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

16.1 Types of Relaxation. Just a basic review, there are always two items to worry about, longitudinal and transverse. The "study of" relaxation can tell you things spectra don't tell you.

16.2 Relaxation mechanisms (514).

(a) **molecular tumbling and the d-d interaction**. Here, if you compute the B_x field of spin 1 at the location of spin 2, the number you get is a function of molecular orientation, so this activity causes **fluctuations** (modulations) of the B_x field (and also B_y and B_z).

(b) **molecular tumbling and the chemical shift interaction**. Here, the induced field say due to a benzene ring current at a spin location varies with molecular orientation, so again we get a fluctuation B_x. In general, the chemical shift is given by a tensor and is not isotropic! This is the **CSA** mechanism.

(c) **molecular rotation and the spin-rotation interaction**. The rotating molecule has charges which make currents under rotation and these make B fields. This is distinct from induced fields in response to external fields as in (b) above. So again, rotation makes B_x fluctuate.

(d) **quadrupole**: I guess as molecule tumbles, the E field at the nucleus (its gradient) tumbles, and this causes something similar to B_x field noise, but I think we will look into this more below. When quadrupole is present, it is usually the largest interaction and so dominates the relaxation. But this chapter won't have anything more to say about quadrupole.

The normal strength ordering is shown of these various effects. In $I > 1/2$, the E2 dominates, and in a gas the spin-rotation dominates.

16.3 Random field Relaxation (515). Malcolm avoids using the word "noise", but this whole discussion is on that subject.

16.3.1 Autocorrelation function (516). The definition is given top of page 517 -- the average of the voltage (or B_x in this case) times itself shifted by time τ. Usual shapes for $G(\tau)$ are shown. **G(0)** is the mean squared field or the "energy". I am familiar with this idea, see Chap 6 of my **Spectral Theory book** and **Sklar**. Top page 519 gives a simple model for G where you use a magnitude and τ_c as a decay width.

16.3.2 Spectral Density. If you write $G(\tau)$ as an integral in the usual way (symbolized by top of page 517), it is a convolution integral of sorts, and if you FT the three functions involved, you find that

$$G(\omega) = | B_x(\omega)|^2$$

which is a very basic FT result: the FT of the autocorrelation function *is* the spectral density. If we use the simple model in (16.2) for $G(\tau)$, we can FT it to get (16.4) as the spectral density which is a one-parameter model. Malcolm will use this function as in 16.5 such that area = 1. All fine so far. [BUT, I later found out that area = π when integrated $-\infty$ to ∞ in $d\omega$.]

16.3.4. Transition probabilities (520).

See separate document entitled "factor of pi" for derivation of the equations below, I will try to summarize here. Saxon shows the following "Fermi's Golden Rule" in its usual form,

$W = 2\pi/\hbar\ \rho(E)\ |H'_{mk}|^2$ $\rho(E)$ = density of states

For use in Levitt, we have to make two modifications. First, we convert to ω instead of E as the argument inside the state density to get

$W = 2\pi/\hbar^2\ \rho'(\omega)\ |H'_{mk}|^2$ $\rho'(\omega)$ = density of states

Next, we convert to Levitt's script Hamiltonian which is in terms or ω instead of E, $H = \hbar\mathcal{H}$. Then we have

$W = 2\pi\rho'(\omega)\ |\mathcal{H}'_{mk}|^2$ $\rho'(\omega)$ = density of states

The correctly normalized-to-unit density of states is given by

$$\rho'(\omega) = \mathcal{J}(\omega)/\pi \quad \text{where} \quad \mathcal{J}(\omega) \equiv \tau_c/(1+\tau_c^2\omega^2) \quad \text{and} \int_{-\infty}^{\infty} d\omega\ \mathcal{J}(\omega) = \pi \quad \text{so} \int_{-\infty}^{\infty} d\omega\ \rho'(\omega) = 1$$

so we end up with the final version of the Golden Rule that applies for Levitt's work

$W = 2\ \mathcal{J}(\omega)\ |\mathcal{H}'_{mk}|^2$

Application #1: Assume that $\mathcal{H}_{RF} = -\boldsymbol{\mu}\bullet\mathbf{B} = -\gamma B_x I_x$ so that $\langle\alpha|\mathcal{H}_{RF}|\beta\rangle = -\gamma B_x \langle\alpha|I_x|\beta\rangle = -\gamma B_x/2$. Then our rate is given by

$W = 2\ \mathcal{J}(\omega_0)\ |-\gamma B_x/2|^2 = (1/2)\ \mathcal{J}(\omega_0)\gamma^2 B_x^2$ // agrees with (16.6) on page 521

Instead of an applied B_x^2 imagine that we have some fluctuation whose mean is $< B_x^2>$. This is then the general meaning of equation 16.6. This would be the rate up or down (before adjustment for TE) between the levels in a spin-1/2 system.

Comment: The *shape* of $\mathcal{J}(\omega)$ corresponds to assuming $G(\tau) = A\ \exp(-|\tau|/\tau_c)$ for the autocorrelation function. The thing called the "**spectral density**" is the FT of $G(\tau)$ which would be $J(\omega) = 2\ A\ \mathcal{J}(\omega)$. We don't care about the constant A because in the end we have to use the *normalized* (to π area) $\mathcal{J}(\omega)$ in our transition rate formula, but the shape of $\mathcal{J}(\omega)$ is determined by the assumed $G(\tau)$ form. Apparently the expo form is a good shape to assume for $G(\tau)$. Levitt does not give it much justification.

