Diffusion

NMR
User Manual

Version 003

think forward

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Table of Contents

Table of Contents

1 Introduction

This manual targets the **installation engineer**, helping them to understand all the features available for the diffusion accessory. This manual also provides valuable information for the **user**, who is getting started with the diffusion system.

New in this version of the Diffusion User Manual is extended background information and reorganized contents, including the addition of a „Troubleshooting" chapter, which will hopefully help both users and service engineers to solve possible problems.

Due to the similarity of the imaging and diffusion hardware and software, this manual overlaps the AVANCE Imaging Manual in parts. Therefore the reference to "**imaging**" will often appear, but can be used interchangeably with "**diffusion**".

1.1 Disclaimer

The diffusion accessory should only be used for its intended purpose as described in this manual. Use of the unit for any purpose other than that for which it is intended is taken only at the users own risk and invalidates any and all manufacturer warranties.

• Service or maintenance work on the diffusion accessory must be carried out by qualified personnel.

• Only those persons schooled in the operation of the diffusion accessory should operate the unit.

• Read this manual before operating the unit. Pay particular attention to any safety related information.

Introduction

2 Installation

This chapter provides information on setting up the hardware and software required in the diffusion system. The chapter is especially important when setting up the system for the first time.

2.1 Installing the Diffusion Software

This manual describes diffusion software version *diff 4.5*, which is delivered with TopSpin version 2.1 pl3. However, most of the content discussed in this manual will be valid for all *diff 4.x* versions and, to some extent, older versions as well.

The diffusion package is part of the micro-imaging package. To activate the package, check the checkbox *Micro-Imaging and Diffusion Systems* during the *expinstall* procedure, which is part of the Micro-imaging installation.

2.2 Installing the Diffusion Hardware

The installation of the diffusion/imaging rack is described in detail in the *Micro-imaging Manual for AVANCE III Systems*. Therefore this step has been omitted in this manual. Nevertheless some details of the imaging rack are provided in the chapter "Imaging and Diffusion Hardware" on page 107.

2.3 Gradres (AVANCE III only)

The parameter *GRADRES* defines the step width for the Digital Preemphasis Processor (DPP). Although this should work over a wide range of values, currently this parameter must be set to 8, i.e. 8 μs for GREAT40/GREAT60 systems. Other values may work as well, but only 8 has been extensively tested.

i Note: Currently the parameter *GRADRES* can only be checked or modified by editing the file: *<TopSpinHome>/conf/instr/spect/uxnmr.par*

2.4 Installing a Diffusion Probe

The following sections describe how to set up the a diffusion probe in TopSpin. For specific details on diffusion probes, refer to the chapter "Probes and Gradients" on page 99.

2.4.1 Defining a Probe in the Probe File

Before a probe can be used in the diffusion system, it must be defined in the probe file as follows:

1. Type `edhead` in the TopSpin command line.

2. Select **New Probe** in the *Probe* pull-down menu.

3. Select **MIC** as *Probe Type* for the diffusion or micro-imaging probe. Afterwards the name can be changed for individual needs. If more probes are in the lab, a meaningful name will be useful.

4. Fill in the **Part Number** and the **Serial Number**, these are mandatory. The other parameters should be filled as far as they are known.

The number appearing in the last column is the identification of the probe.

The description of the probe appearing in `edhead` can be changed manually in the file *<TopSpinHome>/exp/stan/nmr/lists/probes.*

2.4.2 Defining the Diffusion Probe as the Current One

Type `edhead` in TopSpin and select the diffusion probe.

This must be done before adjusting the preemphasis and calibrating the gradient strength. This step is also required each time you switch back from another probe, in order to provide access to the proper gradient calibration. See also "Probe Exchange" on page 33.

2.4.3 Preparation for NMR Adjustments

It is highly recommended to use the *doped water* sample (Z10906) for all setup experiments. If this sample is not available, a similar sample consisting of 1% H_2O in D_2O, plus 0.1% $CuSO_4$ should be prepared. The exact concentration is not important for the preemphasis adjustment, but it is useful for the later gradient calibration. Low concentrations of H_2O are important to avoid radiation damping. The $CuSO_4$ is mainly used to save time, but it also acts against radiation damping. The sample filling height should be about 40 mm.

i Note: Never use pure H_2O for these adjustments.

1. Setup a 1D experiment on protons.

2. Shim the sample to a line width of less than 10 Hz at half height and less than 100 Hz at 10% height. Good shimming at this point provides better sensitivity for the later preemphasis adjustment. The relaxation agent does not allow a line width below about 3 Hz at half height.

3. Adjust the 90 degree pulse. Preemphasis experiments are usually done using 30 degree pulses, but when using the doped sample 90 pulses can also be used.

i Note: All parameters in the following adjustments are controlled by `setpre`, see "Set-pre" on page 91.

2.5 Starting the *Diff* Program for the First Time

At this point the *diff* program can be started in configuration mode, type `diff config`. The *diff* window will appear as shown in Figure 2.1.

In configuration mode adjustments can be done without prior knowledge of the gradient system. Using *diff* in this mode is only necessary if no template files are available, see "Default Preemphasis File" on page 13.

i Note: There is no gradient security in configuration mode!

If there is no preemphasis file available, it will be created first by the *setpre* program, see "Parameter Storage" on page 92.

Installation
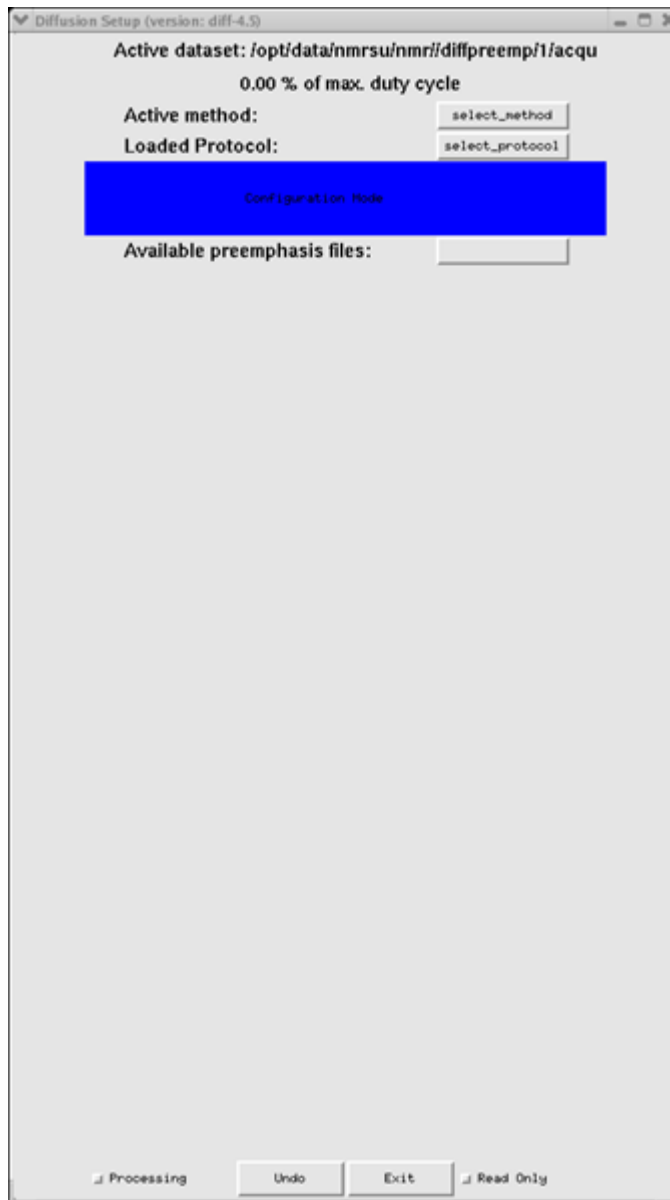
Figure 2.1 *diff* started in config mode

If *diff* is started without a preemphasis file, *diff* will switch to configuration mode automatically, giving a warning after a method has been selected. The *diff* window will then look a bit different:
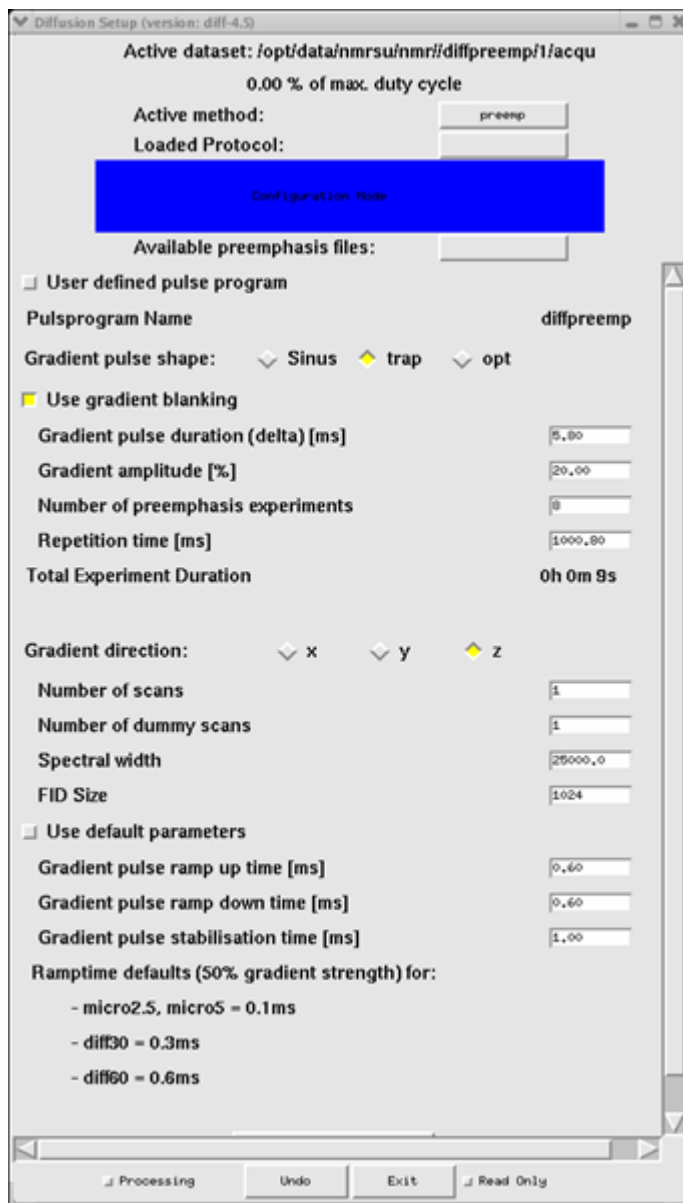
Figure 2.2   ***diff*** after automatic switching to configuration mode

2.5.1   Default Preemphasis File

Preemphasis files are generally stored in the directory:

```
<TopSpinHome>/exp/stan/nmr/parx/preemp
```

The files for the individual probes are then stored in numbered subdirectories.

Usually it is the best to start with a preemphasis file template.

- Beginning with TopSpin version 2.1pl2, templates are provided and can be found in subdirectories called e.g. diff30. In the subdirectory there are different files depending on the amplifier that is used.

- Beginning with TopSpin version 2.1pl4, *diff* can copy the template files into the probe directory. Press the **Available Preemphasis Files** button shown in Figure 2.1. The window will appear as shown below:

Figure 2.3   *Diff* showing preemphasis file copy menu

The list in the pull-down menu in Figure 2.3 shows all available preemphasis files in the actual TopSpin version. The entries beginning with a gradient system name, e.g. diff30/default.GREAT40 as highlighted in the figure, are template files containing all the parameters for the selected gradient system and amplifier type.

Clicking on one of the entries will copy the corresponding preemphasis file to the location of the currently active probe.

i Note: The copy procedure works in the background, i.e. a message will only be displayed when an error occurs.

For earlier TopSpin versions the files must be copied manually:
```
cd <TopSpinHome>/exp/stan/nmr/parx/preemp
cp diff30/default.great60 03/default
```

In the above example, the command copies the default preemphasis file for a diff30 probe driven by a GREAT1/60 amplifier to probe number 03.

i Note: The probe number must always have 2 digits.

Do not overwrite existing, already configured, preemphasis files without making a backup copy.

2.6 Impedance Matching of the Gradient Amplifier to the Gradient System

The following section is a brief description of how to do the impedance matching of the gradient amplifier to the gradient system. This step is explained in more detail in the *Micro-imaging Manual for AVANCE III Systems*.

i Note: This adjustment must be done prior to the preemphasis adjustment.

The default preemphasis file templates (see "Default Preemphasis File" on page 13) provide reasonable loop parameters to get started, but they must be verified during installation. This is particularly important when using the diff60 probe.

Use the same setup as for a preemphasis experiment, see "Preemphasis Adjustment Experiment" on page 19.

Be aware, that the duty cycle calculations may not be correct at this stage of the installation and therefore special care has to be taken not to overheat the gradient system. Using the standard preemphasis protocol should be safe.

1. Set all preemphasis gains of the observed channel to zero (refer to "Preemphasis, B0, and Cross-Preemphasis Parameters" on page 91).

2. Connect an oscilloscope to the output labeled *I* on the gradient amplifier front panel.

3. Look at the gradient pulses in gs-mode and adjust the loop parameters ("Loop parameters" on page 97) in order to match the pulse shape seen on the oscillo-

scope to the input gradient shape.

Usually trapezoidal pulses are the best choice. Examples are given below.
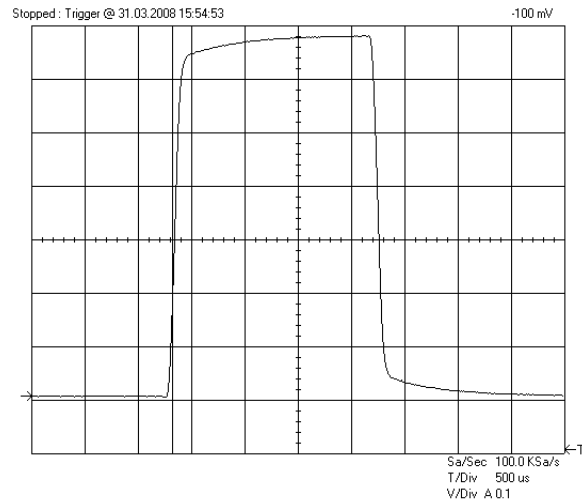
Figure 2.4   Gradient Pulse with too high "Resistors/Capacitors" values, leading to slow regulation behavior
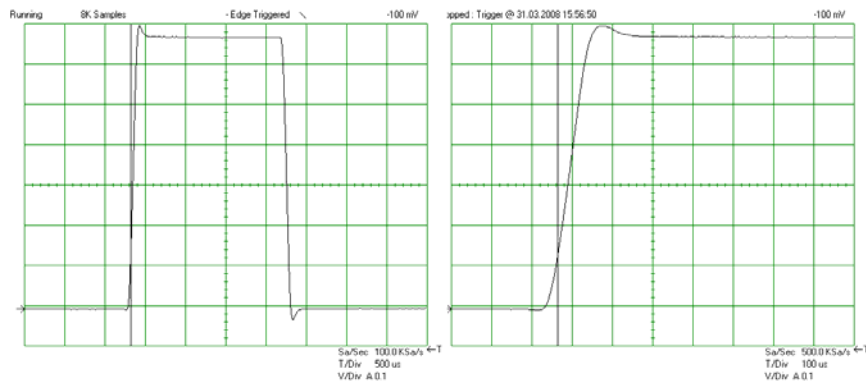
Figure 2.5   Gradient Pulse with too low "Resistors/Capacitors" values, leading to a current overshoot
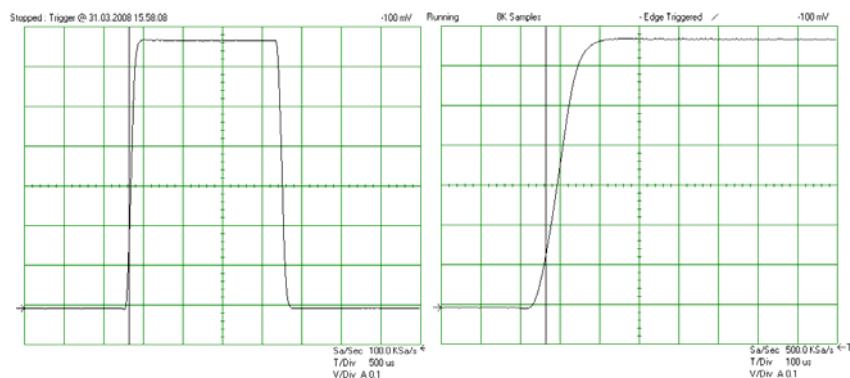
Figure 2.6   Optimal adjusted loop values leading to the fastest rise time without current overshoot

If any changes have been made, save them using *Setpre-->File-->Write default.*

2.7   Offset Adjustment

1. Copy the 1D data set described in "Preparation for NMR Adjustments" on page 10.

2. Change the pulse program to *diffoffset*. Run the experiment in gs mode. The observed spectrum will usually show a much wider line than before.

3. Click on the Auto button in the second row of the preemphasis control window (see Figure 8.1). After a few seconds, the offset should be adjusted and the line shape should be approximately back to the shape achieved using *zg*. In gs mode the signal will be less stable then normal, because the blanking is open during this experiment. This should not be of any concern.

On AVANCE III type instruments using GREAT1/60 amplifiers with part number W1209612, or GREAT1/40 amplifiers with part number W1211690, the auto adjustment might fail. In this case the coarse offset needs to be adjusted prior to the auto adjustment. Set the offset to zero first and then adjust the coarse offset first, followed by the auto offset again. The coarse offset values will usually be in the range of -4 to -6.

In general the offset can be finely adjusted manually, but usually this will not be necessary.

If any changes have been made, save using *Setpre-->File-->Write default.*

2.8   Preemphasis Adjustment

2.8.1   Background

The shape of an FID or an echo, acquired only a short time after a gradient pulse, may be distorted by eddy currents caused by gradient switching. The influence of the eddy currents can be decreased by modifying the shape of the gradient pulses. Three expo-

nential functions, with different amplitude and time constants, are available to accomplish this.

The figure below shows an example of two gradient pulses, one positive, the other negative. In order to get this desired gradient behavior in the presence of eddy currents, the current pulse shapes have to be modified as indicated in Figure 2.8. Usually the required values are much smaller than the ones shown there.
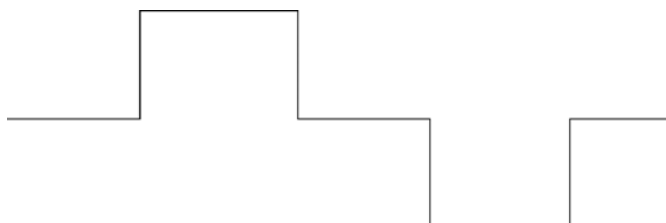
Figure 2.7   Desired Gradient Pulse Shape
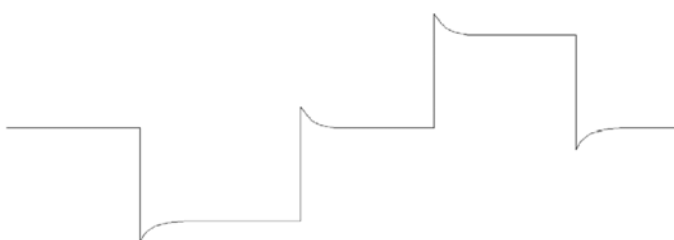
Figure 2.8   Gradient Pulses with Preemphasis (overemphasized)

The amplitudes and time constants are set in a control window and are stored for individual gradient systems. This is described in the following section.

The preemphasis parameters are *adjusted* by observing FID's at varying delays after a gradient pulse. Typical time variations after gradient switching, are in the range between 100 μs and 1 sec, depending on the type of gradient system.
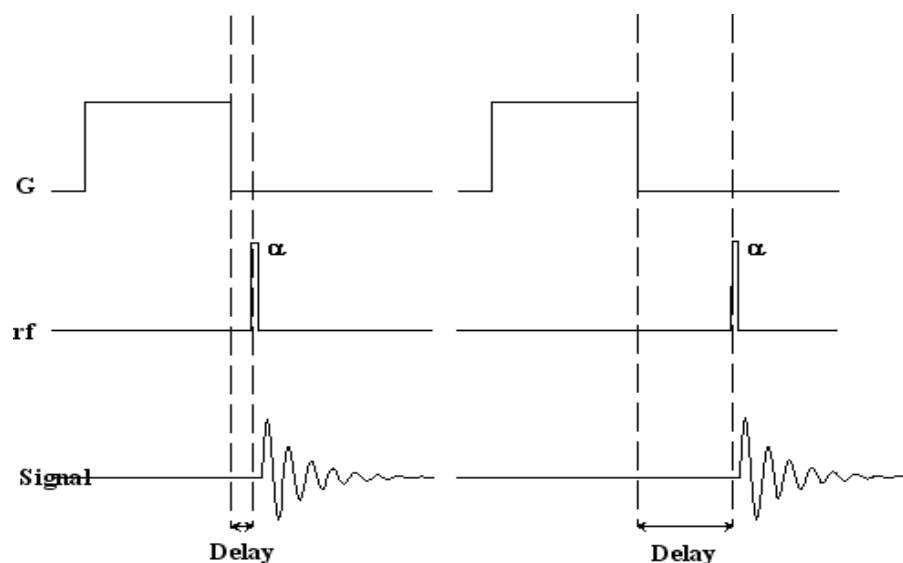
Figure 2.9   Preemphasis Adjustment Program

2.8.2   Preemphasis Adjustment Experiment

1. Copy the 1D data set described in "Preparation for NMR Adjustments" on page 10.

2. Start *diff* and load the protocol ***preemp***.

    Usually all the parameters are already set to reasonable values, only the gradient ramp time must be manually corrected. This is because at this stage the type of gradient system is not yet known to the system. The typical values are shown as comments (see Figure 2.10).

3. Set the offset to about 2 kHz off resonance.
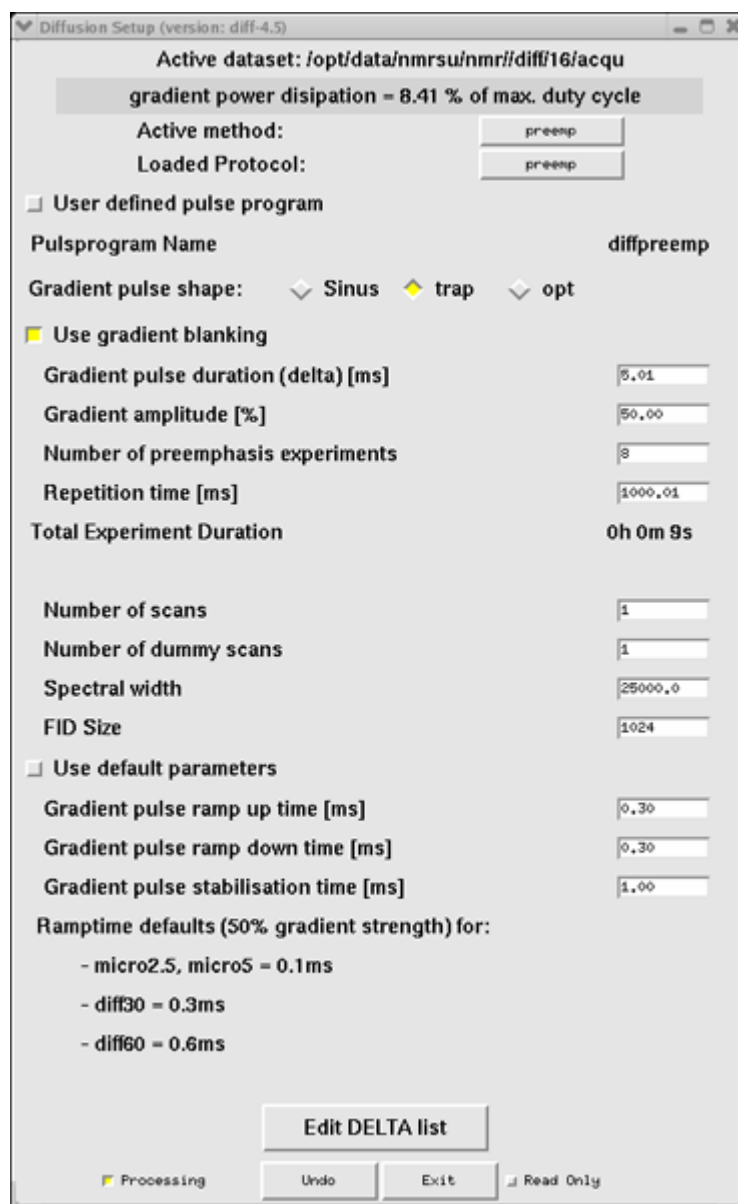
Figure 2.10   *diff* showing preemp

ⅈ   Make sure the water cooling is running properly, the preemphasis adjustment is usually the most demanding experiment in terms of heating of the gradient coil.

2.8.3   Adjustment

Delay After Gradient Pulse
200 µs
400 µs
900 µs
2 ms
4 ms
9 ms
20 ms
200 ms

Table 2.1:   Default preemphasis delay list

As default:

- The gradient amplitude is set to 50%.

- The gradient duration is set to 5 ms.

- And the repetition time is set to 1 s.

- Also the other parameters are set to usually useful values.

The protocol switches the gradient banking on, which is always correct for AVANCE III instruments. If the blanking is active the gradient amplifier will be blanked after the individual variable delay. Using the new BGMU-E (master unit) in the AVANCE III instruments the unblanked period is automatically prolonged until the preemphasis has decayed. This works well, if the offset has been adjusted properly. On older instruments it could be sometimes useful to switch off the blanking to see the effect of the preemphasis.

i Note: The default ramp time setting might not work at this stage. Switch it off and use the values shown at the bottom of Figure 2.10.

If not familiar with this experiment one can first set the gradient amplitude to zero. Start gs and watch the signals in the acquisition window. Then the signals should look like those in Figure 2.11. If this is not the case, go back and check the steps above.
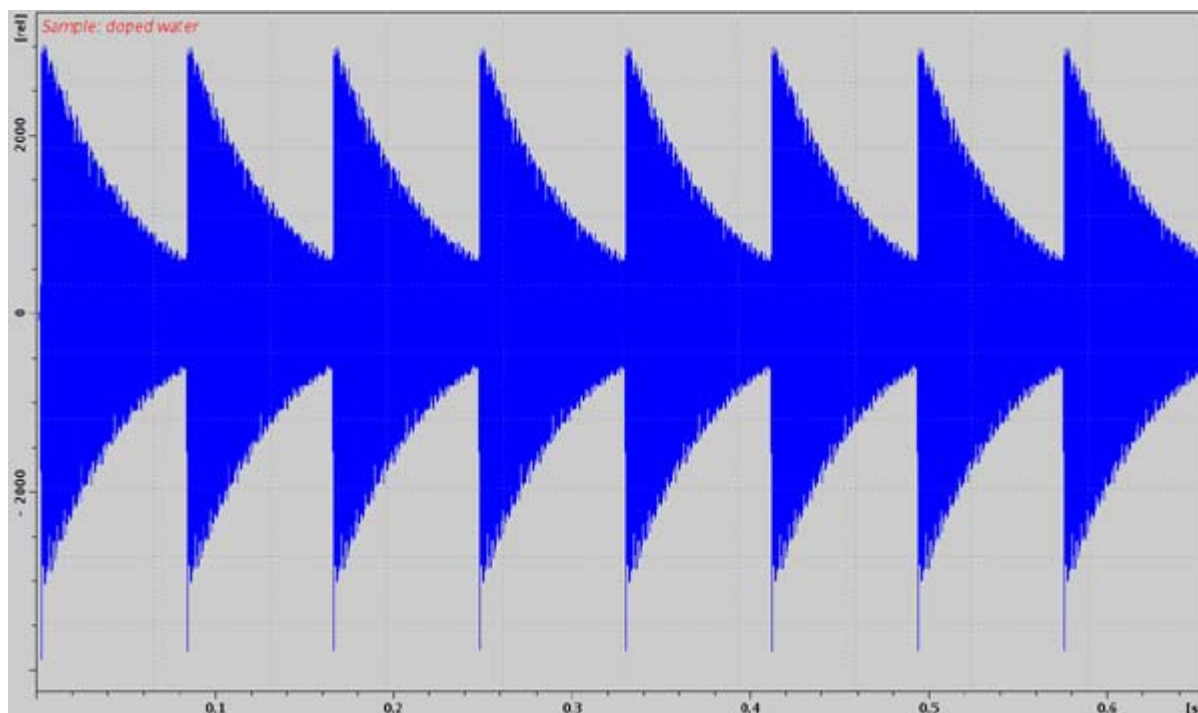
Figure 2.11   Eight FID's Without Gradient Switching

Stop the acquisition and set the gradient amplitude back to 50%.

---

i   Note: Gradient amplitudes and timings cannot be changed in gs-mode. The acquisition must always be stopped and restarted after the parameters have been changed.

Adjustment: Watch the FID's in the acquisition window in gs mode. The screen will now look like that in Figure 2.12.

---

i   Note: If you don't see any effect of the gradients, most likely the gradient rack is not switched on or the master unit needs a reset, e.g. after changing the probe.
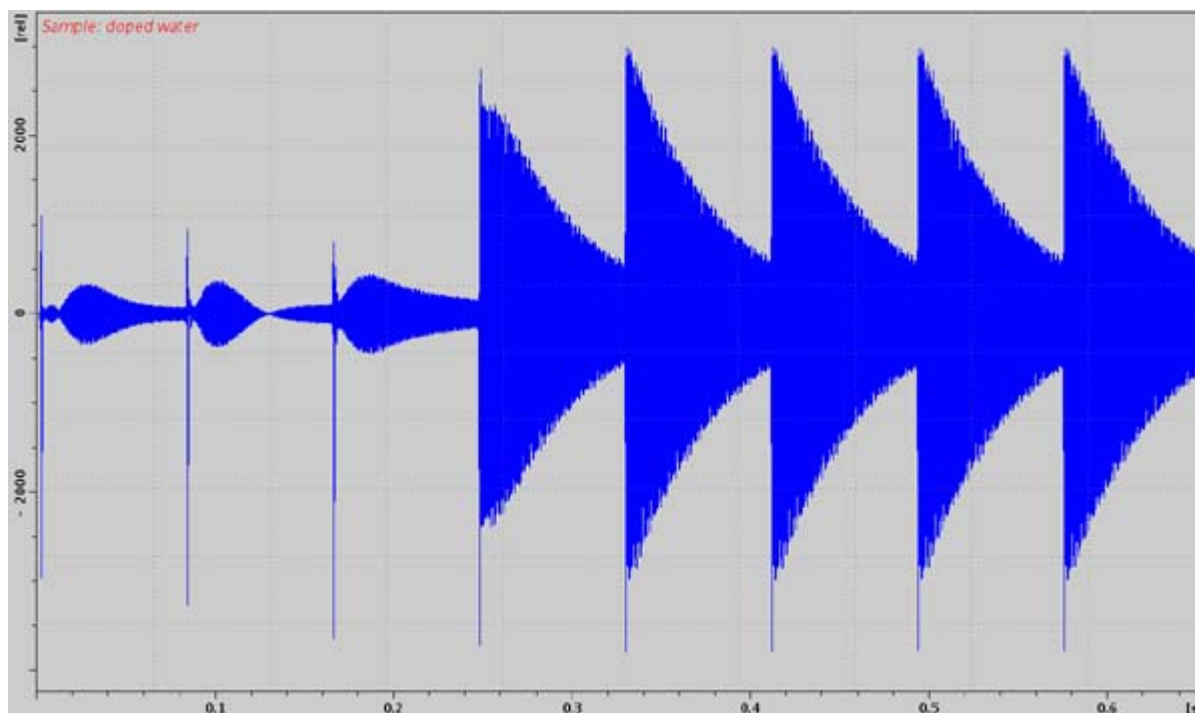
Figure 2.12   FID's After Gradient Pulses.

Modify the gradient pulse shape by changing the time and gain parameters in the setpre menu until all FID's are identical. The FID on the right hand side is used as a reference, since the delay between gradient switching and start of data acquisition is the longest for this FID. It is assumed that all eddy currents are decayed before the last FID.

It is recommended to first adjust the long time constants and continue with the middle and short time constants afterwards. This procedure corrects the shape of the FID's from right to the left.

As a starting point for the time constants the following rules of thumb can be used:

- If FID 7 is distorted a time constant in the range of 100 ms is required.

- If FID's 5 and 6 are distorted a time constant in the range of 10 to 20 ms is required.

- If FID's 3 and 4 are distorted a time constant in the range of 1 to 2 ms is required.

- If FID's 1 and 2 are distorted a time constant in the range of 0.1 to 0.5 ms is required.

This rule can be applied recursively starting with the long time constants, because the long time constants also effect the earlier FID's.

