Flourine-19 Experiments on Varian Spectrometers

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The difficulty with ^{19}F experiments involving decoupling (or 2D heterocorrelation) is the close proximity of the ^{19}F resonant frequency to ^{1}H, e.g., 470 vs 500 MHz. Quad-nucleus probes—as installed only on Athena (our Bruker AC-300) in our facility—provide the simplest route to these double (or triple) resonance experiments. Experiments involving ^{19}F breakdown in the following way in our facility:

^{19}F – ^{19}F spectra coupled to ^{1}H can be acquired in a simple manner on the **UNITY-500**. Temps can range -130 to +120°C. See instructions below (part I). Such data can also be acquired on Athena and the AVANCE-360.

$^{19}F\{^{1}H\}$ – The simplest path to this 1D data is to use **Athena** (Bruker AC-300); only ambient temps are available there. Instructions are posted in the Bruker Users' Guide (BUG) section of the facility website. *If higher sensitivity than provided by Athena, or non-ambient temperatures are required, then the **INOVA-500** must be used.* A probe change is required, along with a non-trivial setup of filters and cabling. See instructions below (part II).

$^{1}H\{^{19}F\}$ – The **INOVA-500** is the only route to this data. A probe change is required, along with a non-trivial setup of filters and cabling. See instructions below (part II).

2D heterocorrelation – Such experiment, including ^{1}H–^{19}F and ^{19}F–^{13}C are possible on the **INOVA-500**. See Charlie for discussions and assistance.

I. Setup for ^{19}F (^{1}H-coupled) 1D Experiments on the UNITY-500

These experiments are simpler to perform on Athena (but are not very hard to do on the U500). Use of Athena is therefore recommended unless higher sensitivity, or non-ambient temperatures are required (or you are obtaining some other data on the sample requiring the U500).

A. (i) Lock-n-shim, (ii) acquire, (iii) reference, and (iv) save a ^{1}H spectrum as normal on the U500. This ^{1}H spectrum will be used to reference the ^{19}F spectrum.

B. Change experiment numbers, leaving the ^{1}H spectrum in VNMR unchanged: if the ^{1}H spectrum is in exp1, perform a **jexp2**; use **cexp(2)** if exp2 does not exist.

   1. Read in 19F parameters using NUC,SOLV .
   2. Note the **sfrq** [will be close to 470.27 MHz] .
   3. Tune the ^{1}H channel of the probe over to ^{19}F .

      → Enter the FREQ above into the HP scope; change the MARKER also to this freq.
   4. The ^{1}H filter in-line should be ok for ^{19}F experiments (so no filter change needed).

C. Acquire a spectrum; use **ns=1e6** if at low sensitivity. *Do not attempt to decouple ^{1}H, i.e., leaving the decoupler turned off (the probe is now tuned to ^{19}F, not ^{1}H)!!*

→ Reference the spectrum by staying in the exp having the ^{19}F spectrum (e.g., exp2), and typing **xref↵** . Answer **1** to the question of where the ^{1}H is located (presuming you took that spectrum in exp1).

D. If ^{1}H couplings, or high resolution in chemical shifts are needed, optimize the sweep width by placing the box about the observe range of ^{19}F resonances, and using **movesw**. Increase **at** as needed, remembering that the limitation on resolution is $\Delta\nu \sim 1/$**at**. Re-acquire the spectrum. The referencing should change properly, but **xref↵** can be run again if desired.

E. Tune the probe back to ^{1}H prior to leaving the laboratory.

II. Setup for Simple Switching between ^{19}F (^{1}H-coupled) ^{1}H (^{19}F-coupled) 1D Experiments on the INOVA-500

These experiments are simple to perform, but a probe change to the **hf** probe is required (with switch back to **hcx** at the end of your session). The U500 is therefore simpler if only a few spectra are needed. The following setup will allow many ^{1}H and ^{19}F 1D experiments to be acquired over an uninterrupted (and unattended, e.g., overnight) session.