16.3.5 Thermally corrected transition probabilities (522). We have assumed rates up and down are the same, and this is wrong for TE. So the idea is to "fix up" the results as in (16.7) which sound very reasonable to me. The middle equation on this page is the balanced rate equation "the rate one way is

equal to the rate the other way in TE". Combining these two equations gives the right ratio for ρ_α/ρ_β as shown on page 283.

Now he presents a question: why does (16.6) say the rates in the two directions are equal? I might then ask, "why does **Fermi's Golden Rule** predict rates are equal" ? After all, the matrix elements $\langle\alpha|H'|\beta\rangle$ and $\langle\beta|H'|\alpha\rangle$ would seem to be equal in magnitude for an I_x in there. Malcolm to his credit addresses this question, and I think he is saying that when the two states are different in energy due to B_0, one state will result in less "field" than the other and this will alter the calculation. We assumed that our spin fields played no role relative to the H' B field, so this is probably the issue. [Perhaps this would show up in higher order perturbation theory.]

16.3.6 Spin-lattice relaxation (523). It is these transition probabilities W which *cause* T1 relaxation. We have a quantum transition rate that is active between our two α β states (in both directions) due to B_x field noise which we represent as $\mathcal{J}(\omega)$ in spectral shape. We start here writing some simple **rate equations** for how our two populations change, and we quickly end up with a simple ODE for M_z as shown top page 524, and I agree with the solution shown. If we then *identify* $T_1^{-1} = 2W$, we have then derived our earlier assumed effect of T_1 relations. We can then make this connection:

$$T_1^{-1} = 2W = J(\omega_o)\,\gamma^2 \langle B_x^2\rangle = \gamma^2 \langle B_x^2\rangle\ \tau_c / [\ 1 + (\tau_c\omega_o)^2\ ]$$

or inverting

$$T_1 = [\ 1/(\gamma^2 \langle B_x^2\rangle)]\ \ [\ 1 + (\tau_c\omega_0)^2\ ] / \tau_c$$

and he has plotted this on page 524 bottom [which is a very characteristic plot for any T_1 model like the one we just did] . As $\tau_c \to 0$, it blows up, and as $\tau_c \to \infty$ it goes as $\omega^2\ \tau_c$ linear. The calculus min is at $\tau_c = 1/\omega_0$. Then in typical Malcolm fashion, he shows graphically why calculus says there is a minimum, but these arguments don't do much for me, two pages consumed 525 + 526.

He then talks a little about temperature. I would assume that somehow $\langle B_x^2\rangle \sim kT$ in some sense, so I expect an effect on T_1 via this mechanism. But he says no, temperature makes things go faster, not more amplitude, so that means τ_c drops as T increases, which seems reasonable. This means high-T puts you to the left on the curve, and that is what top page 527 is showing. If you "warm up a sample", the effect on T_1 depends where you started on "the curve". In this top example, warming lowers T_1, but in the lower case it raises it (warming moves you left). So I am confused about the effect of temperature on $\langle B_x^2\rangle$.
[Answer: $\langle B_x^2\rangle$ is rather abstract right now, just used for illustration. Below we shall do the d-d example in detail and we will get W formulas directly, with no need for any assumed $\langle B_x^2\rangle$. Since this $\langle B_x^2\rangle$ thing does not appear in the result, we don't ask about its temperature dependence!]

Comment: I think I will mention that I thought maybe $\langle B_x^2\rangle \propto kT$ // But now I won't mention it!

16.4 Dipole-Dipole Relaxation.

16.4.1. Rotational correlation times (528). If the noise source is rotation, I agree that the correlation time scale should be on the order of the rotation period, so he is saying roughly that $\tau_c = 1/\omega_{rot}$. It is this

parameter τ_c which controls the shape of the spectrum J(ω). If τ_c is very small, we are rotating very fast, and our spectrum is broad and has lots of high frequency content.

16.4.2 Transition Probabilities. (528). I see how the "unadjusted" W_0, W_1 and W_2 are defined. The W_2 has double the "gap" of energy difference, so Boltzmann adjustments are double.

I went off and computed the three W_i values and I get exactly Malcolm's results. Yes, all the rates are $\propto 1/r^6$. I will summarize the W_i calculations below at the end of this subsection.

Now Malcolm is off again on one of his "physical explanations". Why do we have resonance at the double Larmor frequency? In quantum theory, I see the energy levels and I know the answer, but he wants a classical explanation in terms of magnetic fields, so fine.

(a) the top picture on page 532 shows that if you rotate the molecule shown at ω_{rot}, the B field seen by the #2 spin rotates at $2\omega_{rot}$. But so what??? What is the point being made here??? I guess he is thinking of the molecular rotation rate as the "fluctuation frequency ω" and here it perturbs at 2ω. You would think this would mean that you need $\omega = \omega_0/2$ in order for spin #2 to see effective $\omega = \omega_0$ so this argues the wrong direction.

OK, let's just ignore these two pages. Yes, it is the molecular rotation which is generating the perturbation B field, and which has the J(ω) spectrum. But we are doing quantum mechanics here. We have derived the Ham H from classical arguments, it is true. The energy level diagram shows the possibilities of transition. We calculate the rates between the levels. We know the top and bottom levels are $2\omega_0$ apart. The H' provides its own energy *scale* and rate *scale*. The J(ω) function *does not alter scale*, it just tells how the 100% of noise energy is distributed in ω. We are just "using" the simple form that matches the expo autocorrelation function with its scale set by the correlation time τ_c. I would have to look in some other book to see how this would be justified in a random collision situation. Big Reif has the ingredients, but I don't see him applying to this subject.