After the correction, the FID's should look like those in Figure 2.13 below.
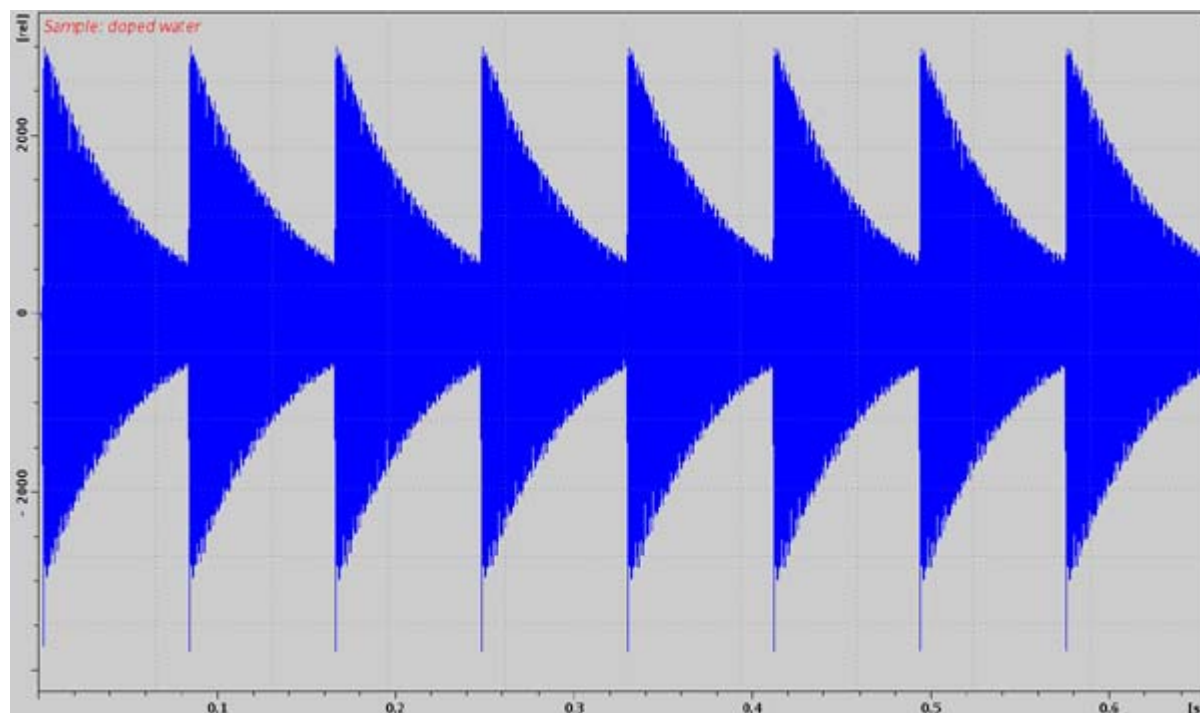
Figure 2.13   FID's After Preemphasis Adjustment.

The preemphasis result may not always look as good as that shown in the figure above.Particularly for the diff60 probe the first, and sometimes also the second, FID cannot be matched with the later ones.

If any changes have been made, save using **Setpre-->File-->Write default**.

2.9   B0 Shift Compensation

The shape of an FID or an echo, acquired with only a short delay after gradient pulses, may be distorted by shifts of the B0 field caused by gradient switching. Such field shifts can be lessened by applying compensation pulses to the field coil of the shim system. The correction works in principle in the same way as the preemphasis, except that the correction pulses are not added to the gradient pulses but to the field current in the field coil of the shim system.

i   Note: For the B0 compensation the optional B0 compensation unit is required.

The procedure is exactly as described for the preemphasis in "Preemphasis Adjustment Experiment" on page 19, except the resonance frequency must be set to on resonance. The corresponding pictures are shown below.
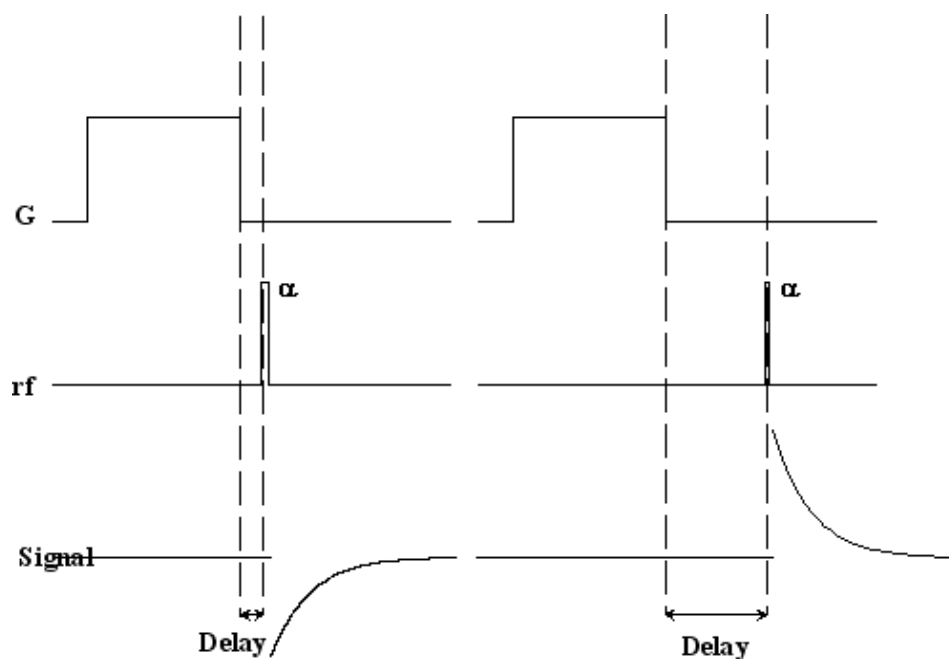
Figure 2.14   B0 Shift Adjustment Program
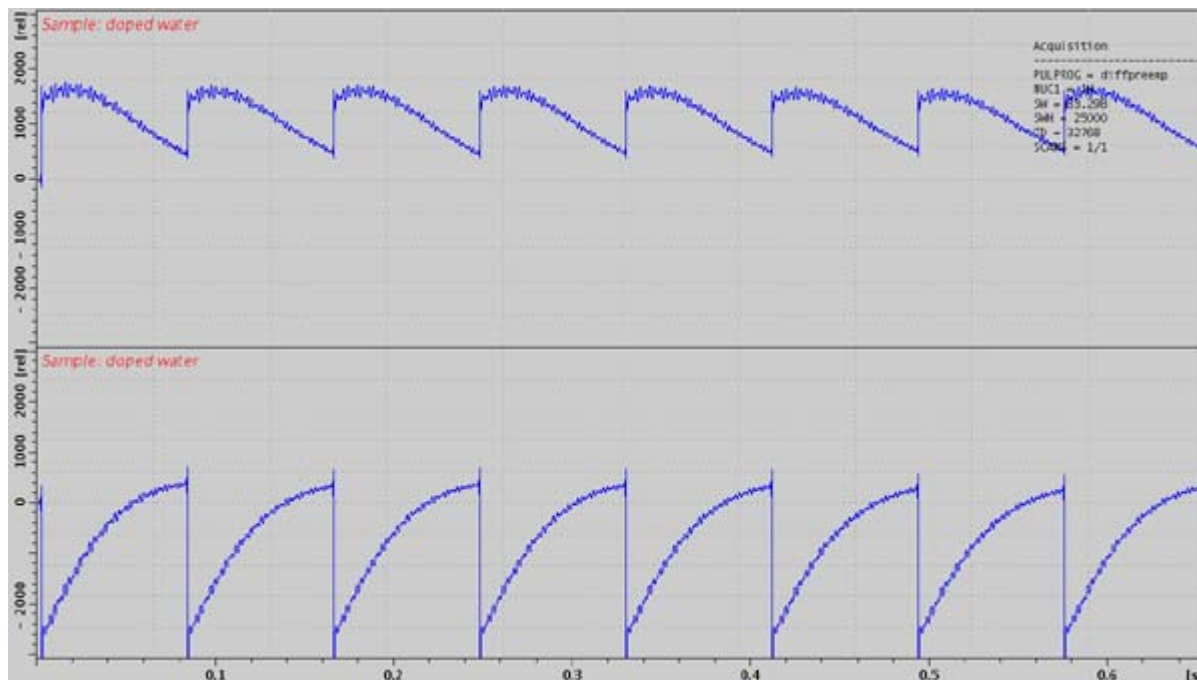
Figure 2.15   Eight FID's on Resonance Without Gradient Switching.
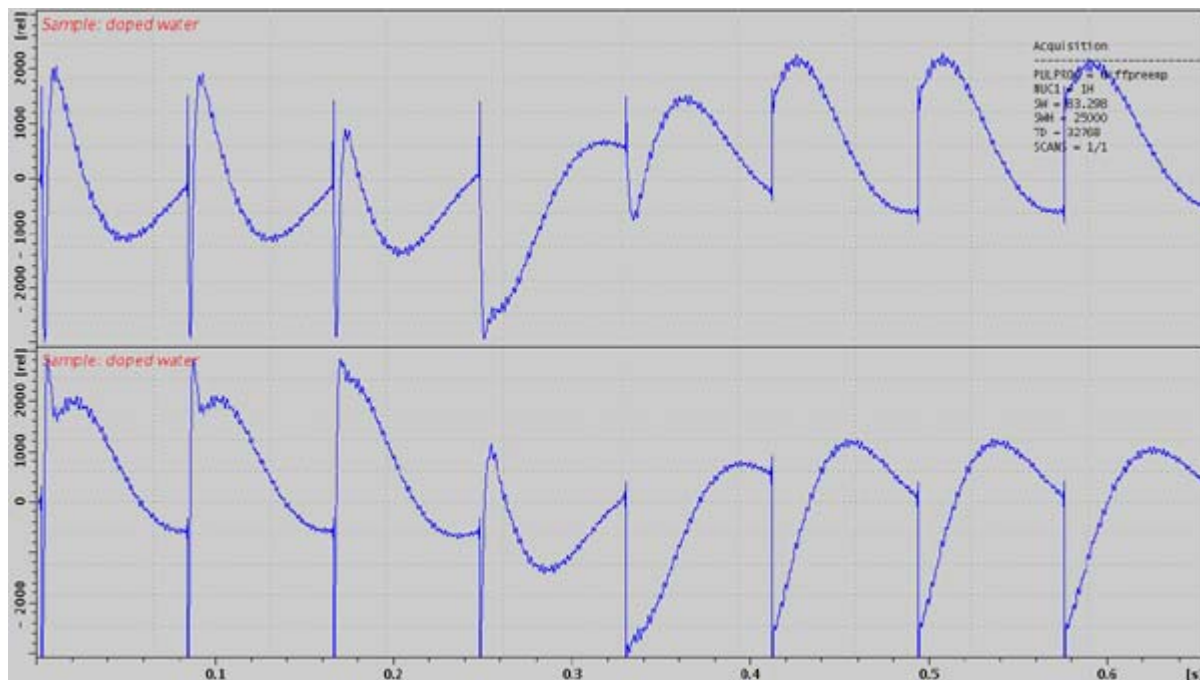
Figure 2.16   Eight FID's on Resonance With Gradient Switching
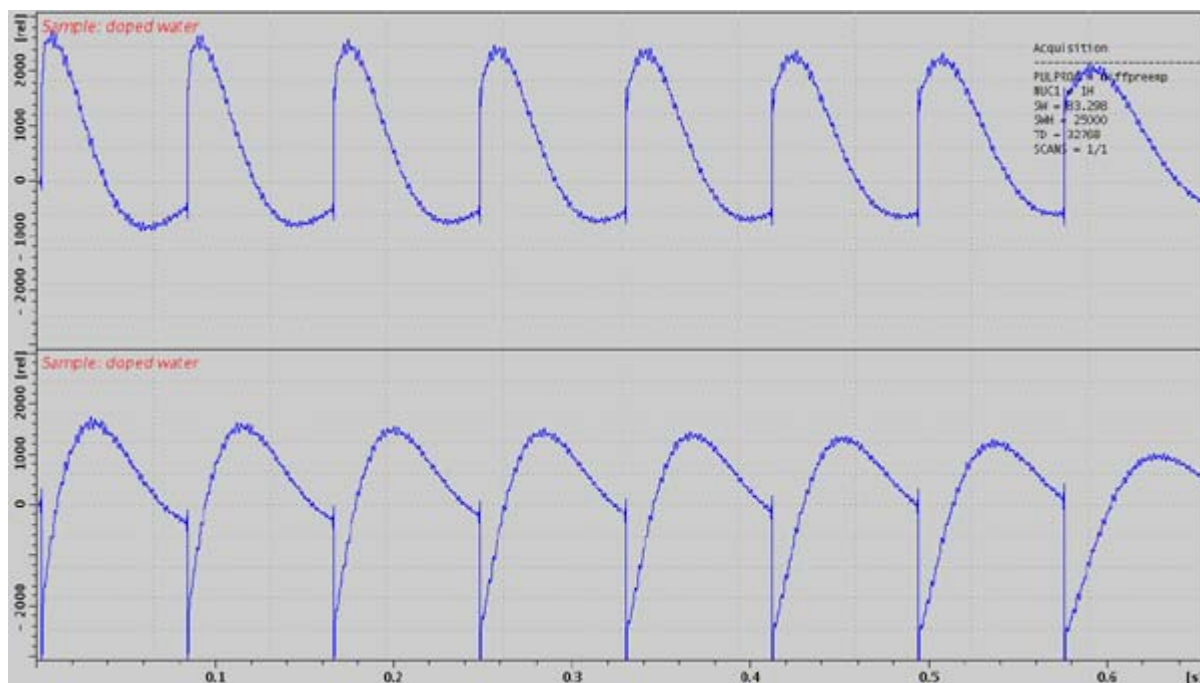
Figure 2.17   Eight Unshuffled FID's After B0 Adjustment

2.10   Gradient Calibration

The entire gradient system must be calibrated in order to make any corrections due to possible mismatching of the components. This is despite the fact that the relative gradient strength of a gradient system and the amplifier are identified from the design. On older systems, with analog preemphasis, mismatches are expected to be larger. In this case the mismatch must be less than 5% of the expected value.

The relative gradient strength (also called gradient sensitivity) is measured in Gauss/ (cmA) or mT/(mA). Values for the different gradient systems and also start values for the gradient calibration constant are give in the table "Gradient Specifications" on page 101.

The only way to precisely calibrate gradient systems is to carefully measure the diffusion coefficients of a well known sample and compare the results with the literature values. Some values are listed below[1], more can be found in the "Bruker Almanac".

Nucleus	Sample	Temperature [C]	D [$10^{-9}m^2$/s]
^{1}H	H_2O	20	2.031
^{1}H	H_2O	25	2.299
^{1}H	D_2O	25	1.872
^{1}H	"Doped Water"	25	1.91
^{1}H	DMSO	25	0.730
^{7}Li	0.25 m LiCl in H_2O (ca. 10 g LiCl /l H2O)	25	0.960
^{23}Na	2 m NaCl in H_2O (ca. 117 g NaCl / l H_2O)	25	1.135

Table 2.2:   Some useful diffusion coefficients

The *doped water* sample already mentioned above in "Preemphasis Adjustment Experiment" on page 19, is used as a standard for the calibration. If the *dope water* sample is not available, other mixtures of H_2O and D_2O can be used. The diffusion coefficient of protons at 25 ^{o}C can be calculated using Equation 2.1:[1]. Low H_2O concentrations are preferable in order to avoid radiation damping.

Equation 2.1:

$$D(x_D) = \left(2.3 - 0.4652 \cdot x_D + 0.0672 \cdot x_D^2\right) \cdot 10^{-9} \frac{m^2}{s}$$

$$x_D = mole\,fraction\,of\,deuterons$$

i   Note: Diffusion coefficients of liquid samples are extremely temperature dependent.

1. Calibration in Accurate Spin-Echo Self-Diffusion Measurements Using 1H and Less-Common Nuclei, Holz et al., JMR 92, 115-125 (1991)

Installation

2.10.1 Calibration Procedure for a Single Axis Gradient System

1. Set the temperature to 25 $^{\mathrm{o}}$C.

   In order to avoid convection artefacts the temperature must be controlled using water cooling. Airflow should not be connected to the probe, as the real temperature may differ from the water temperature. Check the reading for the thermocouple in **edte**. For exact results the temperature must be calibrated using an NMR temperature standard. Refer to the "Variable Temperature Unit User Manual" on the BASH CD for details.

2. Check for the correct initial setting of the gradient calibration constant GCC (see "Gradient Specifications" on page 101).

3. Measure the diffusion coefficient as described in the "Step by Step Guide" on page 33.

4. Calculate the corrected gradient calibration constant:

   Equation 2.2:

   $$G\,CC_{new} = \sqrt{\frac{D}{D_{Literature}} GCC_{old}}$$

5. Store the new constant using **setpre**.

2.10.2 Calibration Procedure for a Triple Axis Gradient System

1. Set the temperature to 25 $^{\mathrm{o}}$C.

   In order to avoid convection artefacts the temperature must be controlled using water cooling. Airflow should not be connected to the probe, as the real temperature may differ from the water temperature. Check the reading for the thermocouple in **edte**. For exact results the temperature must be calibrated using an NMR temperature standard. Refer to the BVT manual for details.

2. Check for the correct initial setting of the gradient calibration constant GCC (see "Gradient Specifications" on page 101).

3. Measure the diffusion coefficient using the actual calibration independently in all 3 gradient directions independently.

4. Correct the relative gradient scaling factors, called S_x, S_y, S_z in Equation 2.3:

Equation 2.3:

$$S_{x,new} = \sqrt{\frac{\min(D_x, D_y, D_z)}{D_X} S_{x,old}}$$

$$S_{y,new} = \sqrt{\frac{\min(D_x, D_y, D_z)}{D_y} S_{y,old}}$$

$$S_{z,new} = \sqrt{\frac{\min(D_x, D_y, D_z)}{D_z} S_{z,old}}$$

5. Calculate the corrected gradient calibration constant:

Equation 2.4:

$$GCC_{new} = \sqrt{\frac{\min(D_x, D_y, D_z)}{D_{Literature}} GCC_{old}}$$

6. Store the new values of S_x, S_y, S_z and GCC using **setpre**.

2.11   Gradient Ramp Time Calibration

Usually the calibration of the ramp time is not necessary, because *diff* automatically sets reasonable ramp times depending on the maximum gradient amplitude used in the actual experiment.

The default values are fixed in the program and cannot be changed in the configuration (this might change in the future).

Therefore user defined ramp times cannot use the automatic adoption to the actual gradient strength, i.e. the user must calculate the proper ramp time. *Diff* uses the simplest method, it sets the ramp time proportional to the maximum current. It is also possible to calibrate the ramp time for different amplitudes individually, but within one experiment the ramp time must be the same.

In order to be able to access the ramp time, the default mode must be switched off, see "Diff Menu of the PGSTE Experiment" on page 76 for details.

i   Note: Switching off the default mode requires the user to manually enter all the parameters controlled by this option.

The ramp time is calibrated in a way, that the output voltage of the gradient amplifier always stays within reasonable limits. For the GREAT40 and GREAT60 amplifiers this means below 100 V. In order to calibrate the ramp time one has to measure the gradient

current and the output voltage of the amplifier at the same time. The newer amplifiers display the current and voltage monitor outputs, please read "Monitor Output" on page 111 carefully. Older amplifiers only have current outputs, whereas the voltage can be measured by connecting to the voltage probes one to the positive and one the negative current outputs and looking at the voltage in differential mode.

Figure 2.18   Oscilloscope view showing current (blue, 30 A/div) and voltage (red, 50 V/div) of a trapezoidal pulse with a ramp time of 300 μs and an amplitude of 60 A.

Figure 2.18 shows a trapezoidal pulse with equal up and down ramp times of 300 μs and a current of 60 A on a diff30 gradient system. The voltage goes just above the limit of 100 V, in this case it shows the limit of a reasonable ramp up time. It also shows, that the ramp down time could be much faster.

Figure 2.19 in contrary shows a case where the ramp up time of 100 μs is too short. The voltage reaches the limit of the power supply, then it decays as the capacitors are discharged. The power supply is overloaded. Although the current pulse shape still looks quite reasonable the next pulse in the sequence will not have exactly the same integral, because the power supply cannot recover completely. The reproducibility of the integral is the most critical point for diffusion experiments, in some cases only a few ppm of mismatch can be detected.

Figure 2.19   Oscilloscope view showing current (blue, 30 A/div) and voltage (red, 50 V/div) of a trapezoidal pulse with a ramp time of 100 μs and an amplitude of 60 A.

For the frequently used half sine the corresponding picture should look like Figure 2.20. But also for this pulse shape the amplifier can be overloaded, just by making the pulse too short. An extreme example is shown in Figure 2.21. Thus *diff* also controls the minimum duration of half sine shapes as a function of the maximum used amplitude.
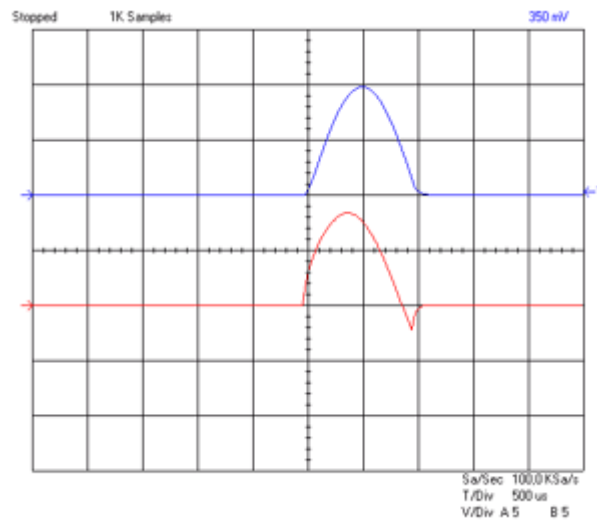
Figure 2.20   Oscilloscope view showing current (blue, 30 A/div) and voltage (red, 50 V/div) of a sine shape pulse with duration of 2 ms and an amplitude of 60 A.
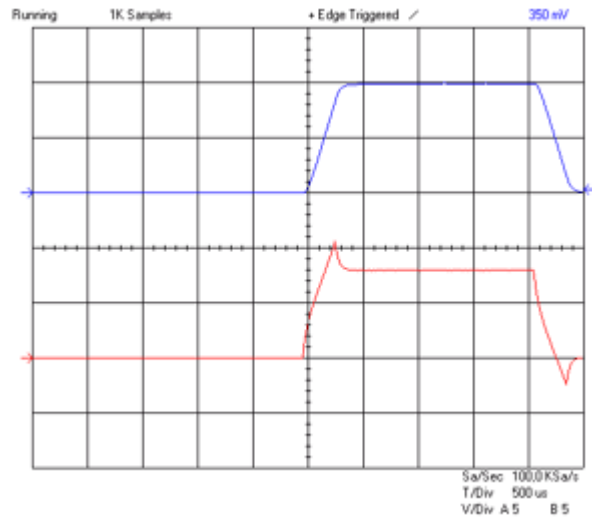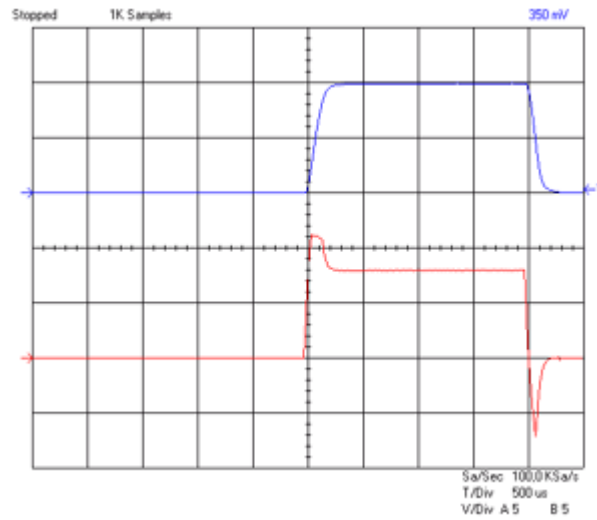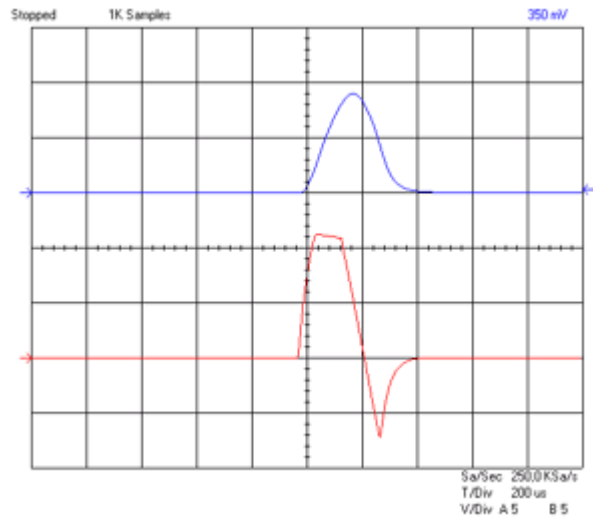
Figure 2.21   Oscilloscope view showing current (blue, 30 A/div) and voltage (red, 50 V/div) of a sine shape pulse with duration of 0.3 ms and an amplitude of 60 A.

3 Step by Step Guide

3.1 Setup

The complete setup described in this chapter usually only have to be fully performed once. At any point during the setup, parameters can be stored as standard parameters and recalled. The degree of changes depend only on the variety of samples to be measured.

The setup is simplified by using the setup program *diff*. *Diff* in it's current version is a TclTk script. Examples of the use of *diff* are described in the description of the experiment setup.

The setup is performed in 3 major steps:

1. The setup of the **spectroscopic parameters**, i.e. RF pulse length, RF power, spectral width and receiver gain.

2. The setup of the **diffusion parameters**, gradient pulse length and maximum amplitude, the diffusion time.

3. The setup of the 2D **measurement parameters**, including the number of gradient steps, scans, and repetitions.

The sample used for all experiments shown below is the Bruker standard sample:

Doped Water (P/N Z10906), consisting of 1% H_2O in D_2O, with 0.1% $GdCl_3$ and 0.1% CH_3OH (^{13}C).

3.1.1 Probe Exchange

If the probe has to be changed, two important steps have to be performed

1. Select the correct probe using **edhead**

2. Read in the corresponding preemphasis parameters and load them in the preemphasis unit.

3. Run *setpre* and execute *Setpre-->Read default*. See also "Preemphasis Adjustment" on page 17.

3.1.2 Spectroscopic Parameters

1. Create a new 1D data-set using your standard method.

2. Perform the standard setup procedure.

   - Tune the probe using wobb.

   - Lock, if a lock channel is available.

i Note: If you don't use the lock, set LOCNUC=off before starting. *Diff* will automatically disable the lock blanking in the pulse program.

3. Shim the probe.

4. Set the RF pulses and the power level. This can be done by typing **"getprosol"**, if this was preset for your probe.

   - Set pl1 to the required power level for the selected nucleus and RF coil.

   - Set p1 to the corresponding 90° pulse length.

   - Set p2 to the corresponding 180° pulse.

i Note: Correct pulse settings are particularly important for diffusion sequences using bipolar gradients.

   - Set SW or SW_h suitable for your sample.

   - Setup the receiver gain, e.g. using **"rga"**

   The receiver gain value found for a 1D experiment is usually a good starting value for the diffusion experiment.
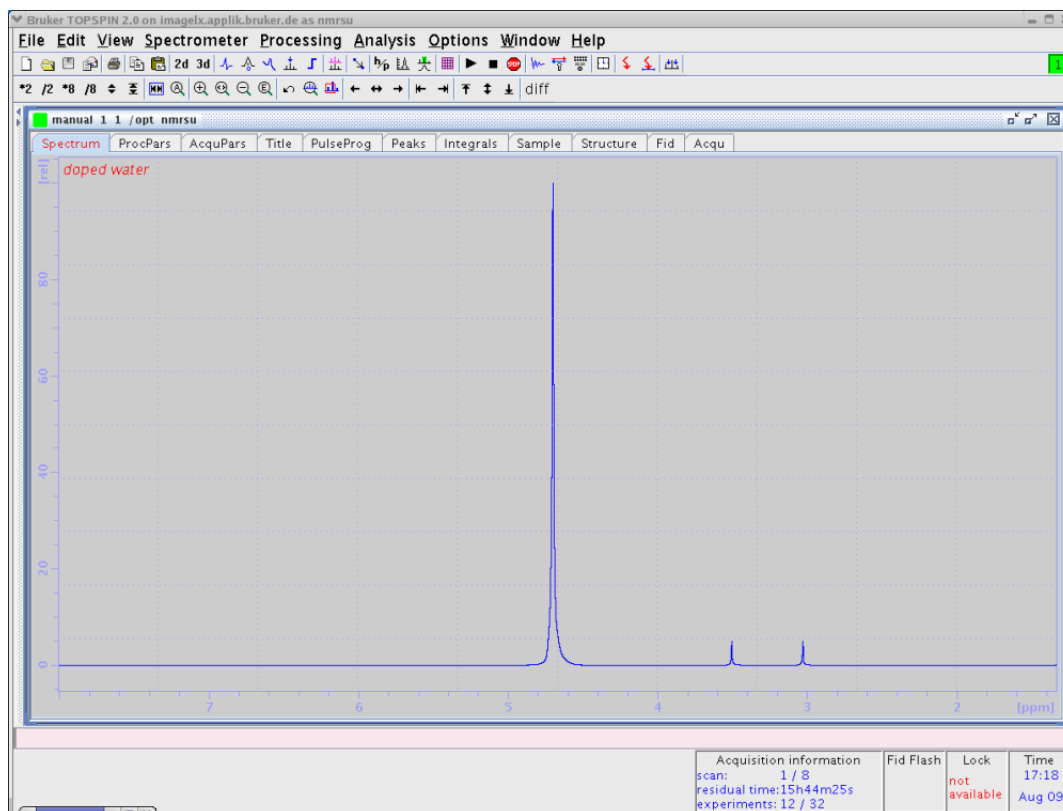
Figure 3.1   1D Spectrum of Doped Water Sample

5.   - After finishing the 1D experiment create a new data-set and change it to 2D

3.1.3 Diffusion Parameter Setup

1. Type **"diff"** to start the setup program. A window as shown in Figure 3.2 will appear. Because it was started on a "fresh" data-set, not much information is visible.
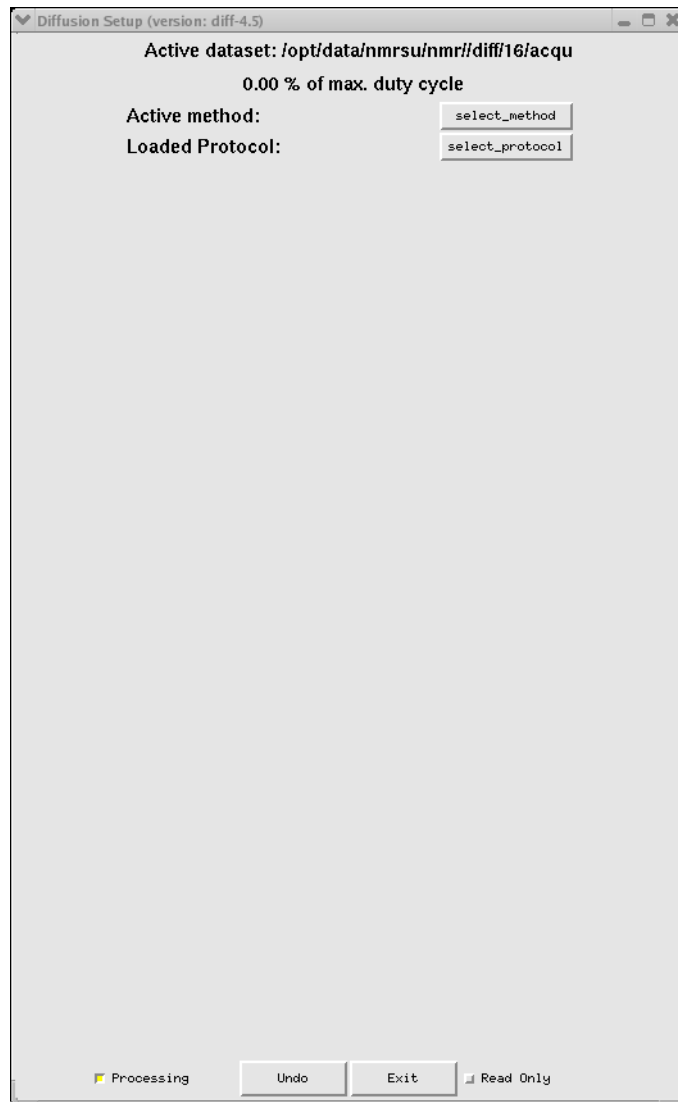
Figure 3.2 **The *diff* cOmmand Started within a Fresh Data-set**

The window can be kept open as long as needed, it will always display the parameters of the active window.

ℹ️ Note: When called from a 2D data set, *Diff* will only allow diffusion experiments!

