NMR NEWS

ENC Conference | 700 Status | Service and Repairs

ENC Update

The Experimental NMR Conference (ENC) was in Boston this year Mar. 23-28. Major themes included **solid state bio-NMR**, **non-uniform & non-linear data** acquisition/processing, and **helium recycling**. See Pg.4 for details.

NMR Users Fees

NMR fees have been introduced starting April 2014. The NMR Facility has evaluated several different methods for tracking NMR usage for fairness and in order to provide requested detail. The spectrometers now track usage directly. Details are provided on Pg.5

Repairs and Service

Many of you may not be aware that several of the spectrometers have been experiencing hardware failures in the recent months. This is due to the hard work of the NMR staff replacing, substituting, and fixing problems before users see downtime. See Pg. 5 for more.

700 Status

The 700 MHz magnet (cryostat) has been successfully replaced, cooled, and energized. Early this year access booking via the website was begun after extensive testing and monitoring (Nov. 2013 - Jan. 2014). The system is functional but a concern exists.

We have been closely monitoring two unstable cryo-shims (Z_1 and Y_1) for several months. Both are slowly settling and we're continuing to work with Agilent to assess the magnitude of changes, and the rate of drift decrease. During our investigations we have also discovered some small environmental impacts on the magnet performance and are working to identify and isolate those effects to the spectrometer. See Pg.2-3 for details.

700 Cryo-Shim Drift - "The Details"

Background: When a magnet is installed it goes through quite a bit of rough treatment. Once arriving on campus (never a guaranteed safe trip) the magnet has to be: unpacked and hoisted into position, transit bolts and restraints removed, high vacuum chamber evacuated, helium chamber pre-cooled with nitrogen gas (vapour from liquid dewars), then cooled to 4.2K, and finally filled with liquid helium. An electrical control rod (called a demountable lead) is plunged into the helium bath and establishes a circuit with the solenoid which is energized while attempting to keep the superconducting coils below 4.2 Kelvin. The energizing magnetic field creates a substantial torque on the coil, and every aspect of connecting to the circuit for energization generates heat. On top of this, adding cryogens into the system to compensate for heating also causes disturbances. Any one of these events (or combination) can result in the loss of superconductivity and subsequent emergency dump of stored energy into the cryogens called a "quench". At this point everything starts over, assuming the magnet is still viable.

During magnet installation not only is the primary field coil energized, but several auxiliary superconducting coils are also separately energized in order to improve the homogeneity of the field. These are called **cryo-shims**. We then use small room temperature electromagnetic coils (shimming coils) to optimize the final quality of the magnet field we all know and appreciate.

Why the 700 was replaced: After the previous magnet was installed and had several months of settling, a highly unusual continuous field drift in the Z_1 cryo-shim was observed. While drift in the primary magnetic field is common due to the size of the amperage and subsequent generated field, cryo-shim drift is certainly not common. The primary field changes are typically measured in Hz (*i.e.* parts per billion) per hour. Acceptable primary field drift of the magnet is contractually negotiated and depending on vendor and magnet is now around 8 Hz/hr. For comparison, the new 700 cryostat is presently showing a main field drift of ~0.5 Hz/hr. Unlike the main field, cryo-shim drift is quite rare, so rare in fact that no accepted magnitude is included in contracts. Unfortunately the previous 700 Z_1 cryo-shim displayed considerable and consistent drift requiring ever increasing compensation from the room temperature shims. This caused two problems, the first was the lack of field stability (poor NMR performance), and the second was that soon the much smaller room temperature shims would be insufficient to compensate. The options were to re-energize the cryo-shim every 1.5 years and accept the risks associated with cryostat disturbance and re-settling , or swap out the magnet for a new cryostat. The magnitude of the drift and failure of all other attempts to stabilize the shim resulted in selecting the replacement of the cryostat.

The new 700: Due to the previous experience, we were prepared to carefully monitor the primary magnetic field drift as well as each of the cryo-shims from the start of installation. Immediately a rather large Z_1 and more modest Y_1 drift was observed. Agilent closely monitored the situation with us, and several methods were tried to stabilize the magnet. We have been monitoring the decreasing cryo-shim drift rate as it continues to approach zero.

Environmental Effects: To quantitate the spectrometer and environmental effects, we have been monitoring the spectra over 3 day periods (5 min interval rate) each month in order to establish the magnitude of the cryo-shim drift in the presence of environmental "noise". This effectively averages out the environmental input, and allows us to see the overall long term trend from the magnet itself.

