(t) & a_{B\to B}(t) \end{pmatrix} \begin{pmatrix} \langle I_z \rangle^A(0) \\ \langle I_z \rangle^B(0) \end{pmatrix} \qquad \text{// "longitudinal mag exchange"}$$

with $a_{A\to A}(t) = \cosh(kt) \exp[-(k + 2W)t]$ etc and $T_1 = 1/(2W)$.

9. In **2D exchange spectroscopy**, starting with a normal 2D pulse sequence, one adds a **"mixing period"** of duration τ_m during which only I_z terms in ρ are allowed to exist (due to phase cycling). The mixing shown above in item 8 happens during this period. The spectrum then has 4 peaks, two diagonal and two cross, with amplitudes given by $a_{A\to A}(\tau_m)$ etc. By varying τ_m one can take the peak ratio cross/diag ~ tanh $(k\tau_m)$ and thereby measure k. This works even if k is very small. Doing the math here, Levitt uses the above mixing of the $\langle I_z \rangle$ values to deduce what ρ must be doing during the mix from time 4 to 5:

$$\rho_5^A = \rho_4^A a_{A\to A}(\tau_m) + \rho_4^B a_{B\to A}(\tau_m)$$
$$\rho_5^B = \rho_4^B a_{B\to B}(\tau_m) + \rho_4^A a_{A\to B}(\tau_m)$$

Chapter 16

1. Other spins and the CSA effect cause a **noise B_x** field at the location of a spin as molecules **tumble** in their Brownian motion. The frequency spectrum of this noise has a standard shape called $\mathcal{J}(\omega)$ with area π, called the **spectral density**. This corresponds to an **autocorrelation function** of the form $\exp(-\tau/\tau_c)$ where τ_c is the **correlation time** and relates to the speed of rotation.

2. In a meta meta review "Phil digression" I tried to see if I can derive Fermi's rule just form our spin formalism, knowing that B_x changes populations. This attempt crudely shows an effect, but is not useful.

3. If you had some explicit noise B_x, you could compute the relaxation rate if causes on a single spin using **Fermi's Golden Rule**. The result is $W = 1/2\ \gamma^2 \langle B_x^2 \rangle\ \mathcal{J}(\omega_0)$ where ω_0 is the Larmor. One can show that $T_1 = 1/(2W)$ and one can then **plot T_1** versus τ_c, given that $\mathcal{J}(\omega_0) = \mathcal{J}(\omega_0, \tau_c)$. It **has a minimum**. We can show that this T_1 produces the expected result on $\langle I_z \rangle \sim M_z(t)$. This is typical of T_1's.

4. We now consider a **2-spin system with a d-d through-space coupling**. There are 4 energy levels and 12 rates W_i which we compute and then "fix" to match TE. We write a 4x4 equation for how the 4 populations change in time, and from this we extract a 2x2 equation that has a solution similar to item 8 of Chapter 15 above. We state the equation of motion as follows: [called the **Solomon Equations**]

$$d/dt \begin{pmatrix} \langle I_{1z} \rangle(t) \\ \langle I_{2z} \rangle(t) \end{pmatrix} = \begin{pmatrix} -R_{auto}(t) & R_{cross}(t) \\ R_{cross}(t) & -R_{auto}(t) \end{pmatrix} \begin{pmatrix} \langle I_{1z} \rangle(t) \\ \langle I_{2z} \rangle(t) \end{pmatrix}$$

where $R_{auto} = W_0 + 2W_1 + W_2$ and $R_{cross} = W_0 - W_2$, and then we state the solution which is this

$$\begin{pmatrix} \langle I_{1z} \rangle(t) \\ \langle I_{2z} \rangle(t) \end{pmatrix} = \begin{pmatrix} a_{diag}(t) & a_{cross}(t) \\ a_{cross}(t) & a_{diag}(t) \end{pmatrix} \begin{pmatrix} \langle I_{1z} \rangle(0) \\ \langle I_{2z} \rangle(0) \end{pmatrix}$$

where $a_{diag}(t) = \cosh(R_{cross}t) \exp(-R_{auto}t)$ etc.