When starting from the scratch, it is easiest to load a protocol. A protocol is a set of "high level" parameters, like the expected diffusion coefficient, from which *diff* can derive all diffusion relevant parameters automatically. For example, select the protocol "steWater"

from the pull down menu, which appears when you click the button next to "Loaded Protocol", Figure 3.3.
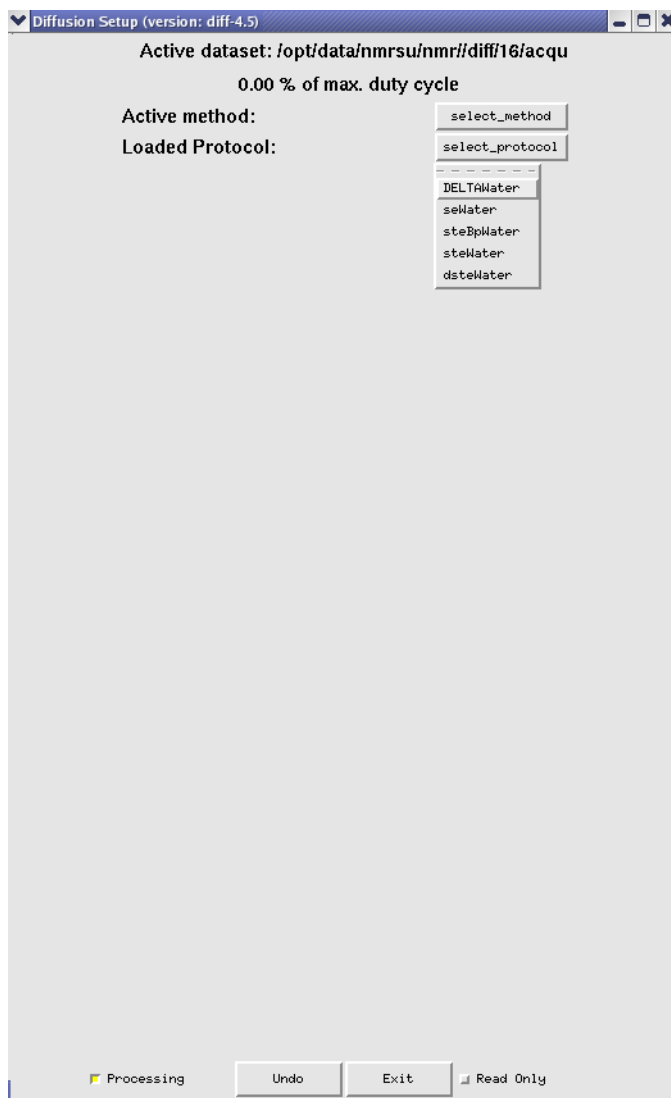
Figure 3.3   **The *diff*** Command Showing Protocol Selection
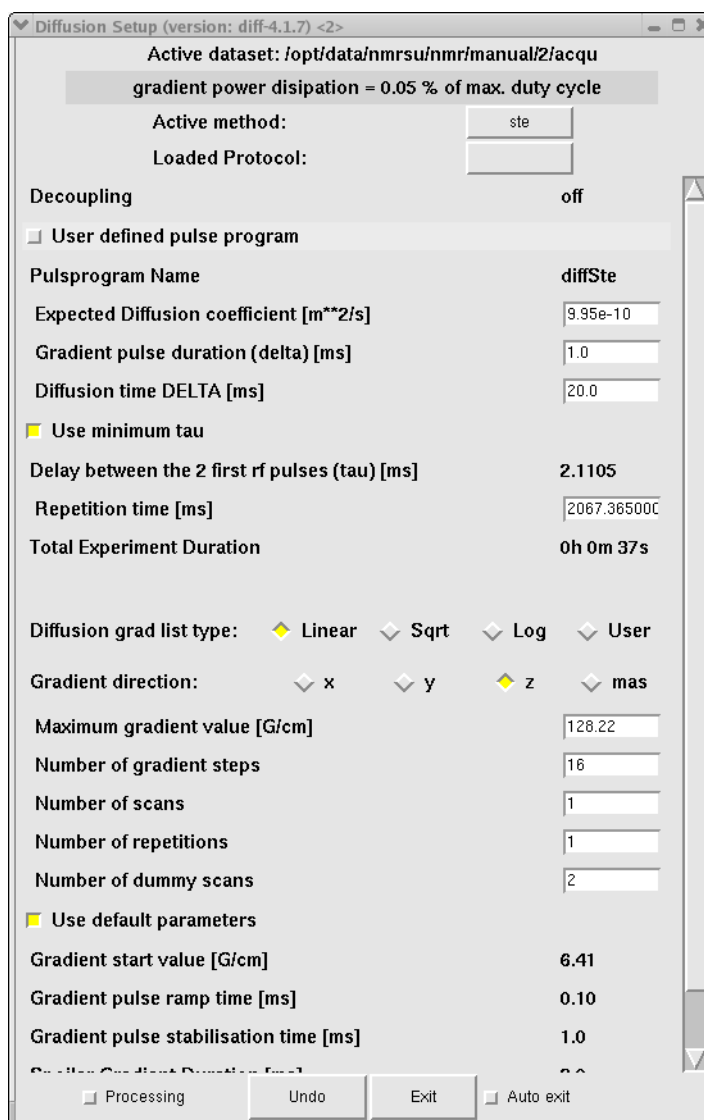
Figure 3.4   **The *diff* Command** Showing Parameters of "ste"

The parameters shown here can be used for water or similar liquids without any change. In general the parameters have to be adjusted according to the sample properties and/or experimental needs. Details about the parameter settings, their meaning, and parameter relations are given in "Diffusion Experiments" on page 51 and in "Diff Program Reference" on page 75.

To change the values:

1.   Click on the entry field.

2.   Delete the numbers and type in the new number you want.

3.   Type "return" or move the cursor out to activate the relations.

Depending on the parameter hierarchy, the parameters will be checked and e.g. set to the minimum possible value, derived from the other related parameters.

When leaving the *diff* window the parameters are automatically stored in the data-set.

i Note: In contrary to older versions of *diff* no active saving is required, the parameters are automatically stored each time the cursor focus leaves the *diff* window. The very first time this action is performed, the AU program "diff_t1pars", which runs in background, will be compiled automatically and the corresponding message will be displayed.

3.2 Running the Experiment

1. Type **zg**.

2. After the acquisition is finished you can display the data as shown in Figure 3.5 by clicking the "FID" tab in the TopSpin data window.
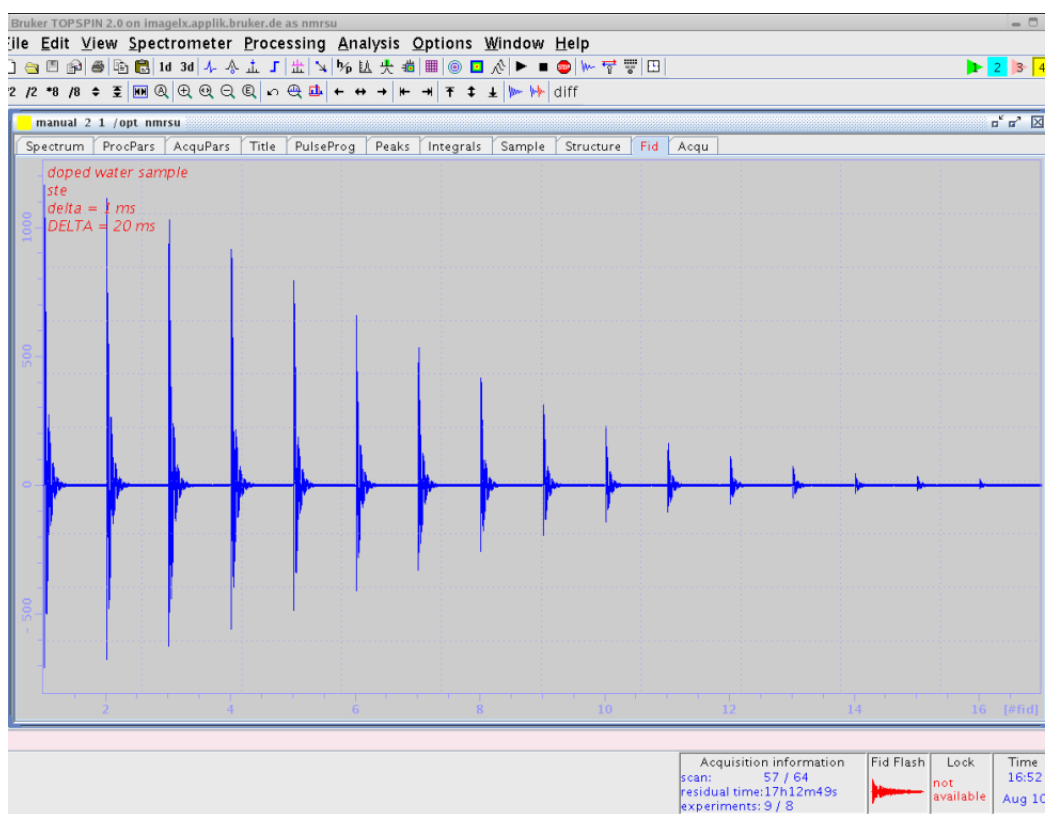
Figure 3.5   Echo Decay Caused by Growing Diffusion Gradients

3.3 Processing

The processing can be done in phased or in magnitude mode depending on the type and quality of the NMR signals. For pure liquids, the phased mode is typically used. This section shows a straight forward way of processing the data. More details are given in

the sections "The T1/T2 Analysis Module" on page 63 and"DOSY Processing" on page 68

1. Type "**xf2**" and phase correct the data in F2 direction. Using the doped water sample, the result should look like that in Figure 3.6.
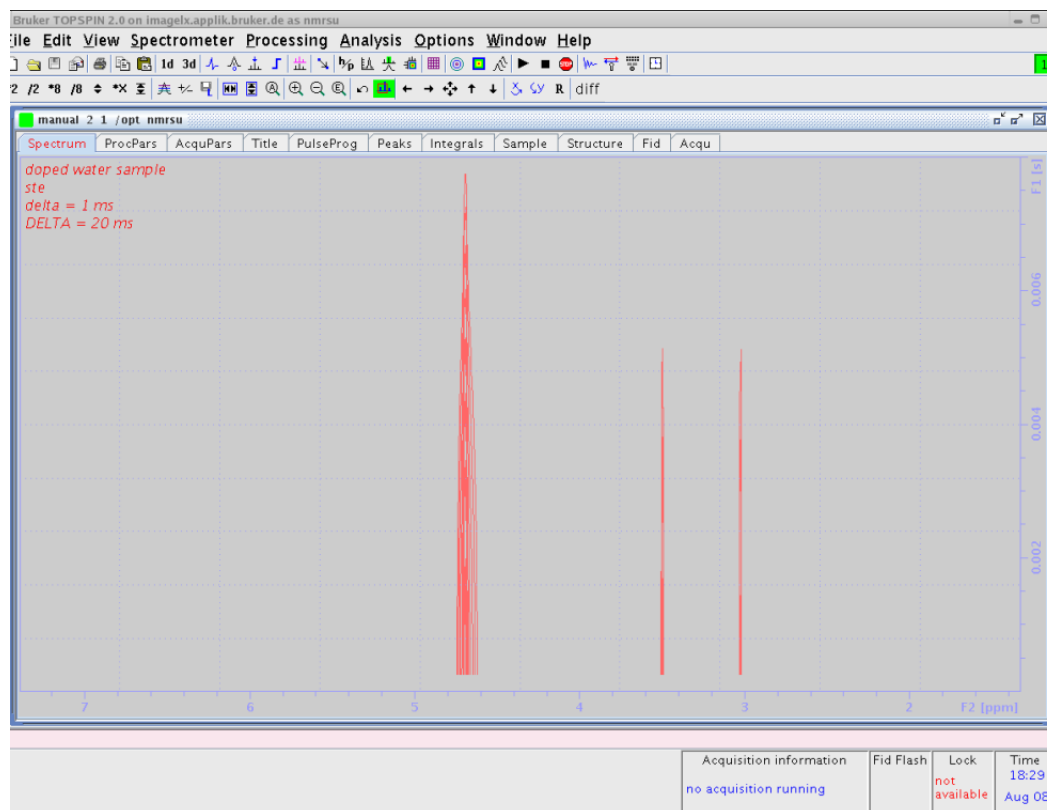
Figure 3.6   Echo Decay After xf2

2. Select the **NMR Relaxation Guide** by clicking on **T1/T2 Relaxation** in the **Analysis** pull-down menu. The TopSpin data window should look like that in Figure 3.7.
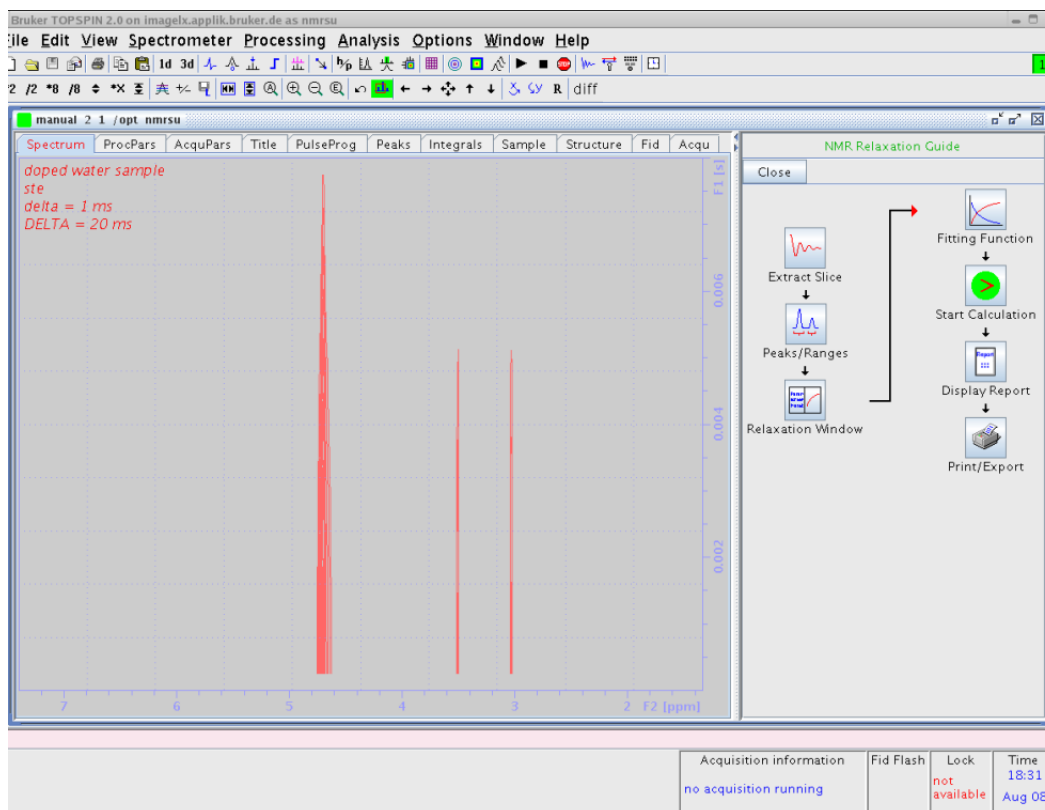
Figure 3.7   Pseudo 2D Spectrum with **NMR Relaxation Guide**

3.   Begin the processing by clicking the icons in the guide sequentially and follow the advice given. When you select the first icon, **Extract Slice**, a section pop-up window as shown in Figure 3.8 will appear.
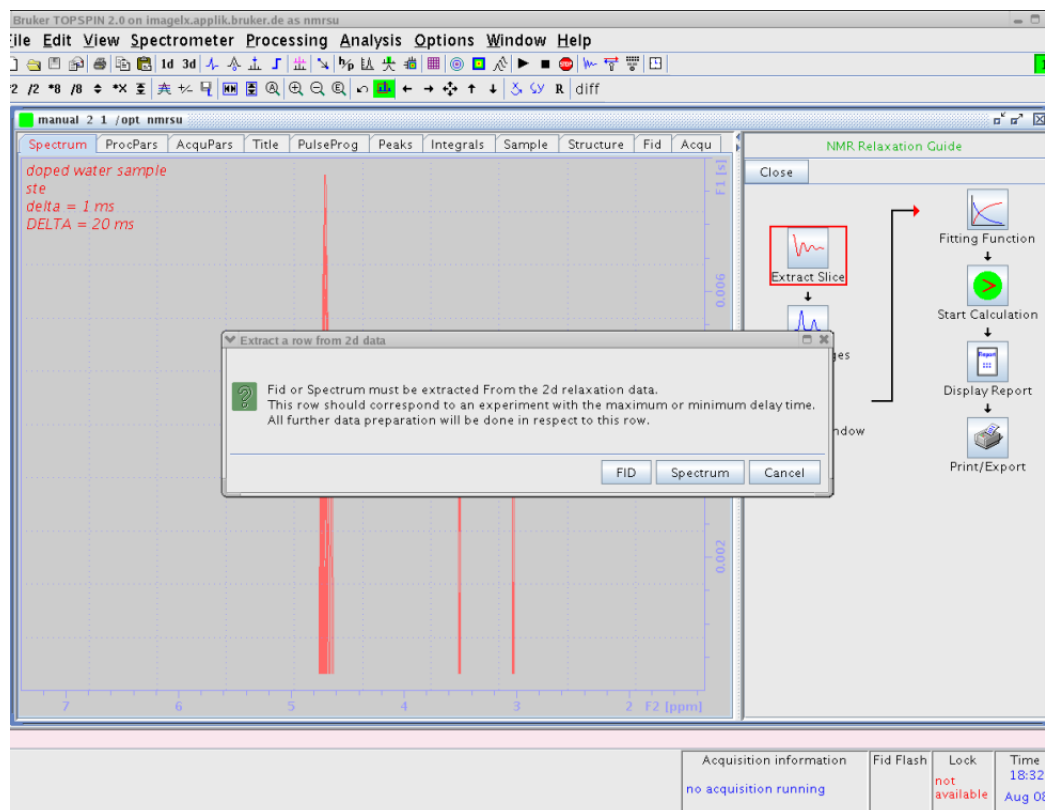
Figure 3.8   Pseudo 2D Spectrum with **NMR Relaxation Guide** 1. step

4.   There are 2 possibilities offered, to start with an FID or to start with a spectrum. As we have already performed the phase correction, select **Spectrum**. This is usually the preferable way.

5.   After selecting **Spectrum** another pop-up window will appear and request the slice number. In diffusion experiments usually the first experiments provide the strongest signals, therefore select one of these. The default is 3, as number 1 and 2 sometimes show artefacts. This is more a tradition than a rule.

The result of this selection is shown in Figure 3.9:
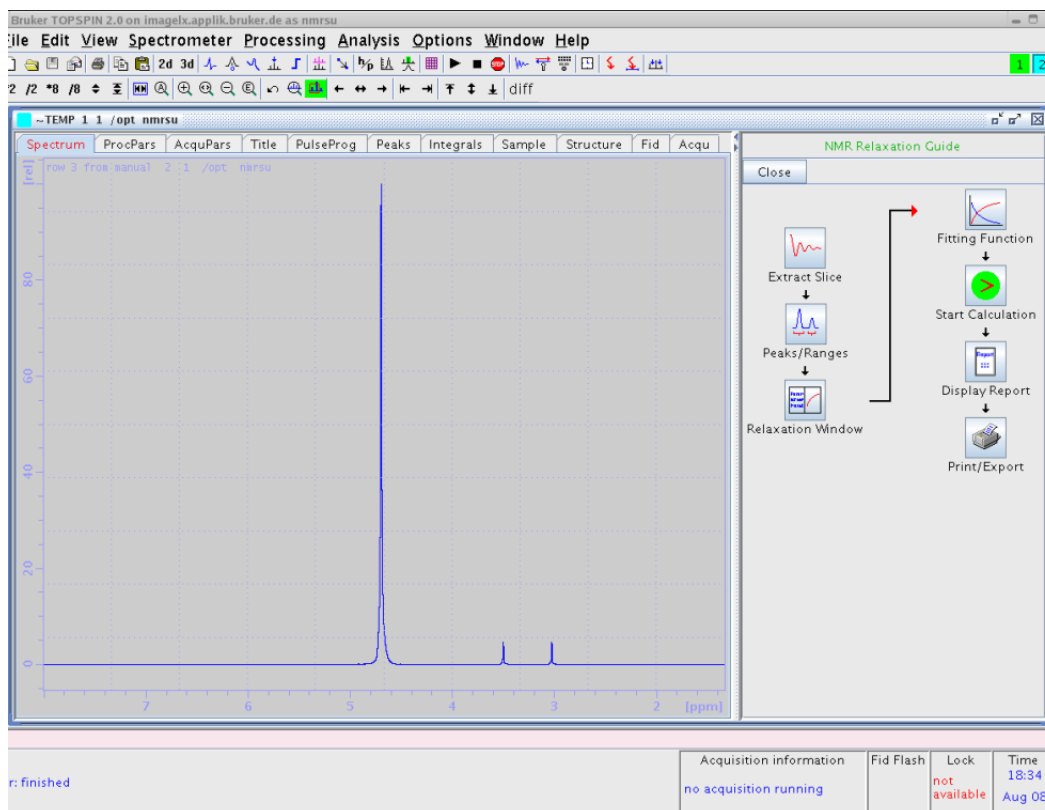
Figure 3.9   Selected 1D Spectrum from the 2D data-set

6.   Click on the next button in the **NMR Relaxation Guide**, **Peaks/Ranges.**

A pop-up window offering **Manual Integration** or **Manual Peak Picking** appears as shown in Figure 3.10.
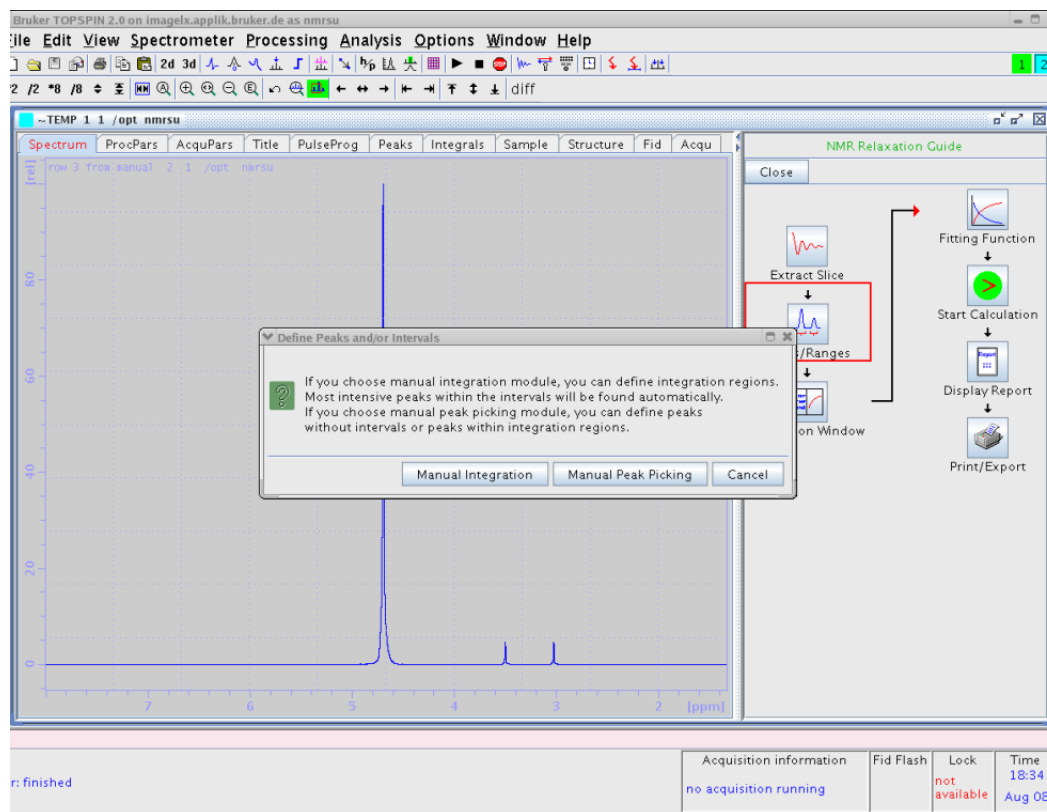
Figure 3.10   Selected 1D Spectrum with **NMR Relaxation Guide** step 2

7.   Select **Manual Integration**. This will open the 1D integration window, where we can select the peaks by dragging the left mouse button. See Figure 3.11
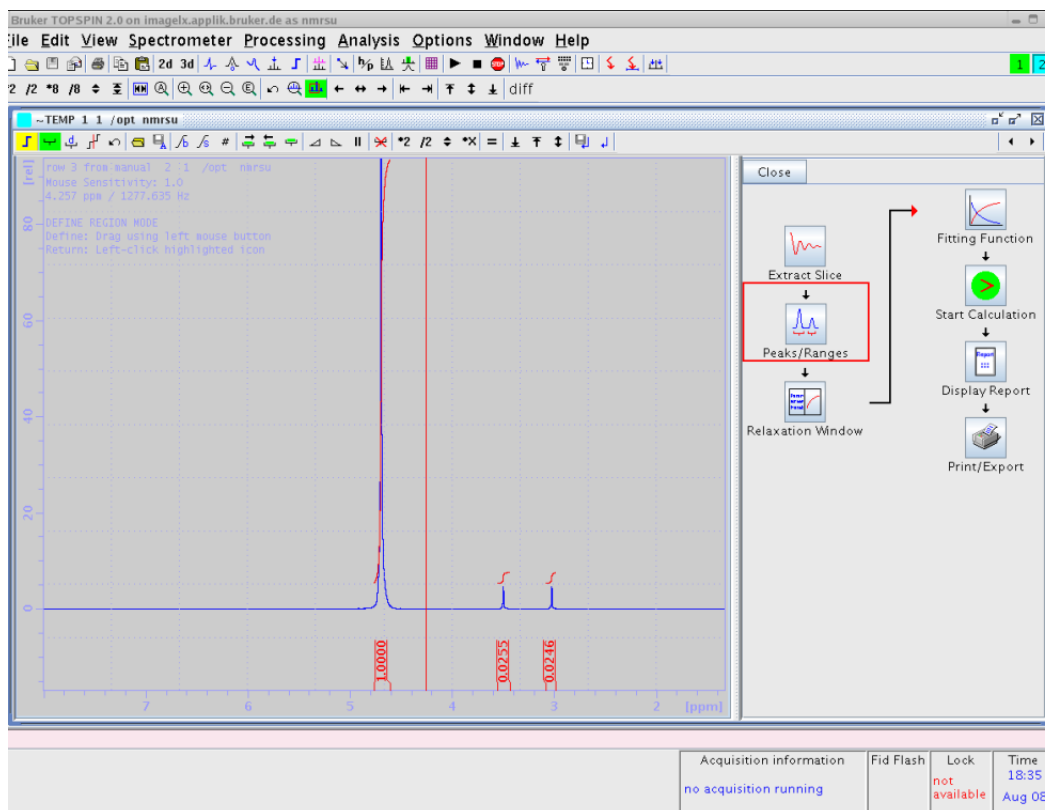
Figure 3.11   Spectrum with integrated Peaks

8. Click on the left floppy button to exit the integration window and select **Export Regions to Relaxation Module and return** as shown in Figure 3.12:
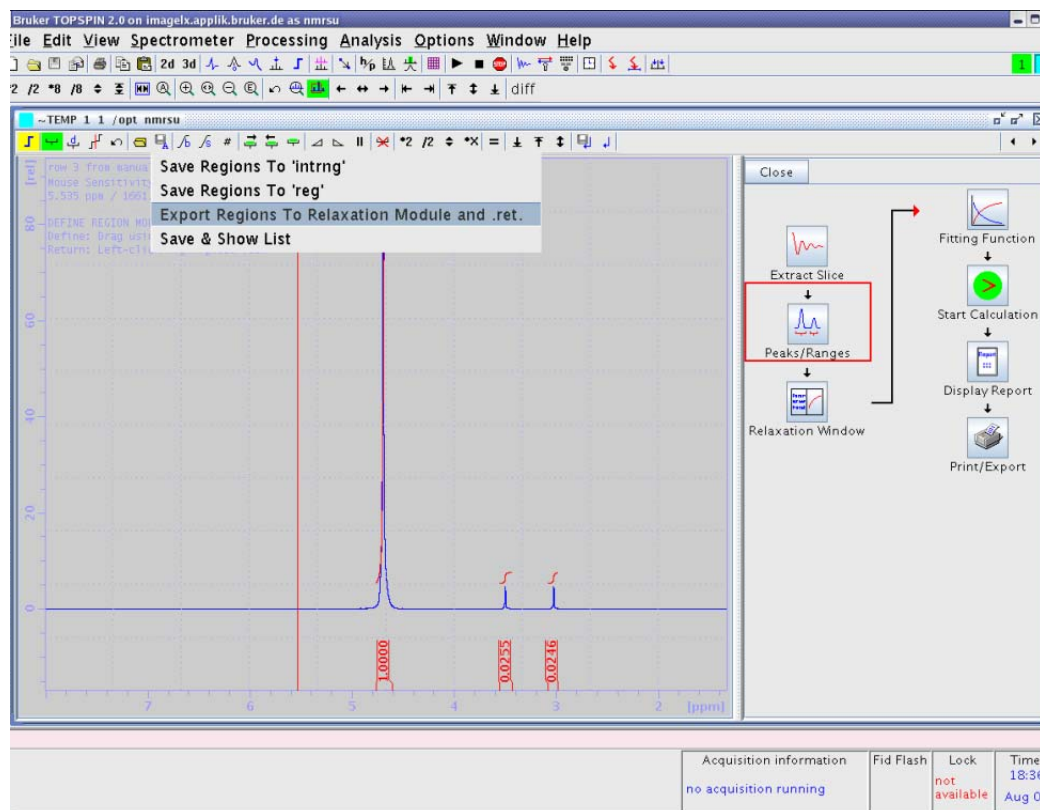
Figure 3.12   Leaving the Integration Module

9.   Click the **Relaxation Window** button. The relaxation window will open showing the automatically selected data points, as shown in Figure 3.13. Automatic peak selection only takes place when this window is opened the first time in a data set. If data are already present, the data will be preserved.
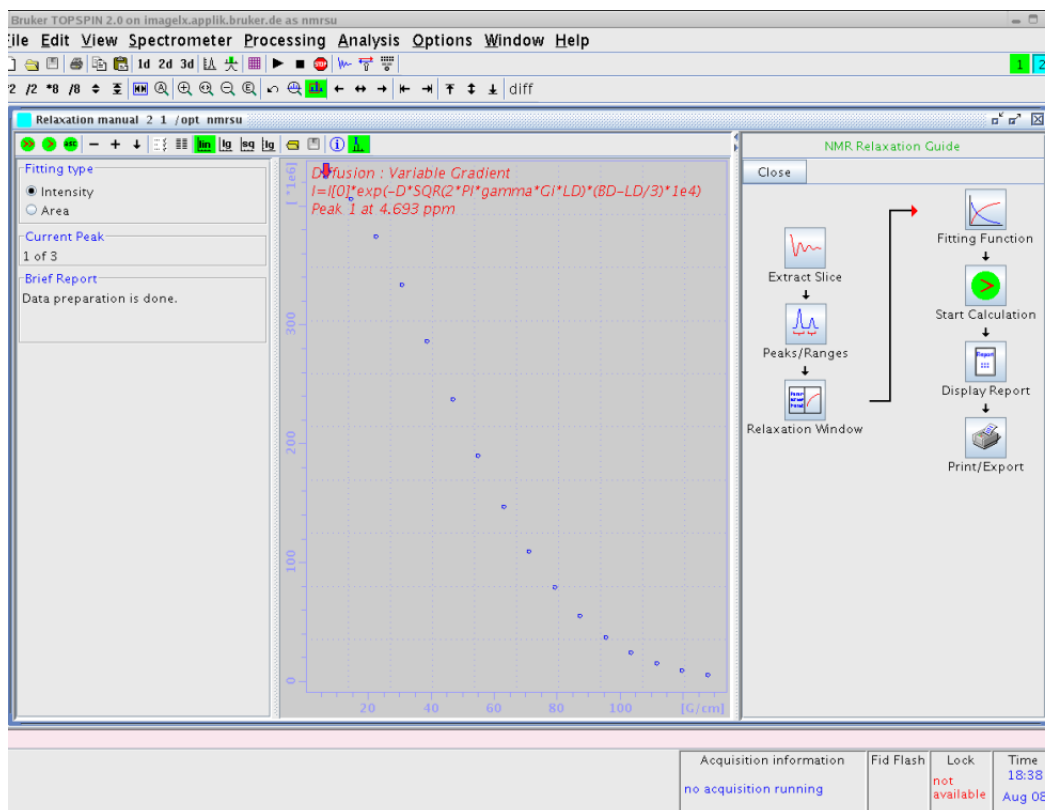
Figure 3.13   Relaxation Window with Data Points

10. Click on the **Fitting Function** button. This will open a parameter editor as shown in Figure 3.14. This editor shows and allows all the relevant parameters for the fitting procedure (e.g. δ and Δ.) to be changed. Details about these parameters are described in "Parameter Dialog Box" on page 65. All of these parameters have been preset by *diff* and usually do not need to be changed.
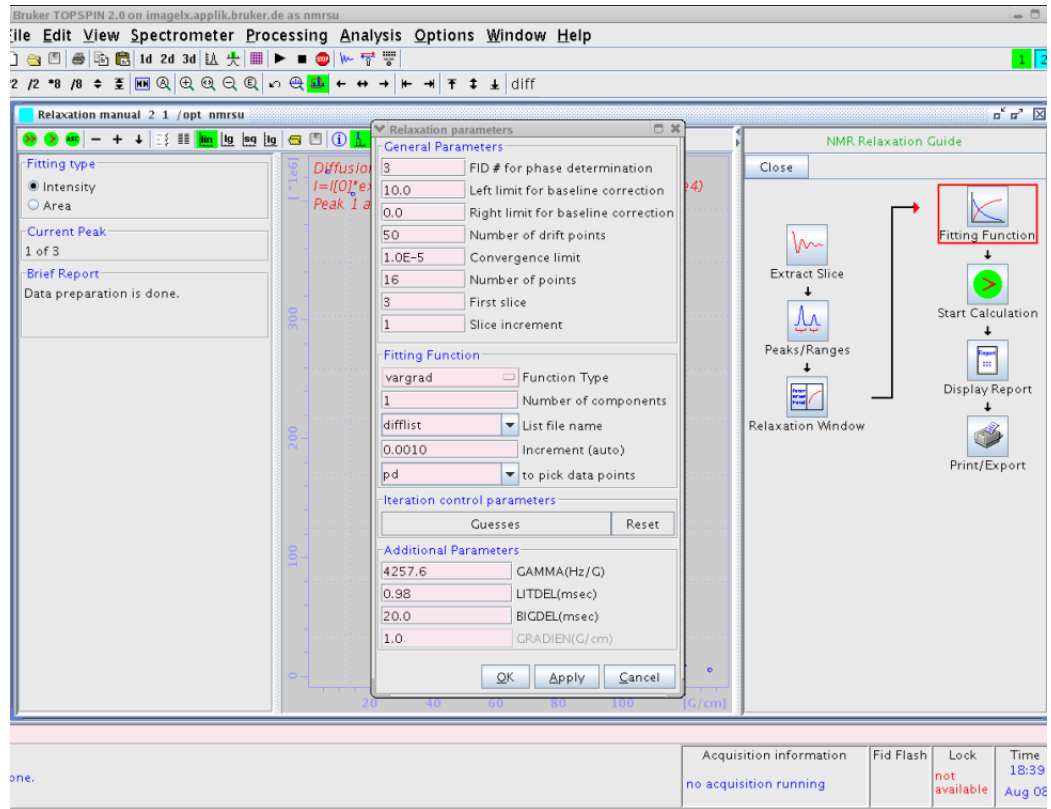
Figure 3.14   Relaxation Parameter Editor

11. Click on the **Start Calculation** button (see Figure 3.15). This fits the fitting function to the data points and plots the curve together with the data points. The results are shown in a brief report field on the left side of the window, and also in title displayed in the plot window.

