MRspa – Magnetic Resonance spectral processing and analysis

Dinesh K Deelchand, PhD

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Manual version 1.0 - based on MRspa v1.5g

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1. Introduction

Magnetic Resonance spectral processing and analysis (MRspa) is a spectral post-processing and analysis package that runs under MATLAB. Various processing steps are currently available: Eddy current, frequency and phase corrections (several algorithms exist), remove and average FIDs (more details in the next section). LCModel package is interfaced with MRspa for quick and easy analysis (either in single- or batch-mode) of MRS data.

Various MRS data formats are currently supported:

- Agilent/Varian
- Bruker
- GE (P-file)
- Philips (SDAT and DATA)
- Siemens (DICOM and raw TWIX).

NOTE: Current version does **NOT** support spaces in data filenames and pathnames.

1.1 Download and Installation

Download MRspa program from https://www.cmrr.umn.edu/downloads/mrspa/

Unzip file and add the full pathname where you install MRspa in your MATLAB startup file. To start the program, execute *MRspa* inside MATLAB.

1.2 First Time Use

The first time you run MRspa, you will be prompted with the following screen (*Figure 1*) to setup LCModel. You need to fill this window if you plan to interface LCmodel to fit your MRS data else please **OK** to skip this setup. Information required are the name of the host computer where the LCModel license is installed, the LCModel license holder name (refer to LCModel manual for more info), the location where the LCModel executable file is located and the location of the user's home directory on the LCModel computer (Windows OS only).

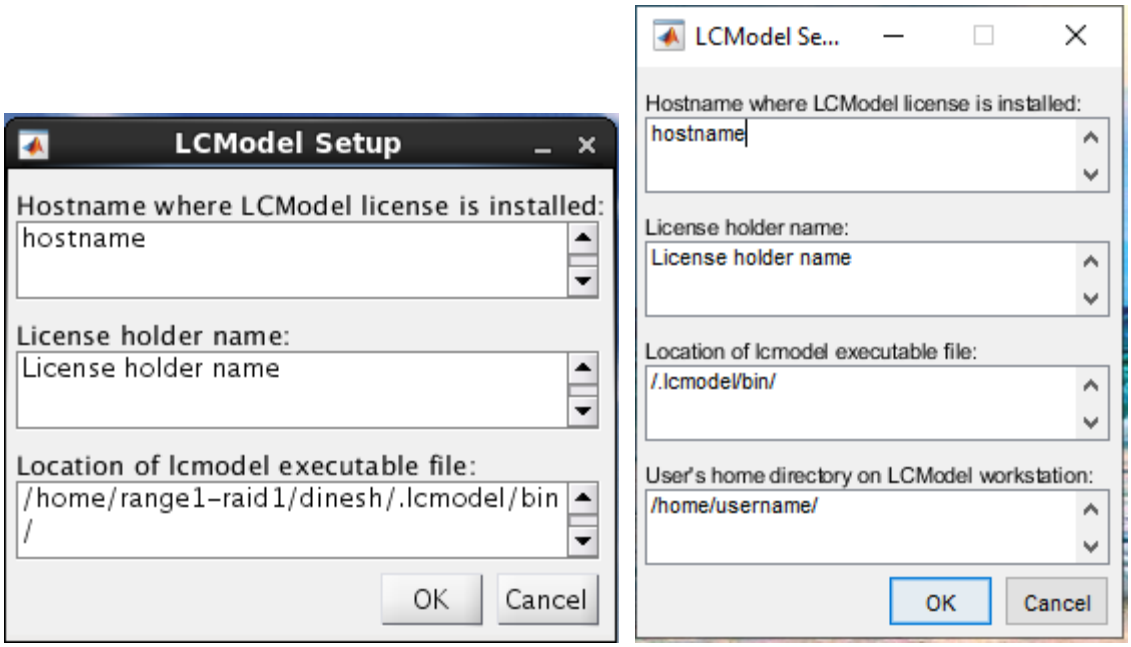

Figure 1: LCModel setup on Windows (left) and Linux or MacOs (right).

After clicking **OK**, a file named MRspa.ini is created inside the MRspa folder which contains these information.

2. MRspa Overview

2.1 MRspa Main GUI

When you start MRspa, you should see the main MRspa GUI (*Figure 2*) with the Processing module enabled by default. The active module is shown by the tab text appearing in red. The MRspa main GUI have many features as described in more details in the next sections.