A. Swap the **hf** probe in. Get assistance/training the first time, and follow all steps carefully. After the switch is completed, use:

1. **hf↵** ;to set **probe='hf'** (also sets the **pfgon** parameter correctly)
2. **rts↵**
   hf.shim↵
   su↵ ;reads in the shims for the probe

B. Use only the VT-style sample spinners (those with the holes along the bottom and upper sections). Keep the VT air with the ball centered at 10cc. Using a normal spin turbine may cause the sample to lift in the detect region, catastrophic for keeping good line shape.

C. Tune the probe, with ^{19}F on the X-port of the probe. *Leave the rf cable on the probe attached to the probe, and connect to the HP sweeper using a male-male BNC connector (located on the shelves in the SW corner of the room); this will reduce variations in tuning that occur with (seemingly) every cable change at the probe.* You should check and retouch the tuning at least one extra time, as the two channels are more strongly coupled to each than on a broadband probe.

D. Modify the filters and cabling as shown on the next page. (You must switch back to the **hcx** probe and "normal" cabling at the end of your session.)

E. (i) Lock-n-shim, (ii) acquire, (iii) reference, and (iv) save a ^{1}H spectrum as normal on the I500. You will use the ^{1}H spectrum to reference the ^{19}F spectrum.

F. Change experiment numbers, leaving the ^{1}H spectrum in VNMR unchanged: if the ^{1}H spectrum is in exp1, perform a **jexp2**; use **cexp(2)** if exp2 does not exist.

G. Setup normal parameters for ^{19}F:

MAINMENU → **SETUP** and select ***nucleus,solvent***

H. Acquire a "normal" ^{19}F spectrum. Note that a **movesw** is often needed, once the range of ^{19}F chemical shifts is observed. Increasing **at ≥ 1** to improve resolution is also common. Use **xref** with the ^{1}H spectrum acquired, FT'd and referenced in another exp.

I. Multiple ^{1}H and ^{19}F experiments can be chained by using other exp areas [**cexp(#)** to create**, jexp(#)** to move to, and **delexp(#)** to delete].

Example: Suppose the ^{1}H setup is in exp11, and ^{19}F in exp12. You want to acquire 4 ^{1}H experiments, and between each 3 ^{19}F, ending with the 4th ^{1}H experiment. Setup a normal ^{1}H in exp11. Then

jexp(11) mp(13) mp(15) mp(17) will setup all the ^{1}H experiments. Use **pad** in the latter three experiments if a delay is needed between the end of the ^{19}F experiments and the start of the following ^{1}H experiment.

Setup the ^{19}F experiments in exp12. Use a **pad** array to acquire three ^{19}F experiments separated by the proper delay [alternatively, you could acquire ^{1}H in exps 11, 15, 19, and 23, with single ^{19}F spectra in the intervening exps]. Use a similar

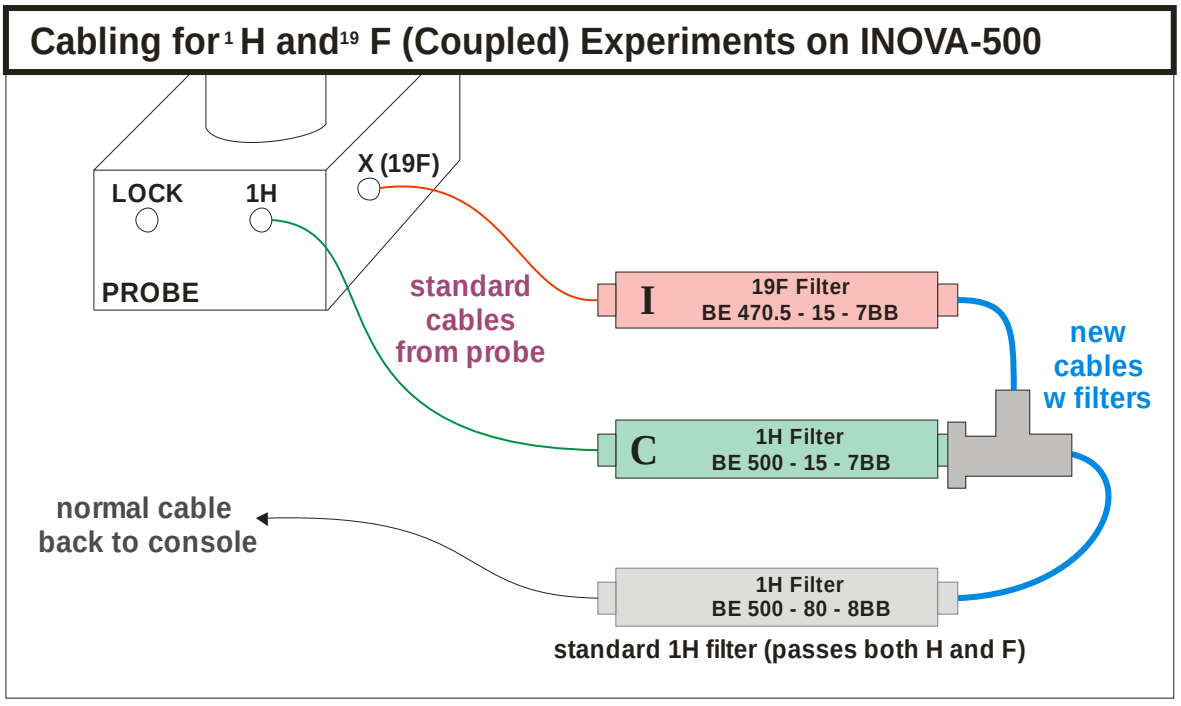
jexp(12) mp(14) mp(16) to copy the setup for all ^{19}F experiments. To acquire, use:

