SmartDriveNMR

SmartDriveNMR

User Manual

Version 009

Innovation with Integrity

NMR

Document Number: Z4D12631

P/N: Z33122

Contents

Contents

1 Introduction

SmartDriveNMR is an advanced acquisition tool optimizing measurement time and delivering high quality data. It is uniquely designed to determine and carry out the ideal combination of experiments for the synthesis control of small organic molecules.

1.1 About this Manual

This manual is intended to provide a basic introduction to the SmartDriveNMR feature. It is organized as a step-by-step walk-through of the SmartDriveNMR workflow.

Please note that the figures shown in this manual are designed to be general and informative and may not represent the specific version you are working with.

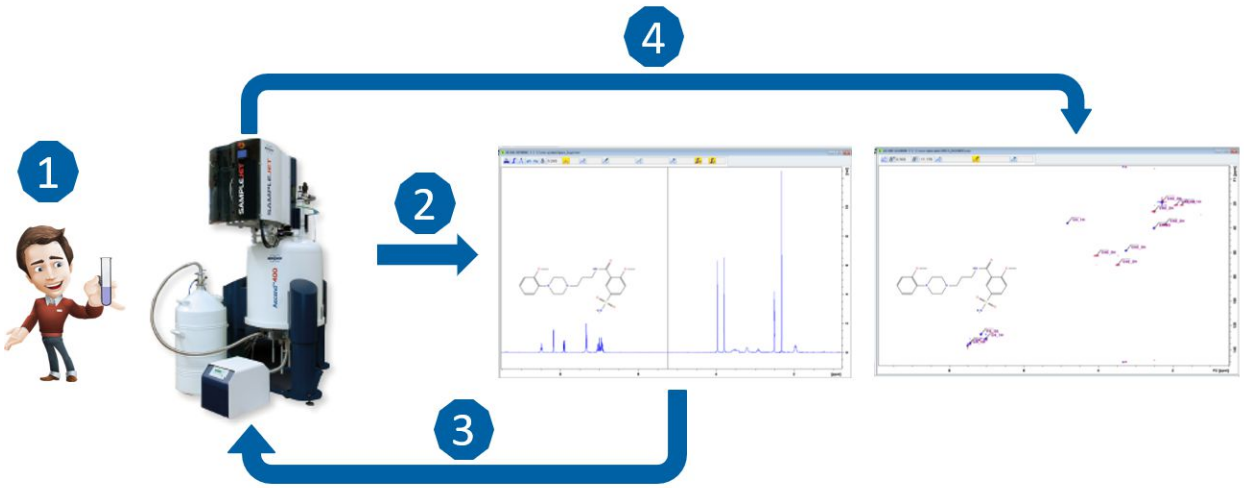
1.1.1 Font Conventions

- Commands that can be entered on the command line, menus, buttons and icons that can be clicked are in **Arial bold.**
- Path, File, Dataset and Experiment names are in *Arial italic.*

1.2 Functionality

SmartDriveNMR is intended to streamline the structure verification task. With intuitive NMR-independent inputs from the user, the software is able to carry out the acquisition for the structure verification synthesis control task independently. It will determine the appropriate experiments to measure and perform an automated analysis within the time allotted.

The workflow of SmartDriveNMR is shown and described here:



1. The user describes and submits the acquisition job using IconNMR. The description can (but does not have to) include structural information (.mol file).
2. A fast 1D proton spectrum is collected and analyzed.
3. Depending on the analysis results concerning complexity of the problem and the signal strength, further experiments with optimal parameters might be requested.
4. Follow-up experiments are scheduled and acquired in full automation if sufficient time is available. Reasoning triggering the acquisition is made available to the user. An automatic structure verification at the end of the run is an integrated part of SmartDriveNMR but not mandatory.

1.3 Required Licenses

SmartDriveNMR requires both a Topspin license and a SmartDriveNMR license.

Both licenses can be ordered online from: *https://www.bruker.com/nmr_license_requests.html*

A short instruction on installing the license will be sent together with the license. In addition, a description how to order and install a license can be found in the help menu of Topspin. Left-click on the **Help** button and select **Manuals (docs)**, afterwards click on **CodeMeter License Management**.

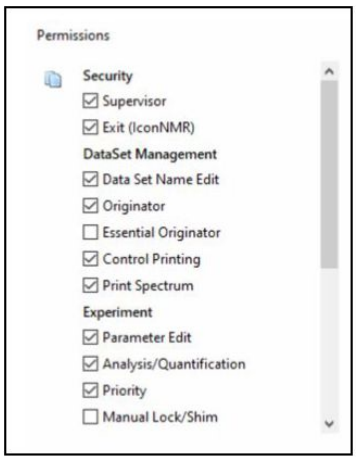
2 IconNMR Settings

SmartDriveNMR is a feature that must be activated from within IconNMR. All relevant settings for SmartDriveNMR are accessed via the IconNMR configuration window.

