DHM | RI NMR Services Guide

DHMRI has one of the best equipped NMR facilities available, anywhere.

- 4 different field strength spectrometers:
  - 400 MHz
  - 600 MHz
  - 700 MHz
  - ultra-high field 950 MHz
- Multiple probe options (RT and cryo):
  - ^{1}H, ^{13}C, ^{19}F, ^{31}P, and ^{15}N
- Sample automation for high throughput applications
- 1D and 2D experimental suite for small molecules, peptides, and small nucleic acids such as HSQC, HMBC, DEPT, COSY, NOESY/ROESY and carbon optimized probe for INADEQUATE or 1D carbon experiments
- Multidimensional 3D and 4D experiments utilizing multiple fields and probe configuration options for macromolecules such as proteins and nucleic acids
- Comprehensive NMR data collection suite, data analysis and statistical support

Bruker Avance III 950 MHz

Our unmatched facility is staffed by a highly experienced team of scientists with over 20 years of NMR expertise who can provide support in study design, data analysis and interpretation.

DHMRI covers a wide variety of applications in sectors including:

PHARMA

BIOTECH

ACADEMIA

FOOD

NUTRITION

AGBIO

Accessed on a simple fee-for-service model to support all your NMR needs, for applications including:

- Structural elucidation or verification
- Fragment based drug design / protein-ligand screening
- Macromolecular assignment and dynamics
- Impurity identification
- Absolute or relative purity determination
- Multiple field strengths for dynamic ^{13}C optimized experiments for (H)CC(H) assignment strategies
- Metabolomics
- Application/method development
- Macromolecular data collection
- Supporting Analytical Services, including LC-MS, GC-MS, ICP-MS etc

DHM | RI

150 Research Campus Drive,
Kannapolis, NC 28081

www.dhmri.org +1 704-250-2600 info@dhmri.org

APPLICATION NOTE - 950 MHz

The ultra-high field strength 950 MHz instrument provides the highest resolution and when paired with a sensitive CryoProbe delivers the fastest, most versatile instrument with the ability to characterize small molecules, impurities and metabolites at very low concentrations. In addition, the high sensitivity of the instrument enables reduced acquisition time, enabling multi-dimensional experiments for assignments and dynamics on macromolecules.

High Field Instrument = Faster Data Collection

- Access to 2D, 3D, and other multidimensional NMR data acquisition
- Less purification required for impurity identifiction
- Faster feasibility studies
- NOESY / ROESY buildup curves for small molecules (high accuracy distance restraints)
- NOESY restraints for macromolecular simulated annealing