How do we leave this somewhat confusing section? The two spin-1/2 system has a d-d interaction, and this interaction results in the transition rates I computed, which pull the system toward equilibrium. Do we have a model for T_1 here? He has not written anything down yet. In the previous book section, we made a model of T_1 for the system containing on spin-1/2 spin which "sees" a fluctuating field. Let's just hold off for a while on T_1 for two spin-1/2's. [We shall soon find that $T_1 = 1/R_{sum}$, just wait.]

Notes added. First, a review of what is going on here. We know that one spin makes a B field at the other spin, we might just call this B_x for want of a name. It is the random banging/tumbling/rotation (with collisions of course) of the molecule containing these two spins that creates $B_x(t)$ varying in time at the site of either spin. This $B_x(t)$ is really a noise signal and when measured at the "other spin", it has some random pattern and has some autocorrelation function. If $B_x(t)$ were $\sin(\omega_1 t)$, it would have no continuous spectrum, but since $B_x(t)$ is a *random* signal, it does in fact have a continuous spectrum of some sort. We have seen examples of noise patterns which make very broad "white noise" with a flat spectrum. But in this application, the noise is best characterized by a decaying expo autocorrelation function, and that results in $\mathcal{J}(\omega)$ being the Fourier spectrum of $B_x(t)^2$. We know that a time-varying B-field induces spin transitions because there is a non-zero matrix element of H' due to the presence of this $B_x(t)^2$ activity. But only the spectral components near 0, ω_0 and $2\omega_0$ will be successful in inducing significant transition rates. This is all built into the derivation of the Fermi Golden Rule. You can imagine if you like that the noisy $B_x(t)^2$ is generating a local EM field cloud with spectrum $\mathcal{J}(\omega)$ and it is this field

of photons that is what makes the transitions. In any event, I would conclude that as we approach absolute zero, the banging/rotating would slow, we could imagine this represented by $\tau_c \to \infty$, and $\mathcal{J}(\omega)$ becomes very low and very flat, and has no energy left anymore at the three sample points just mentioned, so rates $W \to 0$, or $T_1 \to \infty$ and there is then "no relaxation", approach to TE is then very slow.

Second, here is a quick summary review of the three calculations in this section. First, we know that we can write

$\mathcal{H}' = b\,[\,3e_i e_j - \delta_{ij}]\, I_{1i} I_{2j}$ / b and $\mathcal{H}'$ both have units of ω, I's are dimensionless

We first show these trivial facts:

$\langle\alpha|I_i|\alpha\rangle = (1/2)\,\delta_{i,3}$ i = 1,2,3 meaning x,y,z
$\langle\beta|I_i|\beta\rangle = -(1/2)\,\delta_{i,3}$
$\langle\alpha|I_i|\beta\rangle = (1/2)\,\delta_{i,1} + (1/2i)\,\delta_{i,2}$
$\langle\beta|I_i|\alpha\rangle = (1/2)\,\delta_{i,1} - (1/2i)\,\delta_{i,2}$

Case #1: (W_1) Insert formulas from the list above to show that

$\langle\alpha\alpha|\,\mathcal{H}'|\alpha\beta\rangle = b\,[\,3e_i e_j - \delta_{ij}]\;\langle\alpha|I_{1i}|\alpha\rangle\;\langle\alpha|I_{2j}|\beta\rangle = (3b/4)\,e_z\,(e_x - ie_y)$

$|\langle\alpha\alpha|\,\mathcal{H}'|\alpha\beta\rangle|^2 = (3b/4)^2\,e_z^2(1-e_z^2)$ // use $e_x^2 + e_y^2 + e_z^2 = 1$ as needed

If we average the variable part over dΩ we get

$$= (1/4\pi)\int_0^{2\pi} d\phi \int_{-1}^{1} dx\, x^2(1-x^2) = (1/4\pi)*2\pi*2\int_0^{1} dx\, x^2(1-x^2) = 1*[\,1/3 - 1/5] = 2/15$$

Our rate is then

$W_1 = 2\,\mathcal{J}(\omega_o)\,|\,\mathcal{H}'_{mk}|^2 = 2\,\mathcal{J}(\omega_o) * (3b/4)^2 * (2/15) = 2*2*9/(4*4*15)\,\mathcal{J}(\omega_o)b^2 = (3/20)\,\mathcal{J}(\omega_o)b^2$

in agreement with (16.11). All 4 rates involving an ω_0 transition will be the same because the only difference is ± i , as shown above, which difference goes away on abs squared.

Case #2: (W_2). Using the same method we have

$\langle\alpha\alpha|\,\mathcal{H}'|\beta\beta\rangle = b\,[\,3e_i e_j - \delta_{ij}]\;\langle\alpha|I_{1i}|\beta\rangle\;\langle\alpha|I_{2j}|\beta\rangle = (3b/4)\,(\,e_x^2 - e_y^2 - 2ie_x e_y\,)$

$|\langle\alpha\alpha|\,\mathcal{H}'|\beta\beta\rangle|^2 = (3b/4)^2\,(1 - e_z^2)^2$ // use $e_x^2 + e_y^2 + e_z^2 = 1$ as needed

Average again over dΩ. As before, the dϕ gives 2π, so we get for the variable part $(1 - e_z^2)^2$,

$$= (1/2) \int_{-1}^{1} dx\,(1 - x^2)^2 = 1 * \int_{0}^{1} dx\,(1 - 2x^2 + x^4) = (1 - 2/3 + 1/5) = (15 - 10 + 3)/15 = 8/15$$

Our rate is then

$$W_2 = 2\,\mathcal{J}(2\omega_o)\,|\mathcal{H}'_{mk}|^2 = 2\,\mathcal{J}(2\omega_o) * (3b/4)^2 * (8/15) = 2*9*8/(16*15)\,\mathcal{J}(2\omega_o)b^2 = (3/5)\,\mathcal{J}(2\omega_o)b^2$$

in agreement with (16.12).

