Processing NOAH experiments

NOAH (NMR by Ordered Acquisition using 1H-detection) experiments are a class of experiments created by Ēriks Kupče and Tim Claridge (*Angew. Chem. Int. Ed*. 2017, 56, 11779 –11783). They concatenate the pulse sequences required to generated various 2D experiments in such a way that it is not necessary to let spins relax between each scan of each experiment. In effect, the sequences are acquired simultaneously. This greatly speeds up the time required to obtain multiple 2D spectra on the same sample.

The names of the parameter sets include codes for various sequences:

S: HSQC (^{1}H-^{13}C one-bond correlation)

B: HMBC (^{1}H-^{13}C multiple-bond correlation)

C: COSY (^{1}H-^{1}H through-bond correlation)

N: NOESY (^{1}H-^{1}H through-space correlation)

M: 15N-HMBC (^{1}H-^{15}N multiple-bond correlation)

One dataset is generated, regardless of the number of spectra acquired. Processing COSY and NOESY spectra in Mnova poses a problem (see *Processing with Mnova*). Processing any NOAH dataset in TopSpin requires some setup (see *Processing with TopSpin*).

Processing with Mnova

In **Mnova**, it is sufficient to drag and drop the zipped dataset into Mnova to open it. Or, you may save it and find it in the data browser or use any other standard technique to open it. Each spectrum will open on its own page. Use the Pages view to see all of them (go to View and select Pages under Tools).

There is a bug with Mnova, and COSY and NOESY spectra are not processed properly. (HSQC and HMBC spectra are, however, processed properly.) See Figure 1, where the highest field and lowest field signals are separated by 6.8 ppm in the direct (horizontal) dimension and 8.6 ppm in the indirect (vertical) dimension of this COSY spectrum acquired using a NOAH_SC experiment. This indicates that the "spectral width", or total number of ppm acquired, is incorrect in one of the dimensions. Because the horizontal dimension lines up with the 1D spectrum (acquired in a separate experiment), we can see that the spectral width in the indirect (vertical) dimension is the one that is wrong. The **C** (for crosshair) command can help measure this.
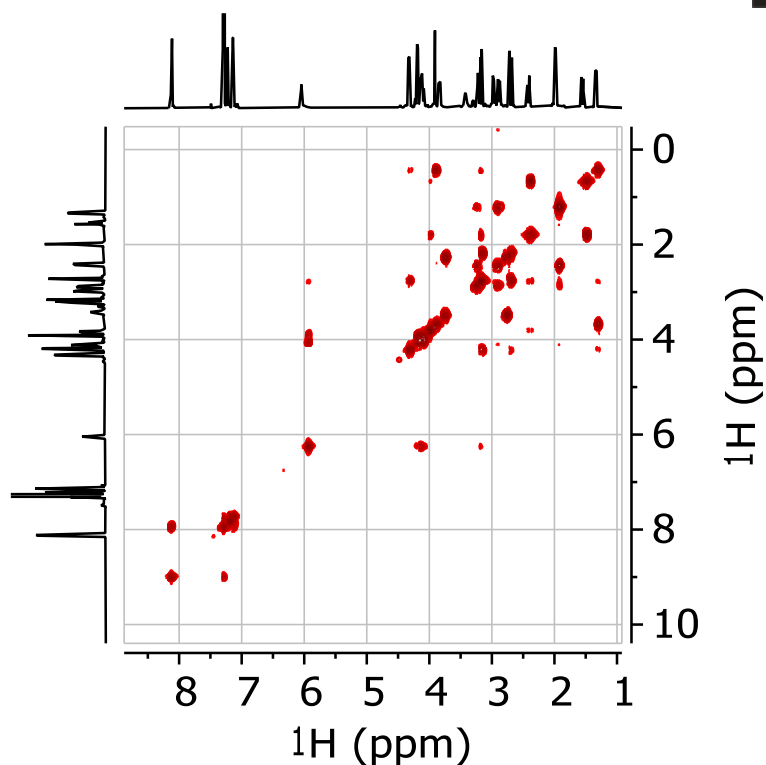
Figure 1. COSY spectrum of strychnine obtained with a NOSY_SC experiment in TopSpin and opened by dragging and dropping in Mnova. The number of ppm between the highest field and the lowest field signal in the spectrum is different in the two dimensions.