Step by Step Guide
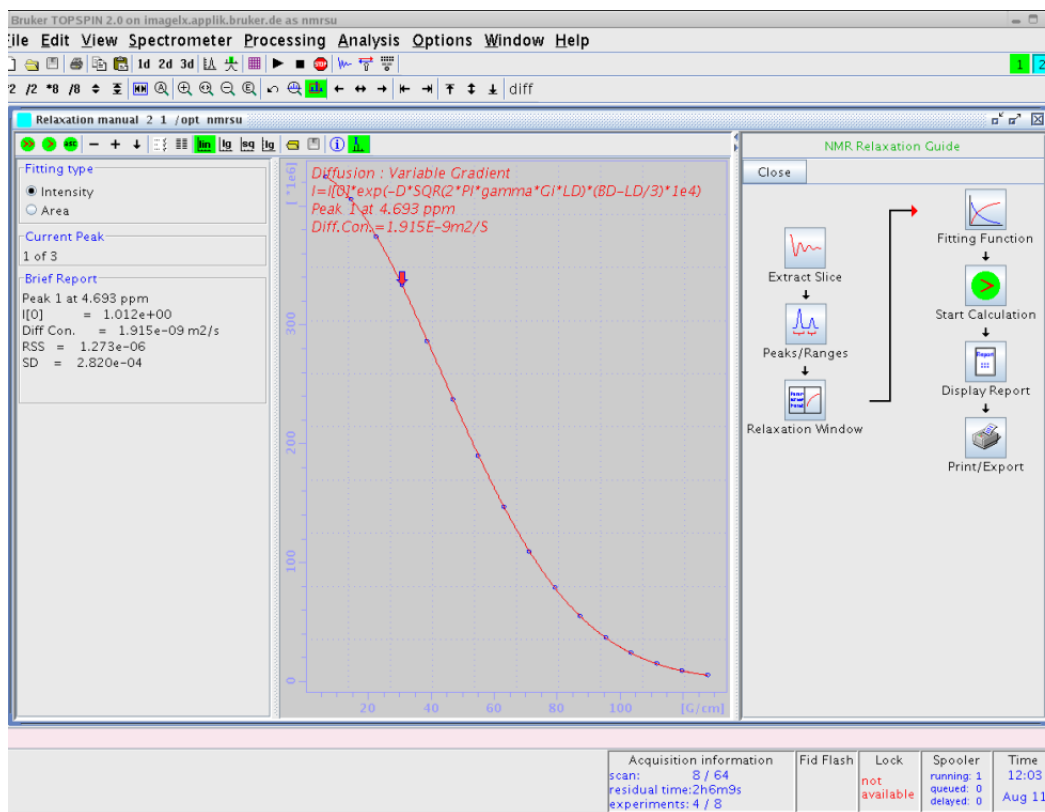
Figure 3.15   Data Points with Fitted Curve

12. Click on the **Display Results** button (see Figure 3.16). An editor window is opened showing the results in a more detailed view, together with the measured data and the calculated points. These are also stored in the file ct1t2.txt in the processed data directory.
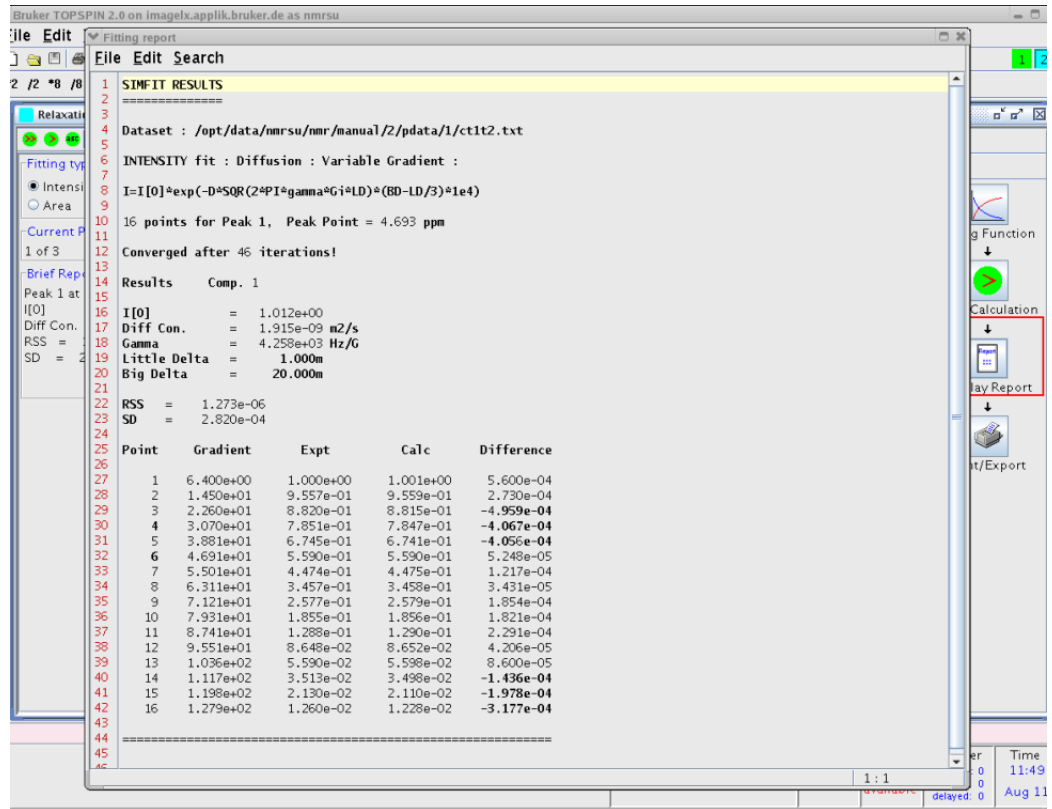
Figure 3.16   Simfit Results

13. Click the Print Option button (see Figure 3.17). A list of print and export options will be shown.
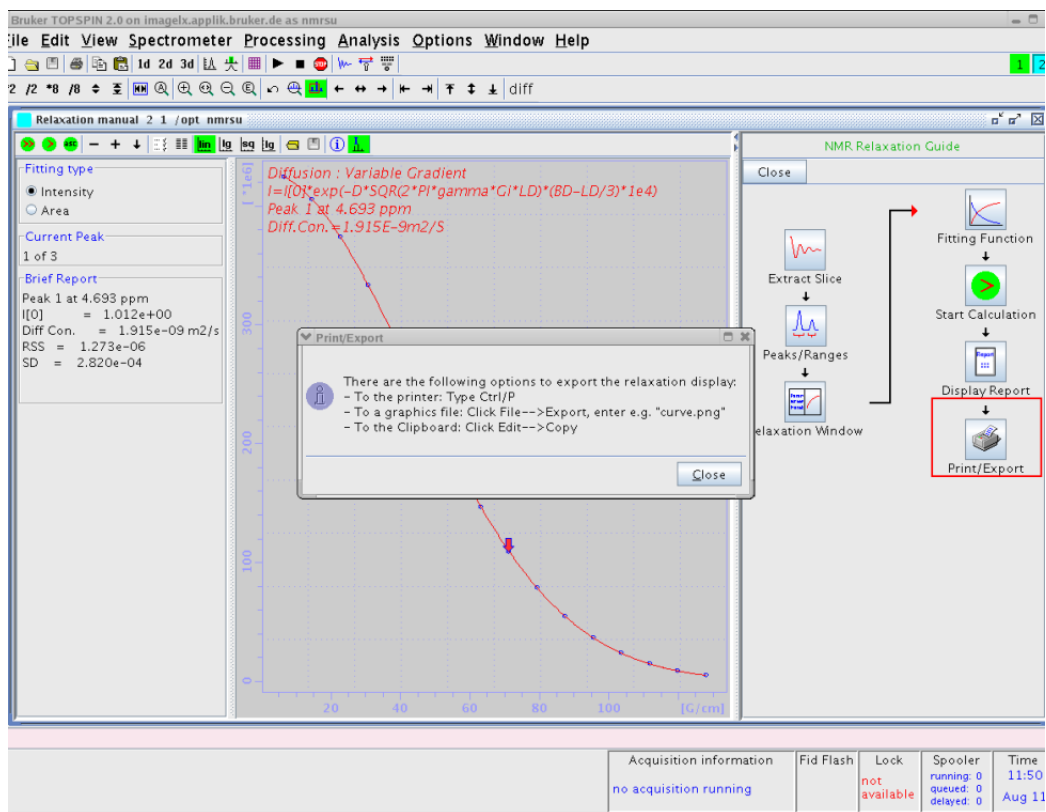
Figure 3.17   Print Options

4 Diffusion Experiments

Diffusion experiments are usually based on two standard types of pulse sequences, the spin echo diffusion sequence[1] (PGSE) and the stimulated echo sequence[2] (PGSTE). All other published sequences can be understood as modifications of theses two sequences. For samples with $T_1 = T_2$ the PGSE sequence is usually the preferred one; for samples with $T_1 \gg T_2$ the PGSTE sequence is often used, as during most of the diffusion time the magnetization can be stored in the Z direction. For the PGSE sequence, the maximum diffusion time is limited by T_2; for the PGSTE sequence the maximum diffusion time is limited by T_1.

A growing number of sequences are supported by the *diff* program, some sequences are explained here in some detail, mainly in order to show the meaning of the parameters

All pulse programs supported by ***diff*** are written in a way, whereas they can all be processed by the same equation, the Stejskal-Tanner-Equation:

Equation 4.1

$$\frac{S}{S_0} = e^{-\gamma^2 g^2 \delta^2 \left(\Delta - \frac{\delta}{3} \right) D} = e^{-BD}$$

$$B = \gamma^2 g^2 \delta^2 \left(\Delta - \frac{\delta}{3} \right)$$

In order to measure the diffusion coefficient *D* usually a series of experiments with different values of *B* are performed. Equation (1) is then fitted to the experimental signal amplitudes S. The algorithm then calculates the signal amplitude using B = 0, S_0, and the diffusion coefficient *D*. The parameter *B* holds all the experimental parameters, the gradient strength *g*, the diffusion time Δ, and the gradient pulse length δ. It also contains the gyro magnetic ratio γ in units of rad/s.

In most experiments the timings are kept constant in order to avoid signal attenuation caused by the spin-lattice relaxation time T_1 or the spin-spin relaxation time T_2. In homogeneous broadening T_2^* is usually canceled by means of spin echos.

The approach of describing diffusion experiments using parameter B, is only valid in the case of non-restricted diffusion, i.e. liquid state samples. In the case of restricted diffusion, i.e. porous media, the NMR diffusion experiments can only measure an apparent

1. E. O. Stejskal and J. E. Tanner, J. Chem. Phys. **42** (1965)

2. J. E. Tanner, J. Chem. Phys. **52**(1970)

diffusion coefficient. The magnitude of the apparent diffusion coefficient will usually depend on the diffusion time Δ. Therefore also experiments varying the diffusion time are also available.

4.1 Gradient Pulse Shapes

To generate rectangular gradient pulses using a real gradient coil having a finite resistance and inductance (described in the literature for simplification), an infinite voltage would be required. Shaped gradient pulses allow the required voltage to be limited to a value the amplifier can reasonably produce. Driving a gradient amplifier with rectangular input pulses leads to more or less distorted output pulses depending on the resistance and the inductance of the gradient coil. Even when this distortion does not matter, there is an issue for the gradient pulse reproducibility. More details and how to measure and adjust the ramp time are given in "Gradient Ramp Time Calibration" on page 29. Therefore only shaped gradients are used within the Bruker diffusion programs.

In older versions of **diff** only trapezoidal gradients with equal ramp-up and -down times were available. Beginning with Topspin2.1 pl1, the new gradient shapes *sin* and *opt* are available in *diff* as well. Additionally, the pulse program syntax has been changed to make it easier to have a matching number of gradient shape steps at any ramp or shape duration. The gradient pulses can be selected by radio buttons in the *diff* interface, (refer to "The diff Command Showing Parameters of "ste"" on page 37).

In order to fulfil Equation 4.1 the gradient pulse duration is calculated in a way, that a fictive rectangular pulse of the length δ would have the same integral as the real pulse. This method is not absolutely accurate, but the error is usually negligible.

The default is now always the sine shape.

4.1.1 Sine Shape

The sine shape should more accurately be called half sine shape, but sine shape is the usual nomenclature. In order to allow to fit the data to the usual diffusion equation, the durations are used as described above.

Equation 4.2

$$\delta = 0.636 \cdot t_g$$

The gradient pulse duration is then:

Equation 4.3

$$t_g = \frac{\delta}{0.636}$$

4.1.2 Trapezoidal Shape

The trapezoidal shape can now have different durations for the up and down ramps, tr_{up} and tr_{down}. Currently stage tr_{down} must not be larger than tr_{up}. The equations Equation 4.2 and Equation 4.3 get a bit more complicated:

Equation 4.4

$$\delta = 0.5 \cdot \left(tr_{up} + tr_{down}\right) + t_{on}$$

Equation 4.5

$$t_g = tr_{up} + t_{on} + tr_{down} = \delta + \frac{tr_{up} + tr_{down}}{2}$$

4.1.3 Opt Shape

The „opt shape" stands for optimal shape, which is mainly useful for gradient systems with a high resistance and inductance.

The opt shape is a composite shape, it starts with a quarter of a sine wave, then a constant gradient and finally a ramp down. Using this sequence will in most cases provide the biggest gradient integral for a given time. The equations Equation 4.4 and Equation 4.5 have to be modified as follows:

Equation 4.6

$$\delta = 0.636 \cdot tr_{up} + t_{on} + 0.5 \cdot tr_{down}$$

Equation 4.7

$$t_g = tr_{up} + t_{on} + tr_{down} = \delta + 0.364 \cdot tr_{up} + 0.5 \cdot tr_{down}$$

The advantages of this pulse are not only that the factor 0.636 shows up in Equation 4.6, but also tr_{up} can usually be significantly shorter compared to the trapezoidal pulse.

4.2 Variable Gradient Experiments

In all of these experiments the times are kept constant while the gradient amplitude is varied. The gradient strength usually starts at a small "gradient start value" and is increased in different ways up to the so-called "maximum gradient value". The selector for the different ways of varying the gradient strength is called **diffusion grad list type**. The first mode is **linear**, were the gradient is incremented in constant increments between the **gradient start value** g_{start} and the **maximum gradient value** g_{max} (see Equation 4.8).

In Equation 4.8 i stands for the index of the gradient value and n for the number of gradient steps. In the **default mode** g_{start} is set to g_{max}/n, but not larger than 5% of g_{max}.

Equation 4.8

$$g_i = g_{start} + \frac{g_{max} - g_{start}}{n-1}$$

The second mode is called *sqrt*, here the gradient values grow following the square root of their index. Here g_{start} is implicitly calculated and therefore not variable:

Equation 4.9

$$g_i = \sqrt{\frac{i}{n}} g_{max}$$

The third mode is the **log** mode, here the gradient values increase exponentially, as shown in Equation 4.10:

Equation 4.10

$$g_i = \exp\left(\ln(g_{start}) + (i-1)\frac{\ln(g_{max} - \ln(g_{start}))}{n-1} \right)$$

The last mode is the so-called **user** mode, where the user can edit the gradient list.

4.2.1   Pulse Gradient Spin Echo (PGSE)

The PGSE is the basic experiment, called **se** in the *diff* program. During a $\pi/2$ - π spin echo sequence two absolutely identical gradient pulses g are applied after the first and the second RF pulse. In this variant of the PGSE sequence, the gradient pulses are placed immediately the RF pulses in order make the available time for gradient ring down as long as possible. The distance between the centers of the two gradient pulses is called diffusion time Δ.
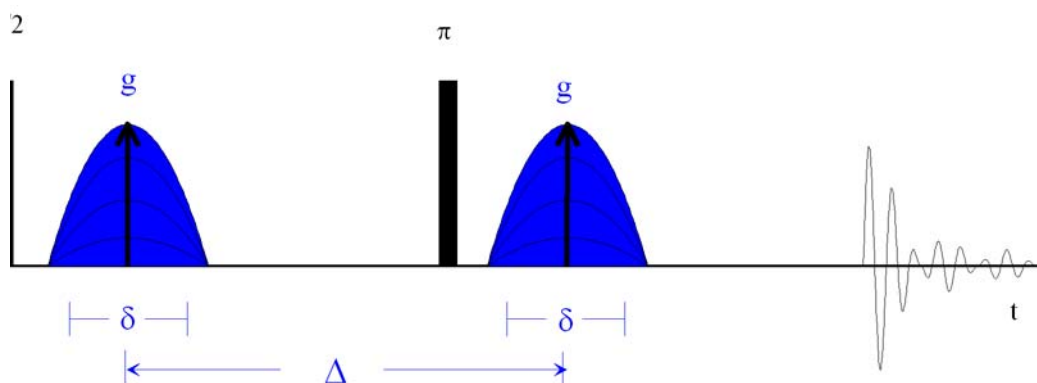
Figure 4.1   PGSE Pulse Sequence (diffSe)

During the sequence the signal decays according to the T_2 value, at an effective echo time (T_e) of 2Δ. Because all delays are kept constant during the whole experiment, the T_2 relaxation delivers only a constant attenuation factor whilst the decay is purely caused by diffusion.

Equation 4.11

$$T_e = 2\Delta$$

The gradient pulses can have different shapes as described above. The effective length of the gradient pulses describing the phase encoding strength of the gradient pulse is called δ. Depending on the pulse shape the duration of the gradient pulse is longer than δ (see Equation 4.3, Equation 4.5, and Equation 4.7).

i Note: If a J-coupling is present, long echo times may lead to spectra, which cannot be phased.

4.2.2   Pulse Gradient Stimulated Echo (PGSTE)

The PGSTE is called **ste** in the *diff* program. During a $\pi/2$ - $\pi/2$ - $\pi/2$ stimulated echo sequence two absolutely identical gradient pulses (*g*) are applied immediately to the first and the third RF pulse. The PGSTE sequence delivers only half of the signal compare to the PGSE sequence. The period between the two first RF pulse is called τ, during τ the magnetization decays according to the T_2 value at an effective echo time of 2τ.

Equation 4.12

$$T_e = 2\tau$$

During the period between the second and the third RF pulse the magnetization points in the z direction and therefore the T_1 value applies. In many cases, this behavior allows use of rather long diffusion observation times. Because all delays are kept constant during the whole experiment, the T_1 and the T_2 relaxation contributions deliver only a constant attenuation factor whilst the decay is caused purely by diffusion.

The amplitude of these gradient pulses is incremented between experiments in order to get a variable attenuation of the NMR signal (see "Variable Gradient Experiments" on page 53). In this variant of the PGSTE sequence, the gradient pulses are placed immediately the RF pulses in order to allow for the shortest possible τ value.
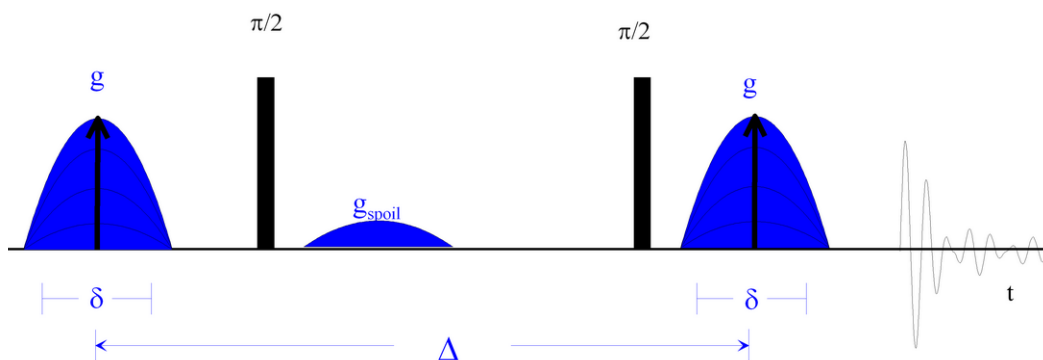
Figure 4.2   PGSTE Pulse Sequence (diffSte)

The gradient pulses can have different shapes, see "Gradient Pulse Shapes" on page 52. The effective length of the gradient pulses describing the phase encoding strength of the gradient pulse is called δ. Depending on the pulse shape the duration of the gradient pulse is longer than δ (see Equation 4.3, Equation 4.5, and Equation 4.7).

The distance between the centers of the two gradient pulses is called diffusion time Δ.

An optional gradient spoiler or crusher gradient pulse is used in this sequence in order to get rid of coherent magnetization during the evolution period.

4.2.2.1   Spoiler Gradients

In the current version of the diff program, only mixing time spoilers are used for all stimulated echo experiments. Mixing time means the spoiler gradient is in the period between the 2nd and the 3rd $\pi/2$ pulse. In this period the usable magnetization is stored in z direction and the spoiler dephases the remaining magnetization using spatial phase encoding. This is particularly important, when running a sample with a long T_2 value. The area of a spoiler pulse should not match the value of any of the diffusion gradients throughout the experiment.

In the default mode the spoiler gradient is calculated so that it's area equals 2/3 of the initial gradient step. If this area is too small for proper spoiling the value is set between the first and the second step, and so forth.

The minimum spoiling gradient $g_{spoil,min}$ area is set arbitrarily to a value which corresponds to $33*360^o$ phase shift over a 1 cm sample length.

Equation 4.13

$$g_{spoil,min} = \frac{33}{\gamma \, \delta_{spoil}}$$

In the equation above, δ_{spoil} stands for the effective spoil pulse duration resulting from Equation 4.2. For protons with a typical spoil duration of 2 ms, the $g_{spoil,min}$ would be 3.9 G/cm (39 mT/m).

4.2.3 PGSTE using bipolar gradients

The PGSTE using bipolar gradients, also called 13 interval sequence[1](PGSTEBP), is quite similar to PGSTE (see). The single gradient pulses of the PGSTE sequence are split into a pair of 2 pulses with opposite signs enclosing a π-pulse. This pulse sequence is used to remove the effect of internal gradients in the sample. The dephasing resulting from internal static gradients is removed by means of the π-pulse. The effect of the applied gradients is kept by reversing the gradient after the π-pulse. In this sequence the gradient pulses are centered in the gaps between the RF pulses.
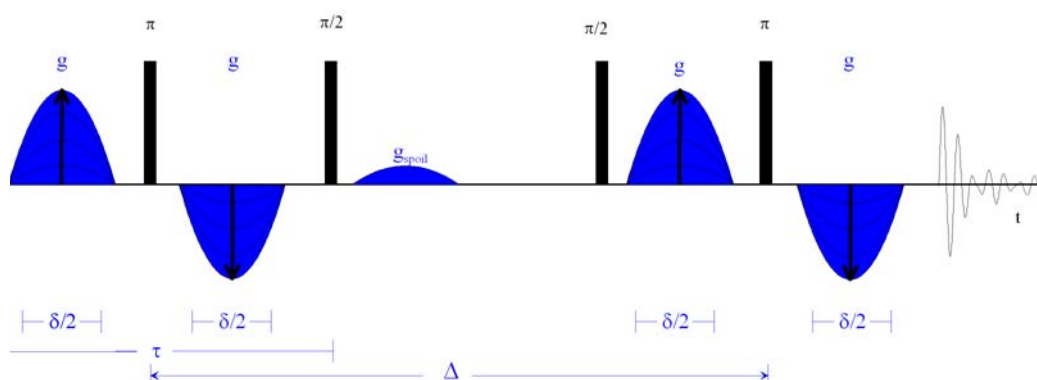
Figure 4.3   PGSTEBP Pulse Sequence (diffSteBp)

The delay between the first two $\pi/2$-pulses, called τ similar to the PGSTE sequence, is usually a much longer sequence, here compared to the standard PGSTE sequence. This is mainly because of the gradient ring down delays, which also have to be in front of the gradient pulses in order to center them.

This sequence is also often used in liquid type experiments using the lock, because the bipolar sequence disturbs the lock less than the monopolar.

The gradient pulses can have different shapes (see). The effective length of the gradient pulses describing the phase encoding strength

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1. R. M. Cotts, M. R. Hoch, T. Sun, and J. T. Markert, JMR **83**, 252-266(1989)

of the two gradient pulses is called δ. The duration of the individual gradient pulse might be shorter than δ here. The equations Equation 4.2 to Equation 4.7 must be converted in this experiment.

Equation 4.14

$$\delta = 2 \cdot 0.636 \cdot t_g$$

Equation 4.15

$$t_g = \frac{\delta}{2 \cdot 0.636}$$

Equation 4.16

$$\delta = tr_{up} + 2 \cdot t_{on} + tr_{down}$$

Equation 4.17

$$t_g = tr_{up} + t_{on} + tr_{down} = \delta - t_{on}$$

Equation 4.18

$$\delta = 2 \cdot 0.636 \cdot tr_{up} + 2 \cdot t_{on} + tr_{down}$$

Equation 4.19

$$t_g = tr_{up} + t_{on} + tr_{down} = \delta - 0.272 \cdot tr_{up} - t_{on}$$

The distance between the two π-pulses, which are the effective centers of the two gradient pulse pairs, is called diffusion time Δ.

An optional gradient spoiler or crusher gradient pulse is used in this sequence in order to get rid of coherent magnetization during the evolution period (see "Spoiler Gradients" on page 56).

4.3 Variable Δ experiments

Currently, only one method using a variable D is built into *diff*, a stimulated echo experiment. The advantage of this method is, that because T_1 is often significantly larger than T_2, the range of possible D values is larger in the stimulated echo experiment compared to a spin echo experiment. The disadvantage is, that the signal amplitude in such an experiment does not only decay caused by the molecular diffusion, but also caused by spin-lattice relaxation T_1. Because of this Equation 4.1 must be modified:

Equation 4.20

$$\frac{S}{S_0} = e^{-\gamma^2 g^2 \delta^2 \left(\Delta - \frac{\delta}{3} \right) D} \, e^{-\frac{\Delta}{T_1}}$$

In order to compensate for this effect, each D increment is performed twice, one increment with g = 0, the other with g = g_0. This way the relaxation Term can be removed by dividing the amplitude of experiment two by the amplitude of experiment one.

4.3.1   PGSTE with variable diffusion time

The PGSTE with variable diffusion time is called **DELTA** in the *diff* program. During a $\pi/2$ - $\pi/2$ - $\pi/2$ stimulated echo sequence, two absolutely identical gradient pulses (*g*) are applied immediately the first and the third RF pulse. The PGSTE sequence delivers only half of the signal compared to the PGSE sequence. The period between the two first RF pulse is called τ. During τ the magnetization decays according to the T_2 value at an effective echo time of 2τ (see Equation 4.12). During the period between the second and the third RF pulse the magnetization points in z direction and therefore T_1 applies. In many cases this behavior allows use of rather long diffusion observation times.

The amplitude of the gradient pulses is constant throughout the experiment. The diffusion time Δ, which is the distance between the centers of the two gradient pulses, is incremented between experiments in order to get a variable attenuation of the NMR signal. In this variant of the PGSTE sequence, the gradient pulses are placed immediately after the RF pulses in order to allow for the shortest possible τ value.

Because the delays are not kept constant during the whole experiment, the T_1 relaxation contribution cannot be neglected. Therefore the experiment is always performed in two steps. For each diffusion observation time the experiment is performed once with and once without diffusion gradients. The experiment without diffusion gradients measures the relaxation contribution, while the experiment with gradient shows the attenuation caused by diffusion and relaxation.

The data are then processed by dividing the spectra with diffusion gradients with the ones without at the same timings. This way the relaxation effect is removed without further calculations. The processing section of the *diff* program handles this automatically, see "Processing using diff" on page 70.
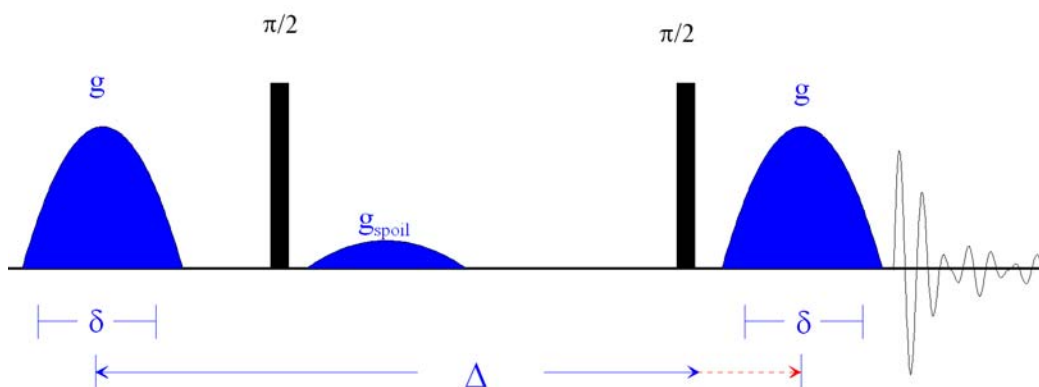
Figure 4.4   PGSTE Pulse Sequence with variable Δ (diffDELTA)

The gradient pulses can have different shapes (see "Gradient Pulse Shapes" on page 52), depending on the TopSpin version used. The effective length of the gradient pulses describing the phase encoding strength of the gradient pulse is called δ. Depending on the pulse shape the duration of the gradient pulse is longer than δ.

An optional gradient spoiler or crusher gradient pulse is used in this sequence in order to get rid of coherent magnetization during the evolution period.

4.4   Convection Compensated Sequences

Diffusion measurements are measurements of slow molecular motion, thus superimposed macroscopic motions can corrupt the results. Vibrations convective flow can also be the source of artefacts in diffusion experiments. The reason for convection are temperature gradients in the sample (see "Convection Artefacts" on page 88). The smaller the viscosity of the solvent or the sample itself, the larger the velocity of the convective flow will be.

To explain the convection compensation a short explanation of the effects of gradients on the signal phase is given here. In general the phase evolution of the spin signal at a certain position (r_0) caused by gradients in any NMR experiment, can be described using the equation:

Equation 4.21

$$\Phi(t) = \gamma \vec{r}_0 \int \vec{g}(t)dt + \gamma \vec{v}_0 \int \vec{g}(t)t\,dt + ...$$

$$\Phi(t) = \gamma M_0 \vec{r}_0 + \gamma M_1 \vec{v}_0 + ...$$

Because the magnetic field is position dependant in the presence of a gradient, the gradient induced phase is dependent on the position r_0, and its derivatives. The expansion shown in Equation 4.21 stops at the first derivative, the velocity v_0. For the treatment of

convection in an NMR tube the constant velocity term v_0 is usually enough in this geometry. This is because one can assume two constant flows, one up, the other down. The time integrals of $g(t) \cdot t^i$ are usually abbreviated using M_i, or *moments*.

In a diffusion experiment like e.g. the PGSE (see Figure 4.1), the effect of M_0 is exactly zero. This is because the phase shifts caused by the two gradient pulses are exactly the same, but with opposite sign because of the π pulse in between. The first *moments* of the two gradient pulses are not identical, because they occur at a different time. If then the velocity is zero, the M_1 term is also zero. In this case only the signal attenuation caused by the random diffusive motion, which is neglected in Equation 4.21, will be visible (see Equation 4.1).

