---------- **Chapter 14: Multiple Spin-1/2 Systems (435-476) ------- 41 p ---------- ###**

14.1 Spin Hamiltonian (435). I agree with formula 14.1 for the Ham. The ω_j^0 are the chemically offset eigenenergies of the states with no J coupling. In the two-spin N=2 systems AX we studied earlier, the two close-to-degenerate states $\alpha\beta$ and $\beta\alpha$ are split because the two ω_j^0 differ. In this case, j = 1,2. The second term is a sum over *pairs* of spins where we delete pairs within mag equiv groups, the meaning of the prime.

Example 1 is shown page 435 which has 3 H's all shifted apart. The Ham for this is shown top p436 and exact values are given for the δ's and the J's. There are (3,1) = 3 pairs of spins in the sum. When you have three differents, you have an **AMX system** using our alphabet soup (implies **J-coupling**).

Example 2 is ethanol which has N=5 spins, but they are in two mag groups so we write A_2X_3. There are then 6 J coupling terms if you pair a black with a white, but now only one J coefficient due to this symmetry. Similarly, the non-J terms are grouped as shown into 2 + 3.

14.2 Energy Eigenstates (436). States (3 spins) enumerated as I would have done, in "binary order". The spin operator I_{jz} is for just one spin, j = 1,2 or 3. Malcolm does not bother with a z subscript on the m_j quantum number, which is traditional. Total M is sum of m_j of course. Now, when you sandwich one of the 8 states "r" around the Ham (to determine the eigenenergies), you get 14.4 using $\langle r| I_{jz}I_{kz}|r\rangle = \langle r| m_j^r m_k^r|r\rangle = m_j^r m_k^r$ and of course $\langle r| I_{jz}|r\rangle = m_{jz}$. The energy level diagrams are shown for N up to 5. In each near-degenerate group, even if J=0 we get splitting from the δ shifts, as we saw in the N=2 case on page 343.

14.3 Superposition States (438). Nothing new here, states should be normalized I suppose.

14.4 Spin Density Operator (438). As expected; I have earlier notes on the general case. When a coherence has a + or – sign, that spin is "**active**", else "**passive**". Nothing new here otherwise.

14.5 Populations and Coherences (439)

14.5.1 Coherence orders. (439). The coherence $\rho_{--+\alpha\beta}$ has order -1, add up the signs. The number of coherences of order -1 in an N=5 system is 210, as table page 440 shows. It is not too hard to compute these numbers (just combinatorics). In organic and biological molecules, you might have N = 100 or 500 (or more), and you see that the number of coherences for the low orders becomes astronomical. Note that number of coherences is on the order of $4^N = 10^{0.6N}$ so if N = 500, you have 10^{300} as shown in the table. These numbers are the same as the number of DNA sequences with N bases.

14.5.2 Combination versus simple coherences. (440) A **simple** case is $\rho_{-\alpha\beta}$ whereas a **combination** is ρ_{--+} , both being of the same order -1. For order 0, you only have combination coherences. Table shows that the numbers of simple coherences are smaller than the combinations. He gives a formula for the simples that I am sure I could derive.

14.5.3. Coherence frequencies.(440) The energy difference exponent for a given coherence is Ω_{rs} as shown 441, and it would be $\Omega_s - \Omega_r$ if we compare (12.11) p351 with (14.5) p441. We can use 14.4 shifted to the rotating frame to get a formula

$$\Omega_{rs} = \Omega_s - \Omega_r = \Sigma_j \Omega_j^0 [m_j^s - m_j^r] + \Sigma_{j<k}{}' J_{jk} [m_j^s m_k^s - m_j^r m_k^r]$$

Malcolm comes up with a graphical way to evaluate the above formula for specific cases. Notice that in the first term, only j = active spins contribute, for example. I put off a derivation of the graphical rule for now, consider an exercise.