Proteins/Nucleic Acids

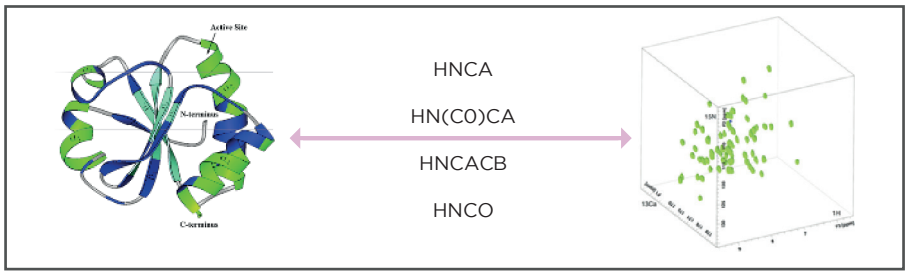


FIGURE 1

Data collection for macromolecular assignment via ^{1}H, ^{13}C, and ^{15}N

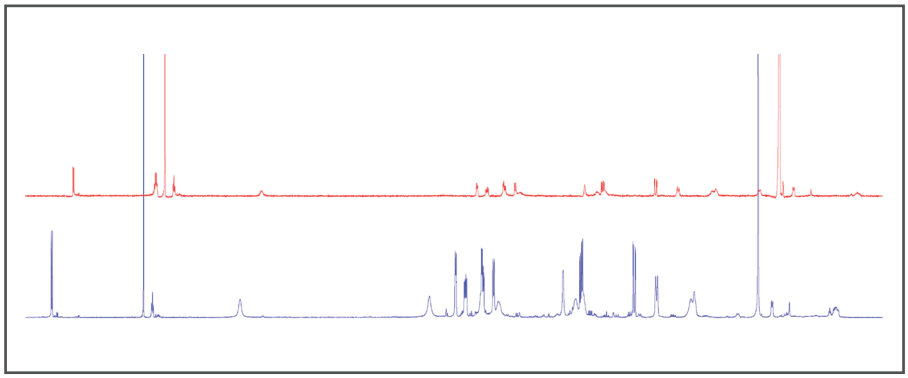


FIGURE 2

Overlay of 1D ^{1}H of strychnine demonstrating multi-suppression pulse sequence for better dynamic range which can be used in 2D experiments

950 MHz – Impurities

^{1}H ^{13}C – 2.34 mg in 5 - 7 hours

- 1D ^{1}H, COSY, ROESY, HSQC,HMBC
- Proton only – 10 µg at 2 days
  1D ^{1}H, TOCSY, NOESY or ROESY

DHM | RI
150 Research Campus Drive,
Kannapolis, NC 28081

www.dhmri.org +1 704-250-2600 info@dhmri.org

APPLICATION NOTE - 700 MHz

The 700 MHz instrument is ideal for screening applications. The flexibility of both proton and fluorine configurations makes this an ideal instrument for ^{1}H-based experiments such as STD and LOGSY protein-ligand screening, while the ^{19}F probe enables experiments such as fragment-based drug design.

The high-capacity SampleJet delivers automation for large sample sets in applications including protein-ligand screening or metabolomics (for complex or simple mixtures). Additional configuration options include the use of ^{31}P for nucleic acids, or other ^{31}P-containing compounds.

- SampleJet Autosampler - up to 480 sample capacity (5mm, 3mm, 1.7mm)
- CryoProbe for enhanced ^{1}H, ^{13}C, and ^{31}P
- ^{19}F (^{1}H) dual probe – fragment-based drug design, HOESY experiments