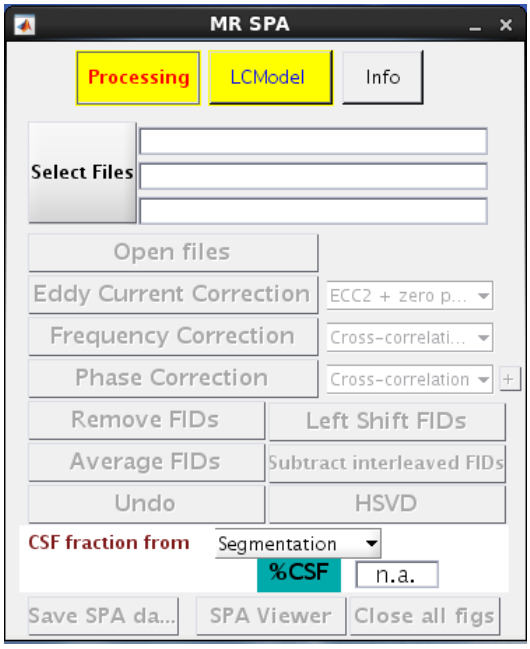

Figure 2: MRspa main GUI where the Processing module is active.

2.2 Load MRS Data (Processing)

To load an MRS data set, click on 'Select Files' On the MRspa main GUI. This opens a dialog box to select the appropriate files (*Figure 3*). There might be several data sets associated with the MRS data based on your acquisition scheme: metabolite scan (i.e. water-suppressed data), water reference scan for eddy current correction (ECC) and another water reference scan for absolute quantification.

For MRS sequences distributed by CMRR, look for data after the calibration data sets (e.g., calib90 or calibWS) that contains 'WS' or ‘avg#” in the title (e.g. MR-SR008-vermis_64 or MR-SE019-dACC_WS64). Do not load filenames with _SUM extension (if available) since this dataset contains a single summed FID instead of individual FIDs suitable for frequency and phase corrections (*Figure 4*).

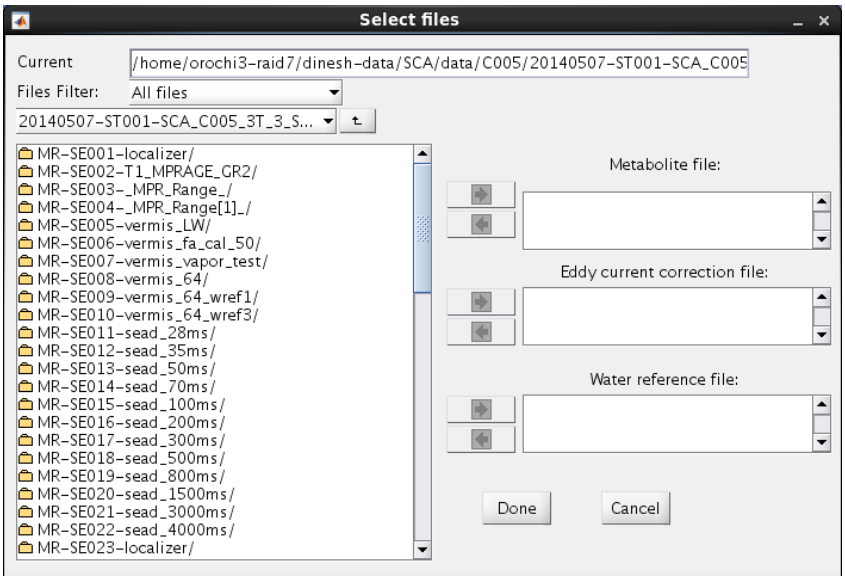

Figure 3: Select files GUI

How to select data file(s):

- Select the appropriate water suppressed dataset and click on the arrow pointing towards the Metabolite File tab (labelled 1 in *Figure 4*). The filename shows up in the Metabolite File window
- Do the same for the Eddy current correction File and Water reference file if applicable.
- Click Done (labelled 4 in *Figure 4*).
- The MRspa main GUI should now display the selected files with the Open files button (*Figure 4*).
- To load the file(s), click on Open files on the MRspa main GUI. Based on the selected files, the appropriate buttons for processing are enabled (*Figure 5*). In addition, the *SPA Viewer GUI* opens up and the spectrum is displayed in Sum mode (more details in the next section).

