What New Solutions for Small Molecule NMR Work Agilent has to Offer: New OneNMR™ Probes, Autosamplers and VnmrJ 3.1 Software
The OneNMR Probe

400-700 MHz

- Performs like a dedicated Carbon Probe
- Performs like a dedicated Proton Probe

- High quality 1D & 2D data
  - Excellent pulse (PW90) performance
  - Excellent lineshape
  - Excellent lock sensitivity
  - Excellent decoupling performance
  - Excellent RF homogeneity on both channels

- Excellent water suppression
- Superior salt & solvent tolerance

A Significant Advancement in Solution-State Probe Technology
The Ultimate Routine Probe

400 MHz OneNMR Probe:

\[ ^1H \text{ S/N} = 575:1 \]

\[ ^19F \text{ S/N} = 642:1 \]

\[ 13C \text{ S/N (ASTM)} = 183:1 \]

\[ 13C \text{ S/N (10\% ETB)} = 301:1 \]

- Performs like a dedicated Proton Probe

- Performs like a dedicated Carbon Probe
High Quality Data Through Outstanding Lineshape, Short Pulses & High Lock Sensitivity

400 MHz OneNMR Probe:

Outstanding lineshape = easy shimming & well resolved spectra

Decoupled Dioxane
0.08 50%
0.67 0.55%
1.40 0.11%

$^{19}$F PW90 < 8 μs
$^{13}$C PW90 < 7 μs

Short pulses = large bandwidth coverage

High lock sensitivity = stability & easy gradient shimming

Gradient profile NT=4
3mm tube, CDCL$_3$
Superior RF Homogeneity
On both channels – A key performance metric

Spin projections (signal intensity along the z-axis of the coil) of a standard dual broadband probe (Coil A), the OneNMR probe (Coil B) and the comparison of the two. The OneNMR probe provides a more uniform signal than a standard broadband probe.

The advantage of good RF homogeneity is easily seen in 2D experiments with multiple pulses like the gHSQC-NOESY (above). The ID probe is 20% more sensitive than the OneNMR probe but the overall performance is similar due to its outstanding RF homogeneity. A dual broadband probe is also shown.
400 – 600 OneNMR PZT Probe

**ProbeID**
- Probe recognition
- On-probe Flash storage
  all probe data, calibrations & history

**ProTune-PZT**
- **Third Generation** Automated Probe Tuning
  - 1st Remote Motors in Drive Modules
  - 2nd On-Probe Rare Earth Magnet Motors
    (more stable in magnetic fields)
  - 3rd On-Probe Piezoelectric Motors
    (not influenced by magnetic fields)
- Available for 400-600
- Fast / Silent Operation

Piezoelectric Tuning

Agilent Technologies
The Ultimate Routine Probe
The Ultimate Automation Probe

The OneNMR Probe
400 – 700 MHz
7600-AS Sample Change

96 sample capacity (2x48)
Random sample access
Free standing (vibration isolated)
Fast and Accurate for Highest Productivity
Compatible with all standard sample tubes & caps
Sample confirmation & monitoring
SCARA robotics – low maintenance & long life
7510-AS (12-Pack) Sample Changer

12 sample capacity (all std tube types)
Full random access
Plug & Play – dynamic adaptation, no adjustments
Fast, accurate, & reliable
Easy One-Handed Operation
Sample confirmation & monitoring
Low-maintenance – reliability
Single cable integrated into console
VnmrJ 3 : Scope and Coverage

VnmrJ 3.1

- For DD2, 400MR, VNMRS & VMRI
- Supports
  - Liquids
  - Solids
  - Imaging and microimaging
  - BioPack/BioSolidsPack
  - LC/NMR/MS
  - VAST
  - Secure Environment
  - DOSY
  - 7600AS / 7510AS / SMS / Carousel / 7800AP
VnmrJ 3 : Scope and Coverage

VnmrJ 3 is :

• A general release for all modalities
• Full integration of ChemPack and its philosophies plus further improvements
• Quality & Reliability improvements
• For a range of PC’s & OS levels
  – RHEL 5.1 and 5.3
  – DELL 390N, Optiplex 755N, T3400, T3500
VnmrJ 3 – Functionality (overview)

Intuitive interface to access / design / edit / continue…

Experiments and Studies
VnmrJ 3 – Functionality (overview)

Intuitive interface to access / design / edit / continue…

Experiments and Studies

A large gamut of experiments at the mouse-tip…
- Each with multiple options such as presat/wet/purge/ss/zfilter/etc.
- Controls to customize (add/hide/remove) access
VnmrJ 3 – Functionality (overview)

Intuitive interface to access / design / edit / continue...

