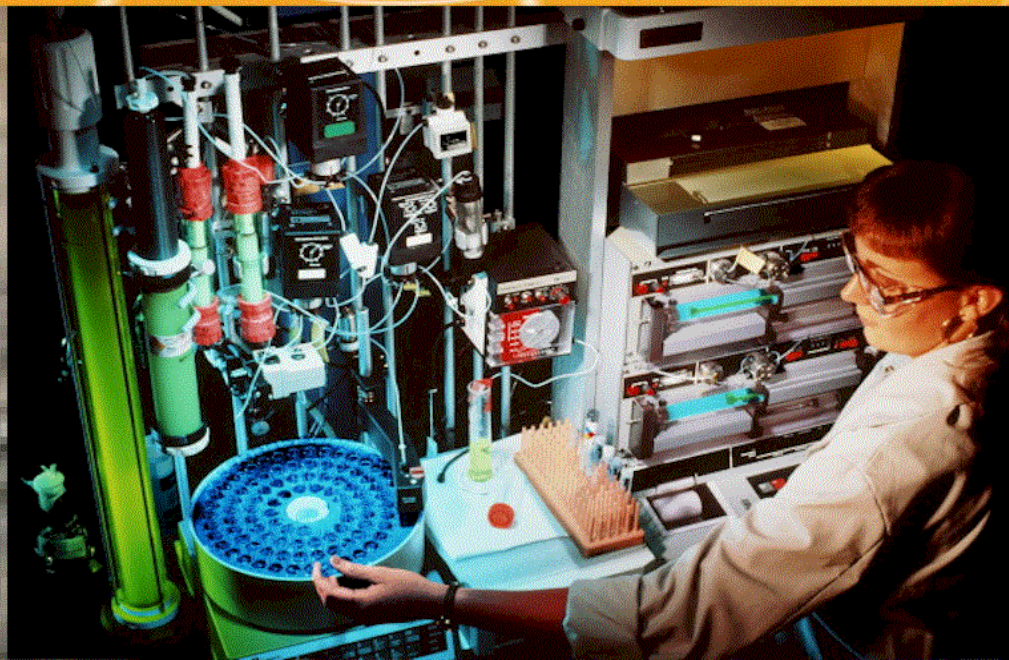


Automation

## Open Access High Throughput NMR

*Add Microplate Automation to Your Facility*

**Explore**  
**Life Science Automation**



# Year-End Perspectives

Dear Colleague:

We typically use the fall SMASH conference to check-in with our customers and learn about new trends in small molecule NMR and this year was no exception. Tim Peck, Bob Albrecht and I were there with a CTC/LEAP liquid handler showing off the robotics, fluidics and software for our record-setting One-Minute NMR platforms.



No less than twenty of our current customers were there and some of these groups are running hundreds of samples per month and supporting dozens of synthesis chemists to create smooth-running trouble-free departmental HT-NMR automation systems. I thought you might be interested to hear what they said:

- ⇒ They told us that our CapNMR probes generate excellent spectra with clean baselines using a small fraction of the sample (e.g., micrograms of material or only a few microliters from prepared libraries) needed using other probes. But when every prepared sample is valuable, *less is more*, even for synthesis chemists who might be making plenty.
- ⇒ Facility Managers and chemists alike told us that traffic to and from our systems was a *one-way street*. Most submitters reserve a space on our platforms at their desk using their web browser, then ‘drop off’ their sample, but never bother to ‘pick up’ their sample. We take so little material from their synthesis or library that they can now say, “Why bother?” Others conveniently recollect in the original or a fresh well or vial. Your choice.
- ⇒ And they told us that chemists like the freedom to work with their choice of plates or vials helps keep the peace when supporting dozens of chemists with different experimental needs. One-Minute NMR supports 96- or 384-well microplates, short or tall, and many varieties of sealed, tapered vials in many different volumes. In fact, CTC/LEAP liquid handlers can support any of the inexpensive, standard lab consumables in the Microliter Analytical catalog.
- ⇒ One customer told us that their system had “paid for itself” in deuterated solvent savings alone in less than eighteen months. They like our comprehensive solvent conditioning (with sparging, blanketing and degassing) to create ‘no-water-peak’ spectra from up to three solvents.
- ⇒ Several customers are integrating One-Minute NMR into their new molecule operations to create well-centric LC-MS-NMR library QC systems. Clearly, LC is needed to clean up and isolate the sample and MS provides the molecular weight. But NMR is the best choice to provide definitive structure confirmation, well purity and quantitation. Microplate automation lets NMR keep up and ‘puts NMR back into the game.’
- ⇒ Facility Managers told us they can now work a *second shift* to gather more information by scheduling runs overnight and keep tabs on what is going on from their web browser at home.

This issue is devoted to the new product brochure that we introduced at SMASH describing our Medicinal Chemistry NMR Automation system. It illustrates how many of our customers are getting more mileage out of their older 400 MHz systems by re-deploying them to One-Minute NMR. These systems rapidly attract routine structure confirmation samples and can typically run hundreds of spectra per day if you have that kind of workload. Even if you don’t yet, you will be surprised how the capability to schedule plates and vials will expand the use of NMR by your chemists. Sound interesting? Then call and ask for our new Open Access HT-NMR Application Note. It shows setup screens, typical spectra and example reports.

Sincerely,

David Strand  
CEO, Protasis Corp.

## Inside This Issue

CICG—CapNMR ICG Probes	4
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### ***What if you could get NMR spectra on your LC/MS wells?***

You could confirm structure, including isomers, without ambiguity. You could get amounts without needing internal standards. And you could determine well purity.

### ***What if you could use the same microplates or vials for NMR that you use on other standard lab equipment?***

You could transfer samples easily and quickly from one instrument to the other without reformatting and without spending the time, cost and effort to fill NMR tubes.

### ***Sound interesting?***

Turn the page to read about Microplate NMR Automation with Capillary NMR Probes.



## Find Even More Information on Our Web Site:

To learn more about:

CapNMR Probes	<a href="http://www.protasis.com/MicroFlowNMR/">http://www.protasis.com/MicroFlowNMR/</a>
One-Minute NMR	<a href="http://www.protasis.com/OMNMR/">http://www.protasis.com/OMNMR/</a>
Natural Products	<a href="http://www.protasis.com/NaturalProducts/">http://www.protasis.com/NaturalProducts/</a>
Medicinal Chemistry	<a href="http://www.protasis.com/MedicinalChemistry/">http://www.protasis.com/MedicinalChemistry/</a>
Newsletter Signup	<a href="http://www.protasis.com/Customersupport/">http://www.protasis.com/Customersupport/</a>
Technical Support	<a href="http://www.microNMR.com/">http://www.microNMR.com/</a>

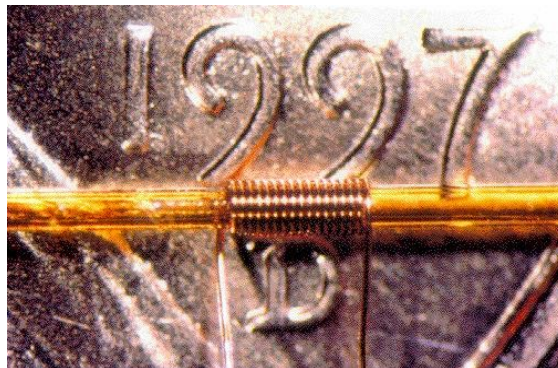
# Sample-Limited Applications for MicroFlow NMR

## Natural Products

When you could have the world's supply in one microplate well, you want the smallest flowcell possible. Get 1D spectra on as little as 1 microgram of sample in a few minutes. Obtain 2D spectra and elucidate structure on New Molecular Entities with about 50 micrograms of material in a few hours. Dereplicate quickly to home in on your important new discoveries. Conserve your resources!

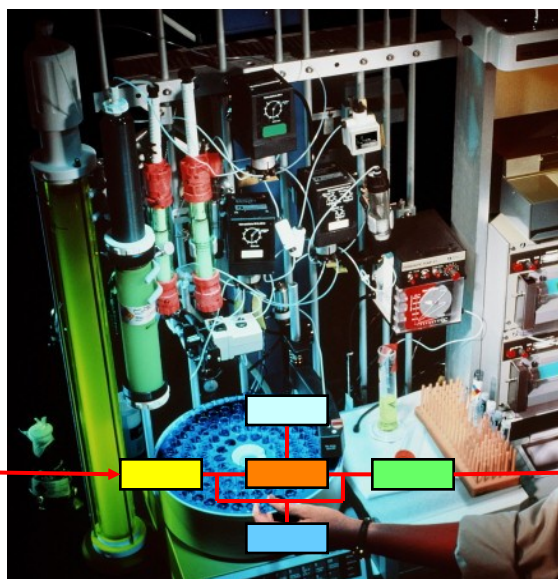
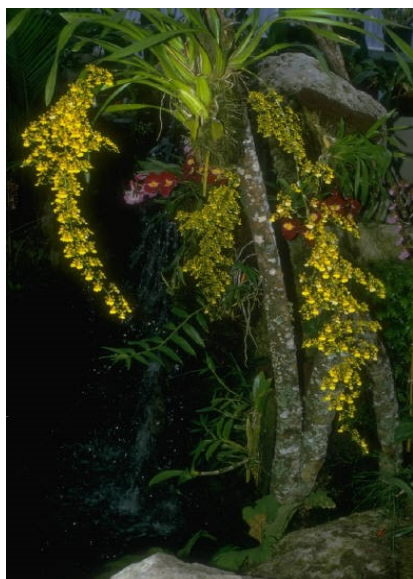
## Sensitivity, Simplicity and Economy

Elegant simplicity. Smooth fused silica with low carryover. Only 5 microliters in volume for the highest mass sensitivity! Fast and spartan.



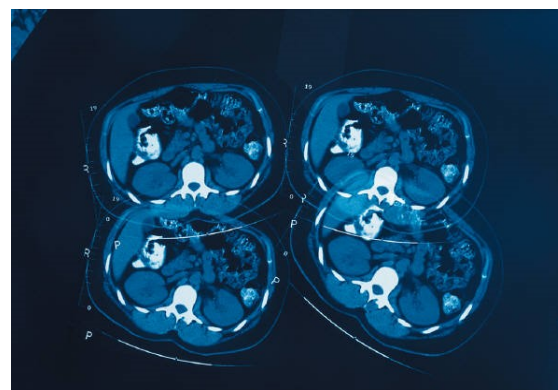
## Organic Synthesis

With organic chemists synthesizing more molecules than ever, you need to fast tools that tell you your program is on track. Did you make what you thought you made? What are those reaction byproducts. Confirm quickly. Improve yield and efficiency in your synthesis. Automate discovery research with high throughput purification and on-line hyphenation to NMR followed by MS on the same sample.



## Metabolites

A promising drug lead can fail suddenly in development if problem metabolites surface. NMR is definitive, but has been too slow and insensitive to compete with MS. Now get these answers sooner with MicroFlow NMR. You can clean up biosamples to reject interferences, isolate and concentrate low-abundance metabolites and load bands automatically with Protasis High Throughput Sample Management (HTSM)..



## Protein Expression

Now you can screen as little as forty micrograms of protein from cell extracts using Protasis MRM's new triple inverse gradient (TXI) probe.

## Product Release – Impurities / Stability

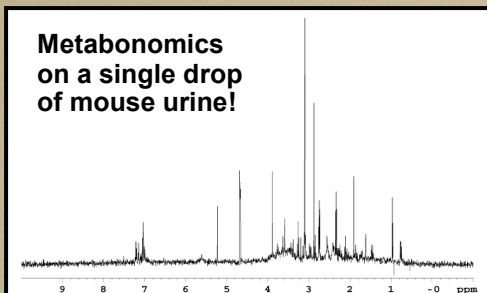
Consumer products must be tested before each batch can be released. The FDA's process analytical technology (P.A.T.) initiative will make monitoring each intermediate step a requirement. Protasis' Stability / Impurities Platform can automate product stability testing to characterize thermal or oxidative degradants. Put HT-NMR on-line to obtain the highest level of QA/QC for your most valuable processes.