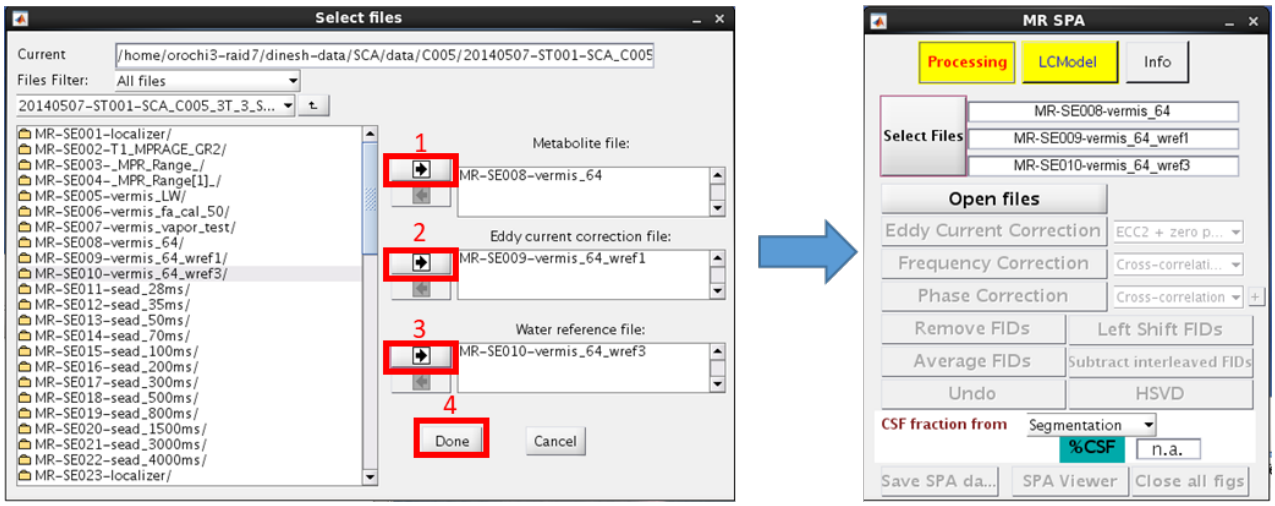

Figure 4: Left dialog box shows how to select the appropriate files in the specific locations. The selected files are displayed in the main GUI (right) after pressing done.

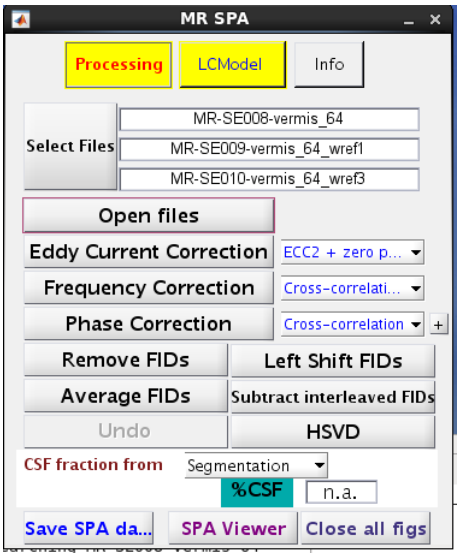

Figure 5: After opening the file(s), the appropriate buttons are enabled.

The most recent implementation of the CMRR semi-LASER sequence [Öz & Tkáč, Magn Reson Med 2011] has embedded water reference scans, so there is no need to select the individual water reference scans (e.g. ECC or water reference) as shown in *Figure 6*.