Experiments and Studies

Experiment Selector

Study Queue

StudyQ - A mouse driven GUI to...
- Access completed data
- Build a new study
- Add experiments to continue study
- Monitor active experiment / study
- Customization of experiments
VnmrJ 3 – Functionality (overview)

Intuitive interface to access / design / edit / continue…

Experiments and Studies

Graphic canvas to display (interact with)…
- Spectrum / fid / image
- Array
- Overlaid viewports
- Interact between viewports
VnmrJ 3 – Functionality (overview)

Intuitive interface to access / design / edit / continue...

Experiments and Studies

**Parameters** (and action control) panels
- Set parameter values
- Controls for setup / process / plot / display

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**Experiment Selector**

**Study Queue**

**Parameter panels**
VnmrJ 3 – Functionality [StudyQ]

Intuitive interface to access / design / edit / continue…

Experiments and Studies

Drag-n-drop a study to recall data OR continue further investigation
VnmrJ 3 – Functionality [StudyQ]

Intuitive interface to access / design / edit / continue…
Experiments and Studies

Submit to:
- Foreground
- Background
- Automation
  - (sample changer)
  - DayQ / NightQ / PriorityQ

All options using similar workflow
Q. What about “my experiment” that already works fine for me? Do I need to edit macro/sequence/parameter to make it work with VJ3 tools?

A. NO !! Add your experiment to the Experiment Selector without “reinventing your workflow”
Q. What about “my experiment” that already works fine for me? Do I need to edit macro/sequence/parameter to make it work with VJ3 tools?

A. ABSOLUTELY NOT!! Add your experiment to the ES without “rediscovering your workflow”.

VnmrJ 3 – Functionality

One-step migration of experiments to VJ3

Take full advantage of VJ3 interface tools with your experiments.
VnmrJ 3 – BioPack integrated

All 390+ experiments integrated without needing to edit/reinvent macros/sequences/parameter sets !!
Q. What about $^{19}\text{F}-^{15}\text{N}$ gHMBCAD (for example)?

A. **Every liquids experiments (macro/sequence/parameter set/protocol) is nucleus independent.** Start current workspace with tn=‘F19’ and dn=‘N15’ – gHMBCAD will setup $^{19}\text{F}-^{15}\text{N}$ gHMBCAD.
Q. What about $^{19}\text{F}-^{15}\text{N} \text{gHMBCAD}$ (for example)?

A. Every liquid experiments (macro/sequence/parameter set/protocol) is nucleus independent. Start current workspace with $\text{tn} = \text{F19}$ and $\text{dn} = \text{N15}$ — $\text{gHMBCAD}$ will setup $^{19}\text{F}-^{15}\text{N} \text{gHMBCAD}$.

Large number of permutations of different experiments, starting from the parameters in current ‘workspace’.
VnmrJ 3.1 – Quantitative NMR made easy!!

Calibrate on a known standard…
– concentration of any sample is a “mouse-click” away!!

- Acquire a single scan 90degree tip spectrum on a known standard.
- Place cursor inside the integral of a known peak; Enter concentration; Click Define Concentration.
- Commit the value in the probe file.
- qNMR is now ready to go!!

Achieve <0.5% accuracy and precision without internal standards or electronic reference!!
DOSY_3.1 – New Features and Functionalities

New functionalities:
- non-uniform gradient (NUG) calibration
- monoexponential fitting with NUG correction
- biexponential fitting, with and without NUG correction (uses a modified SPLMOD)*
- multiexponential fitting, with and without NUG correction (uses a modified SPLMOD)*
- fitting of distributions of diffusion coefficients with CONTIN*

Performance enhancements:
- improved support for 3D DOSY (including N- and P-type absolute value processing)
- “user-friendly” phase-sensitive 3D acquisition and processing
- display of residuals
- optional point-by-point instead of peak-segmented 2D DOSY fitting and display
- removal of peak number limitations in 2D DOSY
- full panel support for every experiment in the package
- full ChemPack compatibility

(* only for 2D DOSY data sets)
VnmrJ 3 – Hadamard Experiments

Routine fast methods…
VnmrJ 3: QuickSubmit ("one-stop shop")

QuickSubmit:
- Run experiments under default conditions
- All operations are in background
- Current workspace is undisturbed
- Mix-N-match submissions between QuickSubmit (default experiments) and StudyQ submission (customized experiments)
VnmrJ 3 – Functionality (Batch Submission)

Use Study Clones to repeat an experiment (set) on multiple samples!

Create “clones” of a study in...
- Current workspace
- A given location (sample changer)

Create “clones” of...
- Experiment in current workspace
- A new study (built from scratch)

Clones are available in Experiment Selector
Clones can be made available in QuickSubmit
Experiment list
VnmrJ 3 : Preferences (Daily automation schedules)
3D Shimming

• Gradient Shimming Introduced in mid-90’s for Z axis only.
• Soon after developed for XYZ using PFGs
• The current solution does not require XYZ PFGs, it works with the shims
• It requires a strong signal so best suited for BioNMR samples in 90% H$_2$O
Routine 3D Shim of Bio NMR Sample

1D spectrum of ubiquitin in 90% water in a Shigemi tube using normal presaturation after 3D shimming. No processing methods for suppressing water were used. The total procedure required less than 10 minutes after the sample temperature reached equilibrium.
Non-spinning lineshape before & after a 2 minute 3D Shim of a very poorly adjusted magnet – Fully automatic result!