If convection is present, v_0 is not zero and will be different in various radial positions in the sample, usually $+v_0$ and $-v_0$. The signal will show a superposition of the attenuation caused by diffusion and the phase shifts caused by two opposite flows.

To compensate for this, the pulse sequence must be modified in a way, that M_1 is inherently zero. This can be accomplished by adding suitable additional gradient pulses in order to fulfill to following condition:

Equation 4.22

$$M_0 = M_1 = 0$$

There are many possible ways to do this, also the compensation of higher order are possible. In diffusion experiments usually the simplest solution is used, the double stimulated echo sequence[1], whereas the second part compensate the first moment of the first part.

4.4.1 Pulsed Gradient Double Stimulated Echo PGDSTE

The PGDSTE sequence is a duplicated version of PGSTE (see "Pulse Gradient Stimulated Echo (PGSTE)" on page 55), whereas only the initial $\pi/2$-pulse is not copied. This pulse sequence is used to remove the effect of constant flows in the sample. In this variant of the PGSE sequence, the gradient pulses are placed immediately after the RF pulses in order make the available time for gradient ring down as long as possible. The distance between the centers of the two gradient pulses is called half diffusion time $\Delta/2$. This allows the data to be processed afterwards in the same way as the PGSTE data. Details about this are given in the section "Conversion of the Cotts 13 interval to the Stejskal/Tanner Equation" on page 84.

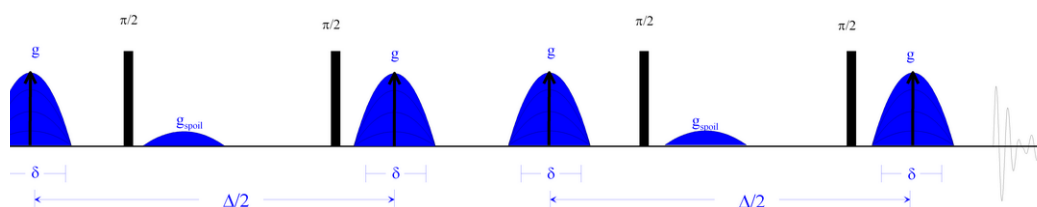In this experiment two identical, optional spoiler gradient pulses are used.

Figure 4.5   PGDSTE Pulse Sequence (diffDste)

1. A. Jerschow & N. Mueller, J. Magn. Reson. A 123, 222-225 (1996)

4.5 Multiple Acquisition in TopSpin2.1 and Later

In general Multizg does not work for diffusion experiments.

Beginning with TopSpin 2.1, the relative gradient amplitudes (diff_ramp) cannot be stored in the data directory together with the other acquisition parameters. The diff_ramp is now stored in the highest priority gradient list directory, usually "*<TopSpinHome>/exp/ stan/nmr/lists/gp/user*". In order to solve this problem a modified *multizg* AU program called *diffmultizg* is provided, which will recalculate these parameters in the background. This works properly beginning with TopSpin2.1pl2. For later versions a more general solution is planned.

This point is only relevant if the *number of gradient steps* or the *grad list type* is changed within the sequence of experiments. When this is not the case, the conventional *multizg* will work anyway.

In case of repetitive experiments where parameters do not change and without prior preparation of the data-sets *diffmultizg* is advantageous in that it prepares the processing parameters which a conventional *multizg* cannot do.

i Note: The spooler in TopSpin can only be used if the *number of gradient steps* or the *grad list type* is not changed within the sequence of experiments.

5 Processing

5.1 The T1/T2 Analysis Module

The T1/T2 analysis tool is described in detail in the TopSpin **User Manual** in the chapter **Relaxation Analysis** (TopSpin2.1). In future TopSpin versions a separate T1 manual may be used. This chapter provides details relevant for diffusion experiments.

5.1.1 New Display Features

Beginning with TopSpin 2.1, the T1/T2 Analysis Tool provides options for plotting logarithmic axis for the x- and y-axis, and a squared axis for the x-axis. The log x-axis has usually no meaning for diffusion experiments, but squared x- plus log y-axis provides the common semi-logarithmic display.

The buttons **lin**, **log**, and **sq** for the x-axis work like radio buttons, while the **log** button for the y-axis can be toggled.

The figures Figure 5.1, Figure 5.2, and Figure 5.3 give examples of how this should like.
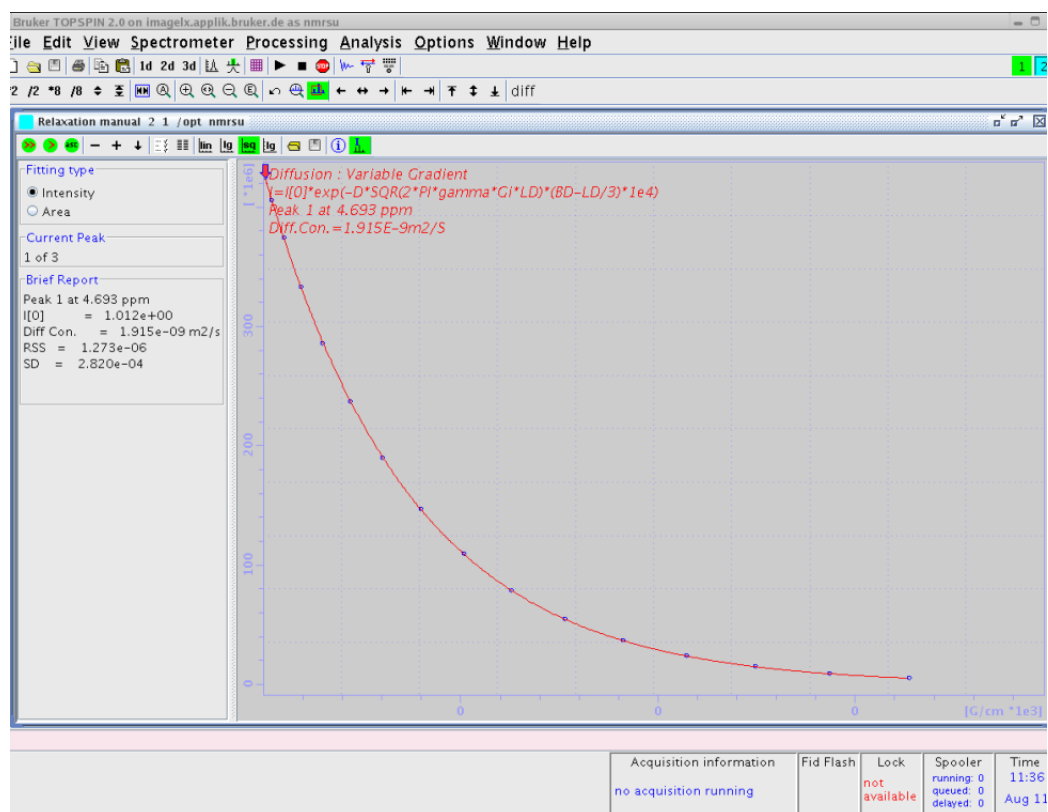

Figure 5.1   Diffusion curve displayed using the sq option of the x-axis
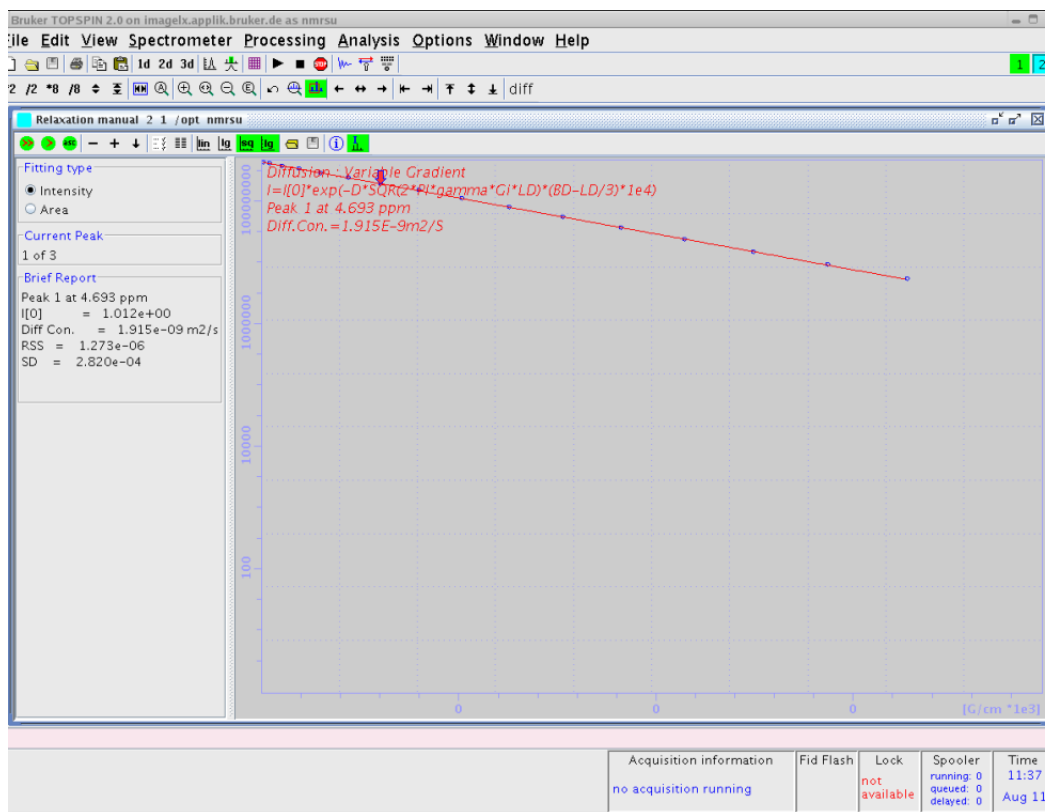
Figure 5.2   Diffusion curve displayed using the sq option of the x-axis and the log option of the y-axis
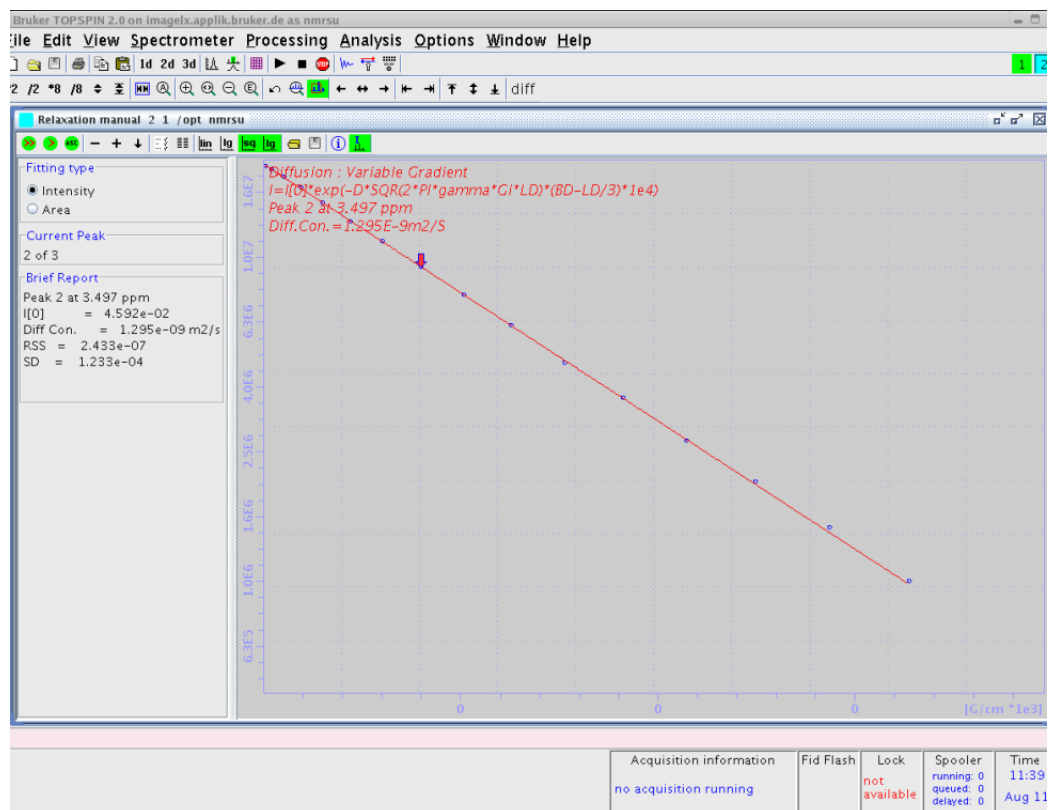
Figure 5.3   After manual scaling

5.1.2   Parameter Dialog Box

In routine operation these parameters do not need to be modified, as the *diff* program sets them automatically. But sometimes it might become necessary to adjust some of the parameters, therefore a description of their meaning is given here.

If it becomes necessary to change parameters, change the values, then click on **Apply** followed by **OK.** If an error occurs due to incorrect parameter setting (see below), the changes made are not lost.

1. **FID # for phase determination**: This parameter has no meaning at the moment, but it must be in the range of the number of the experiments performed. A value of zero, for example, leads to an error message.

2. **Left** and **right limit for baseline correction**: These are the same parameters as in **edp**.
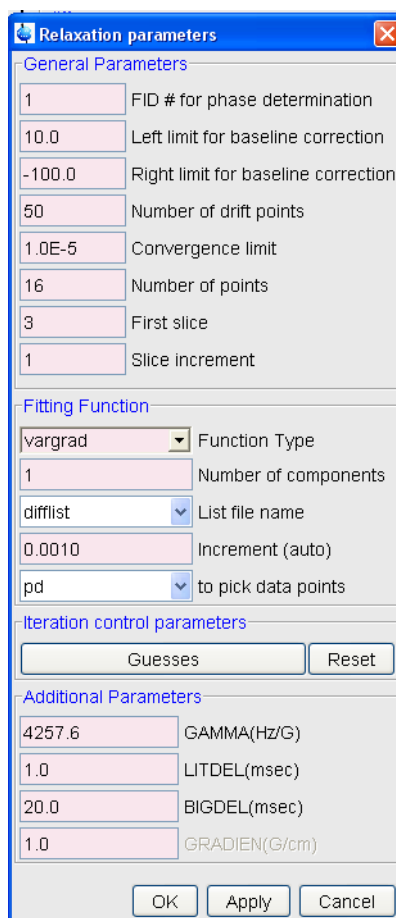
Figure 5.4   Parameter dialog box

3. **Number of drift points**: This number is the maximum allowed drift range for the peak picking method **pd**. The value is preset to 50 by **diff**.

4. **Convergence limit**: Parameter used to control the simfit algorithm. This normally does not need to be changed.

5. **First slice**: Parameter is not used, but must be in the range of **td1**, zero is not allowed.

6. **Slice increment**: Must be a value of „1".

7. **Function type**: The function type can be selected from a pull-down menu. For diffusion experiments only 3 functions apply: **vargrad**, **varlitdel**, and **varbigdel**. The correct value is set by *diff*.

8. **Number of components**: Number of exponential functions to be fitted to the data. Parameter can be 1 to 6, while for diffusion experiments more than 2 or 3 are normally not useful. The default set by **diff** is 1.

9. **List file name**: Name of a file in the acquisition data directory containing the varied experimental values, e.g gradient amplitudes. Besides the file name this parameter can also have one of a list of predefined key words, but they are not used here. **Diff**

always creates a file called **difflist** containing the gradient amplitude for variable gradient experiments, or the delays for large variables, or small delta methods.

10. *Increment (auto)*: This parameter is used by the auto keyword of the parameter *List file name* above, not used by *diff*.

11. *to pick data point*: This parameter is used to select the peak picking mode. The default method *pd* searches for the peak maximum in each individual spectrum allowing for a maximum shift as given in the number of drift points field.

12. *Guesses*: Clicking on the button *Guesses* opens an additional dialog box, shown in Figure 5.5, if one exponential (Number of Components) is used. The fitting algorithm used by the *T1/T2 Analysis Module* needs initial *Guesses* for the fit. For single exponential fitting the algorithm is very tolerant, but for multi exponential fitting these values must be carefully set and sometimes varied a bit in order to get proper fitting.
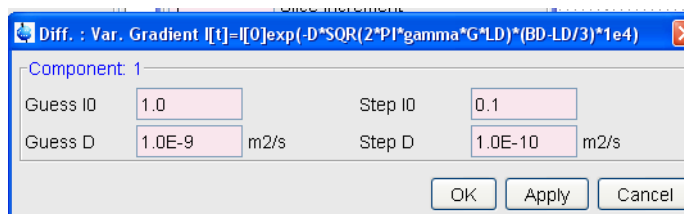

Figure 5.5   Guesses dialog box for one exponential

Diff always presets the *Guesses* for the amplitudes to 1.0. The *Guess* for the diffusion coefficient of the first component is set to the value of the *expected diffusion coefficient (see* "The "Expected Diffusion Coefficient"" on page 83*)*. The *Guess* of the second diffusion coefficient is set 0.1, the third to 0.01 of the *expected diffusion coefficient*. The steps, i.e. the initial step width of the iteration of the algorithm, are always set to 10% of the corresponding *Guess*, which is the maximum allowed value.

The dialog box changes depending on the selected number of exponents, e.g for 2 exponents it looks like Figure 5.6.
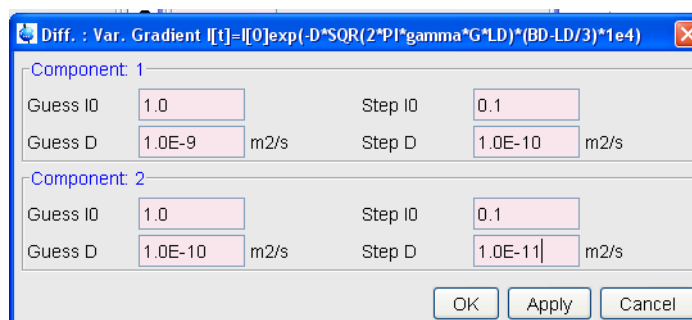

Figure 5.6   Guesses dialog box for 2 exponents

In the title of the *Guesses* window, the actually fitting function used is displayed.

13. ***Reset***: This button also opens the *Guesses* dialog box, but resets the parameters to values present at the start of the ***T1/T2 Analysis Module***.

5.1.2.1 Additional Parameters

The ***Additional Parameter*** section allows adjust of the remaining fixed parameters in the fitting function. All these parameters are automatically set by ***diff***.

14. ***Gamma***: Gyro-magnetic ratio in Hz/Gauss ($\gamma/2\pi$), depends on the observed nucleus.

15. ***LITDEL (ms)***: Little delta (δ), active for ***vargrad*** and ***varbigdel***.

16. B***IGDEL (ms)***: Big delta (Δ), active for ***vargrad*** and ***varlitdel***.

17. ***GRADIEN (g/cm)***: Gradient amplitude (g), active for ***varbigdel*** and ***varlitdel***.

5.2 DOSY Processing

Diffusion **O**rdered **S**pectroscop**y** (**DOSY**), is another way to process and to display diffusion experiments. DOSY is described in detail in a separate manual, so only a few hints shall be given here.

Most of the relevant parameters for the DOSY processing are set by *diff* automatically. To check and set the DOSY parameter type, open the DOSY parameter editor window, **eddosy**, shown in Figure 5.7.
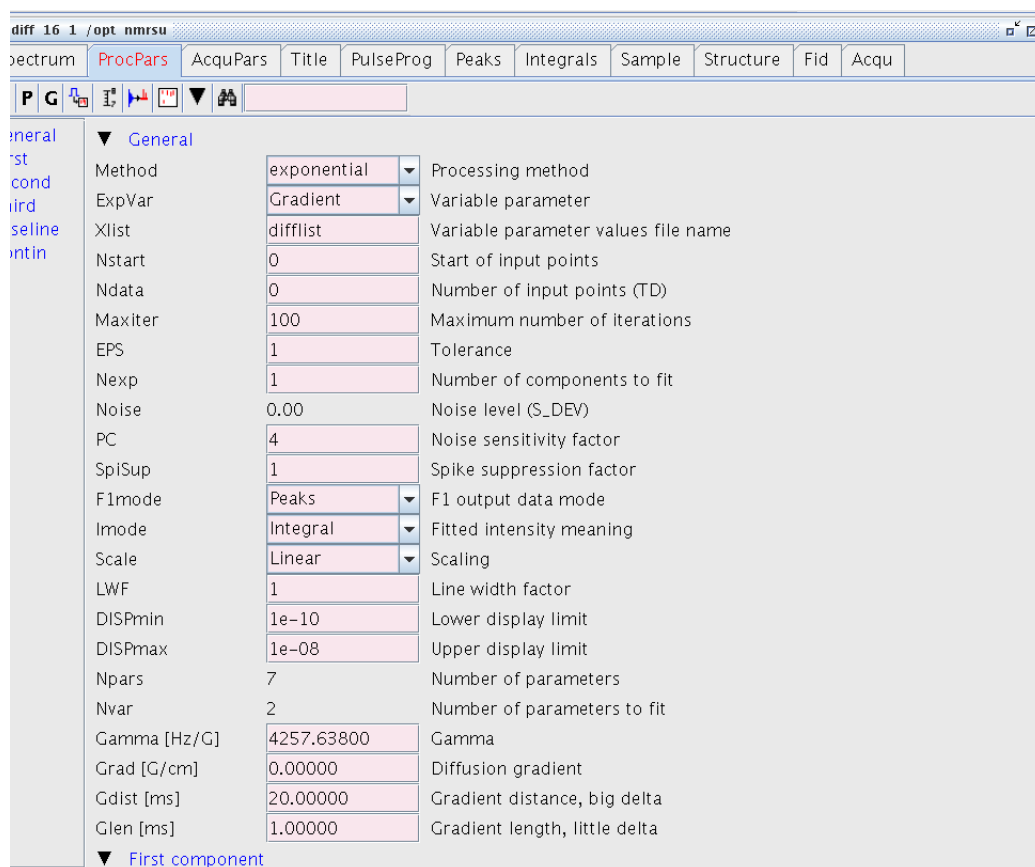
Figure 5.7   DOSY parameter editor window, eddosy

The algorithm must be first selected in the *eddosy* window. The pull-down menu next to the parameter *Method* allows for 4 different algorithms:

- Exponential
- Gifa-maxent
- Decra
- Contin

5.2.1   Exponential

Exponential solves the problem of displaying diffusion experiments by fitting up to 3 exponential functions in the individual columns of the 2D data matrix. By default the *Nexp* exponential is selected. If the number of exponential to fit is increased, the user has to check and in most cases enable the fitting of the corresponding parameters, *I2vary, D2vary, I3vary, D3vary*.

Important is to set the range of the displayed diffusion coefficients, *DISPmin*, *DISPmax* correctly in order to have all expected values in the displayed window.

Usually it is better to select the logarithmic display mode, *Scale*, because often the diffusion coefficients can vary over several orders of magnitude.

For better display quality use zero filling in the F1 direction, i.e. set the *SI* in F1 direction double or 4 times the number gradient steps prior to *xf2*

5.2.2 Gifa-maxent

Gifa-maxent is a special algorithm, which needs an extra software license, and is explained elsewhere.

5.2.3 Decra

Decra is an algorithm, which can separate 1D spectra of different species, if they differ sufficiently in their diffusion coefficient.

Decra requires that the squares of the gradient amplitudes are spaced linearly. In *diff* the *sqrt* list must be selected prior to acquisition.

5.2.4 Contin

Contin is a long established inverse Laplace algorithm. It delivers similar results as the exponential method, but often somewhat smoother and nicer looking. It requires significantly more calculation time, therefore it is useful to keep the number of data points small, 1K or 2K in the F2 direction will usually be reasonably fast.

The scaling and oversampling settings are the same as for exponential.

5.3 Processing using *diff*

The *diff* program is mainly a tool to set-up experimental parameters, but it also provides a processing section. This has mainly two purposes:

- First it can convert the data from the TopSpin t1t2.dx file to different spreadsheet like files containing the experimental data together with formats of the abscissa data, e.g. like gradient strength, q-values, and B-values.

- Secondly it allows processing of a series of similar experiments and creates a spreadsheet file containing all the experiments. This makes the handling of large numbers of experiments a bit more convenient. The spreadsheet files cannot be processed by TopSpin or by *diff*. The files can only be imported by third party programs such as Microsoft Excel.

5.3.1 Single Experiment Processing

In order to use the processing features of *diff,* the data must be processed so that simfit can use it. If the raw data will only be used within another program, it is not essential that simfit delivers useful results. On the other hand, if the simfit results are required later on,

the fitting parameters should be set to allow for a good simfit result.

Be sure to close the T1 analysis window or to switch to another window in TopSpin to display the data-set to be processed before starting *diff*.

If not already selected, click on the *processing* check button, which is always visible on the bottom of the window on the left side (see "The diff Command Showing Parameters of "ste"" on page 37). Once the button is checked you should see the window displayed in the figure below:
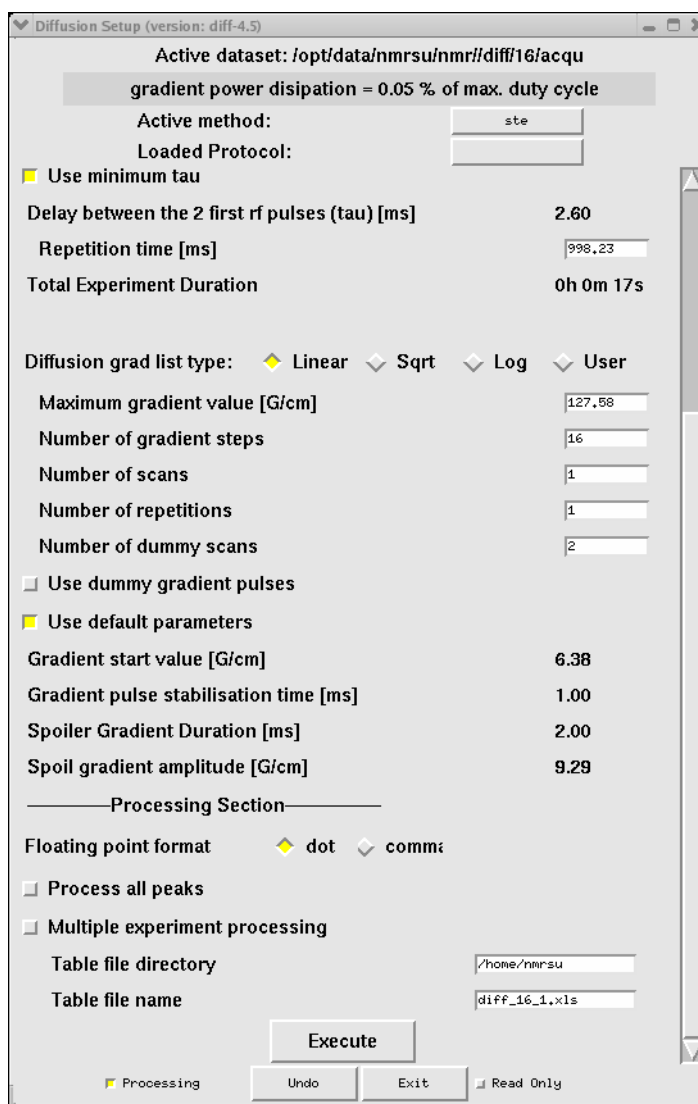

Figure 5.8   *diff* Showing the Processing Section

Pressing the *Execute* button will cause the following actions:

1.   Execution of simfit in TopSpin.

2.   Depending on the experiment type, two column csv files (e.g. SB*i*.dat), which contain the B values in the first column and signal amplitudes in the second will be cre-

ated. The *i* in the filename stands for the index of the peak. If the *process all peaks* check button in Figure 5.8 is not checked *i* will be equal to one, regardless of which peak was selected (e.g. SB1.dat). When only one peak is present *i* will also be equal to 1.

An additional file called DiffData.xls, containing all the columns of the other files plus the fit parameters, is also created. If more than one peak is processed they are sequentially placed in the file from top to bottom. The file is not an EXCEL type spreadsheet as the name implies, but rather a tab separated csv file, which can be read directly using EXCEL or Open Office. In this conversion the data acquired by the DELTA method are treated automatically, i.e. the amplitudes of the odd data points are divided by the amplitudes of the even.

3. The file DiffData.xls is copied to a name and location specified in the setup window (see Figure 5.8). The default values are the users home directory and a name, which is constructed out of the data set name, the experiment number, and the processing number.

5.3.2   Multiple Experiment Processing

This feature is used to process a series of experiments acquired with consecutive experiment numbers and mainly to create a single spread sheet file containing all data from all experiments.

When the *Multiple experiment processing* check button is checked (see Figure 5.8), the window will change as shown in Figure 5.9:
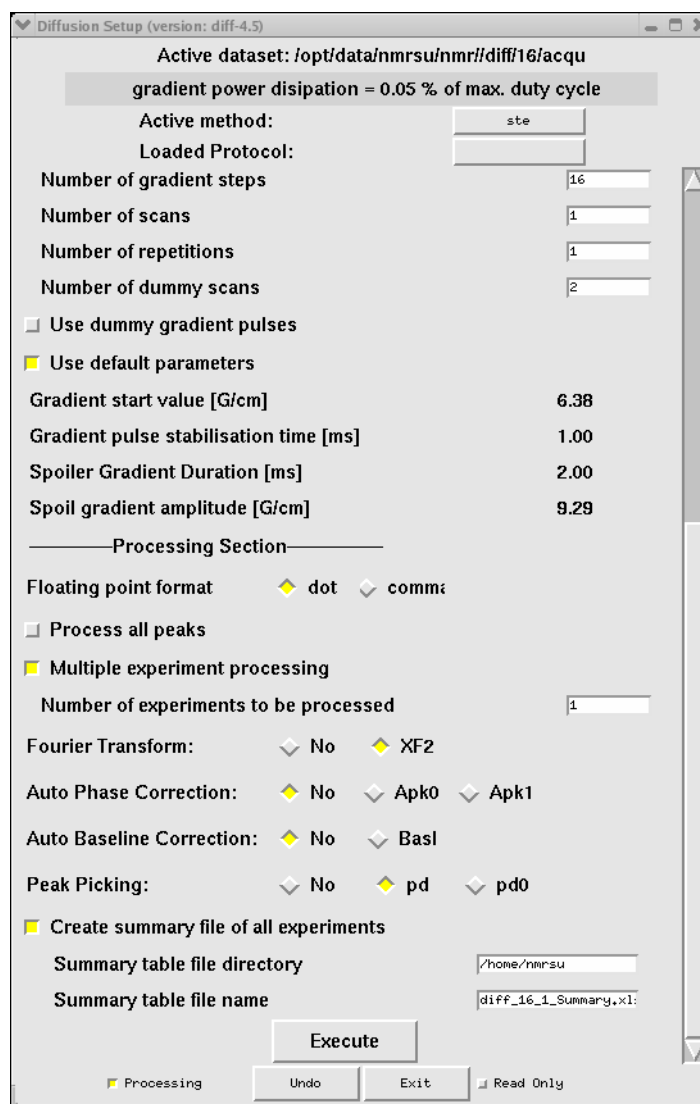
Figure 5.9   *Diff* showing multi experiment processing

If *Fourier Transform* and *Peak Picking* are not selected, and *Create Summary file of all experiments* is not checked, the program will assume that peak picking is already performed and the same actions as described in Chapter 5.3.1 will be performed.

If the check button *Create Summary file of all experiments* is checked, all the Diff-Data.xls files are copied into the specified summary file, sequentially left to right.

If *Peak Picking* is selected, the program uses the same peak picking parameter as for the first in the series for all, i.e. the files *intrg* and *baslpnts* are copied from the first experiment in the series to the rest of the series, and peak picking is performed afterward.

If *Fourier Transform* is selected, than a Fourier transformation is performed on all the raw data prior to the peak picking. Automatic phase correction and/or automatic base line correction can be performed upon request.

6 *Diff* Program Reference

This part of the manual describes the *diff* program, referencing existing material already discussed and providing information not given elsewhere.

6.1 *Diff* Program

The *diff* program is a tool to simplify the set-up of diffusion experiments. The main idea is to replace machine level parameter settings with experiment level parameters representing physically relevant parameters. For example, rather than setting the gradient strength in percent, the gradient strength is given in Gauss/cm. In other words, the user does not need to know, which delays form the diffusion time, they just have to specify the diffusion time and the program will automatically set the other parameters.

Most of the parameters will be checked for reasonable upper and lower limits. Typing 0 in a parameter window, will show the minimum possible value for that parameter return is typed or the entry field is no longer focused[1].

Parameters like the diffusion time and particularly their minima, depend on other adjustable parameters, thus a parameter hierarchy is necessary. Using the PGSTE experiment as an example, the hierarchy of the delays is as follows:

*   Level One: Effective gradient pulse duration, spoiler gradient duration[2], gradient ramp time[3], RF pulse duration, τ[4].

*   Level Two: Diffusion time.

*   Level Three: Repetition time.

Parameters in level one can be adjusted independently, but they will affect the parameters in level two and three.

When changing a parameter in level one increases the minimum diffusion time, and the new minimum diffusion time is larger than the old diffusion time, then the diffusion time will be increased until it is as big as the new minimum.

Likewise, when the minimum diffusion time is reduced by changing a parameter in level one, or the new minimum diffusion time is smaller or equal than the old diffusion time, the diffusion time will remain the same.

The same mechanism applies between members of level one and level two, with respect to parameters in level three.

