NMRSim

Experiment Simulator

User Manual

Version 007

Innovation with Integrity

NMR

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Contents

1 Introduction

NMRSim™ is a program for the simulation of a wide range of NMR experiments. The program is a part of the Bruker TopSpin software package.

NMRSim uses the standard Bruker pulse sequences and experiment definition parameters used on AVANCE™ spectrometer series. All pulse programs are executed in the same way as they run on the NMR hardware. The output of the simulation is a FID or SER file in the standard TopSpin format. The "sample" is defined using simple language, or optionally a chemical structure file may be used. In such case TopSpin internal chemical shift prediction is used to generate the necessary shifts and couplings.

The ability to use Bruker pulse programs offers the possibility of pulse sequence tuning or the analysis of complex NMR experiments under ideal conditions without instrumental imperfections.

NMRSim is designed to simulate the behavior of general homo- and hetero-nuclear spin systems. Spin quantum numbers up to 2 are supported. The simulation is based on the solution of the quantum mechanical Liouville equation. The spin system evolution during the radio-frequency pulse is taken into account, so you can simulate rotating frame magnetization transfer experiments (TOCSY or HOHAHA). The implementation of gradients allows simulation of gradient enhanced experiments.

NMRSim contains several additional modules

- The **NMR-Wizard** allows a basic set of NMR experiments for given structure to be calculated, it is not necessary to enter or modify any parameters.
- The **Bloch Module** allows different features and behavior of shaped pulses to be studied.
- The **Pulse Program Display** may be used for the visualization or editing of Bruker pulse programs.

1.1 New Features

1.1.1 NMRSim 6.4

This version introduces a major enhancement - simulation of non uniform sampled 2D spectra (NUS).

Additional improvements:

pulse program display:

- support for experiments using 3D gradients
- multiple display windows may be opened

1.1.2 NMRSim 6.0

This is a major update for MS-Windows, Linux and macOS. A new user interface replaces the old, platform depended solutions. This makes NMRSim™ independent of obsolete technologies. The installation of X11 server on macOS is no longer required.

- The user interface has been simplified, all parameters or options for the simulation are now available from one dialog.
- Chemical structure (MOL) files may be used now as spin system definition.

- The NMR-Wizard has been completely reworked and offers now a simple user interface for chemists. Only one click is necessary to calculate an 1D or 2D NMR spectrum from your structure.

The following functions are not available in the new release:

- Calculation and display of energy levels.
- Direct calculation of 1D spectra – it was replaced thru new NMR Wizard.
- Parameter optimization.
- Propagator calculation.
- Graphical assistant.
- Several command line options duplicating other functionality were also removed.

1.1.3 NMRSim 5.7

For MS-Windows , RedHat Linux and macOS.

This is the last version using the platform dependent user interface (e.g. MOTIF/X11 on Unix platforms).

1.2 Installation

Bruker software packages are distributed via download from Bruker Webpages, or on the Bruker Software DVD. Please refer to the respective TopSpin installation manual for details.

1.2.1 TopSpin

TopSpin must be configured before you start NMRSim. You should install the pulse programs using the TopSpin command **expinstall** and select the option **Install High Resolution Pulse Programs**.

Start NMRSim from the menu **Analyse/Simulate Fid**, or type in the command **nmrsim**.

2 Theoretical Background

The aim of this section is to provide some brief background information on the physical models and equations used for the simulation.

The simulation of an NMR experiment is based on the density matrix approach. Relaxation phenomena are implemented using a very simple model based on Bloch equations. Cross-correlation and cross-relaxation effects are neglected.

2.1 Liouville Equation

The basic equation describing the time development of the density matrix ρ is the *Liouville equation*:

$$i\hbar\rho(0) = [H, \rho]$$

$$H = H_0 + H_{rf}(t)$$

Where ρ(0) is the density matrix and H is the spin system Hamiltonian.

The Hamiltonian may be divided into two parts. The time dependent part $H(t)_{rf}$ describes the interaction between nuclei and the radio frequency fields from the spectrometer. The constant part H_0 describes the nuclear spin system, or in other words, the sample.

$$H_0 = \sum_i \omega_i I_z^i + \sum_{i<j} 2\pi J_{ij} I^i I^j$$

$$= \sum_i \omega_i I_z^i + \sum_{i<j} 2\pi J_{ij}(I_z^i I_z^j + I_x^i I_x^j + I_z^i I_z^j)$$

The program finds the solution of the Liouville equation in the form of the exponential propagator:

$$U(t) = Te^{\left(-\frac{i}{h}\int_0 H(\tau)d\tau\right)}$$

Only numerical approaches are used to calculate the propagator *U*. Thus there are no approximations resulting from analytical formulas or simplifications (e.g. weak coupling approximation). The time evolution of the density matrix is calculated using:

$$\rho(t) = U\rho(0)U^\dagger$$

Where ρ(0) is the initial density matrix. These formulas are used for delays as well as for radio-frequency pulses. Thus, the exact evolution of the whole spin system during all pulses is taken into account. In this way, we are able to simulate the selective pulses and rotating-frame coherence-transfer experiments exactly. The propagators for radio-frequency pulses are phased using the appropriate phase specified by the pulse sequence, so you can use any general phase cycle. The propagator of the whole pulse sequence U_g is defined as a product of all interval propagators in the sequence:

$$U_g = \prod_{i=1}^{N} U_i$$

From this formula, it is clear that the most frequent numerical operation used by the simulator is *matrix multiplication*.

If you add one non-equivalent spin 1/2 nuclei to your spin system, you will double the dimension of the spin system density matrix, but the time necessary for matrix multiplication will increase by a factor of 8. Thus, there is a significant loss of performance for larger spin systems. Approximately $2*10^6$ floating point operations are needed to multiply two 64*64 complex matrices, which represent operators for six nonequivalent spin 1/2 nuclei.

It is a different situation, if you increase the multiplicity of some nuclei. In this case the program uses the **group theory** to split the spin system into several smaller *fictitious*, independent *systems*. Performance loss is much less than the factor 8 for nonequivalent nuclei. So, if you simulate the behavior of spin systems with equivalent nuclei, use the multiplicity parameter in the spin system definition file. If you specify the equivalent nuclei using different spin labels but the same resonance frequency and couplings, you will get the same result, but the calculation will be far slower and the probability that you will exceed the program limits will be larger.

The acquired FID is calculated using the formula:

$$\mathrm{FID}(n) = \mathrm{Tr}\left\{ e^{-iH_0\tau n} U_g \rho(0) U_g^{\dagger} (e^{-iH_0\tau n})^{\dagger} J^{+} \right\}$$

Where J^+ is the creation operator for the total angular momentum of the observed nuclei, and Tr is the symbol for the trace operator.

2.2 Relaxation

Relaxation is implemented in NMRSim as follows:

During radio-frequency pulses the relaxation effects are neglected. During delays the program uses the Bloch equations for the relaxation of longitudinal magnetization:

$$\dot{M}_z = -\gamma(\overline{B} \times \overline{M})_z + \frac{M_z - \overline{M}_0}{T_1}$$

Where $\overline{M}_0$ stands for the thermodynamic equilibrium value. The rest of the density matrix (i.e. off diagonal elements) is multiplied by the factor:

$$e^{\frac{-t}{T^*}}$$

Where t is the interval length and T* is the effective relaxation time:

$$\frac{1}{T^*} = \sum_j \frac{1}{T_j}$$

When the full relaxation simulation is switched on, the initial relaxation matrix ρ(0) in the equation above is regularly updated to its relaxed value. This allows the simulation of relaxation artifacts in 2D spectroscopy. All cross-correlation and cross-relaxation effects are neglected.

2.3 Flow of the Simulation

The flow of the simulation is the same as the flow of real NMR experiment:

All pulse program transients are calculated in the same order as they are carried out on a spectrometer.

The user can check the flow of an experiment by means of message lines in the NMRSim main window. The message lines display the current pulse program, transient (scan) and experiment numbers. When the program calculates the FID, this box displays the message Acquisition.

Generally it is not necessary to calculate the FID for every pulse sequence transient (scan). It is possible to accumulate the density matrix instead and to calculate the FID after the last scan. In this case the program displays the message Acquisition only at the end of the last transient. This approach substantially speeds up the simulation of multidimensional experiments with phase cycling.

All of the NMRSim calculations are highly optimized for maximum performance, the pulse propagators U are stored in memory for later use in subsequent scans or the next time increment in multidimensional experiment.

3 Using the Program

This chapter provides a short guide through the NMRSim menus and an introduction to the program user interface. Further detailed information about the experiment setup and several example experiments can be found in the section *Examples [▸ 77]*.

3.1 Program Start

The easiest way is to use the **Applications/Simulate/Simulate FID** TopSpin flow menu, or type `nmrsim` on the TopSpin command line.

After the start NMRSim looks for further copies of itself (instances) that might already be running. When another instance is found, its window is display and terminates itself. In other words, every user may run only one instance of NMRSim at any given time.

3.1.1 Parameter Definitions

This set of options allows you to define several experiment parameters on the command line.

- -config <name>

  This command loads the predefined experiment configuration.

  Example: *nmrsim -config example1d.cfg*

  NMRSim starts and loads the predefined configuration file example1d.cfg from the user directory $(HOME)/NMRSIM_SESSION/config.
- -xconfig <path>

  This loads the experiment configuration from the TopSpin acquisition parameters. The path specifies where the TopSpin acquisition parameter file is located.

  Example: *nmrsim -xconfig /u/data/guest/nmr/demo1d/1/acqus*
- -pulprog <name>

  This selects the pulse program <name>.

  nmrsim -pulprog cosydfsh
- -spnam<n> <name>

  Selects the waveform for shaped-pulse (acquisition parameter SPNAM0 .. SPNAM32).

  Example:

  nmrsim -spnam0 gauss

  nmrsim -config selcosy.cfg -spnam0 gauss
- -p<n> <value>

  Defines the pulse length parameter P0..63.
- -d<n> <value>

  Defines the delay length parameter D0..63.

It is possible to combine several parameter definitions on one command line:

nmrsim -config cosy.cfg -pulprog cosydfsh

In this example the program is started and the configuration file *cosy.cfg* loaded, then thes new pulse program *cosydfsh* is loaded. The order of parameters is substantial, the parameters are evaluated from left to right, therefore it does not make any sense to write:

nmrsim -pulprog cosydfsh -config cosy.cfg

The *-config* option will rewrite the pulse program selected in the *-pulprog* parameter!

3.2 Exiting NMRSim

You can exit the program in two ways: using the command **File**/**Exit** from the menu, or using the system menu (upper left corner of the NMRSim window). The first method saves the currents state (selected files, values of parameters) to disk, in the second case nothing is saved.

The saved state will be loaded at the next start from the file *session.cfg* in the user data directory.

3.3 User Data Directory

All private data (pulse sequences, spin system definitions,...), created by the user are saved in the private user directories, but it is also possible to load files from any other directory. In this way possible interference between potential users is minimized, and a common database of sequences and spin system definitions can be created.

The program creates user private directory *NMRSIM_SESSION* in your home directory:

c:\Users\Otto\NMRSIM_SESSION

/home/Otto/NMRSIM_SESSION

All example files are copied here after the first start of NMRSim.

3.4 Main Menu Commands

The NMRSim main window displays basic information about current settings:

- The names of selected experiment definition files.
- The duration of the last experiment in seconds.

The program commands are separated into several logical function groups, which will be described below.

3.4.1 File

The **File** menu allows you to select current pulse sequence and spin system definition data files, as well as the current delay, pulse and offset lists.

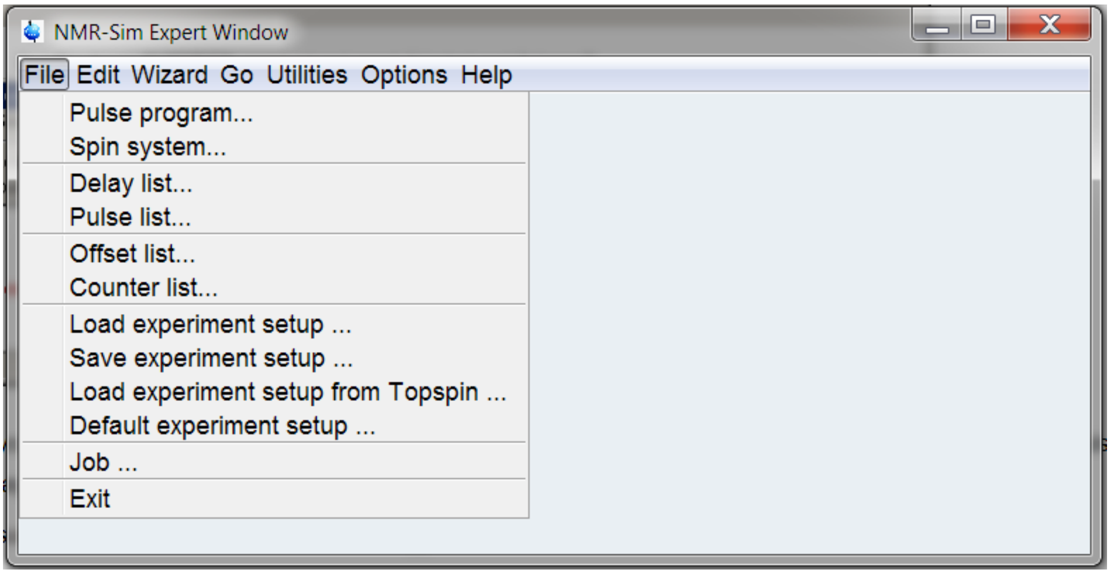


Figure 3.1: File Menu

All information about experiment set-up is saved to disk as well. The configuration is automatically loaded during the start procedure from the file *session.cfg*, however the user has the possibility of creating any number of private configuration files (any name with the extension *.cfg) and read them manually using the **Load from file** command.

The configuration files reside in user private directories. Several predefined configuration files are installed in the demo user directory. You can use them to run several example experiments

The experiment setup menu block contains following commands:

- **Load from file**
- **Save to file**
- **Default settings**

  This command sets the default value for all NMRSim parameters. The default values allow you to execute a variety of NMR experiments without significant changes. Only spin system dependent parameters as evolution delays must be modified.
- **Load from TopSpin data set**

  This command reads the NMRSim experiment configuration from an existing TopSpin data set. Only data sets created on AVANCE spectrometers are supported.
- **Job**

  NMRSim allows execution of several experiments in one job. The job description is saved in a plain text file and contains only the names of configuration files which are loaded and executed. The progress of the job is recorded in a simple protocol file.

  The command **Job** only selects the job description file. The job may be started from the **Go** menu.
- **Exit**

  This command closes all program windows, saves the current configuration on the disk and exits.

3.4.2 NMR Wizard

The NMR Wizard is a tool which allows NMR spectra to be calculated from your own chemical structure. The user must only select or draw a chemical structure, then the required spectra is calculated by pressing the appropriate button. Refer to the section *NMR Wizard* [▹ 63] for further details.

3.4.3 Edit

The experiment definition files, which are saved as general text files in ASCII file format (pulse programs, all lists, spin system definitions), are edited using a built-in text editor.

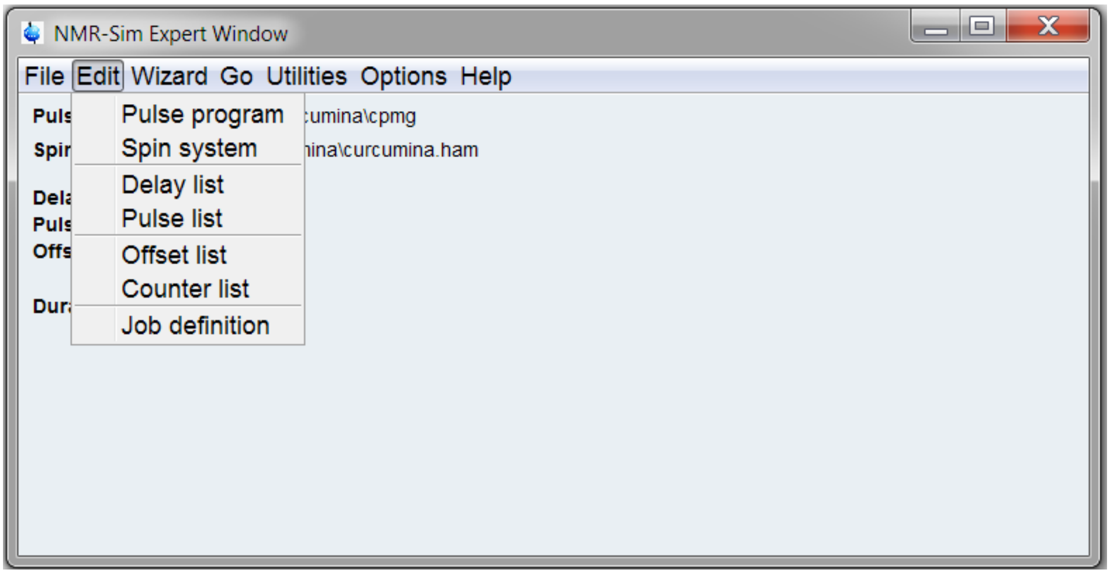
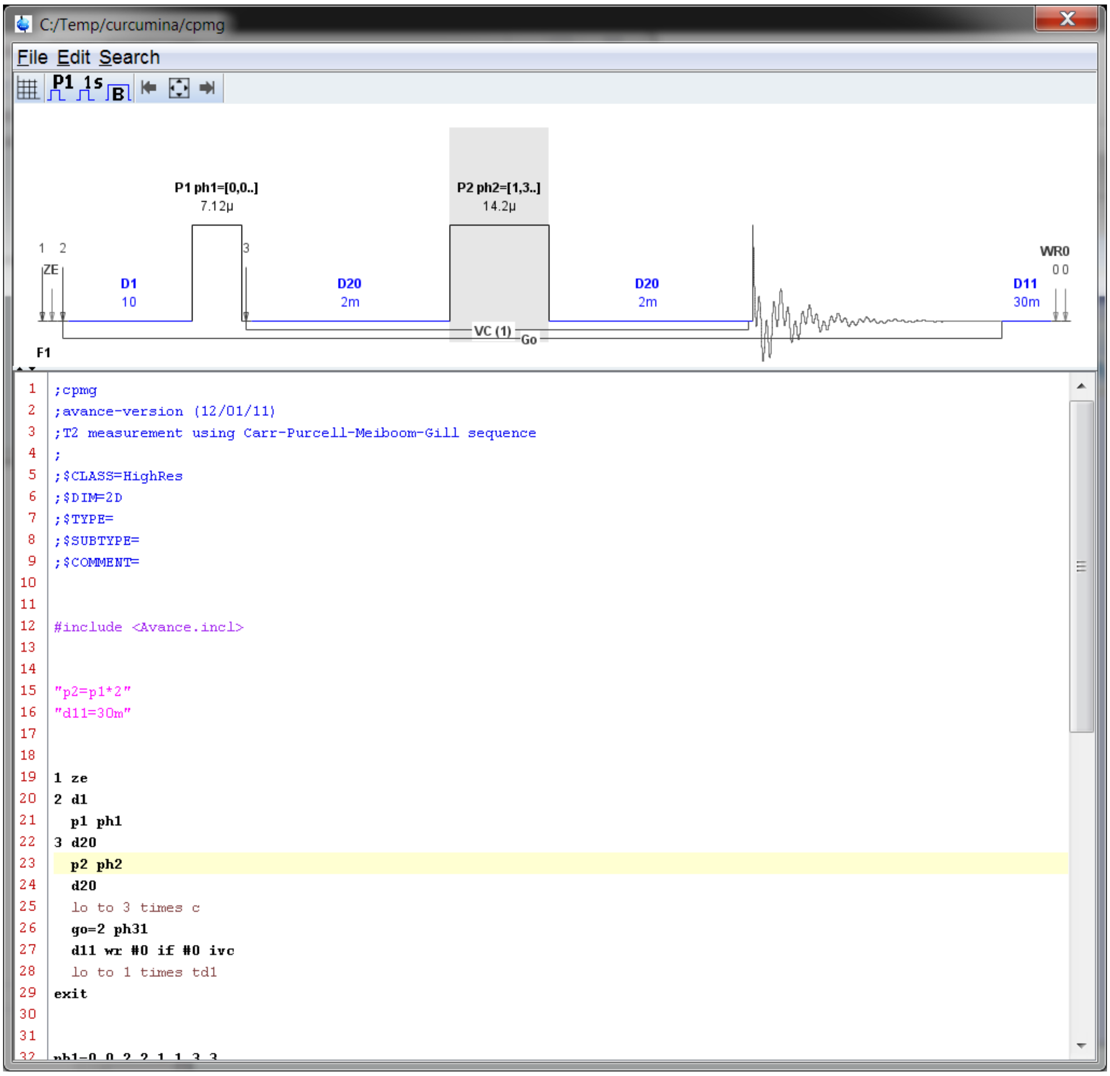


Figure 3.2: Edit Menu

The pulse program editor uses the on line graphical display of pulse programs.

The graphics is updated immediately, so you can follow the text changes in the displayed pulse program scheme.



```
;cpmg
;avance-version (12/01/11)
;T2 measurement using Carr-Purcell-Meiboom-Gill sequence
;
;$CLASS=HighRes
;$DIM=2D
;$TYPE=
;$SUBTYPE=
;$COMMENT=


#include <Avance.incl>


"p2=p1*2"
"d11=30m"


1 ze
2 d1
  p1 ph1
3 d20
  p2 ph2
  d20
  lo to 3 times c
  go=2 ph31
  d11 wr #0 if #0 ivc
  lo to 1 times td1
exit


ph1=0 0 2 2 1 1 3 3
```

Refer to the *Pulse Program Display [▸ 39]* section for further details.

3.4.4 Go

The menu element **Go** starts the simulation.

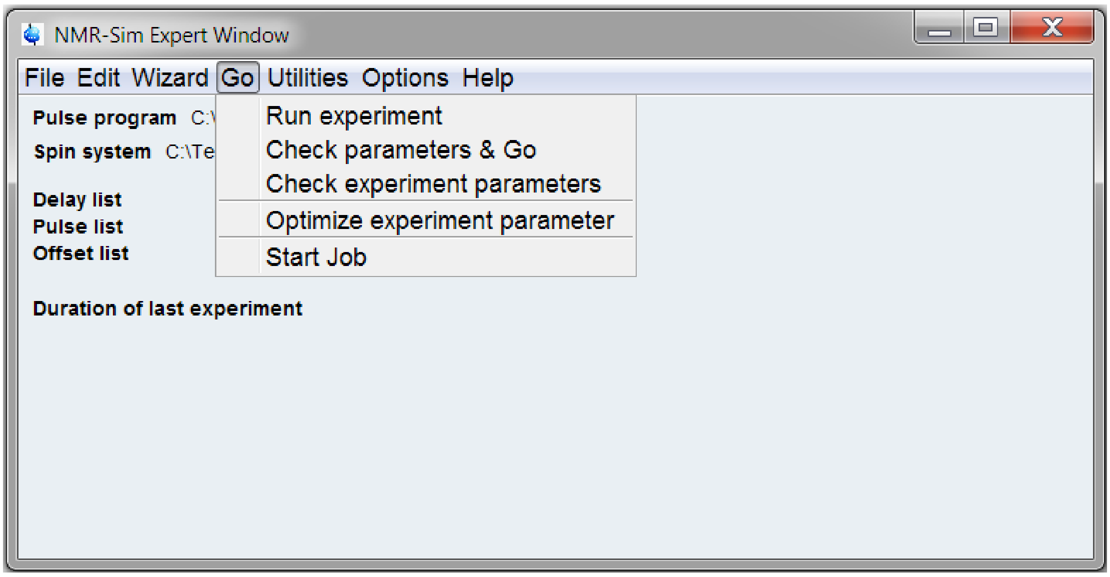
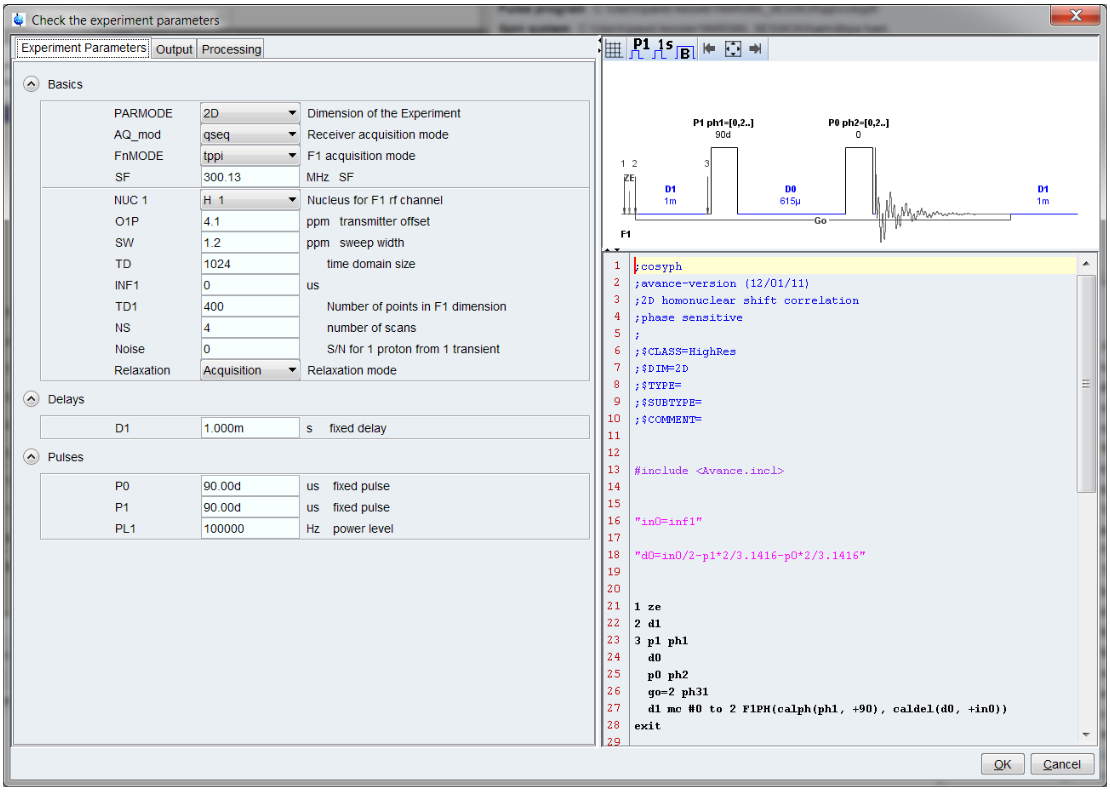


Figure 3.3: NMRSim Go Menu

It is possible to start the simulation immediately, by selecting **Run experiment**, or to check and edit the value of all parameters before the start using **Check Parameters & Go**.

The dialog box for editing the current experiment parameters displays only those parameters which are really used during the simulation.



Basics

PARMODE	2D	Dimension of the Experiment
AQ_mod	qseq	Receiver acquisition mode
FnMODE	tppi	F1 acquisition mode
SF	300.13	MHz SF
NUC 1	H 1	Nucleus for F1 rf channel
O1P	4.1	ppm transmitter offset
SW	1.2	ppm sweep width
TD	1024	time domain size
INF1	0	us
TD1	400	Number of points in F1 dimension
NS	4	number of scans
Noise	0	S/N for 1 proton from 1 transient
Relaxation	Acquisition	Relaxation mode

Delays

D1	1.000m	s fixed delay

Pulses

P0	90.00d	us fixed pulse
P1	90.00d	us fixed pulse
PL1	100000	Hz power level

```
;cosyph
;avance-version (12/01/11)
;2D homonuclear shift correlation
;phase sensitive
;
;$CLASS=HighRes
;$DIM=2D
;$TYPE=
;$SUBTYPE=
;$COMMENT=


#include <Avance.incl>


"in0=inf1"

"d0=in0/2-p1*2/3.1416-p0*2/3.1416"


1 ze
2 d1
3 p1 ph1
  d0
  p0 ph2
  go=2 ph31
  d1 mc #0 to 2 F1PH(calph(ph1, +90), caldel(d0, +in0))
exit
```

Figure 3.4: Check Parameters Dialog Box

The command **Check experiment parameters** displays the parameter dialog box. You may change any parameter. Parameters are stored, but the experiment is not started.

The command **Start job** starts the NMR job.

3.4.5 Utilities

This menu contains several useful tools:

- Show pulse program

  This command opens a new window and presents the current pulse program in a simple graphical form. More details may be found in the chapter *Pulse Program Display [*▷ 39].

- Bloch module

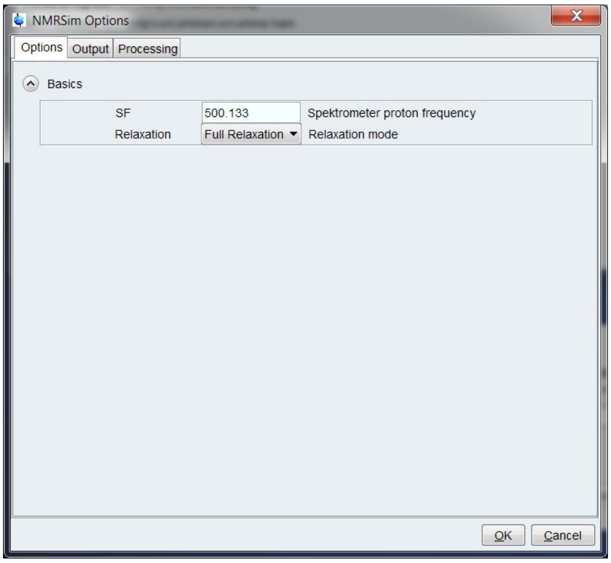
  Opens the Bloch simulator window, which is described in the chapter *Bloch Simulator [*▷ 25].

3.4.6 Options

The option **Upgrade Example Files** copies the latest version of example files to your private NMRSIM_SESSION directory (see *Examples [*▷ 77]).

NMRSim Settings opens a dialog where you can set several parameters. All parameters are also accessible from the "Check Parameters" dialogs (see *Go [*▷ 17]).

3.4.6.1 Options Dialog



SF 500.133 Spektrometer proton frequency

Relaxation Full Relaxation Relaxation mode

Figure 3.5: Options Dialog

Several parameters can be controlled from this submenu.

- Spectrometer frequency (SF).
- Relaxation - here you can select the relaxation mode.
  - None

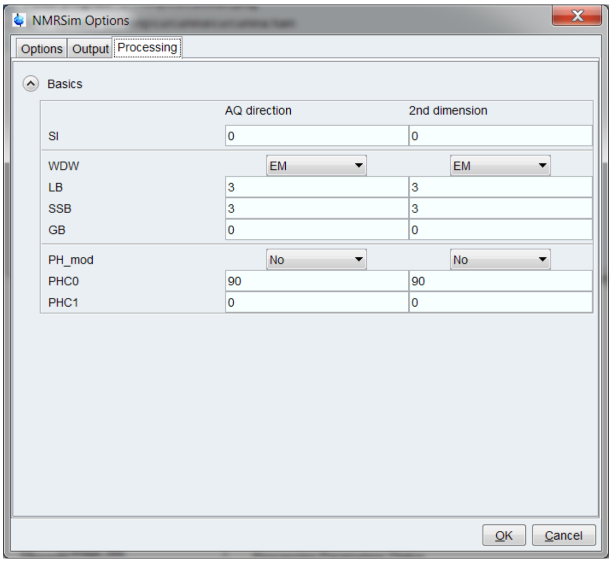
    Relaxation effects are ignored.
  - Acquisition

    Relaxation is only used to simulate the natural line widths (signal decay during FID).
  - Full relaxation

    Full relaxation is described in the section *Theoretical Background [*▷ 9]. This option significantly reduces the speed of calculations.

3.4.6.2 Processing Parameters

This part opens a page which lets you define the processing parameters. These parameters are saved to disk, i.e. you only need to execute the processing command (e.g. xfb) when processing the simulated spectrum.