5. The **NOESY 2D experiment** is *just like* the 2D exchange spectroscopy discussed above, Chap 15 item 9, but here it is applied to a sample which is a 2-spin system with d-d coupling. Again, we get the four peaks, and varying τ_m we can deduce both R_{cross} from $\tanh(R_{cross}\tau_m)$ and then we can get R_{auto} as well. From these we deduce the various W's, and finally we deduce the spacing d between our two spins. This experiment analyses *lots* of spin pairs at the same time, of course, and can help you determine the folding **shape of a protein**, for example, where through-space couplings are determined by the way the peptide backbone loops near itself, etc etc.

6. Backtracking, the NOE effect is derived, the **Nuclear Overhauser Effect**. This is an enhancement of the B factor (of the S spin) in TE due to irradiating the other species (the I spin) in an I-S heteronuclear AX system, result on page 541. This calculation uses the same d-d rates W_i that we used above in the NOESY preparation. It is the d-d coupling between the I and S spins that gives rise to this effect. You can get a boost of at most 4 using I = ^{1}H and S = ^{15}N. Want a large ratio of γ's to get a good result. The upshot is that irradiation *not only* removes multiplet structure for S due to I, it boosts the S signal!

7. **ROESY** is just like NOESY and is used for the same purpose. However, whereas NOESY uses longitudinal relaxation equations like that shown in item 4 above, ROESY uses some similar **transverse** relaxation equations. Although these are quoted, they are not derived. In order to "hold" the mixing action of between transverse spins during the mixing period, you have to irradiate during the mixing period with a strong RF to achieve **spin-locking**. ROESY is better than NOESY for some situations.

8. It is possible to have an interaction between two pairs of dipoles (call it DD/DD) or one pair of dipole spins and the CSA effect (induced B in electron cloud acting as the other DD). This subject is called **cross correlation**. The **DD/DD** example given shows a 4-spin system H-C-C-H and the two outer dipoles interact so as to affect the relaxation of the C-C dipole, as indicated by the width of the C-C spectra lines. This can be used to deduce the orientation of the 4 atoms, two cases shown on page 561. The other example which is **DD/CSA** shows how you can arrange for the CSA to offset the effect of the DD relaxation so as to minimize the width of spectral lines. To achieve this minimum, you have to tune the value of the main field B_o (usually to a quite large value). This is used in spectroscopy of heavy molecules where lines tend to fat up so much you can't even see them. This method is called **TROSY** and minimizes the total relaxation by offsetting the unavoidable d-d against the CSA.

9. Both NOESY and ROESY have the name "Overhauser Effect" in the name. NOESY has the name Nuclear OE, while ROESY is called Rotating Frame OE (due to irradiation and tradition). **Neither** of these pulse sequences makes use of the signal boost called the NOE (item 6 above). ***However***, both involve the transfer of magnetization between two spins via the d-d coupling mechanism, and I guess this general notion is associated with the Overhauser Effect buzz phrase.

ORIGINAL META META REVIEW NOTES for Chaps 15 and 16

Chap 15 reviews **librational** and **rotational** motions, then gives an example of the **"exchange"** process where a spin jumps between two locations we call A and B. Page 481 gives another A and B case where two identical spins simply swap between these two environments, which will be the k' = k situation analyzed later.

A too-short discussion of **"magic spinning"** of solids claims to remove d-d relaxation mechanisms (which we will learn about soon) by making all dipoles "be" at the magic angle which makes d-d go away. When this relaxation goes away, line broadening is reduced and you can see spectral detail again. No theory is given for this, however. General timescales are given both for types of motion, and for effects those motions cause on Hams and spectra.

Finally, the chapter starts into the A B k=k' **exchange problem**. Remember that when an H moves back and forth between two chem shift environments A and B, it is the spin that moves, and this must affect the spectrum somehow! A rather complete math analysis is done with appendix help (17.12.1,2,3) and we learn that the nature of the resultant 1D spectrum varies with the size of k, a measure of the exchange rate. For very slow exchange, you get your **two chem shift peaks** as if k=0. As k increases, these move together and blend into **one broad peak** at a critical value of k. Further increase in k **narrows** the peak. We then see how the case is a little different if one environment (B on page 498) persists most of the time. Then k' ≠ k and in fact K = k/k' = [B]/[A] . In this case the initial pair of lines are **unequal in height** (small k), they merge at a point **offset from the center** and then narrow there. The math for this is not given but is probably not too hard to do.