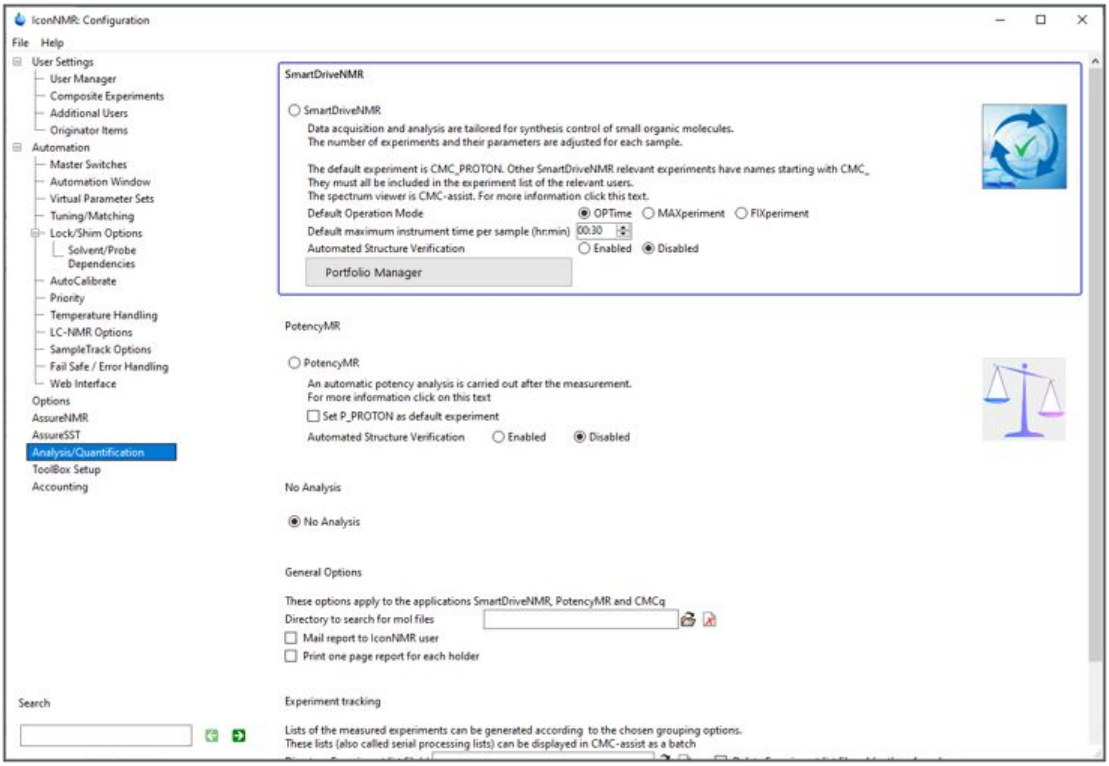
2.1 Enable SmartDriveNMR

- Open IconNMR by typing **icon** on the Topspin command line
- Click on **Configuration** to open the Configuration Menu (this most often is protected by the password of the spectrometer administrator)

- Click on **user manager** to activate SmartDriveNMR by ticking **Verification/ Quantification** for the user/user group to be permitted to use SmartDriveNMR in the permission section



- Click **Verification/Quantification** on the left side of the configuration page to open the Verification/Quantification



- Click the radio button next to SmartDriveNMR to activate SmartDriveNMR as the default for the IconNMR Automation menu and edit the settings for SmartDriveNMR
- Also within the user manager under the section **other settings** each user can be assigned a portfolio which will be the default when using SmartDriveNMR from the automation window from IconNMR. In the picture Paula Miller is associated with "FULL PORTFOLIO". See section *Experiment Portfolios [▶ 17]*of this manual for more details on portfolios.

2.2 Configure Settings

These settings will be used for each SmartDriveNMR job unless further specified for a particular sample. For individual samples, these settings can be changed from within the IconNMR Automation menu. This section describes how to configure the recommended settings. An exception to this statement is the settings for **Automated Structure Verification**: This can only be set here in the configuration section to ensure that only the spectrometer administrator can change this setting. For more detailed information about each setting see Chapter *Further Information [▶ 17]*.

- Click the radio button next to **OPTime** to get optimal usage of the spectrometer time

- Use the arrows to set the default maximum instrument time per sample to 00:30 indicating 30 minutes
- Turn off structure verification by clicking the radio button **disable**
- Click on the grey button labeled **Portfolio Manager** to create a new portfolio or the edit an existing one

2.3 Adding CMC Experiments

In order for SmartDriveNMR to function, each of the CMC experiments must be added to the experiment list for the desired user. These experiments include:

- CMC_PROTON
- CMC_SINGLE
- CMC_SINGLE_H2O
- CMC_WET
- CMC_HSQC
- CMC_13C
- CMC_HMBC
- CMC_COSY
- CMC_TOCSY
- CMC_NOESY
- CMC_F19
- CMC_F19CPD
- CMC_C13DEPTQ135

See Chapter 5 Configuration Suite of the IconNMR User manual for detailed information on adding experiments to the experiment list.

IconNMR Settings

3 SmartDriveNMR Work Flow

This section will walk through the steps required to set up a SmartDriveNMR run. It will use a Quinine sample in DMSO.