14.5.4 Degenerate coherences (442). A few examples are given. Of course in the A_2X_3 type N=5 system, we expect lots of degenerate coherences, meaning simply they are equal. Remember that the Ω_{rs} frequency defined above is the photon energy for the spontaneous radiation FID and so becomes a line in the spectrum. Interesting comment: Not unexpectedly, weak coupling combined with isotropic liquid implies lots of degeneracy, so the number of distinct Ω_{rs} [number of spectral lines] is manageable for a small protein. But go into an anisotropic liquid (still weakly coupled) and the spectrum is out of control for N = 10! You might have $4^N = 10 \cdot {}^{6N}$ = 1,000,000 distinct coherences, even in 2D or 3D that is going to be hard to deal with.

14.5.5 Observable coherences (443) The claim is that things like $\rho_{-\alpha\alpha}$ are observable (simple), but a coherence like ρ_{--+} is not observable directly in the FID.

Page 443 shows classically WHY only the simples appear in the FID! The FID measures $\langle I_x \rangle$ and when you just write this out as he does on page 443, you see that only the simples contribute. This is because each I_{ix} term creates a single I_i^- factor which causes a single − sign. As expected, we end up with the top of page 444 for our FID sum.

[We know that the non-simple coherences are nevertheless indirectly observable using the right pulse sequences, such as when we were able to see things like ρ_{--} for N-2, "double quantum COSY, etc.]

14.6 NMR Spectra (444). Consider N=3 in the most general case. You have 3 places to put the − in ρ_{abc} and for each, there are 4 terms, so 12 terms total. The spectrum then has 12 lines as shown bottom page 444. In the N=2 case we had 4 lines. (and thee ρ_{--+} case did not arise!). The locations of the 12 peaks of course depend on the signs and sizes of the various parameters: the Ω's and the J's. In terms of "topology", the AMX diagram is as I have shown top page 445. If you kill off one of the three coupling J's, then the topology becomes "**linear**", and he uses this term, but still AMX. This of course adds degeneracy to the spectrum wherever that J was the separating factor. If your system is AX_2 , then there is more degeneracy and we might have only 5 lines left with the expect 2,3 splitting pattern, bottom page 445. For the ethanol case with N=5 and with A_2X_3 structure, we know there are 80 simple −1 coherences, but there is lots of degeneracy, and all 80 are shown page 446. We now have the expected 4 + 3 peak structure. [I am spotting lots of errors in the text, by the way, and am marking them. They are not in his errata!]

14.7 Multiple-Spin Operators (447).

14.7.1 Construction of Product Operators (447) Well, we have a direct product of N spin-1/2 subspaces, but here we use the usual compact notation when there are 1's in one or more subspaces, just don't write them, they are implicit. Another notion is that for a non-trivial product of N factors, you have the constant 2^{N-1} out front. We saw how the "2" was natural for the N=2 system in terms of commutators and sandwich rotations, so that idea must extend here.

14.7.2 Populations and coherences (447). As usual, you "blow out" a transverse spin like I_{1y} in raising and lowering operators, unities in projection operators, as shown bottom of page. If you have I_z, then you will get some sign changes.

Now we look at some spectra examples for N=3 cases.

First, consider AMX and term $-I_{1y}$. The relevant FID coherences have the form ρ_{-ab} so there are four cases, so in general four lines. Assuming the #3 split is relatively small, we draw this as in Fig 14.11. Now consider term $-I_{1y}I_{2z}$. This makes a peak sign change for lines with #2 = β, so get Fig 14.12. Another possibility is a term $-I_{1y}I_{3z}$ where now the #3 β's get negated, shown in Fig 14.13. A final case in this world would be $-I_{1y}I_{2z}I_{3z}$ where now the negative peaks are those when #23 = αβ or βα, as shown in Fig 14.14.

Second example is when the AMX case degenerates into AX_2 where for example #1 and #3 are mag equiv. In this case, whether #3 is α or β makes no energy difference for a ρ_{-bc} peak [I should prove this but skip for now, not quite obvious to me] so we get Fig 14.15 for $-I_{1y}$. As before, you can add the various z-factors and get peaks to negate. If peaks become negative and degenerate, they cancel and leave you with no peak.