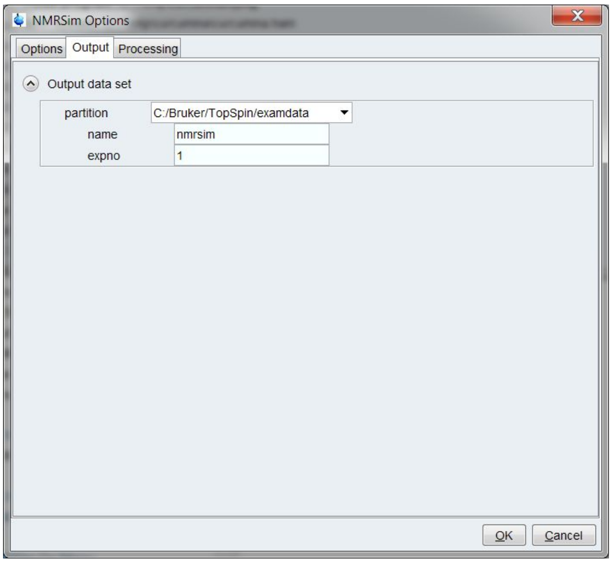


	AQ direction	2nd dimension
SI	0	0
WDW	EM	EM
LB	3	3
SSB	3	3
GB	0	0
PH_mod	No	No
PHC0	90	90
PHC1	0	0

Figure 3.6: Processing Parameters Dialog

3.4.6.3 Output File

This table defines the default output file.



partition C:/Bruker/TopSpin/examdata
name nmrsim
expno 1

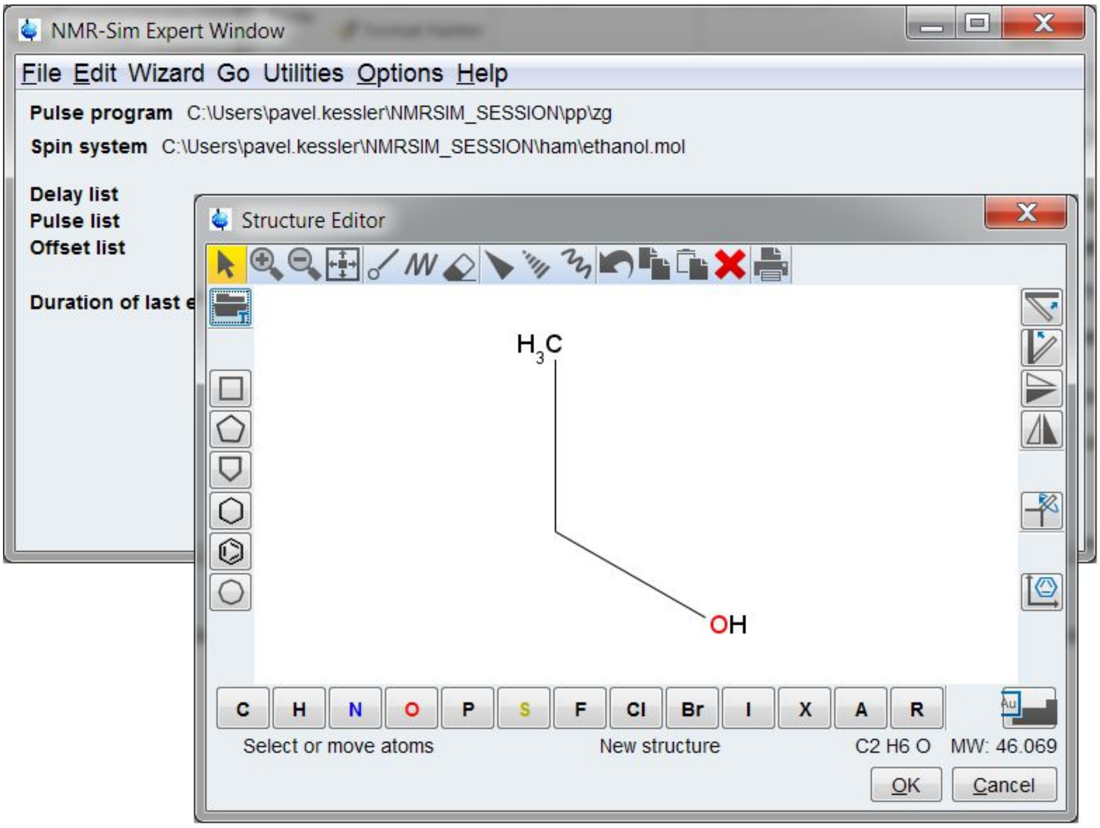
The partition allows you to either select one of data partitions defined in the TopSpin data browser, or define your own path.

3.5 The “sample” - Spin System Definition

The spin system in definition is the “sample” for the simulation of NMR experiment. It is defined using a simple language, the definitions are saved in text files with the extension *.ham. The program constructs the Hamiltonian operator H_0 from the spin system definition file. So, in some cases we will refer to this file as the Hamiltonian definition.

Alternatively, you may select a chemical structure file (“*.mol”) as your spin system definition. In this case NMRSim uses built-in NMR prediction to generate a temporary spin system definition for the sake of simulation.

The spin system may be edited using a built-in editor (**Edit/Spin System**). In the case, a structure file must be selected as you spin system, and the structure editor is used.



Pulse program C:\Users\pavel.kessler\NMRSIM_SESSION\pp\zg

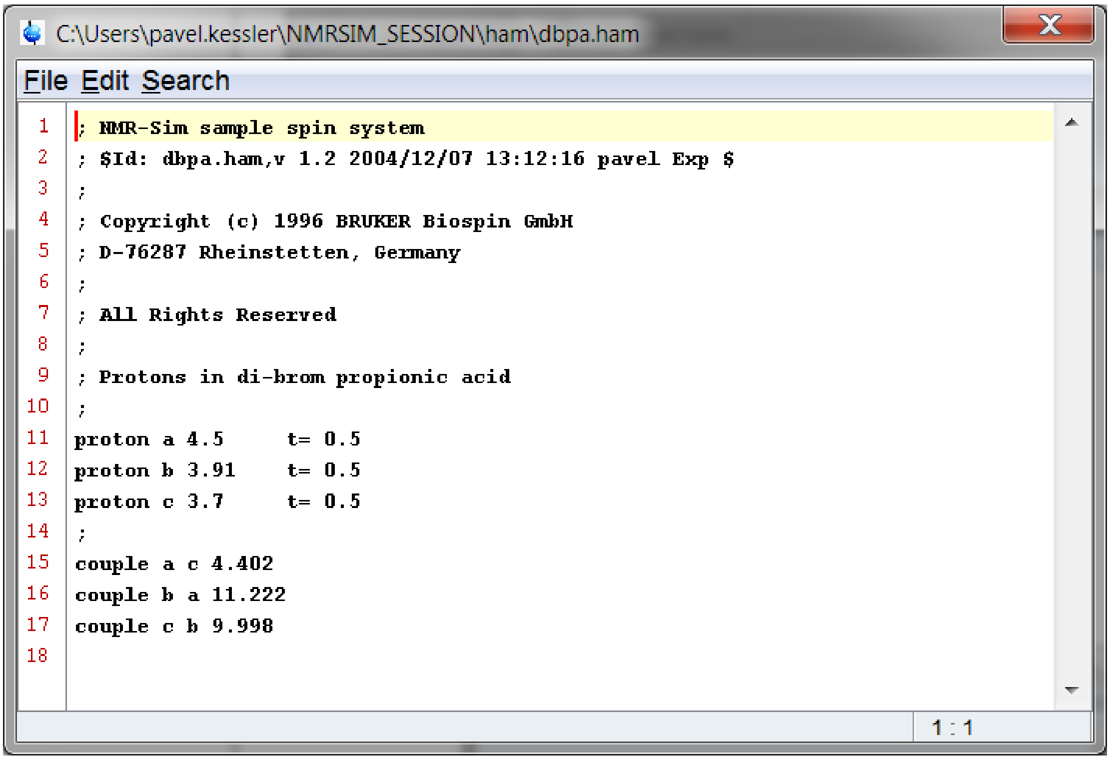
Spin system C:\Users\pavel.kessler\NMRSIM_SESSION\ham\ethanol.mol

Select or move atoms New structure C2 H6 O MW: 46.069

Figure 3.7: Editing the Spin System: The Molecular Structure Editor

Please refer to the structure editor documentation for further details (“Structure Analysis Tools”, chapter “2D Structure Editor”).

The built-in text editor uses the same user interface as any TopSpin text editor.



```
; NMR-Sim sample spin system
; $Id: dbpa.ham,v 1.2 2004/12/07 13:12:16 pavel Exp $
;
; Copyright (c) 1996 BRUKER Biospin GmbH
; D-76287 Rheinstetten, Germany
;
; All Rights Reserved
;
; Protons in di-brom propionic acid
;
proton a 4.5     t= 0.5
proton b 3.91    t= 0.5
proton c 3.7     t= 0.5
;
couple a c 4.402
couple b a 11.222
couple c b 9.998

```

Figure 3.8: Editing the Spin system: The Text Editor

Chemical shifts of all nuclei in the spin system and nuclei multiplicities should be defined here. If the nuclei multiplicity is 1, it is possible to define its spin quantum number larger than 1/2. The nuclei chemical shifts are defined in ppm.

If necessary, the user can specify a different start value of the density matrix $\rho(0)$ than the thermodynamic equilibrium ρ_0.

Chemical shift parameters in the spin system description can be specified as a variable. There are 32 such variables *var1-32*, their values can be changed from the same dialog box as the general set of experimental parameters. Each Hamiltonian variable is defined by two values:

- The start value *HV1-32*.
- The step *HS1-32*. The user can change their values from the pulse sequence: it is possible to increment only one parameter (*ihv1-32*) or increment all parameters by one command (**ihc**).

The full description of spin system definition commands may be found in the chapter *Spin System Definition Summary* [▷ 49] and *New Commands* [▷ 47].

3.6 Pulse Sequence Definition

The program uses standard Bruker pulse sequences for the definition of the experiment. However, there are some restrictions and enhancements.

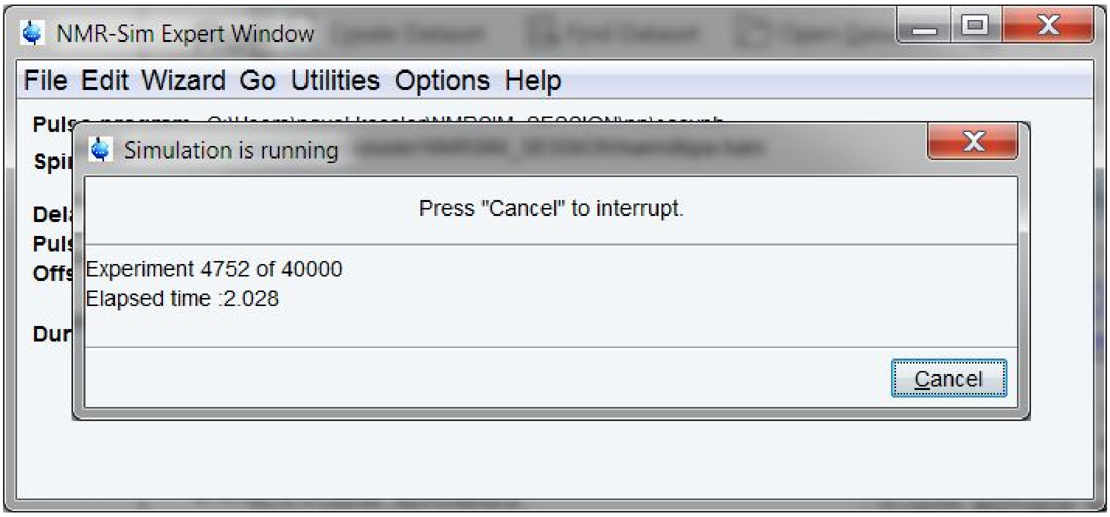
The pulse sequence is syntactically checked before the start of an experiment. In the case of errors in the sequence, the user has the possibility of editing the file with a simple editor.

The editor can be invoked from the **Edit** menu, or directly from the error message box. After opening the editor from the error message box, the cursor placed on the line with the syntax error and the whole line is highlighted.

If the user starts the simulation using the command **Go** or **Check Parameters & Go**, they are asked for the value of all parameters (pulse and delay lengths, RF intensities...), which are used in the sequence.

3.7 Running the Simulation

After starting the simulation from the NMRSim menu a progress dialog is shown.



Press "Cancel" to interrupt.

Experiment 4752 of 40000
Elapsed time :2.028

The **Cancel** button interrupts the simulation, the program finishes the phase cycle and the data will be saved on the disk.

The information about the current state of the running experiment is displayed in two lines below the menu bar. The first line, the **Experiment counter** is incremented when the acquisition command finishes the last transient (scan). The limit displayed is identical to the TD1 variable. The bottom line of the progress dialog shows the elapsed time for the current calculation.

Simulated data are written to disk and immediately processed and displayed in TopSpin (we assume that the TopSpin option “Enable automatic data processing” is on).

This automatic cooperation between the simulation program and processing software combines them in a software-only based Bruker spectrometer.

4 Bloch Simulator

The command **Utilities**/**Bloch** module in the main NMRSim menu opens a new window with its own menu bar. You may also start the Bloch simulator as a stand-alone application using the following option:

nmrsim -bloch

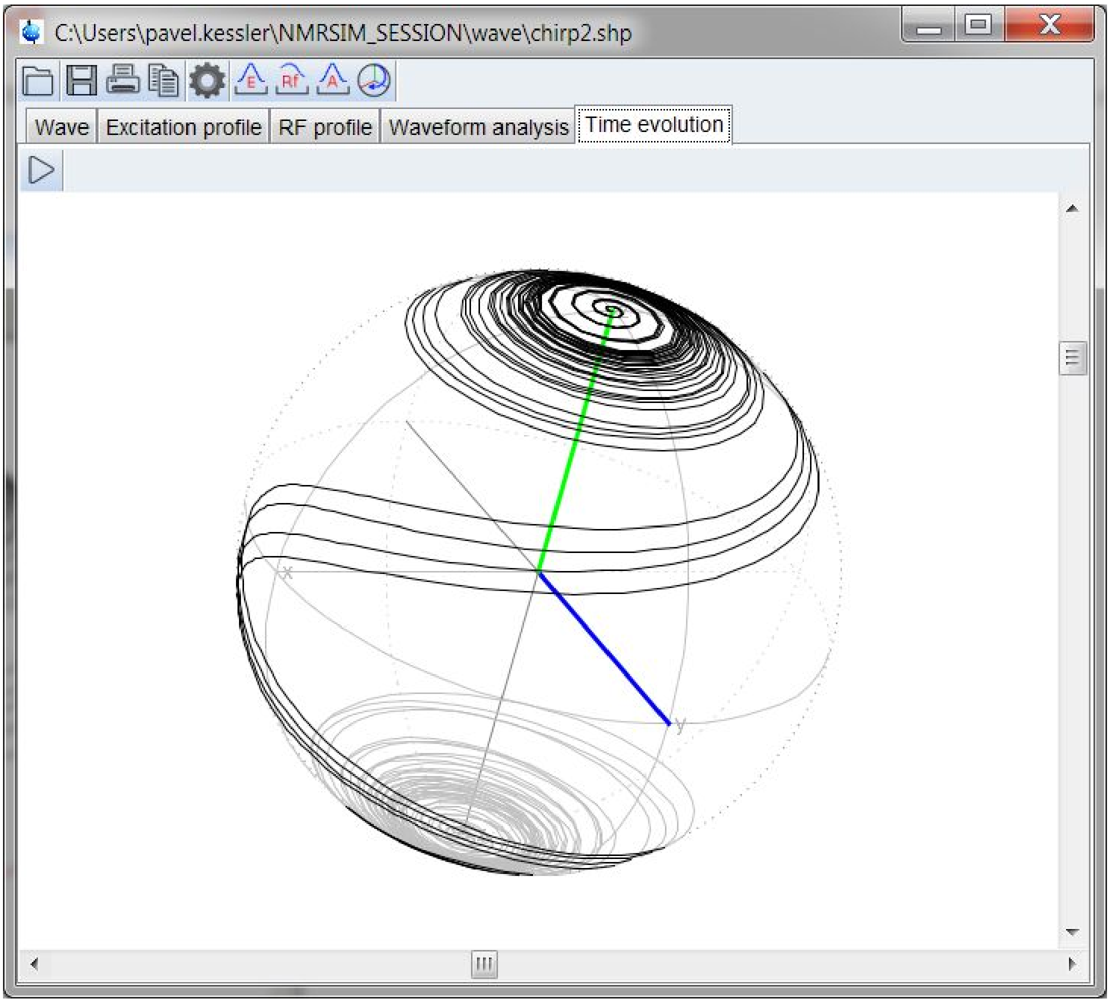


Figure 4.1: Time evolution of a nuclear magnetization vector during an adiabatic pulse calculated for several offsets, is shown as a projection on the sphere

Additional parameters **-excit_profile** and **-time_evolution** may be used to immediately start the calculation of the excitation profile, or the time evolution of the nuclear magnetization.

The stand-alone module contains only the functionality described in this chapter.

The Bloch simulator module is designed to calculate and visualize the motion of the nuclear magnetization vector during an NMR experiment. The calculation of excitation profiles and waveform analysis brings important information about the behavior of pulses or pulse sequences in a real experiment.

The motion of the magnetization vector is described by the Bloch equation:

$$\overline{\mathrm{M}} = -\gamma(\overline{\mathrm{B}} \times \overline{\mathrm{M}})$$

This is a classical equivalent of the Liouville equation for spin 1/2.

4.1 Toolbar

- Selects the waveform for the calculation. The waveform is immediately shown on the screen.
- Saves the calculated information to disk. The displayed profile or waveform analysis will always be written. This information can be imported into other programs (it is a plain text file).
- Prints the current picture.
- Copies the picture to the clipboard. Currently, only Windows supports this feature.

4.2 Calculate

The calculations are started from the corresponding icon in the Bloch module toolbar. It is also possible to start the calculation from the command line. The arguments *-excit_profile* and *-time_evolution*, combined with the *-bloch* argument, will start the calculation immediately.

Example:

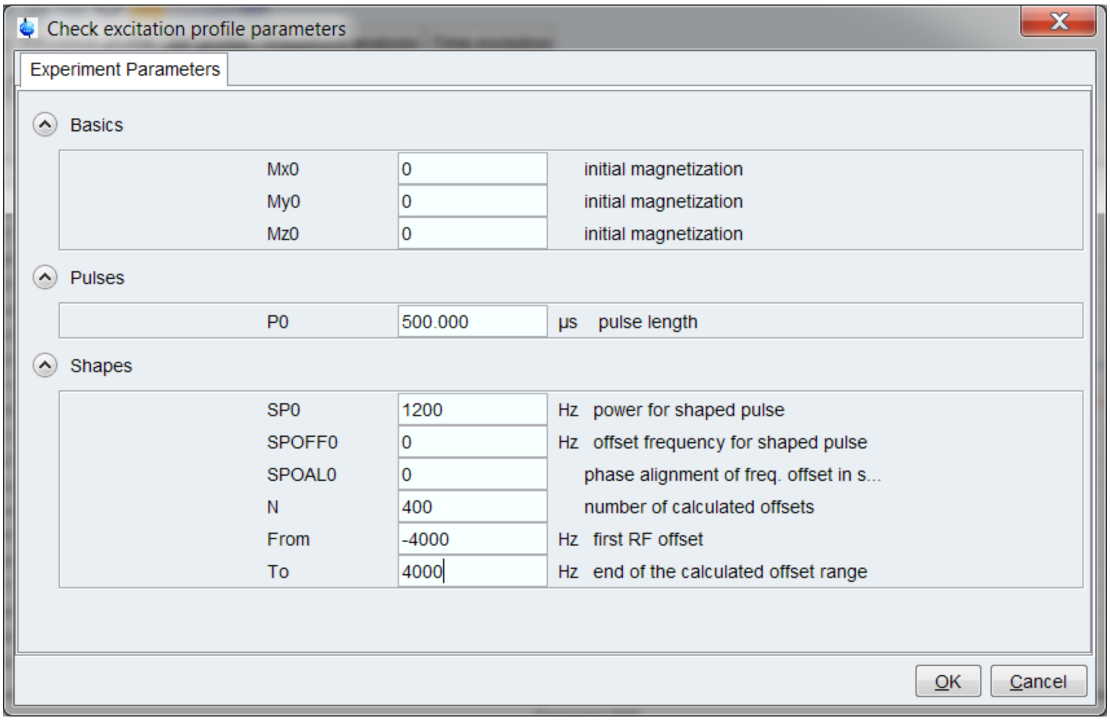
nmrsim -config chirp.cfg -bloch -time_evolution

Starts the Bloch module, loads all settings from the configuration file *chirp.cfg* and calculates the time evolution of the magnetization.

4.2.1 Time Evolution

The toolbar button starts the time evolution simulation. It calculates the motion of the magnetization vector during the pulse for several radio frequency offsets and shows it on the sphere.

The command opens a dialog box, where the following experiment parameters can be defined:



Basics

Mx0	0		initial magnetization
My0	0		initial magnetization
Mz0	0		initial magnetization

Pulses

P0	500.000	µs	pulse length

Shapes

SP0	1200	Hz	power for shaped pulse
SPOFF0	0	Hz	offset frequency for shaped pulse
SPOAL0	0		phase alignment of freq. offset in s...
N	400		number of calculated offsets
From	-4000	Hz	first RF offset
To	4000	Hz	end of the calculated offset range

Figure 4.2: Parameters for the Calculation of the Time Evolution of the Magnetization Vector

- MX(0),MY(0),MZ(0)

  The initial value of the magnetization vector. The values are later so normalized, that the vector length is 1.

  Example:

  (0,10,0) is equivalent to (0,1,0),

  (1,1,1) is equivalent to $(1/\sqrt{3}, 1/\sqrt{3}, 1/\sqrt{3})$

  The value (0,0,0) is identical to the equilibrium value (0,0,1).

The following is a list of all pulses, delays and variables that occur in the pulse program:

- SP 0

  The radio frequency field intensity for the shaped pulse.
- N

  Number of slices (offset values) which will be calculated. One slice represents the simulated experiment for one radio frequency offset.
- From

  The first value of radio frequency offset used for the calculation.
- To

  End of calculated offset range.

The result of the calculation is shown using spherical coordinates. The scroll-bars on the bottom and on the side of the window may be used to adjust the angle of view. Double-clicking with the mouse on the sphere restores the original angle of view.

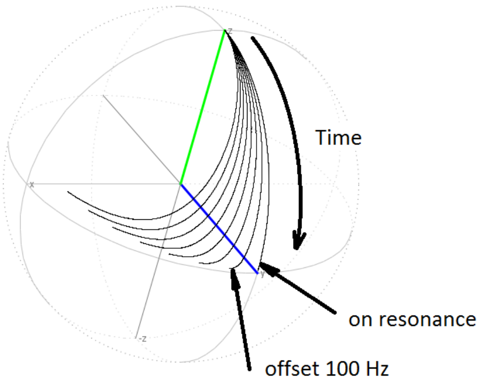
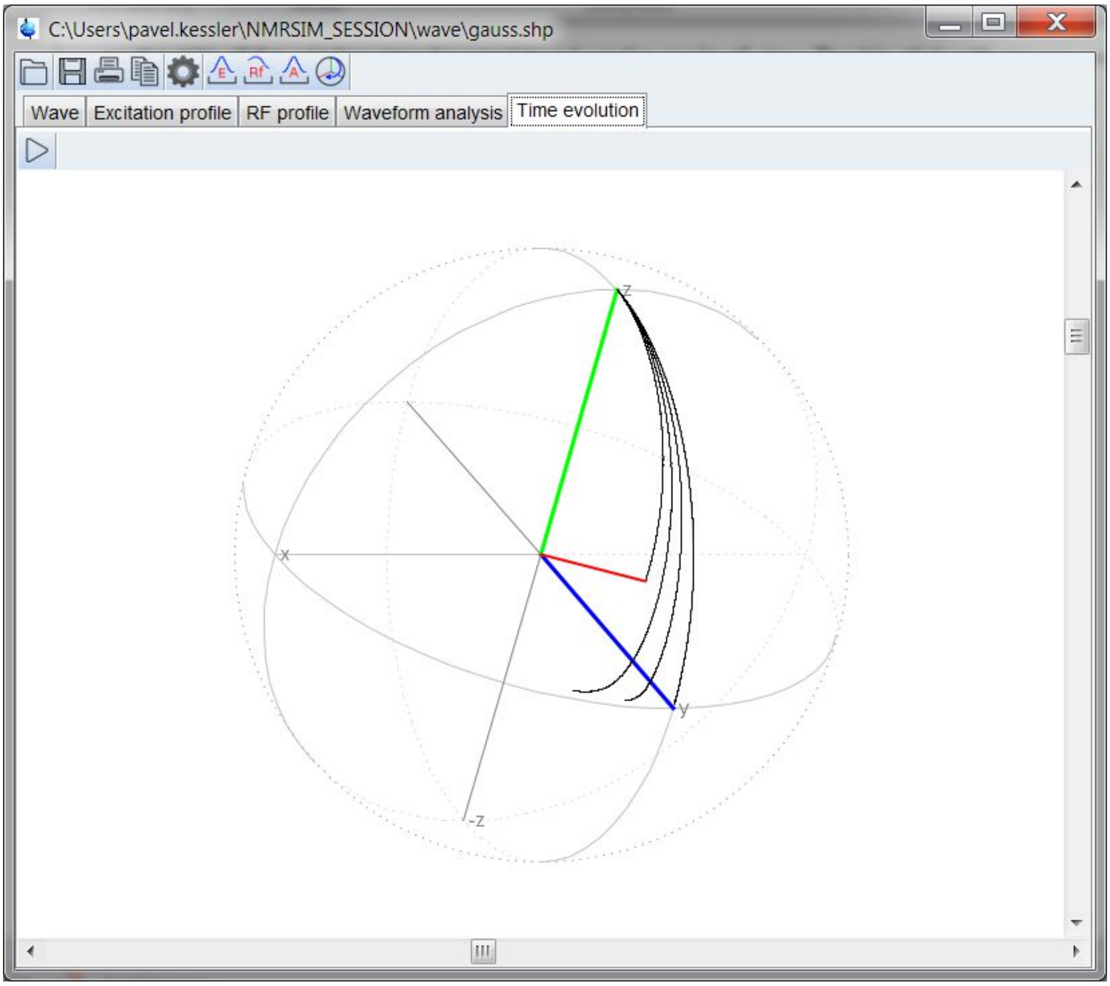


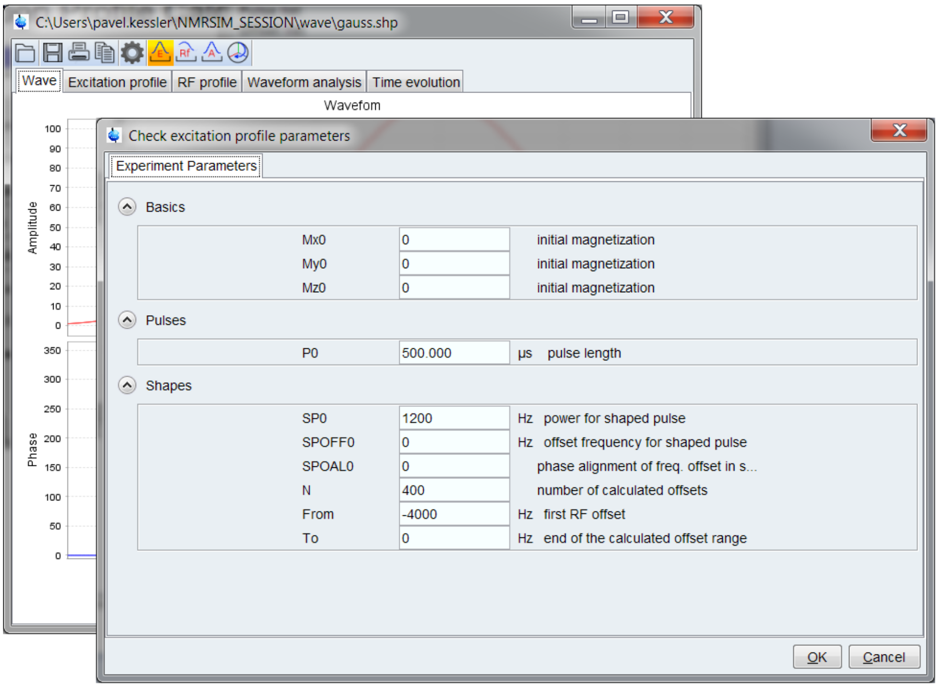
Figure 4.3: The Time Evolution of the Magnetization Vector Shown as a Projection on the Sphere

The button ▷ starts (or stops) a movie – the movement of magnetization vector is shown.



4.2.2 Excitation Profile

The button opens the calculation of the excitation profile of a shaped pulse.



C:\Users\pavel.kessler\NMRSIM_SESSION\wave\gauss.shp

Check excitation profile parameters

Experiment Parameters

Basics

Mx0	0		initial magnetization
My0	0		initial magnetization
Mz0	0		initial magnetization

Pulses

P0	500.000	µs	pulse length

Shapes

SP0	1200	Hz	power for shaped pulse
SPOFF0	0	Hz	offset frequency for shaped pulse
SPOAL0	0		phase alignment of freq. offset in s...
N	400		number of calculated offsets
From	-4000	Hz	first RF offset
To	0	Hz	end of the calculated offset range

Figure 4.4: Parameters for the Excitation Profile Calculation

The parameters are the same as for the time sequence. The window layout changes and the calculated excitation profile is shown.

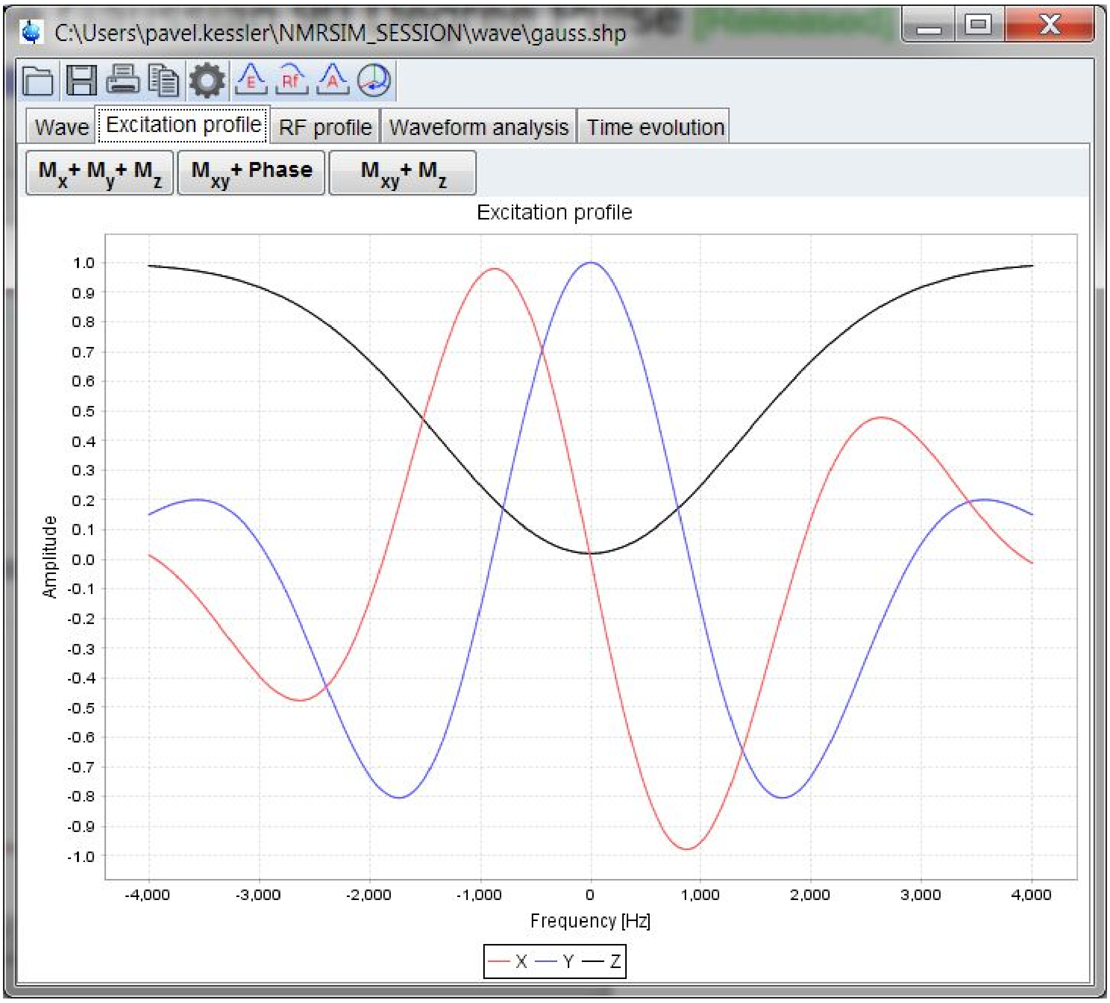
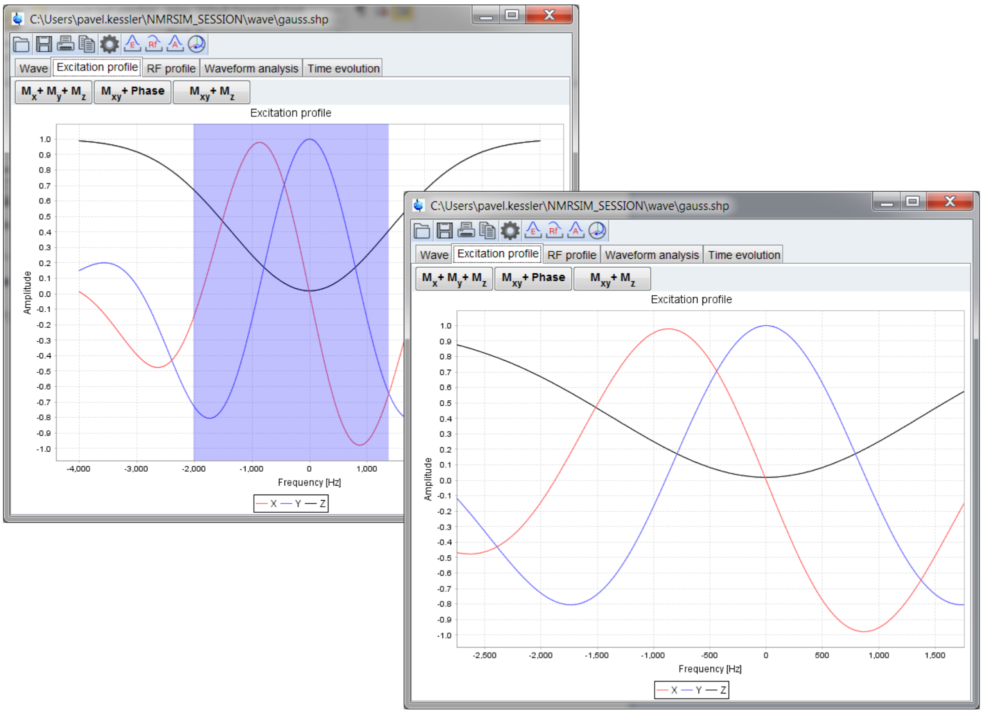


Figure 4.5: The Excitation Profile of the Gaussian 90 Degree Pulse

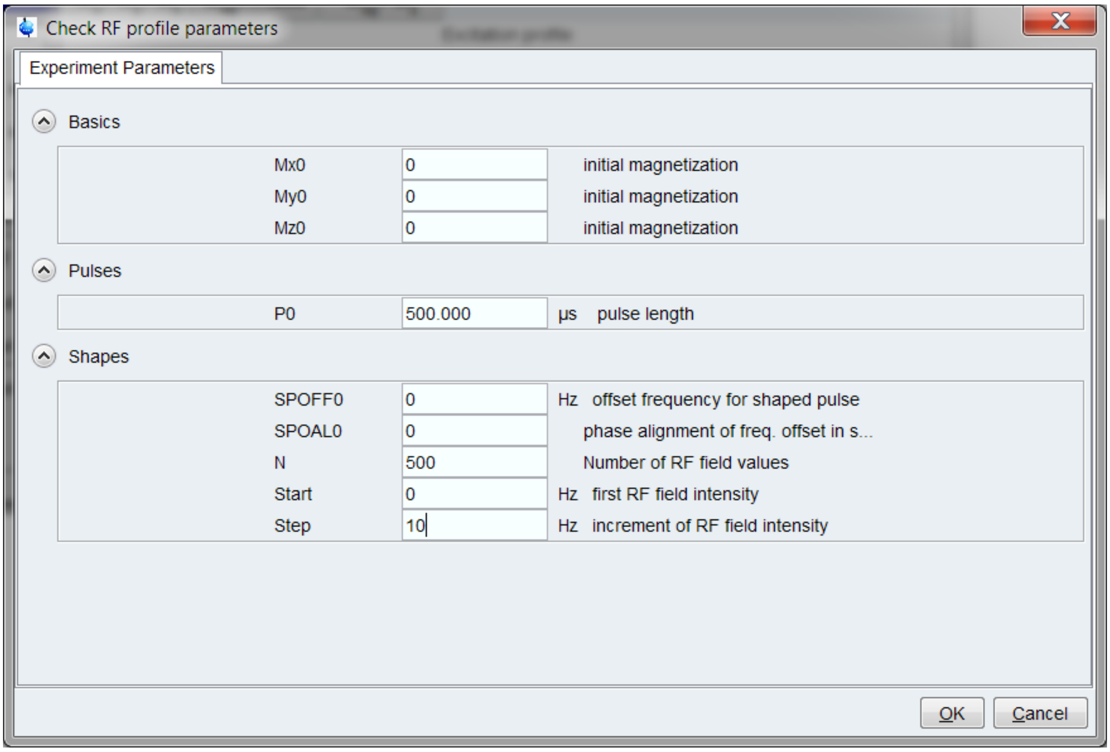
The buttons on the top of the window allow you to select the visible component.