---

1. How this works in detail depends on the operating system and the desktop settings

2. If default mode is off

3. If default mode is off

4. If minimum echo time id off

6.2 *Diff* Menu of the PGSTE Experiment

The contents of the menu shown in Figure 6.1 is described here line by line as an example, as other methods use similar menus.
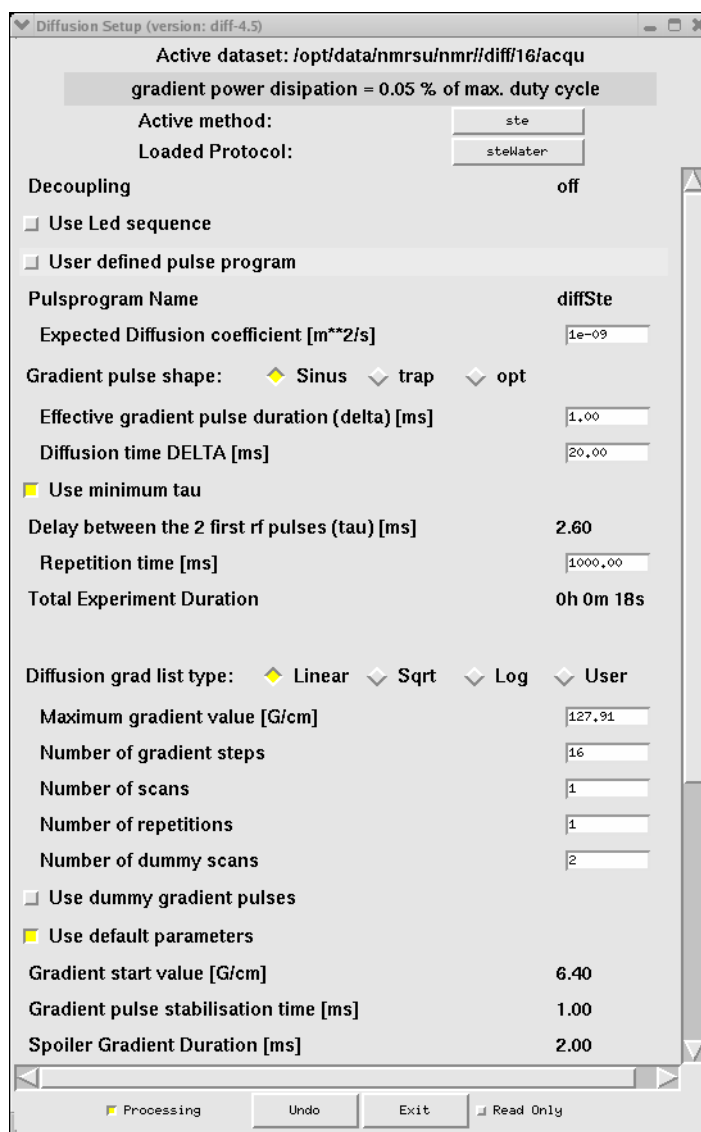

Figure 6.1   *diff* showing parameters of **ste**

1. The title of the window "Diffusion Setup (version 4.1.7) <2>" also displays the actually running version of the *diff* program and, if more than one *diff* window is open, which is selected.

2. The location of the *acqu* file for the active data-set.

3. The Gradient power dissipation is calculated from the resistance of the gradient system and the applied current scheme. This value is then compared to the maximum allowed duty cycle of the gradient system. If the duty cycle exceeds 90% the display

changes (see Figure 6.3). If the duty cycle exceeds 100%, the repetition time is automatically increased in order the reduce the duty cycle to 100%. If an individual pulse exceeds the maximum allowed value, the gradient strength is reduced.

The gradient system parameters are taken from the data given in the preemphasis files, if available, see "Default Preemphasis File" on page 13 for details. If not, the type of gradient system is guessed from the gradient strength, and standard parameters for the type are then used. If the parameters are not already set, they can be set via setpre, see "Gradient Safety Parameters (AVANCE III only)" on page 95 for details.
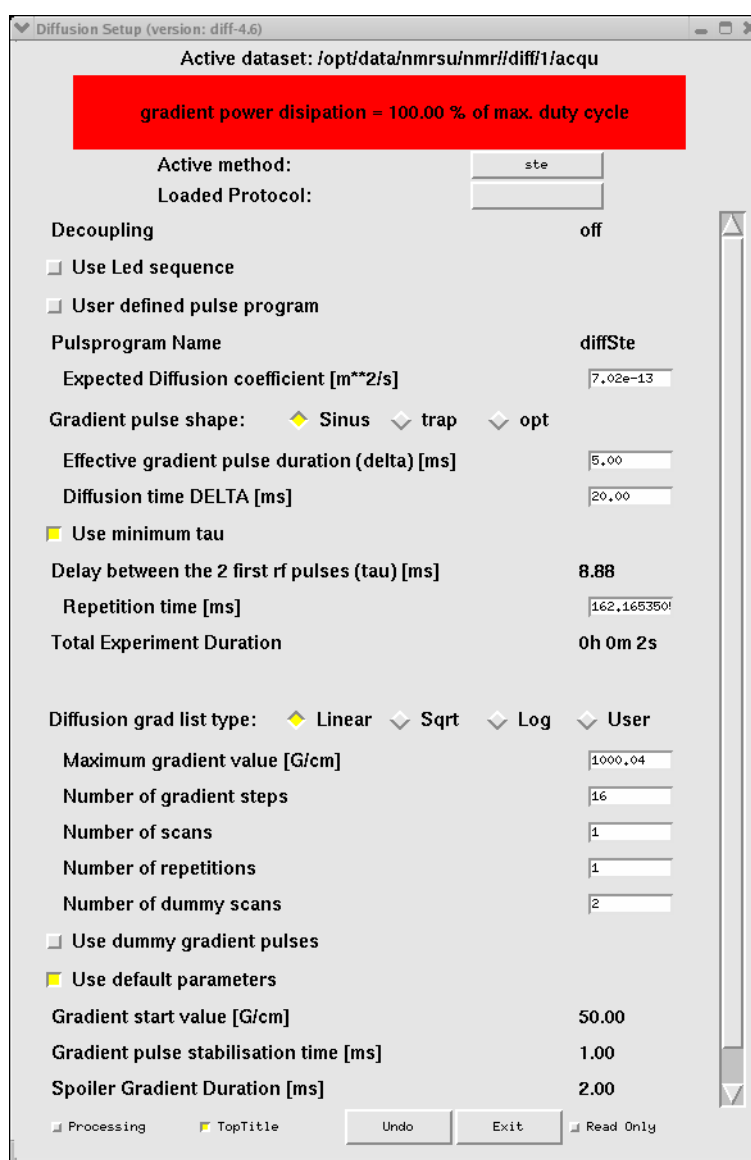

Figure 6.2   *Diff* showing duty cycle warning

4.   The *active method button* shows the selected method out of the list of installed methods shown when clicking the button. The main methods are described in "Diffu-

sion Experiments" on page 51.

The method files are located in *<TopSpinHome>/prog/tcl/xwish3_scripts/difflib.* Details about the syntax are given in the method file ste.

5. The ***loaded protocol button*** shows the last protocol loaded during the current run of ***diff***. If no protocol was loaded it will show ***select-protocol***. Clicking the button displays a list of available protocols (see "The diff Command Showing Protocol Selection" on page 36), which can be selected by clicking on the name.

Protocols are prepared lists of parameters, which can be used to easily setup an experiment. The different protocols are in different files in the directory *<TopSpin-Home>/prog/tcl/xwish3_scripts/difflib/protocols.* The file name is used as the protocol name. With the current software version, protocols can only be changed by editing the protocol file using a text editor. Likewise, protocols can only be created by copying existing protocols and modifying the content using a text editor.

All protocols must be located in the directory named previously and must begin with the line:

```
#DiffProtocol --Don't change this line--
```

6. ***Decoupling*** will show ***off***, if a second nucleus is not defined in ***TopSpin***. If a nucleus is selected, ***diff*** assumes this nucleus should be decoupled and shows ***on***.

   Diff sets the pulse program parameter l14 = 0 for off, and l14 = 1 for on. During the pulse program compilation decisions will be made on which parts of the pulse program to be selected depending on whether the decoupling is on or off.

7. The check button ***Use LED sequence*** will activate the ***LED*** module used to move the echo away from the last gradient, which will reduce the effect of eddy currents. When this option is selected, the applied ***LED*** delay will be visible and can be adjusted. Currently this option is only available for ***ste***. The LED option uses a separate pulse program.

8. The check button ***User defined pulse program*** allows the user to change the pulse program name, e.g. to make small modifications in a pulse program, but still use the general set-up with ***diff***.

9. The Pulse program name displays the name of the pulse program. If ***User defined pulse program*** is checked, the pulse program name can be edited.

10. The parameter ***Expected diffusion coefficient*** allows the user to see, for which value of a diffusion coefficient the selected parameter are useful. It also can be changed in order to calculate a suitable gradient strength for the expected diffusion coefficient (see "The "Expected Diffusion Coefficient"" on page 83 for details).

11. ***Effective Gradient Pulse Duration (delta)*** is the effective duration of the gradient pulse δ. Details are given in "Gradient Pulse Shapes" on page 52.

12. ***Diffusion Time (DELTA)*** is the diffusion observation time Δ.

13. ***Use minimum tau***: If this check button is selected, the program calculates the minimum possible tau (τ), the delay between the first two RF pulses (see "Pulse Gradient Stimulated Echo (PGSTE)" on page 55), for the given delays. If not, the parameter τ is accessible for the user and can be set longer than the minimum.

14. ***Repetition time*** means the sum of all delays within one scan, see "Relaxation Parameters" on page 84 for details.

15. The radio buttons ***Diffusion Gradient List Type*** are used to select the way the gradient amplitude is varied between the different rows in the 2D experiment, for details

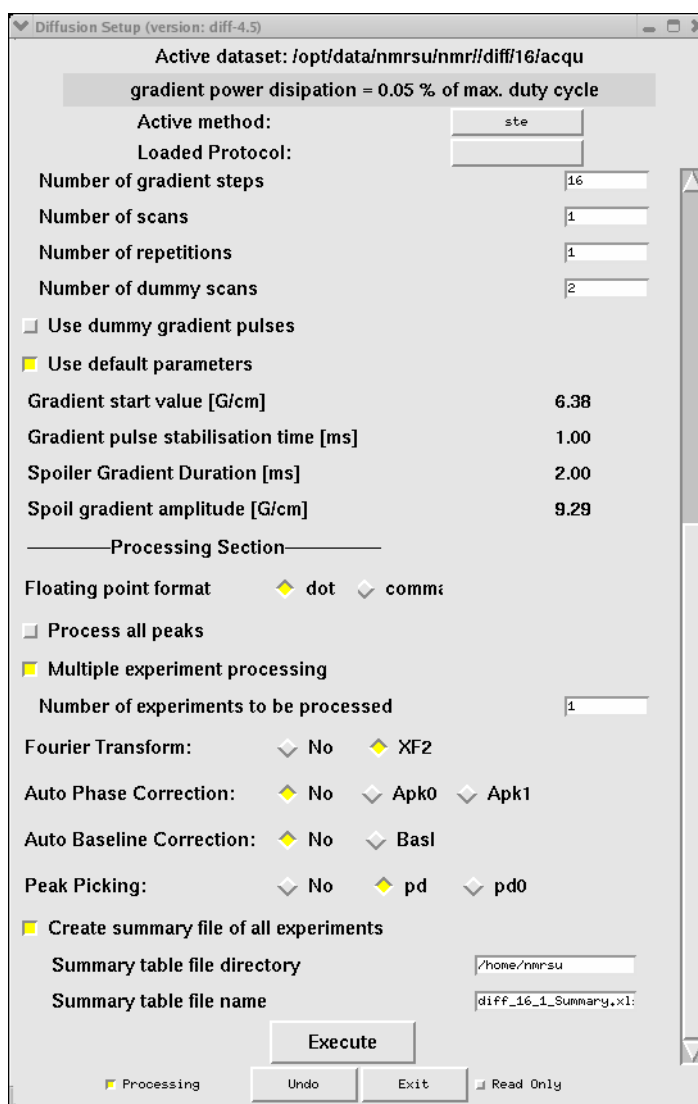see "Variable Gradient Experiments" on page 53.

Figure 6.3   *diff* showing parameters of **ste**, second part

16. The radio buttons **Gradient direction** allow selection of the gradient direction when using a 3 axis gradient system. Using a single axis gradient, these buttons will usually not show up. The direction **mas** means a combination of all 3 gradients then pointing in direction of the magic angle. Which combination is used is defined in the configuration, see "Configuration Parameters" on page 81

17. The **Maximum Gradient Value** is the maximum amplitude of the gradient in the sequence. It is related to the **expected diffusion coefficient** as described in 10.

18. The **Number of gradient steps** is the length of the gradient list, or the number of increments in the 2D experiment, or the value TD1.

19. The **Number of scans** is the same as **NS** in **TopSpin**, in can be from either program, i.e. in **diff** or in **TopSpin**. The NS value should usually be a multiple of the

number of steps in the phase cycle, but most experiments will also work with smaller numbers.

20. In contrast, the **Number of repetitions** repeats the entire experiment summing up the data in the same file. In the pulse program it is represented by the loop counter "l1". This parameter corresponds to the parameter **NAE** "number of averaged experiments" in ParaVision. A **NAE** value larger than one is particularly useful, when many averages are required and the experiment uses a larger variation of gradient strength. This may cause temperature changes caused by different heating of the gradient system during the experiment.

---

i Note: When multiple accumulations are required, it is a good practice to set the **number of scans** to the length of the phase list in the pulse program, and to increase the number of averages by increasing the **number of repetitions**.

---

21. The **Number of dummy scans** is the same as **DS** in **TopSpin**, it can be from either program, i.e. in **diff** or in **TopSpin**.

22. The option **Use Dummy Gradient Pulses** allows pre-gradient pulses to be sent with the same distance as in the measurement part, before the first RF pulse in order to warm up the amplifier. When selecting this option the number of dummy pulses becomes accessible. This option is normally not used and under normal circumstance not required. It is available in all *diff* pulse programs, but only shown in the menu **ste**.

---

i Note: Dummy gradient pulses will increase the duty cycle. Do not use them unless required!

---

23. If the option **Use default parameters** is selected, which is done by default when loading a protocol, a couple of parameters are set to typical values, otherwise they can be adjusted by the user.

- The **Gradient start value**, see "Variable Gradient Experiments" on page 53 for details.

- The **Gradient pulse stabilization time** is set to the default value, see "Configuration Parameters" on page 81 for details

- The option **Use Spoiler gradient** is activated and is not visible in the default mode.

- The **Spoiler gradient duration** is set to the default value, see "Configuration Parameters" on page 81 for details.

- The Spoiler gradient amplitude is calculated as described in "Spoiler Gradients" on page 56

The processing parameters shown were described in detail in "Processing using diff" on page 70.

6.3   Configuration Parameters

There are a couple of parameters, which can be configured. They are set to typical values used, so in most cases there is no interaction required. As there is no configuration user interface, configuration parameters can only be modified by means of a text editor. The configuration parameters are located in the main program file, <TopSpinHome>/prog/tcl/xwish3_scripts/*diff*. The corresponding section is shown below. The sequence of parameters was developed historically, only a few of them can be modified by the user. Before changing any parameter a backup copy of *diff*, e.g. *diff*.orig should be made. This copy can also run directly by typing ***diff.orig*** in the ***TopSpin*** command line.

Be aware, that modifying parameters here can lead to ***diff*** program malfunctions, as well as with the experiments setup using ***diff***.

Diff program code showing configurable parameters mixed with others.

```
##-------------- define some constants -----------

set diffVersion "diff-4.5"
variable maxDutyCycle 32400.0
variable maxPulsePower 16200000.0
variable gradstabDefault 1.0
variable spoilDurDefault 2.0
variable constSlopeRampConst 0.0004
variable grampMin 0.1
variable backUp 0
variable Focus 1
variable pid [pid]
##-------------- check and create directory $HOME/.diff ----
##-------------- used to store default values -----------

variable diffHome [Gethome .diff]
variable diffHistory 1
variable diffHistFile [createDiffHome $diffHome $diffHistory]

variable configUnblank 0.01
variable is1D 0
variable minDelay 0.005
variable DigPnts 2
set gradresDefault 0.008
variable gradres [readGradres $gradresDefault]
variable minGradDelay [expr 10.0 * $gradres]
option add *RadiobuttonFont: *-helvetica-bold-r-normal-*-14-*-
iso8859-1
variable labelFont "-*-helvetica-bold-r-normal-*-14-*-iso8859-1"
variable xMasFactor 1
variable yMasFactor -1
variable zMasFactor 1
variable maxGrad 0.99
```

Note: Parameters which must not be changed are not displayed:
```
variable gradstabDefault 1.0
```

Default gradient stabilization delay [ms]:
```
variable spoilDurDefault 2.0
```

Default spoiler duration [ms]:
```
variable grampMin 0.1
```

Default minimum ramp duration, up and down [ms]. Should not be set to less than 0.05:
```
variable configUnblank 0.01
```

Unblank time before the gradient pulse [ms]. Must be set to 0.15 for BAFPA amplifiers:
```
variable xMasFactor 1
variable yMasFactor -1
variable zMasFactor 1
```

Definition of the MAS direction in a micro2.5 gradient system: Normally this should be already set correctly, but in older installations the gradient wiring might be different and therefore changes may be required.

Please note that this will be changed in future versions of the program. Check **diff config** to see, whether the parameters are accessible in the user interface.

6.4 *Diff* command line options

The **diff** program offers a couple of command line options. They are not necessary for the standard work flow, but are useful. Typing **diff help** in the **TopSpin** command line will result in:

```
diff command line options

syntax:diff [options]

options:help config ii -exec readOnly r status s

options:help:Print this text.
config: Switch to configuration mode.
r, readOnly:Switch to read only mode.
ii:Reset experiment type.
-exec cmd1 cmd2 ...cmdn:Switch to noninteractive mode and execute
cmd1 .. cmdn.
cmdi can be any Tcl script, defined within the method.
```

Here is a brief description of the options.

1. The **config** option switches **diff** to configuration mode, which means it can run without a preemphasis file. Currently only **preemp** configuration methods are available. The figures Figure 2.1, Figure 2.2, and Figure 2.3 show **diff** working in configuration mode.

2. The **ii** option makes the data-set forget, that **diff** was working on it. Using the **ii**

option the parameters remain unchanged, except for the parameter *USERA1*, which normally contains the method name now being cleared.

3. In *readOnly* mode *diff* only shows the parameters, but does not allow them to be changed. The *readOnly* mode can also be switched on by checking the **Read Only** check button on the bottom right side of the *diff* window, but this will delete any changes made. The readOnly mode was introduced to be able to safely look at data-sets, when it is unclear, whether they have been setup by *diff*, or by an older version. The readOnly mode will remain until the **Read Only** check button is unselected.

4. In *status* mode *diff* will start reading the status parameters, whereas it will automatically switch to the *readOnly* mode, i. e. without changing anything. Once the *readOnly* check button is released, the parameters are saved in the background. This option was introduced to help prevent parameters of previously acquired data sets from being accidentally deleted.

5. The *-exec* option allows the method specific procedures to be executed in the background. This is used e.g. in the *diffmultizg* au program.

6.5   Background information

6.5.1   The "Expected Diffusion Coefficient"

The expected diffusion coefficient D_e is calculated using Equation 6.1, assuming a signal attenuation of one order of magnitude. In other words S/S_0 is set to 0.1 and D_e can be calculated:

Equation 6.1

$$D_e = -\frac{\ln(0.1)}{B}$$

If D_e is modified by the user, the g_{max} value is recalculated using the equation:

Equation 6.2

$$g_{max} = \sqrt{-\frac{\ln(0.1)}{\gamma^2\delta^2\left(\Delta - \frac{\delta}{3}\right)D_e}}$$

6.5.2 Relaxation Parameters

The relevant time for the T_2 relaxation, the echo time T_e is implicitly defined in most of the experiments.

In the spin echo experiment T_e is defined as:

Equation 6.3

$$T_e = 2\Delta$$

In the stimulated echo experiments T_e is defined as:

Equation 6.4

$$T_e = 2\tau$$

Where τ stands for the delay between the first $\pi/2$ pulses. Usually τ is set to the minimum possible value τ_{min}, but it can also be increased in order to act as a T_2 filter.

The value of τ_{min} depends on the type of the experiment, it will usually contain the gradient pulse length t_g and the gradient stabilization time.

For the T_1-Relaxation *diff* uses the parameter repetition time t_r, which is not the relaxation delay, but rather the sum of all delays in one scan. Nevertheless t_r is usually dominated by the acquisition time aq and the relaxation delay d1. In the spin echo experiment it is defined as:

Equation 6.5

$$T_r = 2\Delta + aq + d1$$

In the stimulated echo experiments it defined as:

Equation 6.6

$$T_r = 2\tau + \Delta + aq + d1$$

6.5.3 Conversion of the Cotts 13 interval to the Stejskal/Tanner Equation

The idea to use the standard Stejskal/Tanner calculation for the 13 interval Cotts sequence can be described as follows:

The equation [5] in the Cotts paper[1], neglecting the background gradients, looks like:

Equation 6.7

$$\ln\left(\frac{M}{M_0}\right) = -\gamma^2 D\delta^2 g^2\left(4\Delta + 6\tau - \frac{2}{3}\delta\right)$$

This replaces:

Equation 6.8

$$\Delta^* = \Delta + \frac{3}{2}\tau + \frac{\delta}{2}$$

$$\delta^* = 2\delta$$

where Δ^*, and δ^* stand for the corresponding parameters used by *diff*. This results in the following equation:

Equation 6.9

$$\ln\left(\frac{M}{M_0}\right) = -\gamma^2 D\delta^{*2} g^2\left(\Delta^* - \frac{1}{3}\delta^*\right)$$

Equation 6.9 is an exact representation of the Stejskal-Tanner equation introduced in Equation 4.1.

---

1. R. M. Cotts, M. R. Hoch, T. Sun, and J. T. Markert, JMR **83**, 252-266(1989)

7 Troubleshooting

7.1 Static Line Broadening

7.1.1 No Blanking

If the lines in a spectrum are broadened as soon as the gradient cable is connected and the amplifier reset, it usually means the blanking is not active and the offset is not adjusted.

1. Adjust the amplifier offset, see "Offset Adjustment" on page 17.

2. Check, whether the pulse program unblanks the amplifier. All Bruker pulse programs called *diff*... include gradient blanking commands. If not, check the imaging rack wiring (see "The Imaging Accessory Wiring" on page 120).

7.1.2 Cooling Water

When the lines in a spectrum become broadened after the cooling water was inserted to the empty case, this is to some extend normal, because the environment has been modified. However, this effect can become severe in the following cases:

1. When there are air bubbles in the gradient system. The air bubbles create a field gradient because of the different susceptibility of air and water. In this case remove the air bubbles by taking the probe out of the magnet with the water running. Turn the probe upside down and back a couple times, then the bubbles should be out. Often air bubbles can be heard clicking when putting the gradient system next to one's ear. See also "Water Cooling Set-up" on page 106.

2. When the water is dirty and contains magnetic, or conducting materials. If uncertain, exchange the cooling water.

7.2 Dynamic line broadening

Instabilities in the line shape can result due to a couple of reasons:

• No blanking.

• Air bubbles.

7.2.1 No Blanking

When the blanking is disabled by the pulse program, switch to a standard pulse program, e.g. *zg*, and check whether the pulse program unblanks the amplifier. If not, check the imaging rack wiring (see "The Imaging Accessory Wiring" on page 120).

7.2.2 Air Bubbles

When air bubbles are in the gradient system, they can move there driven by the flowing cooling water. The air bubbles create a field gradient because of the different susceptibility of air and water. If they are moving the line shape can be modulated by these fluctuating gradients. See also "The Imaging Accessory Wiring" on page 120.

7.3 Convection Artefacts

Convection in the sample usually occurs due to temperature gradients. For samples having a very low viscosity, even smallest temperature gradients can lead to convection.

Convection effects usually lead to an artificially increased diffusion coefficient. Sometimes phase changes in the signal function of the gradient strength are visible. In extreme cases the signal can change the sign and oscillations of the signal amplitude, as a function of the gradient strength can be observed.

Other macroscopic motions, like flow or vibrations, can lead to similar effects as convection. These are summarized under the term convection in the following section.

If the diffusion of big molecules in low viscous solvents is investigated, even small convection artefacts as compared to the diffusion of the solvent can lead to a significant error for the small diffusion coefficient of the big molecule.

7.3.1 Diagnosis

When the existence of convection is suspected, the safest test is to measure the diffusion coefficient at different diffusion times. In case of convection the apparent diffusion coefficient will grow as a function of the observed diffusion time. This effect is only observed in case of convection or other macroscopic motions as mentioned above.

Diffusion Results @ 45°C (doped water)

Legend:
- ◆ DELTA = 200 ms
- — D = 8.9e-9
- ▲ DELTA = 100 ms
- — D= 5.6e-9
- ■ DELTA = 20 ms
- — D = 3.4e-9

y-axis: relative signal intensity (1, 0.1, 0.01)

x-axis: $B[s^2/m]$ (0.00E+00, 2.00E+08, 4.00E+08, 6.00E+08, 8.00E+08, 1.00E+09, 1.20E+09)
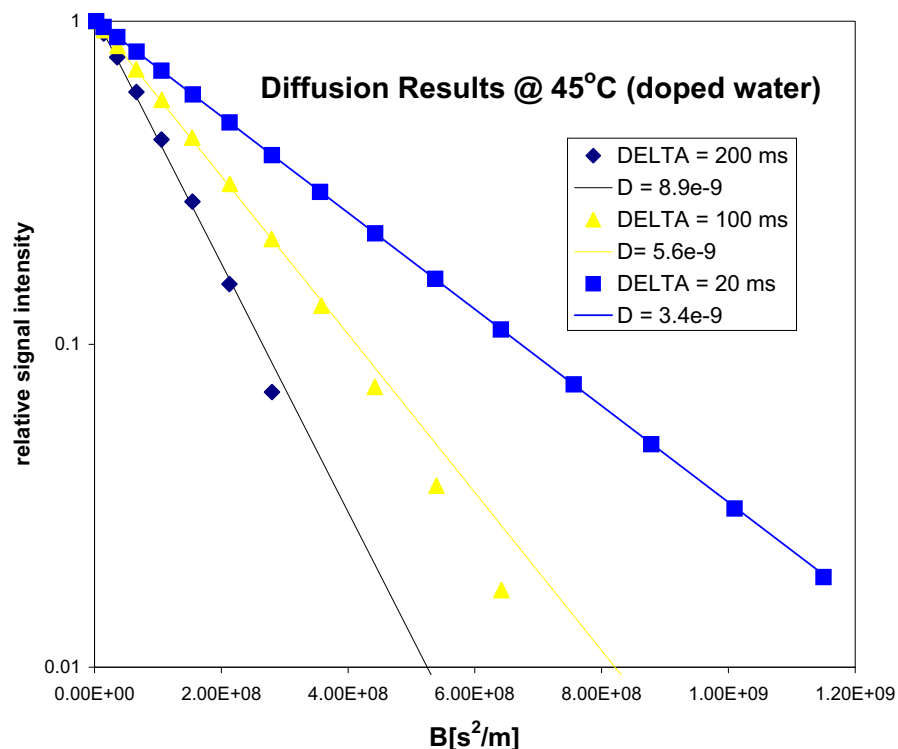
Figure 7.1   Diffusion time dependence of the apparent diffusion coefficient in the presence of strong convection

7.3.2   Avoiding Convection

There are a few general rules on avoiding convection, which of them applies and/or is necessary depends on the individual situation.

1.   The sample should be as short as possible. In order to allow proper shimming usually a compromise value of 40 mm in 5 mm samples is used.

2.   In water cooled probes the water temperature should be set to the desired sample temperature, if possible within the allowed temperature range. The airflow should be switched off if the desired temperature can be reached by means of the water temperature and no decoupling is required.

3.   In extreme cases, double sample tubes should be used. With double sample tubes, the sample is put into the inner tube and a low viscous, fully deuterated (for proton observation) solvent is filled in the outer tube. The convection in the outer tube will equilibrate the temperature in the inner tubes.

7.3.3   Compensating Convection

In order to compensate for convection, flow compensated pulse sequences can be used to some extent. Usually the double stimulated echo *dste* is used to remove the effect of constant flow, which will be the main component in case of moderate convection.
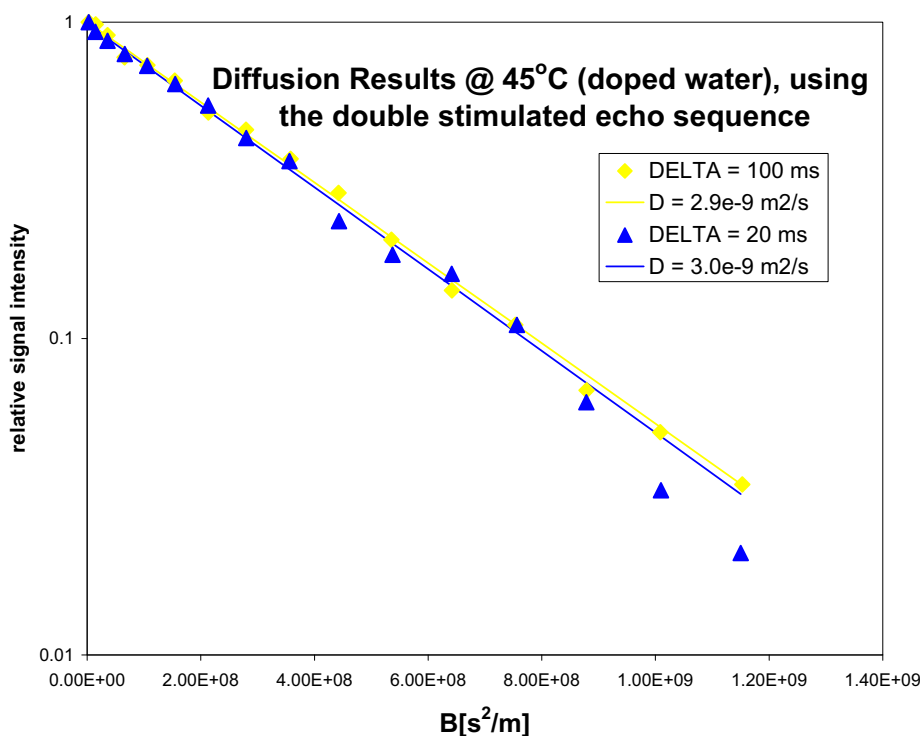
Figure 7.2   Results obtained using dste in the presence of strong convection

---

i   Note: The double stimulated echo causes at least 50% of the signal to be lost. Therefore avoiding convection is always preferable.

7.4   Software

If problems concerning the *diff* program show up, save the file *diffHistory* in the *.diff* sub-directory of the user file running TopSpin, then send it together with the data-set in a tar or zip file, and a description of the problem to:

micdiff@bruker-biospin.de

7.4.1   Error: No gradient parameters found, only configuration mode possible

Often this means, that an incorrect probe was selected in edhead (see "Probe Exchange" on page 33).

If a properly configured probe is not available, follow the description given in "Installing a Diffusion Probe" on page 9.

8 Setpre

The program module **setpre** is used to adjust all gradient related parameters. A short description of how to use setpre is give here.

8.1 Preemphasis, B0, and Cross-Preemphasis Parameters

The parameters for preemphasis adjustment are shown in the following figure, the menu is activated using the **setpre** command.
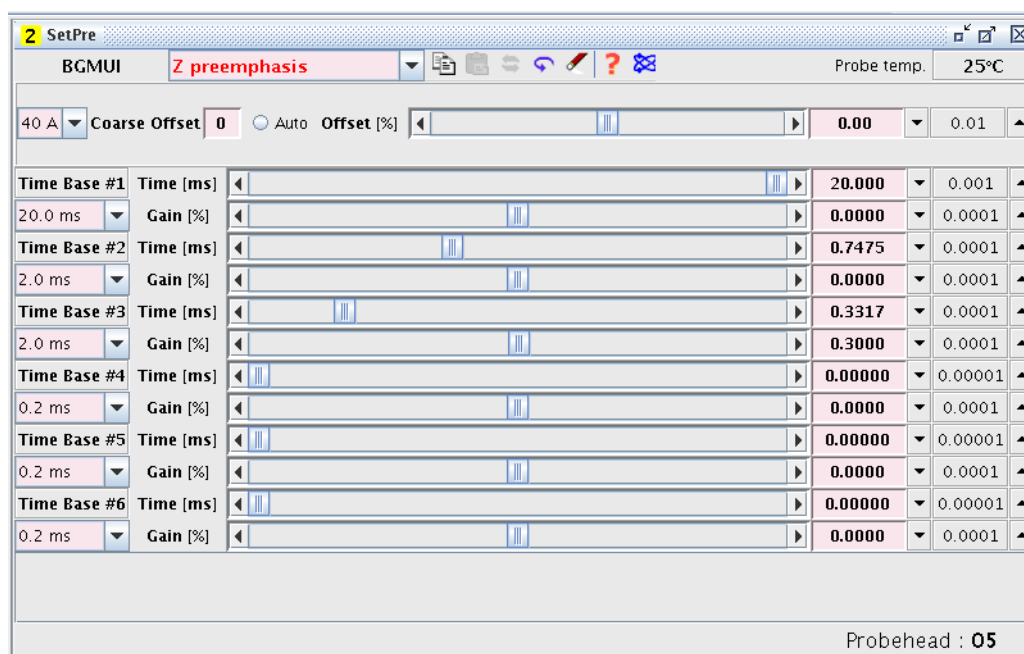
Figure 8.1   Preemphasis Control.