Case #0 (W_0). Again using the same method we have:

$$\langle\alpha\beta|\,\mathcal{H}'|\beta\alpha\rangle = b\,[\,3e_ie_j - \delta_{ij}]\;\langle\alpha|I_{1i}|\beta\rangle\;\langle\beta|I_{2j}|\alpha\rangle = (3b/4)\,(1/3 - e_z^2)$$

$$|\langle\alpha\beta|\,\mathcal{H}'|\beta\alpha\rangle|^2 = (3b/4)^2\,(1/3 - e_z^2)^2$$

Average over $d\Omega$. As before, the $d\phi$ gives 2π, so we get for the variable part $(1/3 - e_z^2)^2$,

$$= (1/2) \int_{-1}^{1} dx\,[\,1/9 - 2/3\,x^2 + x^4] = \int_{0}^{1} dx\,[\,1/9 - 2/3\,x^2 + x^4] = 1/9 - 2/9 + 1/5 = 1/5 - 1/9 = (9-5)/45 = 4/45$$

Our rate is then

$$W_2 = 2\,\mathcal{J}(0)\,|\mathcal{H}'_{mk}|^2 = 2\,\mathcal{J}(0)\,(3b/4)^2 * (4/45) = 2*9*4/(16*45)\,\mathcal{J}(0)b^2 = (1/10)\,\mathcal{J}(0)b^2$$

in agreement with (16.13).

16.4.3 Solomon Equations (533). Equation (16.15) and (16.16) and (16.17) all come from the appendix and are correctly transcribed. I then verified the expressions given for R_{auto} and R_{cross}. Malcolm then plots these two R factors as functions of τ_c which we know appears inside the J(ω) functions. He uses typical <r> for the spacing of two protons, throws in their gammas, sets the field B_0 to a large value which controls the value of ω_0 which appears in these factors. He notes that there is a critical value of τ_c which causes $R_{cross} = 0$ as shown in the lower graph. Equations (16.15) are the Solomon Equations.

I sense that we are in a "set up phase" here, getting ready to do something significant with all this machinery, but so far I am in the dark.

16.4.4 Longitudinal Relaxation (536). We use our machinery now to solve a very simple problem. If you are away from TE, how does $\langle I_{ztot}\rangle$ restore to TE? Our equation for this problem is (16.19) with R_{sum} as shown in (16.20) and rewritten in (16.21). The solution is "the usual" restoring expo shown at the bottom of the page, and for this problem (only), we find that $T_1^{-1} = R_{sum}$. If you plot T_1 we get a curve similar to our earlier one on page 524 (*that* T_1 came from B_x noise that we just assumed there). In general, T_1 is caused by many mechanisms and sources at once, so you cannot very easily go backwards

to find something like a bond length directly from T_1 measurements. The main point here is that we have completely calculated T_1 *due to the d-d interaction* "from first principles" !

16.4.5. Transverse Relaxation (537). Presumably we could redo all our theory (another appendix would be needed) to derive this result which Malcolm just states without comment or derivation. It has a similar structure to the other things we have seen, just the coefficients are different. If you plot this, however, you find a falling value as τ_c increases. Why would that be? Well in general we have

$J(\omega) = \tau_c/ (1 + \omega^2\tau_c^2)$ goes as τ_c at small, goes as $1/\tau_c$ as large.

In general, then, things like $R_{sum} \rightarrow 0$ for large τ_c so T_1 grows without limit, as shown. Why would this not also apply to the expression on page 537 for T_2^{-1}? The ω=0 term makes $J(\omega) = 1/\tau_c$ for small τ_c so the J(0) gets very large for small τ_c. For *large* τ_c the J(0) term goes as τ_c and this causes $T_2^{-1} \sim \tau_c$ and therefore $T_2 \sim 1/\tau_c \rightarrow 0$ as shown correctly in the graph on page 538.

Comment: I am not sure how I would start to derive (16.22) for T_2. I guess a variation B_z^2 would act to perturb the Larmor frequency of a spin, and that result in dephasing and hence T_2. Maybe you treat the Larmor angle $\phi(t)$ as a noise-like variable which responds to noise like B_z^2 and then look at $\langle\phi(t)^2\rangle$ and when this is π, you are done.

Or perhaps you would start with the Bloch Equations which talk about transverse stuff as well as long,

$dM_x/dt = \gamma[\mathbf{M} \times \mathbf{B}]_x + M_x/T2$
$dM_y/dt = \gamma[\mathbf{M} \times \mathbf{B}]_y + M_y/T2$
$dM_z/dt = \gamma[\mathbf{M} \times \mathbf{B}]_z + (M_{0z} - M_z)/T1$

but I don't see these predicting T2. You need to see how the W rates affect the coherences. You know that the coherences do in fact phase along at the frequencies 0, ω_0 and $2\omega_0$ from page 351. Consider the coherence ρ_{rs} perhaps it is $\rho_{\alpha\alpha\rightarrow\alpha\beta}$. We know that coherences change in time when we apply an RF pulse, so they ought to change in time due to a noise created RF pulse. I would have to first figure out what a noise B_x^2 does to the density matrix ρ, then I could look at off-diagonal matrix elements of this altering ρ to see how the coherences were changing in time. It is the rate at which they fade back to zero that determines T_2. The noise here will have the same $J(\omega)$ spectral shape. The time derivative of ρ I don't think was much explored in Levitt earlier chapters, but I would guess something like $d\rho/dt = [\rho,H']$ is what pulls you away from the basic phasing frequencies, and this will involve matrix elements of H' etc etc. I think I could do this exercise problem in a few days at most, but let's let it be for now. As you can see, I have several possible starting points.