A mouse can be used to zoom in a part of the displayed graphics, a double-click returns you back to the overview.



4.2.3 RF Field Profile

The RF filed profile command calculates the dependency of the magnetization on the RF filed intensity. You can define the pulse length, the RF offset, the starting value of used radio frequency filed, number of calculated points and the step:



Basics

Mx0	0	initial magnetization
My0	0	initial magnetization
Mz0	0	initial magnetization

Pulses

P0	500.000	µs	pulse length

Shapes

SPOFF0	0	Hz	offset frequency for shaped pulse
SPOAL0	0		phase alignment of freq. offset in s...
N	500		Number of RF field values
Start	0	Hz	first RF field intensity
Step	10	Hz	increment of RF field intensity

Figure 4.6: Parameters Used for the Calculation of Radio Frequency Profiles

The calculated profile is shown as a dependency of magnetization components on the RF field intensity.

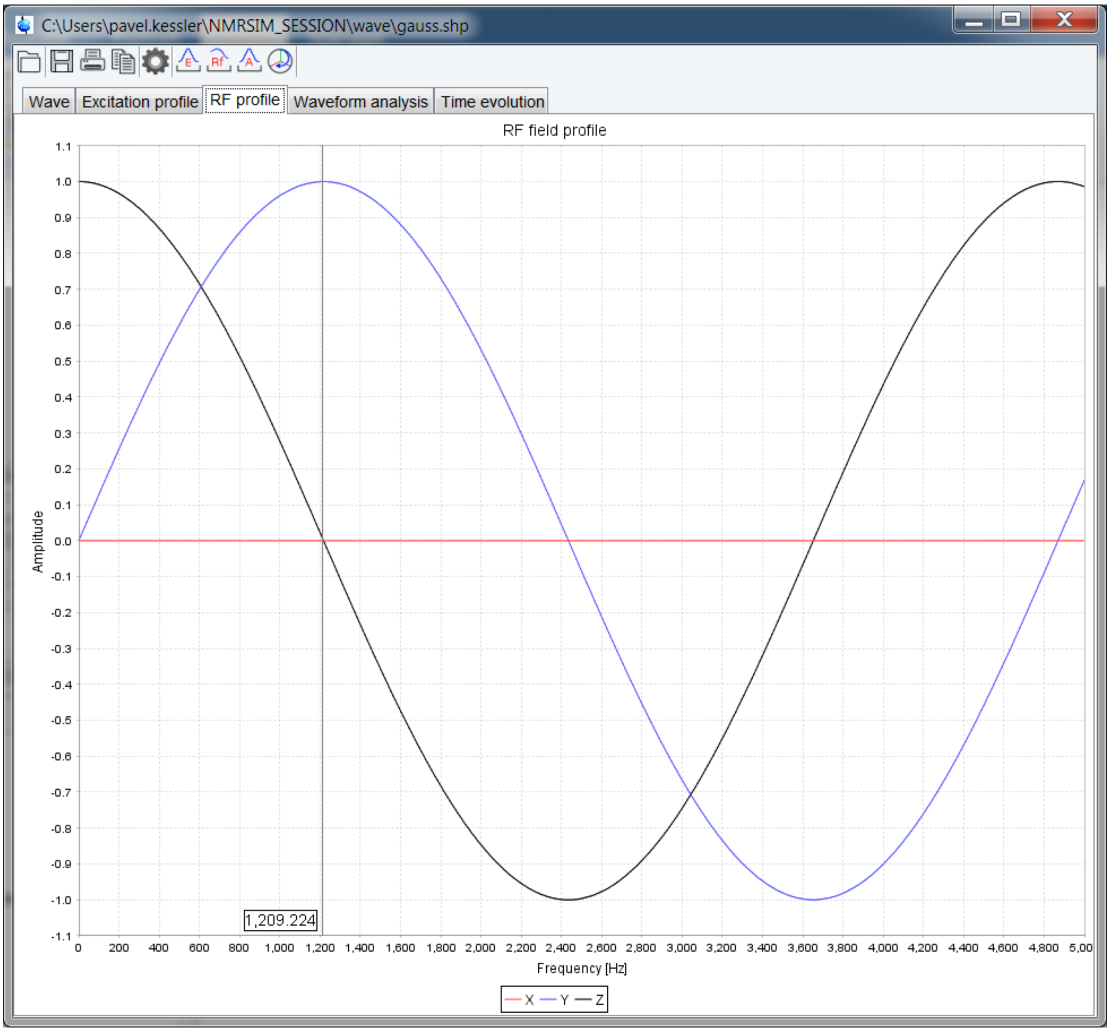
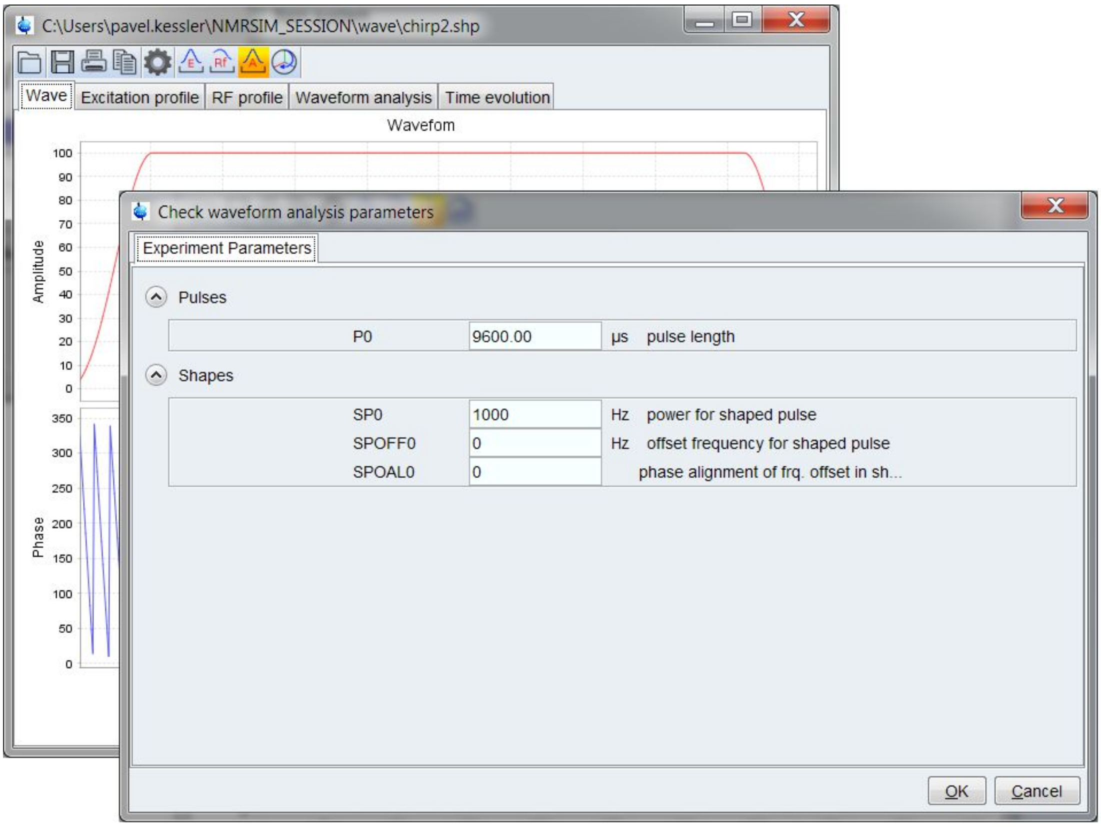


Figure 4.7: Calculated Radio Frequency Profile.

The RF field for a 500 ms 90 degree pulse is about 1209 Hz.

4.2.4 Waveform Analysis

The command **Calculate/Waveform analysis** is used to analyze features of adiabatic pulses.

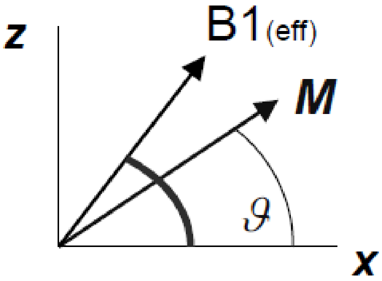


P0	9600.00	µs	pulse length
SP0	1000	Hz	power for shaped pulse
SPOFF0	0	Hz	offset frequency for shaped pulse
SPOAL0	0		phase alignment of frq. offset in sh...

Figure 4.8: Parameters Used for the Waveform Analysis.

The program requires the pulse length, the RF intensity and the offset of the examined pulse and calculates following output:

- Φ_M and Φ_{Bleff} are the angles between the magnetization or B_{1eff} vectors and the **xy** plane



The definition of the adiabatic condition requires that the magnetization vector M follows the trajectory of the effective radio frequency field vector B_{1eff}.

- Quality factor
- Frequency sweep.

The following figure show the same pulse analyzed under two experimental conditions - on resonance and off resonance. The on resonance picture shows very good adiabatic condition, the off resonance case shows rising misalignment between the magnetization and RF field vectors - the adiabatic condition is no longer valid.

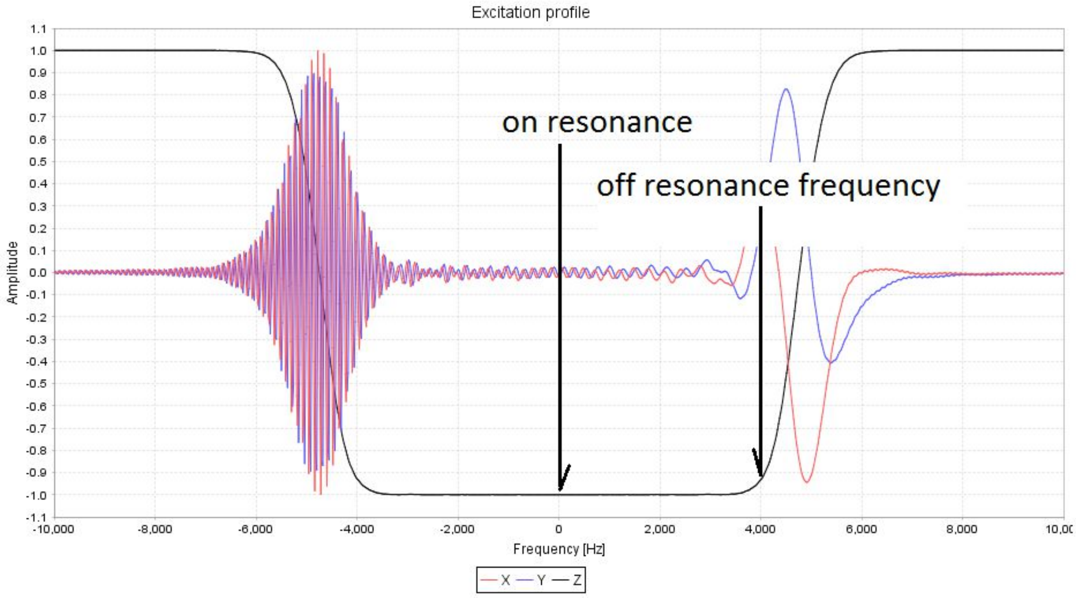


Figure 4.9: Excitation Profile

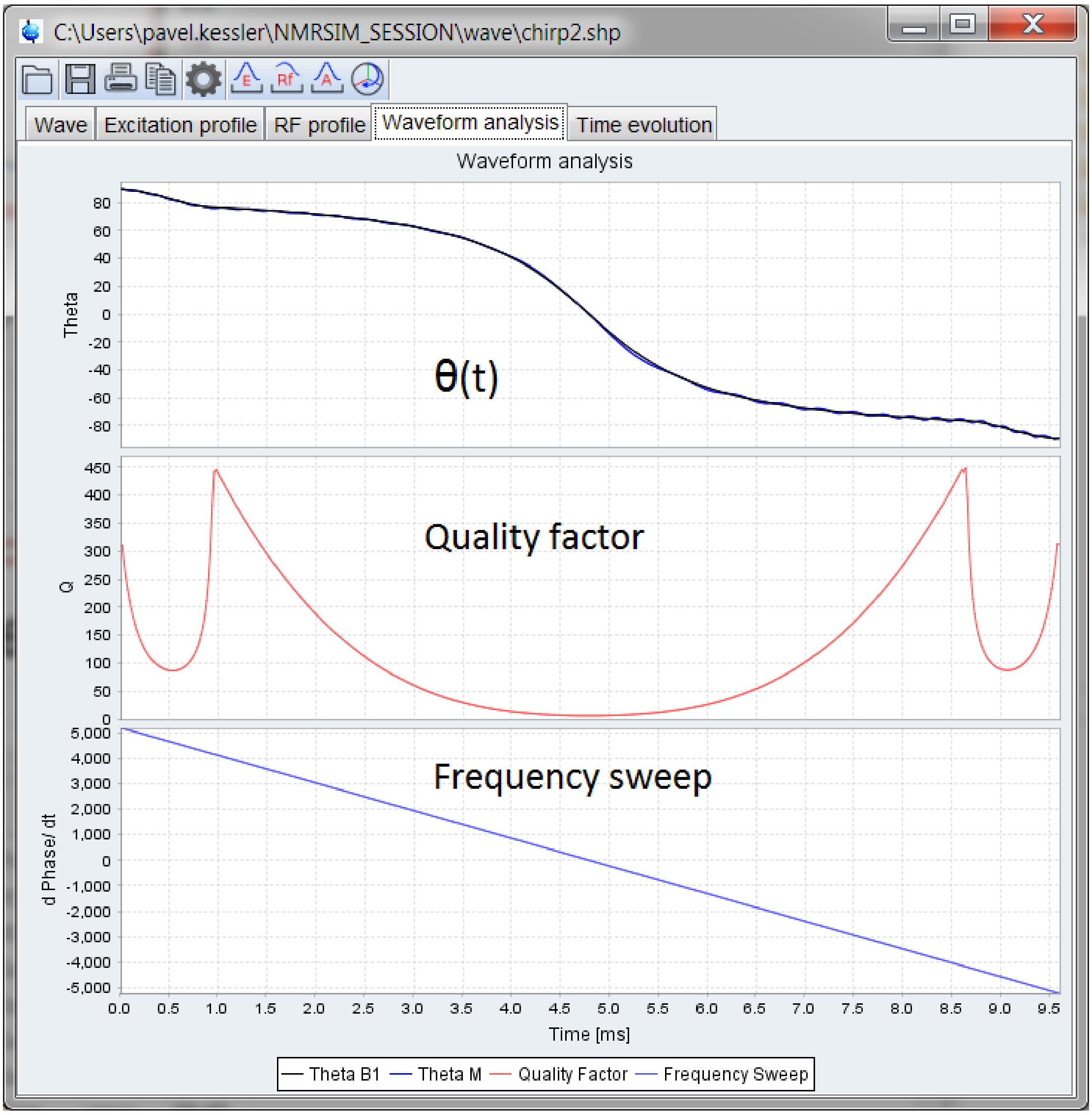


Figure 4.10: On Resonance

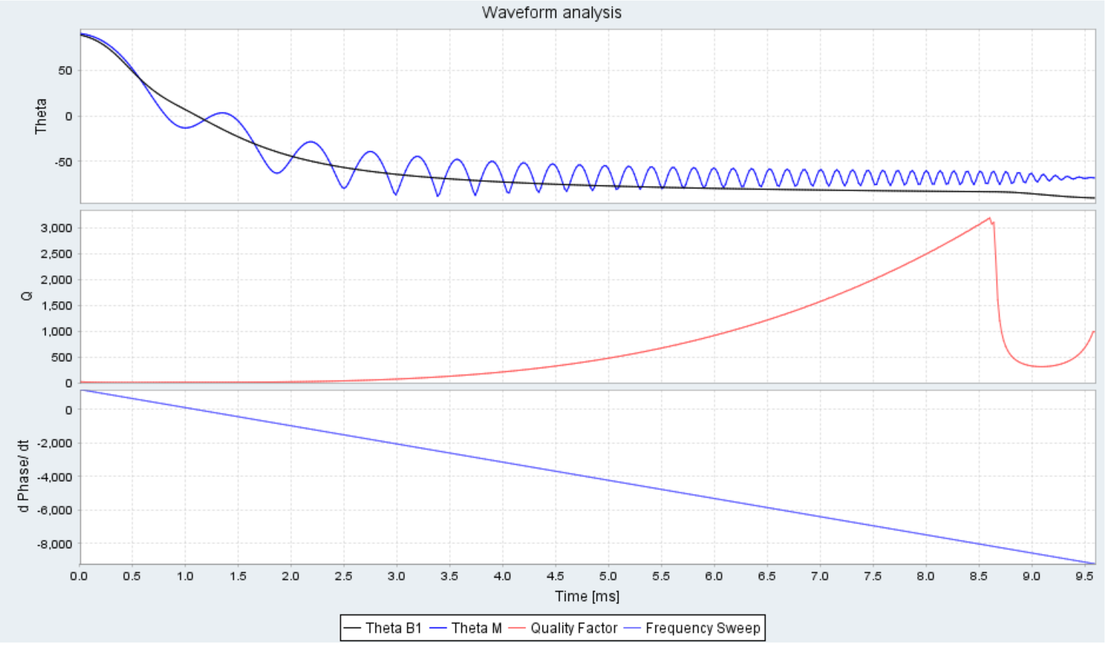


Figure 4.11: Off Resonance, the Adiabatic Condition is Violated

4.3 Examples

There are two predefined configuration files which may be used to start your own work with this part of program: *bloch.cfg* and *chirp.cfg*.

Load the configuration saved in the *bloch.cfg* (use the main menu command **File**/Load **Experiment Setup…**) and calculate the excitation profile. The result is shown in the next figure. The picture was copied into the MS-Windows clipboard and pasted into this document

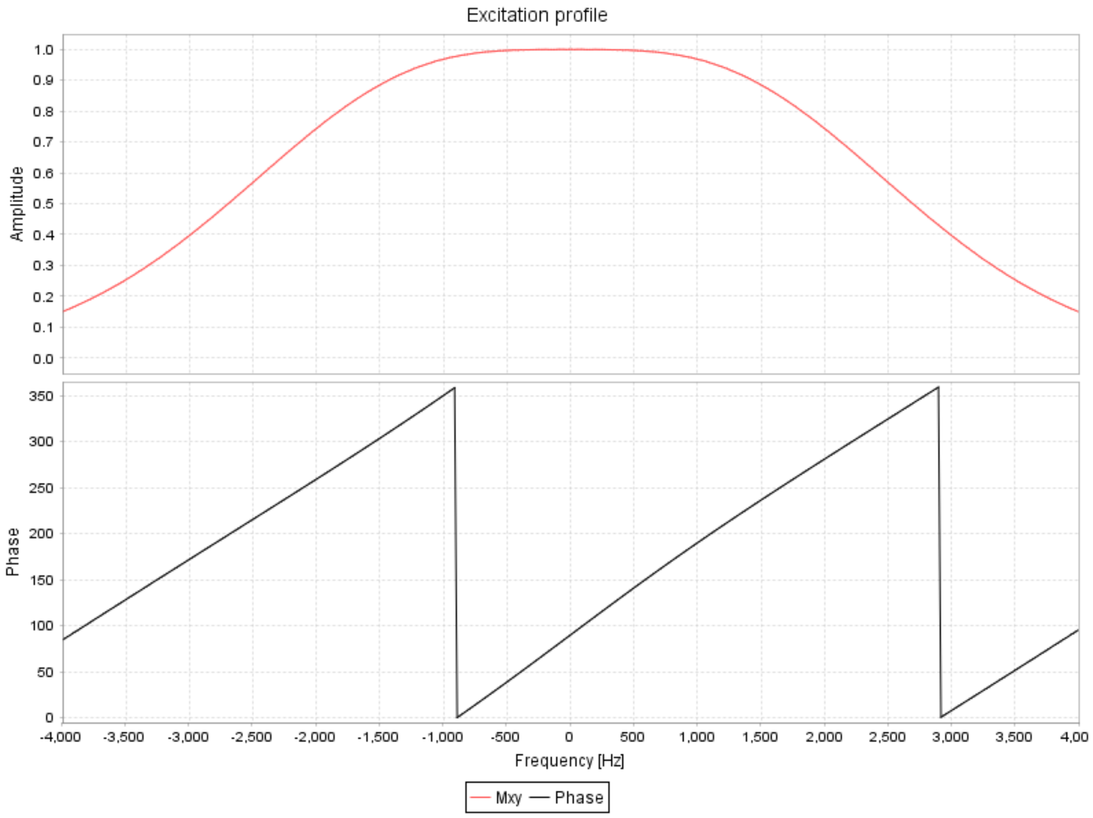
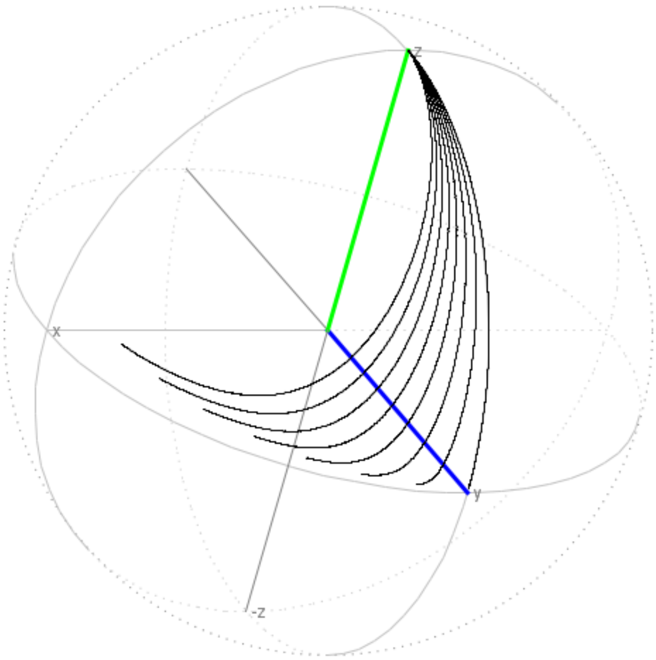


Figure 4.12: Excitation Profile of Shaped Gauss Pulse.

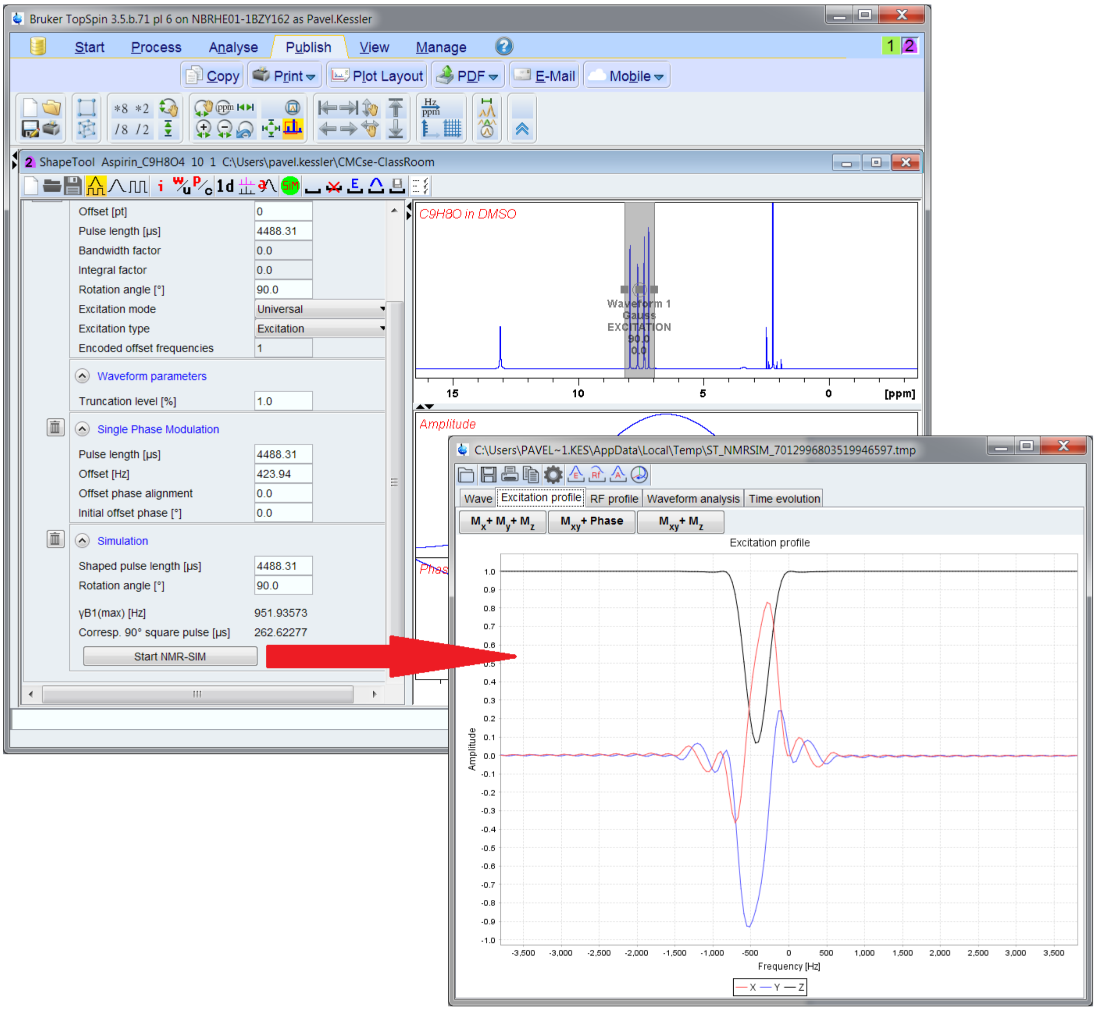


The time evolution calculation shows trajectories of the magnetization for a gaussian 90 degree pulse

4.4 Waveform Analysis using the TopSpin Shape Tool

The Shape Tool is the standard tool for the definition and manipulation of waveforms in TopSpin. You can start it using **stdisp** command on the TopSpin command line. The button **Start NMR-Sim** opens the Bloch simulator window and shows the excitation profile of your pulse.

You may now use all Bloch module functionality to investigate the features of your pulse.



Offset [pt] 0
Pulse length [µs] 4488.31
Bandwidth factor 0.0
Integral factor 0.0
Rotation angle [°] 90.0
Excitation mode Universal
Excitation type Excitation
Encoded offset frequencies 1

Waveform parameters

Truncation level [%] 1.0

Single Phase Modulation

Pulse length [µs] 4488.31
Offset [Hz] 423.94
Offset phase alignment 0.0
Initial offset phase [°] 0.0

Simulation

Shaped pulse length [µs] 4488.31
Rotation angle [°] 90.0
γB1(max) [Hz] 951.93573
Corresp. 90° square pulse [µs] 262.62277

Start NMR-SIM

Figure 4.13: TopSpin Shape Tool and Bloch Simulator Windows.

5 Pulse Program Display

The command **Utilities/Show pulse program** in the main NMRSim menu opens a new window, which shows the selected pulse program in a graphical form.

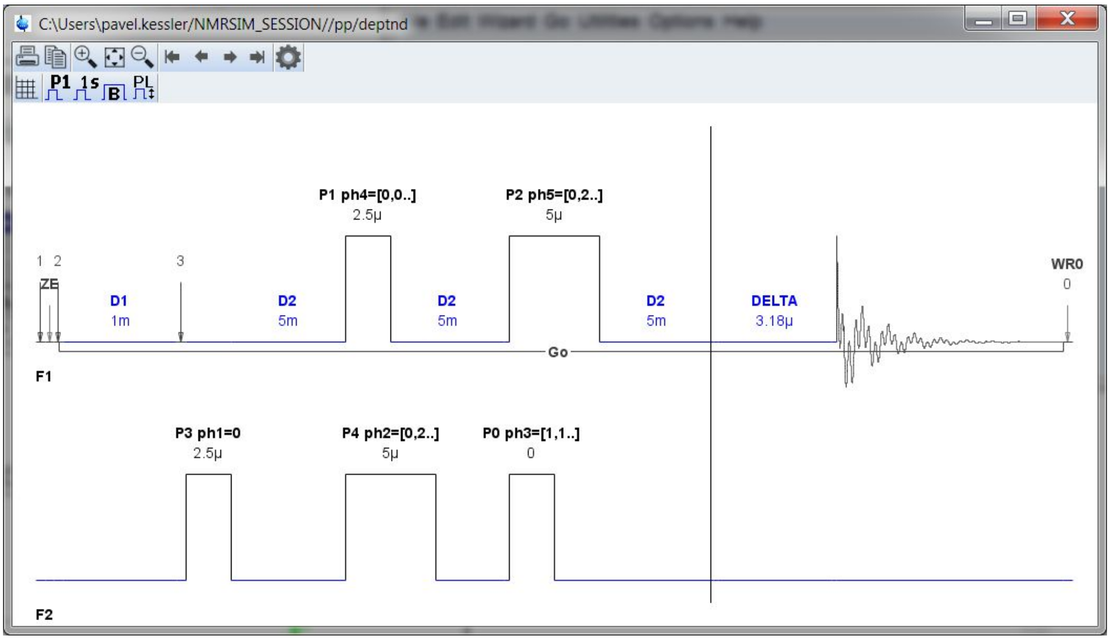


Figure 5.1: Window with the Pulse Program Scheme

The pulse programs are shown in a symbolic form, i.e. the lengths of pulses and delays do not represent the actual durations, but they use artificial proportions which make the pulse program more understandable.

The pulse program display may be also started as a stand-alone application using the command:

nmrsim -showp <pulse program name>

This command opens a pulse program display window without any simulation functions. Here is possible to start any number of copies of the stand-alone display (the NMRSim program may be started for each user only once).

An equivalent command is also available directly from TopSpin:

- *spdisp <pulse program name>*

  Displays the pulse program.
- *spdisp*

  Reads the pulse program name from the current data set.