3.1 Experiment Setup

- Load the sample into position one in the sample changer

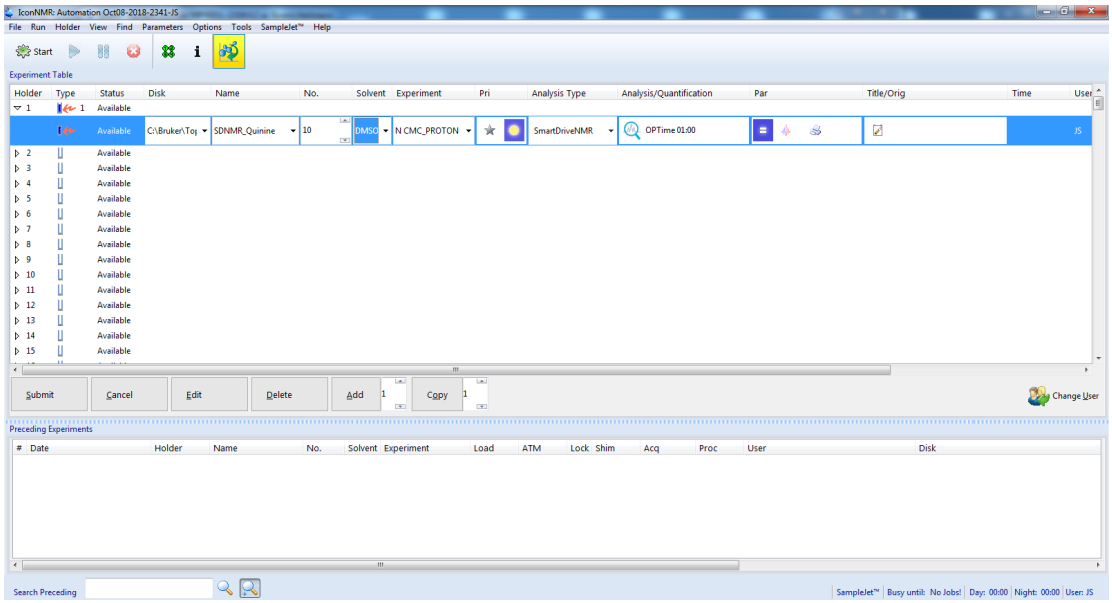
SmartDriveNMR can still be used when the Manual Inject/Eject mode is being used in IconNMR instead of a sample changer.

- Click **Automation** from the main IconNMR window to open the Automation Window

- Double-click on the first line to begin an experiment
- Enter **SDNMR_Quinine** in the Name field
- Enter **10** in the No. field
- Select **DMSO** from the **Solvent** pull down menu
- Select **CMC_PROTON** from the **Experiment** pull down menu

Every SmartDriveNMR experiment should be set up using the parameter set CMC_PROTON; other possible options are CMC_SINGLE, CMC_SINGLE_H2O and CMC_WET.

- Select SmartDriveNMR in the column **Analysis Type**
- Click  in the Analysis Settings column to view and possible adjust the default settings for the SmartDriveNMR run for this holder
- Click  to browse for a Quinine.mol file
- Select **OPTime** for **Mode** and 1h for the **Time**
- Click **Ok** to select the desired file
- At this point the automation window should look like the one below



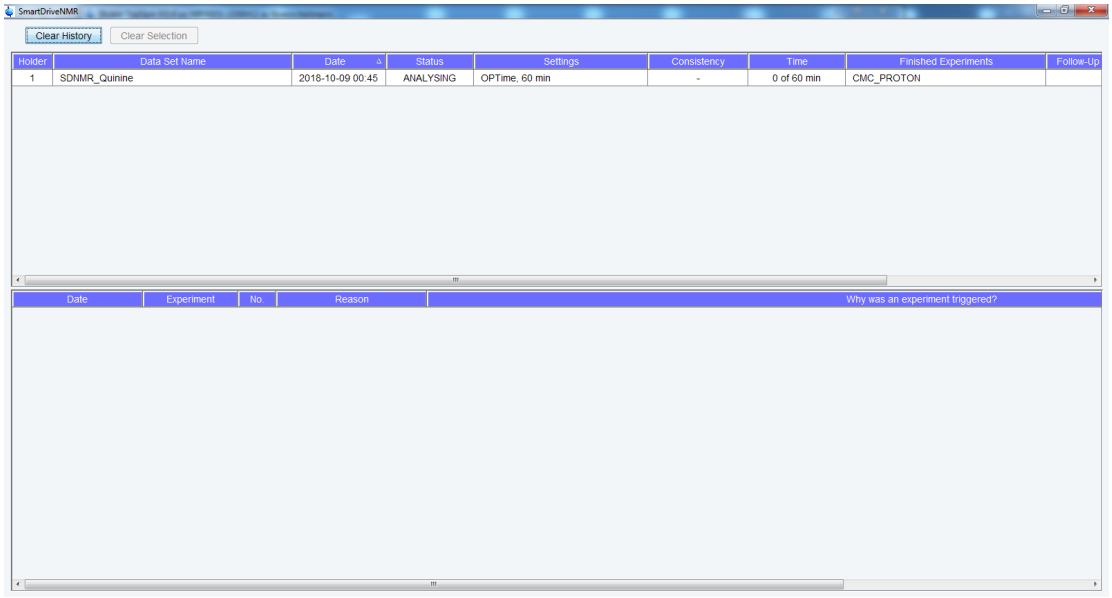
- Click **Submit** followed by **Start** to begin the acquisition