In this example many key radial shims were set to be far from optimal values, with several simply set to zero. From this poor state of adjustment, 3D shimming with an existing 90% H2O 3D shimmap followed by submission of the lineshape sample with only the typical Z-PFG adjustment shows the incredible improvement attained by fully automated means. Only 2 minutes were required for the 3D shim and 20 seconds for the Z-PFG shim once the lineshape sample was inserted in the magnet.
Lineshape after 3\textsuperscript{rd} order only 3D shim from typical shims

Routine 3D shim of basic shims on a water sample serves to be an excellent method for fast maintenance shimming.
ProShim

- ProShim is a new suite of programs and macros for automated shimming.
- It is complementary and greatly enhances the traditional Simplex lock autoshim.
- It works with shim methods provided as text files simulating the way an experienced “shimemr” would have worked.
- A collection of methods is provided that can shim the low order or all the shims, in a short or long time.
- The user has got the ability to define its own shimming methods.
Non-spin lineshape after 3D shim starting from very poor shims followed by Proshim.
Simply choose desired method from menu and click Proshim Now button! One would have typically first do a Z-PFG shim on the sample prior to using proshim. When an extensive proshim methods such as “allshims” or 4th-order_xyz, is used, it can be useful to finish with a final Z-PFG shim.
Proshim Panel – Admin user

Note the Automation Shim Tools group that appears for the admin user of the account. With these tools the admin user can pre-define how to conduct maintenance shimming and, if desired, schedule such service. AutoLineshape Now is not active because the Shim Scheduler has not yet been used to define the spreadsheet that defines the sample and method to use.
Define the desired name for the shimming study and the position of the lineshape sample in the sample rack. Choose the desired method from the ShimMethod menu and select the solvent the lineshape sample is in (typically acetone). Click Create and the shimming spreadsheet is in place. The Help facility guides the user in these steps.
Proshim in Action

When Proshim Now button is evoked in foreground the graphics window shows progress and tells when proshim is done.
This example was chosen to illustrate the “one DAC/line” format and how spin control is done is desired. This is in fact the same method used to re-shim the prednisone/DMSO-d6 sample in the misset shims experiment.

Note that addition of the keyword page=‘doped’ in parameters will prompt proshim to move very quickly. In the prednisone/DMSO-d6 misset shims experiments this was done.

Note that your console’s shimset is checked and that DACs which do not exist in hardware or are typos (eg z2x rather than xz2) are skipped. Proshim just moves on to the next DAC.
Effect of Deliberately Missetting Shims

Using a 40mM sample of Prednisone dissolved in DMSO6, the amount of change in individual shims required to drop the lock level 20% was determined. To produce these spectra z1, z2, x1, y1, xz, yz, xy, and x2y2 were all collectively miss set by that amount. The effect on the spectrum of such a large shimming error is quite pronounced in both the sample of prednisone and of course the lineshape sample.

Expansion of prednisone in DMSO6 with misset shim

Effect of same shim condition with the lineshape sample
After ~4 minute Proshim
Non-conventional probes

- Proshim is a unique tool for adjusting the shims in non-conventional probes, like nano probes.
- Specific care is taken for the peculiarities of such probes, like increased sensitivity to non-axial shims and practically insensitivity to higher order shims.
- A special ProShim method for such probes is provided.
A 234-page Guide. Two to three pages per Experiment. “Tips and Tricks” from the applab (at least half a page per experiment!)

“This manual has been created for the benefit of organic chemist/novice NMR spectroscopists to intermediate level NMR spectroscopists.”

“The purpose of this document is to provide more information about the small-molecule liquids experiments available in the VnmrJ 3.1 experiment selector. Users will find descriptions of the experiments, their utility, guides to parameter selection, processing, and references for further reading.”
VnmrJ 3 – Functionality (more…)

- **Sample-centric data management**
  - Migrate between spectrometers / day / automated acquisition / manual acquisition
- **csv2cpQ**
  - Submit samples to automation using spreadsheet (perhaps generated by local LIMS)
- **Automated shimming**
  - Gradient shimming / Proshim / 3D shimming (mix-n-match)
- **Run-time decision making**
  - CMD protocols and/or execprocess
- **Dynamic Data Mirroring**
- **e-Options**
  - Automatic messages, fids, spectra, plots, study
- **“Spectrometer View”**
  - Dynamic snapshot of completed / pending / active / errored studies on a day-to-day basis
- **“Convert current parameters” concept**
  - Every liquids experiments (macro/sequence/parameter set/protocol) is nucleus independent
- …
Thank you!