To correct the spectral width, go to the View flowbar (at the top) and choose Parameters (Figure 2).
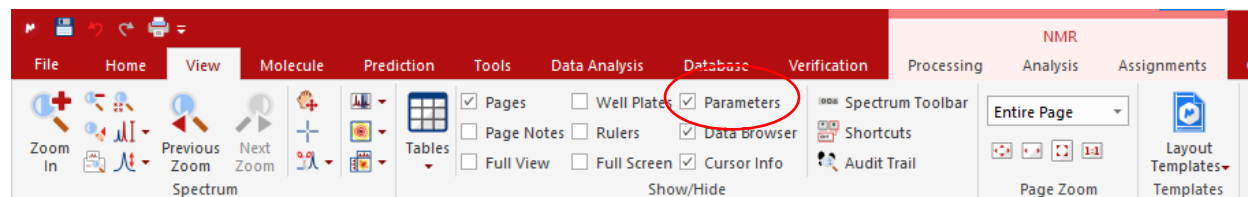

Figure 2. View flowbar, with Parameters option circled in red.

Scroll down in the Parameters window to the entry for Spectral Width. Double click in the Value field and modify the second (f1) number so that it is the same as the first (f2) value (Figure 3).

Figure 3. Parameters window showing, at left: Incorrect spectral width in f1. Right: correct spectral width in f1.

The spectral width is now correct, but the referencing in the indirect (vertical) dimension is wrong: the signals in the 2D spectrum do not line up with those in the 1D spectrum.
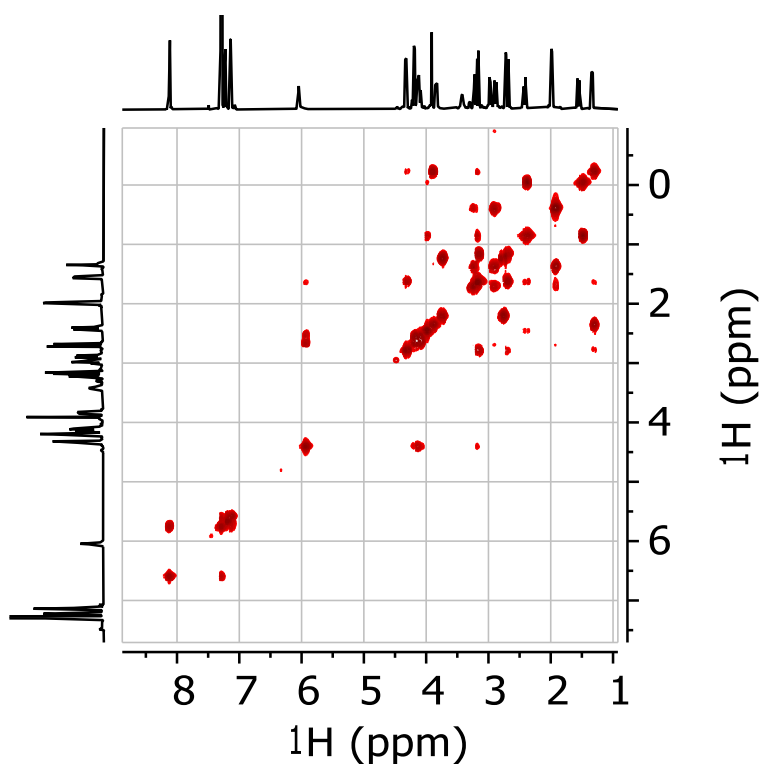

Figure 4. COSY spectrum obtained with NOAH_SC parameter set, with indirect dimension spectral width corrected.

To reference the spectrum, use the reference command. Type **L**, or go to the Analysis flowbar and choose Reference). Click on a signal along the diagonal of the COSY spectrum. The chemical shift of the signal in the f2 (horizontal or direct) dimension will appear. Use Ctrl-C or Cmd-C to copy this number. Now click on f1. Paste in this correct chemical shift over the incorrect chemical shift and click OK (Figure 5).
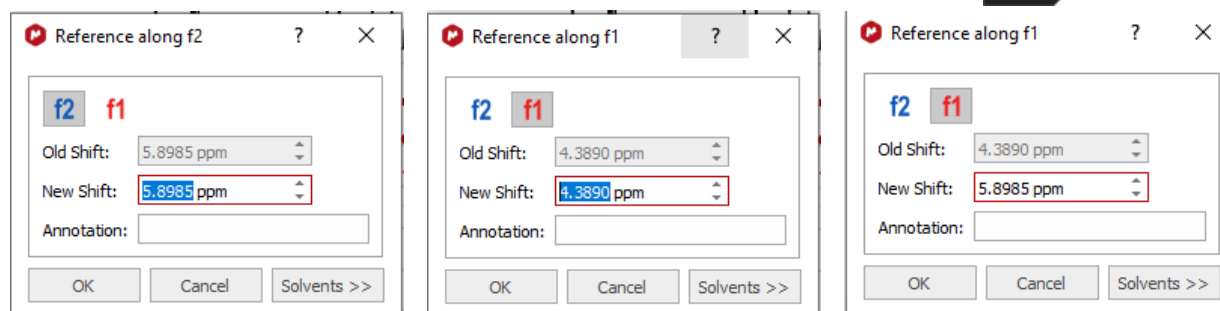
Figure 5. Left: correct chemical shift, in the f2 dimension; copy this number. Middle: incorrect chemical shift in the indirect dimension. Paste the copied number into this field. Right: correct chemical shift in the indirect dimension.