16.5 Steady State Nuclear Overhauser Effect (NOE). (538). We have a hetero AX system with I and S as usual, and γ_I is assumed larger. The results for the rates shown bottom page 538 and top 539 all follow from previous page notes, as does the TE value of ρ. Then the specific rates like W_{1S} all follow from previous calculations, nothing new except the ω points of sampling the spectrum. Of course b_{IS} has both gammas. So page 539 is fine.

Now on page 540, we are supposed to irradiate our system with I-spin signal, just apply it all the time. We regard the four levels as two systems (gray blob), and compute the rates in and out. We have two equations in two unknowns, namely

A+B = 1/2
aA = bB so that A = (1/2) [1 + a/b] B = 1/2 - A

where a and b are the sum each of four rates as shown. I went into Maple and entered all these rates and had Maple compute A. Maple gave this result for A

$$A = \frac{1}{8}\,\frac{(2-bi+bs)\,w0+(2+bi+bs)\,w2+(4+2\,bs)\,w1s}{2\,w1s+w2+w0}$$

I then had to switch to hand calculation and we then able to verify that

A = (1/4) [1 + bs/2 { ε_{NOE} }] with ε_{NOE} exactly as shown in (16.28)

I then used B = 1/2 - A to get the rest of the pair of equations above (16.28). In all this algebra, *no approximations or assumptions of any kind were made*, so I think Malcolm's comments are misleading and I will comment to him on that. Of course the initial equations assume things are small.

Now, the result is that, with this I-irradiation, we get ρ_{TE} = diag(A,B,A,B). If we just enter the values for A and B, we get that ρ_{TE} = 1/4 diag(1,1,1,1) + 1/4 (ε_{NOE} bs/2) diag(1,-1,1,-1). This last matrix is recognized as 2[1 $\otimes$ S_z] using the rules Levitt gave earlier for interpreting these matrix. So we get

ρ_{TE} = 1/4 1 $\otimes$ 1 + 1/4 (ε_{NOE} bs) 1 $\otimes$ S_z = 1/4 1 + ε_{NOE} bs/4 S_z

which is then the bottom result on page 541. Here is the point: this I irradiation has changed the TE value of the population matrix ρ. It has not created off diagonal elements, but it has changed the diagonal elements. It makes it appear that you have only species S present, and that its population is "enhanced" above what it was in the normal TE (see 16.24) by factor ε_{NOE}. So assuming ε_{NOE} > 1, doing this irradiation on I will increase the final FID signal for any NMR experiment you do on S. So the irradiation supplied on I not only "decouples" I from the problem [which we already knew, and here we see specifically how I_z no longer appears in ρ_{TE}] , it also boosts the signal on the S channel FID.

Page 542 the computes ε_{NOE} in both the small and large τ_c limits. It was easy to verify the small limit on the top of the page, but the large τ_c limit cost me about 3 scratch pages of algebra . I did obtain exactly the result he states, however.

Next, we can use the general expression with a specific case like hydrogen and carbon and a specific B_0 and plot a curve for $\varepsilon_{NOE}(\tau_c)$. The solid line is for ^{13}C and in its two limits, it agrees with the limiting calculations, being 3 at the left end. The other line is for ^{15}N which has γ of opposite sign. You can see that in both cases you get considerable "enhancement" in the small τ_c regime (up to factors of 3 and 4 for C and N). In the other limit, benefits go away.

The paragraph on page 542 bottom does not yet make sense to me, I think maybe I first have to read the next sections to see what he is talking about.

Historical Note: the original effect was between one nuclear spin and one electron spin: see http://bouman.chem.georgetown.edu/nmr/noe/noe.htm for a review of key NOE facts.

Overhauser Effect

A phenomenon discovered by Albert Overhauser in 1953

Saturating the electron magnetic resonance in a paramagnetic system would cause the nuclear resonance intensity to be enhanced by a factor of the order of 10^3

The ratio

$$\frac{\gamma_{electron}}{\gamma_{nucleus}}$$

16.65 NOESY (543) (NOE Spectroscopy)

I have no idea where we are heading here, so just keep reading. In footnote, Malcolm says that the thing we are about to study is in fact unrelated to the NOE effect we just read about, despite the name!!!

16.6.1 NOESY pulse sequence (543). Luckily, we are going to reuse the pulse sequence we used back in Chapter 15 for doing "exchange spectroscopy".

16.6.2 NOESY signal (543). We did the "theory" here already for just one spin, and here we repeat things for 2 spins, so we can look back to page 505 to red-check-off the results. As before, at point 4 we keep only the I_z terms due to our "phase cycle filter" process indicated by the black line marking order 0 only in the τ_m gap. Now, during the "mixing time" τ_m the Solomon equations tell us that the 1 and 2 systems intermix their z-spin expectation values. It is the T_1 longitudinal dipole-dipole relaxation process that causes this mixing, as developed in Appendix 17.13 see page 633. The situation is mathematically similar to the exchange mixing study we did earlier and we obtain a set of four peaks, two diagonal and two cross. Each peak is associated with a coefficient a_{diag} or a_{cross} which in turm are functions of the Solomon equation matrix factors like R_{cross} which are calculated from those Golden Rule rates like W_1.

In this section Malcolm has two errors which I have fixed in pencil and which I will report.

16.6.3 NOESY spectra (546). Here we just look at two cases for τ_c . If it is large (slow rotating molecules), then page 535 [rightmost red dot] shows that $R_{cross} > 0$ (for our sample numbers). In this case, the sinh function is positive and then bottom page 546 shows our expected peak size as we vary τ_m in our pulse sequence. On the other hand, if τ_c is small (fast rotation) page 535 (bottom red dot) shows that $R_{cross} < 0$, then the sinh thing is negative and our prediction for our experiment is on page 548, and now the cross peaks have the opposite sign!