3.2 Acquisition Management

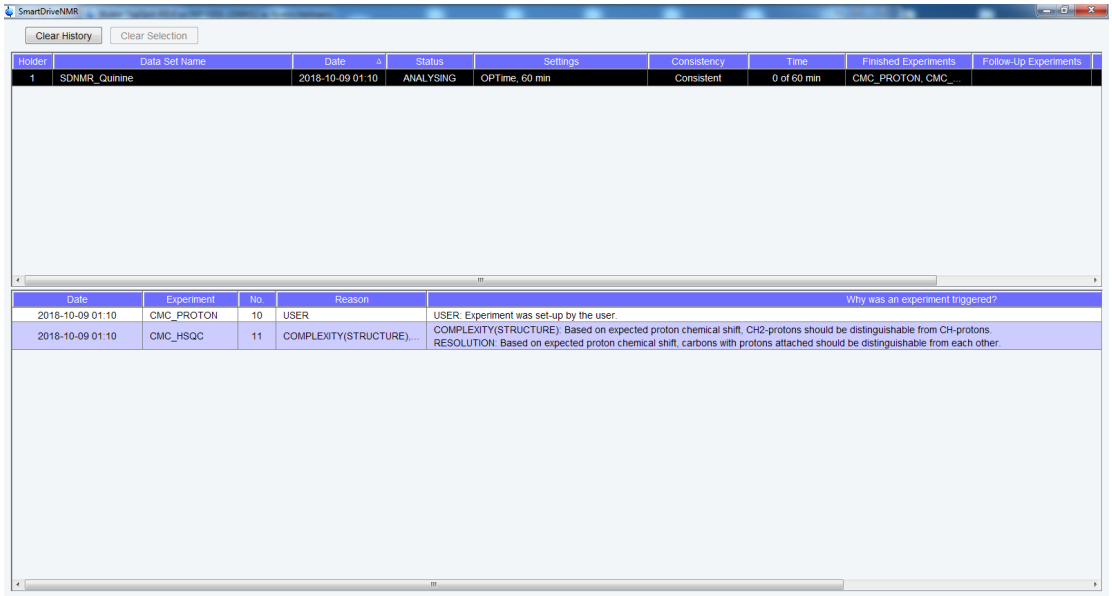
The progress of SmartDriveNMR experiments can be viewed from the SmartDriveNMR monitor. From here one can view the status of current and previous jobs.

To access the monitor, type **smartdrive** on the Topspin or CMC-assist command line. Alternatively the monitor can be opened by Right Click in the bottom part of the automation window on a dataset and Left Click on **Show in SmartDriveNMR monitor.**

- During the acquisition of the first spectrum the monitor will display the chosen settings as well as the currently running experiment.



- After analyzing the spectrum, the current consistency result is displayed along with the spent time. Furthermore, the next experiment is started in IconNMR automatically and the reason for such a follow-up is displayed in the bottom part of the SmartDriveNMR monitor.



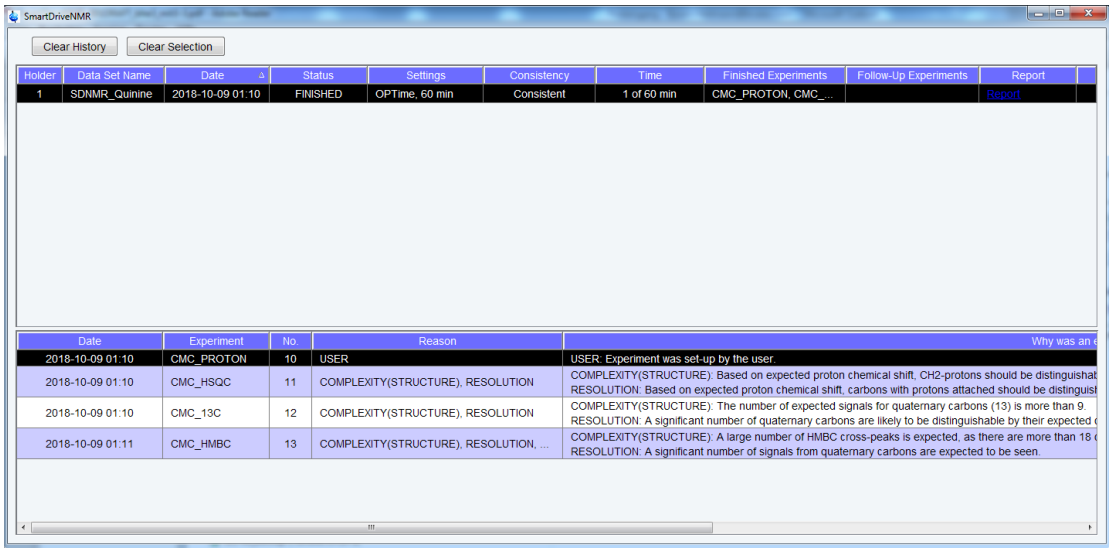
- When the final experiment was acquired and analyzed, the **Status** switches to “Finished“. The consistency result is shown as well as the complete history of the SmartDriveNMR run in the bottom part of the monitor.