Now comes a temporary **Malcolm digression** where he, in the middle of Chapter 15, takes conclusions from Chapter 16. He does this because the spectral results one obtains are analogous mathematically to what we have just discussed above. If you have a 2-spin system that is J coupled, you will have for example $\rho_{\alpha-}$ and $\rho_{\beta-}$ as two of your -1 coherences. The claim is this: As one spin moves back and forth from α to β due to a T_1 relaxation mechanism, the process creates two different environments for the second spin *which are like* the A and B discussed above. Offhand I can imagine that the $\alpha \leftrightarrow \beta$ "flipping" cause the B field from the first spin to change polarity, and this acts via the through-space d-d coupling to in effect change the chem shift environment for the second spin. The claimed connection between this and our "exchange process" described above is this: $k = 1/2T_1$ and $\Omega_\Delta = 2\pi J$. Granting that this analogy is valid (and survives rotational averaging), we expect that normal J-coupling peak doublets (spaced by $2\pi J$) should move together, merge and then narrow as k increases (T_1 decreases). Earlier in the book, we assumed long T_1 so this never happened. This idea is further developed in Chapter 16 where I will look at it harder. [no, it was never brought up again.]

An example of the exchange "variant" discussed in the last paragraph is the **Knight shift**. In this case, the one spin "moving back and forth α to β is a metallic conduction unpaired *electron*, and this creates two environments for the other spin which is a normal *nuclear* spin. In this case, the flip rate is fast, which means k is large, which means you are always in the regime with the single narrow peak. Because the α and β states differ a lot in energy (μ_e is large), we have a k≠k' situation (β exists more than α, say),

and we have the final narrow peak being shifted from the central position it would be have there no flipping, and this is the Knight Shift.

At this point, I now have to add **my own digression to get clarity on the regular exchange issue** we were discussing before the above digression. Consider the k'=k situation shown on page 481 with two methyl groups. Due to the asymmetry of the left side of this molecule, if you are an H atom in one of the methyl groups on the right side, you are thrown back and forth between the two environments A and B which have different chemical shifts. But because the two methyl groups are chemically the same, it is not easy to talk about a solution having "two species" A and B, because both species look exactly the same. This example was used because it clearly must have k'=k. Notice in this example that the NMR spins are actually within the object that is swapping around.

For me a better picture for exchange is provided on page 509 and it is different in nature. Here we have to distinct molecular species (I don't know the correct technical term, isomers perhaps). Notice that the molecule is not left-right symmetric because there are some metal atoms only on the right side. The species are different because some $Br(CO)_3$ group can take up residence at two different locations, left side or right side, as shown, and this will be a $k' \neq k$ situation, as it notes with 75% and 25%. In this case, the spins of NMR interest are NOT inside the thing that moves between the two positions. The spins of interest are any of the H atoms in the molecule. For example, consider the H spin called H_B on the far left of the left picture, and called H_L on the far left of the right picture. As the exchange takes place, this spin sees two different chem environments which go back and forth. Although we have not done the math for the $k \neq k'$ problem. we think it will be similar to what we have done and have talked about. We expect that for small k's, we will have two peaks of unequal side that are separated by the chemical shift difference created by the existence of the two species. This is in fact what we see in the spectrum at the top where you see the B and L labels -- two unequal height peaks, with the B peak larger because it is in the 75% species.

To summarize: here we have an example with two cleanly defined "species" of molecules called A and B. The NMR spins of interest are the various H nuclei in the two species at the same location, and these are sort of bystanders to the swapping action of the $Br(CO)_3$ group.

Now we need to go off on another **Malcolm digression** and look at Appendix 17.12.4 on page 631. Here we are discussing a system (like that in the above paragraph) where we have two species A and B and each of these has a spin-1/2 system of interest to us (like the H_B and H_L mentioned above). We want to write an equation for d/dt of ρ_α^A for example. Here is the claimed result:

$$d\,\rho_\alpha^A/dt = -k\,\rho_\alpha^A + W\,\rho_\beta^A + k\,\rho_\alpha^B - W\,\rho_\alpha^A$$

As one sees, there are two types of terms here. Due to exchanges $A \rightarrow B$, we are "losing" ρ_α^A at the rate k, and this is the first term. But due to changes from $B \rightarrow A$, we are "gaining" ρ_α^A at the rate k, and this is the third term. This seems pretty reasonable to me. But now we postulate another mechanism going on at the same time, indicated by W. Within our A molecule, there is some rate $\beta \rightarrow \alpha$ due to "noise" and this increases ρ_α^A. This same noise causes $\alpha \rightarrow \beta$ and this decreases ρ_α^A. All this time, we are talking about one spin location in an A molecule, and the corresponding spin in a B molecule. We don't bother to show how the up and down rates are slightly different, because they are roughly the same at high temperature. so these two terms are due to a "relaxation mechanism" of unspecified origin which is causing transitions

of our spin A. We assume that our spin in the B species has exactly the same relaxation rate W, but one could imagine how it might be a little different since the molecule the spin lives in is different.