# MicroFlow NMR

Sensitivity, Simplicity, Economy

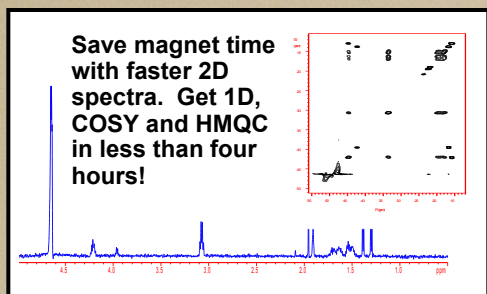
## Efficient Sample Utilization

Metabonomics  
on a single drop  
of mouse urine!



## Efficient Magnet Utilization

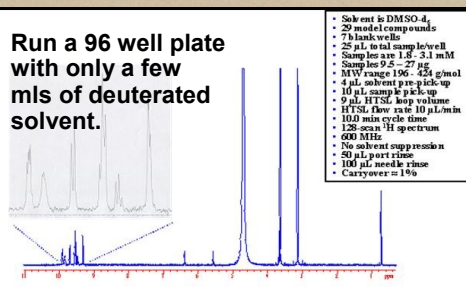
Save magnet time  
with faster 2D  
spectra. Get 1D,  
COSY and HMQC  
in less than four  
hours!



For Varian, Bruker or JEOL  
300MHz —800 MHz  
FEP Flowpath  
<sup>1</sup>H, {<sup>13</sup>C, <sup>15</sup>N / <sup>31</sup>P}

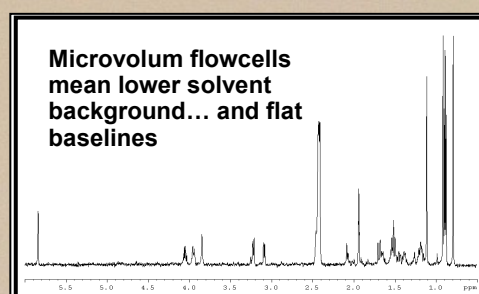
## Miniscule Reagent Cost

Run a 96 well plate  
with only a few  
mls of deuterated  
solvent.

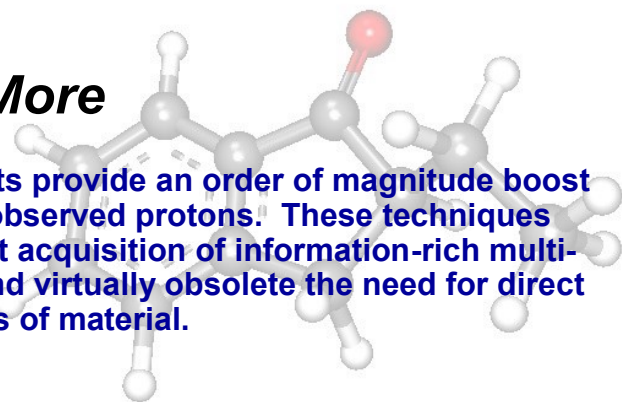


## Low Solvent Background

Microvolum flowcells  
mean lower solvent  
background... and flat  
baselines



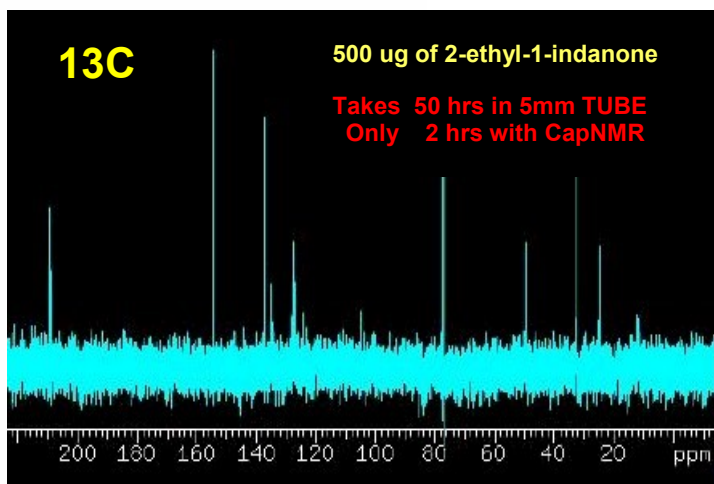
Benefits accrue quickly at the  
capillary scale. Let Protasis  
show you how to get started!



## Q: Direct vs. Indirect? A: Less is More

Modern 2-dimensional indirect NMR detection experiments provide an order of magnitude boost in sensitivity due to the larger gyromagnetic ratio of the observed protons. These techniques coupled with a new generation of RF microcoils allow fast acquisition of information-rich multi-dimensional datasets from only micrograms of sample and virtually obsolete the need for direct detection of low-sensitivity gamma nuclei from milligrams of material.

### Historical



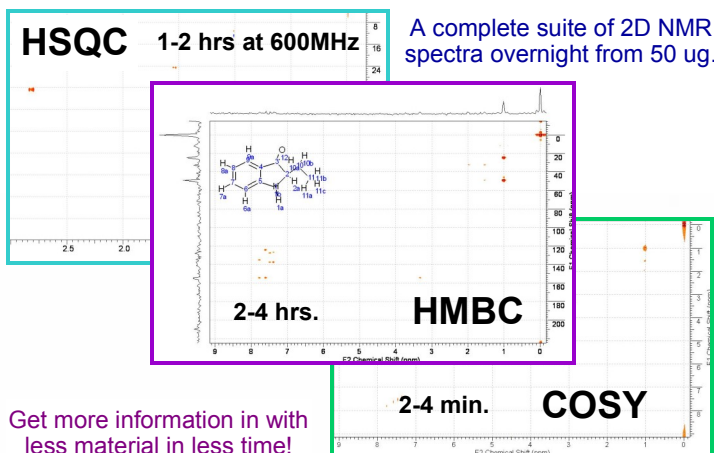
#### Pros:

- Historical significance
- Large  $\delta$  bandwidth and high resolution
- Easy digitization for recording

#### Cons:

- Does not provide connectivity info
- Requires impractical quantities of sample
- Low sensitivity, long acquisition times
- High susceptible to artifacts and electronic noise
- High susceptible to misinterpretation
- Costly

### A Better Way...



#### Pros:

- ✓ Highly sensitive to  $\gamma$  proton
- ✓ Easily acquired using modern pulse sequences
- ✓ Needs only micrograms and microliters of sample
- ✓ Provides connectivity information invaluable to chemical assignments
- ✓ Practical, economical
- ✓  $^{13}\text{C}$  shifts can be simulated using software, if desired
- ✓ Working knowledge of pulses sequences is readily mastered with minimal time investment

#### Cons:

- May not digitize as easily for legacy library recording

Call For The Complete 8-Page Application Note

Want to learn more about advanced 2-dimensional heteronuclear techniques? We can help by sending you an introductory tutorials and some references. The miniaturized detector cells in CapNMR probes make these advanced techniques more useful than ever before. Microcoils are ten times more sensitive than 5mm probes. That translates into 100-fold speed improvement to allow you to acquire complete suites of 2-D spectra in a reasonable timeframe. Now you can get you all of the information you need for library quality control from a miniscule amount of sample that you won't even miss.

CALL 508-481-4163

# CICG

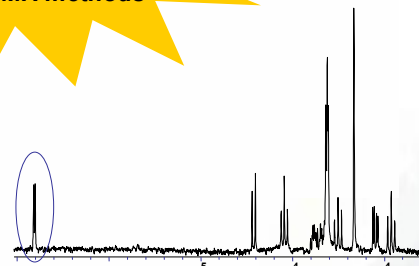
## CapNMR™ Indirect Carbon Gradient Probes *NMR Provides Quality Assurance for Molecular Libraries*

Meet the heart of Protasis' wellplate-centric Microflow NMR systems...



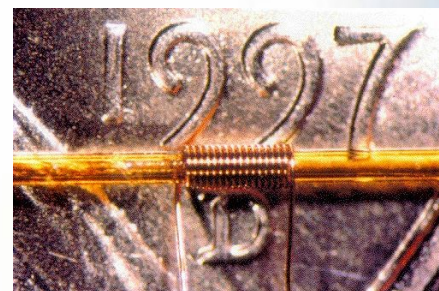
Get more information  
with fast, sensitive  
indirect NMR methods

In 2002, Protasis MRM overcame the limitations of traditional NMR with its original CapNMR Indirect Carbon Gradient NMR Probe. Then in 2004, we increased the observe factor to make the best even better. The enhanced mass sensitivity offered by this unique microcoil design enables NMR data to be obtained using only micrograms of sample mass and only a few microliters of sample volume. These reasonable sample amounts put NMR onto common ground with other modern laboratory instruments and enables sample interchange of standard wellplates and microvials directly.



Highest Sensitivity!

Typical homonuclear and heteronuclear NMR spectra are now possible using 100 nmol or less of analyte. A strong z-directed pulse field gradient allows for complete access to modern NMR pulse programs utilizing water suppression techniques and coherence selection pathways. Sensitivity translates into speed, allowing 2D spectra in minutes instead of hours.



Twice as Fast!

The ICG microflow probe utilizes a unique, patented NMR flowcell that provides excellent spectral resolution. The ICG probe is available with flowcell volumes of either 5 or 10 uL with an effective observe factor of 50%. The solenoid coil architecture is wound directly over the flowcell and provides maximum signal strength, exceptionally clean baselines and short pulse widths that enable

Protasis CapNMR probes use small diameter (0.075um I.D.) Teflon FEP transfer lines to minimize band broadening, maximize solvent compatibility and virtually eliminates analyte wall-coating. Solvent consumption is drastically reduced over conventional scale systems, making the use of NMR-compatible (deuterated) solvents cost-effective and practical. CapNMR probes are engineered, manufactured and calibrated to extremely high standards to deliver world-class proton and correlation spectra with less material in less time. Protasis probes are easy to use, reliable to operate and proven with all major spectrometer systems.

CNMR- XXX-10-075-FFF

Protasis CapNMR ICG Probe

B = Bruker  
V = Varian  
J = JEOL

XXX = 300, 400, 500, 600, 700 Mhz  
075 = 075 micron I.D. Teflon FEP transfer tubing  
FFF = 05E or 10E microliter flowcell volume  
(\*E' for enhanced 50% active volume)

### NMR Compatibility:

Protasis/MRM probes are compatible with Bruker, Varian and JEOL NMR spectrometers. These proton detect / deuterium lock probes are designed for 300 MHz — 700 MHz operation. Call about 800 MHz probes – available now.

## CapNMR™ ICG Probe Performance Benefits

- High mass sensitivity lets you reduce sample preparation time and get results faster.
- Up to 100X faster than 5mm probes. Improve utilization for your existing magnets.
- Rapid 2D experiments enable more information with less sample in less time.
- Small flowcell volume lets you take less sample from valuable, prepared libraries.
- Go shimless. Reshimming is typically not required between samples in the same solvent.
- Save the cost and time of filling NMR tubes. Use standard lab consumables and techniques.
- Excellent hydrodynamic and NMR spectral resolution. Exceptionally clean baselines.
- Short pulse widths enable broadband experiments without overheating sample.
- Miniscule solvent consumption for economical operation and minimal waste.
- Compatible with all HPLC and NMR solvents (e.g., DMSO, chloroform, acetonitrile).
- Flow-through probe design virtually eliminates sample carryover. Easy cleaning protocols.
- Load samples manually with a simple syringe or fully automatically with a liquid handler.
- Exchange solvents (protonated-to-deuterated) with vacuum centrifuge or SPE.
- Solvent management available to protect deuterated solvents from atmospheric contaminants.

