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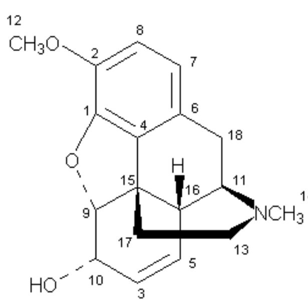
Multiplet Analysis with wxNUTS

A useful tool for multiplet analysis in 1D NMR spectroscopy is spin-spin calculation to reproduce an observed multiplet's pattern. Doing so gives the spectroscopist confidence that he knows and understands spin-spin couplings that give rise to the observed multiplet.

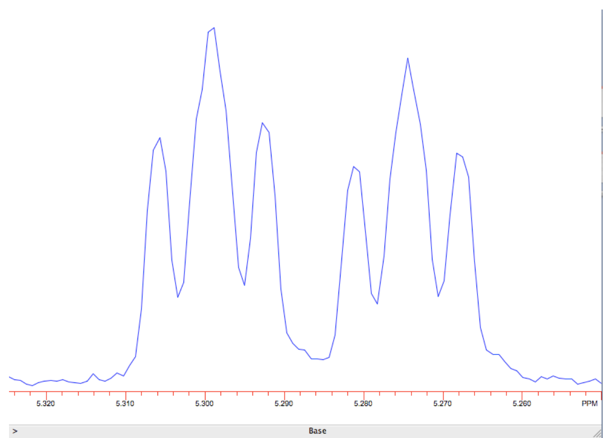
As the size of a molecule grows, doing a spin-spin calculation can be slow or can exceed the software's size limitations. However, focusing on a particular multiplet makes the simulation process faster and allows the use of Simplex optimization to fine tune the values. It is only necessary to include all couplings for the multiplet of interest, not the entire spin system.

This discussion of multiplet analysis will use the NMR spectrum of Codeine.



Codeine

The proton spectrum of Codeine has a multiplet at 5.29 ppm which looks like a doublet of triplets. This multiplet arises from the vinyl proton on the carbon labeled 5 as shown in the structure above.

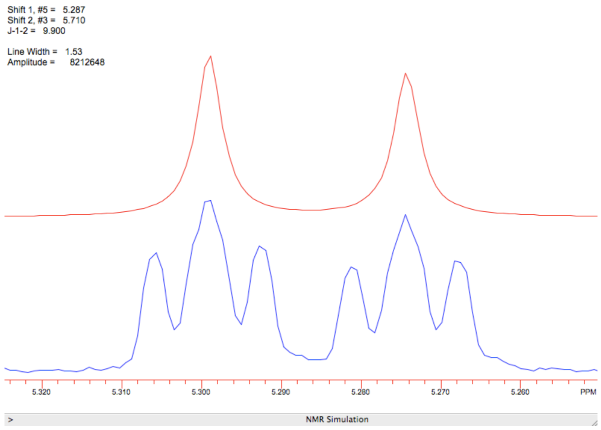


Multiplet for H-5

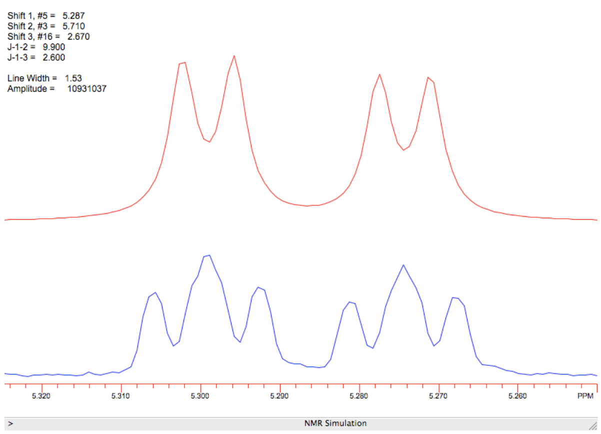
The complete assignments for Codeine can be found at:
http://www.acornnmr.com/codeine/assignments.htm

Our goal will be to simulate this multiplet with the NS (NMR Simulation) subroutine of wxNUTS.

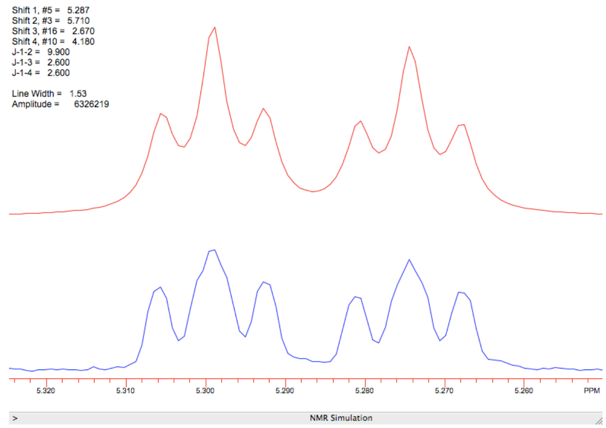
To start our analysis we use the cursor tools in wxNUTS to measure the splitting between the triplets in the doublet of triplets, which is 9.9 Hz. We then enter the NS subroutine and enter two chemical shifts: H-5 (2.87 ppm) and H-3 (5.71 ppm) with a coupling constant of 9.9 Hz. The spectral region and the simulation are shown below.