Prior to the real preemphasis parameters being display, a group of other parameters appear in the preemphasis control window:

- The first row in Figure 8.1 shows the type of gradient generation hardware connected, here the **BGMUI**. This is followed by the selected channel for adjustment, then actual gradient coil temperature.

- The second row shows the gain, the coarse offset (AVANCE III only), the auto offset adjustment button, and the offset accessible by slider or number.

- Following the header information is the preemphasis block. Three timeframe's out of a possible four can be specified for the time constants of the exponential functions. The precise values of these time constants and the amplitudes are adjusted using the slider control on the Time and Gain bars. Values can also be typed in

directly after selecting the corresponding field with the mouse. Each value change is loaded directly to the preemphasis unit.

In Avance systems previous to Avance III, the timeframe's for the analog preemphasis system were related to hardware components, therefore it was useful to use a very short timeframe. For the new digital preemphasis (AVANCE III) these switches have no real meaning and are only there for compatibility.

When **setpre** is started it first reads the parameters from the preemphasis unit, e.g. the GREAT Master Unit (BGMU), or from the DPP (AVANCE III), and displays the parameters for the Z-gradient channel. The channel can be changed using the channel pull-down menu (see Figure 8.2).

The channel pull-down menu also gives access to the B_0 compensation parameters, if the corresponding hardware is available. These parameters are referred to as X-B_0, Y-B_0, or Z-B_0 cross preemphasis parameters in the pull-down menu inFigure 8.2

If more than one gradient amplifier is active, cross preemphasis parameters are also available (only AVANCE III).

i Note: Setpre always shows the parameters corresponding to the available gradient hardware generation. Some probes will not react on all possible channels, e.g. a Z-only gradient probe will not react on any non Z-adjustment.
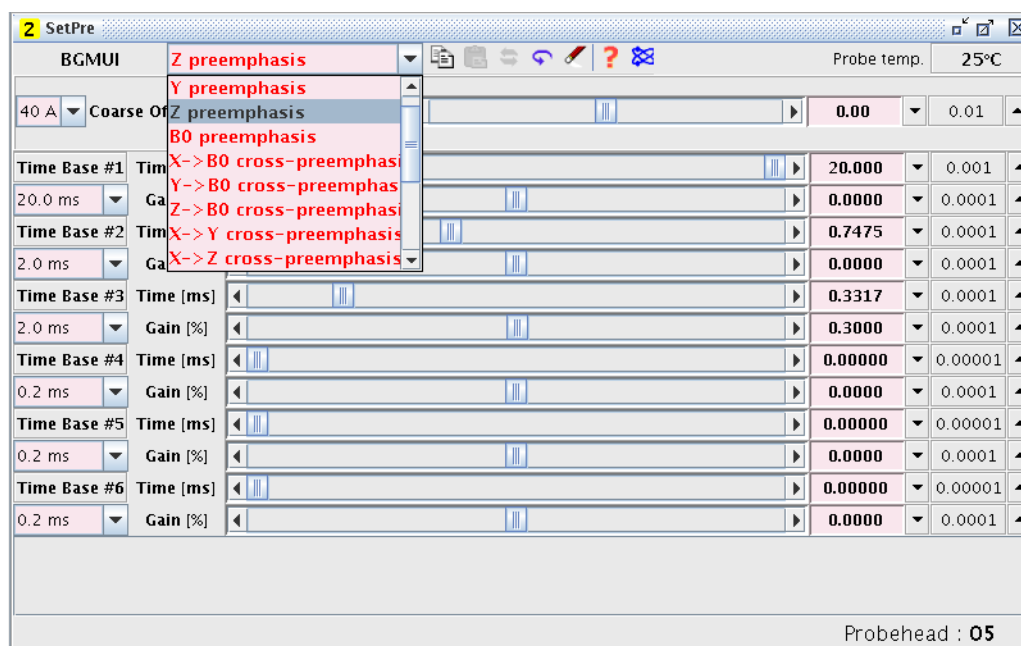
Figure 8.2   Channel Pull-down Menu

8.2   Parameter Storage

All preemphasis parameter are stored in the preemphasis files. There is a special file, the "default file", also named "default", see "Default Preemphasis File" on page 13. Other

files can be created and read in from the same directory. Preemphasis parameters can be read from a file or written to a file by selecting the **File** entry in the **Setpre** pull-down menu (see Figure 8.3).

Each time preemphasis files are read or written, the file *<TopSpinHome>/conf/instr/ gradient_calib* is updated in order to provide the proper gradient calibration for the older imaging au programs and the DOSY *au* programs.
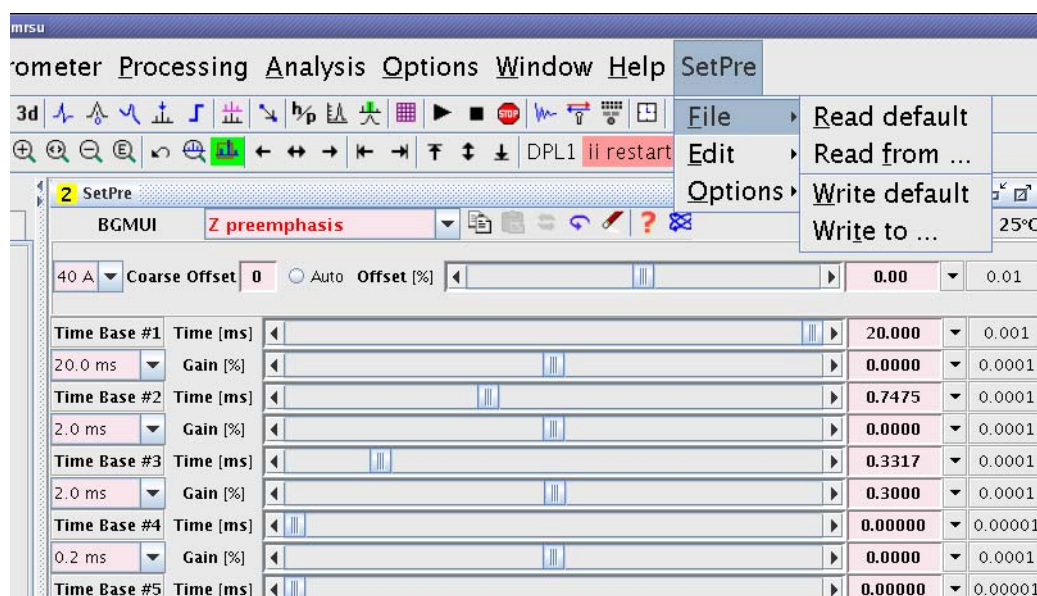
Figure 8.3   Reading and Writing Preemphasis Files

8.3   Gradient Parameters

The gradient calibration and the relative gradient scaling can be edited using the option **Gradient parameters** in the **Setpre-->Edit** pull-down menu (see Figure 8.4 and Figure 8.5).

After changing any parameter press **Apply** and afterwards use **Setpre--> File--> Write default** to save the parameters to disk and to update the gradient_calib file.
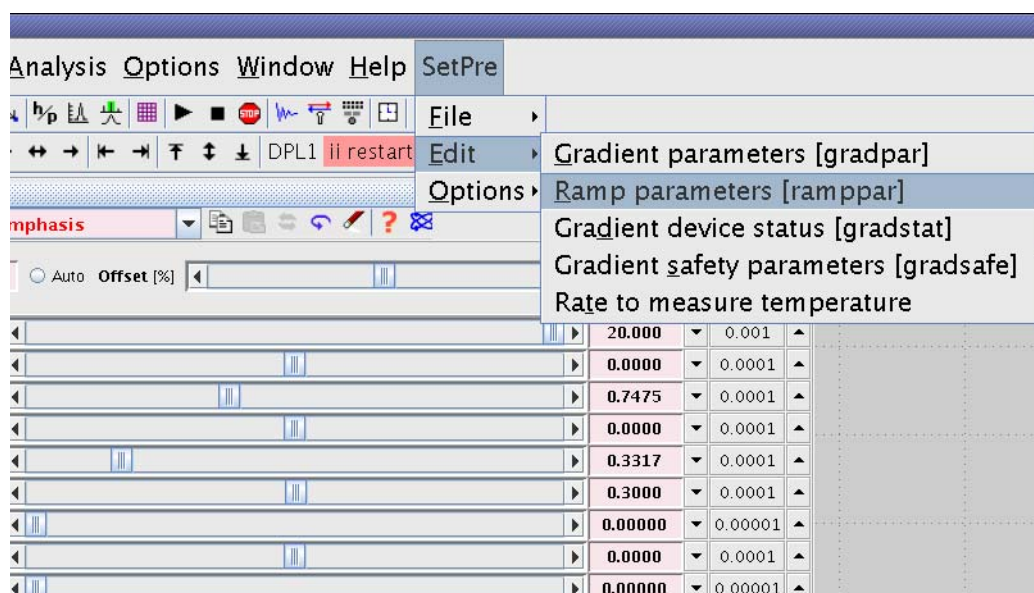
Figure 8.4   Other Parameters
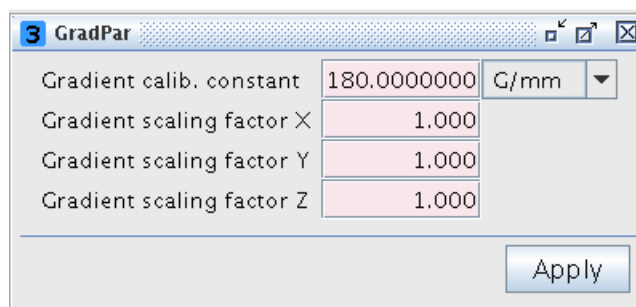
Figure 8.5   Gradient Parameters

8.4   Ramp Parameters

The ramp parameters must be set to *Ramp off* in all TopSpin 2.x versions, in older versions these parameters are not available. The ramp parameters are found under *Setpre--> Edit--> Ramp parameters* (see Figure 8.4).

After changing any parameter press *Apply* and afterwards use *Setpre--> File--> Write default* to save the parameters to disk.
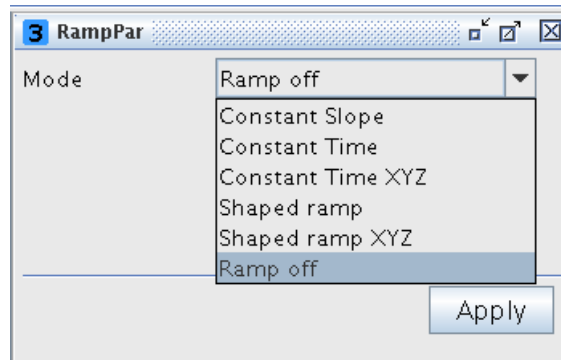
Figure 8.6   Ramp Parameters

8.5   Gradient device status (AVANCE III only)

The gradient device status can be displayed by selecting **Setpre--> Edit--> Gradient device status** (see Figure 8.4).

Figure 8.7   Gradient Device Status

8.6   Gradient Safety Parameters (AVANCE III only)

The safety parameters are found under **Setpre--> Edit--> Gradient safety parameters** (see Figure 8.4). The gradient safety parameters should normally be provided within the default preemphasis files, no interactions should be necessary. A list of standard safety parameters is given in *Micro-imaging Manual for AVANCE III Systems*, the values might change in future due to technical development.

If the safety parameters are not set, the master unit will not switch on and a C01 status

error will result.

Figure 8.8   Gradient Safety Parameters

After changing any parameter press **Apply** and afterwards use **Setpre--> File--> Write default** to save the parameters to disk.

8.7   Rate to Measure Temperature

The rate to measure temperature parameter is found under **Setpre--> Edit--> Rate to measure temperature** (see Figure 8.4). This parameter defines the rate the gradient temperature for the display in **setpre** is measured.

Figure 8.9   Rate to Measure Temperature

After changing any parameter press **Apply** and afterwards use **Setpre--> File--> Write default** to save the parameters to disk.

8.8 Setpre Options

The options submenu is found under **Setpre-->Options** as shown in the following figure. The options available will be discussed in the following section.
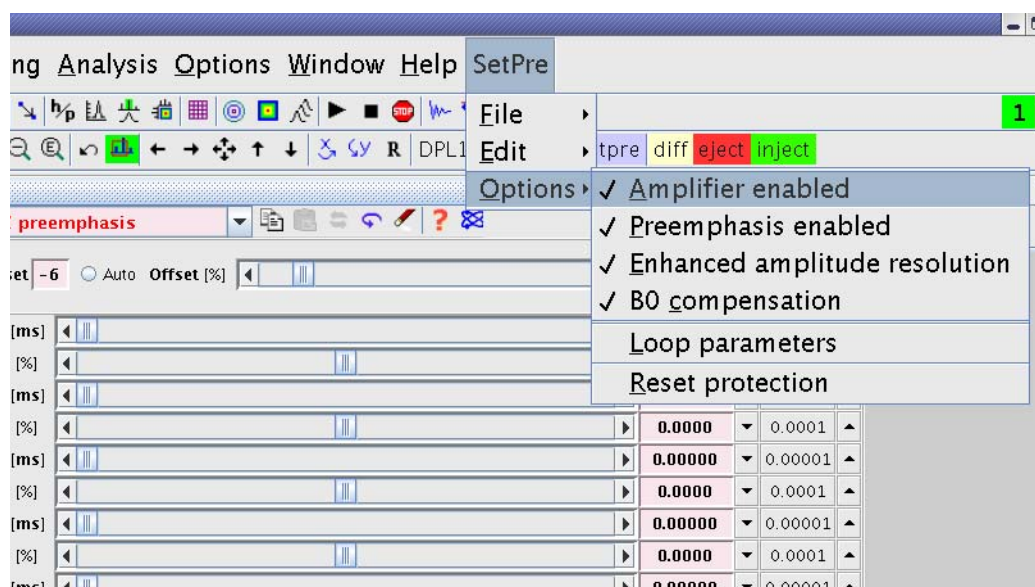
Figure 8.10   Setpre Options

Amplifier enabled

Allows the amplifiers to be disabled/enabled (default on).

Preemphasis enabled

If this option is checked the preemphasis corrections will be applied (default on).

Enhanced amplitude resolution (AVANCE III only)

Allows switching between enhanced (19 bit) and standard (16 bit) amplitude resolution. This option was added for testing, normally enhanced should be used (default on).

B0 compensation

This option appears if a B0 compensation unit is present. It allows the unit to be switched on or off. This switch also switches the relay for the field current from the BSMS.

Loop parameters

Clicking on this button will enhance the setpre menu by the loop parameters, which are used to match the output impedance of the amplifier to the gradient coil (see Figure 8.11). This option will first ask for the **NMR Administrator** password, it should be only necessary at installation.

Reset protection

Does the same as the red reset button on the front panel of the master unit.
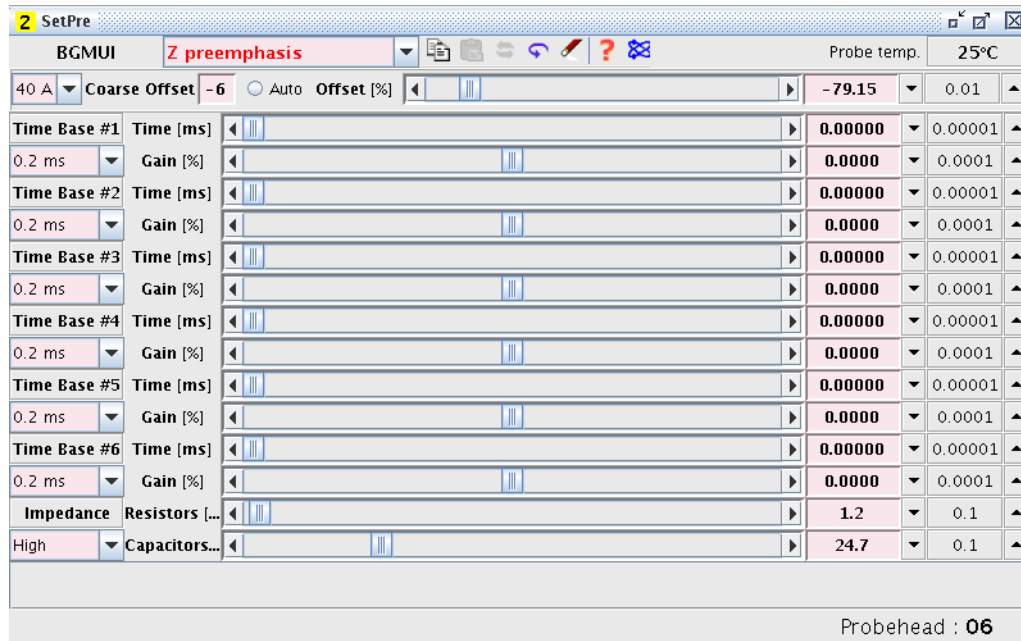
Setpre

Figure 8.11   Setpre Window Showing Loop Parameters

9 Probes and Gradients

9.1 Diff30, Diff60, Micro5

Figure 9.1   Diff30 (left), diff60(right) probe

The diff30, the diff60, and the micro5 probe consist of a probe body with exchangeable RF coils of different diameters and type. The bodies and most of the RF inserts are identical for all the 3 probes. They only differences in the gradient system. These probes have 2 RF channels, which can be used in different ways depending on the RF insert mounted on the probe. The X-channel normally has a low pass filter to reduce cross talk between the channels.

9.1.1 Rf Inserts

There are two different types of RF inserts:

• Single-tuned

• Double-tuned

9.1.1.1 Single-tuned Inserts

Saddle coil inserts with a diameter of 5 mm, 8 mm, and 10 mm are available. They can hold a ^{1}H or a ^{19}F coil on the ^{1}H-channel. Coils tunable from ^{1}H to ^{19}F can be built upon request. Usually the load range will be reduced in the tunable case.

Alternatively fixed frequency X nucleus saddle coils with a diameter of 5 mm, 8 mm, and 10 mm are available for the X-channel. The range of possible nuclei is ^{31}P down to 40 MHz. Below 40 MHz modifications on the probe body might be necessary.

Additionally EVT (extended variable temperature) 5 mm inserts are available. The handling of the EVT inserts is described separately in the section "Mechanical EVT Insert Handling" on page 104.

Single tuned solenoids coils can also be built on request.

9.1.1.2 Double-tuned Inserts

Double tuned inserts with 2 crossed saddle coils can be built as direct inserts, i.e. X on the inner coil and ^{1}H or ^{19}F on the outer coil, or as inverse inserts, i.e. ^{1}H on the inner coil X on the outer. The X range is the same as described above.

^{1}H - ^{19}F double tuned coils are also possible, but need a modification of the probe body.

9.1.2 Diff30L, diff60L

Direct or inverse double-tuned probes with an additional lock channel are also available. These probes have fixed frequencies, no exchangeable inserts. The frequency ranges are the same as above.

9.1.3 Gradient systems

The gradient system specifications are shown in the following table:

Gradient system	diff30	diff60	micro5
Part number	M81113	M81163	M81111
Gradients	z	z	x, y, z
Gradient sensitivity [mT/Am] ([G/Acm])	300 (30)	600 (60)	50 (5)
ID/OD	19/40 mm	19/72	19/40
Usable volume diameter / length [mm / mm] (nonlinearity < 3% peak-peak)	10 / 15	10 / 15	10 / 18
Inductance [μH]	250	1000	10 - 20
Resistance [mΩ]	1000	1500	120
Rise time [µs] from 10% to 90% of 40 A @ 120 V	< 200	< 800	< 50
Usable ring-down time [µs] @ current [A]	500 @ 60	1200 @ 50	100 @ 60
Maximum current tested [A]	60	50	60
Expected gradient calibration constant [G/mm] @ Gain [A][a]	120 @ 40 180 @ 60	240 @ 40 300@50[b]	20 @ 40 30 @ 60
Maximum average power ($R*I^2$) [W]	40	40	35
Loop parameter R[c]	12.5	1.0	50.2
Loop parameter C[d]	30.0	30.0	5.0

Table 9.1: Gradient Specifications
a. The gain of the GREAT amplifiers is defined by the current at maximum input.
b. Maximum possible current using GREAT1/60 amplifiers.
c. The loop parameters are start values and must be checked, particularly for the diff60
d. The loop parameters are start values and must be checked, particularly for the diff60

9.1.4 Handling of the Diff30, Diff60, Micro5 Probes:

Take extreme care when changing inserts, they are fragile.

9.1.4.1 Removal of the gradient coils from the probe body

1. Remove the cooling water using forced air, before disconnecting the gradient coil system from the probe body.

2. Unscrew the coupling nut (counter clockwise looking from the bottom of the probe), see also "Mounting of the gradient system" on page 104. Hold the probe at the gradient system while unscrewing.

3. Carefully detach the gradient from the probe body by using a screwdriver as shown in "Gradient Coil Removal" on page 102.

4. Remove the gradient system completely without tilting it, otherwise the glass on the RF insert will break!

Figure 9.2   Gradient Coil Removal

9.1.4.2   Exchanging saddle coil RF inserts

After the removal of the gradient system, the RF insert can be just pulled off. Another insert can just be plugged onto the socket on the probe.

Check the orientation, the insert fits in only one position. No force is required.

9.1.4.3   Mounting solenoid coils

Solenoid coils must be fixed by a screw. This is accomplished by removing the ground pin and using this thread for fixing, see "Mounting of a solenoid coil" on page 103.
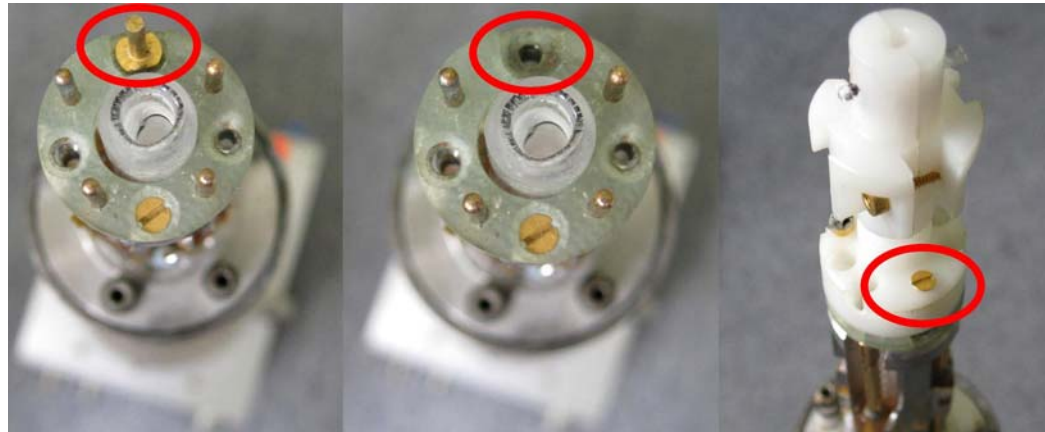
Figure 9.3   Mounting of a solenoid coil

9.1.4.4   Mounting the gradient coils

1.   Make sure no water drops from the gradient cooling interfere into the electronics of the probe body. Remove any water drops with a tissue or a fan.

2.   Push the gradient coil system carefully over the RF inserts, see "Mounting of the gradient system" on page 104.

⚠ CAUTION

Equipment or personal damage from glass breakage

Tilting the gradient system while pushing it over the RF insert may lead to glass breakage and bending of the connectors.

▶   Do not tilt the gradient system while pushing it over the RF insert.

---

3.   Screw the coupling nut on (clockwise looking from the bottom of the probe). The gradient system fixes the glass type RF inserts on the probe body, see "Mounting of the gradient system" on page 104.

Do not use too much force to fix the ring.
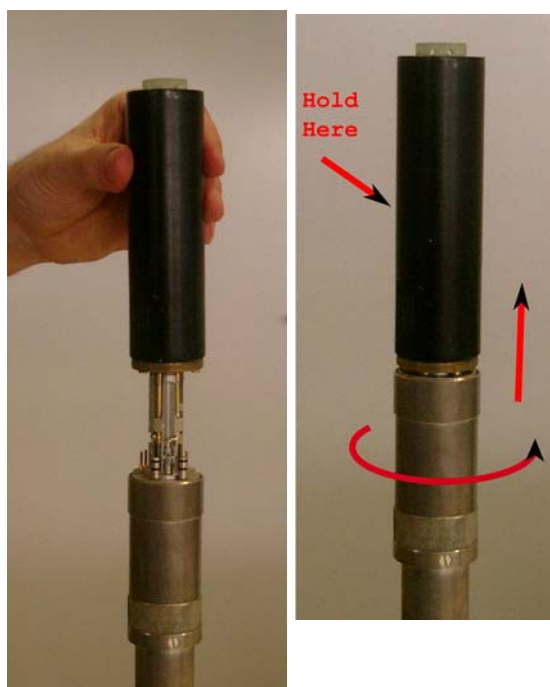
Figure 9.4   Mounting of the gradient system

9.1.5   Mechanical EVT Insert Handling

The mechanical installation of the EVT inserts is in principle very simple, just a few points must be carefully checked in order to ensure the correct sealing of the gas channel. This is both important for the correct variable temperature operation and for the protection of the gradient system, especially in the case of high temperatures.

Figure 9.5   Bottom view showing silicon rubber sealing

1.   First check whether a sealing ring is present at the bottom of the insert (see Figure 9.5). This can be either a silicon rubber or a Teflon ring.

2. Place the insert on top of the probe body, only one position is possible, for details check "Handling of the Diff30, Diff60, Micro5 Probes:" on page 101.

3. Without applying any additional force, ensure that there is a gap of about 1 mm between the insert bottom and the probe body (see Figure 9.6). If the gap is too small a thicker silicon rubber ring must be installed. Use 2 rings if necessary, but if at least one of them must be silicon rubber.

4. Set the gradient onto the gradient system. After fixing it, there must be no gap at the top between the upper end of the insert and the greenish epoxy ring on top of the gradient system - no copper must be visible (see Figure 9.7).

5. If a gap shows up at this point, this can usually be corrected by means of increasing the gap at the bottom.

   The gap at the bottom should not exceed 2 mm, this would cause too large of a thermal bridge. If bigger gaps seem to be required one must use a Teflon ring on the top of the insert in order to compensate for it.

Figure 9.6   Bottom gap
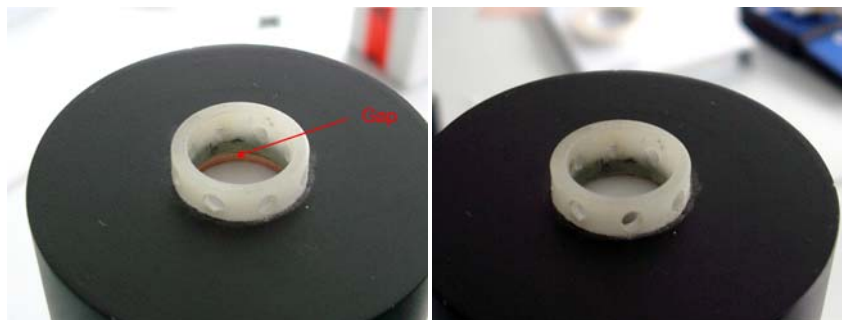
Figure 9.7   Top View with (left) and Without (right) Gap

9.2   Water Cooling Set-up

Never run a diff30, diff60, or micro5 probe without water cooling!

1.   Connect the water cooling to the probe before putting the probe into the magnet.

2.   Start the BCU20 and set the 3 way valve to **flow**.

3.   Wait a couple of minutes, then check, whether the wheel on the front of the BCU20 is spinning. If not, most likely the filter is blocked, (see "Cooling Unit BCU20 (W1210722)" on page 117).

On newer system the gradient generation is automatically interrupted, when the water is not flowing. On older systems the operator has to monitor this.

4.   The next step is to remove air bubbles from the gradient system. This is done by putting the probe upside down and back a few times.

5.   After this the probe can be installed in the magnet as usual.

10 Imaging and Diffusion Hardware

The AVANCE III compatible micro-imaging system is based on 3 Great gradient amplifiers (Great1/40 or Great1/60), a Master Unit (BGMUI-E), and optionally a B0 compensation unit (B0-2). The components are installed in a single bay stainless steel rack, called the imaging rack.

Additionally, all micro-imaging systems are equipped with a DPP board (Digital Preemphasis H12513F1), which modifies the gradient shapes by numerically adding preemphasis terms to compensate for eddy currents. This DPP board is located inside the IPSO 19" rack, connected to the systems internal PCI bus and to the gradient controller.

10.1 Master Unit BGMUI-E (W1522066)

The Master Unit BGMUI-E is a dedicated unit to interface the Great 1/40 or Great 1/60 amplifiers to the AVANCE III system. In addition to the main function of distributing the digital signals to the Great amplifiers, the Master Unit contains a PT100 temperature and an external enable security feature. A DSP based feedback structure is implemented which allows calculation of the applied power rate and comparison with maximum values for coil protection.

Figure 10.1   Master Unit BGMUI-E Front Panel

The Master Unit must be the last device which is switched on in the imaging rack since it detects the connected amplifiers only during the boot process. During the boot process, the Master Unit will stop with a 'C01' message in the 7 segment LED display, whereas in normal operation mode the LEDs show the coils PT100 temperature (11). The error message 'C01' means, that safety parameters for the coil protection need to be loaded. Refer to chapter "Gradient Safety Parameters (AVANCE III only)" on page 95 for details about this procedure.

The LED display is also used for numerous error messages, which are indicated as 'Exx', where xx is an error code that can be found in the Web interface of the unit (accessible by the 'ha' command in TopSpin). If the source for the error message is eliminated, the unit can be reset to normal operation mode by pressing the red reset button (1).

10.1.1 Master Unit In/Out Data Connection

The Master Unit can be connected either to a DPP (Digital Preemphasis board) or directly to the GCtrl (gradient controller) of the IPSO board via LVDS (48 bit wide and 80 MHz bus clock) (5). The maximum allowed cable length for this connection is 5 m. The internal logic distributes the incoming digital signals to the desired gradient/B0 output connectors (10), where the Great amplifiers or B0-2 compensation unit can be directly connected. The communication between the Master Unit and the mentioned amplifiers is via an unidirectional parallel bus for the gradient shape data, and a bidirectional I2C bus for the communication between the units.

The Master Unit can be controlled via the Web interface. Thus the unit is connected directly to the systems ethernet switch (3) to allow any browser to access the service pages, e.g. for firmware updates.

10.1.2 Security Features

The Master Unit includes 3 security features:

- A PT100 temperature check.

- A check of the external enable signal e.g. from the gradient cooling water chiller.

- A DSP based power calculation.

A PT100 can be connected directly to the PT100 connector (6). If the PT100 shows a resistance which indicates a temperature below 5°C (101.95) or above 50°C (119.4), the Master Unit will switch the Great60 amplifiers off. Valid temperatures for the Great operation are between 5°C and 50°C. The PT100 is measured in 4-wire mode, to eliminate cable resistances. This guarantees an accuracy of +/- 1°C from the actual value.
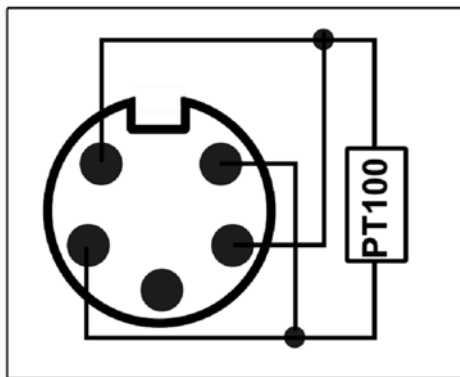
Figure 10.2   Pin Layout of the Pt100 Connector

The external enable connector (7) is used to check the current state of the BCU20 cooling unit. In case the BCU20 is switched off, or no water is flowing, the BCU20 opens a short between 2 pins. This is detected at the Master Unit by the external enable connector. If the short is missing, the Master Unit switches the Great amplifiers off.
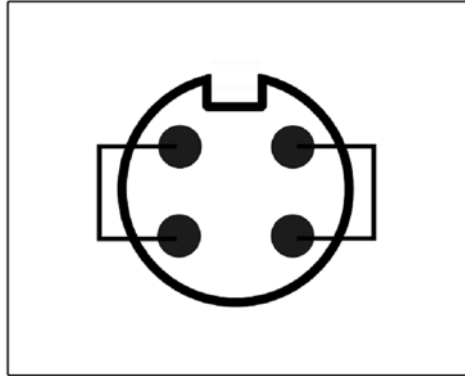
Figure 10.3   Pin Layout of the 'External Enable' connector

The DSP security feature uses the 6 analogue monitor output signals of the Great amplifiers to calculate the power dissipation in the gradient coil on the fly. From each amplifier the current signal and the voltage signal is fed back to the 'U mon' (8) and 'I mon' (9) input connectors of the Master Unit. A 10V U-monitor voltage corresponds to the maximum voltage (100V for the Great1/40 and Great1/60), a 10V I-monitor voltage to the maximum current (40A for Great1/40, 60A for Great1/60). The analogue signal is AD-converted within a 25usec dwell time, and the power applied to each individual gradient coil is calculated by the formula:

Equation 10.1:

$$\frac{1}{T} \int_T R_{ch} \cdot i_{ch}^2(t)dt < P_{\lim_{ch}}$$

R_{ch} is the DC-resistance (stored in the safety parameters in setpre) of the gradient coil, i_{ch} is the current detected by the 'I-mon' input and T is the time in which the energy is integrated. P_{lim-ch} is the maximum power value, which is specific for each channel of each gradient system. On triple axis gradient coils, the power sum of all 3 channels must be less than 3 times the maximum power for one channel.