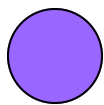
## Product Specifications (5 µL 500 MHz shown)

<b>Enhanced CapNMR ICG Probe</b>	
<i>Nuclei</i>	$^1\text{H} \{^{13}\text{C}\} / ^2\text{H}$ lock
$^1\text{H}$ Frequency Gradient	500 MHz z-Directed
<i>NMR Flowcell</i>	5 µL
<i>Fluidic Lines/Connectors</i>	75 mm I.D. x 1/32" O.D. Teflon FEP with Upchurch Fingertight Connectors 1/16" O.D. Hastalloy Unions compatible with aggressive cleaning protocols
<i>Resolution/Lineshape (<math>^1\text{H}</math>)</i>	(5% $\text{CHCl}_3$ in acetone- $d_6$ , stopped flow, flowcell filled, LB=0)
50%	< 1 Hz
0.55%	< 10 Hz
0.11%	< 20 Hz
<i>Proton 90° Pulse Width</i> <i>Indirect Detect Carbon 90° Pulse Width</i>	≤ 5 ms ≤ 15 ms
<i>VT Control*</i> (gas source supplied by customer)	0 - 50 °C
<i>Proton Signal to Noise</i>	
10 mM sucrose in 100% $\text{D}_2\text{O}$ with 0.1 mM $\text{NaN}_3$ , quantity sufficient to overfill flowcell. Anomeric proton. LB=0.7 Hz.	> 27:1 single scan
RF connectors	BNC
RF Homogeneity (450°/810°)	75%/50%
<i>Gradient Specifications</i>	
Strength: (typical)	35 G/cm/A
Maximum recommended duty cycle	< 10 %
Maximum recommended drive current	< 10 A

\* Bruker and JEOL systems, probe interfaces to spectrometer manufacturer's heater, supplied by customer.

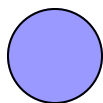


# How to Make Short Work of Your *Medicinal Chemistry* Samples Implementing Open-Access HT-NMR in an Active Department using One-Minute NMR™



← **Your Department  
Full of Eager  
Synthesis Chemists**

Now you can go from sample to results in one step. One-Minute NMR lets you transfer your prepared samples directly from your HPLC to a fast liquid handler for NMR analysis. Now you can load plates and vials directly.



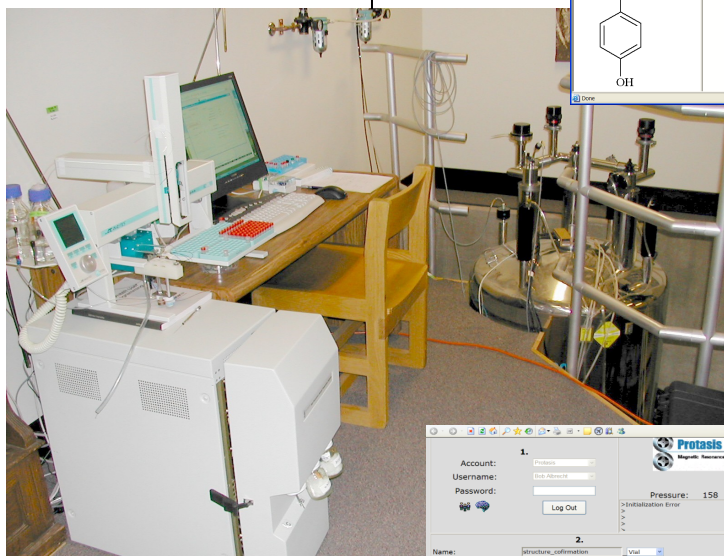
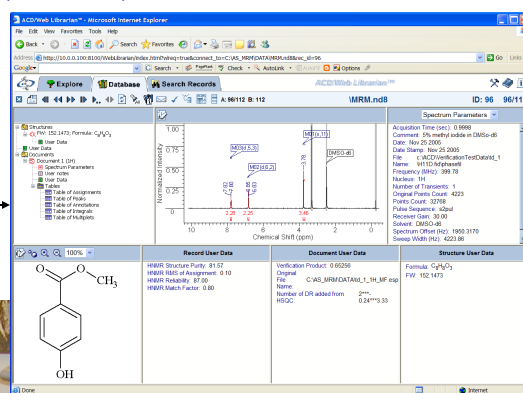
**Did I Make What  
I Thought I Made?**

Chemists and their managers will immediately appreciate the indispensable convenience of walk-away, unattended operation, with special support for overnight samples. When you consider shorter sample prep times, tiny sample withdrawals from valuable libraries, scant reagent and solvent consumption, elimination of the cost and effort to fill tubes plus improved magnet utilization due to faster spectral acquisition, this is a system that easily justifies itself in any NMR facility with multiple users or many samples.

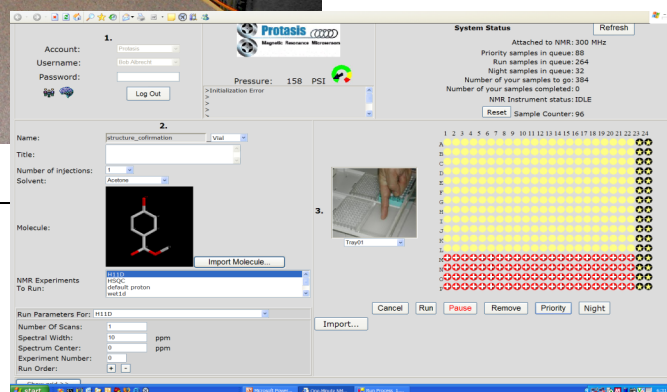


"For quality control of chemical libraries, 1D NMR spectra are acquired under full automation from 384-well plates on as many as 130 compounds within 24 hours using 128 scans per spectrum and a sample-to-sample cycle time of about 11 min. Because of the low volume requirements and high mass sensitivity of the microflow NMR system, 30 nmol of a typical small molecule is sufficient to obtain high quality, well-resolved, 1D proton or 2D COSY NMR spectra in approximately 6 or 20 min of data acquisition time per experiment, respectively."

Bernhard Geierstanger, The Genomics Institute of the Novartis Research Foundation, *Analytical Chemistry*, October, 2005,



View acquired spectra and compare match and purity scores using ACD/Lab's Web Librarian. Results are emailed to each user. Flexible scripts allow any experiments using your spectrometer commands.



The workflow diagram shown is used in major pharmaceutical companies to process thousands of samples per month.

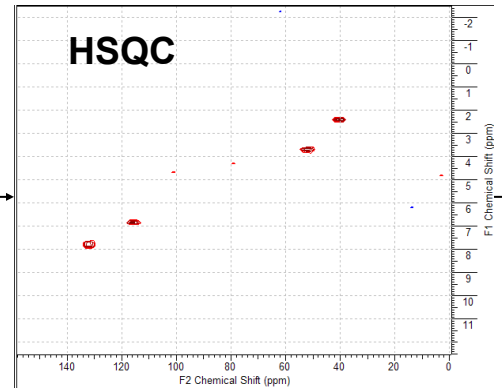
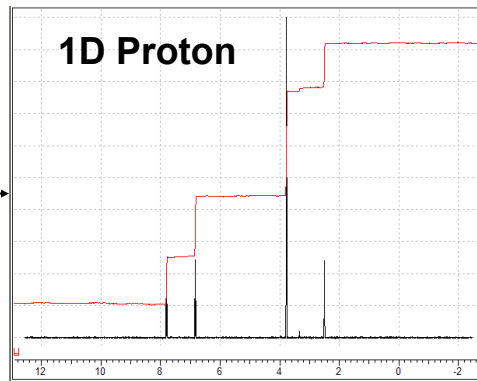
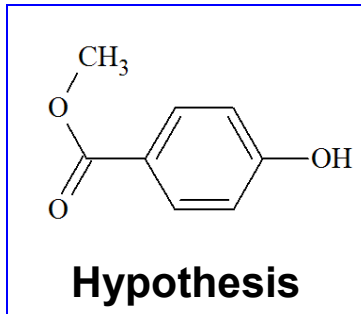
Log in samples quickly and monitor analytical progress from any web browser. Or import sample lists directly from your HPLC or other instruments. Support for 96 or 384 well microplates and your choice of low-volume vials. Supports up to three solvents.

**Sample Cleanup  
(e.g., HPLC,  
filtering)**



**Reconstitute  
And Boost  
Concentration  
In Deuterated  
Solvent**

# Obtain Excellent Results



Building or qualifying a library? NMR is the best technique to provide definitive structure verification and complements your MS spectra. And once you confirm the identity of the NMR spectral peaks, then you can also easily obtain the amount and purity of molecule in each well using ERETIC quantitation.

**YES**

**>= 1D Proton  
Acceptance Level?**

**NO**

If more information is needed, schedule additional experiments automatically while the sample is still in the flowcell.

**YES**

**>= AVG(HSQC + 1H1D)  
Acceptance Level**

**NO**

**Confirmed**

**Rejected**

**Match Score**

**Amount,  
%Yield**

**Well or Vial  
Purity**

## Structure Confirmation

These NMR spectra show the results of the first complete structure verification done by the One-Minute NMR interface to ACD Automation Server 9. The 1D match factor acceptance level was intentionally set high so that an HSQC experiment would be performed.

## Target Amount and % Yield

Once you know confirm the molecule you can integrate over selected peaks using ERETIC quantitation. One-Minute NMR lets you import original sample amounts so that % Yield or % Active can be calculated in your final printed or emailed report.

## Sample Purity

Once the amount of target material has been calculated, additional calculations can be performed and reported.

Call To Get our  
Structure  
Confirmation  
Application  
Note

508-481-4163

# HTSC

## Get Structure Confirmation, %Yield and Purity *NMR Provides Quality Assurance for Molecular Libraries*

### Protasis High Throughput NMR Structure Confirmation System

#### Typical Configuration

- ✓ Protasis CapNMR™ ICG Probe
- ✓ Protasis One-Minute NMR™ Software
  - Talks to Varian or Bruker Spectrometers
  - Seamless Interface to ACD Structure Confirmation Software
  - Accurate %Yield and Purity in a single step with ERETIC
- ✓ Protasis MultiSolvent HTSL + DSCM
- ✓ CTC/LEAP PAL Liquid Handler
- ✓ Vacuum Centrifuge
- ✓ Varian or Bruker Spectrometer
- ✓ 400 MHz Shielded Magnet



Get an optimized solution that can power your entire department! This Protasis High Throughput NMR Structure Confirmation System is supporting a sample workload of 2500+ samples per month in a departments with 150+ synthesis chemists.

Protasis can help you assemble a complete, dedicated multi-user NMR system for your Medicinal Chemistry department to serve all of your synthesis chemists. It is capable of processing hundreds of samples per day in up to three different solvents. Multiple methods can be defined for each sample using flexible, editable scripts that are sent to your spectrometer over a standard LAN.

The Protasis One-Minute NMR platform is a great way to introduce NMR automation to your synthesis chemists. You can mix and match laboratory-standard microplates and microvials freely on the fast, reliable CTC/LEAP liquid handlers that have proven themselves so well in mass spectrometry applications. Samples can be loaded directly from any HPLC system without the additional cost or time required to transfer samples to NMR tubes.

Protasis CapNMR probes are already sensitive and fast. To take full advantage of this revolutionary capability, Protasis adds convenient fully-automated sample loading using a standard injection loop. You can walk away with confidence knowing that your precious sample will be positioned accurately in the

center of the NMR flowcell. Then your complete set of experiments can be executed and monitored efficiently by One-Minute NMR software.

Once acquired, One-Minute NMR can automatically send your 1D spectra to ACD/Lab's Structure Confirmation algorithm to determine match and purity scores. If you need more information, it will automatically schedule additional 2D experiments. A report with links to the results is emailed to each user. All acquired spectra can be reviewed in exquisite detail using ACD/Lab's spectral viewers.

The Protasis Structure Confirmation System is the highest performing system available for active departments that are building and certifying molecular libraries. Use mass spectrometry to provide molecular weight. But use One-Minute NMR to provide high-certainty structure confirmation, % yield and purity so that you can fully characterize your valuable molecules.