3.3 Viewing the Results

The details of the analysis can be viewed from CMC-assist, but also from TopSpin. Along with the structure consistency check, the analysis includes integration regions, proton numbers, multiplet interpretation and assignment, concentration determination, and purity.

To view the details about the SmartDriveNMR run use the SmartDriveNMR monitor directly which displays the complete history of the run. Alternatively, this information can also be found in the SmartDriveNMR run report. To access this report:

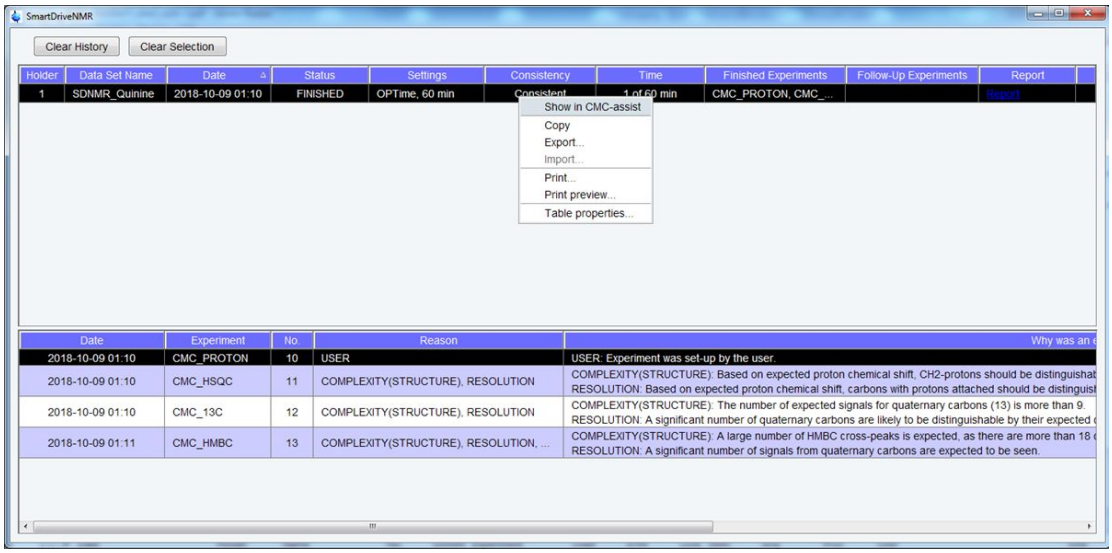
- Open the pdf report accessible from the report column of the SmartDriveNMR monitor. The report lists next to the run itself also general information about the data acquisition (e.g. used NMR system including probe type)



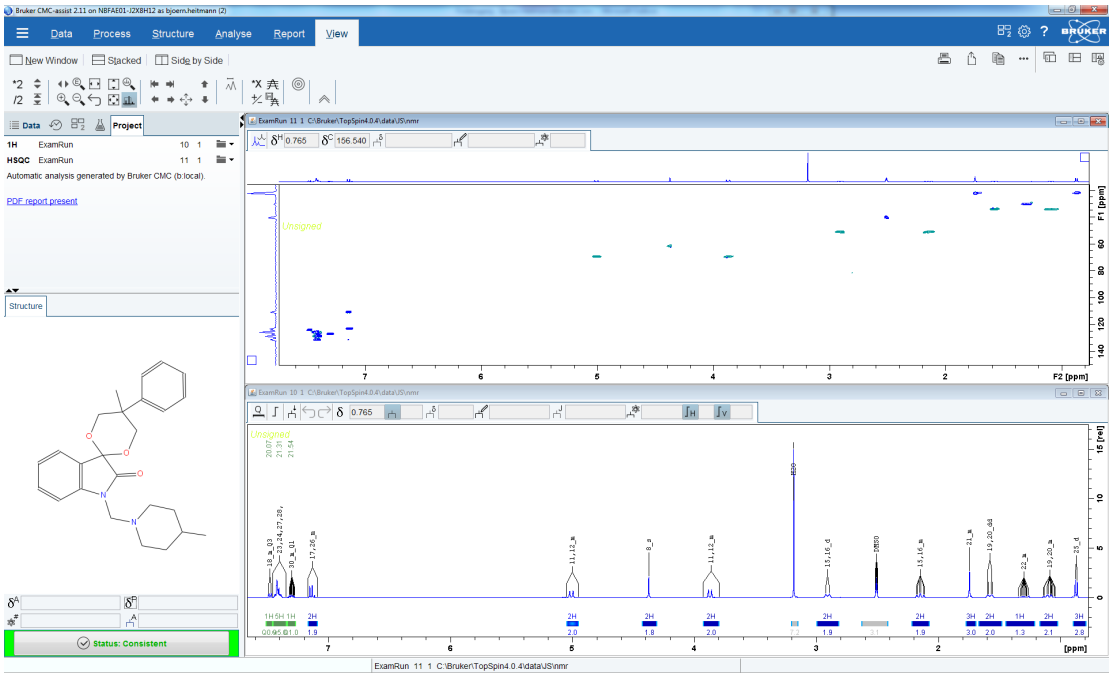
Of special interest is the report concerning experiments that could not be acquired due to time limitations but which are considered highly useful for the structure verification task. They are listed in the report as recommended follow-up experiments.