However, as the changes in the cryo-shim became smaller it became harder to measure, and the environmental impacts drew more of our attention. Regardless of the eventual cryo-shim outcome, these environmental effects are relevant and it is always beneficial to reduce them as much as possible. We therefore began investigating the possible sources of environmental noise.

To start we began tracking the spectrometer responses to atmospheric pressure changes, external temperatures, and internal building temperatures (*i.e.* the usual suspects) over several weeks (Figures 1). Close monitoring of room EB-44 for temperature fluctuations (Figure 2), has revealed an interesting link between small temperature changes in the room over weekend/evening periods to external building temperatures. Attempting to correlate room temperature changes with external temperatures yielded an expected positive correlation on the weekends, but surprisingly an inverse correlation during the week. This is presumably due to air conditioner flow changes for evening/weekend versus work week periods.

We have also discovered a correlation between room temperature changes and spectrometer primary field responses (Figure 3). Specifically we have a direct observable link between the small room temperature changes and the spectrometer magnetic field. We are presently working with Building services to reduce and/or compensate for these room temperature changes. Desired specifications for room stability are less than 0.1°C difference per hour. Exceeding this has long been reported (Wüthrich, K. (1986) NMR of proteins and nucleic acids., 1-292.) and is most often seen as apparent T_1 "streaks" in indirectly detected dimensions.

Summary: So what will happen to the new 700? Our present options are to continue to monitor the system and evaluate further settling with the possibility of cycling the energization of the cryo-shims. With the predicted summer demands on the system we have opted to wait for more monitoring data. If the settling rate for the cryostat is unsatisfactory, we will schedule a cryo-shim power cycle for later this summer.

Should both time and cycling prove insufficient, then we will have to devise a new method of further reducing the drift. There is always the last resort of replacing the cryostat, but this is unlikely unless the settling halts.

We are continuing to monitor the 700 cryostat closely and expecting that settling will continue during the subsequent months. Projections based on current data show slow but continuous drift reduction. Agilent is involved at all stages and will continue to assess the situation with us. We are grateful for their unflagging support. Agilent has been clear from the start that their job will not be done until the highest quality, fully functional system is delivered and meets our approval.

ENC Update

EXPERIMENTAL NUCLEAR MAGNETIC RESONANCE CONFERENCE

The conference this year contained a large emphasis on bio-molecular solid-state NMR especially from groups like Chad Reinstra (Illinois-Urbana) and Mei Hong (Iowa State). The full conference abstract book is available if anyone is interested. Other prevalent topics included non-uniform and non-linear data sampling, *e.g.* Hyberts, S. G., Robson, S. A., and Wagner, G. (2012) *J Biomol NMR - online*, and the possible application of residual dipolar coupling to small molecular stereochemistry problems, *e.g.* Roberto Gils' *Magn. Reson. Chem.* (2012) 50, s86-91.

Non-Uniform/Non-linear Data Sampling (NUS) and Processing

This is an aspect of NMR that has been tantalizingly close for quite awhile. The idea is to save time by skipping acquisition of data points, especially in spectral regions dominated by noise. While the application has been around for about a decade, the practicality aspect has been missing. The processing, or rebuilding of the partial dataset back into something useful, had required specialized software, a lot of computer processing power, and more time in some cases than collecting the full data set would have needed. Also one never knew if the processing was correct unless the full dataset had also been acquired eliminating all time saving advantages. Several new processing schemes have been introduced into the latest spectrometer software making non-uniform and non-linear data virtually "push button". The time savings are compounded in higher multi-dimensional experiments. While beneficial, you never get something for free with NMR and there is a price to be paid in terms of signal to noise. Anyone interested in trying NUS is encouraged to contact the NMR staff, and we would be happy to assist.

Conference Evening Sessions

Evening sessions included exploratory panels on defining the need for ultra-high field liquids national facilities in the United States (*e.g.* three separate sister facilities at 1.2 GHz costing 50M+ USD each), and the ongoing helium crisis. The crisis topics ranged from the availability of helium, quality concerns, pricing, and the possibility of recycling and re-liquefaction of the boil off gas from present systems. On this note the two primary vendors had additional developments. Bruker Inc.'s answer at the ENC was the introduction of helium recycling spectrometers. A "cold-finger" can be employed at the top of the magnet that continuously re-liquifies the gases back into the helium bath. The challenges to this type of system include: higher initial magnet costs or retrofit costs, dependence on uninterrupted electricity supply (or the magnet quenches), pump vibration elimination, and biennial maintenance costs for cold-finger piston refurbishment (similar to requirements for cold-probes). The new magnets do not contain a liquid nitrogen shield therefore no weekly fills, no helium fills, and helium hold times measured in years. Agilent's proposed solution was 3rd party collaborations supplying after-market separate helium liquefiers that can support single or multiple spectrometer installations. The advantages are no additional magnet costs, no worries about electrical interruptions, and pump maintenance does not impact spectrometer availability. Disadvantages are that weekly nitrogen fills and periodic helium fills are still required and additional infrastructure (*e.g.* piping, larger equipment footprint) costs are involved. Complications involving helium recovery were a hot topic.