16.6.4 Both at Once (546): In this "experiment" we have a homo AX system and by varying τ_m, we could do a fit to our predicted curves and in that way we might be able to deduce values for R_{cross} and R_{auto}. Then looking back at page 534, we might be able to figure out that various W_i rates and that might let us figure out a value for "b" and hence we can know r, the bond distance [but he is not saying all this] . All this "stuff" is deriving from the dipole-dipole interaction between our spins A and X. That is how we computed all those rates like W_2

In our previous "experiment" with the same pulse sequence, we also had an AX system, but we had the A and the X spins "exchanging" at a certain rate we called k. That experiment made four peaks in exactly the same location as the previous paragraph, but from fitting the curves we were trying to decide a value for k.

16.6.5 Molecular Structure (549). Take a protein with 120 AA's and throw it into this experiment and do the proton spectrum. For each value of τ_m , you get a spectrum like that shown on page 549, where somehow it must distinguish + and - peak amplitudes. You presumably resolve this into a "set of squares". For each square, the upper right corner tells you Ω_1 say, and the lower left tells you Ω_2 , so you then know your chemical shifts for a pair of protons which are d-d interacting (*through space*!!!) The size of the cross peaks relative to the diagonal peaks give you information on the separation in space of these two spins! Here is a reminder of the connection to this distance:

(a) $peak_{cross} / peak_{auto} = R_{cross}/R_{auto} = \tanh(R_{cross}\tau_m)$ // use experiment to find R_{cross}

(b) $R_{cross} = (1/10)\, b^2 \{ J(0) - 6\, J(2\omega_0) = W_0 - W_2$ // from R_{cross} find b

(c) $b = -(\mu_0/4\pi)\ \gamma^2 B_o^2 / r^3$ // from b find r

Now look at plate 5 facing page 273. Within the molecule, we already know all about the spacings between H atoms that are rigidly connected. The issue is the spacing between H atoms between two pieces of the strand -- that is, highly separated H atoms. The spacings that the NOESY spectrum gives you act as constraints on what shape the molecule can have. The claim is that you can completely nail down the shape of the molecule as in this plate example. This work of Lu must have taken a lot of analysis effort, but this doubtless let them build a "machine" that could do this for any molecule, a shape analyzer. Right up my alley. The caption says they did NOESY and two other kinds of NMR to nail this thing down.

The NOESY experiment involves "cross relaxation" between the I_z components of the two spins, according to the Solomon equations.

16.7 ROESY

16.7.1 Transverse Cross Relaxation (550). Suppose you had such a process (we will study it soon), you would expect something like top page 551 to happen. The M_x transfers from spin 1 to spin 2 (just as we got this for M_z above). The problem is as follows: if you go into a rotating frame where I_1 does precess, then of course I_2 is going to precess and that is what is shown here. The problem is, then, as spin 1 transfers little "doses" of M_x mag over to spin 2, it keeps adding M_x at a different time when spin 2 is at a different location, so in the end, you end up adding nothing to spin 2 because it averages out over the precessional rotation of spin 2.

In other words, the fact that we have a relative rotation between the two precessing spins (which Levitt calls a **mutual precession**), you can not "build up" any amount of transverse transfer.

16.7.2. Spin Locking (551) Levitt now digs way back in this book to some set up he did earlier, we look back at page 266. The subject being treated there was what happens when you apply some strong RF that is off resonance. We go first of all into a rotating frame trying to match the spin precession. With no RF, spin just sits there, and if you go off resonance in either direction, the spin precesses slowly one way or the other about z.

But if you have a strong x directed B_{RF} and you go into this same rotating frame, you find that the spin axis is no longer the z axis, it wants to be the x axis because in this frame, the I_z term in the Ham is very small relative to the transverse terms like I_x . The larger B_{RF}, the larger ω_{nut} , and the more the spin axis in the rotating frame is knocked down toward the x axis. This is what the arctan function is saying, and see also my picture on page 267. If you are a little off resonance, you get precession about this funny tilted down axis. The rate of precession is given by ω_{eff} on page 266 which is roughly ω_{nut} if ω_{nut} is large.

So, now consider our two spins that have a chemical shift. If you go into a rotating frame of spin 1, we see spin move relatively. However, if we smoke this system with B_{RF}, then in the rotating frame both spin axis are going to be tilted down close to 90 degrees. This is shown on page 552 in the drawing. If you are exactly on resonance for spin 1, it is exactly at 90 degrees, and the precession axis for spin 2 is perhaps at 88 degrees. Although the two resulting transverse spins move a little relative to each other, they are always very close. In this example, they are both sitting basically along the y axis. This is far cry from what we had with no B_{RF} as just discussed above. Basically, the B_{RF} is locking the two spins together. We did not talk much about the opening angle of the precession, but it seems to be 0 degrees for the spin 1 and perhaps 2 degrees for the spin 2.

The point, then, is that if you supply such a strong B_{RF}, in this rotating frame the two transverse spins won't rotate relative to each other (except a tiny amount) despite the fact that they might have a large chemical shift! This is pretty amazing to me, and I have seen "spin locking" mentioned on the web. On says that "spin locking inhibits mutual precession between to chemically shifted spins".

16.7.3 Transverse Solomon Equations (552). No derivation is given for these, but it must surely parallel the longitudinal development, though I am not sure how to "get started". I will defer this until the book is done and errata are sent out. The R's all have T on them for transverse. Malcolm plots these new R^T's and compares them to the R^L,s we used earlier. The $R_{cross}{}^T$ has a nicer shape without a confusing zero crossing.