To view the detailed analysis:

- Right Click on the desired experiment from within the IconNMR Automation window or the SmartDriveNMR monitor



- Choose **Show in CMC-assist**



For detailed information about the CMC-assist analysis and interface, please see the CMC-assist manual.

4 Further Information

This chapter is intended to provide more detailed information about SmartDriveNMR and the various relevant parameters.

4.1 Operation Modes

SmartDriveNMR offers three different operation modes: **FIXperiment**, **OPTime**, and **MAXperiment.**

FIXperiment: Experiments are carried out exactly as they are set up by the user WITHOUT any parameter optimization. The measurement time results directly from the set up experiments.

OPTime: Only the experiments highly beneficial for the given synthesis control task that fit in the given time are carried out with optimized parameters. E.g. for a simple molecule like ethanol only a 1D 1H experiment is carried out – this will take about 2 min.

MAXperiment: All experiments that are technically possible and fit into the given time, will be carried out with optimized parameters. E.g. for a simple molecule like ethanol the complete portfolio will be carries out for the standard portfolio this would lead to the acquisition of a 1D 1H, HSQC, 1D 13C, and HMBC - depending on the concentration this will take about 50 min.

All three modes can be used with but also without providing structural information via a .mol file.

4.2 Experiment Portfolios

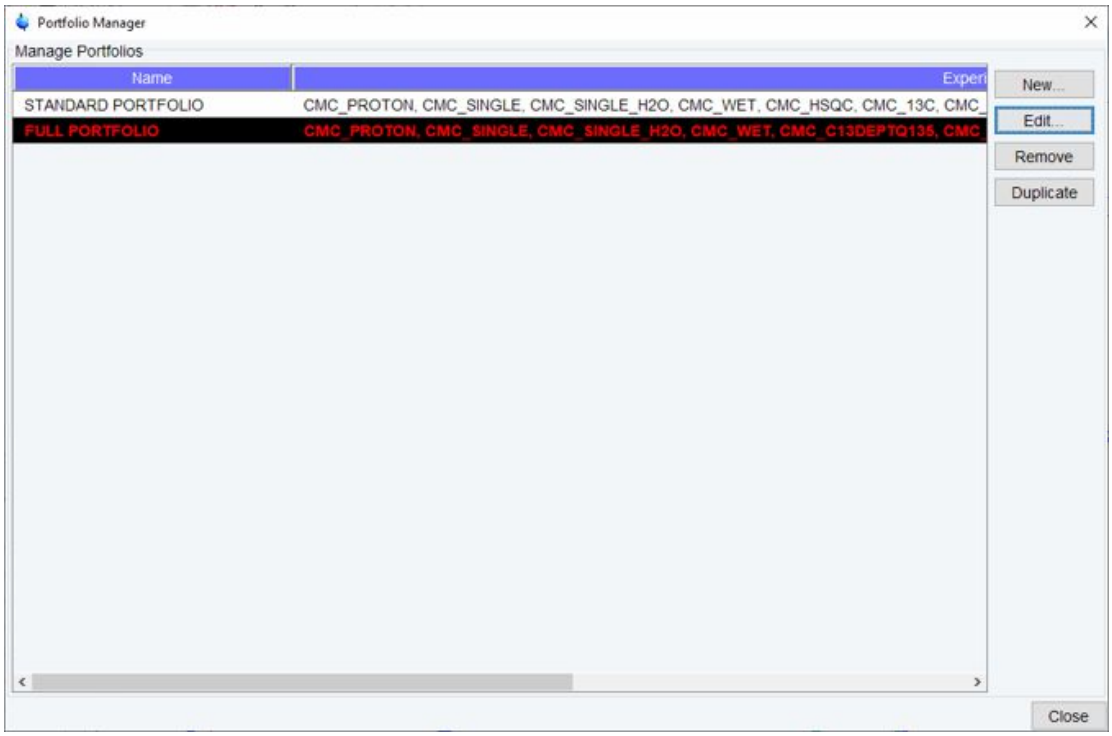
The type of experiments, their order and their specific settings which are considered during a SmartDriveNMR run are defined in the "Portfolio". Per default two portfolios are available named STANDARD PORTFOLIO and FULL PORTFOLIO. The standard portfolio contains:

- a 1D 1H block (consisting of CMC_PROTON, CMC_SINGLE, CMC_SINGLE_H2O, CMC_WET)
- a 2D 1H-13C HSQC (CMC_HSQC)
- a 1D 13C (CMC_13C)
- a 2D 1H-13C HMBC (CMC_HMBC)

The full portfolio contains the experiments from the standard portfolio and additionally:

- three homonuclear 2Ds CMC_COSY, CMC_TOCSY, and CMC_NOESY
- two 1D 19F experiments (CMC_F19 and CMC_F19CPD)
- a 1D 13C Dept including quaternary Carbons (CMC_C13DEPTQ135)

These two portfolios can be found by Left Click **Portfolio Manager** (see section *Configure Settings [▶ 8]* of this manual). They can not be reduced or extended but their parameters can be edited and new portfolios can be derived from them by Left Click **duplicate** then selecting the new portfolio named **Copy of ...** and then Left Click **edit**.



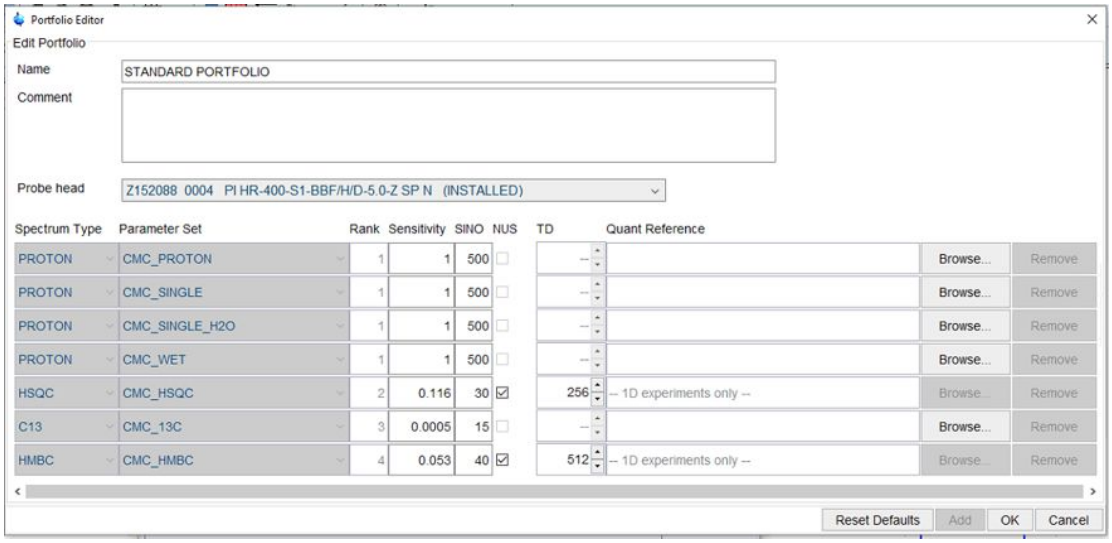
4.2.1 Manage a Portfolio

A portfolio can be given a name and a comment. It is always associated with a specific probe head and per default the currently installed probe is preselected. To manage a portfolio of a different probe select this by Left Click the arrow pointing down next to the current probe name.

Any portfolio contains these options:

- Spectrum Type: This lists all the supported types of spectra.
- Parameter Set: All parameter sets (experiments) that fit to the selected spectrum type are listed here. The display criteria is the setting of the processing parameter SPECTYP inside of a parameter set.
- Rank: This influences the order in which the experiments in the portfolio are carried out. The lower the rank the earlier the experiment will be considered.
- Sensitivity: This is a number that is used to calculate the needed amount of scans (acquisition parameter NS) to reach the desired signal-to-noise ratio.
- SINO: This is the desired signal-to-noise ratio of the selected parameter set; the signal refers to the strongest signal in the spectrum that is not the solvent. The sensitivity value indicates how the sensitivity of an experiment compares to a reference experiment like the CMC_PROTON which had been assigned the value of 1.0 . E.g. a sensitivity of 0.3 indicates that this experiment is 0.3 times less sensitive than an experiment with a sensitivity value of 1.0.
- NUS: By selecting this the acquisition of selected parameter set is carried out using Non Uniform Sampling (see section "Non Uniform Sampling" for more details).
- TD: Here the number of increments in the indirect dimesion of a 2D parameter set can be set. This value replaces what is in the parameter set when used with SmartDriveNMR.
- Quant Reference and Browse: Each 1D parameter set can be associated with a quantification reference experiment of the same kind which allows a concentration determination using the eretic2 functionality of TopSpin.

- Remove: Here a whole line of the portfolio can be removed (please note that none of the four 1D 1H experiments can be removed for any portfolio and that none of the parameter sets of the standard and full portfolio can be removed).
- Reset Defaults: This will restore the default settings associated with the selected probe head.
- Add: Here additional experiments can be added to the current portfolio (please note that this is note possible for the standard and full portfolio).
- OK: This will terminated the portfolio management process by saving all the changes on the current portfolio.
- Cancel: This will terminated the portfolio management process by ignoring all the changes on the current portfolio.