14.7.3. Physical interpretation of the multiple spin terms in ρ (450). Fine, see picture. Notice the "non-linear" graphics used in this picture for the AMX case -- triangle with three different shapes.

14.8 Thermal Equilibrium (450). You can see that we are "just going through all the same subjects" that we first did with N=1, then with N=2 and now with N = N. I skip the details and accept the results here (I could easily derive them). For homo case, only one Boltzmann B factor, so get 451 top. Notice that the constants are different from N=2, but often we don't care at all about these constants, as he points out. For the hetero case, we put specific B factors on each I_z term in TE. Recall how this played a role in our magnetization transfer example of INEPT.

14.9 RF pulses (451). What does a $(\pi/2)_x$ pulse to do an arbitrary spin term in ρ? The examples here remind is that we already know that answer to this question, you just "do it in the usual way". Homo and hetero cases are considered. OK to here

14.10 Free Precession (451). Well, this is like the N=2 case but for N=3 AMX there are 6 Ham terms to worry about instead of 3: three z δ terms and three z-z J terms. This just shows up the need for automation of ρ matrix processing.

14.10.1 Chemical shift evolution (452). If we ignore the J's we can do the three δ rotations for the AMX as shown here.

14.10.2. J coupling evolution (453). If you are thinking about J_{jk} evolution, there are lots of terms that do NOT evolve and just stay put. These are the ones with zero commutators on page 377. He describes these NON evolving terms in words here as four cases. All very good. The picture page bottom is a typical non-zero commutator combination. So on page 454 we process just one possible ρ term doing all three J coupling double-z rotations on it.

14.10.3 Relaxation (454). Just throw it in as usual. // I am very comfortable with all this mechanical stuff because I worked pretty hard on it in the N=2 case, there is no mystery here.

14.11 Spin Echo Sandwiches. (455) In the general N case, for the short and long τ cases shown in that appendix 17.9, we can slide the central π pulse to the left (first in time) and have a full τ period after it where only the J couplings are active. On page 455, Malcolm does an example where he takes a particular ρ term and applies first a π_x , then the three J rotations. The result is the effect of a SES on this term. As usual, if you tune the τ value to the magic value that makes π/2 or whatever, you end up with a very simple result. On page 456 he uses a graphical labeling method showing the results of each activity transformation. Here we are in the N=5 case so there are 5*4/2 = 10 J rotations to worry about, but for mag equivs, we drop the intragroup J's, so this removes 4 leaving 6, and his graphical method shows the action of all 6. I don't understand this method, but I am sure I could figure it out, and it looks like something I would come up with, but I would provide a wordy explanation! Fine.

14.12 Refocused INEPT in the I_2S system (457). He shows the same pulse sequence we had before, separate I and S lines. We start as usual in TE and apply the pulses mechanically, and we end up with result R.1 on page 459. At this point, the half-size of the second sammy is left as variable τ'/2 so τ' of free J run. If you plot this result R.1 versus τ', you get the sine curve shown page 460. We are getting the usual INEPT mag transfer effect here, and to max out the FID we want to have the sin argument be π/2.

In the IS case we find (found earlier but did not do this detail) the optimal τ' is the same as the first τ, and this is twice as much as in the I_2S case.

Comment: when we write something like A_2X_3, we imply mag equiv in each group.

If we repeat the treatment for an $\mathbf{I_3S}$ system, we get a third different result. Looking at page 458, where things differ first is that now we have $I_{1y} + I_{2y} + I_{3y}$ which goes into the J terms. Somehow having the extra term changes the nature of the result so we get R.2. For this system, the optimal τ' to max the FID is different again, as shown in the plot! Also, the max FID amplitude is more than in the other two cases, being 1.155 as he says. Lots of calculation work is needed here. I wonder if there is a good visible program like MAPLE, MATLAB or REDUCE that can do all this stuff?