16.7.4. ROESY spectra. (554). The name ROESY is misleading. This is really going to be a "transverse relaxation" experiment, but historically if you have a wide RF pulse in your sequence, the experiment is called a "rotating frame" one, so this is Rotating Frame Overhauser Effect Spectroscopy. Sometimes NOESY is called "laboratory NOE". The name Overhauser is associated with the notion of a *transfer* of spin between two species due to a relaxation mechanism. In NOESY we transferred between I_{1z} and I_{2z} during the "mixing period", whereas here we will mix between I_{1x} and I_{2x}. The pulse sequence mixing period has a constant irradiation which is used to achieve the spin locking discussed above, so that the transverse mag can not be washed out by the mutual precession. It has nothing to do with the irradiation one supplies in the official "nuclear Overhauser effect" which is used to cause enhancement ε_{NOE}.

So the pulse sequence is shown page 554 (a simple form) and it has the usual States phase cycling. As we have done several times now, we do the math to show there are 4 peaks with magnitudes given by the combination cosh * exp decay, with R_{cross} and R_{auto}, with the T label. Because R_{cross} is always negative, the spectrum always looks like page 556.

Both NOESY and ROESY have the same purpose. You vary τ_m of the mixing period, and then you do a fit to determine your constants R_{cross} and R_{auto} . You can then deduce the value of b, and finally a value of "r" separating the two spins. Both these methods are making use of the dipole-dipole interaction Hamiltonian. Page 557 compares NOESY and ROESY and shows which is better for a given regime of τ_c magnitude. ROESY makes larger peaks for small τ_c (second row of pix) , NOESY wins for large τ_c (correlation time) as seen from the bottom pair of pix. A key idea is that ROESY avoids the problem of a critical value of τ_c where R_{cross} vanishes completely (second row of pix).

16.7.5 ROESY and chemical exchange (556). The cosh-business 4 peak spectrum first appeared in our exchange application, and the cross peaks there were always positive. We had $R_{cross} = k > 0$. For ROESY we always have $R_{cross} < 0$. So I guess the point is that you can tell from the sign of the cross which mechanism is happening.

16.7.6. ROESY and TOCSY (556). Recall that TOCSY (discussed end of Chap 14) was a method of disambiguating the spectra of a mixture of AMX and A'M'X' triple-spin-1/2 J-coupled systems with some degeneracy. It used a mixing period of hundreds of π_x pulses or SES's. The only comment made here is that these two pulse sequences are "similar" (page 554 versus 469) and you can get the AMX J-coupling action showing up in your ROESY spectrum, and you can get the dipole-dipole transverse relation AX effect showing up in our TOCSY spectrum, so each can affect the other. For this reason, there are fancier pulse sequences for ROESY which attempt to eliminate TOCSY contamination.

16.8 Cross Correlated Relaxation (557).

16.8.1 Cross correlation (557). This is like autocorrelation, but between two different signals.

16.8.2. Cross correlation of spin interactions (559). We are not surprised to find that spin effects caused by the same process of molecular rotation are correlated. A "common physical link" is what makes for correlation.

16.8.3 Cross correlation in dipole-dipole interactions: angular estimations (560). Look back at page 206 where we were talking secular d-d. Suppose you have two C-H bonds as shown with one having angle 0 and the other angle θ. Then we have $d_{1jk} = b_{jk}*1$ and $d_{2jk} = b_{jk}*(1/2)\ [\ 3\cos^2\theta - 1\ ]$. So the ratio of the two Ham terms will be $(1/2)\ [\ 3\cos^2\theta - 1\ ]$. And signals obtained from these two terms will have this ratio to each other, so if you can measure the ratio, you can deduce θ.

We now have a long example starting page 561. Both molecules have ^{13}C in the two gray locations, so we have a 4-spin system to think about (a la Chapter 14). In the α form, the C-H bonds are perpendicular and so we expect the above ratio to be - 1/2. In the β form the C-H bonds are antiparallel so we ratio should be +1. So we want to concoct an experiment that distinguishes these two forms.

I do recall various experiments in earlier chapters involving "double quantum filters", so let's just accept that we could isolate the four double-coherences listed here (they eventually get mapped by the

phase cycle filter to -1 order of course). Each double quantum coherence [such as $\rho_{\alpha--\alpha}$] has a characteristic frequency, and some of these are listed on page 561. These are the ones that are near the value $\Omega_2 + \Omega_3$ which are the frequencies for the two carbons, see ordering 1-2-3-4 mentioned. So if we look at the "double carbon spectrum" we expect to see the four peaks given here, which differ by various combinations of the J-couplings. The 1D spectrum is shown top page 561 for the β case [the word anomer is new to me:

"In sugar chemistry, an **anomer** is a special type of epimer [itself a certain kind of isomer] . It is a stereoisomer (diastereomer, more exactly) of a saccharide (in the cyclic form) that differs only in its configuration at the hemiacetal (or hemiketal) carbon, also called the anomeric carbon. If the structure is analogous to one with the hydroxyl group on the anomeric carbon in the axial position of glucose, then the sugar is an alpha anomer. If, however, that hydroxyl is in the equatorial position, then the sugar is a beta anomer".

Now Malcolm is going to explain the appearance of these four peaks based on some orientation pictures. The main idea is that a strong relaxation coupling means a broader peak. Notice the labeling on the peaks in the picture.