Notice how the mechanism for W does not require the two molecules to be next to each other at some time. We are not saying that W for spin H_B is caused by a d-d interaction from H_L on the other molecule, as I once thought. Within molecule A, W is caused by *whatever* spin-relaxation mechanisms are present and certainly this would include any that arise from collisions between A and B molecules. More likely W is coming from mechanisms within the A molecule caused by its rotation.

We do this with the other three populations as well, and obtain a little 4x4 equation. We then convert this to $\langle I_z \rangle^A$ and $\langle I_z \rangle^B$ in the usual way, and then we have a 2x2 equation. We then solve this equation and we get this result (my confusion arose here because this result was never cleanly stated in the appendix):

$$\begin{pmatrix} \langle I_z \rangle^A(t) \\ \langle I_z \rangle^B(t) \end{pmatrix} = \begin{pmatrix} a_{A\to A}(t) & a_{B\to A}(t) \\ a_{A\to B}(t) & a_{B\to B}(t) \end{pmatrix} \begin{pmatrix} \langle I_z \rangle^A(0) \\ \langle I_z \rangle^B(0) \end{pmatrix} \qquad \text{// "longitudinal mag exchange"}$$

where for example

$$a_{A\to A}(t) = \cosh(kt) \exp[\, -(k + 2W)t \,] \qquad T_1 = 1/(2W).$$

Notice that the above 2x2 matrix equation concerns $\langle I_z \rangle^A$ and $\langle I_z \rangle^B$ in two different molecule species, and it is NOT called the Solomon equation. In the *next* appendix section, we have an analysis of a 2-spin system (both spins in same molecule) and we find an equation for $\langle I_{1z} \rangle$ and $\langle I_{2z} \rangle$ which has the same form as our equation above, but it applies to a different situation and is not relevant for our current discussion!

Now finally, with all this preparation, we can talk about **"2D exchange spectroscopy"** which does not have a fancy capital letters name like INEPT. The pulse sequence is shown page 501 where the two Fourier times are t_1 and t_2. We arrange to have a long mixing period τ_m during which only order 0 coherences are allowed to exist due to some fancy phase cycling, as shown on page 502 (table). The question then is: how do we model the change in ρ between time 4 and time 5?

First, let's review how we start this ρ analysis. We regard our NMR sample as a mixture of the two chemical species A and B, as described in my personal digression above. We assume k = k' to make the math simple, and that is why we start off with $\rho = (\rho^A + \rho^B)/2$ as if we had a 50/50 mixture instead of a 75/25 mixture. We analyze the two density matrices separately, as if they were independent chemicals inside our NMR sample container. At point 4 we have these results:

$$\rho_4^A = I_z \cos(\Omega^0_A t_1) \exp(-\lambda' t_1)$$
$$\rho_4^B = I_z \cos(\Omega^0_B t_1) \exp(-\lambda' t_1)$$

where we show the different Larmor frequencies for the two species A and B and we assume the same T_1 time for both. We have filtered out all other basic spin matrix terms from the ρ's.

We now go back to our "longitudinal magnetization exchange" 2x2 matrix equation quoted above and we apply that during our mixing period. At time 4 we have what I have shown above for the two ρ's. At time 4 we must therefore have

$$<I_z>^A(\tau=0) = tr(\rho_4^A I_z) = \cos(\Omega^0_A t_1) \exp(-\lambda' t_1)\, tr(I_z^2) = (1/2)\cos(\Omega^0_A t_1)\exp(-\lambda' t_1)$$
$$<I_z>^B(\tau=0) = tr(\rho_4^B I_z) = \cos(\Omega^0_B t_1) \exp(-\lambda' t_1)\, tr(I_z^2) = (1/2)\cos(\Omega^0_B t_1)\exp(-\lambda' t_1)$$

So this is our little 2-vector of $<I_z>$ at time $\tau=0$. We let this propagate until time $\tau=\tau_m$ at time 5 and we have

$$<I_z>^A(\tau=\tau_m) = <I_z>^A(\tau=0)\, a_{A\to A}(\tau_m) + <I_z>^B(\tau=0)\, a_{B\to A}(\tau_m)$$
$$<I_z>^B(\tau=\tau_m) = <I_z>^A(\tau=0)\, a_{A\to B}(\tau_m) + <I_z>^B(\tau=0)\, a_{B\to B}(\tau_m)$$

where I am just writing out the 2x2 matrix equation above.