User Fees

There have been some questions regarding how usage is determined, users charged, and what detail on experiments is available for primary investigators. After reviewing several options and comparing to other facilities, a system was selected we felt to be the most fair. Mark has been busy writing and testing software for each spectrometer to track and summarize individual usage for monthly reporting to the department. When a user logs in at the spectrometer the usage is recorded until log out. **Please log out of systems when done** to be fair to colleagues and minimize charges. To address concerns about accidentally forgetting to log-off for long periods, Mark has included software to cross-reference the computer login with the spectrometer usage. We can go back and check, however logging off is best. For robotic auto-sampling systems the total experiment acquisition time is used for charges.

The spectrometers track individual usage to the second, sum the total usage for each research group and report at the end of each financial month. To include submitted service samples the total time is recorded, added to self measurement time, and then the total fees calculated at a rate of $2/hr. We then send the data to the department along with a breakdown of each investigator in each group. These charges are intended to account for a predicted cost recovery of approximately 10 to 15% of the facility. We hope this will provide the simplest and fairest system with the right balance of of detail (*i.e.* useful but not burdensome) while we gain experience collecting data and reporting it to the department. Should you have any questions regarding time, charges, or usage please do not hesitate to contact us.

Repairs and Service

While our priority is to minimize the downtime experienced by users, some delays can not be avoided. Both the U500 and V700 cold probes have received replacement of their gas compression pistons due every ~10,000 hours of operation. Total replacement time was 1 day of service with a day each for warming and then re-cooling. The cost of this replacement was covered under a service contract with expires this year. Subsequent maintenance for these probes has been added to projected facility costs.

The IBD5 spectrometer's 5mm AutoX DB probe has been sent to Agilent for refurbishment. The constant bombardment of high voltage excitation energy involved in NMR pulsing eventually takes its toll and occasionally small electronic components need replacement. Fortunately Mark was able to find a backup probe from another instrument, and the backup has been fully tested, calibrated for the IBD5 spectrometer, and is presently running samples. The original probe is in California awaiting Agilent's evaluation. We are very fortunate that a backup probe could be employed so quickly as probe repairs can take up to several months.

Lastly the U500 sample carousel has been experiencing some inconsistency. The problem seems to be intermittently related to valve pressures and we're trying to isolate the source of the issue. Let us know if you see anything misbehaving as it may help us narrow down the cause.

Figure 1 - Monitoring of EB-44 room temperature (blue), external temperature(red) and atmospheric pressure (green) over one week.