Pulse Program Display

You may also switch to the **Pulse Program** tab in the TopSpin data set window and press the **Graphical Pulse Program Display** button:

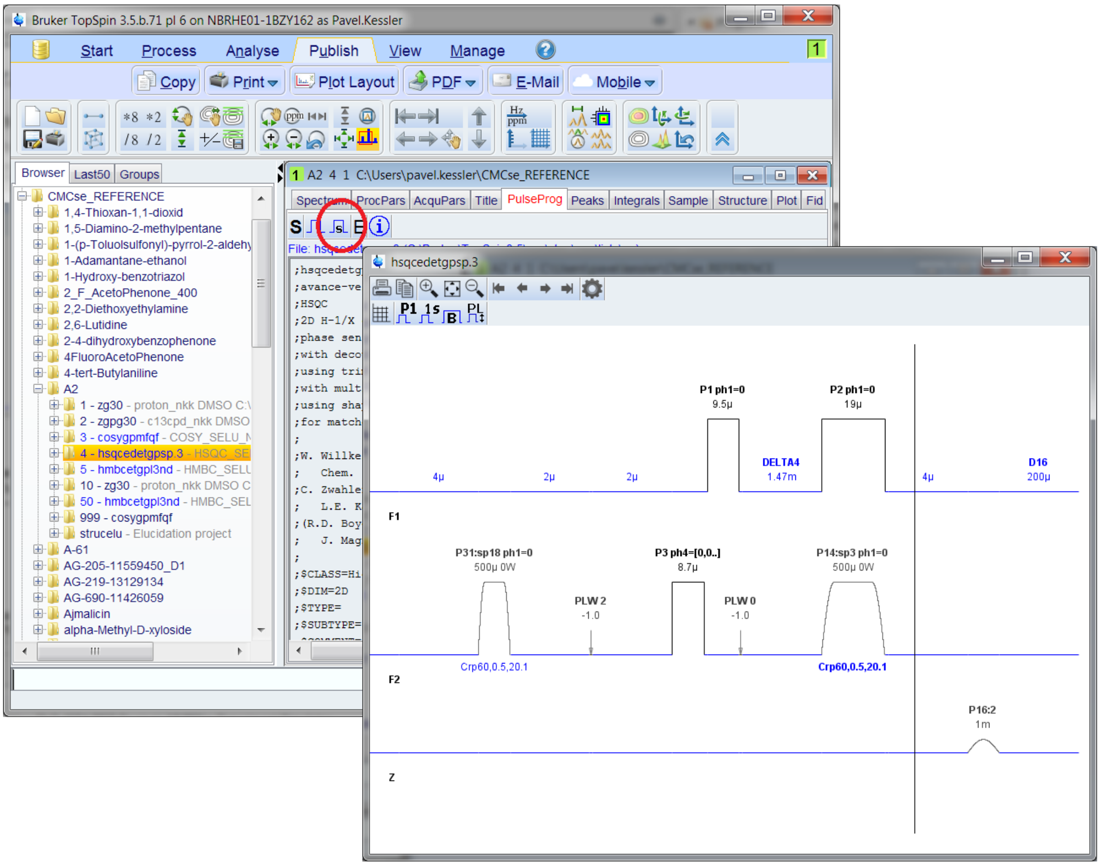


Figure 5.2: Pulse Program Display from TopSpin PulseProg Table

The buttons on the top of the pulse program window and the scroll bar on the bottom can be used to zoom and scroll the pulse program display.

You may also zoom using the mouse. The procedure is the same as zooming in TopSpin: press the left mouse button on the start of zoomed area and drag the mouse to the end. The expanded area is highlighted by two vertical cursor lines and middle thick line:

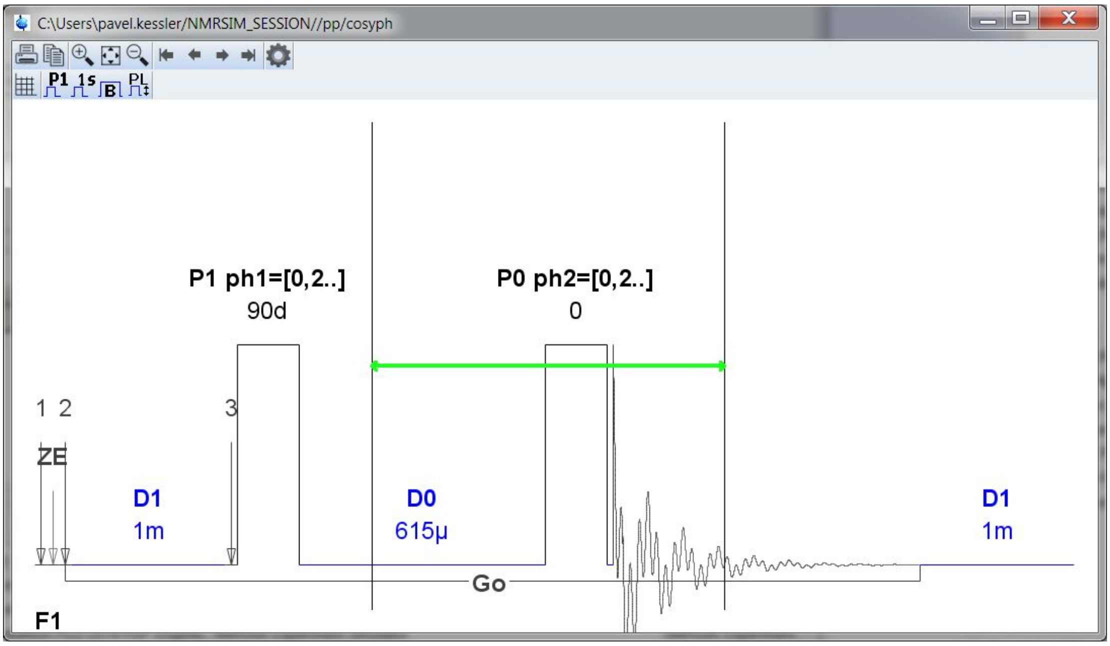


Figure 5.3: Releasing the left mouse button displays the selected part of pulse program.

- Selects the pulse program for the calculation. An alternative selection method is to use drag & drop:

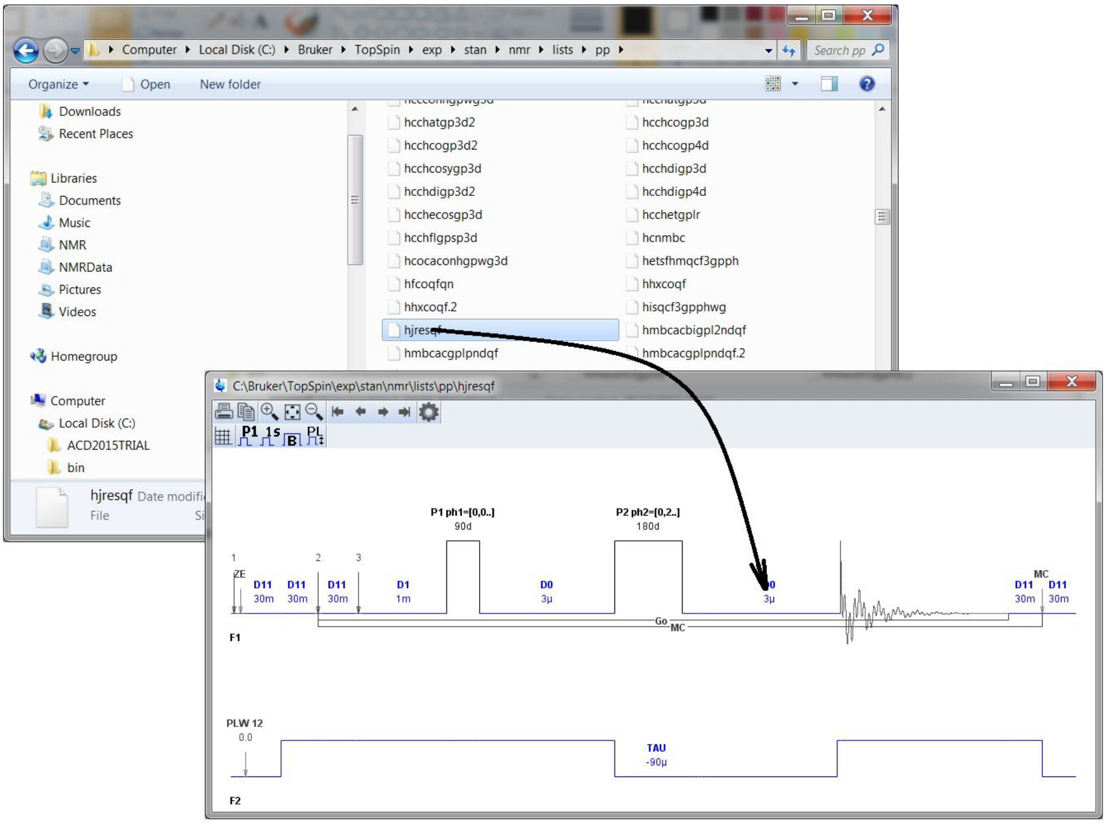


Figure 5.4: Pulse Program Display Window with the MS-Windows Explorer Window in Background.

- Saves the calculated information to disk. The displayed profile or waveform analysis will always be written. This information can be imported into other programs (it is a plain text file).
- Prints the current picture.
- Copies the picture to the clipboard. Currently, only Windows supports this feature.
- ⚙ The display options.
- You may select channels visible in the pulse program display and toggle between the external window and TopSpin internal frame for the pulse program display.

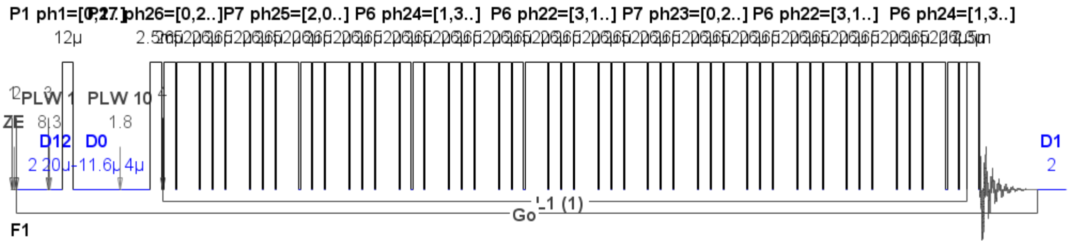
5.1 Display Control

The 2nd toolbar row controls the display features.

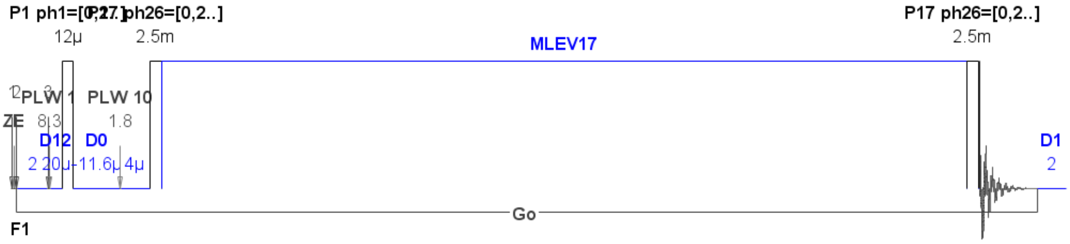
- Switches the grid lines in the pulse program display. The grid lines between different channels connect synchronous points in the pulse program. This is an important feature for the visualization of “pulse trains”. A pulse train is a parallel asynchronous execution of pulses and delays in two or more channels (see *Pulse Trains, Virtual Channels [▸ 44]*).
- P1 Toggles the display of pulse and delay names.
- 1s Parameter Values

  Toggle the display of parameter values.

- B Toggles the display of blocks in pulse programs. Blocks in pulse programs need to be annotated in the pulse program text. Typical example is the MLEV mixing sequence:



- Toggling the display of blocks radically simplifies the display:



- PL Pulse height

  Controls how the pulse program display shows the pulse height.

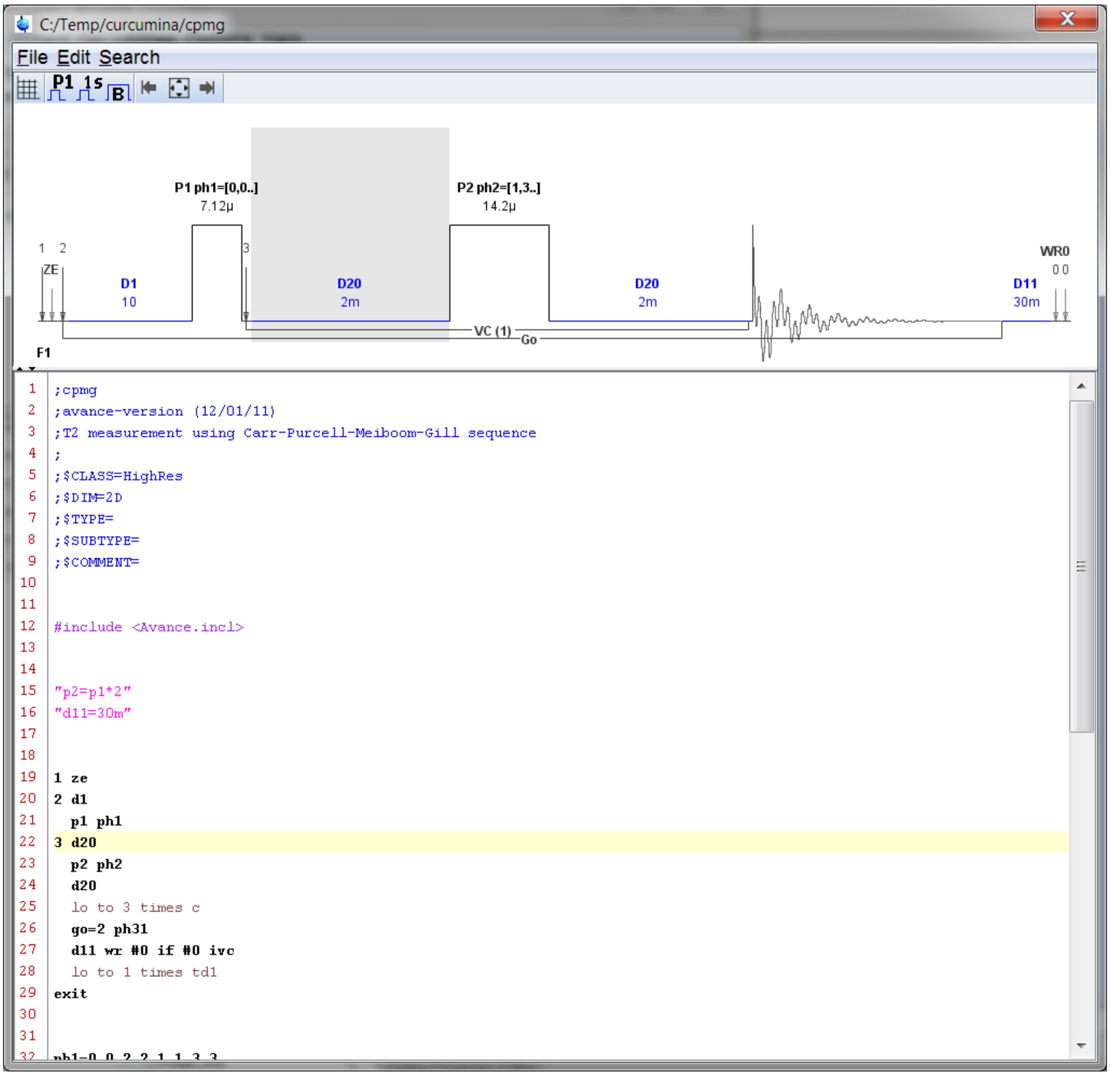
  Constant - all pulses have the same height.

  Proportional to power level - the program uses following formula to calculate the pulse height.

```
if(powerLevel < 20 dB)
height = exp(-(powerLevel+6)*0.0266595);
else
height = 0.7598*exp(-(powerLevel+6)*0.0160944);
```

5.2 Pulse Program Text Editor

NMRSim couples the pulse program text editor to the pulse program display.



```
;cpmg
;avance-version (12/01/11)
;T2 measurement using Carr-Purcell-Meiboom-Gill sequence
;
;$CLASS=HighRes
;$DIM=2D
;$TYPE=
;$SUBTYPE=
;$COMMENT=


#include <Avance.incl>


"p2=p1*2"
"d11=30m"


1 ze
2 d1
  p1 ph1
3 d20
  p2 ph2
  d20
  lo to 3 times c
  go=2 ph31
  d11 wr #0 if #0 ivc
  lo to 1 times td1
exit


ph1=0 0 2 2 1 1 3 3
```

Figure 5.5: Pulse Program Editor.

The cursor position in the text window is highlighted on the pulse program display.

The graphical display is updated after each change of the pulse program text. It is possible, that the actual version contains a syntax error. In such a case the pulse program display shows the respective error message.

5.3 Pulse Program Visualization Details

5.3.1 Spectrometer Channels

The pulse programs use spectrometer conform labels *F1..F8* and *Grad* for gradient channel. The switch *F1 bottom* defines the position of the *F1* channel, either on the top, or on the bottom of display. Visible channels may be selected in the display options dialog.

5.3.2 Pulse Trains, Virtual Channels

A pulse train is a part of the pulse program, executing several pulses or delays simultaneously on one or more channels.

The pulse program *colocqf* contains the following line:

```
(d6):f1 (d0 p4 ph2):f2 (d0 p2 ph4):f1
```

There are two independent fragments which are executed on the same channel *F1*. In such a case NMRSim creates one additional *virtual* channel which allows the overlapping pulses and delays to be split visually.

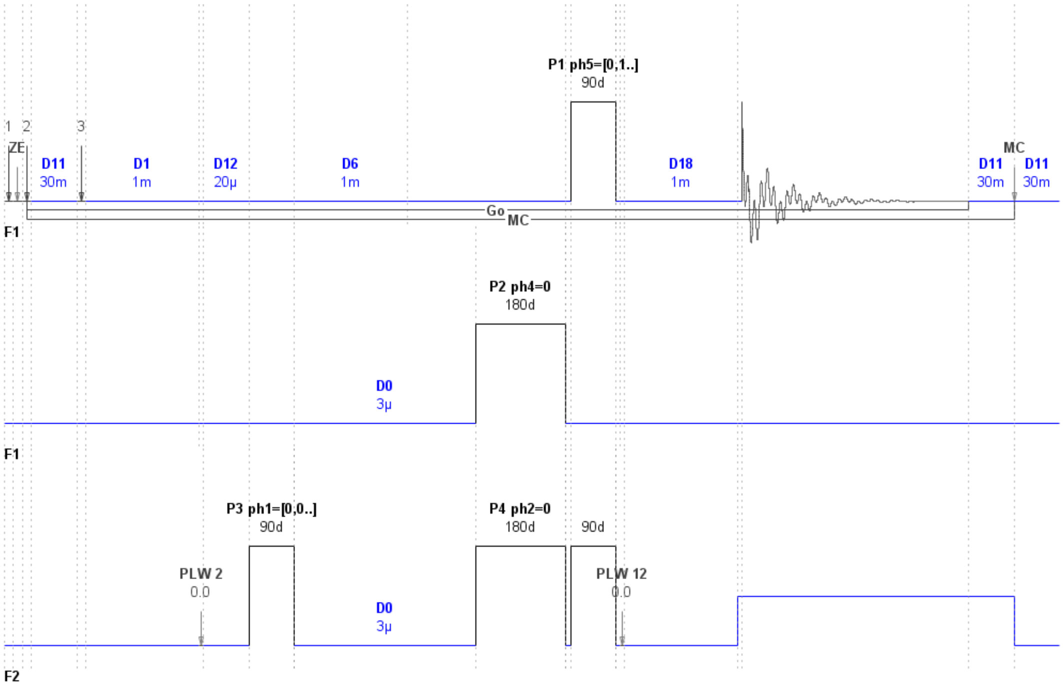


Figure 5.6: Example of a Virtual Channel.

6 Pulse Programs

This section contains the information about Bruker pulse program language implementation in the NMRSim program. A complete description of Bruker pulse program syntax is included in the TopSpin documentation.

6.1 Pulse Program Commands Implemented in NMRSim

NMRSim implements all substantial commands necessary for pulse program execution. All trigger commands, and commands used to set spectrometer control words, are ignored. The pulse program display and the pulse program interpreter support only four radio frequency channels.

6.2 Decoupling

Only simple, ideal decoupling have been implemented. Any decoupler command (e.g. **cpd**, **cw**, ...) switches on the total decoupling of all heteronuclear interactions, whereby participate nuclei are assigned to decoupled channel: the heteronuclear coupling are set to zero.

The interactions are restored to the original state, when the decoupler is switched off (e.g. command **do**).

Example: An H-C-O group. Setting the decoupler to the O nucleus will decouple all couplings to the oxygen, but the C-H coupling remains intact.

6.3 New Commands

- ihc, dhc, rhc

  Increments, decrements or resets all spin system variables *var1-32*. The increment or decrement step is defined by *HS1-32*.
- ihv1-32, dhv1-32,rhv1-32

  Increments, decrements or resets one spin system variable var1-32 by HS1-32.

  Example:

```
1 ze
2 p1
....
; this is not allowed !
Ihc
....
go= 2
; the end of acquisition loop
ihv1 ; increment var1 by HS1
lo to 1 times l1
```

Please note that commands manipulating the spin system variables may not be used in the acquisition loop (e.g. *ihc* in the example above).

The change of a spin system variable forces the recalculation of the spin system Hamiltonian and its eigenvalues. This means that the resonance frequencies in the spectrum may change! Such an operation does not make any sense in the acquisition loop. It will not crash the calculation, but you will get false results!

The change of a spin system variable after the **go=** command allows you to efficiently simulate the experiment dependency on the spin system parameters.

- sample

  This command is used in the Bloch simulator for the sampling of magnetization values.

7 Spin System Definition Summary

In this chapter all the commands used for the definition of spin systems will be summarized. The spin system description has the same role in the simulation as the sample does for the real experiment.

The nuclear spin system is defined using a simple language. The definition is based on a plain text file and can be edited using any ASCII text editor such as Notepad. However, NMRSim implements a simple editor to do this.

7.1 Syntax

Each line contains at most one command. The lines starting with a semi-colon (;) are comments, the language does not discriminate between upper and lower case. The following predefined commands are available:

- Nucleus or isotope name
- Couple
- Weak
- Dipolar
- Qpolar
- Add
- Molecule
- Endmol

It is also possible to use the C language preprocessor macro definitions and conditional expressions.

7.1.1 Nucleus

The **nucleus** command has the following syntax with each parameter separated by one or more spaces (the fields in square brackets are optional):

nucleus [multiplicity *] label [spin number] [isotope] chemical shift [relax. time]

- label

  This is an arbitrary label denoting a particular nucleus. The maximum length is 31 characters.

- isotope

  This is a label denoting the isotope. The defined isotopes are listed in table the table below:

Symbol	Isotope	Name	Spin	g
h1	proton	proton	1/2	1
d2	deuterium	deuterium	1	0.15351
li6	lithium 6	lithium6	1	0.14717
li7	lithium 7	lithium7	3/2	0.38866
b11	bor 11	bor11	3/2	0.32809
c13	carbon 13	carbon	1/2	0.25144
n14	nitrogen 14	nitrogen14		
n15	nitrogen 15	nitrogen	1	0.10133
f19	fluorine 19	fluorine	1/2	0.94077
si29	silicon 29	silicon	1/2	0.19867
p31	phosphor 31	phosphor	1/2	0.40481
y89	yttrium 89	yttrium		
rh103	rhodium 103	rhodium		
sn115	tin 115	sn115		
sn117	tin 117	sn117		
sn119	tin 119	sn119		
yb171	ytterbium 171	yb171ytterbium		
hg199	mercury 199	hg199mercury		

Table 7.1: Nuclear isotopes defined in the NMRSim program.

- chemical shift

  This parameter shows the chemical shift in ppm units. The acquisition parameter SF is used to define the spectrometer frequency, which is used to convert the values in ppm to absolute frequency:

  ω = (offset+1)*SF*γ

  Instead of writing the number, you could use the spin system variable symbol *var1..32* or the pulse program constants cnst0..63.

  The nuclear chemical shift can be also defined in absolute units - Hz. To do that, you must specify the unit Hz after the value of chemical shift.

  Example:

```
proton p1 350.5 Hz
proton p22 6 ; 6 ppm
proton atom22 var1
proton d cnst11
```

- multiplicity

  An integer number denoting the multiplicity of nucleus (spin equivalence). The maximum allowed value is 4, the default value is 1. This parameter is not allowed for nuclei with spin quantum numbers greater than 1/2.
- spin number

  Defines the spin quantum number of the nuclei. The following values are available:

  j1/2, j1, j3/2, j2,

  The default value is j1/2. For spin quantum numbers greater than 1/2 the multiplicity parameter is not allowed.
- relaxation Time

  This parameter defines the relaxation times for the nucleus. The relaxation times T1 and T2 are defined in seconds with following formats and values:

  `t= value`

  T1 = T2 = value

  `t1=value`

  T1 = T2 = value

  `t2=value`

  T1 = infinity, T2 = value

  `t1=value_1 t2=value_2`

  T1 = value_1, T2 = value_2

  The default value is infinity (no relaxation). The relaxation time is used for the simulation of line widths (T2*) and for the relaxation of z magnetization (T1) when the option full relaxation is selected.

Example:

```
; 3 equivalent spin - 1/2 nuclei labeled "a"
; with a chemical shift of 3.6 ppm
nucleus 3*nuc1 3.6
;
; nucleus b has spin 3/2, shift 8.3 ppm and t1 = t2 = 0.32 s
;
nucleus b j3/2 8.3 t= 0.32
; nucleus c is C13 , we define t1 and t2
nucleus c c13 83 t1= 0.32 t2=0.1
```

7.1.2 Isotope Labels

To simplify the work with different isotopes, you may omit the command **nucleus** and use the isotope name directly. The isotope names used for the spin system definition are listed in the isotope table.

The following nuclei definitions are equivalent

```
; 3 equivalent protons labeled "a"
; with a chemical shift of 3.6 ppm
nucleus 3*a 3.6 ; default isotope is h1
nucleus 3*a h1 3.6
proton 3*a 3.6
;
; nucleus b is carbon, shift 83 ppm
;
nucleus b c13 83
carbon b 83
```

```
;
; phosphor 10 ppm
;
nucleus c phosphor 10
phosphor 10
```

We prefer to use the isotope names described here, because the spin system definition is more readable and simpler. All examples in this manual will use the isotope names and not the command **nucleus**.

7.1.3 Couple

This is the command for the full scalar coupling between two nuclei using the operator I_xS_x + L_yS_y + I_zS_z. This should be used to define all homonuclear couplings (no X approximation).

- couple nucleus1 nucleus2 coupling

  The parameters nucleus1 and nucleus2 are the spin labels, the parameter coupling is the scalar coupling constant in Hz, spin system variable or the pulse program constants *cnst0..63*.

Example:

```
couple a b 10.32
; spins a and b are coupled with J = 10.32 Hz
couple a b var1
couple a b cnst11
```

7.1.4 Weak

This command is used to define a weak scalar coupling (X approximation) between two nuclei I_zS_z. It is normally used for heteronuclear J couplings or to simplify the AX type homonuclear spin systems.

- weak nucleus_1 nucleus_2 coupling

  The parameters nucleus_1 and nucleus_2 are the spin labels, the parameter *coupling* is the scalar coupling constant in Hz, spin system variable or the pulse program constants *cnst0..63*.

Example:

```
; nuclei a and x are coupled with J = 56.2 Hz
weak a x 56.2
weak a x cnst31
weak a x var1
```

7.1.5 Dipolar

This command defines a dipolar coupling between two nuclei (only energy conserving parts of the dipolar Hamiltonian are implemented).

$H_{DD}=J_D(I_z*S_z-(I_x*S_x+I_y*S_y)/4)$

The dipolar coupling JD also includes the geometrical factor $(3\cos(\theta)^2 -1)/r^3$.

- dipolar nucleus_1 nucleus_2 coupling

  The parameters nucleus_1 and nucleus_2 are the spin labels, the parameter coupling is the coupling constant J_D in Hz.

Example:

```
dipolar a b 100
dipolar a b cnst11
```

The dipolar coupling may be used to simulate the spectra of solid state *monocrystals*.

7.1.6 Qpolar

This command is used to define a quadrupolar coupling of one nucleus. The quadrupolar coupling is only allowed for nuclei with spin > 1/2.

- qpolar nucleus coupling

Example:

```
;the nucleus a has the quadrupolar coupling constant 100 Hz
qpolar a 100
qpolar b var11
```

The quadrupolar coupling may be used to simulate the spectra of solid state *monocrystals*.

7.1.7 Molecule

This command starts the definition of a molecule. You can define several molecules in one spin system description file.

Every molecule must have a unique name, the labels of atoms in one molecule need to be unique. The label of atoms in different molecules may be the same (see the example below). The molecules are completely independent, NMRSim calculates the resulting signal as a weighted mixture of signals from single molecules. It is not possible to define an interaction between nuclei in different molecules.

- **molecule** molecule_name weight

  molecule_name is any string with no more than 31 characters.

  weight Is a float number defining the relative concentration of this molecule in the mixture. It is also possible to use the spin system variable here. It is good practice to keep the weights of molecules close to 1. You may also use the spin system variable *var1..32* or the pulse program constants *cnst0..63*.

Instead of

```
molecule alpha 0.00001108
...
endmol
molecule alpha 0.00099
...
endmol
```

use

```
molecule alpha 1.108
...
endmol
molecule alpha 99
...
endmol
```

Example: Mixture of two CH_3 groups, one with C^{13}, 2nd with C^{12}. The weights are identical to the natural abundance of C^{13} isotope:

```
molecule alpha 1.108
```

```
proton 3*a 10
carbon x 130
weak a x 80
endmol

molecule beta 98.882
;
; the proton labeled a has nothing to do with the proton a from
; the molecule alpha
;
proton 3*a 10
endmol
```

The nuclei from different molecule definitions with the same label are different.

Omitting the **molecule** command in your spin system definition means that all nuclei in the spin system are part of one molecule. The following two definitions are equivalent:

```
;
molecule any_name 1.108
proton 3*a 10
carbon x 130
weak a x 80
endmol
```

and

```
; the same spin system definition without the molecule command
proton 3*a 10
carbon x 130
weak a x 80
```

The weight factor 1.108 does not play a role in this case.

7.1.8 Endmol

The command **endmol** finishes the definition of a molecule. Every **molecule** command must be followed by **endmol**.

7.1.9 Add

The spin system definition commands described above are used to define general nuclear spin systems in liquid. For special purposes you can use the command **add**. This command lets you create user-defined types of interaction between nuclei which you can use to create virtually any spin system Hamiltonian. The command multiplies a spin operator by a real constant and adds it to the specified inner matrix of the simulator:

- **add** matrix_name real_constant operator

Where *matrix_name* is the internal name of a spin system matrix. At present one can only use the symbol *ham* to specify the Hamiltonian matrix and *ro0* - to specify the initial density matrix.

operator is any operator expressed in product operator formalism, e.g.

```
   operator notation
   Ax = ax_
   Ax*By = ax_by = by_ax
   Ax*By*Cz = ax_by_cz = by_ax_cz = .......(any permutation is
allowed )
```

Example: Define a scalar coupling interaction between the nuclei *I* and *S* with coupling constant 3.5 Hz, i.e. $I_xS_x + I_yS_y + I_zS_z$.

```
proton i 10.3
proton s 9.2
add ham 3.5 ix_sx
add ham 3.5 iy_sy
add ham 3.5 iz_sz
```

You may use the **add** command and the C preprocessor macros to build your own interactions.

7.2 Initial Spin System State

The system sets the value of the initial density matrix ρ(0) to be proportional to the thermodynamic equilibrium value $\rho(0) = \sum I_z^i$.

If you use the command **add ro0** in your spin system definition file, the program assumes, that you have set the value of ρ(0) yourself and will not modify it.

This feature allows you to start the experiment from any state which may be far from equilibrium. A particular interesting feature is that you can use initial states that are very hard to create with a simple pulse (e.g. pure double quantum coherence I^+S^+ in a coupled system).

Example: The initial state of the spin system is $I_z + S_z + C_x$

```
add ro0 1 iz
add ro0 1 sz
add ro0 1 cx
```

7.3 Spin System Variables

To simplify the calculation of an experiment dependence on various spin-system parameters, the program offers a set of variables which can be used in the spin system definition. These variables are controlled from the pulse sequence.

Example:

```
   ; here the three chemical shifts and coupling constant are
written
   ; as variables which can be altered from one FID to the next
   nucleus 3* a var1
   nucleus b var2
   nucleus c var3
   couple a b var11
```

At the beginning of the pulse sequence the variables have their initial values set by the parameters *HV1..32*. When the pulse program encounters a command to increment a variable, the variable is incremented by the value *HS1..32*.

All spin system variables use Hz as the unit.

The command to increment the spin system variable recompiles the spin system Hamiltonian, and the program continues the experiment with the new settings. To use these commands it is necessary to observe the following rule:

- The pulse program commands manipulating the spin system variables (dhc, rhc, ihc , ihv,.., see *Pulse Program Commands Implemented in NMRSim [*▶ 47]) should not be used inside the acquisition loop. The program will not detect such programming violations. Such command in the acquisition loop will probably not crash the calculation, but will lead to nonsensical results.

Example:

```
 ;
   1 ze
   2 d1

   ;
   ; spin system modified in the acquisition loop !!
   ; this is forbidden
   ihv1
   go = 2
   ;
   ; this is allowed , the modification is done outside the
acquisition    loop
   ihv2
   loto 1 times td1
```

The spin system variables are also used in the calculation of shaped pulse excitation profiles.