Now, the next question is this: what ρ_5^A and ρ_5^B would replicate these results at time 5? We are then sort of computing these things a bit indirectly. The answer must be:

$$\rho_5^A = \rho_4^A\, a_{A\to A}(\tau_m) + \rho_4^B\, a_{B\to A}(\tau_m)$$
$$\rho_5^B = \rho_4^B\, a_{B\to B}(\tau_m) + \rho_4^A\, a_{A\to B}(\tau_m)$$

so we saying that the ρ's transform just as do the $<I_z>$ objects. No doubt this is only true for the I_z terms in ρ's, but the phase cycling makes these be the only terms. So we then end up with

$$\rho_5^A = I_z \cos(\Omega^0_A t_1)\exp(-\lambda' t_1)\, a_{A\to A}(\tau_m) + I_z \cos(\Omega^0_B t_1)\exp(-\lambda' t_1)\, a_{B\to A}(\tau_m)$$
$$\rho_5^B = I_z \cos(\Omega^0_B t_1)\exp(-\lambda' t_1)\, a_{B\to B}(\tau_m) + I_z \cos(\Omega^0_A t_1)\exp(-\lambda' t_1) a_{A\to B}(\tau_m)$$

and this agrees with the top of page 507.

In any event, we are seeing "longitudinal magnetization transfer" between two different molecules in this example during the mixing period of duration τ_m. This entire effect did not exist in earlier chapters of the book, because we never talked about the idea of exchange between two species.

After we do the last knockdown pulse of the pulse sequence, we find using our usual methods that our 2D spectrum is a square of peaks, two diagonal and two cross. The ratio of cross/diag is given by $\tanh(k\tau_m)$ and by varying the parameter τ_m we can deduce a value for k. A major motivation for this entire spectroscopy method was that when you have a small-k exchange situation, it is very hard to measure the value of k from the widths of peaks, as outlined above, and here we have something that works even for very small k. And so finally ends Chap 15.

Chapter 16 begins with a sort of symbolic explanation of relaxation, and this is all new material to a reader of this book. One has to keep in mind: as a molecule tumbles, the spins are on perfect frictionless gimbals bearings and they stay pointed as they were. As a result, if you have two spins, as the molecule tumbles, the B field due to one spin at the location of the other changes direction and magnitude. This action with some characteristic time τ_c is the cause of noise in the B field near one spin due to the

motions of the other spin. A good picture is shown page 514. A similar noise is created by currents induced into the electron cloud, because the cloud tumbles but the spin does not. This is the CSA action, the first case is the d-d interaction.

Now one can wonder about the nature of this noise-like $B_x(t)$ field (as we call it, just to pick a direction). The only books I have with noise discussions are: Bleaney, Big Reif (where the expo at least appears), Sklar and its partner Dig Comm book). None of these books attempts to derive the shape of the autocorrelation function, but Reif seems close. I see several web comments which say that the simple expo decay shape of the autocorrelation function is a characteristic of "Brownian motion" of rotations. I cannot find a derivation of this fact on the web, one guy quotes the Reif graph I found. I guess this is one of those things you have to find buried in a real textbook. I seems a reasonable shape, so I will accept it as applicable to this situation.

Given the expo shape of $G(\tau)$, you must then accept the $J(\omega)$ shape of the spectral density. So we conclude that if we did a spectral analysis of our noise random process $B_x(t)$, we would find $J(\omega)$ as its spread in frequency.

The next ingredient that goes into the cake here is **Fermi's Golden Rule** which Malcolm failed to highlight, but I do it here. In this whole book, Malcolm never really talks about radiation and transitions between energy levels, which seems odd since he has done so much quantum work in the book. He does not treat the RF pulses and FID pulses as radiation, these are classical things, although the spin's reaction to these things is treated with quantum mechanics. In the FID we have $M_x = \langle I_x \rangle$ which links the quantum spin matrix/operator to the classical M_x which induces the FID voltage. In the pulse, the B_{RF} is just a B field we throw into the $\mu \bullet B$ quantum Ham world. So basically, radiation and transitions don't fit into this book very well, but now we need them.