4.2.2 Hints on how to Add Your "Own" Parameter Sets to a Portfolio

When creating your own portfolio it is possible to add experiments that are not part of the standard or full portfolio. To formally make a parameter set available to SmartDriveNMR it needs to have the processing parameter SPECTYP set to any of the types that SmartDriveNMR supports. To list all the available ones Left Click in a field of the Spectrum Type column of the portfolio. Please note that only parameter sets that contain only one experiment (in contrast to "composite" experiments) and experiments that carry a single FID that is linked to a single spectrum are supported by SmartDriveNMR. The last restriction excludes NOAH super sequences and multireceive experiments for use within SmartDriveNMR. The settings for Rank, SINO, NUS and TD follow straight forward out of the users requirements and in the list above in section *Manage a Portfolio [▶ 18]* more explanation are available if needed.

Choosing a proper value for the sensitivity for your "own" parameter set is not that obvious and here are some hints that should help to find a good value:

- Use the sensitivity values given in the full portfolio as a guidance. If the new parameter set is similar to an existing one concerning the way magnetization is excited, evolving, and being detected than the sensitivity will be similar (e.g. the sensitivity of an HMQC will be in the range of the sensitivities of the HSQC and the HMBC from the full portfolio).
- For an experiment like an HSQC-TOCSY the sensitivity is roughly the product of the sensitivities of the HSQC and the TOCSY of the full portfolio.

- An indication for a sensitivity value that is set too low is an achieved Signal-to-Noise value that is significantly higher than the value specified in the SINO column of the portfolio. The achieved signal-to-noise value can be found in the SmartDriveNMR run report (see section *Viewing the Results* [▷ 14] of this manual).
- An indication for a sensitivity value that is set too high are repeated measurements of the same experiment. The reason for this is that the achieved Signal-to-Noise value of the first experiment did not reach the desired signal-to-noise ratio that was specified in the portfolio and a follow-up with more scans was submitted to reach the criteria. Changing the sensitivity by a factor of four will result in a Signal-to-Noise value change of a factor of two.

4.3 Maximum Instrument Time per Sample

This is the amount of time that will be allotted to each sample for the entire verification task. This includes acquisition time as well as analysis time but does not include the time for loading, locking, and shimming the sample. This time will respect the night and day time limits set by IconNMR. So e.g. if a SmartDriveNMR run is set for a maximum of 3 hours but only 2 hours are allowed by IconNMR then the SmartDriveNMR run will not exceed 2 hours.

4.4 Non-Uniform Sampling (NUS)

The data acquisition of all the 2D experiments can be carried out using NUS. The settings for this acquisition option can be found in portfolio which can be edited via the Portfolio Manager. The settings for NUS is another source that influences the time spent on the acquisition. Depending on the settings for TD in the indirect dimension NUS can be used to save time (with TD values of e.g. 256 and lower) or to gain resolution with TD values of e.g. 512 and higher. During the acquisition of the spectrum with NUS some of the data points for the indirect dimension are not acquired but reconstructed later on. The percentage of the actually acquired points (NusAMOUNT) is determined for each sample individually and ends up typically between 20% and 60% which directly results in the percentage of time spent compared to the traditional experiment. During the acquisition the quality of the spectra is determined and the NusAMOUNT is on-the-fly increased if needed this behavior is controlled by the acquisition automation script named ta_acqu. For the 2D experiments of the standard and full portfolio this script is already set. To benefit from this targeted acquisition approach the acquisition parameter AUNP needs to be set to "ta_acqu". The usage of NUS can be recommended in general with the exception of experiments of the type NOESY and ROESY.

4.5 Temperature Handling

When SmartDriveNMR is setting up a new experiment, it will respect the temperature set for the initial experiment. E.g., if the first experiment was set-up at 305 K and in IconNMR the settings were chosen that way, that IconNMR is controlling the temperature via the parameter TE, the follow-up experiments of the SmartDrive run will as well be acquired at 305 K. If the temperature is not controlled by IconNMR SmartDriveNMR will naturally acquire at the same temperature as the initial experiment.

5 Contact

Manufacturer

Bruker BioSpin GmbH
Silberstreifen 4
D-76287 Rheinstetten
Germany
http://www.bruker.com

WEEE DE43181702

NMR Hotlines

Contact our NMR service centers.

Bruker BioSpin NMR provides dedicated hotlines and service centers, so that our specialists can respond as quickly as possible to all your service requests, applications questions, software or technical needs.

Please select the NMR service center or hotline you wish to contact from our list available at:

https://www.bruker.com/service/information-communication/helpdesk.html

Phone Germany: +49 721-5161-6155
Phone USA: 978-667-9580 ext 5444
Phone France: +33 3 88 06 60 00
Phone UK: +44 24 7685 5333
E-mail: *nmr-support@bruker.com*

Contact

Lastpage

Lastpage

Bruker Corporation

info@bruker.com
www.bruker.com

Part No: Z33122