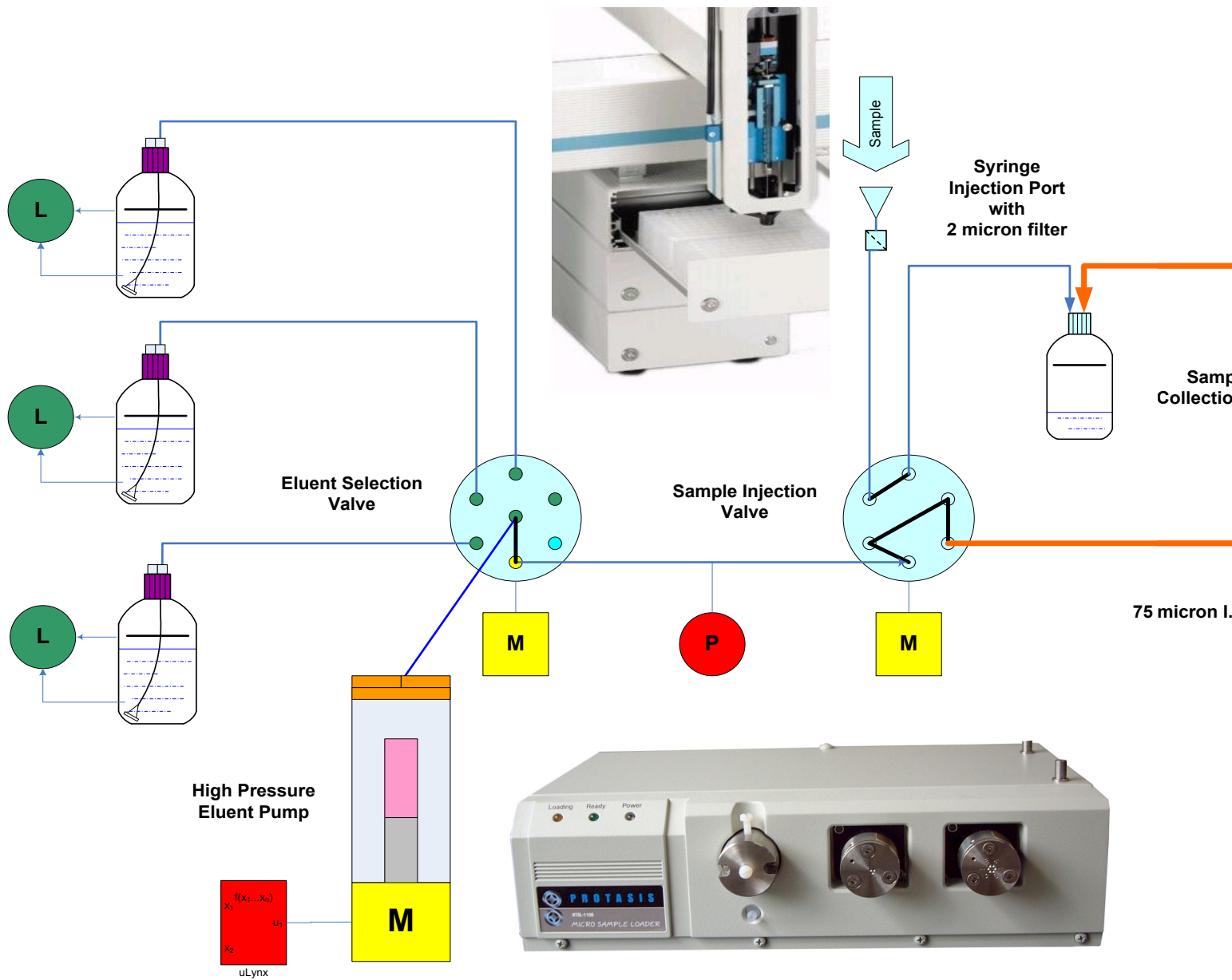
HTSC-2006-LC

High Throughput NMR Structure Confirmation System

CALL

*Protasis—Leading the Way in NMR Automation*

# OAHT One-Minute NMR™



**Power-Up Diagnostics**

When One-Minute NMR powers up, it performs a suite of diagnostics, including leak testing and transport time calibration.

**Method Setup**

One-Minute NMR allows you to define a complete set of NMR experiments ahead of time and then run them in sequence.

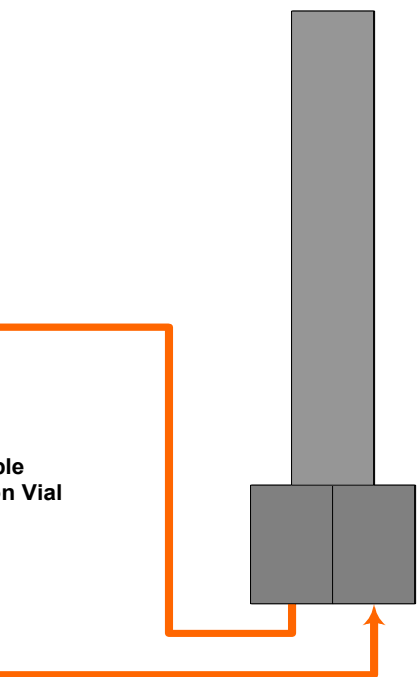
**Rapid Shimming**

Protasis CapNMR probes shim up quickly upon installation and rarely requires reshimming between samples.

**Easy Sample Loading**

Log in quickly from any web browser. Drop your microplate or vial into the LEAP. One-Minute NMR will take over from there.

# Convenient Loading of NMR Samples



D. Transfer Line



## Sensitivity

Performance outweighs everything else in research. CapNMR probes provide you with the highest mass sensitivity and highest data quality attainable. That means that you only need miniscule amounts of material to obtain full suite of proton and correlation spectra to fully characterize your novel molecule. That saves valuable time up front because you can collect less, make less or grow less material. And sensitivity and low noise can also save you time in the magnet, so that you can get more work done. One-Minute NMR optimize these performance attributes.

## Simplicity

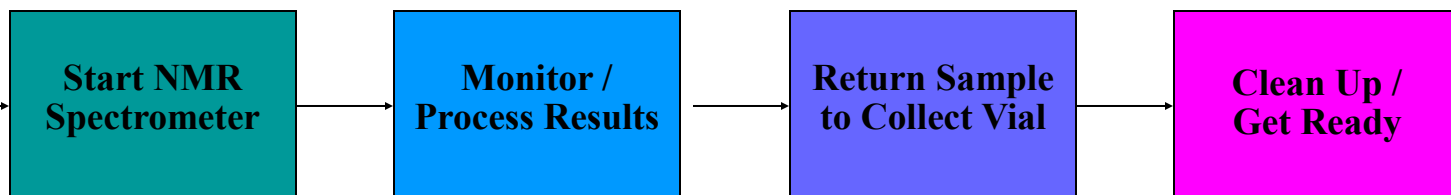
Effective tools must be quick and easy to use. One-Minute NMR manages every step in the process of collecting your spectra from powering-up and checking the fluidics, to installing and shimming the probe, through monitoring the results for quality, to returning your precious sample and cleaning up at the end. Protasis recognizes that streamlining the process of gathering data will make your research go faster. One-Minute NMR's software remembers small details for you to let each step flow seamlessly from one to the next to get you to publications sooner.

## Economy

One-Minute NMR quickly pays for itself. You will find your research group spending less time preparing samples. You will stop worrying about the cost of deuterated solvents or isotopically labeled reagents. You can eliminate NMR tubes from your budget. Magnet time will no longer be a bottleneck. These benefits accrue naturally, through miniaturization. One-Minute NMR will ease your exploration of capillary NMR by managing the fluidics and spectral acquisition to boost your productivity immediately.

***“Our professors don't want to wait even one extra day to hold up their research publications. They need to walk up to the NMR and get quality results right away.”***

*[University NMR Facility Manager, Pharmacy Dept.]*



One-Minute NMR talks to your spectrometer the same way that you do, using scripts through the command line interface.

One-Minute NMR watches over your sample and alerts you of any problems. Automatic processing with ACD/Labs.

After all spectra are collected, One-Minute NMR safely pushes your precious sample back into a collection well or vial you choose.

One-Minute NMR cleans up after itself by flushing with one or more wash solvents to prepare for the next sample. Check baseline.

# Medicinal Chemistry: Automated MicroFlow NMR

## One-Minute NMR™ Supports Multi-User Departmental Automation

This journal paper in Analytical Chemistry describes the redeployment of a Bruker 400 MHz NMR system for microplate and microvial automation using a Protasis CapNMR ICG Probe, LEAP HTS PAL liquid handler and One-Minute NMR software. The system supports a department of about twenty medicinal chemists who

typically confirm their synthetic molecules using MS and NMR after cleanup with HPLC. Only a few micrograms of sample in five microliters of solvent are needed for rapid spectral acquisition. Chemists may choose multiple NMR experiments for each sample based upon editable spectrometer scripts. Results are e-mailed to each user. Supporting spectra are available upon request.



Bruker DPX-400 NMR System with LEAP HTC Liquid Handler, 10µL Sample Volume, 5µL Injection

*Anal. Chem.* 2005, 77, 6509–6515

### Automated Microflow NMR: Routine Analysis of Five-Microliter Samples

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A microflow CapNMR probe double-tuned for  $^1\text{H}$  and  $^{13}\text{C}$  was installed on a 400-MHz NMR spectrometer and interfaced to an automated liquid handler. Individual samples dissolved in  $\text{DMSO-}d_6$  are submitted for NMR analysis in vials containing as little as 10  $\mu\text{L}$  of sample. Sets of samples are submitted in a low-volume 384-well plate. Of the 10  $\mu\text{L}$  of sample per well, as with vials, 5  $\mu\text{L}$  is injected into the microflow NMR probe for analysis. For quality control of chemical libraries, 1D NMR spectra are acquired under full automation from 384-well plates on as many as 130 compounds within 24 h using 128 scans per spectrum and a sample-to-sample cycle time of  $\sim 11$  min. Because of the low volume requirements and high mass sensitivity of the microflow NMR system, 30 nmol of a typical small molecule is sufficient to obtain high-quality, well-resolved, 1D proton or 2D COSY NMR spectra in  $\sim 6$  or 20 min of data acquisition time per experiment, respectively. Implementation of pulse programs with automated solvent peak identification and suppression allow for reliable data collection, even for samples submitted in fully protonated DMSO. The automated microflow NMR system is controlled and monitored using web-based software.

Automated methods for synthesis and compound screening in drug discovery have resulted in an increasing need for high-

down to 1-mm-diameter tubes that accommodate sample volumes as small as 5  $\mu\text{L}$ .<sup>1</sup>

Although the benefits of flow NMR have been recognized, namely, an increased throughput because samples are directly introduced into the detector from 96-well microtiter plates without the need for sample transfer to and from tubes, these systems have until recently required sample volumes between 100 and 600  $\mu\text{L}$ .<sup>2–4</sup> The newest generation of cryogenically cooled probes has accomplished mass sensitivity enhancements of 4-fold relative to conventional flow designs.<sup>5</sup> However, progress in conventional NMR flow analysis has been slowed by sample management challenges, such as peak dispersion, sample dilution, and excessive carryover that are problematic traits common to conventional-scale (several millimeter diameter and higher) fluidic systems. The recent development of capillary-scale microflow probes has provided an ability to accurately flow-inject and analyze sample volumes of several microliters. By combining small radio-frequency microcoils that wrap directly around the NMR flow cell for high fill factor with 75- $\mu\text{m}$ -i.d. fluidic transfer lines, these capillary probes provide enhanced mass sensitivity, negligible dispersion, and excellent fluidic performance by maintaining in real time the integrity of the fluidic flow path.<sup>6–15</sup> Microflow cell volumes are typically 3–10  $\mu\text{L}$  with RF observe volumes of 1.5–

(1) Schlotterbeck, G.; Ross, A.; Hochstrasser, R.; Semm, H.; Kuhn, T.; Marek, D.; Schett, O. *Anal. Chem.* 2002, 74, 4464–4471.  
(2) Haner, R. L.; Llanos, W.; Mueller, L. J. *Magn. Reson.* 2000, 143, 69–78.  
(3) Keller, P. A.; Smallcombe, S. H.; Williams, E. H.; Sakamoto, K. E.; Mendez, G.; Bolintin, L. L.; Moore, C. D. *J. Comb. Chem.* 2000, 2, 151–171.

Courtesy, Bernhard Geierstanger  
The Genomics Institute of the Research Foundation of Novartis

### System Used For:

#### 1. Med Chem Support / Library QC

Users submit reserve space on the system from their desktop and then submit their day's work in 384-well plates. System can hold up to six (optionally cooled) plates to process more than 1000 1D NMR samples per day



#### 2. Open-Access MedChem Analysis

Users can walk-up at any time and log in individual microvials. 'Priority' or 'night' samples may be selected based upon Administrator-assigned permissions.



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*The search is on.  
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is waiting. The  
clock is counting  
down and you're  
already tired and  
starting to panic.  
You need NMR con-  
firmation of struc-  
ture in a hurry to  
meet your publica-  
tion deadline.*

**Photo 1.** The Entry-Level One-Minute NMR system used by Protasis at our facility in Illinois.



The Entry-Level configuration of the Protasis One-Minute NMR™ platform is a great way to introduce NMR automation into your natural products, medicinal chemistry or other research departments. You can mix and match laboratory-standard microplates and microvials freely on the fast, reliable CTC/LEAP PAT liquid handlers that have proven themselves so well in mass spectrometry applications.