Bruker Avance III 700 MHz

Fragment/protein-ligand screening

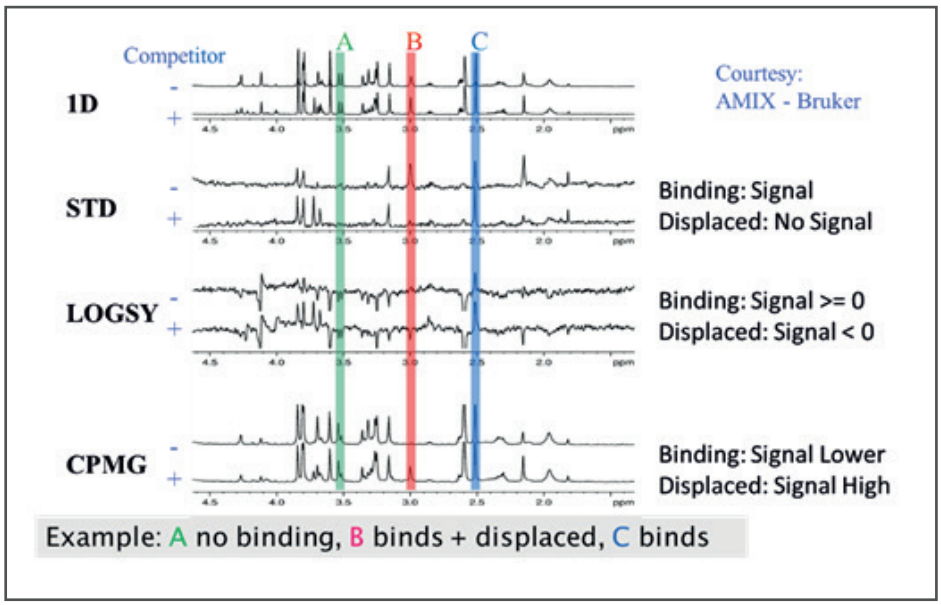


FIGURE 3

1D ^{1}H protein ligand screening with STD and LOGSY

APPLICATION NOTE - 600 MHz

The 600 MHz instrument is equipped with a highly sensitive ^{13}C CryoProbe. This probe enables fast structure elucidation of small molecules, enabling assignment and definitive through-bond determination of C-C connectivity in proton-poor compounds (e.g. quartenary carbons). Data collection such as 2D INADEQUATE or 1D selective-INADEQUATE provide detailed connectivity and coupling constants.

The direct-detect ^{13}C Probe at this field strength is flexible enough to be used alongside carbon labeled macromolecules such as those used in (H)CC(H)-based assignment strategies.

- BACS Autosampler for high-throughput screening - up to 60 sample capacity
- CryoProbe for enhanced direct-detect ^{13}C, also with cold ^{1}H channel

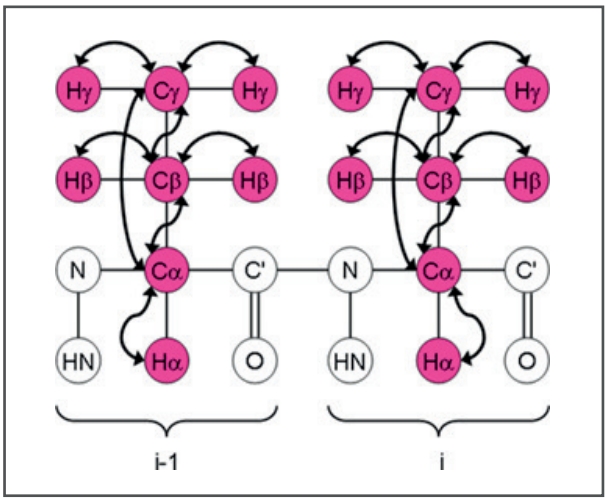
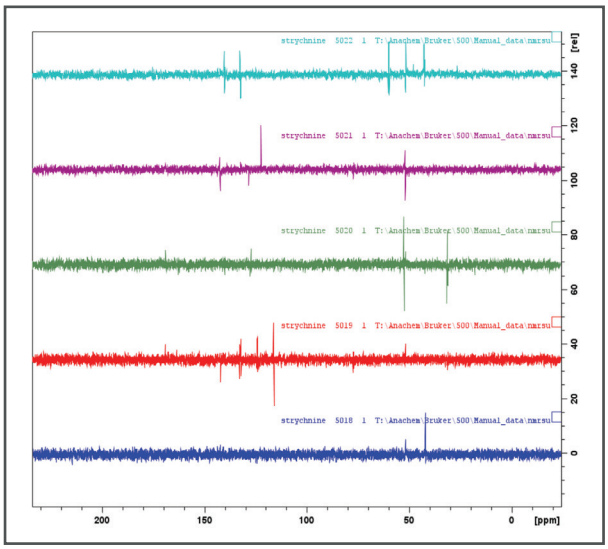


FIGURE 4

Schematic representation of HCCH-TOCSY, by Victoria A. Higman (CCPN)



Coupling	Atom	Bifulco, et al, (Hz)	SELINA 1D (Hz)
$^{1}J_{CC}$	4,20	49	48.3
	11,22	64	65.3
	6, 12	34	Overlap with 6, 10
	6, 10	34	Overlap with 6, 12
	12,13	32	33.1
	11,14	61*	59.8
	12,14	43*	43.8
$^{3}J_{CC}$	11,23	Not reported	9.1

*Reported from INADEQUATE spectrum.

FIGURE 5

Selective INADEQUATE overlay for sequential assignment of strychnine, including extracted C-C coupling constants

DHM | RI
150 Research Campus Drive,
Kannapolis, NC 28081
www.dhmri.org
+1 704-250-2600
info@dhmri.org