He then poses an interesting question: is there a better pulse sequence that produces a larger FID for the I_nS systems? Aha! This relates to the voyage through k-space mentioned in my MRI readings. There is work going on in this area he says and he gives references, something I might like. *****

14.13 COSY for General N systems (460). We use the exact same pulse sequence as before. In MRI, this would not be very exciting for the isolated H spin which is just an "A" system. The second knockdown would produce a small result after the first. But here we are talking an AMX system, say, where J couplings operate during the τ free propagation time.

14.13.1 AMX Spectrum (461) . I know how messy the simple COSY was, so I expect a large mess for the AMX COSY "cos" result. I would guess he uses the ... to imply perhaps a 2↔3 set of terms in his 14.9 which is the result of propagation for time t_1. Then he applies the final knock-down and gets what I will call 14.9' (he has a goof here for sure!). He then claims there are three terms in there that are -1 and he argues where this terms generally appear in the Ω_1-Ω_2 plane. Each of the three terms goes with a little multiplet in the picture on page 462. I guess if you write out the trig products as sums of differences, you will get a set of peaks in each multiplet. I think I see only 4 peaks from the sin*cos*cos in the t_1 variable,

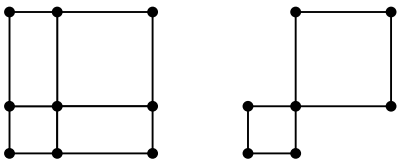
and we somehow know from symmetry that you will get 4 peaks from four different coherences in the t_2 direction, and this makes the 16 peaks we see in each multiplet. Fine. I agree with the locations of terms 1,2 and 3 as he shows on page 462 along the top. These are all near Ω_1 for t_1. If you start with the I_{2z} term in ρ, you will get the second row of stuff, and if you start with the I_{3z} term in ρ, you get the bottom row of stuff. He has plotted this for specific values of the Ω's and this causes each 16-plet to have a slightly different spacing. Now *that* would be a tough exercise to verify I think.

14.13.2. Active vs Passive Spins (463). We already defined this for a single coherence. But we have this notion of objects in the pulse sequence converting one coherence into another [or linking them] -- recall my theory somewhere where I use Z and P for pulses and propagators (phil theory of coherence flow.doc), where my indices like r,s are coherences. In the present context, a pulse sequence process turns one coherence into another such as, for example, the term I have shown circled in pencil on page 461. You can show that the activeness for a given ρ term applies to all its matrix elements (all coherences), so if a spin is active in either the initial or the final coherence (or in both), you say that spin is **"active in the coherence transfer process"** , otherwise it is passive in same. He uses this definition on the top of page 466, but I don't really want to follow through on that right now. These are all rules attempting to simplify this gargantuan mess when you have N > 2.

14.13.3. Cross-peak multiplets (463). Malcolm now derives the peak polarity structure of one of the peak 16-plets. He writes our ρ term which gave rise to the "Term 2" multiplet on page 462. We know that this ρ matrix term has -1 order coherences of the form ρ_{a-b} because we have an I_{2y} sitting there. There are four such terms, one being $\rho_{\alpha-\beta}$, and these will have four spectral peaks, and the I_{1z} factor causes the peaks with the 1-state = α to have one polarity, and those with β to have the other polarity, so we get the Ω_2 1D spectrum shown top of page 464, I like it. then we multiply out the t_1 trig functions as I mentioned above and we get four terms and for his values, the ones with I_{2z} = β are plus, the others -, and we get the lower picture on page 464. I then labeled these peak signs on page 462 and this then verifies the pattern or black and white circles shown in the Term 2 multiplet. This is repeated top of page 465. He says you can figure out the other multiplets using the same method.

14.13.4. Diagonal Peaks (466). In COSY the diagonal peaks come out all dispersion with the States procedure, just as they did in the N=2 case, see page 398. You can fix this with the same double-quantum filtration trick using a phase cycled back end, but I am surely not going to get into *that* right now, I did it for N=2, that was bad enough.