Phil Digression: We *do* know that the B_x of the RF pulse makes the polarization vector rotate, and one can interpret that as causing transitions between the up and down states α and β. We know you can make inversions this way. You could associate some sort of transition rate then with $W = \omega_{nut} = 1/2\ \gamma B_x$. Here is a crude derivation of a rate:

$$P_z(t) = P_z(0)\ [\ \cos(\omega_{nut} t)\ ] = 2\rho_\alpha(t) - 1$$

so that at t=0 we have $P_z(0) = 2\rho_\alpha(0) - 1$. Perhaps $\rho_\alpha(0) = 1$ so that $P_z(0) = 1$.

Now we then get

$$2\ d\rho_\alpha/dt = P_z(0)\ \omega_{nut}\ [\ -\sin(\omega_{nut} t)]$$

Then for very small times we get

$$d\rho_\alpha/dt \approx -(1/2)\ P_z(0)\ \omega_{nut}^2\ t \qquad \text{// at least it is now quadratic in } B_x\ !$$

which is not really a rate.

Schiff showed this as well. In his page 283 (35.12) you get for small times that

$$|a|^2 \sim t_0^2 \text{ so that } |a|^2/t_o = \text{rate} \sim \text{constant x } t_0$$

so you get a rate that increases with radiation time t_0. However, when you integrate this thing into a density of states $\rho(\omega)$, you then get a constant rate because of this fact [see Schiff (35.12) and (35.13)] , really a dimensional argument only, we have

$$\text{rate} = (1/t_0) \int_{-\infty}^{\infty} d\omega\, \rho(\omega)\, t_o^2\, \text{sinc}^2(\omega t_0) = t_0\, \rho(0) \int_{-\infty}^{\infty} d\omega\, \text{sinc}^2(\omega t_0) = t_0\, \rho(0) * (1/t_0) \int_{-\infty}^{\infty} dx\, \text{sinc}^2 x = \pi\rho(0)$$

So we cannot really reproduce the correct Fermi rates from the above amateur formulas for rotation of polarization vector, but we are in the right general area.

So we consider a spin which sees some $B_x(t)$ noise function with spectral density $J(\omega)$, and we then treat that as an EM field density which causes a transition rate between α and β states according to Fermi's Golden rule.

But what Hamiltonian are we using for H' in this rule? Well we can use just $\mu \bullet B_x \sim \gamma B_x$ and this leads to a rate of the form page 521 of Levitt, $W = 1/2\ \gamma^2 \langle B_x^2 \rangle\ J(\omega_0)$. Malcolm does this, then adjusts the up and down rates to match TE.

Now we apply this idea to a single spin-1/2 system, and we say we have W_+ and W_- as our two rates linking the α and β states. We can write a little 2x2 equation as on page 523, and then we can convert this to a single equation for M_z, and we can solve it for $M_z(t)$, and we find the major result that $M_z(t)$ behaves exactly as we assumed earlier in the book if we identify T_1 as 1/(2W). We still have the mysterious factor $\langle B_x^2 \rangle$ floating around, but ignoring that, we have T_1 as a function of W and therefore of $J(\omega_0)$ and therefore of τ_c, our rotational correlation time. This then gives a characteristic shape to the plot of T_1 versus this time, with the famous **minimum**.

We now go the next step: instead of some mysterious B_x^2 that comes from Brownian motion, we now consider *specifically* a 2-spin system with d-d coupling. We could write this as $H' = \mu \bullet B_{x(d\text{-}d)}$ if we wanted, but it ends up being H' = the dipole-dipole usual thing with $[3\ e_i e_j - \delta_i \delta_j]\ I_{1i} I_{2j}$. This 2-spin system has four energy levels as on page 528. We have 4*3 = 12 potentially different rates and we go ahead and compute them all using this H'. The rates pick off the spectral density at three different ω points, which are 0, ω_0 and $2\omega_0$.