The spectrum should now be displayed correctly, although you may need to play with the view (**F** for full, **Z** for zoom) to display it as you want (Figure 6).
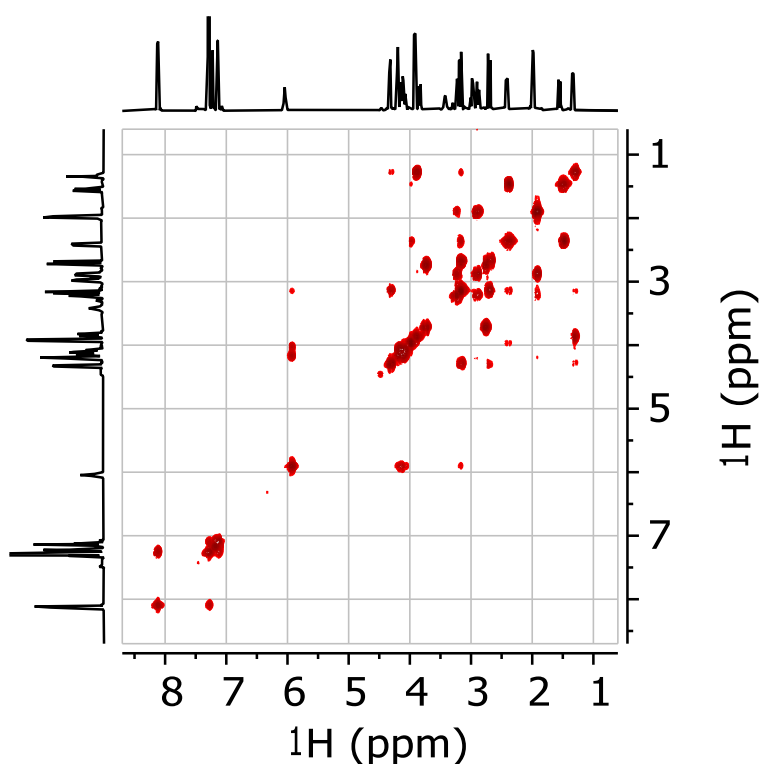

Figure 6. COSY spectrum obtained with NOAH_SC parameter set, with indirect dimension spectral width corrected and signals properly referenced.

Processing with TopSpin

In **TopSpin**, however, you must type the command `splitx_au` (one word) in order to force it to separate the data into separate experiments. Type this at the bottom of the TopSpin window. If the command `splitx_au` gives an error message, then you must run the command `expinstall` in order to install the command `splitx_au`. The password is likely "mcgill" or perhaps something you chose yourself. It may also be blank. Accept all defaults while running the expinstall procedure. When it is finished, run `splitx_au`. This will generate additional datasets within TopSpin. To see them, in the data browser, right-click and choose "Scroll to active dataset". This should highlight your dataset in the data browser. If no other numbers are

shown there, then close and open the display of the current dataset. The other numbers contain the other experiments, and you can now drag and drop them. Alternatively, use the `re` command to change datasets. For example, if your NOAH_SC dataset was in expno 2, then NOAH datasets will be in 2001 (HSQC) and 2002 (COSY) and higher numbers. If your NOAH_BSCN dataset was in 5, then the HMBC will be in 5001, the HSQC in 5002, the COSY in 5003, and the NOESY in 5004.a