Equation 10.2:

$$\frac{1}{T} \sum_{ch=x,y,z} \int_T R_{ch} \cdot i_{ch}^2(t)dt < P_{tot}$$

The Master Unit checks the power on 2 different time bases. One time base is fixed to 1sec, which checks for the average power applied to the gradient coil. Another time base is configurable between 25usec and 1sec and is mandatory to detect short (msec range) gradient pulses with high currents, which might burn the coil in <<1sec. See chapter "Gradient Specifications" on page 101 for typical values for different coils.

10.1.3 Blanking Pulses

The Master Unit BGMUI-E delivers 3 blanking output signals (4), which can be directly connected to the gating input of the Great1/40 and Great1/60 amplifiers. The blanking pulses are TTL level, TTL-low (0V) forces the amplifiers to switch on (unblank) its output, TTL-high (5V) disables (blank) the amplifiers output.

The blanking output of the BGMUI-E is 'soft-blanking'. In contrast to the 'hard-blanking' which was used in previous imaging systems, the 'soft-blanking' takes care of residual amplifier output currents. The blanking is switched off by a command in the pulse program (see "Gradient Amplifier Blanking Modes" on page 121), and stays off until a second command is executed in the pulse program and until the digital input signal to the individual Great amplifier is 0. As a result, the blanking takes care of preemphasis adjustments and keeps the Great output enabled, until the added preemphasis terms are fully decayed. The previously used 'hard-blanking' switched off the Great output immediately when the particular command was executed in the pulse program without taking care of any residual currents.

10.1.4 Control LEDs

The Master Unit has 3 LED groups (12, 13, 14), which show the status of the connected amplifiers. If an „Error"LED is illuminated, the connected amplifier is switched off because of an error or because it is not initialized. If the amplifiers are fully operable, the „Enable"LED is switched on. If an amplifier delivers a current, the „Pulse"-LED shows this by flickering. The pulse LED is only switched on for currents >3% of the maximum amplifier current, for lower currents the LED stays off. A 2nd mode can be selected in the Master Units Web interface which displays digital input data at the Master Unit LVDS input instead of the amplifier output current. If a B0-2 compensation unit is connected to the Master Unit and the „Field" value of the BSMS-2 is not 0, the B0 „Enable" LED is always on, since the B0-2 unit has to deliver a DC current.

10.2 Great 1/40 (W1211690 or W1215322) and Great 1/60 (W1209612 or W1215323)

The Great1/40 and Great1/60 are current regulated amplifiers that provide the gradient current to the gradient coils at dedicated times. Both amplifiers are basically identical; the only difference is the maximum output current, which is 40A for a Great1/40 and 60A for a Great1/60. The signal input of the amplifiers is digital. The digital to analogue converter is located inside the amplifiers to avoid ground loops from non ideal analogue cable wiring.

Figure 10.4   Great Amplifier Front View

10.2.1   Gate Input; Blanking

The Gate input (1) of the Great amplifiers enables an external signal to enable or disable the output of the Great amplifier. In case the output is disabled, the amplifier output is disconnected from the gradient coil, so that no amplifier noise is introduced to the sample spin system. The gate pulse must be TTL level, where TTL-LOW enables the amplifier output and TTL-HIGH disables the output. If nothing is connected to this input, the amplifier is always enabled.

The gating pulse is delivered by default from the BGMUI-E Master Unit (output 4 of the Master Unit) or alternatively from the IPSO T0 connector (see "T0 Trigger Signals" on page 125).

10.2.2   Data Input

The Data input (3) is directly connected to the Master Unit. The gradient data are delivered parallel, whereas the bidirectional communication between the Master Unit and Great amplifier is handled by an I2C bus. Both communication protocols can be found on the Data Input connector and are distributed via a single cable (HZ10202).

10.2.3   Signal Output

The gradient coil current is provided at the red and black clamps (2). Typically, the gradient filter cable with ring cable lugs is connected to the output clamps, which lead to the gradient filter (see chapter 1.4). The output can have a maximum of 100V/ 40A at the Great1/40, or 100V/ 60A at the Great1/60.

Be sure to switch off (7) the amplifier before manipulating the output clamps or the connected cables

10.2.4   Monitor Output

Both Great amplifiers have a monitor output for the output current, labelled „Monitor I" (5) and a monitor output for the output voltage, labelled „Monitor U". Both can be used to

control the output current on an oscilloscope, e.g. to adapt the amplifiers regulator to the connected load.

The scaling for the outputs is 1V/10V for the voltage monitor of both Great amplifiers and 1V/4A at the current monitor output of the Great1/40, and 1V/6A at the current monitor output of the Great1/60. The maximum monitor voltage is 10V on each monitor output. If an externally connected device, such as an oscilloscope or a voltage meter is not ground free, it can lead to ground loops which heavily disturb the output stability of the amplifier and thus the NMR signal.

During routine work, these monitor outputs have to be connected to the 'U mon' and 'I mon' inputs of the BGMUI-E Master Unit (see chapter 1.1.2). The Master Unit can only calculate the power dissipation to the gradient coils and protect them from over power when this connection is established.

10.2.5   LED Bar

The LED bar on the bottom right of Figure 10.4 (6) is an easy way to control the output current during an experiment. The bar shows the output current of the amplifier in 10% steps, so currents below 10% cannot be seen, but for typical experiments the resolution is sufficient.

10.2.6   Fuses

The Great amplifier itself has 2 different fuses, the line fuse and the power supply fuse.

The **line fuse** is located directly in the housing of the mains adapter. If this fuse is blown, nothing on the amplifier will work anymore, even the illumination of the mains switch. After removal of the mains connector, a little insert can be pulled out of the mains plug (#1 in Figure 10.5) with the help of a small screwdriver. The fuses are 20 mm x 5 mm in size and have values of 6.3 A (Great 1/40) or 10A (Great 1/60).

If the mains switch illumination is still working but nothing else on the amplifier, the **power supply output fuses** might be blown. These fuses are located below or to the right of the mains connector (depends on the hardware revision, see #2 in Figure 10.5). There are 2 separate fuse housings that can be opened manually or by the help of a screwdriver, which contain fuses 32 mm x 6 mm in size with a value of 20A.

Figure 10.5   Back side view of the Great Amplifier showing the location of the fuses

10.3   B0-2 Compensation Unit (W1214106)

The B0-2 compensation unit is the 4th amplifier, which can be connected to the Master Unit. A B0-2 compensation unit is required to compensate for 0th order field distortions caused by gradient switching of non ideally shielded gradient systems. In this case, a current is introduced in the surrounding conductive material, which leads to a shift in the B0 field and thus in the behavior of the samples spin system. To eliminate these effects, a current which causes an opposite field shift is introduced to the field coil of the shim system. This coil is typically used to control the field stability (Lock), to shift the field by a static value, or by the automatic drift compensation.

Figure 10.6   Front Plate of the B0-2 Compensation Unit

10.3.1   Digital Data Input

The digital data is handled via the connector „To Master Unit B0-2 Comp" (4). The communication between the B0-2 unit and the Master Unit BGMUI-E is via an unidirectional parallel bus for the B0 compensation current data and a bidirectional I2C bus for the communication between these units. The digital input data for the B0 current is already fully calculated including all direct and cross terms by the DPP. This means, as opposed to the Great gradient amplifiers, that the B0-2 unit will not work without a DPP in the ISPO (if the Master Unit is directly connected to the GCtrl).

10.3.2   Analogue Signal Input/Output

The analogue B0 current is provided by the „H0 Output" (4) connector. Through this connector the B0-2 unit is directly connected to the „Field"coil of the BOSS shim system. The BOSS shim system is used by the BSMS to stabilize the magnetic field (Lock), to shift the field by a static value and for the automatic drift compensation. Since the BSMS-2 functionality must still be operable, the output signal from the BSMS-2 (ELCB board) is feed into the B0-2 compensation unit through connector (4) as well and added to the B0 compensation terms. The output signal of the B0-2 unit is then the B0 compensation and BSMS-2 output, which includes all the required signals. Since this is an active summation with analog devices, the B0-2 unit might introduce a bit of noise to the BSMS-2 signals.

When the B0-2 compensation unit is switched off, an internal relay is set in a way that the BSMS-2 signals are passed passively through the unit, without any modification and without any additional noise or hum.

The maximum output voltage of the B0-2 compensation unit is of 100V, and the maximum output current is 200mA.
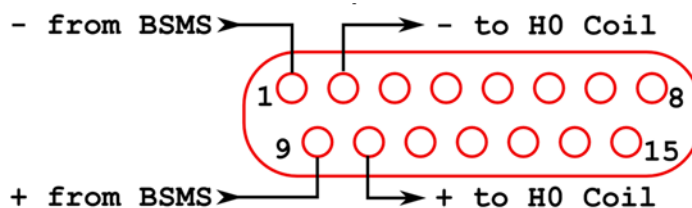
Figure 10.7   Pin Layout of the analogue input/output connector at the B0-2 front plate

10.3.3   Monitor Output

The analog monitor outputs (3) of the B0-2 unit can be used to check the field coil current since it shows the sum of the BSMS-2 output current plus the B0 compensation terms. The ratio is 1V/10V of the voltage monitor and 1V/20mA on the current monitor. During the routine work, these connectors are not connected and it has to be taken care that no grounded devices are connected to them, since they can create ground loops.

10.3.4   Link to the BSMS-2

To connect the B0-2 unit to an existing BSMS-2/BOSS system, an adaptor board with part number Z108181 is required. This board is mounted on the right most SCB20 board in the BSMS-2 between the output of the board and the cable leading to the shim system (see Figure 10.8). It is basically a 1-1 connection of the shim connections, but the connection going to the field coil is cut and wired to the connector on the lower part of the adaptor board.

A cable (HZ12200) is connected from the adaptor board connector to the analogue signal input/output of the B0-2 unit. This connector provides the 'Field' output current to the BSMS-2. This field current reaches the B0-2 unit via the cable, is summed up with the B0 current or shifted through, and then returned via the cable to the BSMS-2 adaptor board, where it is directly connected to the field coil of the BOSS shim system. As a result, if the adaptor board is installed, but no cable to the B0-2 unit, the field coil is not connected to the BSMS-2. In this case no lock, field shift, or field drift compensation is active.

Figure 10.8   BSMS-2 to B0-2 Adaptor Board, mounted on the most right SCB20 Module

10.3.4.1   Gradient Filter (W1212109)

The gradient filter is integrated in the gradient cable, which is connected between the Great outputs and the gradient coil. Its basic function is to eliminate high frequency distortion, which can be introduced to the gradient cable itself. Additionally, the filter has some standard fuses included, to protect the gradient coil from any gradient amplifier failure or programmer errors. The fuses are accessible after removal of a little metal cover, fixed by 4 screws. There are 5 fuses in the filter box, where only fuse 1, 3, and 5 are in the gradient lines and fuses 2, and 4 are spare parts. Each fuse has a value of 15A.

Gradient Filter box

Fuse Box Cover

15 A Fuses used for gradient coil safety
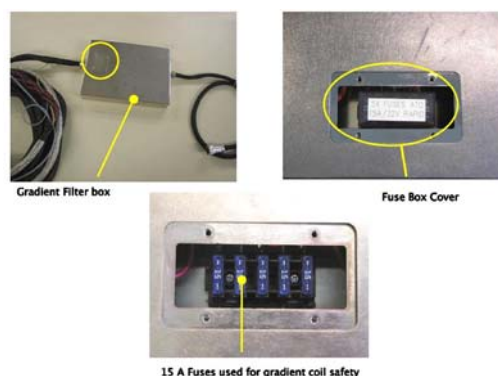
Figure 10.9   Gradient Filter and Fuses

Since the gradient filter is used to remove high frequency noise from the gradient cables, ground conditions are important. The filter must have a good ground connection to the gradient body. This is established on new gradient bodies, but on older bodies the connection might be missing. To check this, the probe body can be controlled. There must be a pin in position G of the Burndy gradient connector, which leads to a ring cable lug connected to the metal of the probe base. If this connection is missing, it has to be established to provide full shielding performance.
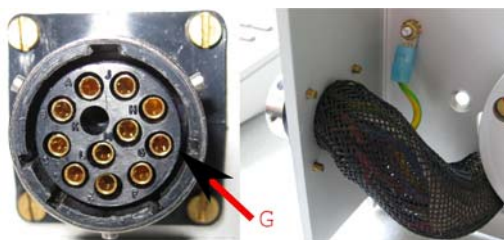
Figure 10.10   Location of Pin G at the probe base connector (left) and grounding of the pin (right image)

For AVANCE III systems, filter cables with part number W1212109 and ECL2 have to be used. If a lower ECL or a different filter cable exists, it needs to be upgraded. By using filter cables with part number W1212109/ECL2, 2-wire and 4-wire gradient probe bodies can be driven by the AVANCE III imaging rack.
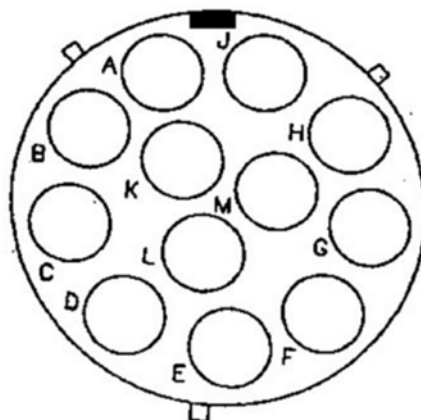
Burndy Connector	Signal
C	+X Gradient
D	-X Gradient
E	+Y Gradient
F	-Y Gradient
A	+Z Gradient
B	-Z Gradient
L	PT100 Current
M	PT100 Current
H	PT100 Sense
J	PT100 Sense
G	Ground

Figure 10.11   Pin Layout of the 12 Pin Burndy Connector (front view of the plug at the probe base)

10.4   Cooling Unit BCU20 (W1210722)

The standard cooling unit for the water cooled micro-imaging and diffusion gradient systems is called BCU20. The BCU20 is a closed loop chiller unit, with a water volume of about 3.5 liters which can actively heat and cool the water with a power of approx. 250 W. Thus the water temperature can be set to values between 5 and 50 °C at standard flow rates of up to 1litre/min. at 0.35 bar.

In addition to this basic functionality, the BCU20 provides more features such as:

*   A 3-way valve to blow out the water of the gradient before removal,

*   manual and software controlled temperature control,

*   a flow control,

*   a water filter and noise optimized air-bubble free operation.

The figure below shows the schematic of the cooler.
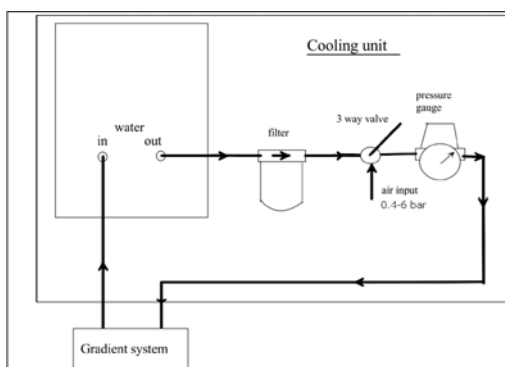
Figure 10.12   BCU20 Schematic Diagram

10.4.1   Installation of the BCU20

During the installation of the BCU20, the flow needs to be adjusted to its maximum. This must be done by opening the top cover of the BCU20 and screwing down the flow needle as far as possible (#1 in Figure 10.14). At the same time, distilled water can be filled in (#3 in Figure 10.14) until the level reaches the maximum mark. A water conditioner should be used to prevent the growth of algae. The recommended concentration is 0.5 ml water conditioner (Art. 9025.1 ROTH) for 3.5 liters of water. On the backside of the BCU20,

10.4.1.1 Hose and Cable Connections

Various cables and hoses need to be connected to the backside of the BCU20. The rest of this section will discuss this in detail. The numbers listed in the text, refer to the following figure.
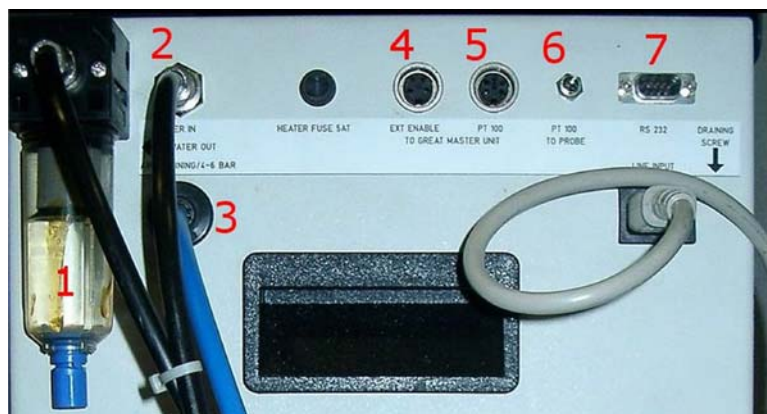
Figure 10.13 Backside View of the BCU20

The **water and air hoses** are connected to the rear of the BCU20, on the left side, as shown in the figure above. The cooling water output is equipped with a filter (1), which prevents small particles from entering the gradient coil. Over time they may block the water flow and thus destroy the gradient coil. For this reason the filter element needs to be checked from time to time and, if its color of the exchangeable filter element is no longer white, it has to be replaced.

The 8 mm water hose leads from this filter to the gradient coil and from there another 8 mm hose returns to the „**Water In**" (2) connector providing a closed loop system.

Below the „Water In" connector is the „**Draining**" connector (3) which is connected to the system's compressed air or nitrogen supply. This enables water to be blown out from the gradient coil before it is disconnected from the chiller unit.

The „**Ext**. **Enable**" connector (4) is connected to the Master Unit. The BCU20 delivers a continuous signal to the Master Unit through this cable, when the BCU20 is fully operational. When the water level becomes too low, the BCU20 stops the water flow and sounds an alarm. Whenever the water flow stops, the BCU20 no longer delivers the enable signal, and the Master Unit switches off the amplifiers to protect the gradient coil from overheating.

The PT100 of the gradient coil is directly connected to the BCU20 via the "**PT100 to Probe**" connector (6). Since its cable is in the gradient filter cable, the connection has to be established by an extension cable from the imaging rack to the BCU20. As a consequence, the BCU20 receives the temperature information from the gradient coil and has to remit it to the Master Unit.

The "**PT100 to Great Master Unit**" (5) is the connection for the PT100 signal to the Master Unit. Since the PT100 thermo-resistor of the gradient probe is not directly connected to the Master Unit, a connection is needed that transfers a signal indicating whether the unit is operating within a temperature range of 5 to 50°C, which is required to enable the Great amplifiers. This signal is provided through the output connector (5).

The BCU20 has a serial connection via the "**RS232**" connector (7) to the IPSO unit. This enables the BCU20 temperature to be set and controlled through software using the TopSpin command 'edtg'. The command 'edtg' behaves identical to the BVT control program 'edte', for which a manual can be found under TopSpin help. The TTY configuration information (default is TTY04) has to be entered during 'cf'.

10.4.2   Operation of the BCU20

During normal operation the BCU20 is only switched on and runs without any user interaction. Prior to this a few settings have to be checked or set. The following section describes these settings, for the location of the parts refer to the following figure:

Figure 10.14   BCU20 Top view with opened Cover

It is critical that the **3-way valve** (2) is set to flow during gradient operation. This position lets the cooling water flow through the gradient coil. In case the gradient coil needs to be disconnected, the water can be blown out of the coil by switching the valve to "Draining". After a few seconds air bubbles in the **water reservoir** (3) can be observed. This is an indication that the gradient and the water hoses are empty. The 3 way valve can be rotated by 90 degrees (pointing downward in Figure 10.14), in this position the output is disabled and the gradient coil can be removed.

The BCU20 can regulate the temperature in 2 different ways:

1. The BCU20 uses its internal PT100 to regulate the temperature of the water in the water reservoir. In this case the switch (4) has to be set to "PT100 BCU20". In this operation mode, the water may heat up or cool down during the flow to the gradient coil, so the gradient coil may indicate a slightly different water temperature. The PT100 of the gradient coil is looped through the BCU20 to the Master Unit in this mode, so the real gradient coil temperature can be read at the Master Units temperature display. This is the default mode for imaging, since it is often helpful to control the gradients temperature in high duty cycle experiments.

2. The BCU20 uses the PT100 of the gradient coil to regulate the temperature of the water. In this case switch (4) has to be set to „PT100 Probe". In this mode, the BCU20s regulator regulates the temperature of the gradient coil, so the water itself can have a different temperature. The coil, however, should have exactly the set temperature. The temperature of the gradient coil is visible in the upper line of the

Eurotherm temperature regulator unit (1, Figure 10.15) on the front of the BCU20. The temperature value which is forwarded to the Master Unit is only a dummy value (due to technical reasons). Thus the Master Unit only shows a temperature values between 5 to 50°C, which is not related to the real gradient coil temperature. This operation mode is the default mode for diffusion applications, since the temperature of the gradient coil (and much more important the temperature of the sample) is a critical parameter for precise measurements.

Figure 10.15   Front View of the BCU20

The above mentioned temperatures can be set manually at the Eurotherm (1) with the up and down arrows, or computer controlled by the 'edtg' program in TopSpin. The set temperature is displayed in the lower line of the Eurotherm. The upper line shows the temperature of the water in the reservoir („PT100-BCU20") or the temperature of the gradient coil („PT100-Probe").

10.5   The Imaging Accessory Wiring

The imaging rack is internally wired, so there should be no need to change any wiring. Externally there are up to 7 cables that need to be connected, they will be discussed in this section.

Figure 10.16   External Imaging Rack Cables

1. Hook the mains plug (1) to a 240V/32A socket.

2. Plug the control cable (2) to the backside of the consoles. This cable switches off the rack when the console is switched off.

3. Connect the LVDS-in cable (3) to the DPP-Out connector of the DPP board.

4. Connect the Ethernet connection (4) to the switch.

5. If available, connect the B0-Out cable to the BSMS-2 adapter board, typically on the right side of the SCB20 board in the BSMS-2.

6. If required (typically not with AVANCE III systems), the external blanking cable (6) can be plugged into the T0 interface of the IPSO board.

7. The gradient filter (7) is connected between the imaging rack and the gradient coil.

For the full wiring of the imaging rack, including the BCU20 refer to the following illustration:
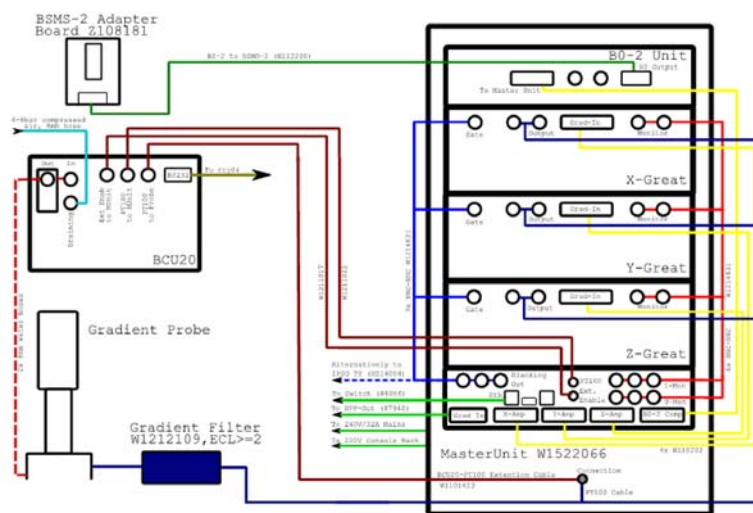
Figure 10.17   Wiring of the Imaging Accessory

10.6 Gradient Amplifier Blanking Modes

The Great amplifiers can operate in 2 different blanking modes, soft and hard blanking. A low level (TTL) at the 'Gate' input of the Great amplifiers enable their outputs; a high level (TTL) disables the outputs. In imaging experiments the amplifiers are often unblanked during the complete experiment (realized in the include file MRI.include) due to 2 reasons:

1. The experiments are quite fast, so there is almost no time to blank the amplifiers.

2. The current to gradient ratio is not as high compared to the diffusion gradient systems.

Blanking is essential for experiments with diffusion gradient systems (Diff30/60), since they have a high current to gradient ratio, so even weak amplifier noise introduces strong effects to the spin system.

The amplifier needs about 10 µsec to enable its output. The blanking command must be executed minimum 15 µsec before the 'grad' command in the pulse program. Shorter times can lead to unforeseeable effects.

10.6.1 'Hard Blanking'

On previous instruments, there was only one blanking mode available which is now called „hard blanking". This blanking mode is controlled by a 'setnmr' command in the pulse program, which enables or disables the amplifier output exactly at that moment, where it is executed, independent from any residual gradient current. This can be well controlled if all preemphasis values are set to zero, but if the preemphasis compensation adds an exponential decaying current to the gradient shape, it can hardly be predicted in the pulse program when the current will be dropped down to zero and blanking can be switched. In this case, the preemphasis compensation current will be cut off and doesn't produce the desired effect. The gating input of the Great amplifiers is directly connected to the IPSO T0 connector for the hard blanking mode. For the T0 pin connections please refer to "T0 Trigger Signals" on page 125.

To **blank** all amplifiers in this mode, bit 32, 33 and 34 of nmrword0 have to be set to 1 (5V at the T0 connector) using the command 'setnmr0^32^33^34' in the pulse program.

To **unblank** the amplifiers, the bits have to be set to 0 (0V at the T0 connector) using the command 'setnmr0|32|33|34', where bit32 is for AmpX, bit33 for AmpY, and bit34 for AmpZ.

The following lines show a pulse program example for the hard blanking:

…

15u   setnmr0|32|33|34

1m   grad { (10) | (t0) | (0) }

200u   groff

2m   ; time for the preemphasis current to decay

10u   setnmr0^32^33^34

…

setnmr ppg command	AmpX	AmpY	AmpZ
setnmr0^32^33^34	D	D	D
setnmr0^32^33|34	D	D	E
setnmr0^32|33^34	D	E	D
setnmr0^32|33|34	D	E	E
setnmr0|32^33^34	E	D	D
setnmr0^32|33^34	D	E	D
setnmr0|32|33^34	E	E	D
setnmr0|32|33|34	E	E	E

Table 10.1:   Hard blanking parameters. D=amplifier disabled (blanked), E=amplifier enabled (unblanked)
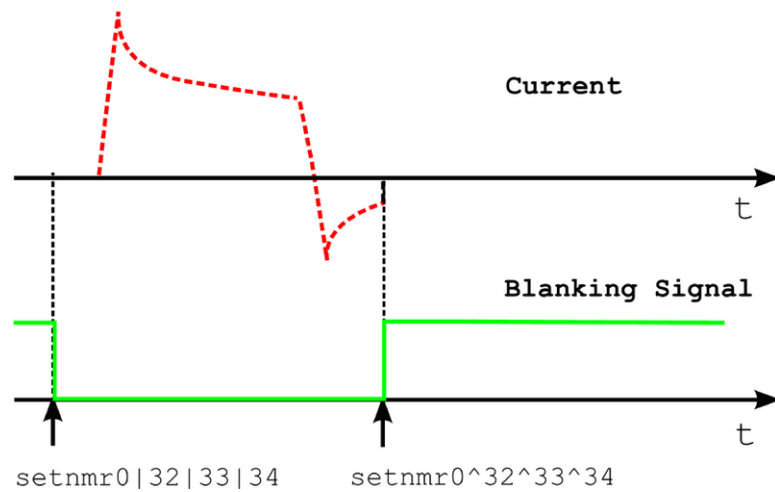
Figure 10.18   Hard blanking of a gradient pulse with preemphasis components

10.6.2   'Soft Blanking'

The Master Unit BGMUI-E used on AVANCE III systems can generate 'soft blanking' pulses. The 'soft blanking' is controlled in the pulse program using the 'ctrlgrad' com- mands. If a 'ctrlgrad' command is executed in the pulse program to blank an amplifier, the Master Unit checks if the digital data of the amplifier is zero. As long as the input data is not zero, the amplifier stays enabled (unblanked). As soon as the input becomes zero, the Master Unit generates the blanking signal for the amplifier.

The main advantage of the 'soft blanking' is that residual currents from the preemphasis are no longer clipped. If, for example, all the preemphasis values are zero, the amplifier is blanked immediately when the 'ctrlgrad' command is executed. If the preemphasis compensation adds an exponentially decaying current, the amplifier is first blanked when the compensation current is fully decayed. The gating input of the Great amplifiers has to be connected to Master Unit, see chapter "Master Unit BGMUI-E (W1522066)" on page 107.

The following lines show a pulse program example for the soft blanking:

…

15u   ctrlgrad 7

1m   grad { (10) | (t0) | (0) }

200u   groff

2m   ctrlgrad 0   ; blanking stays open for preemphasis decay

…

The 'soft blanking' of the amplifiers is executed using the keyword 'ctrlgrad <value>' in the pulse program. To unblank the amplifiers, the <value> bits must be set. To blank the amplifiers, the bits must be reset to 0, where bit0=AmpX, bit1=AmpY, and bit2=AmpZ.

Value (bin)	ppg command	X	Y	Z
000	ctrlgrad 0	D	D	D
001	ctrlgrad 1	D	D	E
010	ctrlgrad 2	D	E	D
011	ctrlgrad 3	D	E	E
100	ctrlgrad 4	E	D	D
101	ctrlgrad 5	D	E	D
110	ctrlgrad 6	E	E	D
111	ctrlgrad 7	E	E	E

Table 10.2:   Soft blanking parameters. D=amplifier disabled (blanked), E=amplifier enabled (unblanked)

The command *Ctrlgrad* opens the amplifier at the next gradient command in the pulse program. If a 'ctrlgrad 7' is not immediately followed by a grad{…} command, the amplifiers remains blanked.
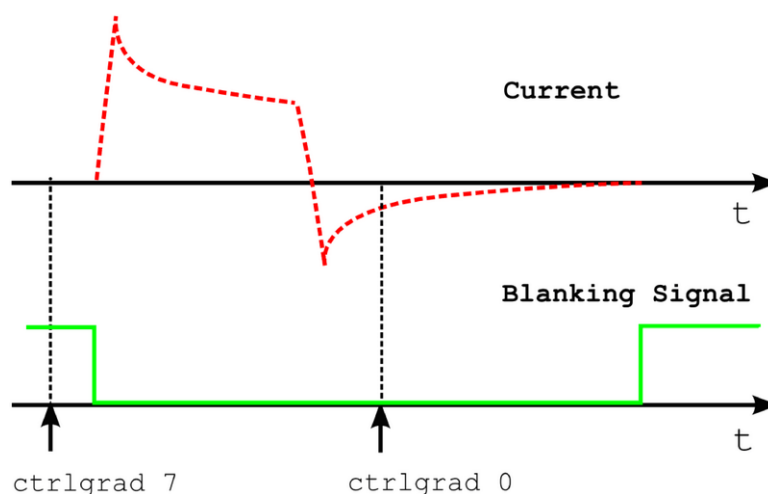
Figure 10.19   Soft blanking of a gradient pulse with preemphasis components

Typically all amplifiers are blanked/unblanked at the same time. Therefore the macros BLKGRAD and UNBLKGRAD are defined in the include file pp/Grad.incl. These macros execute a 'soft' and a 'hard' blanking event, so the behavior of the amplifier depends on where the gating input is connected.

10.7 IPSO

This section contains useful information about the IPSO.

10.7.1 Trigger Signals (in and out) at the T0 connector

T0 Name	Description/Label	ppg Command	Connection Point
Signal Outputs			
TTL1	TTL Out 1	TTL1_LOW TTL1_HIGH (nmrword 3#28)	T0 / I1
TTL2	TTL Out 2	TTL2_LOW TTL2_HIGH (nmrword 3#29)	T0 / I2
TTL3	TTL Out 3	TTL3_LOW TTL3_HIGH (nmrword 3#30)	T0 / I3
TTL4	TTL Out 4	TTL4_LOW TTL4_HIGH (nmrword 3#31)	T0 / I4
STAMP1	ECG_STAMP	STAMP1_LOW STAMP1_HIGH (nmrword 3#6)	T0 / C1
NV_CLOCK	DPP NV_CLOCK		T0 / Z1
BlankXAmp		nmrword0#32	T0 / A4
BlankYAmp		nmrword0#33	T0 / A5
BlankZAmp		nmrword0#34	T0 / A6
Signal Inputs			
TRIG_IN1	ECG_TRIG	trig[np][le]1	T0 / C5
TRIG_IN2	TTL IN 1	trig[np][le]2	T0 / C6
TRIG_IN3	GRAD_SYNC	trig[np][le]3	T0 / E1
TRIG_IN4	TTL IN 2	trig[np][le]4	T0 / E2

Table 10.3:   T0 Trigger Signals

11 Contact

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Contact

Appendix   A

A.1   Warning Signs

C
Caution
N
Note

A.2   Figures

A.3 Tables

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