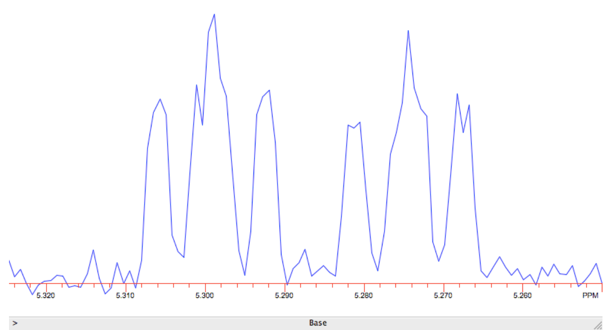
Next we measure the smaller triplet splitting to be about 2.6 Hz. So we add another resonance for H-16 (2.67 ppm) with a coupling constant of 2.6 Hz.



This gives us a doublet of doublets at the correct position, but we need a doublet of triplets. When we add H-10 (4.18 ppm) with coupling to H-5 of 2.6 Hz, we get the desired doublet of triplets.



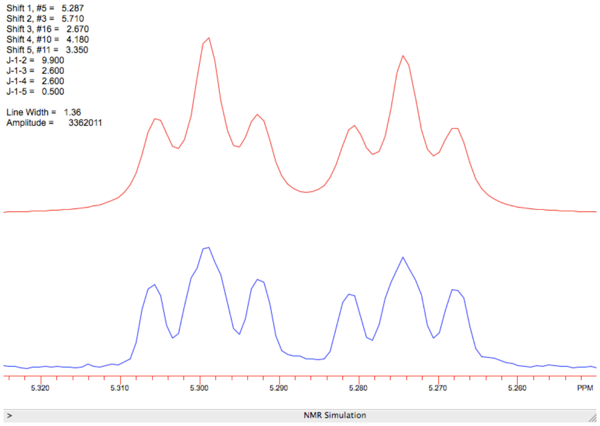
We now have a doublet of triplets similar to the observed multiplet pattern. Now we notice that each of the peaks in the triplets has some fine structure. Using the tools in wxNUTS, we do some resolution enhancement on the spectrum and see that there is an additional small splitting of about 0.5 Hz. This must arise from H-11 (3.35 ppm).



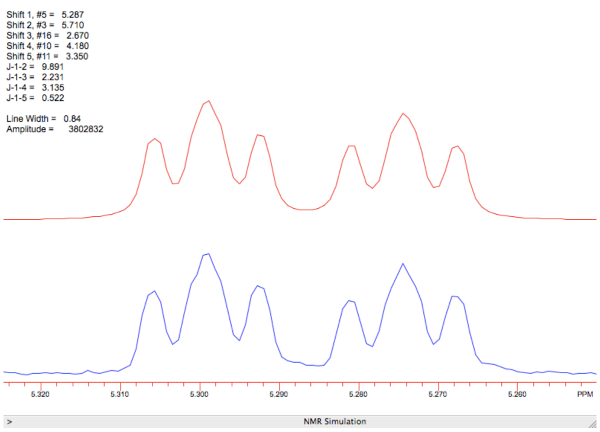
Description of resolution enhancement using wxNUTS can be found at

www.acornnmr.com/wxNUTS/resolution_enhancement.htm

We now add H-11 to our simulation.



This is getting close to the observed pattern. Next we use the Simplex optimization in the wxNUTS NS routine to iterate the coupling constants. Only the displayed region is used in the optimization, so it is not necessary to include the entire spin system in the calculation.



This gets us a very close match.
Because we can simulate the multiplet, we gain confidence in the assignment. We also gain better values for the coupling constants.

It is interesting to note that the COSY data for this molecule does not show the correlation between H-5 and H-11 that was necessary to reproduce the multiplet's splitting pattern.

Simplex Optimization

The Spin-Spin simulation routines used in wxNUTS are based on the proven routines in the original NUTS program. There have been several advancements in the wxNUTS routines, mostly in areas to aid in Simplex optimization of chemical shifts and coupling constants:

- Identical individual spins can be grouped into “Spin Groups” with a multiplicity number. For example a methyl group’s three spins can be grouped into one Spin Group with a multiplicity number of three.
- Coupling constants are entered as the J value in Hertz between Spin Groups. This allows the spins of a Spin Group such as a methyl to be iterated together in a Simplex optimization process instead of iterated as three separate spins.
- The chemical shifts of any Spin Group can be locked so it will not be iterated in a Simplex optimization process.
- The chemical shift of any Spin Group can be locked to the chemical shift of another Spin Group so that they will be iterated together in the Simplex optimization process.
- Any coupling constant can be locked so it will not be iterated in a Simplex optimization process.
- Any coupling constant can be locked to another coupling constant so that they will be iterated together in the Simplex optimization process.

These changes greatly improve the usefulness of the Simplex optimization routine. Details can be found at

www.acornnmr.com/wxNUTS/SpinSpinSimulation.pdf

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