See https://www.mcgill.ca/mc2/documentation/software and https://www.mcgill.ca/mc2/using-mc2/workshops/workshop-information for further information about setting up TopSpin.
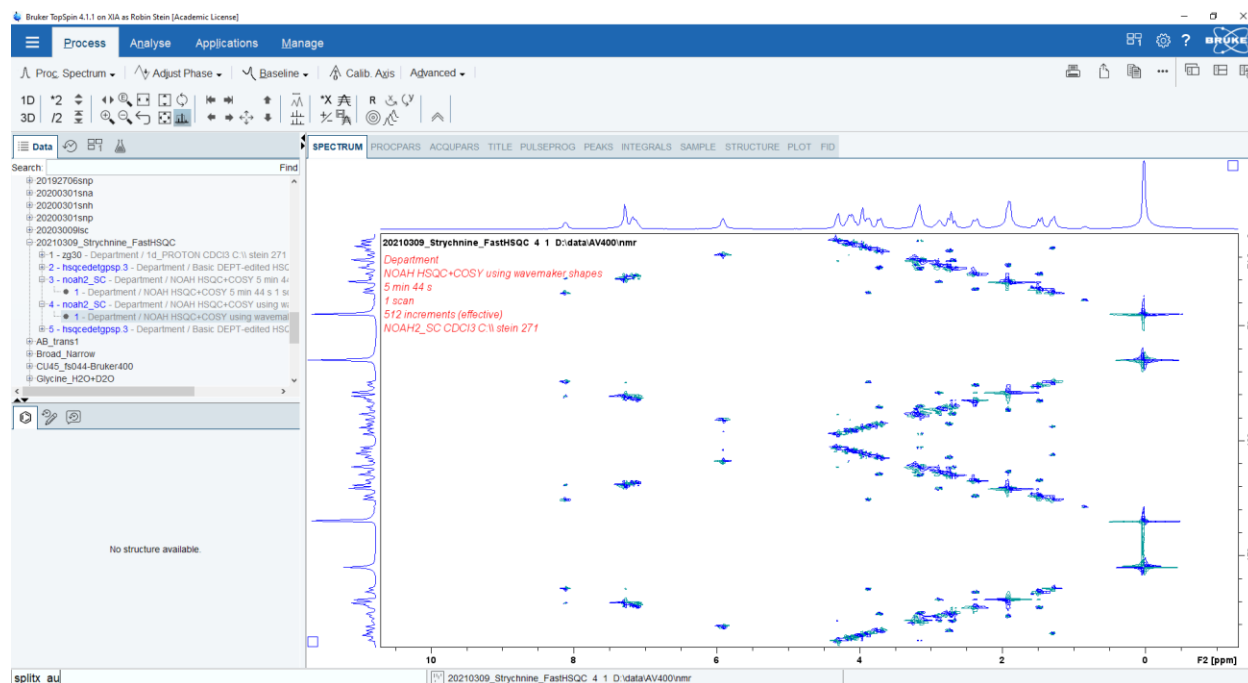

Figure 7. View of TopSpin window before running the command `splitx_au`. *Note that the spectrum is not usable.*

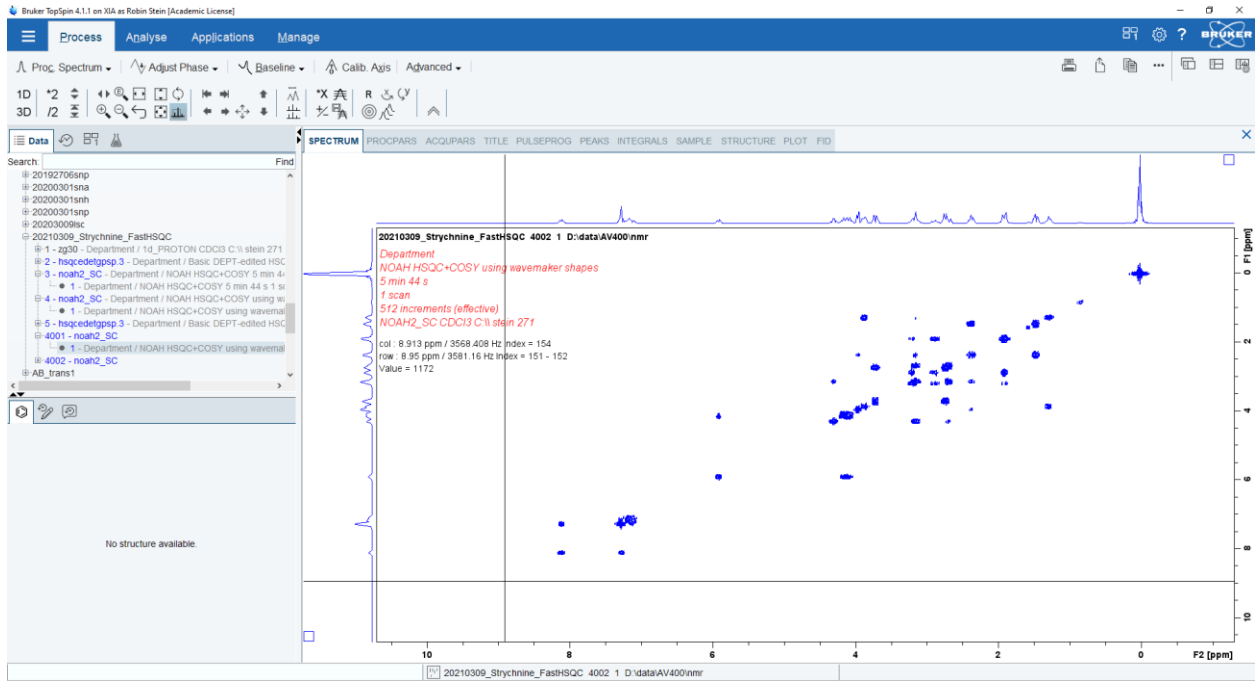*Figure 8. View of TopSpin window after running the command* `splitx_au` *and reading in one of the newly created datasets (see data browser).*