The CapNMR probe is already sensitive and fast. To take full advantage of this revolutionary probe, Protasis adds a convenient fully automated sample loader that allows to fill a standard injection loop, push a single button and then walk away with the confidence that your precious sample will be positioned accurately in the center of the flowcell and your complete set of experiments will be executed and monitored by OneMinuteNMR Lite.

On power-up, this sophisticated microfluidic system

will check itself for leaks using its built-in pressure transducer and then calibrate the transport time from the injection port to the flowcell by talking directly to your Varian, Bruker or JEOL spectrometer. Shim settings for your probe will be loaded automatically.

Once you inject a sample, a high pressure micropump will 'push' the sample from the injection loop precisely to the center of the flowcell with the push solvent of your choice.

During the NMR experiments, One-Minute NMR will monitor the acquired signals and let you know if any problems develop. It can even halt the run if samples lineshape is degrading, a potential symptom of precipitation of other problems.

And after the run, One-Minute NMR will push the sample back into a collection well or vial or your choice and then 'clean up after' by flushing the entire flowpath with you wash solvent to get ready for the next sample.

OAHT-2006-EL      One-Minute OAHT-NMR System—Entry Level

CALL

HTSL-1100-16      HTSL for LEAP OAHT-NMR

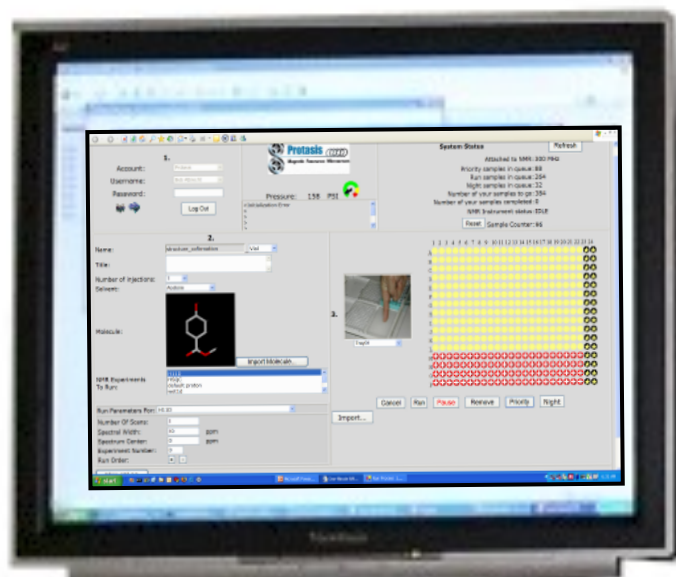
CALL

# Open Access HT-NMR Platform

Support multiple users and run thousands of samples per month with the best in MicroFlow NMR automation

## Featuring:

- ✓ Support for LEAP liquid handler
- ✓ High Throughput Sample Loading
  - ✓ Solvent Management
  - ✓ Rapid Sample Login
- ✓ Runs on Web Browser
- ✓ e-Reporting over Network
- ✓ Secure Data Server



Drug leads become increasingly more valuable as they are qualified. Why take more sample than you need or risk contamination using uncertain recovery? Now you can build NMR spectral databases using only 10  $\mu$ L of your precious sample!



*Outfit your laboratory with an integrated, fast Open Access HT-NMR platform designed expressly for capillary NMR. Give your researchers rapid access to structure and watch productivity climb!*



**One-Minute NMR™ can automate your entire department and keep up!**

**Applications:**

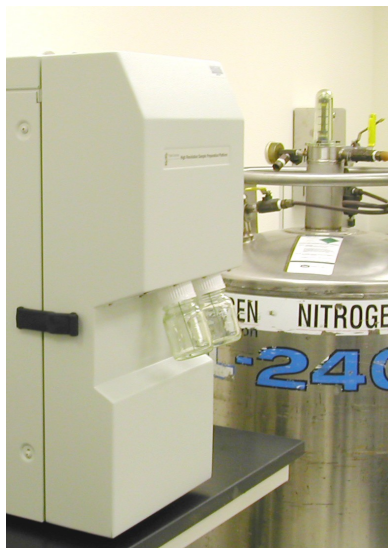
- ✓ Synthesis Confirmation
- ✓ Medicinal Chemistry
- ✓ Integrated LC-NMR
- ✓ Natural Products
- ✓ Trace Impurities
- ✓ Metabolomics
- ✓ Build NMR Libraries



**Pictured: CTC/LEAP HTC PAL Liquid Handler with Discovery Tower (containing Instrument Server and one High Throughput Sample Loaders (three possible solvents) and 19" LCD Monitor running One-Minute NMR Software.**

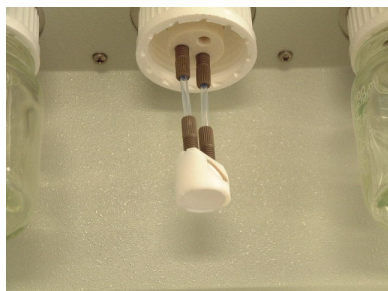
# Active Solvent Management

*Can I Support Multiple Users with Samples in Different Solvents?*



## Comprehensive Features:

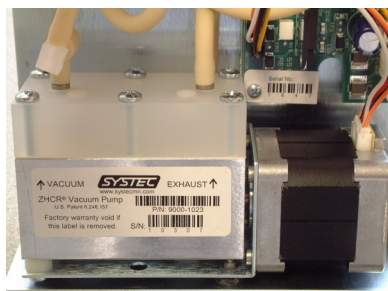
- ✓ Three Solvent Channels
- ✓ Integral Vacuum Degasser
- ✓ Helium Sparging
- ✓ Helium Blanketing
- ✓ Fast Solvent Changeover
- ✓ Ease Pump Priming
- ✓ Vacuum Sensing



Each bottle incorporates integral 2 micron bottle filters with sparging ports. Wetted materials are PPS and stainless steel (or Teflon PTFE) for the highest compatibility with most NMR solvents.



The Solvent Conditioning Module includes helium supply and vent valves to allow timed sparging and blanketing under program control.

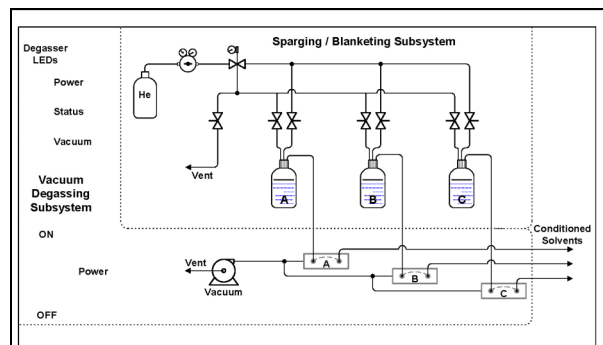


Dissolved gases are removed efficiently and reliably through fluoro-polymer membrane cartridges by a compact, quiet vacuum pump and vented. Wetted surfaces are compatible with all NMR solvents.

**Preserve Expensive Solvents**  
Managing solvents is critically important to your analytical success. Do it automatically with the Protasis Deuterated Solvent Conditioning Module (DSCM).

Located conveniently in the door of the Discovery Navigation Tower, this sophisticated subsystem includes a full complement of operations, sensors and software to protect you valuable NMR solvents.

Degassed systems operate more reproducibly. Let the DSCM rapidly execute and keep track of solvent changeover to optimize dissolution and prevent solute precipitation caused by mixing incompatible solvents.



**Compatible with D2O, DMSO, methanol, chloroform, acetone and other common NMR solvents.**

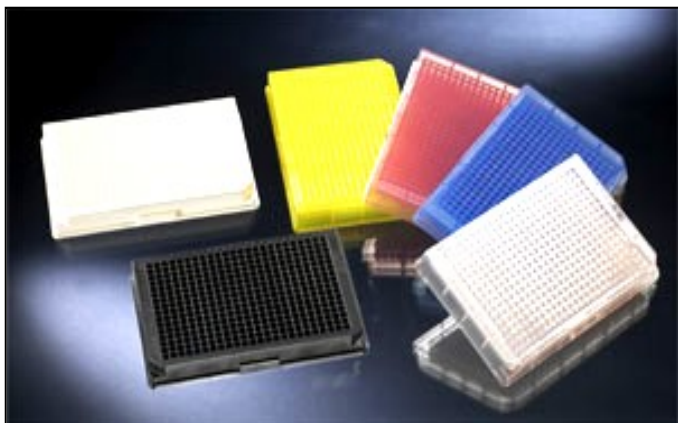
**CALL 508-481-4163**

# Efficient Sample Log-In

*Log-In Your Samples Over the Web in Less Than a Minute*



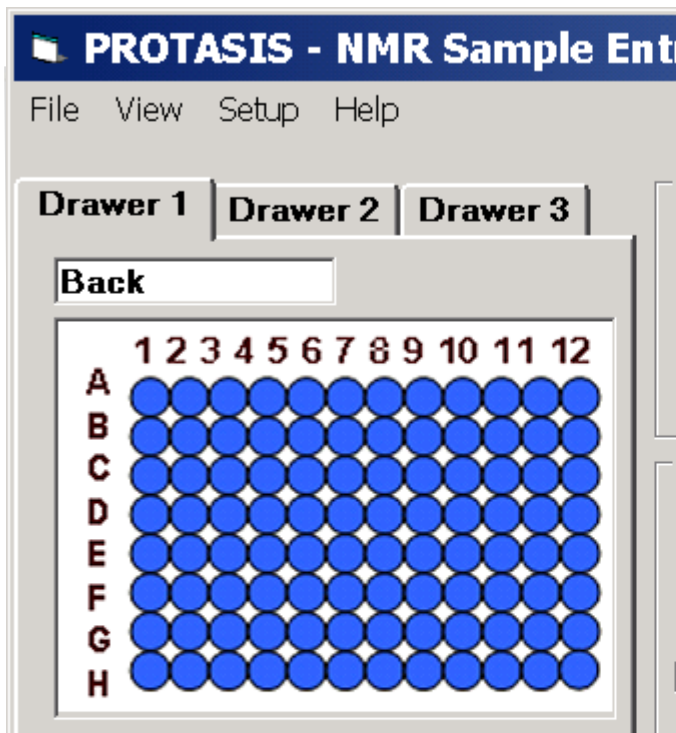
*Nobody wants to wait in line to fill out forms. Create your sample list automatically and log in your samples in less than a minute..*



Protasis *Open Access HT-NMR* provides a flexible walk-up interface to log-in your samples quickly and efficiently.

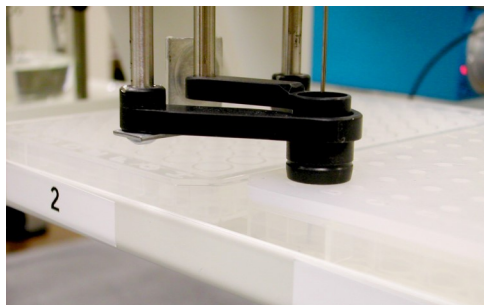
### **Features:**

- Log in your samples quickly and efficiently.
- Import sample lists from your management system.
- Plates or vials
- Sample bar code
- Temperature control (4 – 25 deg C)
- Schedule spectral acquisitions
  - 1D
  - 2D
- Schedule solvent changeover
- Auto Archive to Secure Data Server
- Auto e-Mail data and reports
- Convert data to universal formats



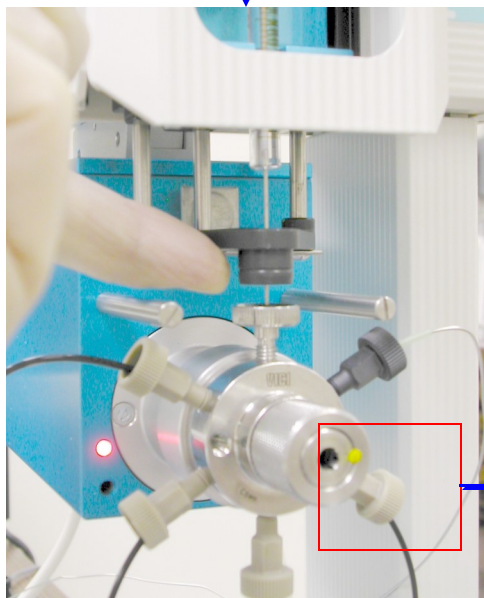
# High Throughput Sample Loading

*How Fast Can I Load Samples?*



## Load 5-10 uL without Dispersion

Get your sample loaded quickly using the Protasis High Throughput Sample Loader (HTSL). The key to effective transport of microliter volumes is small diameters. To ensure rapid loading without dispersion, Protasis uses narrow diameter (50 to 75 mm I.D.) fused silica tubing to transport microvolume samples from the liquid handler over to the CapNMR probe (and magnet). This requires chromatography-grade pumps to deliver precisely metered microliter per minute flows at up to 2000 psi backpressures. The result is fast, efficient high pressure sample loading in one to two minutes.