jexp(11) go jexp(12) go jexp(13) go jexp(14) go jexp(15) go jexp(16) go jexp(17) go

Macros can be written to simplify and extend this procedure. Use of the following:

wexp='svf(\'H1.001\')'

can be used to automate file saves. In this case, best to create a unique folder (using a UNIX terminal window, or the CDE folder tool), and move to it in VNMR using MAIN MENU → FILE → *select folder* → SET DIRECTORY prior to initiating the set of **go** commands.



III. Setup for 1H{19F} or 19F{1H} 1D Experiments on the INOVA-500

A. Switch to the **hf** probe on the INOVA-500 using the normal probe switching notes (as posted on the spectrometer). After the switch is completed, use:

1. **hf**↵ ;to set **probe='hf'** (also sets the **pfgon** parameter correctly)
2. **rts**↵
   hf.shim↵
   su↵ ;reads in the shims for the probe

B. Use only the VT-style sample spinners (those with the holes along the bottom and upper sections). Keep the VT air with the ball centered at 10cc. Using a normal spin turbine may cause the sample to lift in the detect region, catastrophic for keeping good line shape.

C. Tune the probe, with ^{19}F on the X-port of the probe. *Leave the rf cable on the probe attached to the probe, and connect to the HP sweeper using a male-male BNC connector (located on the shelves in the SW corner of the room); this will reduce variations in tuning that occur with (seemingly) every cable change at the probe.* You should check and retouch the tuning at least one extra time, as the two channels are more strongly coupled to each than on a broadband probe.

D. Lock and shim as normal.

E. Setup normal parameters:

MAINMENU → **SETUP** and select ***nucleus,solvent***

Then use either:

hf_HobsFdec↵ for 1H{19F} or

hf_FobsHdec↵ for 19F{1H}

These macros create the parameter **ampmode='cddd'**, and read in proper observe (**pw**, **tpwr**) and decoupling (**dm**, **dmm**, **dpwr**, **dmf**, **dseq**, **dres**) parameters from the probe file.

F. Adjustment of **dof** may be needed, as suggested by the macros. It is critically important that the decoupler center (**dof**) be within the decoupling range available; e.g., the ^{1}H decoupler only works over ~8 ppm width. **dof** will typically be close enough, but for a strongly upfield methyl, some adjustment (to lower values) of **dof** will insure proper decoupling.

G. Cable the rf as shown on the next page. The order of filters (and perhaps even cables) is important to the quality and reproducibility of the probe tuning. The proper placement of the crossed-diode block is crucial for obtaining good signal-to-noise (as first discussed by Rich Shoemaker at http://chemnmr.colorado.edu/ammrl/19F-Decoupling-Note-RKS.pdf).

Cable Connections for 1H/19F Experiments