Consider the picture on the bottom of page 562 (drawn for the β anomer). Look at the left side C spin. Because we are talking the $\rho_{\alpha--\beta}$ coherence, the left H is up, the right H is down. Malcolm now makes a claim which is not obvious to me: he says that the size of the relaxation rate is proportional to the size of the *average* B field that the two C spins see. I will just accept that for the moment. Then in the picture page 562, the left C sees an up B field from its local H, but the right C sees a down field, so the average is near zero, so there is a low relaxation rate, and therefore the spectral line is narrow. The spectrum on this page does indeed show narrow central peaks, of which α--β is one.

The picture top of page 563 applies to the α--α peak. Here the two H spins both point up, so each C atom sees an up local d-d field [white arrows in all figures]. So here we have a large average for the C's and that means a high relaxation coupling and therefore a broad line, and again, the spectrum on page 562 shows a broad line for this peak.

Fine. Now let's look at the α anomer situation. Claim is that the spectrum is as shown page 563. Now we have a right-angle arrangement for the α--β situation. Even though the H's point in opposite directions, because of location of the C's, we have a large value for the average B seen by the C's, so in this case we expect to see broad peaks for α--β and that is what the picture shows.

Here we have just done arm waiving, but you can work out the detailed theory of all this stuff and come up with a way to measure relative bond angles by looking at the widths of the spectral lines!

A case of particular interest is the peptide bond. This is C - (C=O)(N-H) - C . I think as the four spins of interest we take the N-H and a C-H on the right side, and the angle between them tells you how the protein is twisted at that linkage, and the game is to figure out the entire secondary protein structure. You have to somehow get labeled ^{15}N and ^{13}C.

16.8.4 TROSY

In our previous example, we were looking at special dipole-dipole interactions between two C-H bonds and we used it to learn about the angle between the bonds. Here we are instead looking at the interaction of a single C-H bond (actually, an N-H one), and the B field caused by paramagnetic induction of the electron cloud of the N atom by the B_o field. That induction creates an M which makes a B. [note that this does not involve the electron spin] In the upper figure on page 565, the induced B field from the H electron cloud is "up" at the location of the N spin, so this B field adds to the external B_o [this picture

does not really emphasize this point very well] . In the lower picture, where H is off to the side, the induced B field from the H electron cloud is "down" at the N spin location. The electron cloud induction is usually referred to as CSA, the "chemical shift anisotropy". As the molecule rotates, you then get a varying B field at the N atom location, and this causes relaxation there, so we have "CSA relaxation" causing more width of the N spectral lines. The interaction here is $\mu B = (\alpha B)B \sim B^2$ so is more dramatic at large B fields like 20 T.

The pictures on page 566 then examine the effect of the H atoms spin B field on the N atom. Again, the two positions of the H atom cause different modulation of the total N B field seen. Malcolm has some logical errors here, but I get the point despite them. In both figures I have shown the direction of the B field induced by the CSA mechanism. With the H in the β down state, in both pictures the CSA effect and the H spin effect oppose each other. If H were in the up state, α, then in both pictures the CSA effect would add to the H spin effect to make a large B field. Therefore, when the H is in the β state, we have a small relaxation interaction between our two effects so we have a narrow line. And when H is in the α state, we have a broader line. This is an example of a "cross correlation" between to effects (namely, the CSA relaxation and the DD relaxation). Both effects are correlated because both arise from the same physical mechanism: rotation.

Recall that the CSA portion of this CSA/DD mixture changes with the value of B_o. You could tune B_0 to make the two effects cancel in the H = β case. The more perfect this cancellation, the narrower will be the N peak. In a protein [we are thinking in all these pictures of the peptide bond!] this cancellation would occur at 25 T, which was beyond the range of 2001 NMR machines.

But even without perfect cancellation, you can still get a difference in the peak widths, and the spectrum on page 567 shows an example. The β peak is narrower as expected, and this is for some specific protein where they have somehow caused a particular N to be labeled as ^{15}N.

People design special pulse sequences to get the spectra like the one shown page 567, so you can see the different line widths and measure them. Since we did not expose the theory here in detail, it is not clear what parameters you are measuring by evaluating these line widths, but certainly you learn something. These pulse sequence experiments are called **TROSY** for "Transverse Relaxation Optimized Spectroscopy", though I am not sure how the word "transverse" fits in here. Here are the things you want to have in a TROSY experiment: (1) don't do blasting on the H spins because you want to resolve the little split lines to measure their widths. (2) select B_o to optimize; (3) design pulse sequence to optimize signal; (4) deuterize uninvolved H's to remove their signals!

Wiki has some extra useful information about TROSY. It points out that as molecules get larger, τ_c gets larger (slower) as we know. From page 553, we see that this makes things like R_{cross} get larger, see also page 535 for the longitudinal case. This means relaxation *increases*, and that means effective T values *decrease*, so line widths *increase*. This makes it hard to determine the position of a spectral line with accuracy. The TROSY method allows you to in effect reduce the relaxation rate by causing the DD and the CSA mechanism of relaxation to cancel each other, giving slower total relax rate, giving a narrower line and therefore giving you better spectroscopy. Thus, TROSY lets you look at heavier molecules that otherwise, though large B_o fields are required to get the desired cancellation.

This analysis seems at odds with the picture on page 524 which shows that T_1 increases with τ_c. However, on page 538 we see that T_2 decreases with τ_c [due to the math details I examined above] and so TROSY's job is to make T_2 be larger in effect by getting this cancellation, making widths narrower. That is why the T of TROSY stands for Transverse Relaxation Optimized Spec. It is not clear to me why the mechanisms described above were "transverse", but I will have to defer that to a rainy day when I can

look at the details. Wiki gives the reference which is 1997, so TROSY is only 10 years old. Malcolm gives some references as well.

And so ends this book on 3/31/08 !