7.4 Preprocessor Commands

Following C preprocessor commands may be used in the spin system definition:

```
   #define
   #ifdef
   #if
   #else
   #endif
   #include
```

Example:

```
   ; include your private definitions
   #include <my_definitions.ham>
   ;
   ; define some constants
   ;
   #define SHIFT_1 10
   #define SHIFT_2 15
   #define COUPLE_1 10.3
   #define noSOLVENT
   molecule alpha 1
   proton 2*a SHIFT_1
   proton 3*b SHIFT_2
   couple a b COUPLE_1
   endmol
;
   ; the include file water.ham contains the definition of water
   ; it is placed in a subdirectory my_library
   #ifdef SOLVENT
   #include <my_library/water.ham>
   #endif
```

The files included must be in the same directory as the spin system description files. The definition of symbols for the preprocessor is available in the NMRSim *Options Dialog* [▸ 19].

7.5 Spin System Limitations

The current NMRSim release supports up to 255 nuclei in the spin system definition. The nuclear labels are characters from the English alphabet, so you may use up to 26 different nuclei in one molecule. The nuclei from different molecule definitions with the same label are different.

But the limit of 26 interacting nuclei is not realistic. A group of 10 interacting nuclei with spin 1/2 without any symmetry is described by a 1024*1024 density matrix (about 8 MB). The NMRSim program needs at least 10 matrices for the simplest experiment. This means that the memory requirements for a simple experiment with 10 interacting nuclei, exceeds 80 MB.

So, the limits of the spin system you may use are determined by the computer used and not by the NMRSim program.

Let us compare this to a 10 nuclei spin system consisting of two interacting clusters with 5 nuclei. One matrix representing the operators in this case requires about 16 kB, this means that the whole experiment needs less than 200 kB.

The limit of 255 nuclei is a sensible one when defining large, complex mixtures of many simple molecules.

8 NMRSim Parameter Definition

Parameter definition is based on the standard Bruker parameter set. For the sake of simplicity and flexibility, some new features and new parameters have been added.

8.1 Durations

All the parameters specifying pulse durations use microseconds as default units, delay parameters use seconds as default. You can override this default by specifying the time units directly as a terminator for each entry:

- 10µ = 10 microseconds
- 13.5m = 13.5 milliseconds
- 5s = 5 seconds

Pulse length can be specified in two ways: as a time, or as a tilt angle. In the second case the actual pulse length is calculated from this angle and using the current radio frequency field strength parameter (*PLi*).

- 90d = 90 degree pulse
- 10µ = 10 microsecond pulse

8.2 Radio Frequency Field Intensities

The radio frequency field strengths are defined in Hz. The dB units used on the spectrometer are not available here. The dB is a relative unit and need an absolute value.

Example:

Specify the power level PL2 for the f2 channel 100 kHz and the channel is assigned to proton frequency. You will then get (approximately) a 2.5 µs long 90 degree pulse. Assigning the same channel to carbon, you will have get a 90 degree pulse which is also 2.5 µs long.

See also

🗎 Options Dialog [▸ 19]

8.3 Size Parameters

The parameters which specify the number of points or increments (TD, TD1,...) may be specified in multiples of 1024, you simply append the letter k: 1k, 8k, etc.

8.4 Error Checking

Most of the parameters are syntactically checked before closing the dialog box. When the program finds an error (e.g. a negative value, when a positive is expected), the bad parameter is highlighted and short error message is shown on the bottom of the dialog box.

8.5 Parameter Description

- Parmod

This parameter defines the dimension of the experiment. Possible values are 1 .. 2 (NMRSim for Unix 1..4). The value of this parameter defines the dimension of the experiment and the output file name type (*fid* or *ser*). The function of the file increment command differs in 1D and nD modes. The experiment number is incremented and a new file is created in 1D mode. In nD mode, the program only shifts the position in the file for the next write command.

- F1

  This parameter defines the nucleus assigned to the acquisition channel of the spectrometer. The basic frequency of the channel is calculated as $SFO_1 = SF*\gamma_{OBS}/\gamma_{proton}$, where g_{OBS} is the gyromagnetic factor of the selected isotope.

- F2

  This parameter defines the nucleus assigned to the channel F2 of the spectrometer. The basic frequency of the channel is calculated as $SFO_2 = SF*\gamma_{DEC}/\gamma_{proton}$, where γ_{DEC} is the gyromagnetic factor of the selected isotope.

- F3

  This parameter defines the nucleus assigned to the channel F3 of the spectrometer. The basic frequency of the channel is calculated as $SFO_3 = SF*\gamma_{DECB}/\gamma_{proton}$, where γ_{DECB} is the gyromagnetic factor of the selected isotope.

- SF

  This variable defines the *proton resonance frequency* of your spectrometer.

- OFS

  This variable defines the offset between the receiver and transmitter frequencies in ppm.

- O1

  The difference (in ppm) between the basic frequency of the F1 channel and the transmitter irradiation frequency.

- O2

  The difference (in ppm) between the basic frequency of the F2 channel and the decoupler irradiation frequency.

- O3

  The difference (in ppm) between the basic frequency of the F3 channel and the 2nd decoupler irradiation frequency.

- AQ_mod

  Acquisition mode. Possible values are *qf*, *qsim* or *qseq*. For more details refer to the pulse program manuals.

- TD

  The total number of time domain data points to be acquired.
- TDn

  The total number of time domain data points in higher dimensions for multidimensional experiments.
- NS

  The number of pulse program transients (number of scans).
- DS

  The number of pulse program transients without acquiring data (number of dummy scans). This parameter only has meaning for experiments with *full* relaxation. In other cases dummy scans are not executed and you are not prompted for this parameter.
- P0..63

  The length of pulse p0-31 in the pulse sequence
- PL0..31

  The radio frequency field intensities in Hz.
- D0..63

  The length of the free precession delay d0-31 in the pulse sequence.
- IN0..31

  The increment of delay D0-31 in the pulse sequence used by id0-31 commands. You may use the symbol *sw*. In this case the time increment is calculated from the formula 1/SW. This feature automatically guarantees the same spectrum width and calibration in both dimensions for *homonuclear* 2D experiments.
- FnMODE

  The parameter *FnMODE* is used to define the expansion of the **mc** command in multidimensional pulse programs. It defines which quadrature detection scheme will be used in the indirect detection directions (e.g. F1 for 2D experiments). The parameter can be defined in the Frequencies dialog (see Parameters).
- L0..31

  The loop limits used in pulse program loops.
- HV1..32

  The start value of the spin system variable *var1..32*.
- HS1..32

  The step value for the spin system variables *var1..32*.
- SP0..31

  The radio frequency intensity used for the shaped pulse, the unit used is Hz.
- SPNAM0..31

  The name of the file which contains the shape pulse definition.
- GPZ0..31

  The gradient intensity modifier. The shape gradient intensity is multiplied by this factor. Possible values are -100 ... 100%.

8.6 Expressions in Pulse Programs

The AVANCE spectrometer series allow one to define their own pulses and delays. For example:

```
define delay MY_DELAY
define pulse MY_PULSE
```

```
"MY_PULSE=p1*0.3333+3/4*p2+10u"
"MY_DELAY=d2+d3/2"
ze
.
.
MY_DELAY
MY_PULSE
.
.
.
```

Defines one pulse and one delay. Every pulse declared must be initialized in the pulse program. The **Check all parameters** dialog box shows all the actual values of all user defined delays and pulses.

The pulses used in any expression in the pulse program cannot be defined using the tilt-angle value, exact time values must be used instead. The value of the actual radio frequency field is not known at setup time and therefore is not possible to convert the tilt angle to the time unit.

9 NMR Wizard

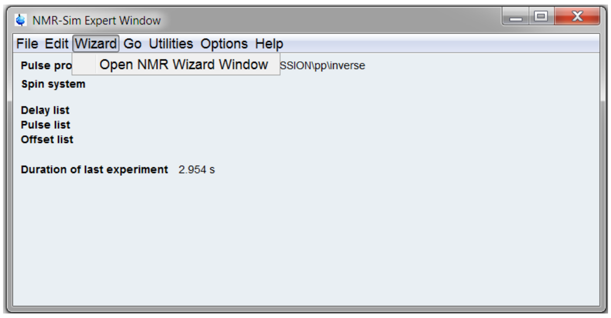
9.1 What is NMR-Wizard

The NMR-Wizard is a new tool which calculates the NMR spectrum (i.e. the time domain signal) without any user input. The user simply draws a chemical structure and selects which spectra should be calculated.

The whole complexity of NMR experiments (pulse programs, parameters, …) is hidden. This makes the NMR-Wizard an ideal teaching tool for chemist, or other people who are interested on the results (NMR spectra), but do not need know the experimental details.

9.2 Using NMR-Wizard

NMRSim always starts in an „Expert mode”. This is the classical user interface offering a lot of complex functionality. Use the Wizard menu to open the NMR Wizard window:



NMR-Sim Expert Window

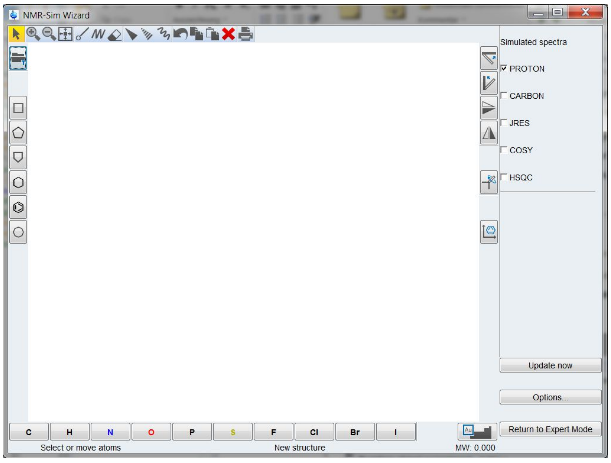
Pulse pro SSION\pp\inverse
Spin system

Delay list
Pulse list
Offset list

Duration of last experiment 2.954 s

Figure 9.1: NMRSim Expert Window

NMRSim main window closes and you see now only the NMR-Wizard window:



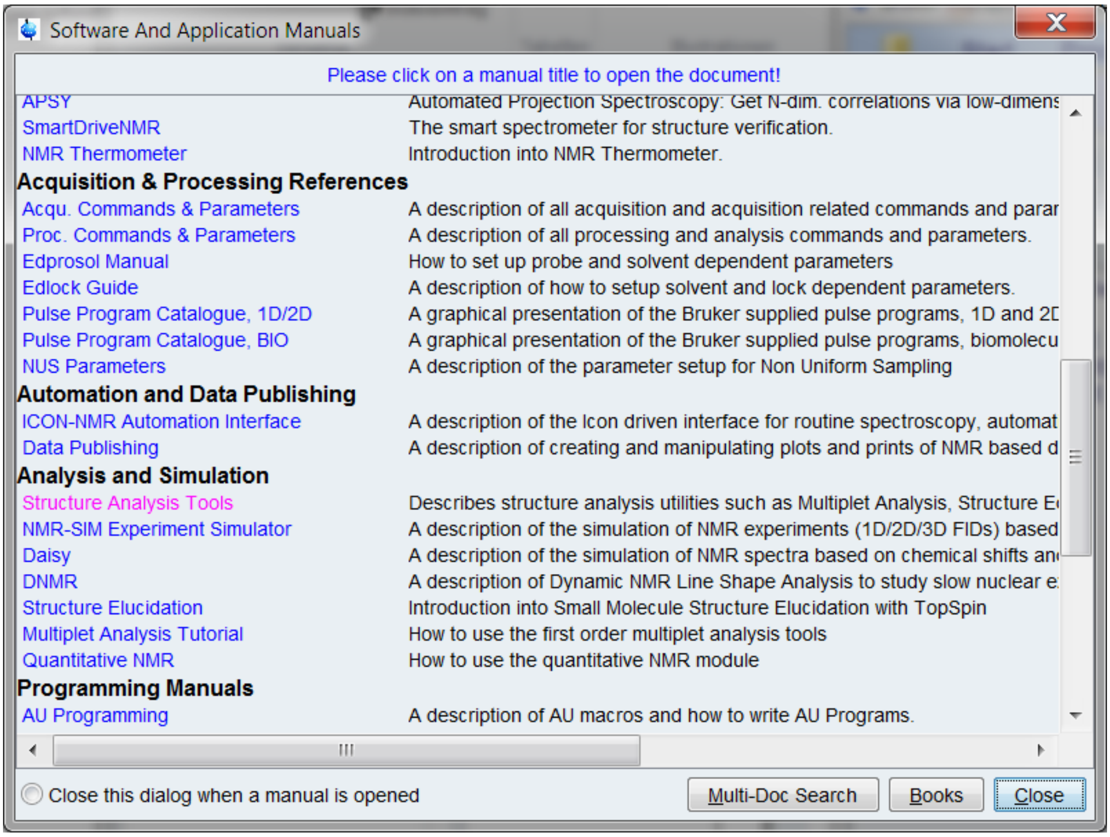
NMR-Sim Wizard

Simulated spectra
☑ PROTON
☐ CARBON
☐ JRES
☐ COSY
☐ HSQC

Select or move atoms
New structure
MW: 0.000

Figure 9.2: NMRSim NMR Wizard Window

The user interface enhances the Bruker chemical structure editor component, which is used in several applications (TopSpin, CMC-se,…). Please refer to the structure editor documentation for further details (“Structure Analysis Tools”, chapter “2D Structure Editor”).



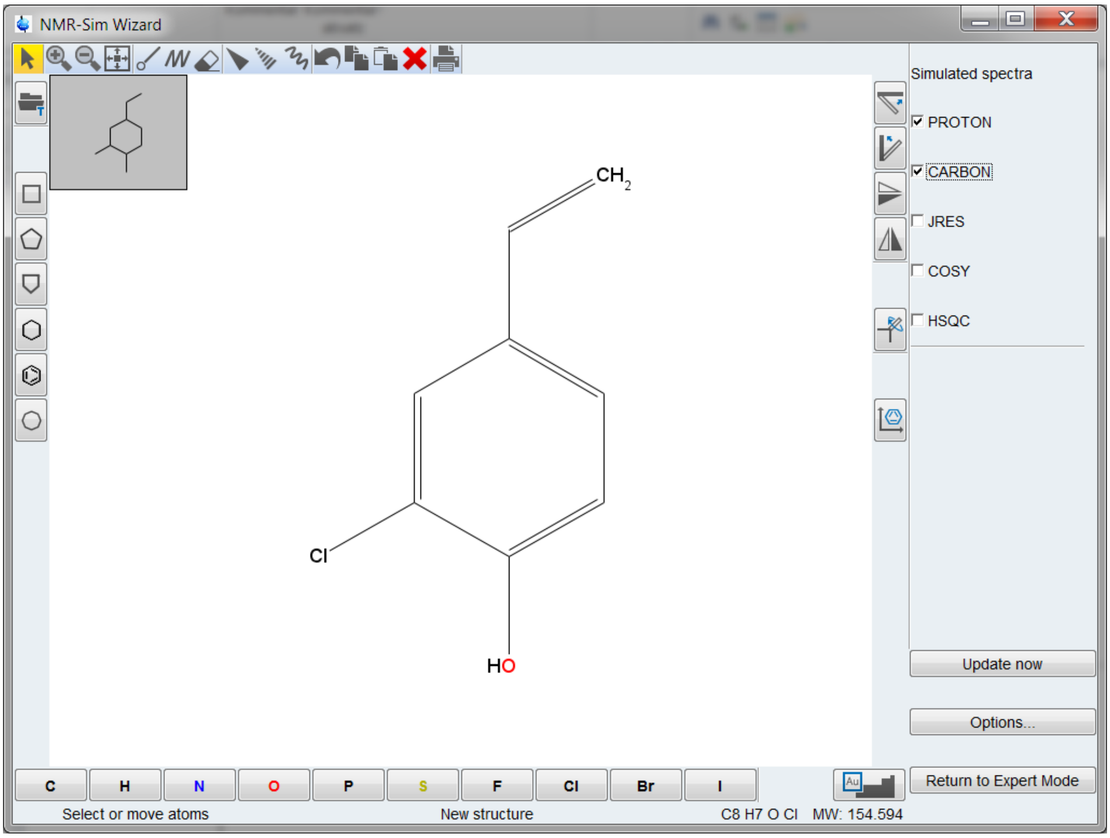
Please click on a manual title to open the document!

APSY	Automated Projection Spectroscopy: Get N-dim. correlations via low-dimens
SmartDriveNMR	The smart spectrometer for structure verification.
NMR Thermometer	Introduction into NMR Thermometer.
Acquisition & Processing References	
Acqu. Commands & Parameters	A description of all acquisition and acquisition related commands and para
Proc. Commands & Parameters	A description of all processing and analysis commands and parameters.
Edprosol Manual	How to set up probe and solvent dependent parameters
Edlock Guide	A description of how to setup solvent and lock dependent parameters.
Pulse Program Catalogue, 1D/2D	A graphical presentation of the Bruker supplied pulse programs, 1D and 2
Pulse Program Catalogue, BIO	A graphical presentation of the Bruker supplied pulse programs, biomolecu
NUS Parameters	A description of the parameter setup for Non Uniform Sampling
Automation and Data Publishing	
ICON-NMR Automation Interface	A description of the Icon driven interface for routine spectroscopy, automat
Data Publishing	A description of creating and manipulating plots and prints of NMR based d
Analysis and Simulation	
Structure Analysis Tools	Describes structure analysis utilities such as Multiplet Analysis, Structure E
NMR-SIM Experiment Simulator	A description of the simulation of NMR experiments (1D/2D/3D FIDs) based
Daisy	A description of the simulation of NMR spectra based on chemical shifts an
DNMR	A description of Dynamic NMR Line Shape Analysis to study slow nuclear e
Structure Elucidation	Introduction into Small Molecule Structure Elucidation with TopSpin
Multiplet Analysis Tutorial	How to use the first order multiplet analysis tools
Quantitative NMR	How to use the quantitative NMR module
Programming Manuals	
AU Programming	A description of AU macros and how to write AU Programs.

○ Close this dialog when a manual is opened

Figure 9.3: TopSpin Manuals Selector. The “Structure Analysis Tools” Document

Now, you can start to draw a structure (or load existing structure using the clipboard or drag & drop).



Simulated spectra

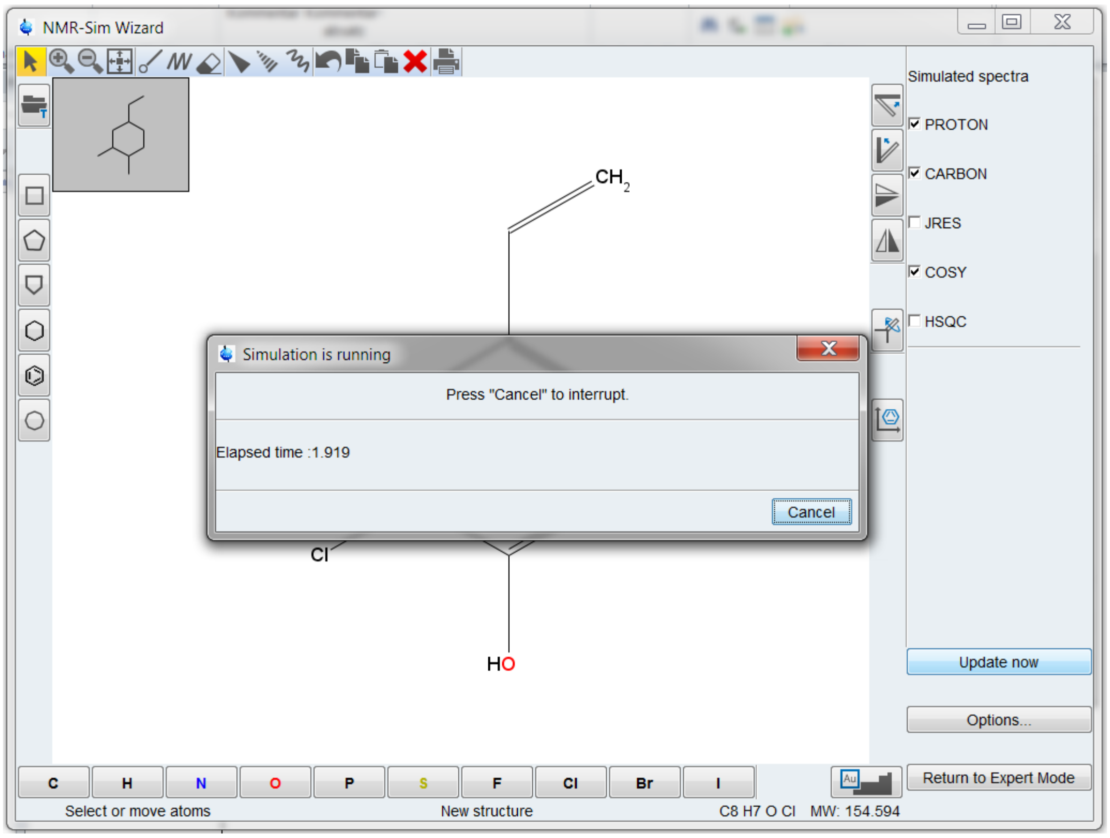
☑ PROTON
☑ CARBON
☐ JRES
☐ COSY
☐ HSQC

Select or move atoms

New structure

C8 H7 O Cl MW: 154.594

Select the spectra you need and press the **Update now** button. The simulation starts:



NMR-Sim Wizard

Simulation is running

Press "Cancel" to interrupt.

Elapsed time :1.919

Simulated spectra

☑ PROTON

☑ CARBON

☐ JRES

☑ COSY

☐ HSQC

Select or move atoms

New structure

C8 H7 O Cl MW: 154.594

Figure 9.4: NMR-Sim Wizard during the Calculation

The simulated spectra are shown in TopSpin after the simulation finished:

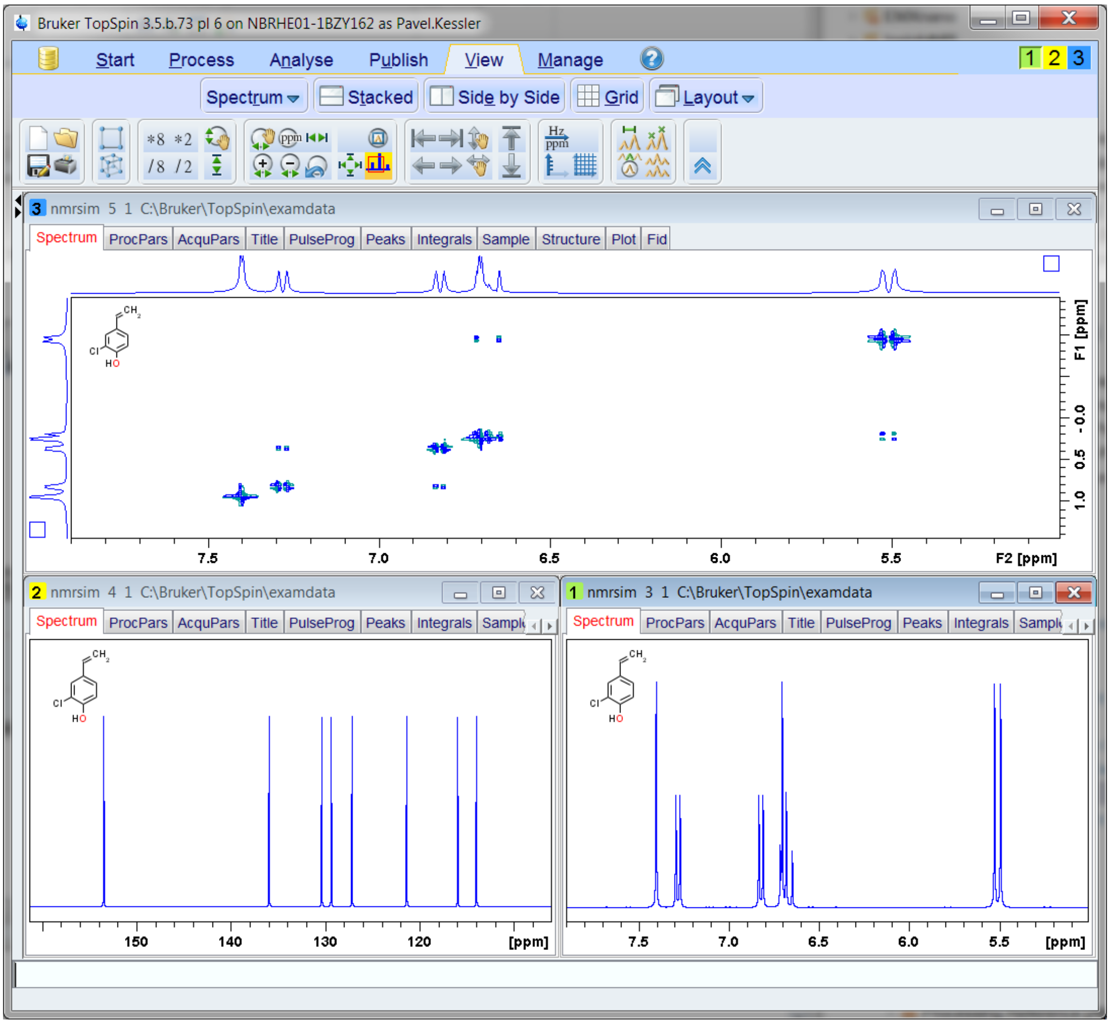
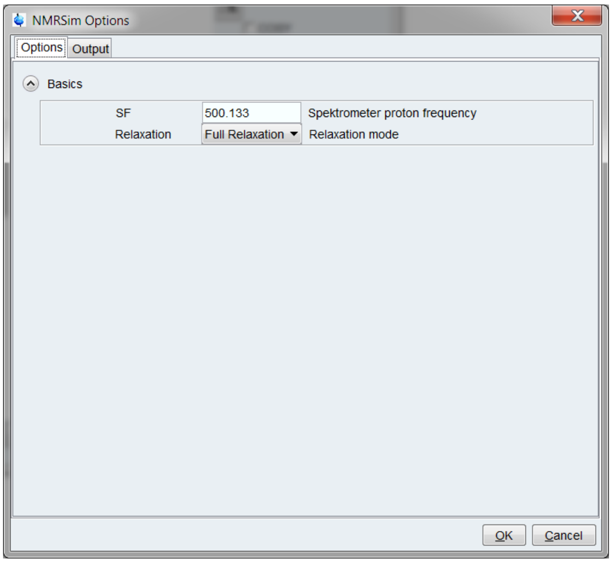


Figure 9.5: A Simulated Spectra after the Simulation is Finished

Press the **Return to Expert Mode** button to close the wizard window and reopen the expert view. The chemical structure was automatically saved to disc and will be reloaded if you open the wizard for a second time.

The **Options** button allows you to set basic NMR parameters and the target dataset.



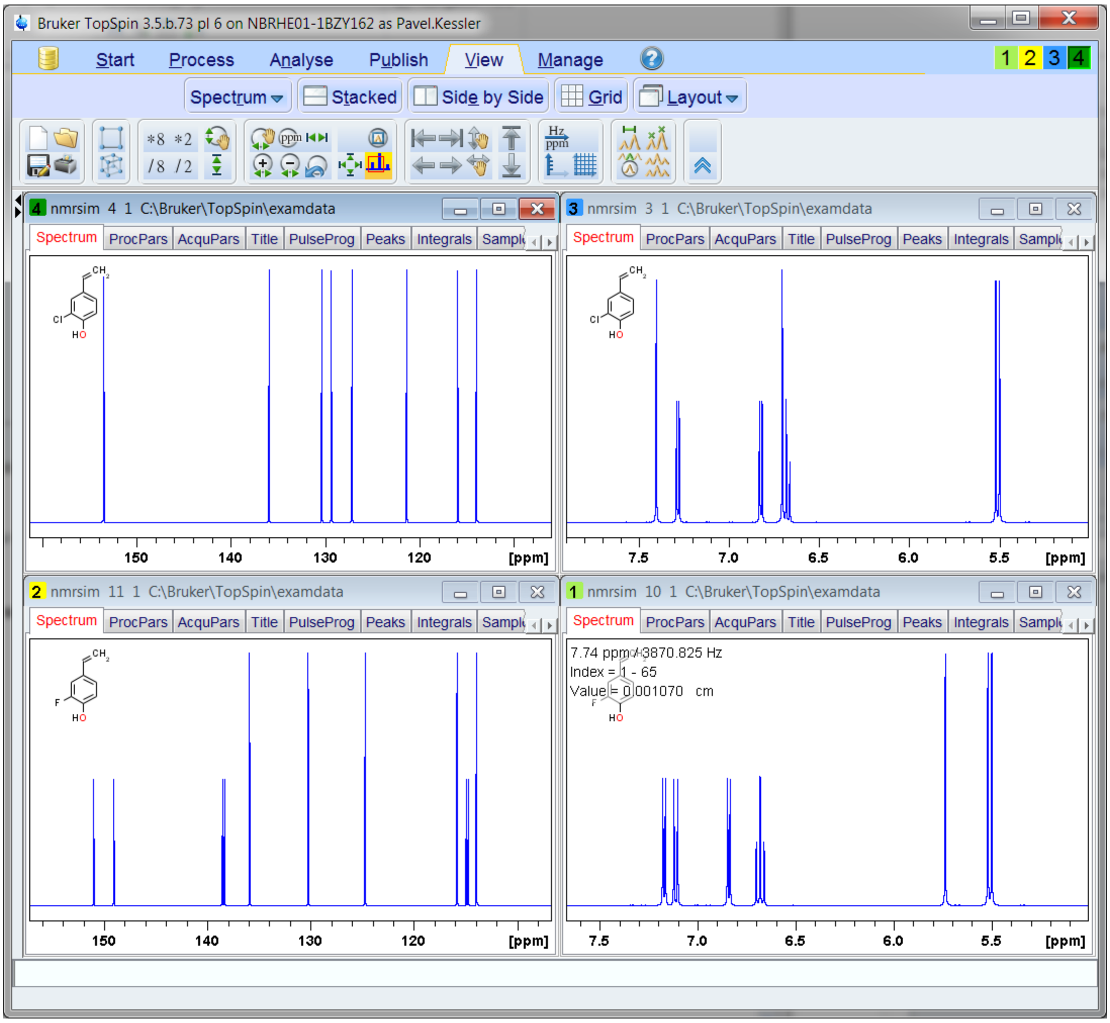
SF 500.133 Spektrometer proton frequency

Relaxation Full Relaxation Relaxation mode

Figure 9.6: NMRSim Options

Changing the target data set allows easy investigation of changes in spectra prompted through modification of the chemical structure.

Example: Compare spectra of the original structure and a different one, where the Chlorine atom was replaced by Fluorine.



7.74 ppm / 3870.825 Hz
Index = 1 - 65
Value = 0.001070 cm

Figure 9.7: Visible Signal Splitting though the Fluorine Coupling in H^1 and C^{13} Spectra

9.3 Where are the limits ?

As described in the section *Theoretical Background [▸ 9]*, the complexity of NMR experiment simulation grows exponentially with the number of simulated nuclei. NMR Wizard tries to split the system of interacting atoms in a set of smaller isolated subsystems (e.g. neglects long range couplings,..). So, it is not simply possible to define a limit (e.g. molecular mass, number of atoms,…) where the simulation of spectra fails. This section demonstrates it on two molecules with comparable number of NMR relevant atoms.