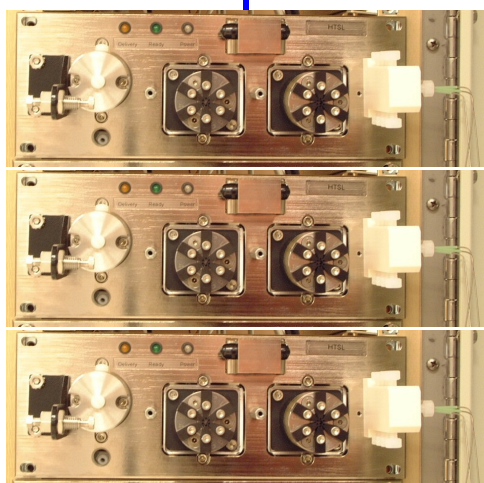


## Syringe-Only Technology

The syringe-only concept of the PAL series of sample loaders combines the manual sample injection procedure with the precision and throughput of a robotic liquid handling system. Samples are aspirated with a conventional liquid syringe and are transferred directly into the sample loop. No error prone teflon tubing or transfer lines are involved during the sample loading process. Before and after each injection the syringe and syringe needle



(needle inside and rinsed in a Wash Station different cleaning solvents. This unique design virtually eliminates sample carryover and adsorption problems.



**Multiple Solvents**  
Manage up to three different solvents with the Discovery Tower

## Transfer Up To 5 Meters To You Magnet

Have an unshielded magnet? The Protasis HTSL can transfer your sample up to 5 meters away with minimal band broadening. Pressure monitoring during the run with automatic shutdown upon overpressure. Flowrates from 1 to 40 uL/min.



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# Sample Management

★★★★★ *Service for Your Samples*

## Advanced Performance

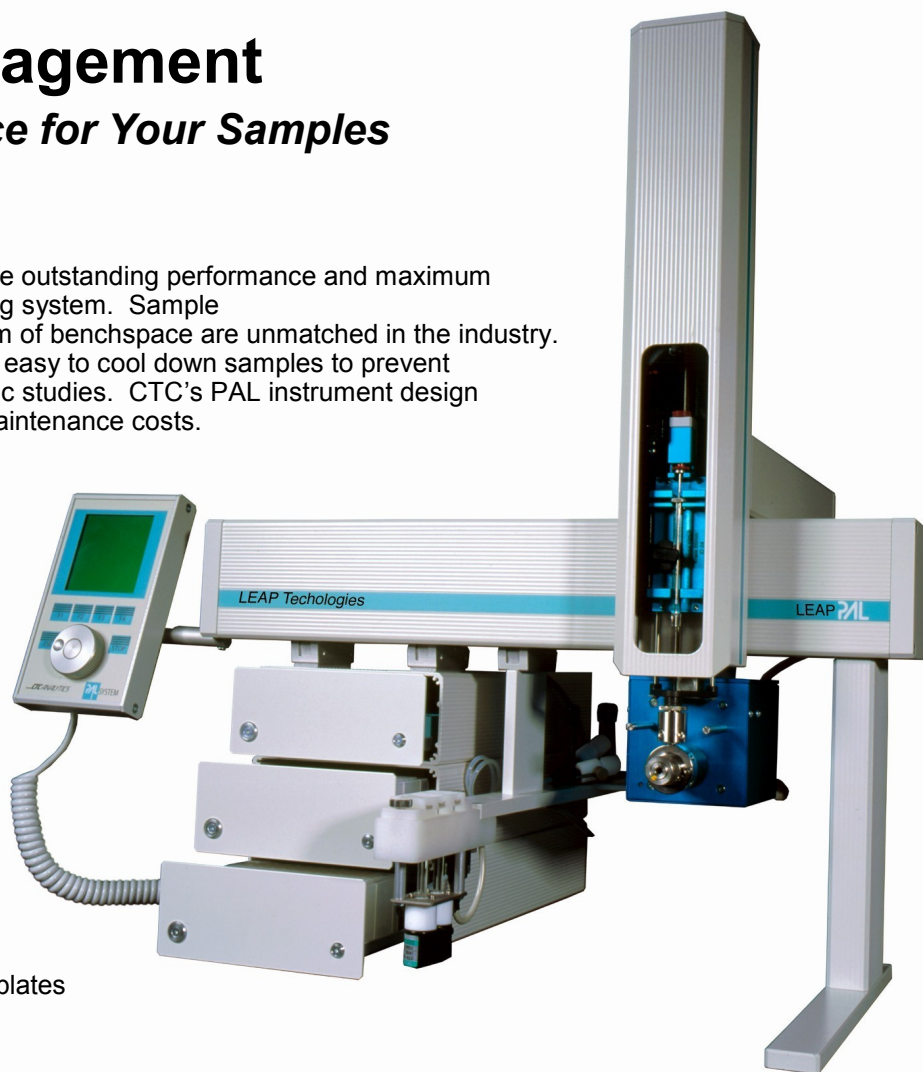
The PAL series of sample loaders provide outstanding performance and maximum flexibility for your NMR sample processing system. Sample capacity up to 24 microplates within 50cm of benchspace are unmatched in the industry. Temperature controlled storage makes it easy to cool down samples to prevent degradation or heat up samples for kinetic studies. CTC's PAL instrument design provides worry-free operation and low maintenance costs.

## High Performance Features:

- Lowest Volume Pickup (< 1  $\mu$ L)
- Compatible with HTSL-1100
- 2 minute cycle time or less
- Sample makes contact with syringe and needle only; short flow path
- Sample is pushed into loop for quick loading
- Active Wash Station washes syringe and outside of needle.
- Lowest carryover possible.

## Flexible Sample Storage

- 12 regular or 6 deep-well microtiter plates
- 1ml vials
- 2ml vials
- Or use your own format
- Heated or cooled (to 4 deg. C)



## Read Bar Codes on Vials or Plates

- Automatic sample login from scripts

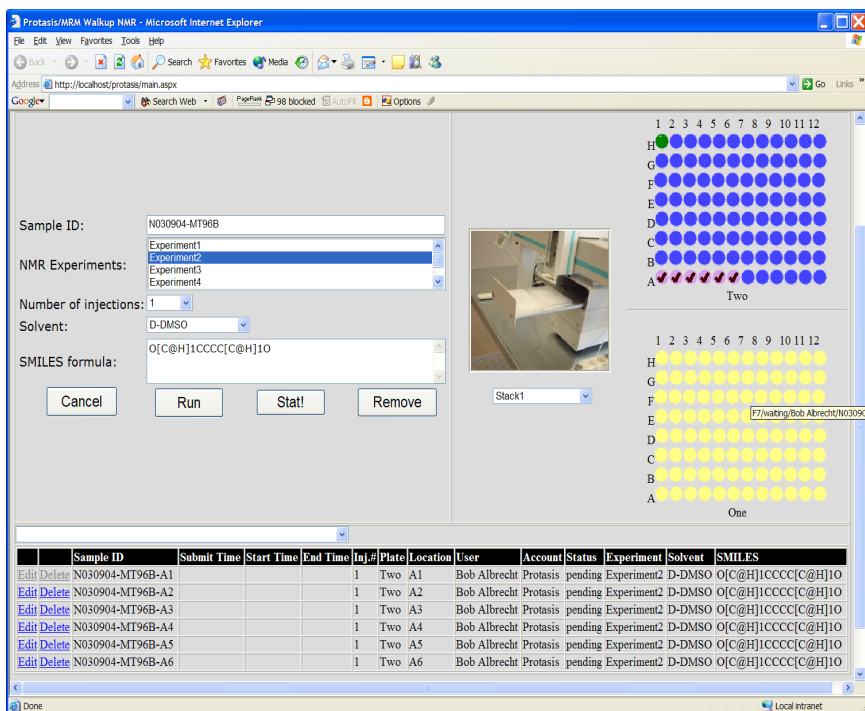
## Reconstitute / Dilute Samples

- Automatic functions
- Reconstitute dried samples
- Dissolve samples in appropriate solvent
- Enables return of sample to vial



# Spectrometer Control

## Do Any NMR Experiment with Your Flexible Scripts



**Sample Scheduler**  
From auto-calibration to performance monitoring to emailing your results, One-Minute NMR is designed for unattended operation. Its intelligent scheduler can program sampling based upon time interval or clock time.

Schedule one or multiple experiments for each sample to collect an entire suite of archival-quality spectra.

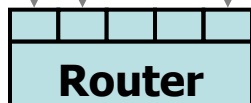
Automatically send spectra to ACD/Labs Structure Verification for processing.

Run 384-well microplates plates in the background and give higher priority wells or vials priority.

CapNMR is compatible with all standard NMR pulse sequences.

**1H NMR**  
**COSY**  
**HSQC**  
**HMBC**  
**TOCSY**  
**NOESY**

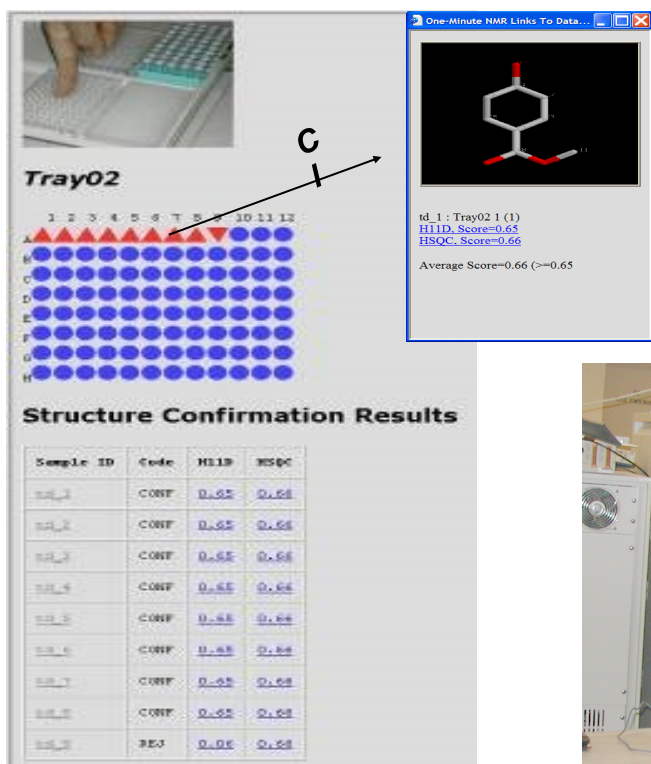
```
RSH(a.shimFile)
RPAR(a.experiment, "all")
SETCURDATA
XCMD("gpro")
RGA
STOREPAR("NS", a.scans)
STOREPAR("SW", a.sweepWidth)
STOREPAR("o1p", a.centerOfSpectrum)
exptime = CalcExpTime();
```



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# Efficient Reporting

## E-mail Results Automatically to Each User

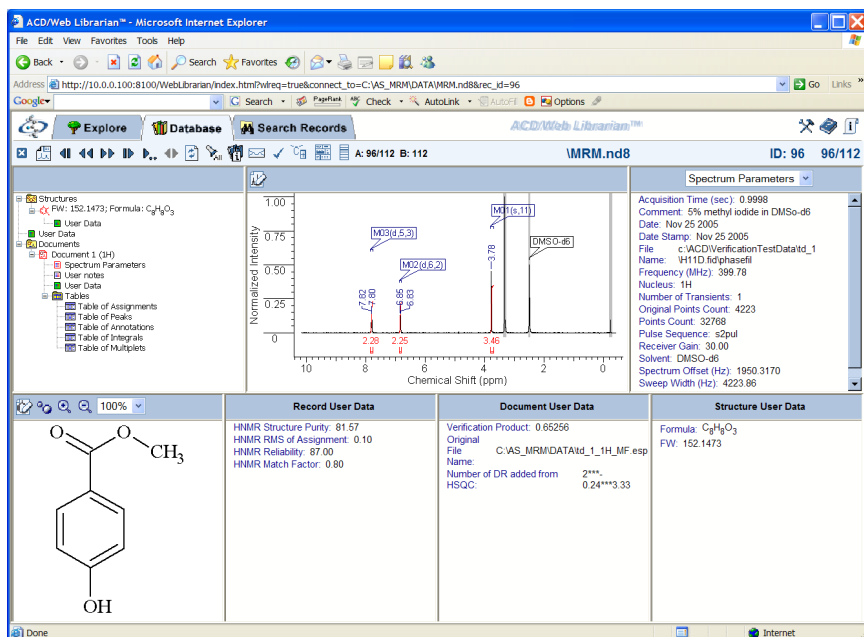


- ✓ Send reports to your network printer
- ✓ Login to the server and view results
- ✓ Send signed and encrypted e-mail



**E-Mail Reporting**  
 Protasis One-Minute NMR software enables complete front-end log-in of samples from multiple users, archival to a secure data server and back-end reporting of results over your network. Solvent changeover is managed safely and automatically. Support for fast capillary liquid handler.