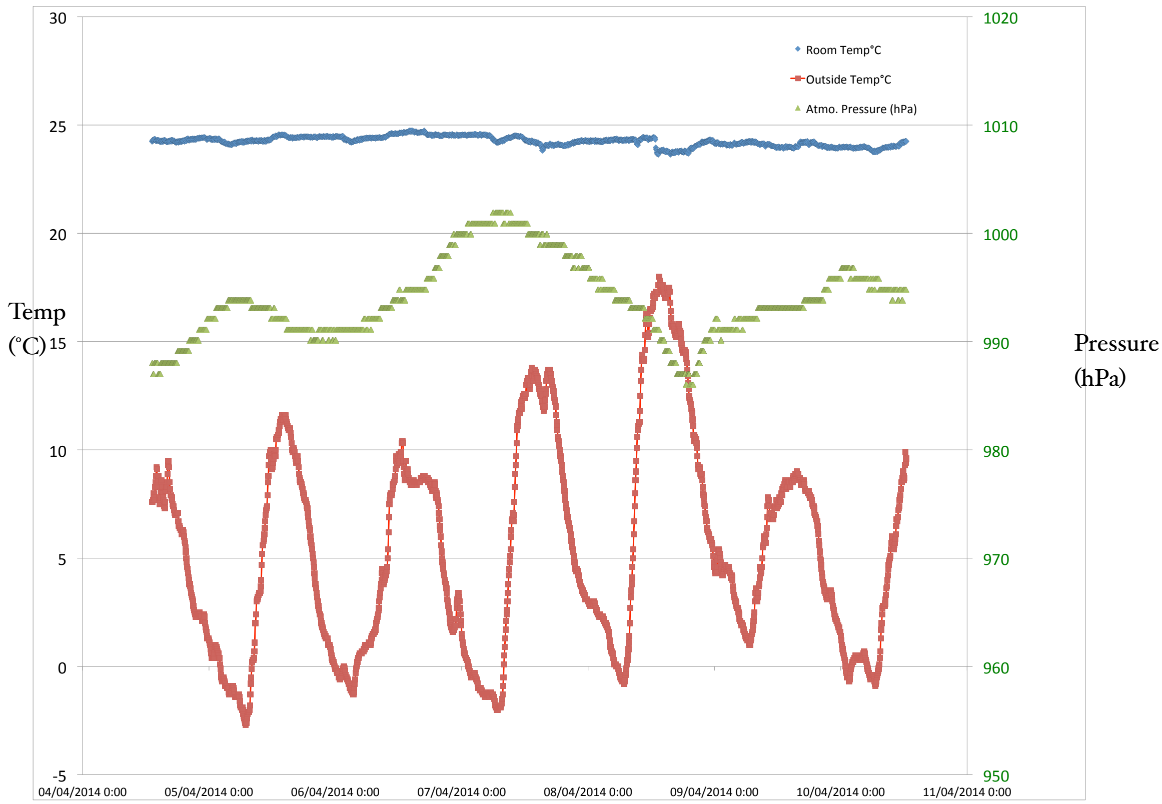

Figure 2 - Closer comparison of internal room EB-44 temperatures (blue) and external temperatures (red) for the same time period as Figure 3. Room temperature changes less the 0.1°C per hour are highly recommended for long term NMR spectral acquisition.

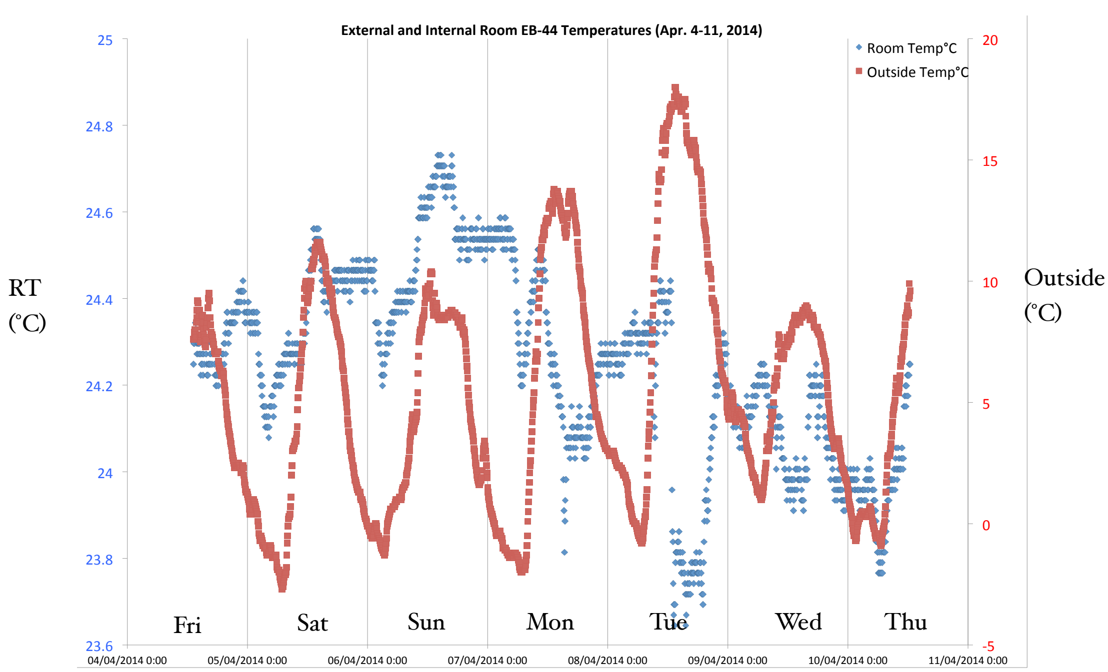

Figure 3 - Correlation between the small temperature changes found in the spectrometer room and the Z1 gradient compensations needed by the spectrometer to maintain field homogeneity. Typically rooms are controlled to less than 0.1°C per hour for long term data acquisition. Solutions that have worked in other facilities include easy changes such as diffusing the incoming conditioned air throughout the room more evenly, and replacing the thermostat with a more responsive unit. More invasive solutions can include passive heat-exchangers (no compressor cycling) to newer local room air conditioners.