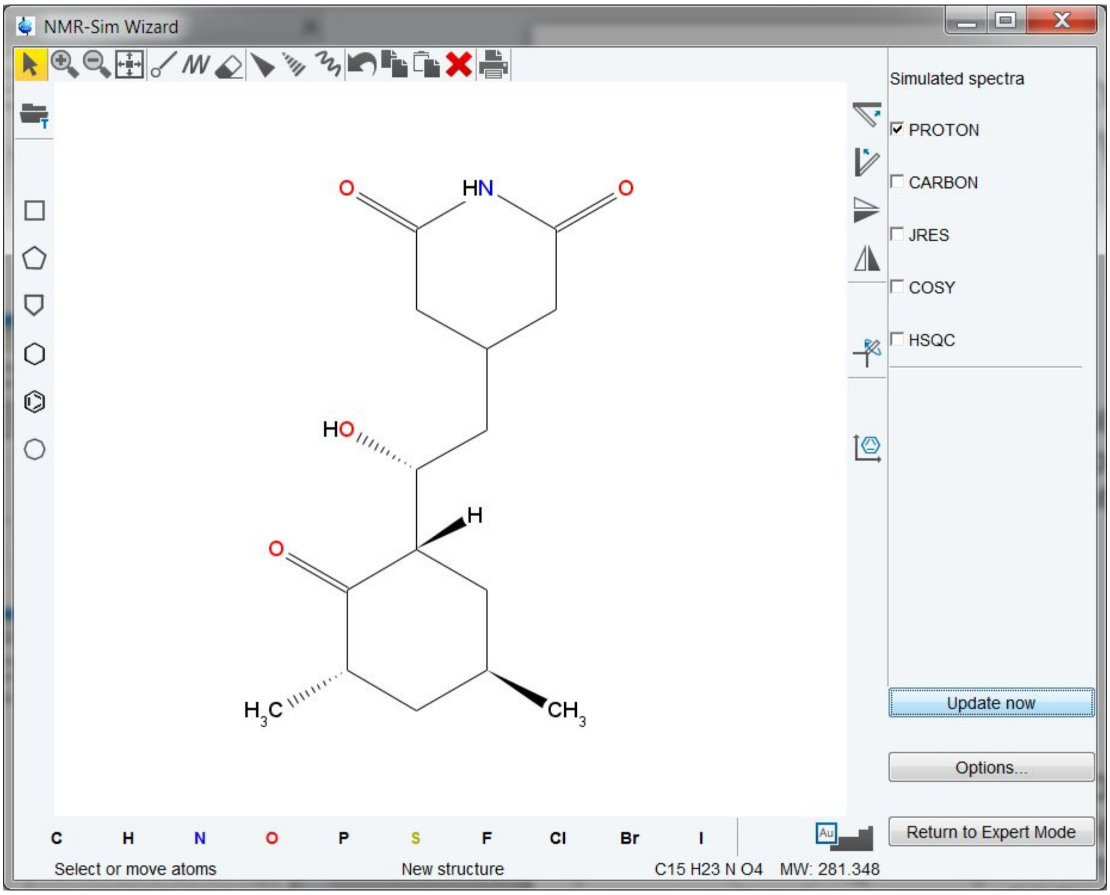
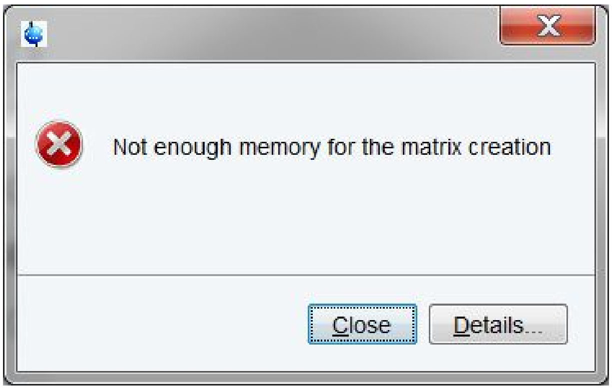


Figure 9.8: 4-[2-(3,5-Dimethyl-2-oxocyclohexyl)-2-hydroxyethyl]-2,6-piperidinedione

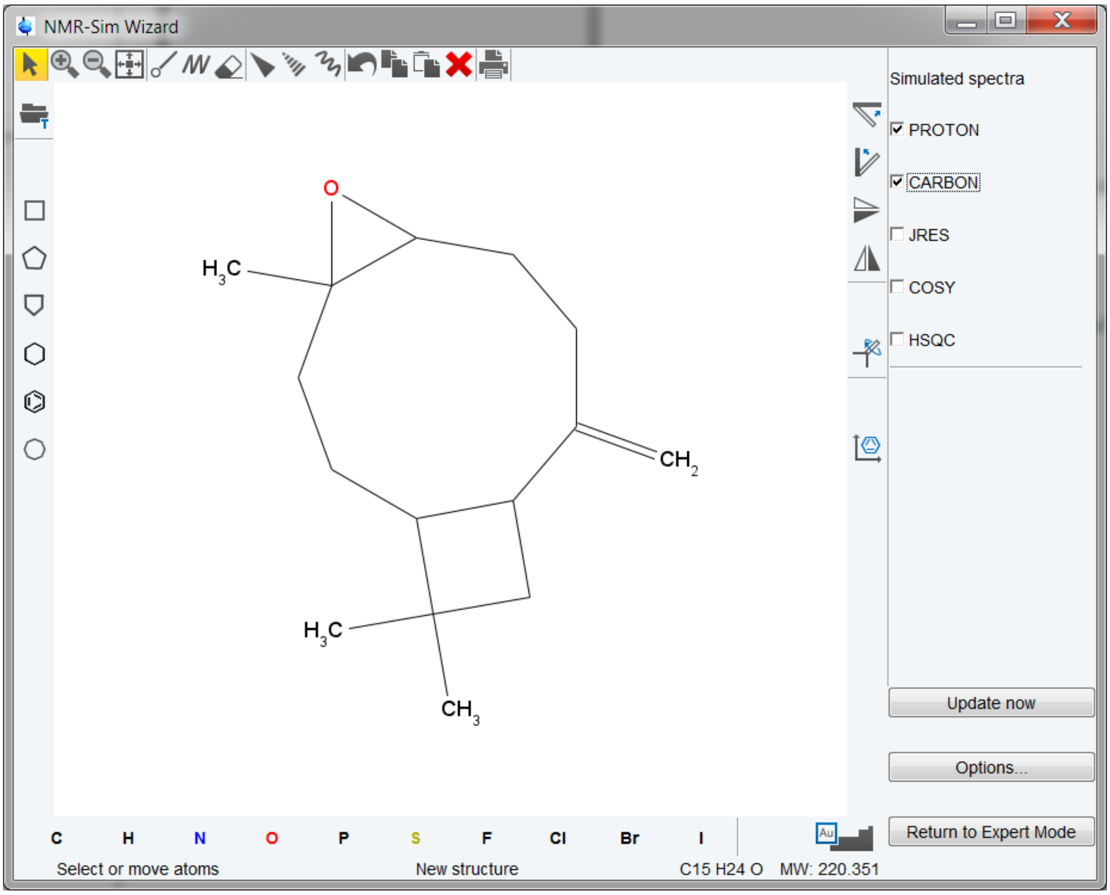
The first structure (see picture above) is too big to calculate the proton spectrum. You get following error message:



Not enough memory for the matrix creation

The C13 spectrum may be calculated, because the simulation uses only 2 spheres of neighborhood atoms to get correct splitting due to the CH coupling.

Next example is even larger structure (24 protons), however the calculation of proton spectra works fine.



NMR-Sim Wizard

Simulated spectra

☑ PROTON

☑ CARBON

☐ JRES

☐ COSY

☐ HSQC

Select or move atoms

New structure

C15 H24 O MW: 220.351

Figure 9.9: Caryophyllene Oxide alias (4R)-4,12,12-Trimethyl-9-methylene-5-oxatricyclo[8.2.0.04,6]dodecane

The calculation is very fast, only few seconds are necessary to get both proton and c13 spectra

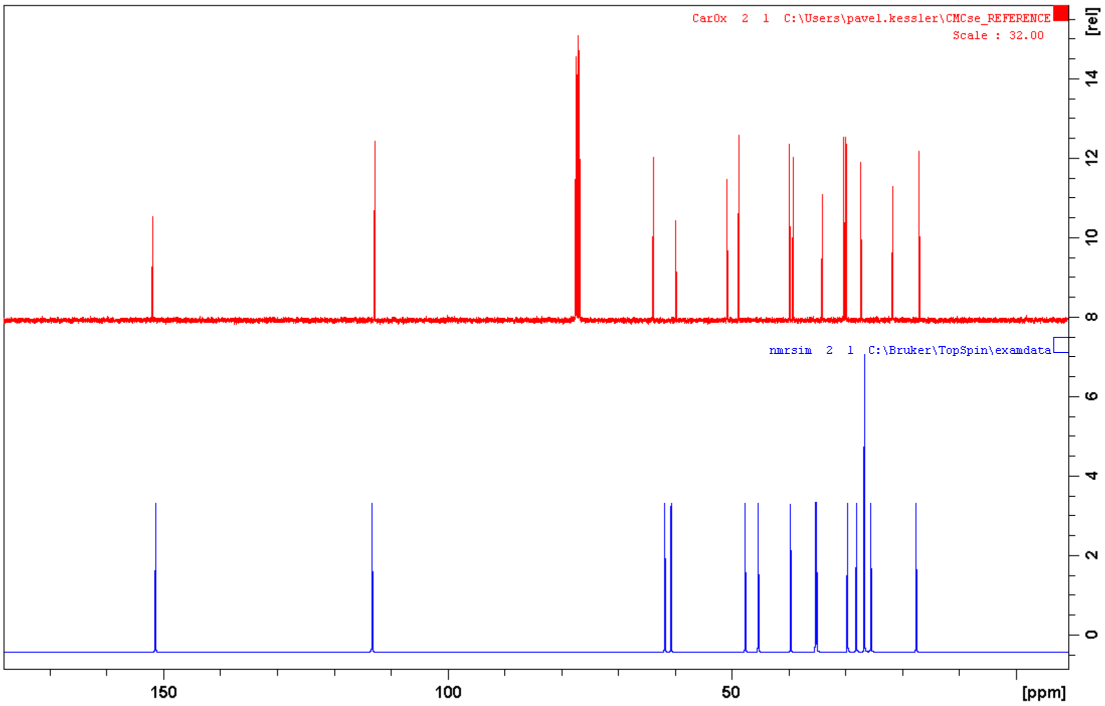


Figure 9.10: Comparison of simulated and experimental C_{13} spectra of Caryophyllene Oxide.

Calculation of COSY spectrum demonstrates the overall performance. Simulation of the COSY experiment on the Caryophyllene Oxide sample required only 30 seconds.

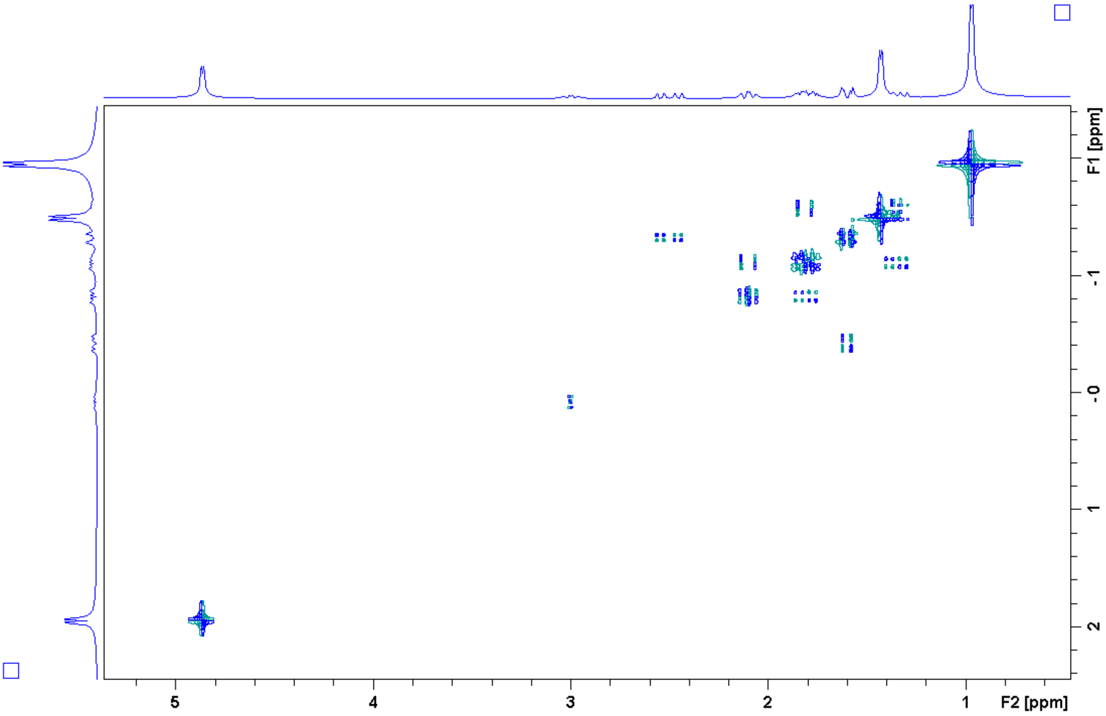


Figure 9.11: Caryophyllene Oxide, simulated COSY spectrum,

10 Gradient Spectroscopy

This chapter describes the basics of the gradient spectroscopy implementation in NMRSim. The chapter *Examples* [▸ 77] contains several examples of *Gradient Experiments* [▸ 99].

10.1 Gradients in Pulse Programs

The Bruker pulse program language has several different gradient control methods. The NMRSim implementation uses the *AVANCE shaped gradient syntax*.

p16:gp2

This command invokes a gradient pulse with a length P16 and a gradient shape of 2. The parameter *GPZ2* defines the relative amplitude (in %) of gradient number 2. It is possible to use values between -100 and 100.

10.2 Gradients in NMRSim

NMRSim does not use gradient shapes. Shaped gradients in NMR spectroscopy are used to suppress the experimental artifacts induced by the rapid static field change. The theoretical calculations in NMRSim do not require this. For spectroscopy, there is no difference between x, y or z gradients. So, NMRSim only implements the gradients along the z axis.

10.2.1 Numerical Simulation of Gradients

The gradient pulse applied to the sample introduces a rapid dephasing of the coherent magnetization. The global magnetization is not destroyed, but it is dephased. The measured NMR signal is a sum of all magnetization vectors. Using a second gradient pulse with inverted magnetic field reconstructs the original magnetization (neglecting the spin system evolution due to J-coupling).

It is not possible to use one density matrix to describe such systems. NMRSim divides the sample into a number of layers. Each layer is taken to be a system with homogenous fields, so it is possible to use the density matrix formalism. The evolution of the spin system in this layer is described by the Liouville equation. The NMR signal is then calculated as a sum over all layers. This approach allows for the simulation of gradient experiments the main goal of NMRSim program: *Flexibility*.

This approach is a challenge for the program performance. The Liouville equation must be solved separately for each layer in the sample. This means, that the simulation will be much, much slower compared to the simulation of “classical” experiments without gradients. A trade-off between program speed and the output quality should be found. NMRSim implements a lot of optimizations to achieve acceptable performance. The number of layers used for the simulation is defined on-the-fly using an *adaptive algorithm* which guarantees good quality of results and acceptable speed. In fact, the calculation of sample gradient experiments presented in this manual takes only a few seconds on modern hardware.

The current implementation of gradient experiments neglects any *diffusion effects* and the *full relaxation mode* is not available for gradient experiments.

10.3 Examples of Gradient Experiments

This section presents some principles of gradient spectroscopy.

10.3.1 Decay of Magnetization Under the Influence of Gradients

The dephasing (decay) of the magnetization under the influence of a homogeneous static field gradient may be described using the following formula:

The figure below shows a simulated decay. The vertical axis is proportional to the pulse length, the full vertical scale is about 4 ms. The absolute value of the resulting display is shown. The projection on the side of the spectrum shows, that the calculated decay is in a form very near to the theoretical formula above.

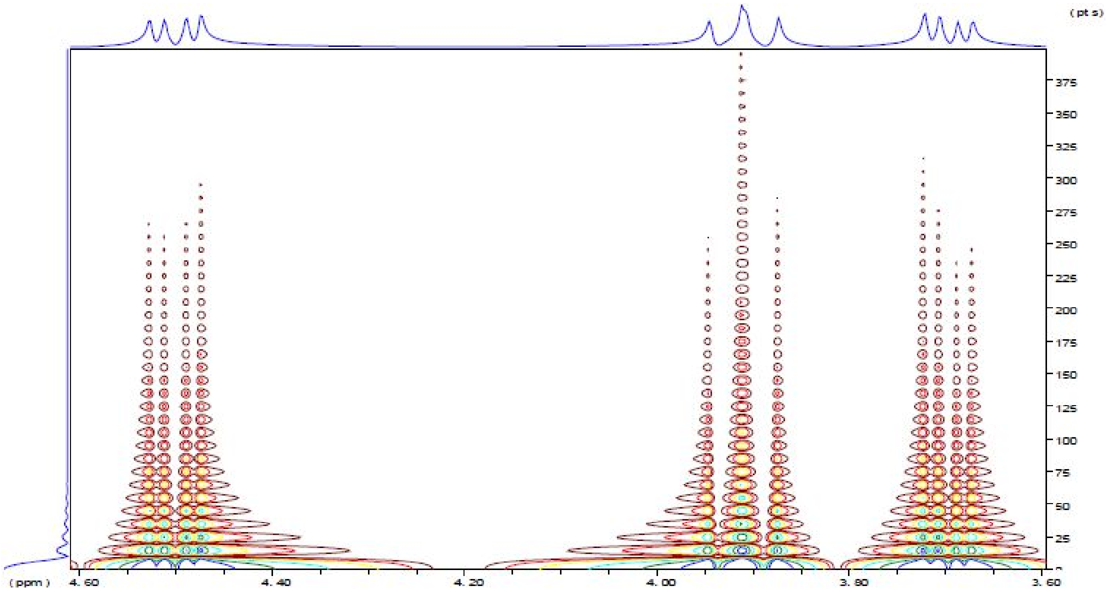


Figure 10.1: The Magnetization Decay During a Gradient Pulse.

10.3.2 COSY Experiment

The gradient COSY demonstrates the ability to select the coherence to be observed using gradients.

The classical COSY pulse program uses phase cycling to achieve the coherence selection. Thus, at least two transients (scans) are necessary to get a two dimensional spectrum.

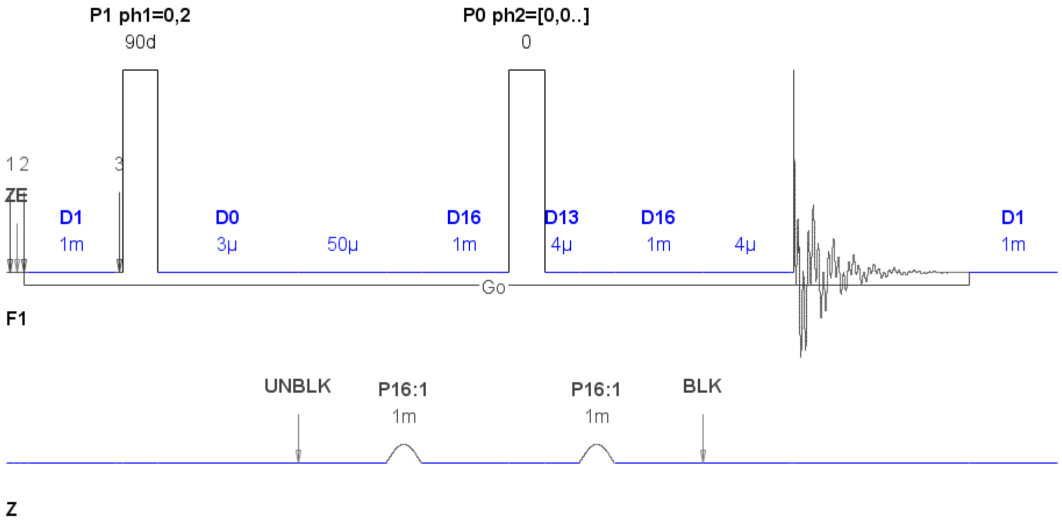
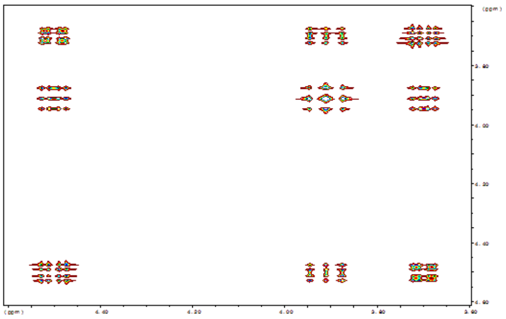


Figure 10.2: The cosygp Pulse Program.

The gradient pulse program selects the coherence using a static field gradient. Only one transient is required. The figure below demonstrates the coherence selection. The gradient ratio 10:10 selects the “normal” +1 coherence. Inverting the sign of the second gradient selects the -1 coherence and the sign of the indirect detection axis changes.

a) p-type spectrum



b) n-type spectrum

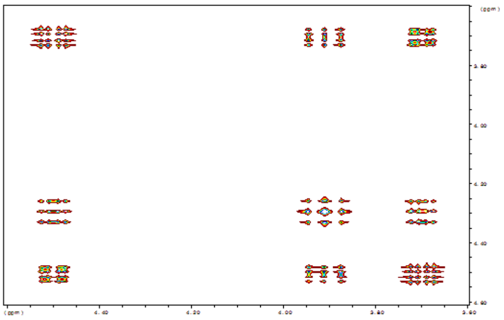


Figure 10.3: Gradient COSY Spectrum, Gradient Ratio 10:10 and 10:-10.

The suppression of the unwanted coherence achieved in this case is better than 1:1000. The configuration of this experiment is stored in the file *gradient_cosy.cfg*.

11 Examples

This chapter describes several example experiments.

Start the NMRSim program typing **nmrsim** on the TopSpin command line.

After the first start NMRSim copies all the example files into the user directory: $HOME/NMRSIM_SESSION.

The command **Options**/**Update example files** in the NMRSim main menu bar may be used to reload a full set of the original example files. This should be invoked after each installation of new NMRSim version.

In your user directory you will find the configuration files, which will assist you in starting these examples. Load the specified settings into the simulator using menu command **File**/**Experiment setup**/**Load from file**. This step properly defines all parameters for your experiment. In this step only the experiment parameters are defined, it does not create the spectra.

To start the experiment, execute the main menu command **Go**/**Run** or **Go**/**Check parameters & Go**. This will start the simulation and the time domain signal will be generated. Use TopSpin to process the calculated spectra.

The NMRSim installation contains the following example configuration files:

demo1d .cfg	1d spectrum of ethanol.
selco .cfg	Selective COSY of di-brom propionic acid.
select .cfg	A selective excitation experiment in a strongly coupled system (di-brom propionic acid).
dept.cfg	Dept experiment on a sample CH-CH2-CH3 spin system.
hohaha.cfg	Selective excitation and magnetization transfer using the MLEV mixing sequence.
invreco.cfg	Simple inversion recovery experiment.
profile.cfg	Excitation profile.
jres.cfg	J-resolved experiment on di-brom propionic acid spin system.
cosytp.cfgcosydtp.cfg, cosytftp.cfg cosyph.cfg	COSY experiments on dbpa. Cosyph.cfg uses the new mc command for F1 phase sensitivity.
hetcor.cfg	Heteronuclear correlation experiment on a sample C-H spin system.
invitp.cfg	Inverse heteronuclear experiment.
inv_1d.cfg	1D H-X correlation via heteronuclear zero and double quantum coherence.

Table 11.1: Example Configuration Files

inv_1d.cfg	1D H-X correlation via heteronuclear zero and double quantum coherence using gradients.
gradient_cosy.cfg	Gradient COSY experiment.
gardient_calibrate.cfg	Simulates the magnetization decay in the gradient pulse as a function of time.
watergate.cfg	Water signal suppression using binomial pulse sequence and gradients.
Bloch Module	
bloch.cfg	Investigation of a gaussian pulse.
chirp.cfg	Investigation of a phase modulated chirp inverse pulse.

Table 11.2: Example Gradient Spectroscopy Configuration Files

These example files may also be used as a template for the definition of your own experiments. You only need to change necessary parameters and save the configuration on the disk under a new name.

The spin system used in all the examples is small, so you will get the results in very short time on any computer. It takes just a matter of seconds to calculate most of the 2D experiments described here.

The following section describes details of selected example experiments. Every part contains a listing of the experiment configuration file. To reduce the storage requirements the files contain only parameters which are non-zero or different from the Bruker default settings.

The negative values of pulse lengths in configuration files are in fact the tilt angles. The program uses this coding for the sake of simplicity.

11.1 How to Setup a New Experiment

- Load the existing experiment configuration.

  Load an existing experiment configuration that is similar to the new experiment you want to calculate. Select a new spin system or pulse program and modify the existing parameters.

See also

🗎 NMR Wizard [▸ 63]

11.2 The First 1D Experiment

The configuration file *demo1d.cfg* contains the description of a simple one dimensional experiment. The spin system description file is *ethanol.ham*.

```
; Protons in ethanol
;
; Bruegel, Handbook of NMR Spectral parameters,
; vol 2, p 316
;
proton 3*a 1.19 t=1
proton 2*b 3.66 t=1
proton c 5.27 t=1
couple a b 6.9
couple b c 4.76
```

The file *ethanol2.ham* contains the protons, and the protons and carbons, from ethanol molecule respectively.

The file *ethanol2.ham* uses the molecule definition to create the natural *mixture* of molecules with c13 and c12 isotopes. The c12 atoms are omitted, because the c12 nucleus does not have any magnetic moment.

```
;
; Carbons and protons in ethanol
; Bruegel, Handbook of NMR Spectral parameters,
; vol 2, p 316
;
molecule alpha 0.98
proton 3*a 1.19
proton 2*b 3.66
proton c 5.27
;
couple a b 6.9
couple b c 4.76
endmol
;
; follow two molecules with carbons
molecule beta 0.01
proton 3*a 1.19
proton 2*b 3.66
proton c 5.27
carbon e 56.30
couple a b 6.9
couple b c 4.76
;
; H/C spin coupling in Hz
;
weak a e 100
endmol

molecule gamma 0.01
proton 3*a 1.19
proton 2*b 3.66
proton c 5.27
carbon f 16.95
;
couple a b 6.9
couple b c 4.76
;
; H/C spin coupling in Hz
;
weak b f 100
endmol
```

The resulting 1D spectrum:

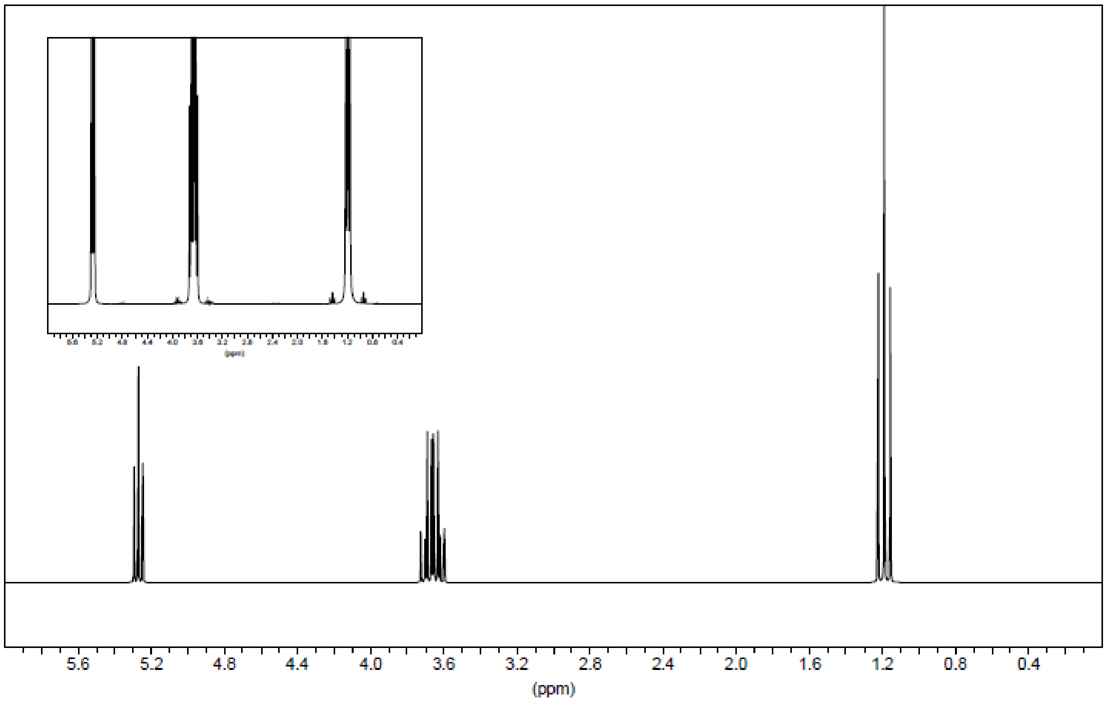


Figure 11.1: The Proton Spectrum of Ethanol at 200 MHz, Experiment Definition File demo1d.cfg.

The inset in the figure above shows the C13 satellites (vertical scale with 8 times magnification).

11.3 Excitation Profiles of Shaped Pulses

The **ihc** command allows for the simulation of rather complicated experiments, you can study the dependence of NMR experiments on various spin system parameters.

The results of such an experiment is shown part "c" “Excitation profile of a gaussian pulse on a two spin system” in the figure below. Chemical shift of one nucleus varied in the range ± 700 Hz, the chemical shift of the second nucleus was fixed on 1000 Hz. A comparison to the excitation profile of isolated nucleus ("b" in the figure below) shows, that the excitation profile is not affected by the spin-spin interaction.

```
[NMR-Sim-Experiment]
sequence= $root$\usr\demo\shape.seq
hamiltonian=a.ham
SF=200
p5=5000
l1=81
sh1=gauss.shp
Relaxation=1
TD=8192
NS=4
HL1=100000
HL2=200
```

SW=8.192
hv1=-800
hs1=200

Table 11.3: Configuration File profile.cfg

Please note, that the values of spin system variables used for chemical shift definition are interpreted as frequency in Hz!

The use of the flip angle (e.g. 90d) instead the pulse duration is available only for pulses without phase modulation!

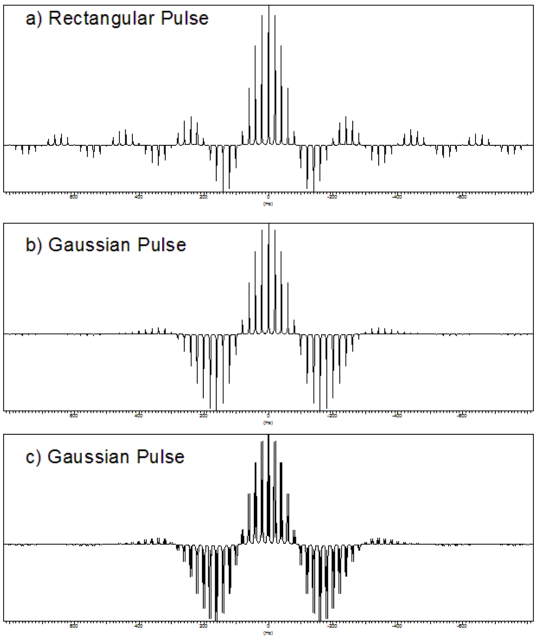


Figure 11.2: The Comparison of Excitation Profiles of Three Different Selective Pulses.

The length of all pulses is 5 ms, tilt angle 90 degree (effective field amplitude 50 Hz). The configuration file name is *profile.cfg*.

11.4 Selective COSY

This example demonstrates the practical use of a shaped pulse for the selective excitation.

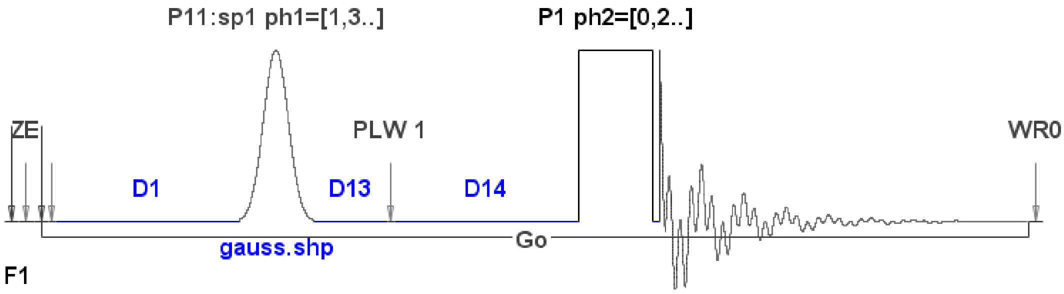


Figure 11.3: Schema of 1D Selective COSY Experiment.

The comparison of the experimental and simulated spectra shows a very good agreement between the theoretical and experimental results. The pulse program being used is the standard Bruker pulse program *selco*.

```
   ;selco
   ;1D COSY using selective excitation with a shaped pulse
   ;C.J. Bauer, R. Freeman, T. Frenkiel, J. Keeler & A.J. Shaka,
   ; J. Magn. Reson. 58, 442 (1984)
   ;H. Kessler, H. Oschkinat, C. Griesinger & W. Bermel,
   ; J. Magn. Reson. 70, 106 (1986)
   1 ze
   2 d1 tlo
   p11:tp1 ph1
   d13
   d14 thi
   p1 ph2
   go=2 ph31
   wr #0
   exit
   ph1=(360) 90 270 270 90 180 0 0 180
   ph2=0 2 0 2 1 3 1 3
   ph31=0 2 2 0 1 3 3 1
   ;hl1: ecoupler high power level
   ;tp1: power level for shaped pulse tp1 in tlo mode
   ;p1 : 90 degree transmitter high power pulse
   ;p11: 90 degree transmitter shaped pulse
   ;d1 : relaxation delay; 1-5 * T1
   ;d13: short delay (e.g. to compensate delay line) [3 usec]
   ;d14: delay for evolution after shaped pulse: (p11)/2 + d14 ~ 1/
(2J)
   ;NS: 8 * n
   ;DS: 4
   ;x : phase difference between thi and tlo output
   ;choose p11 according to desired selectivity
   ;the flip-angle is determined by the amplitude
   ;the use of an external attenuator might be necessary
   ;O1 has to be on resonance on the multiplet to be excited
```

```
[NMR-Sim-Experiment]
sequence=selco
hamiltonian=$root$\usr\demo\dbpa.ham
p11=80000
d1=0.003691
sh1=gauss.shp
Relaxation=1
TD=4096
NS=8
HL1=100000
SF=300.13
SFO1=4.1
```

```
SW=1.2
```

Table 11.4: Experiment definition selco.cfg

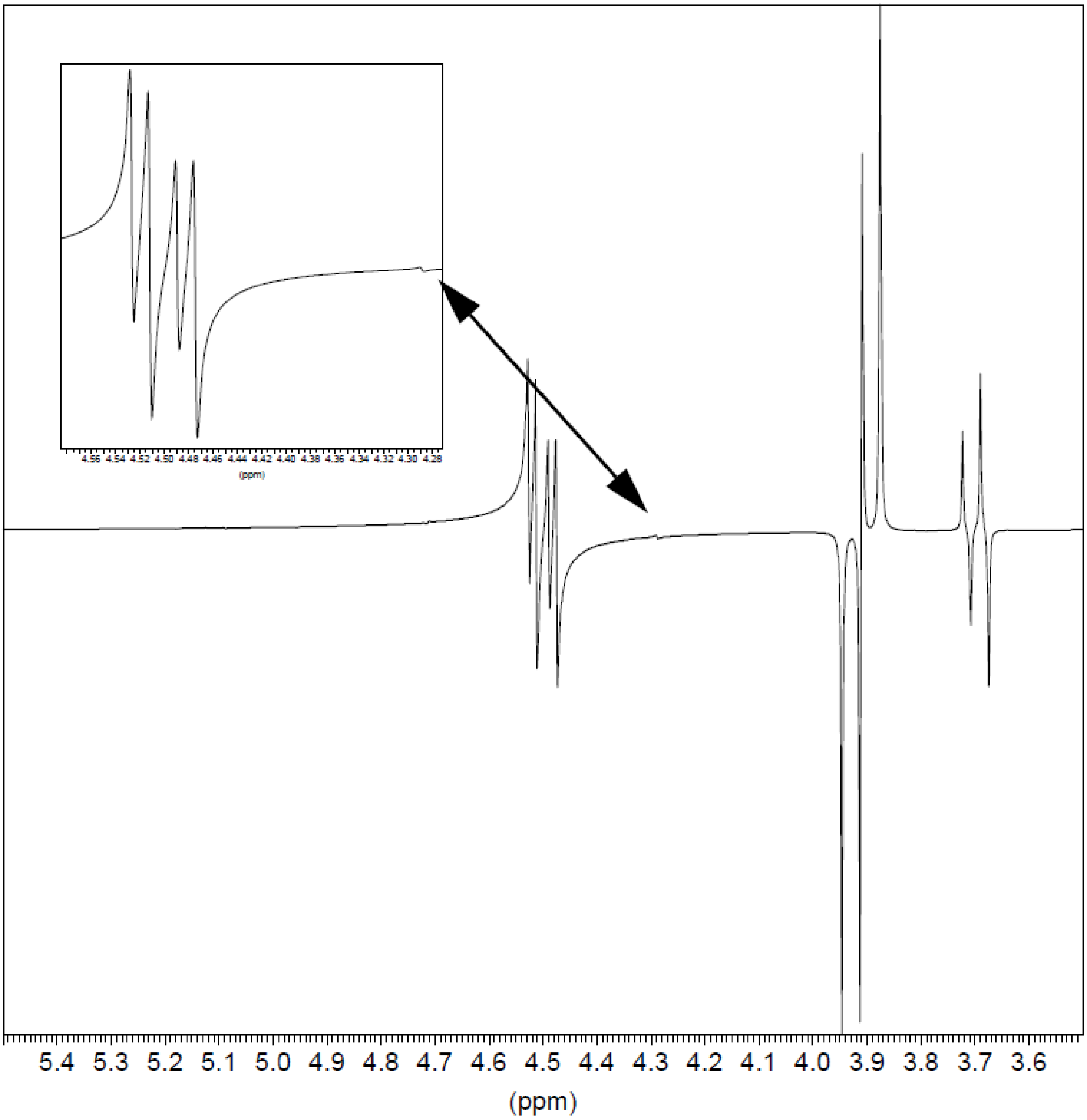


Figure 11.4: Selective COSY Experiment.