**Links to Spectral Viewer**  
 Just click on the links for your data set and you can easily see all of the original spectra for each of your experiments.



# One-Minute NMR Fact Sheet

<i>Easy</i>	
<b>Open Access</b>	Ease of use, security, accounting, multiple spectrometer support, sensitivity, speed and common sample formats brings NMR to more applications than ever before.
<b>Easy Graphical Sample Entry</b>	Pick solvent, experiment(s), and sample location and the just click <Run>.
<b>Single Web Page</b>	Operator control panel with steps labeled 1, 2, 3... for sample login. Works with IE, Mozilla, Netscape on Windows/UNIX/Linux/Macintosh.
<b>One-Minute Plate Login</b>	Choose plate name and experiments, then shift-click to select whole or partial plates.
<b>Sample List Import</b>	CSV file import with custom import templates allows plates from MS to be logged in without rekeying data.
<b>Priority Samples</b>	Keep the system busy with plates/arrays, but interrupt with individual samples as needed.
<b>Night Samples</b>	Give long-running samples priority at night, but do not run them during the day.
<b>Direct-Edit Samples</b>	Alternative sample grid with direct editing of rows for entering detailed samples and experimental information.
<b>Remote Intranet / Internet Login</b>	Log in samples and monitor status from your spectrometer, desk, lab or home from any web browser.
<b>Multiple Configurable / Selectable NMR Experiments</b>	One or more NMR experiments are selected from a list and run in the order specified. All existing experiments suitable for the CapNMR probe can be used.
<b>E-Mailed Alerts and Completion Messages</b>	Uses your e-mail server to send batch completion reports and error alerts. Errors are sent to a list of administrators.
<b>Direct-Edit Sample Grid</b>	Alternative sample grid with direct editing of rows for entering detailed sample and experiment information.
<b>Consistent Interface</b>	The same easy operator interface for all spectrometers.
<i>Secure</i>	
<b>Data Overwrite Protection</b>	Overwrite protection as samples are entered and before each sample is run. Rules allow data to be saved to safe locations anywhere on your network.
<b>Password Security</b>	User protection with permissions for selecting other's samples, user administration and changing automation settings.
<b>Run Lockout</b>	Remote systems can be prevented from starting the NMR while allowing samples to be logged in and status monitored from your desk.
<b>Error Handling, Retry and Recovery</b>	Errors reported on web pages and by e-mail. Errors are recoverable and your sample is never lost.
<b>Optimized TCP/IP Spectrometer Interfaces</b>	Closed-loop spectrometer control and feedback through TCP/IP link. Optimized for speed, security and error correction / detection.

<i>Controllable</i>	
<b>Administration</b>	Web-based user administration. User-based permissions, e-mail, NMR account information.
<b>Accounting</b>	Users run samples under one or more accounts. Run time is tracked by sample, user or account. System operators may use multiple accounts.
<b>Individual User Directories</b>	NMR data directories are associated with user accounts. Directories are created when new users are created.
<b>Sample Data Overview</b>	Drop-down queries to find out how many samples ran, by whom, what the results are, and where they are located.
<i>Expandable</i>	
<b>Open SQL Database</b>	Standard SQL database allows ODBC connections from custom programs for connection to Enterprise software systems.
<b>Macro Capability for LEAP, HTSL and NMR</b>	Enables special operations such as combining reagents with a sample before a run, or addition of stabilizer after a run.
<i>Technology</i>	
<b>CapNMR, The Probe for Everyone</b>	Excellent for most solution-phase NMR samples, including small molecules, lipids, peptides, proteins, salty samples, tiny samples and metabolites.
<b>Low Sample Volume</b>	Samples as small as one microliter and up to 12 microliters can be used effectively.
<b>Intelligent Automatics Solvent Selection</b>	Three program-selectable degassed solvents with intelligent switching to prevent immiscibility problems.
<b>Flexible Injection Sequence</b>	Adjustable numbers of pre-washes, post-washes, injector cleans, sample pickup volumes, filter rinse, fluidic speed and macros.
<b>High Throughput</b>	Super-sensitive probe and fast liquid handler runs up to one thousand samples per day.
<b>Low Maintenance Costs</b>	High sensitivity without electric bills, maintenance fees, special siting requirements and extensive downtime.
<b>Sample Return</b>	Samples are optionally returned to their original or a mirror location. Easily create a mirror plate.
<b>Embedded Web Server</b>	A pre-configured web server is embedded in the Discovery Tower platform.
<b>Automatic Dilution</b>	Dilute immediately before injection for samples that easily oxidize, are vulnerable to solution phase or that you don't want to dilute manually.
<b>Automatic Probe Wash</b>	Keep the probe clean with a wash every Nth sample. Use solvent, acid, detergent or enzymes.
<b>Sample Filtering</b>	Samples are automatically filtered with a pre-injector 2 micron particle filter.



734 Forest Street  
Marlboro, MA 01752

TEL : 508-481-4163  
FAX : 508-481-4190

e-mail : [sales@protasis.com](mailto:sales@protasis.com)

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Protasis MicroFlow NMR Catalog - 24



Probes	PFG	ICG	TXI (‘BioFlow NMR’)	DPC	MultiFlow NMR
Description	Proton with Gradient	Indirect Carbon Gradient	Triple, Inverse Gradient	Dual Proton Carbon Gradient	Ask about Custom Configurations
Nuclei	<sup>1</sup> H / <sup>2</sup> H lock	<sup>1</sup> H{ <sup>13</sup> C} / <sup>2</sup> H lock	<sup>1</sup> H{ <sup>13</sup> C}{ <sup>15</sup> N} / <sup>2</sup> H lock  Also available with { <sup>31</sup> P}	<sup>1</sup> H{ <sup>13</sup> C} / <sup>2</sup> H lock  <sup>1</sup> H{ <sup>13</sup> C} / <sup>2</sup> H lock	How Would You Use Multiple Flowcells?
Flowcells	10 μL	5 or 10 μL	10 μL FEP	10 μL	Your Choice!
Gradient	z-Gradient	z-Gradient	z-Gradient	z-Gradient	z-Gradient
Applications	Library Building Compliance	Natural Products Synthesis Confirm Metabolite ID Trace Impurities	Expression / Screening Protein / DNA / RNA Serum / Urine / CSF	Ultra-High Throughput	Multi-User Foreground / Background

### Researchers, Get Published Faster!

Protasis CapNMR probes let you get the spectra to elucidate and confirm spectra in record time. MicroFlow NMR provides you with the highest mass sensitivity and highest data quality attainable. That means that you only need a miniscule amount of material to obtain a full suite of proton and correlation spectra to fully characterize your novel molecule. That saves you valuable time up front because you can collect less, make less or grow less material. And sensitivity and low noise can also save you time in the magnet, so that you can get more work written up to keep up with new trends in discovery research.

### Managers, Automate Your NMR Operations Efficiently!

MicroFlow NMR probes quickly pay for themselves. You will find your research group spending less time preparing samples. You will stop worrying about the cost of deuterated solvents or isotopically labeled reagents. You can eliminate NMR tubes from your budget. Magnet time will no longer be a bottleneck. These benefits accrue naturally, through miniaturization. When you’re ready, ramp up the samples to hundreds per day using Protasis [One-Minute NMR](#) automation.

### Analysts, Prepare for Integrated Metabolomics!

Markers in biofluids can provide a detailed and specific view into pharmaceutically relevant processes and conditions; most importantly metabolism and disease state. One popular approach is to collect data on a large number of samples and treat these data statistically to tease out patterns that can lead to better understanding of the underlying biochemistry and, ultimately, better pharmaceuticals. MicroFlow NMR can speed this workflow on the front-end by requiring less sample for analysis and on the back-end with trouble-free high throughput analysis. Automated cleaning protocols ensure low carryover.



MicroFlow NMR for  
Varian, Bruker &  
JEOL  
300 MHz—800 MHz

**USPY-Ag**



*“Where Innovation Meets Quality Workmanship”*

Telephone Support	Web Training	Umbrella Coverage	Software Updates	Consumables Kit
X	X	X	X	X

*Protasis leverages the Internet to offer efficient Uptime Assurance through a series of subscription services to answer questions, provide training, handle repairs efficiently and update consumables and software.*

Many service options come

your purchase to ensure that your startup experience with a Protasis product is smooth and productive. Over time, we encourage most customers to budget ahead for their routine servicing requirements. This prevents unanticipated downtime and cost. Support plans come with the comprehensive telephone support and web training to help you get the most use of your CapNMR probe. For about 10% of your initial purchase, the Protasis Uptime Assurance Plan, Silver Level lets you budget ahead for your routine probe maintenance and provides a package of value-added subscription services to keep the results flowing in your laboratory.

with

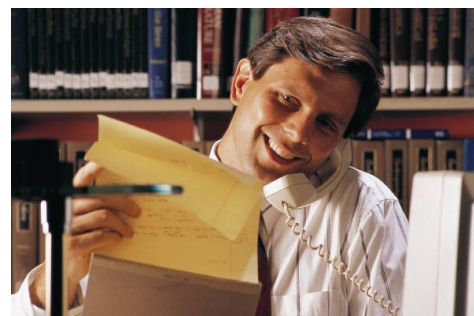
**Features**

**Telephone Support**

We're available to help you and your staff. One year of unlimited access by telephone to our application and design team. Consider value to you – protection of the resource in shortest supply - your valuable time!

Includes:

- Assistance in maintaining peak probe performance
- Diagnostic assistance
- Guidance in the application and use of probe
- Guidance in fluidic management
- Referrals to latest application notes / journal papers



the



USPY-AG-MI	CapNMR Probe-Only Support – Silver Level	\$5995
USPY-AG-EL	Support Plan with Sample Loading Accessories	CALL
USPY-AG-DT	Support Plan with Sample Loading Accessories	CALL



## Web Training

Recognizing that your work environment is constantly changing, Protasis makes it easy for you to brush up on specific skills and quickly train new operators. This year we have expanded our Uptime Assurance Plans to include subscriber access to a suite of narrated slidesets that can be accessed at any time from any web browser.

### Topics include:

- Probe Installation on Varian, Bruker or JEOL systems
- Intro for New Operators
- Capillary Sample Loading

## Umbrella Coverage for Repairs

The Silver Plan lets you budget ahead for normal maintenance\*. That lets you buy peace of mind. Then you can rely upon our factory and efficient depot repair to keep your probe running at top performance levels. Simply call us and arrange a return of your probe to our Service Center in Illinois. Turn-around in less than 4 weeks (typical).

- Covers:**
- Line Broadening
  - Component Failures
  - Plugging or Coating
  - Flowcell Replacement
  - Transfer Line Replacement
  - Factory Retuning



model of probe. Does not cover misuse, modification, droppage or spills.