14.13.5 Linear Spin Systems (466). Now, for the general AMX system, we get a pattern of 9 peak groups which form two squares which are connected at once vertex, as shown here on the left:



However, if you have a linear AMX system such that J_{13}= 0, then the two corner multiplets vanish and you get the picture shown above on the right.

14.14 TOCSY (467).

14.14.1 The ambiguity of COSY spectra for mixed AMX systems. (467) Suppose you have a mixture of AMX and A'M'X' chemicals in your NMR sample, and each is a linear system. If it comes out looking like the bottom of page 467, you can distinguish the two "double square patterns" and there is no ambiguity. BUT, if there is some degeneracy such as the two M' chemical shifts are the same (so $\Omega_2 = \Omega_{2'}$ which he writes as M = M'), then you get a picture as shown top page 468, and now you have an ambiguity problem. If you could just "bring back" those missing J_{13} peak multiplets, then you could resolve the ambiguity, as shown bottom of page 468. It is the purpose of the TOCSY version of COSY to do just that!

14.14.2 The TOCSY pulse sequence (469). You take your regular COSY sequence and replace the final knockdown with a sequence of *several hundred* closely spaced spin echo sandwiches! This looks a little like MRI multiple spin echo stuff. You want the total time of all the pulses long, but the space between pulses to be short.

14.14.3 The Theory of TOCSY (470). Because the gap τ is short, you get to use the approximation shown on page 598 where you in effect are running the full "strong" (non-secular) Hamiltonian for the entire time of all these π pulses. This is called the TOCSY "mixing time".

Because the strong spin-spin Ham is a rotational scalar (unlike the secular Ham), it commutes with the total angular momentum vector and with its component in any direction. Think of $\mathbf{L}\bullet\mathbf{S}$ in this regard. As a rotational scalar, it commutes with total $\mathbf{J} = \mathbf{L} + \mathbf{S}$. In our present context, think of $L\bullet S$ as $\Sigma\, \mathbf{I}_j\bullet\mathbf{I}_k$ as appears in the Ham, and think of $\mathbf{J}$ as $\Sigma\, \mathbf{I}_j$. So I agree with (14.17).

In our 3-spin AMX example, the claim then is that $I_{1y} + I_{2y} + I_{3y}$ is conserved. In (14.15) we start off our analysis of the COSY-like pulse sequence as before and end up with I_{1z} giving a term proportional to I_{1y}. We are then unable to analyze the π pulse sequence because the Hamiltonian is too complicated since we are not in the secular approximation. BUT, the argument is that I_{1y} must decrease in size as the terms of ρ get battered around by the π pulse sequence. As I_{1y} decreases, the I_{2y} and/or I_{3y} must increase to take up the slack so the total is conserved. Even if there is no direct J_{13} coupling, this battering process is going to activate I_{3y}. The way this happens is very well illustrated by the figure on page 471 which shows, at the top left, how we start with 100% in I_{1y}. It splits into 1+2, then 2 can couple down to 3 using J_{23} and the argument is that we end up with 1/3 on each spin. This must be some sort of virial or equipartition theorem at work.

Page 472 shows how this process occurs in a computer simulation of the messy equations of motion. The claim is that there is no steady state, but the equal distribution is achieved more or less.

Now, then, the effect of the TOCSY mixing of the π pulses is shown on page 473 -- the I_{1y} of our particular term is spread into three such terms. The important result for us is that we now have "action" in the off diagonal multiplets even if $J_{13} = 0$. So this achieves the goal of "lighting up" the marker corners of the spectral peak pattern allowing you to disambiguate the two spectra of AMX and A'M'X' in the case that M =M', as outlined above.

Now look back at page 469. Suppose we skipped all the π pulses. We then have the result shown in the middle of page 461 after the t_1 arrow (t_1 is just longer now). I guess the point is that in this case, we remain in the secular approximation all the time rather than the strong limit, so the mixing of the I_{1y} onto

all the spins does not happen. Obviously there is a lot more to this story than he is explaining. Also, the π pulses keep reconverging the spin echo as in MRI, this must be useful, but is not mentioned.

And on this note, this interesting chapter comes to an abrupt end.