The length of the Gaussian shaped pulse was 80 ms, the D13 delay ≈ 3.7 ms. Note the magnified parts of spectrum which shows a small artifact, probably generated due the strong J-coupling in the spin system. The same artifact is also present in the real experiment.

11.5 1D HOHAHA with Z-filter

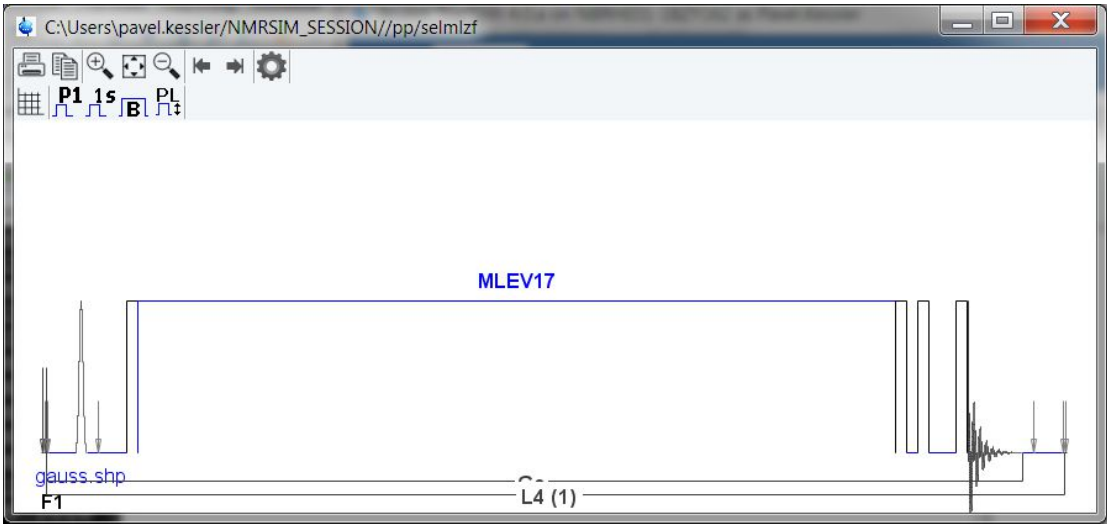


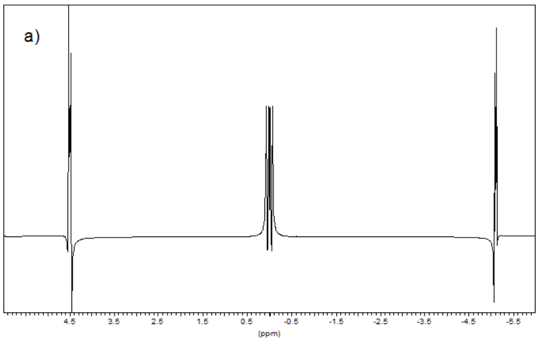
Figure 11.5: Scheme of 1D HOHAHA Z-filtered Experiment

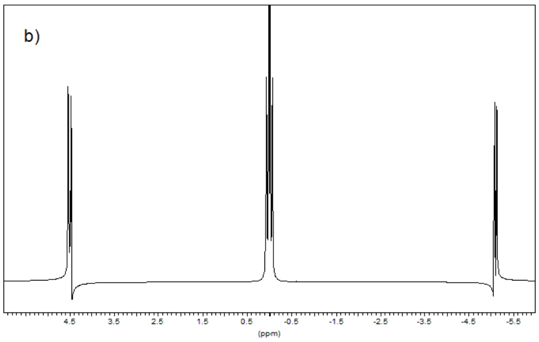
One of the most exciting areas in the NMR spectroscopy are the homonuclear Hartman Hahn experiments, which helps to elucidate the molecular structure. The next example shows the 1D version of such an experiment, the configuration file is *hohaha.cfg*.

This experiment shows the efficiency of the pulse program compilation in NMRSim. The first scan needs the most run time. The shaped pulse for the selective excitation and the magnetization transfer sequence are compiled and saved in memory. Following scans use the previously compiled segments and execute much faster - the number of calculated pulses is reduced by a factor ~ 200.

The result of the short experiment with only one delay, is that the z-filter contains a large number of artifacts ("a" in the figure below).

The “full” experiment with 8 delays in the z-filter exhibits the significant suppression of artifacts ("b" in the figure below). The pulse program requires the delay table *hoha_z.ld*.





The delays in the z-filter (hoha_z.ld) are calculated for the example ABC spin system and for the spectrometer frequency SF = 200 MHz. To use a different spin system or frequency, you should create a new delay list file. The delay values τ are calculated using formula:

$$\frac{1}{\tau\pi} = \sum_{i<j} \pi\alpha_{ij}(\omega_i - \omega_j)$$

Where ω_i, ω_j are the chemical shifts of the nuclei and $\alpha_{ij}\pi$ is 0 or 1. Every possible combination of 0 and 1 in this formula defines one delay time t_π.

11.6 DEPT Experiment

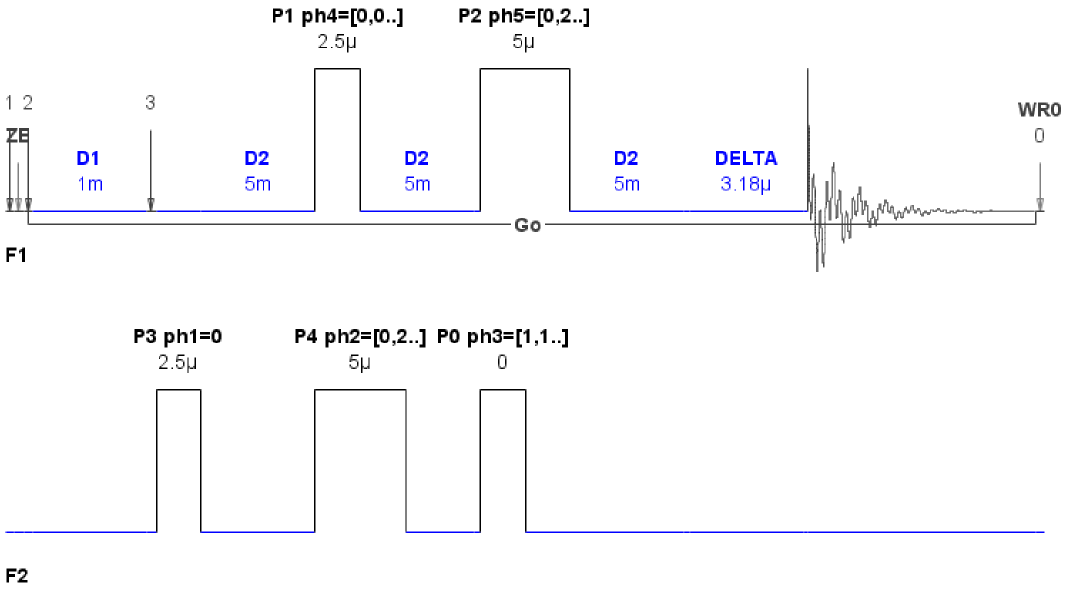


Figure 11.6: The Scheme of DEPT Pulse Sequence without Decoupling

This example presents a simple heteronuclear experiment. The spin system used is an artificial CH3-CH2-CH molecule. The picture demonstrates the dependency of C13 spectra on the number of coupled protons and the tilt angle of the P0 pulse in the DEPT pulse sequence:

```
;deptnd
;dept polarization transfer
;no decoupling during acquisition
1 ze
2 d1 do s1
3 (p3 ph1):d
d2
(p4 ph2):d (p1 ph4 d2)
(p0 ph3):d (p2 ph5)
d2
go=2 ph31
wr #0
d2 do
exit
ph1=0
ph2=0 2 1 3
ph3=1 1 1 1 3 3 3 3
ph4=0 0 0 0 0 0 0 0 1 1 1 1 1 1 1 1
2 2 2 2 2 2 2 2 3 3 3 3 3 3 3 3
ph5=0 2 0 2 0 2 0 2 1 3 1 3 1 3 1 3
ph31=1 1 3 3 3 3 1 1 2 2 0 0 0 0 2 2
3 3 1 1 1 1 3 3 0 0 2 2 2 2 0 0
;S1: ecoupler high power level
;p0 : 45, 90 or 135 degree decoupler high power pulse
; 45 degree - all positive
; 90 degree - XH only
; 135 degree - XH, XH3 positive, XH2 negative
;p1 : 90 degree transmitter high power pulse
;p2 : 180 degree transmitter high power pulse
;p3 : 90 degree decoupler high power pulse
;p4 : 180 degree decoupler high power pulse
;d1 : relaxation delay; 1-5 * T1
;d2 : 1/(2J(XH))
;NS: 4 * n
;DS: 4 or 8
```

The evolution delay D2 has been matched to the CH coupling 100 Hz. The phase distortions in the resulting spectra results from the deviations of CH2 and CH3 coupling constants from this value.

You may try further experiments using the same setup and changing only the pulse program. The pulse program *dept* contains the same experiment, but with decoupling during the acquisition. Another possibility is the pulse program *ineptnd*. The evolution delays for the inept experiment are already set.

[NMR-Sim-Experiment]
sequence=deptn
hamiltonian=chmodel.ham
p0=-135
d2=0.005
Relaxation=1
TD=16384
NS=4
HL1=100000
HL2=200
SF=200
SFO1=50
SW=40

Table 11.5: Experiment Definition File dept.cfg

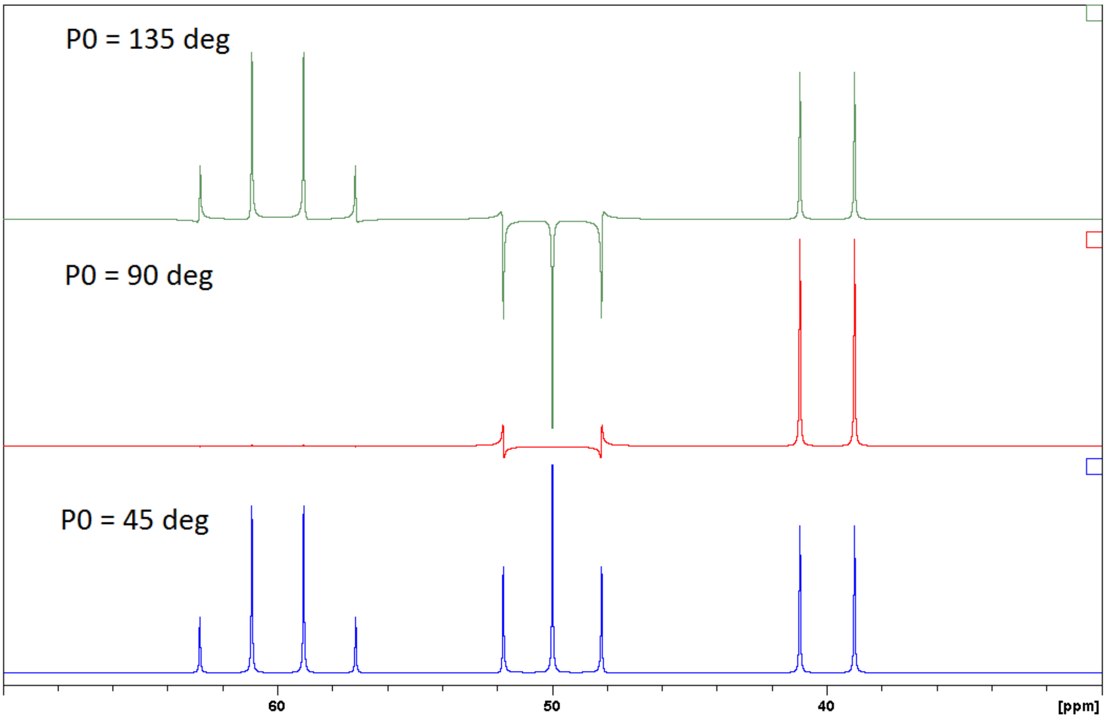
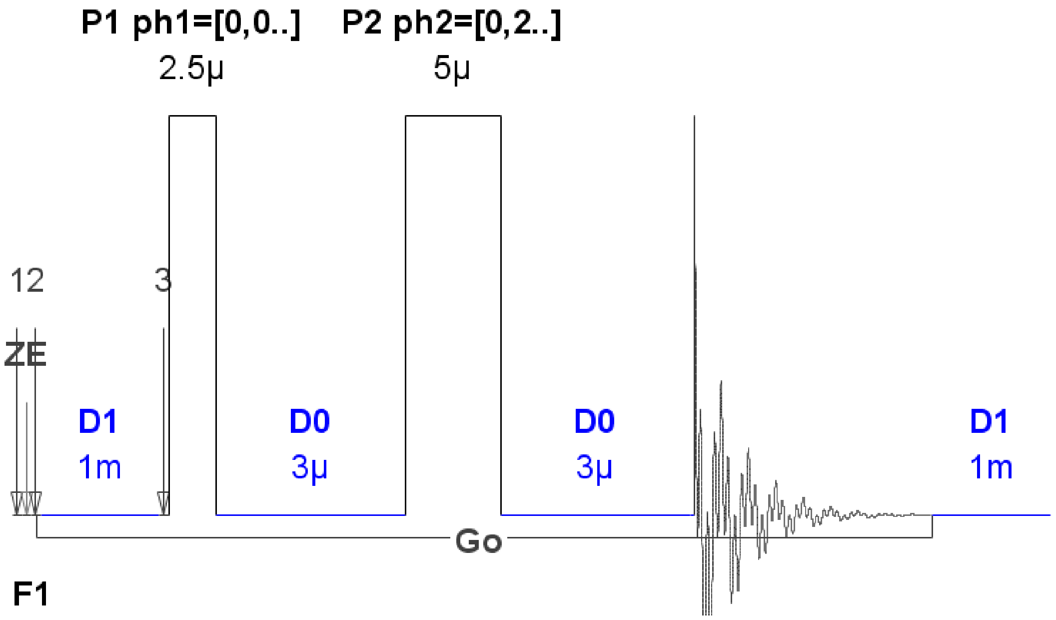


Figure 11.7: Comparison of Simulated C13 DEPT Spectra for Three Different Leading Pulses P0.

11.7 J Resolved Experiment

This simple 2D experiment shows the ability of NMRSim to calculate 2nd order spectra. The comparison of the same J-resolved spectra on 300 MHz and 600 MHz shows the significant reduction of strong coupling artifacts for the higher resonance frequency. Both spectra in the figure were processed using the *qsine* window function with SSB= 3.



[NMR-Sim-Experiment]
sequence=jres
hamiltonian=dbpa.ham
in0=0.01
Relaxation=1
TD=1024
NS=4
HL1=100000
SF=300.13
SFO1=4.1
SW=1.2

Table 11.6: Experiment Definition jres.cfg

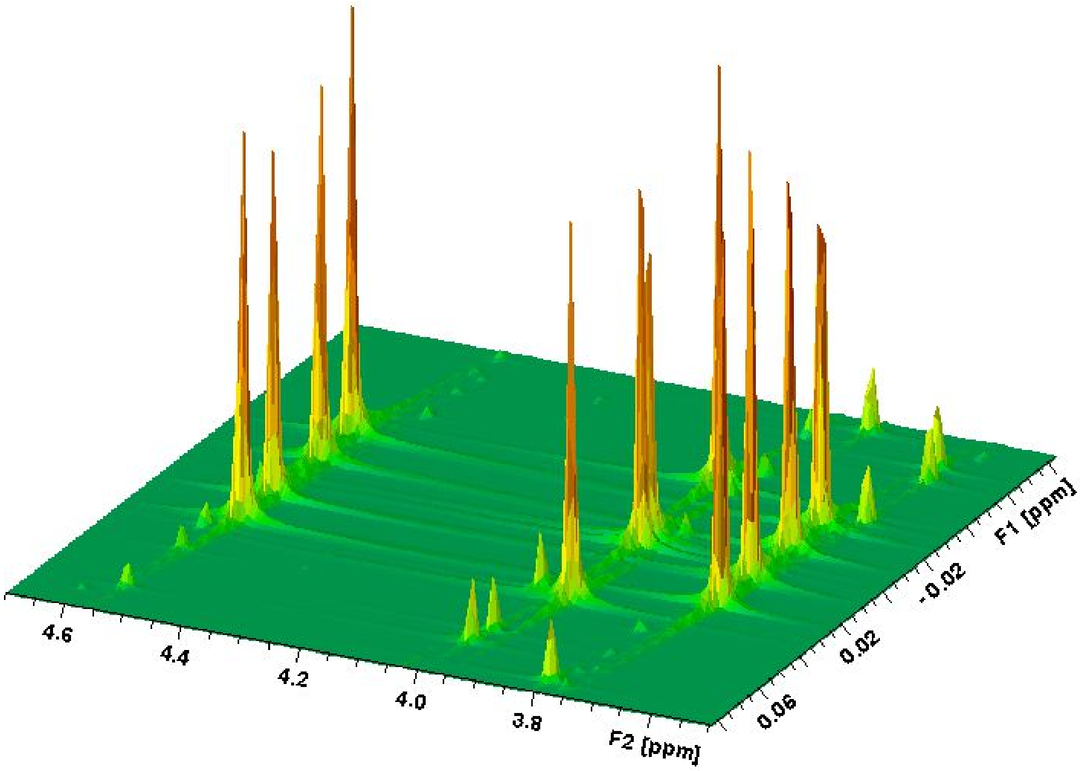


Figure 11.8: The 300 MHz Spectrum Shown as a Stacked Plot.

The intensity of 2nd order artifacts is remarkable.

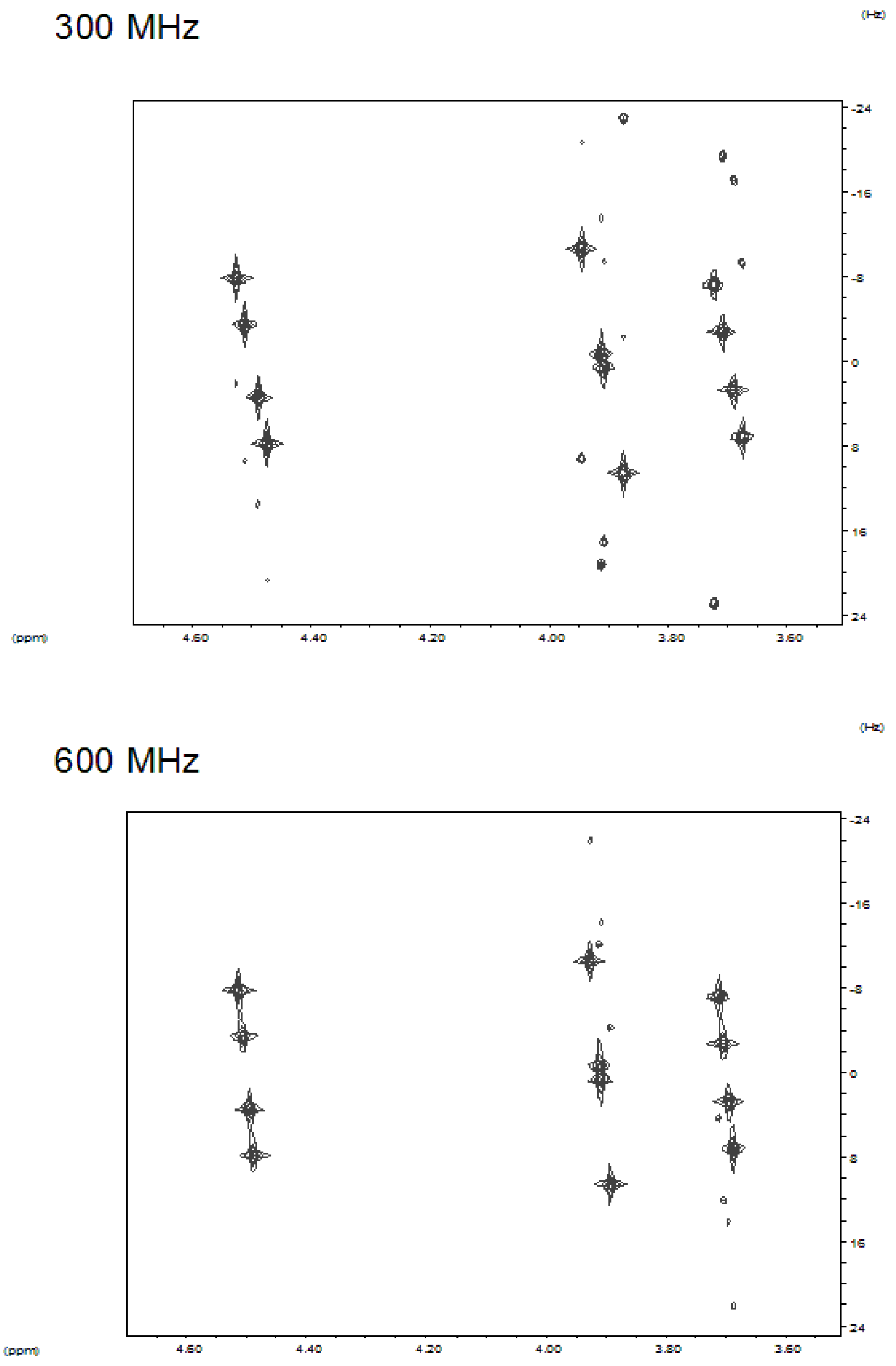


Figure 11.9: The Comparison of J-resolved Experiment for two Different Frequencies.

11.8 Phase Sensitive DQ COSY Experiment

The experiment definition is stored in cosydtp.cfg.

```
[NMR-Sim-Experiment]
sequence=cosydftp
hamiltonian=dbpa.ham
```

in0=sw
Relaxation=1
TD=1024
NS=4
HL1=100000
SF=300.13
SFO1=4.1
SW=1.2

Table 11.7: Experiment Definition cosydtp.cfg

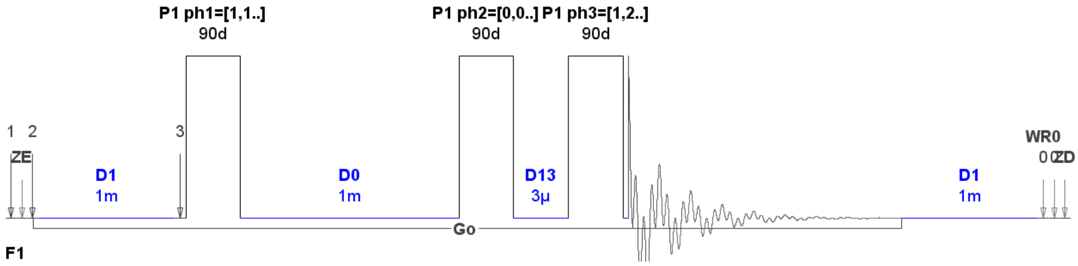


Figure 11.10: Double Quantum Filtered COSY Pulse Program Scheme.

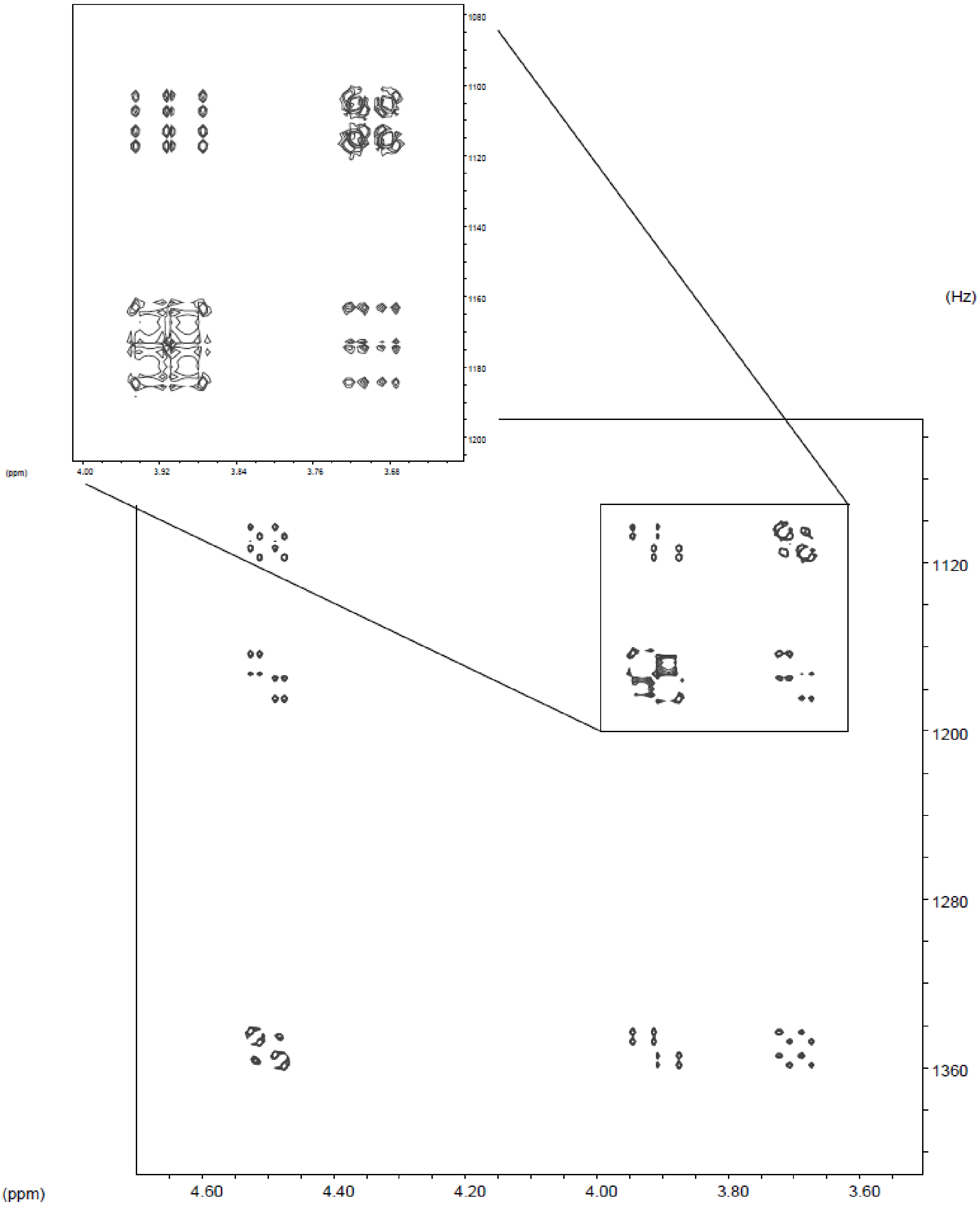


Figure 11.11: The DQ-COSY Spectrum of Di-brom Propionic Acid at 300 MHz.

11.9 Inversion Recovery Experiment

The configuration file *invreco.cfg* contains a simple inversion recovery experiment setup.

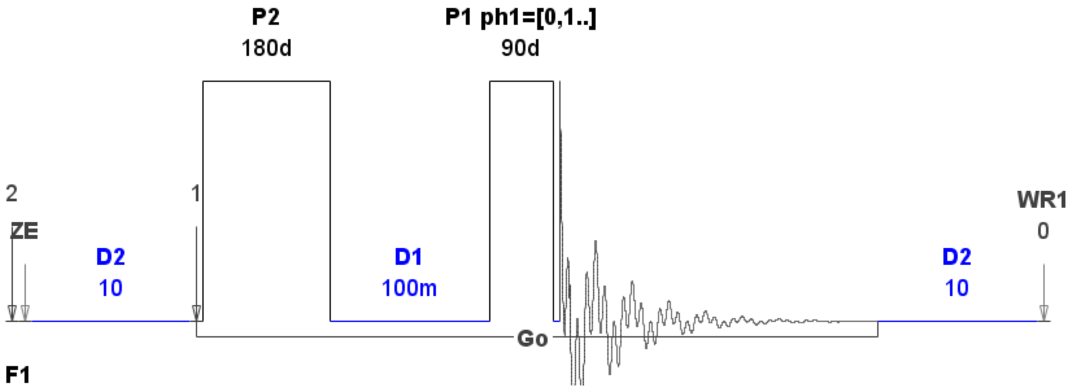


Figure 11.12: The invreco Pulse Program.

The picture shows the relaxation procedure on 10 1D spectra. It may also be possible to present the experiment in 2D form, just change the experiment type from 1D to 2D. Transforming the acquisition dimension f2, you will get an equivalent picture.

```
[NMR-Sim-Experiment]
sequence=$root$\usr\demo\invreco.seq
hamiltonian=$root$\usr\demo\abc.ham
p1=-90
p2=-180
d1=0.0
d2=10
in1=0.03
l1=1
Relaxation=2
TD=16304
NS=1
HL1=100000
SF=200
AQ_mod=1
SW=12
```

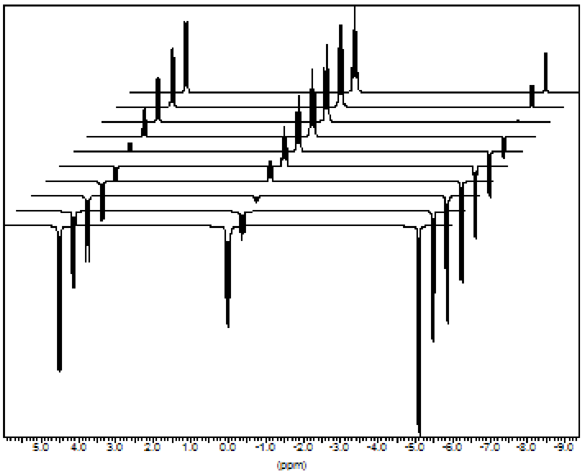


Figure 11.13: Inversion Recovery Experiment.

11.10 Heteronuclear Correlation

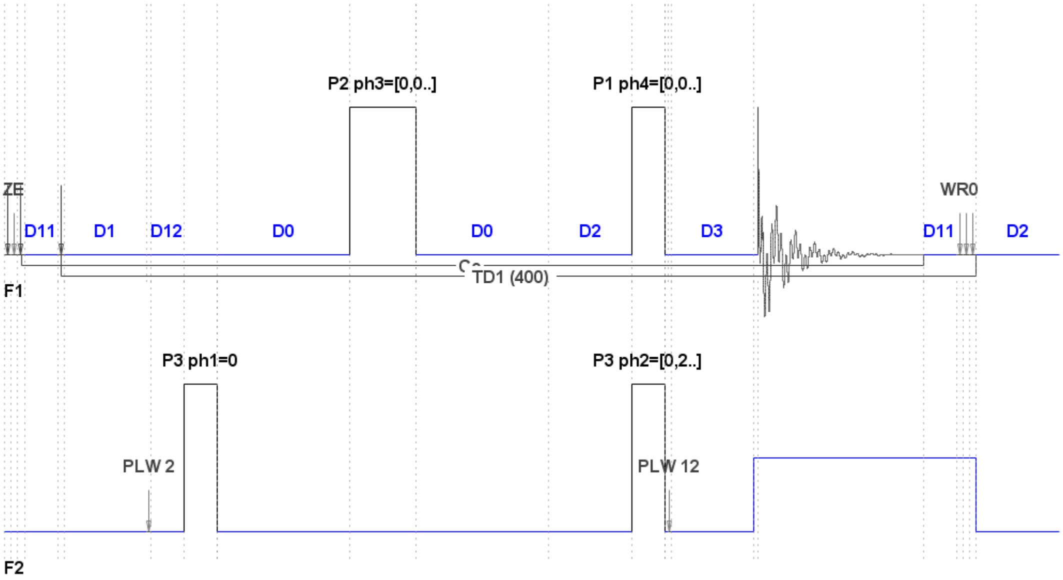


Figure 11.14: The hxco Pulse Program.