## Software Updates

Silver Plan customers that have HTSL-1100 or other sample management accessories can count on free software updates. As they become available, we'll notify you and discuss an update schedule that meets your needs.



## Consumables Kit

Plan customers receive a comprehensive kit of parts and tools, to quickly and conveniently perform minor repairs, filter changes or other operations common to flow-based instruments. These are the same parts that have been tested in use by the experienced installers in our Field Service organization.

\* Covers degradation of performance in normal use including plugging, coating, electronics or failure, leaks or other fluidic breakage or failures for the same



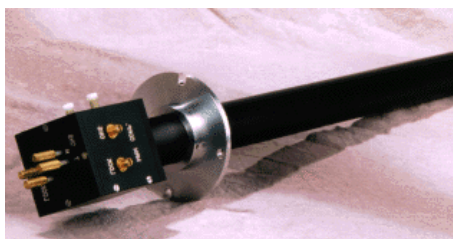
**For ordering information, please contact our sales office:**

Protasis Corporation  
734 Forest Street  
Marlborough, MA 01752

TEL: (508) 481-4163  
Fax: (508) 481-4190  
Email: [info@protasis.com](mailto:info@protasis.com)

or visit us on the web at: [www.protasis.com](http://www.protasis.com)

*Protasis—Leading the Way in NMR Automation*



# Protasis

## 2007 Configurations

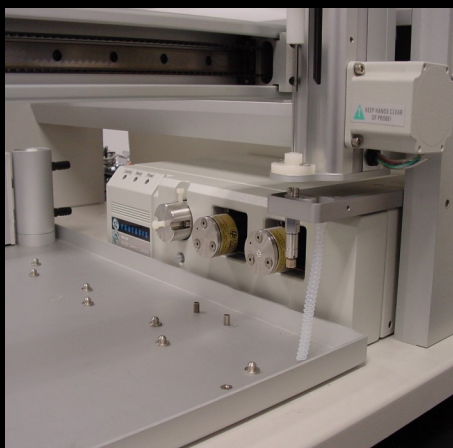


### MicroFlow NMR™ w/ High Precision Manual Injector

**Get the Probe**  
**\$59-75K** U.S. List  
(with enhanced flowcell)

- Sensitivity
- Simplicity
- Economy

**Ask About Our  
Evaluation Offer  
to Qualified  
Researchers!**

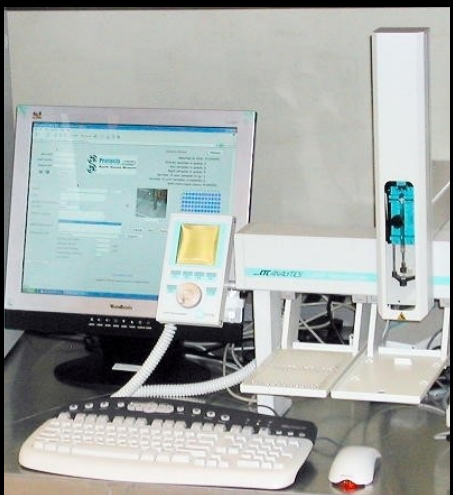


### MicroFlow NMR w/ High Throughput Sample Management

**Add MicroFluidics**  
**\$15-28K** U.S. List  
(loader, degasser, etc.)

- Flexibility
- Reliability
- Speed

**Share your work and  
we'll help stretch your  
budget with our  
Developer's Program**

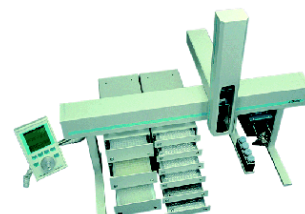


### MicroFlow NMR with Integrated Platforms for:

- Natural Products
- Medicinal Chemistry
- HT-NMR Screening
- Metabolite Profiling
- Impurity / Degradents

**Add Automation**  
**\$35-50K** U.S. List  
(robotics & software)

**We'll build your  
custom system!**



# Justification Analysis to Management for Purchase of **MicroFlow NMR**

## + Increase Revenues

**BETTER ANSWERS.** High Sensitivity (spectra from as little as one microgram of sample). Faster spectra acquisition (up to 100X faster than 5mm probes). Short pulse widths enable new NMR experiments.

**INCREASE FACILITY CAPACITY.** Increase utilization of existing magnet(s). Bring in revenue from other researchers wanting magnet time. Get NMR spectra directly from existing LC-MS fractions.

**OBTAIN IMPROVED SPECTRAL QUALITY.** Flat, clean baselines with reduced solvent background.

## - Decrease Expenses

**CREATING BIOSAMPLES?** *Reduce* sample preparation from 1 month to 1 week. Use smaller quantities of reagents/lab supplies and reduce labor. Technician payroll (w/overhead) at \$90,000/year = labor savings of about \$34,000.00/year. (Assume six studies/year.) Reagent costs (DMSO =\$1,400/liter) (e.g., peptide synthesis, isotopically labeled) could be scaled back by \$9,000/study assuming solvent use reduced by 90%.

**GOT MASS-LIMITED SAMPLES?** Mouse urine, spinal fluid? It is no longer necessary to use hard-to-acquire, large quantities for analysis. Save on collection costs by using micrograms of sample. And save on animal costs – lab quality animals are not sacrificed to obtain NMR data. (Multiple animals in studies brings additional variables – you get clearer data sets.)

**GOT TUBES?** *Eliminate* tube costs. At approximately \$7.00/tube and using approximately 30 tubes/day (220 days/year), cost savings could be approximately \$46,000/year.

**USING CONVENTIONAL-SCALE CHROMATOGRAPHY?** No problem! Run your HPLC in protonated solvents. Collect your fractions into standard 96– or 384-well microplates or microvials. Mass-limited analyte fractions can be concentrated using vacuum centrifugation while keeping the samples in the plate or vial. The LEAP liquid handling robot in the Protasis One-Minute NMR system takes over from there. The LEAP can reconstitute the dry samples in precisely calibrated volumes of deuterated solvents for optimal NMR detection. The tiny capillaries and sample volumes used in MicroFlow NMR dramatically reduce consumption of expensive deuterated solvents. Customer laboratories that switch to MicroFlow NMR typically pay for their CapNMR probe and One-Minute NMR system in one to two years based upon solvent savings alone.

**REDUCED HAZARDOUS MATERIAL RECYCLING COSTS.** \$500/month or more in typical labs.

<b>\$ Return on Investment Calculations</b> (simplified) (Payback Period = Original Investment/Annual Cash Flow)	<b>Savings</b> \$ / yr	<b>Payback</b> (months)
<b>✓ Creating Biosamples</b> ⇒ Payback = \$60,000 / \$88,000 = ~ 8 months (conservative)	<b>\$88,000+</b>	<b>8</b>
<b>✓ Limited Samples</b> ⇒ Payback = results unattainable by other means	<b>Large (Enabling)</b>	<b>Immediate</b>
<b>✓ Eliminate Tubes</b> ⇒ Payback = \$60,000 / \$46,000 = ~ 15 months	<b>\$46,000</b>	<b>15</b>
<b>✓ Solvent Savings</b> ⇒ Payback Period = \$60,000 / \$36,000 = ~ 20 month payback	<b>\$36,000 (Enabling)</b>	<b>20</b>

# University Evaluation for Funding Program

*We'll Help You Get the Data You Need to Get Funding*

## You need:

- A Problem to Solve
- A Stream of NMR Samples
- Buyer's Intent

## We'll Help

- You Get the Data You Need To Write the Grant or To Write the Justification

## Get:

- A Six Month Loan
- CapNMR Training
- Sample and Reagent Savings
- Your Next Journal Paper

## Costs:

- Installation Fee (US \$3500 typ.)\*
- Host a User Workshop (optional)



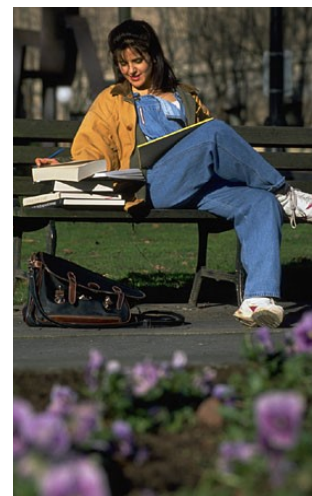
Protasis is committed to supporting innovative research in Life Science Automation.



***Protasis can help your students get published, graduated and on with their lives!***

Our evaluation program can help you get started today. We have already boosted productivity in research groups at Princeton, Stanford, UCLA, Cornell, Imperial, York and many other major universities. Many of these probe placements have already produced world-class data sets that immediately become the focal point of new journal papers and grant applications. Our quick installation and setup and convenient, manual syringe loading makes MicroFlow NMR the fastest way to get mass-limited spectra to speed up your research.

***But hurry to sign up. Protasis can only initiate a limited number of evaluation agreements each quarter!***



## Notes

1. A letter of commitment from your Department Head is suggested.
2. After the six month evaluation period, the customer is encouraged to purchase or lease the probe. If more time is needed to secure funding, the collaboration may be extended by mutual agreement, provided that a Protasis Uptime Support Plan (Silver Level) is maintained on the loaned equipment.
3. Ask about our Developer's Program to stretch your research budget even further. We'll grant you credits when you help us write an application note about your work that we can share with the NMR community.



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Protasis MicroFlow NMR Catalog - 30

*Protasis offers a range of laboratory services from routine 1D NMR analysis to more sophisticated sample cleanup and analyte preconcentration designed to make the most of our simple, sensitive and economical capillary techniques. Services are performed at our state-of-the-art regional laboratories in Massachusetts and Illinois.*



## Lab Services

**Biofluids NMR Analysis (Metabolites).** Protasis has partnered with Novatia to perform high throughput NMR analysis on serum and urine samples for routine metabolite identification. A complete OneMinuteNMR system installed at Princeton University and operated by Novatia is available to process hundreds of biofluids samples per day. Let Protasis and Novatia reduce your backlog from routine samples. Call Novatia directly to schedule work. Call Protasis about acquiring this instrumentation for your own laboratory.

**General NMR Analysis.** Protasis can accept routine 1D samples from Natural Products and Impurities applications at its facility in Champaign, IL.

**Biofluids Purification.** Protasis can perform the following operations (currently in Massachusetts) using free-solution counterflow electrofocusing (aka Dynamic Focusing) to prepare samples for NMR, MS or other instrumental techniques.

- Trap and Release
  - Pre-Concentration (x100 or more)
  - Ultra-Pure Sample Cleanup
  - Quantitative Buffer Exchange
- Analyte Subtraction
- Coarse Fractionation

**Instrument Demos.** Protasis operates three working laboratories at capacity that process customer samples at

prevailing analysis rates. Prospective customers are invited to observe these operations free of charge whenever scheduling (and confidentiality restrictions) permit.

**Evaluation Study.** Customers wishing to evaluate their own samples using MicroFlow NMR or Dynamic Focusing will be quoted standard laboratory analysis rates. Protasis specializes in novel applications for its high sensitivity and high throughput technologies and encourages customers to present their real challenge problems for method development. To perform these services requires that Protasis recover its labor and reagent costs at the time of analysis.

**Evaluation Discount.** Customers that purchase an Evaluation Study will receive an Evaluation Discount Coupon worth up to 5% of the price of Protasis equipment purchased within 120 days of the study. Customers receiving this discount are also asked to release a (nonproprietary) portion of the Evaluation Study data for viewing on the Protasis web site. Good for study account location only. Only one discount per transaction. Some restrictions may apply.



Join dozens of other authors who have published papers based upon MicroFlow NMR spectra!\*

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Optimized Delivery and Direct Carbon Detection for Two Microcoil Flow Probe Designs ENC 2005 Abstract #237, Andreas Kaerner, Tim A. Smitka, Lilly Research Center

NMR Structural Studies of Mass-Limited Modified DNA Using a Protasis/MRM CapNMR Probe ENC 2005 Abstract #330, Monique Cosman, *et al.*, Lawrence Livermore National Laboratory.

A New Era in the Structure Elucidation of Natural Products Using the CapNMR Probe ENC 2005 Abstract #389, Mark O'Neil-Johnson and Jean-Luc Wolfender, *et al.*

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