Now, given that we have these 12 W rates, we can write a very simple 4x4 matrix equation [Appendix page 633] which says how the four populations change in our J-coupled 2-spin system, populations like $\rho_{\alpha\alpha}$ and $\rho_{\alpha\beta}$, etc. We just treat the rates as inbound or outbound, very simple. We can then convert the 4-vector of populations to a 4-vector [1, $\langle I_{1z} \rangle$, $\langle I_{2z} \rangle$, $\langle I_{1z}\, I_{2z} \rangle$] using for example the fact that $\langle I_{1z} \rangle \sim\ \rho_{\alpha\alpha} + \rho_{\alpha\beta}\ -\ \rho_{\beta\alpha} - \rho_{\beta\beta}$. That is, $\langle I_{1z} \rangle$ gets positive contributions from populations where spin1 is "up" (first index is α), and negative contributions from populations where spin1 is "down" (first index is β). When we convert our 4x4 equation to this new 4 vector, we find that the dynamics matrix is in 1,2,1 block diagonal form, so we then get a private equation for just [$\langle I_{1z} \rangle$, $\langle I_{2z} \rangle$] . This is the **Solomon Equations** and it says this: as time goes by, $\langle I_{1z} \rangle$, $\langle I_{2z} \rangle$ "intermix with each other" according to a very simple equation **involving constants R_{auto} and R_{cross} which are functions of the W_i.**

This equation is *similar in form* to the "longitudinal relaxation equations" we got earlier for a two-species exchange system A and B, but this is a different equation and it applies to a different situation! This equation applies to a pair of spin-1/2's which have a d-d interaction between them. The two spin-1/2's are in the same molecule.

If we consider the total M_z in this 2 spin system, we can derive that $T_1 = 1/R_{sum}$ page 536-7, so again we have a model for T_1.

Let's skip NOE and to right now to the 2D **NOESY** experiment which we apply on our d-d coupled 2-spin system. The pulse sequence is similar to our exchange pulse sequence mentioned above, and there is good reason for the similarity. Again, we want a mixing period τ_m during which only I_z terms are allowed to exist. Again, we compute ρ at time 4 and we ask: what happens to ρ during the mixing period. We can use the exact same method above to answer this question. We first let the $<I_{z1,2}>$ intermix according to the Solomon's, and then we claim that the $I_{z1,2}$'s which make up the ρ matrix must do this same mix! [before we made the two ρ's do this mix] In the exchange case we had separate ρ for A and B, while here we have only one ρ for the 1+2 system.

The upshot then is that our ρ_5 contains a mixture and exactly as before we get a 2D spectrum with four peaks. Now, however, the peak ratio cross/diag = $\tanh(R_{cross}\tau_m)$ whereas before we had $k\tau_m$ inside the tanh function. So by trying several values of τ_m , we can measure R_{cross} (maybe also R_{auto}), we can then deduce the rates W_i , and we can then deduce the d-d coefficient b, and finally we can determine the spacing r between our two spins. So this is how NOESY is used, page 549, to find the structure of a protein.

We now backtrack a moment to pick up the NOE effect. This is an enhancement of the B factor in TE due to irradiating the other species in an I-S heteronuclear AX system, result on page 541. This calculation uses the same d-d rates W_i that we used above in the NOESY preparation. It is the d-d coupling between the I and S spins that gives rise to this effect.

ROESY is next. All I will say is that it is a transverse version of NOESY. Everything looks the same, but the R_{cross} and R_{auto} coefficients are different functions of the W_i , *and* you have to irradiate during the τ_m mixing period to get spin-locking or it does not work. The shape of the two coefficients as functions of τ_m gives ROESY certain advantages, but the purpose of NOESY and ROESY experiments is the same, but find the r spacing between pairs of spins, hence the structure of the molecule in question.

As if this were not enough for this long chapter, Malcolm has stuffed in one more related subject, which is calls **"cross correlation"** effects, and he gives two examples.

The first example DD/DD involves four spins, and the idea is that the two C-H dipole pairs affect the dipole pair C-C. We don't learn details of the pulse sequence used here, although it does make use of double-quantum coherences. The upshot is that the angular orientation of the H-C-C-H system affects the spectral peak widths of the C-C system in a certain unnamed experiment you can do. The reason is that the orientation affects whether the two C-H systems exert an additive or subtractive effect on the C-C systems in terms of relaxation due to the C-H systems. Additive means more relaxation means wider lines.

The second example is a DD/CSA interaction and I just quote the meta review comment:

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.