This example presents a simple heteronuclear correlation experiment. The sample CH3-CH2-CH spin system (*chmodel.ham*) was used. The result of the simulation is shown below:

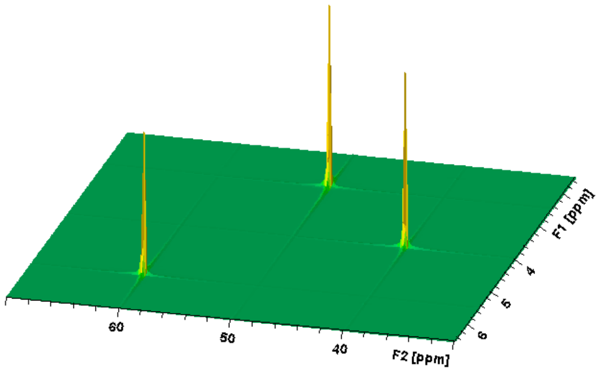


Figure 11.15: Result of the Heteronuclear Correlation Experiment.

11.11 Inverse Experiment

The configuration file *invitp.cfg* contains a setup for a sample inverse experiment.

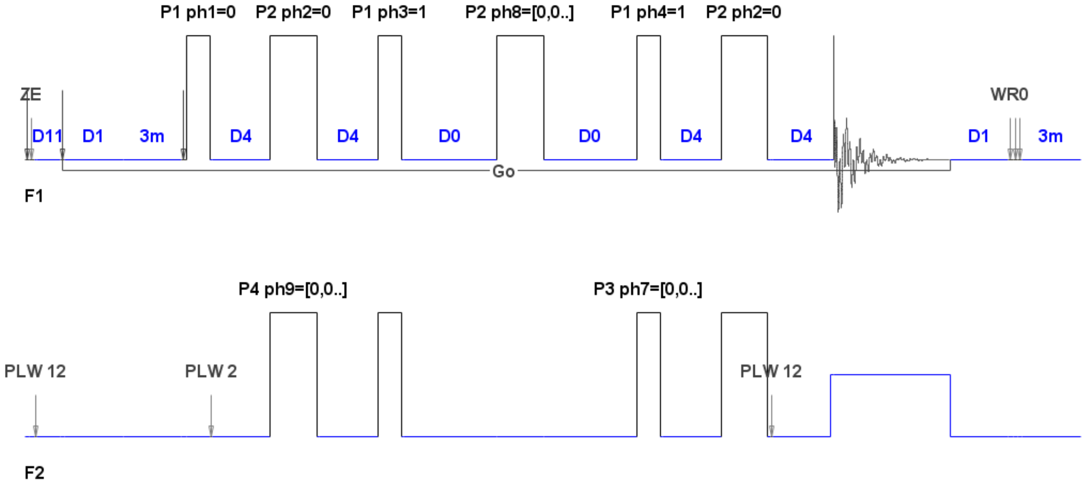
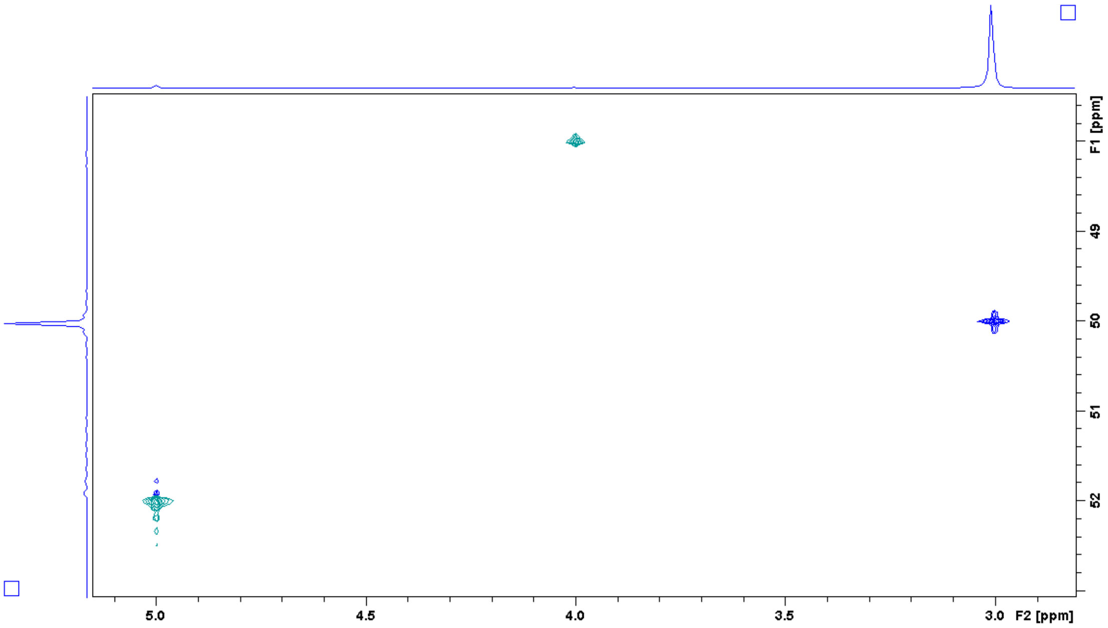


Figure 11.16: invitp Pulse Program - Inverse Correlation Using the inept Sequence.

The double inept sequence is used for the magnetization transfer.

The sample CH3-CH2-CH spin system was used. The figure below shows the result:



11.12 1D Heteronuclear Correlation

The 1D inverse heteronuclear correlation experiment may be used to detect the protons attached to selected X nuclei.

Two versions of this experiment exist: The *classical* one uses a phase cycle to select attached nuclei. The second one uses magnetic field gradient for the coherence selection.

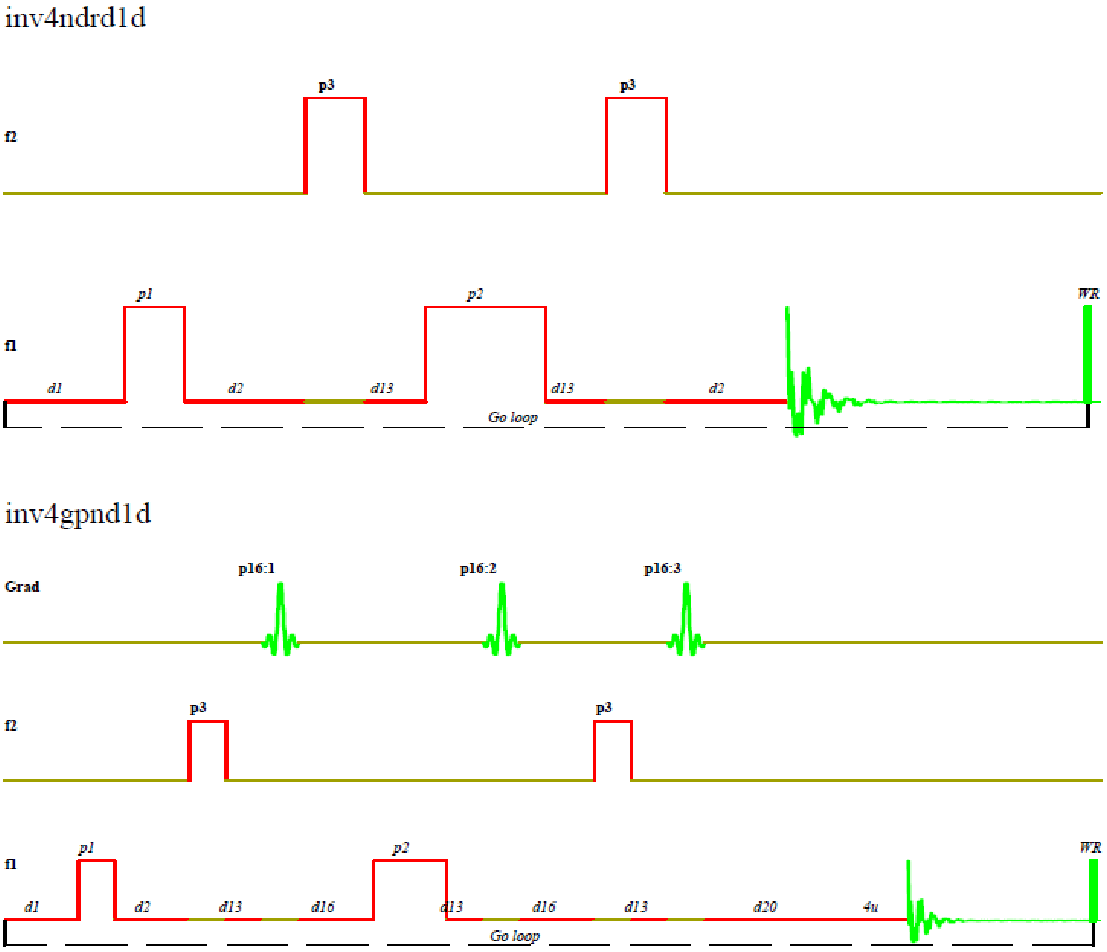


Figure 11.17: Comparison of the "Classical" and Gradient Versions of the Inverse 1D Correlation Experiment.

The experiment parameters are stored in the configuration file *inv_1d.cfg*. Ethanol (*ethanol2.ham*) was used as a model spin system.

The gradient version should use the gradient intensity ratio 50:30:40. This ratio is valid for the H-C13 spin systems. Other X nuclei will require different values.

The results are shown in the next figure. The signals of protons without the C13 coupling are suppressed and we see only the C13 coupled nuclei. A 1D spectrum of the molecule is shown for comparison.

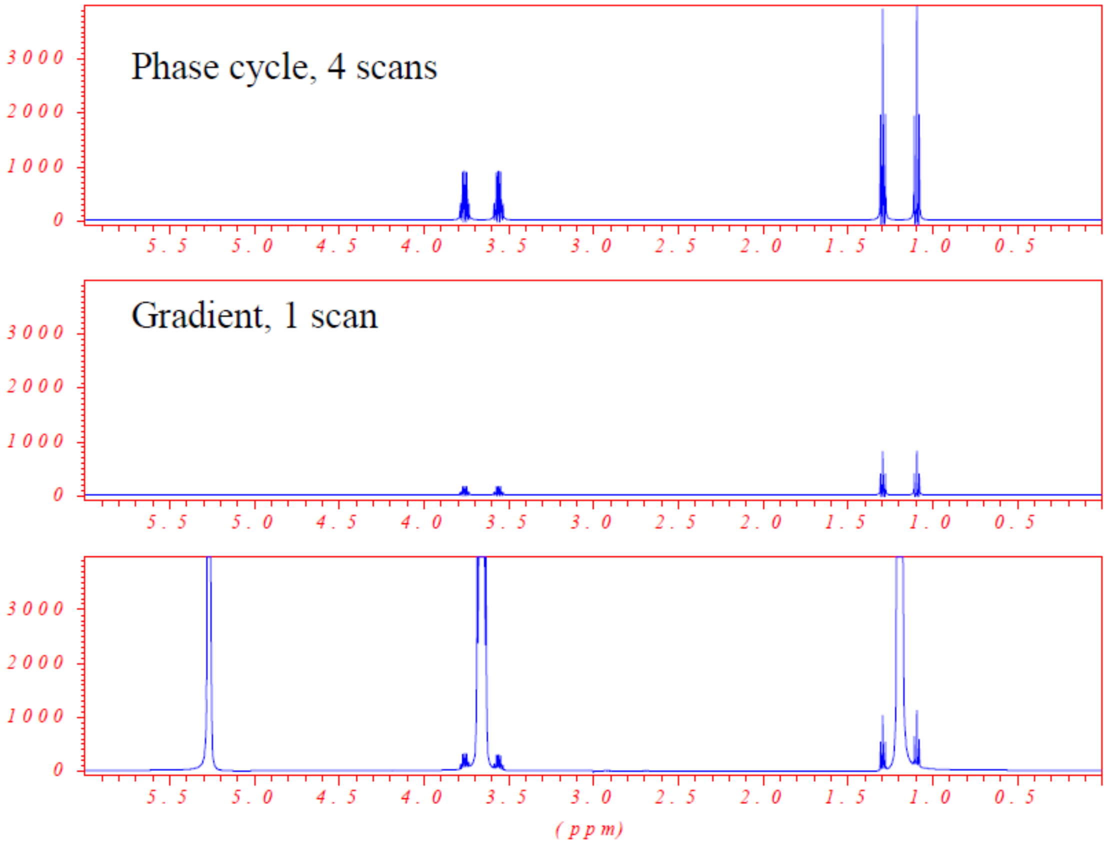


Figure 11.18: Comparison of the 1D Inversion Experiment Using a Traditional Pulse Program with Phase Cycling to Gradient Version.

No decoupling was used during the acquisition. The gradient version uses only one scan, so the signal intensities are lower.

11.13 Gradient Experiments

The details of the implementation of gradient spectroscopy are described in the chapter *Gradient Spectroscopy [▸ 73]*.

11.13.1 Gradient COSY Experiment

The basic gradient experiment is the *cosygp* pulse program. Here we use the *cosygpmfph* pulse program: multiple quantum filtered COSY using gradients.

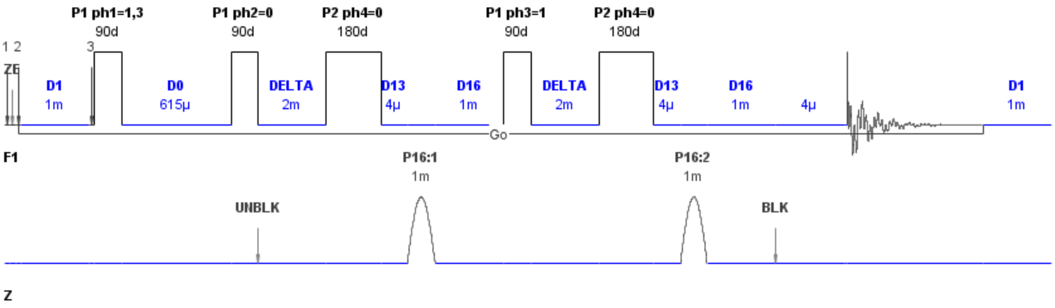
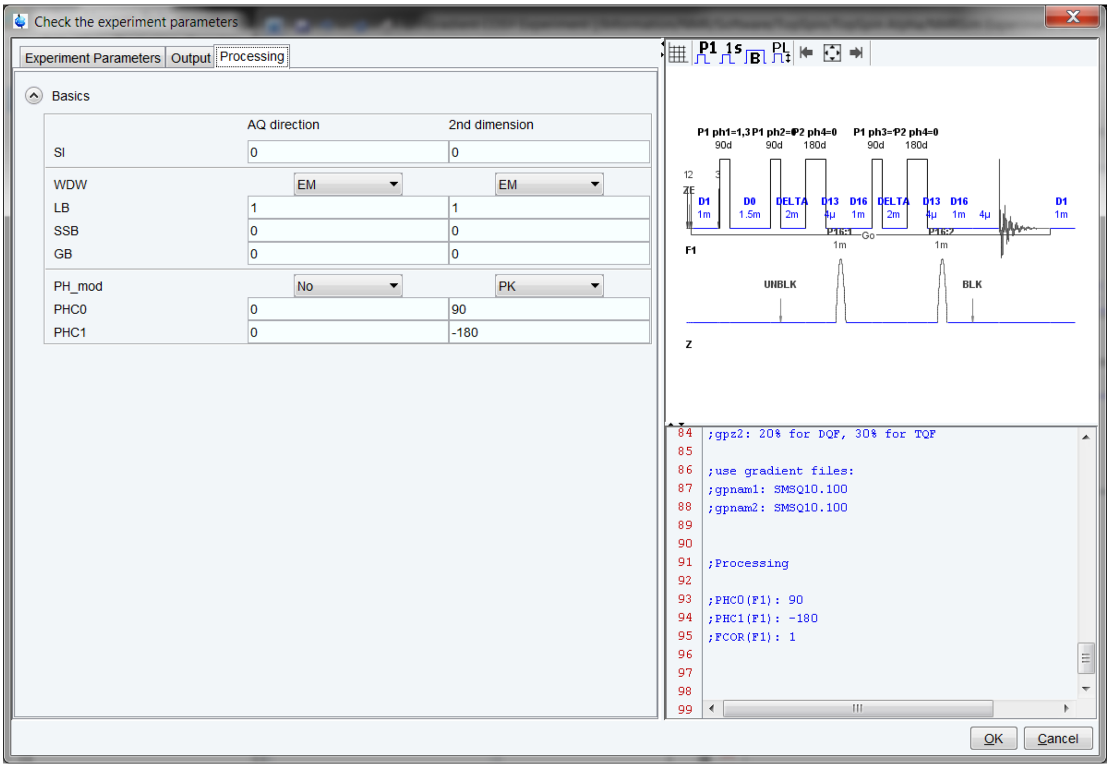


Figure 11.19: COSYGPMFPH Pulse Program.

This pulse program may use different gradient intensity ratios for the coherence selection. Ratio 10:20 gives a double-quantum filtered experiment, ratio 10:30 gives a triple quantum spectrum. The experiment is phase sensitive using the TPPI phase modulation, only one transient (scan) is required.

Please, note the required phase correction: it is always a part of the pulse program documentation.



	AQ direction	2nd dimension
SI	0	0
WDW	EM	EM
LB	1	1
SSB	0	0
GB	0	0
PH_mod	No	PK
PHC0	0	90
PHC1	0	-180

```
;gpz2: 20% for DQF, 30% for TQF

;use gradient files:
;gpnam1: SMSQ10.100
;gpnam2: SMSQ10.100


;Processing

;PHC0(F1): 90
;PHC1(F1): -180
;FCOR(F1): 1
```

Figure 11.20: Required phase correction as a comment in pulse program text

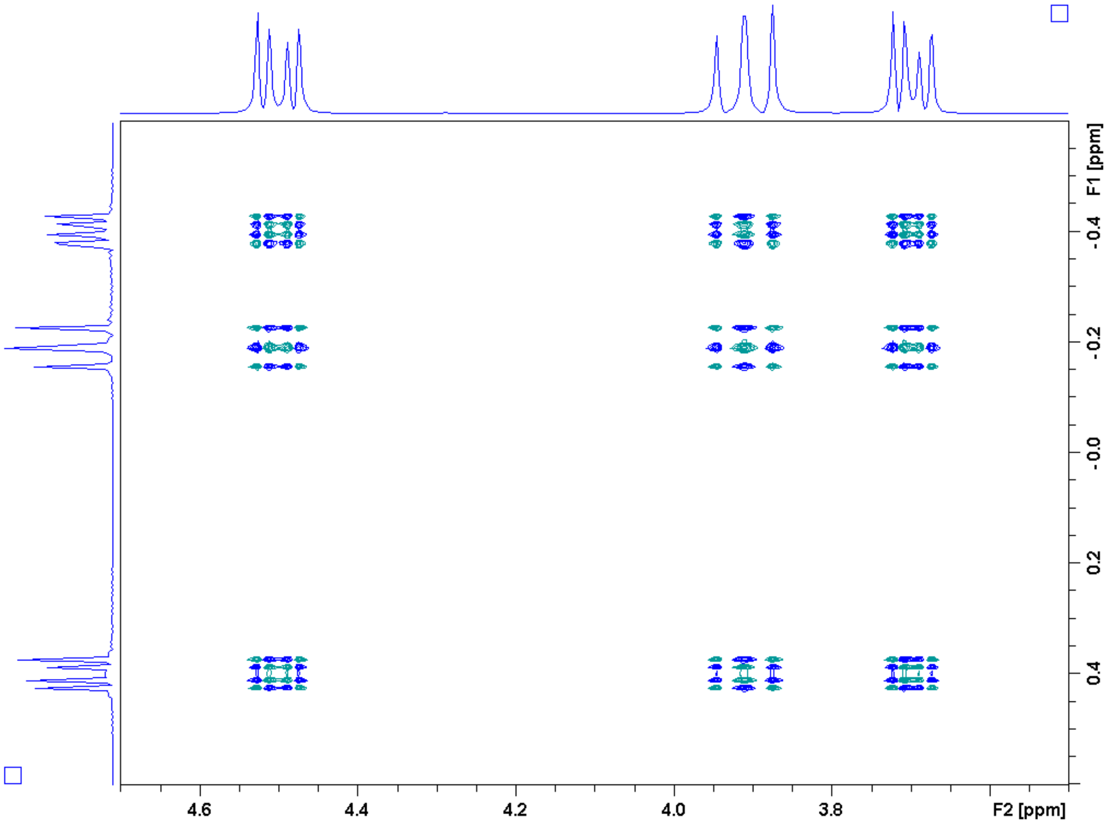


Figure 11.21: Triple-Quantum Filtered Gradient COSY Spectrum of a Di-brom-propionic Acid.

11.13.2 Watergate

The watergate pulse program is used for the efficient suppression of solvent signals. The pulse sequence contains a “sandwich” of two gradients separated by a selective inversion pulse. The version presented here uses a popular binomial sequence of hard pulses as the inversion pulse.

The following pulse program calculates the excitation profile of the watergate sequence. It uses the NMRSim spin system manipulation commands to imitate the shift of the spectrometer carrier frequency which is necessary to measure such a dependence. The name of the pulse program is *watergate.seq*, the configuration file is *watergate.cfg*.

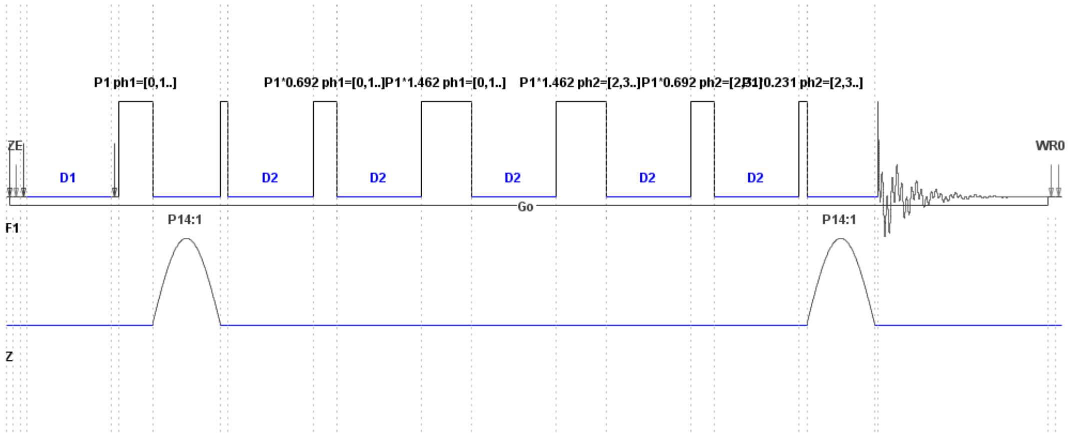
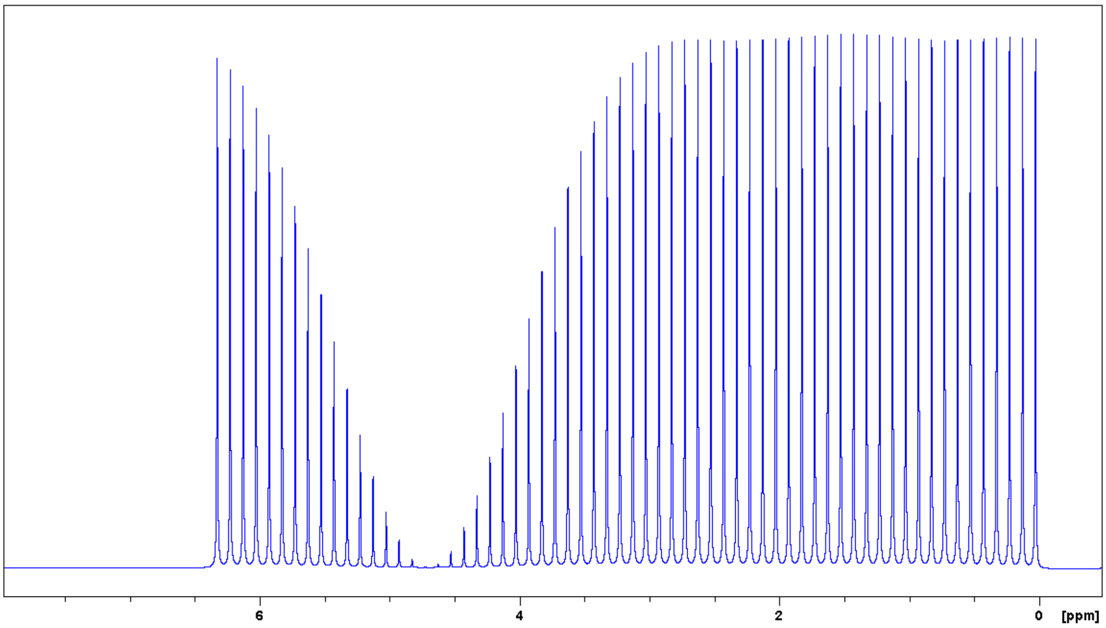


Figure 11.22: Watergate Pulse Program.

```
;watergate
;avance-version
;
; Pulse program for the solvent suppression
; using the watergate pulse sequence
;
1 ze
2 d1
3 p1 ph1
p14:gp1
;
; The binomial selective pulse starts here
p1*0.231 ph1
d2
p1*0.692 ph1
d2
p1*1.462 ph1
d2
p1*1.462 ph2
d2
p1*0.692 ph2
d2
p1*0.231 ph2
p14:gp1
go=2 ph31
; this command increments the spin system variables
ihc
lo to 2 times l1
wr #0
exit

ph1=0 1 2 3
ph2=2 3 0 1
ph31=0 1 2 3

;NS: 4 * n
```

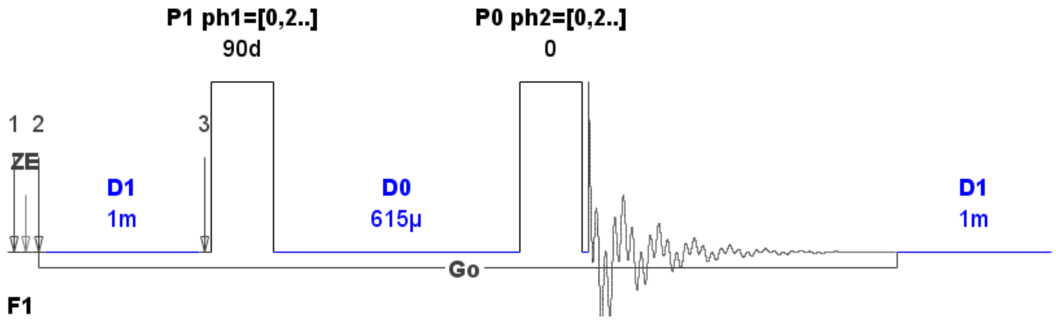


The experiment requires 4 transients (scans), the gradient pulse length was 2 ms, the gradient power GPZ1 10%.

The delay D2 is an important parameter defining the periodicity of the binomial inversion pulse. The value 0.3 µs used here, guaranties that the next minimum lies always outside of the spectrum bandwidth.

11.14 Phase Sensitive COSY Experiment Using the mc Command

The configuration file *cosyph.cfg* contains a setup for a sample experiment using the cosyph pulse program.



The **mc** command was introduced to the Bruker pulse programming language to simplify the usage of different techniques for the phase sensitive detection in the indirect detection directions. The next table compares the new *cosyph* sequence and the old *cosytp* pulse program.

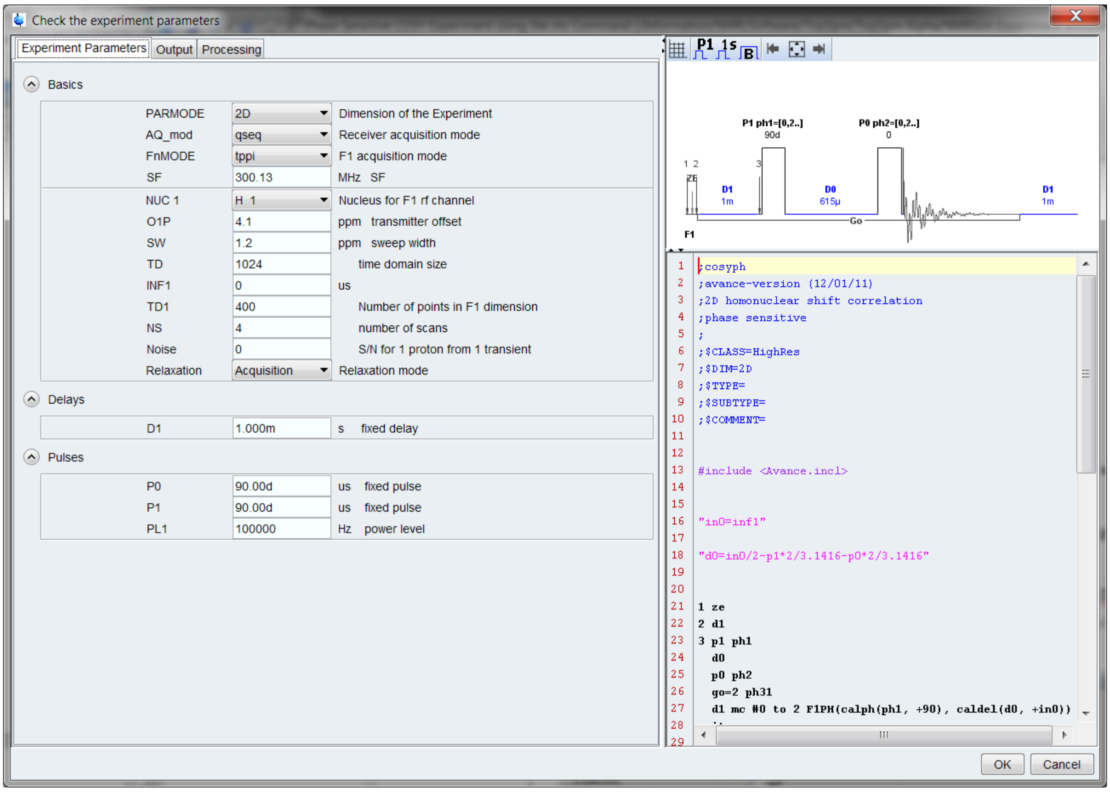
COSYPH	COSYTP
1 ze 2 d1 3 p1 ph1 d0 p0 ph2 go=2 ph31 d1 mc #0 to 2 F1PH(ip1, id0) exit	1 ze 2 d1 3 p1 ph1 d0 p0 ph2 go=2 ph31 d1 wr #0 if #0 id0 ip1 zd lo to 3 times td1 exit

Table 11.8: Comparison of COSYPH and COSY Sequences

You see, that the original handling necessary for the TPPI quadrature detection was replaced with much simpler syntax.

The pulse programs containing the **mc** command are expanded in the pulse programming language compiler to a new pulse program, which is similar to the original cosytp.

The way, in which the pulse programs are expanded is defined using the *FnMODE* parameter. These parameters (for each indirect detection dimension one) may be set in the **Check Experiment Parameters** dialog:



Basics

PARMODE	2D		Dimension of the Experiment
AQ_mod	qseq		Receiver acquisition mode
FnMODE	tppi		F1 acquisition mode
SF	300.13	MHz	SF
NUC 1	H 1		Nucleus for F1 rf channel
O1P	4.1	ppm	transmitter offset
SW	1.2	ppm	sweep width
TD	1024		time domain size
INF1	0	us	
TD1	400		Number of points in F1 dimension
NS	4		number of scans
Noise	0		S/N for 1 proton from 1 transient
Relaxation	Acquisition		Relaxation mode

Delays

D1	1.000m	s	fixed delay

Pulses

P0	90.00d	us	fixed pulse
P1	90.00d	us	fixed pulse
PL1	100000	Hz	power level

```
;cosyph
;avance-version (12/01/11)
;2D homonuclear shift correlation
;phase sensitive
;
;$CLASS=HighRes
;$DIM=2D
;$TYPE=
;$SUBTYPE=
;$COMMENT=


#include <Avance.incl>


"in0=inf1"

"d0=in0/2-p1*2/3.1416-p0*2/3.1416"


1 ze
2 d1
3 p1 ph1
  d0
  p0 ph2
  go=2 ph31
  d1 mc #0 to 2 F1PH(calph(ph1, +90), caldel(d0, +in0))
```

The cosyph pulse program contains a macro F1PH. This means, that this pulse program may use any phase sensitive scheme (tppi, states, statest-tppi). The non-phase sensitive schemes and the echo- anti echo require other macros. Details are discussed in the TopSpin acquisition manual.

12 Contact

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

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