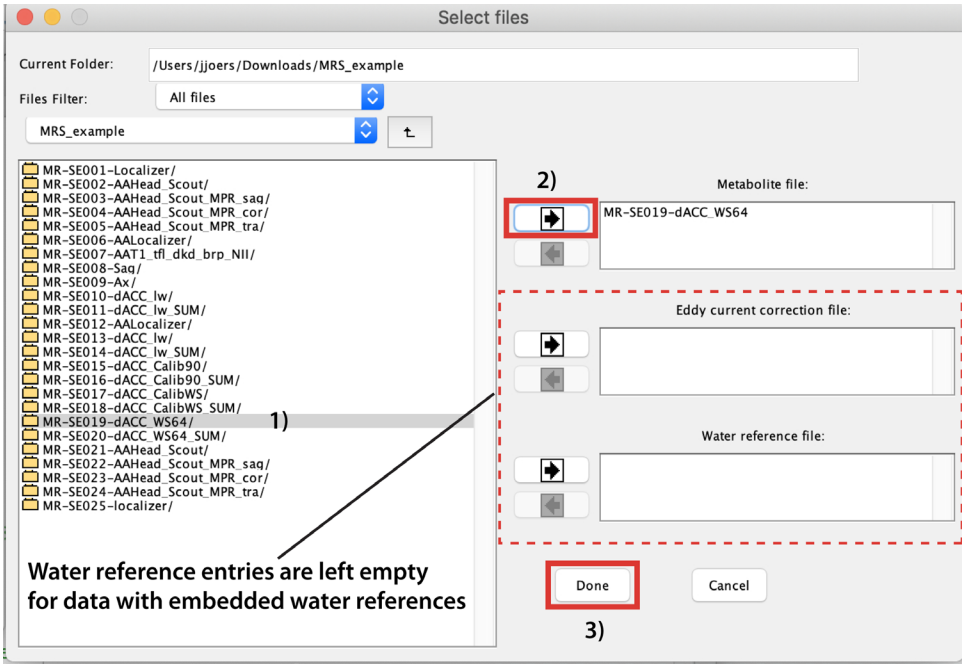

Figure 6: For metabolite-suppressed data with embedded water, select the file as Metabolite file and the water references entries are left blank.

2.3 SPA Viewer GUI (Processing)

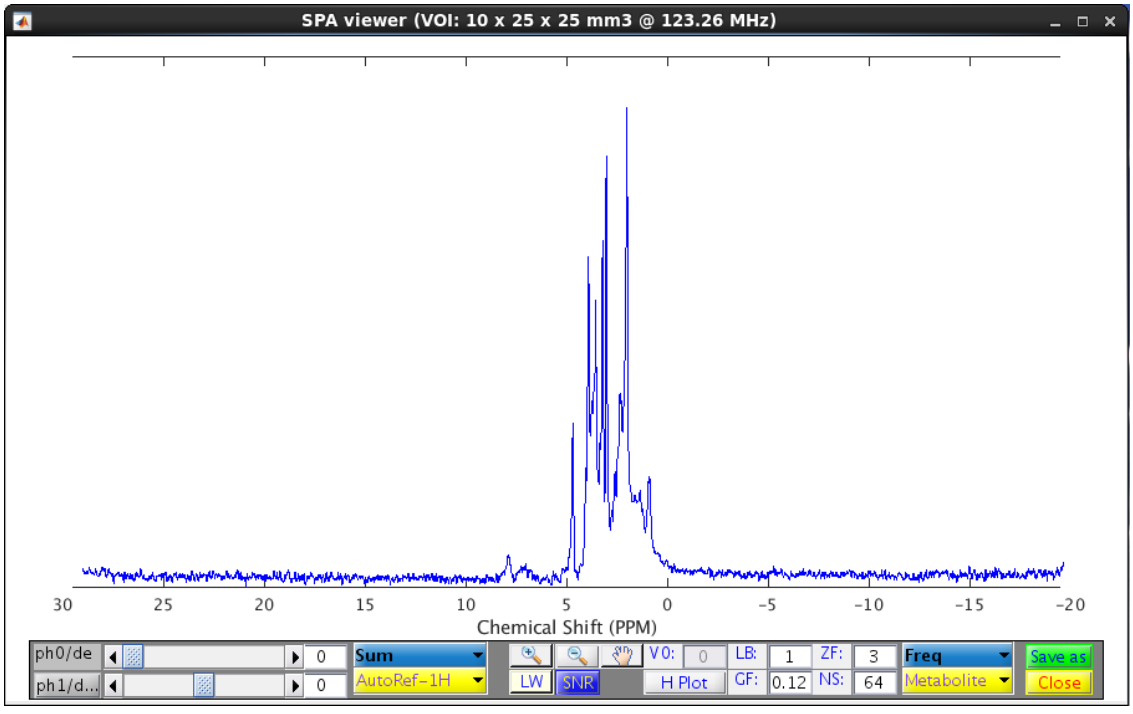

Figure 7: SPA Viewer GUI

After the MRS data have been successfully loaded, the *SPA Viewer* GUI opens up automatically (*Figure 6*). This GUI displays the MRS data during post-processing. There are various features available on this display:

- The VOI dimension (if available in the file header; not applicable when SPA file is loaded) and B_0 frequency (in MHz) are displayed in the window header.
- Manual zero (ph0) and first order (ph1) phase corrections
    - Automatic zero and first order phase corrections are performed when clicking the ph1/deg button
- Option to visualize data
    - Sum, Individual and Stacked plot mode
- Option to automatic/manual referencing of whole spectrum
    - AutoRef-1H: NAA is set at 2.001 ppm for 1H MRS data
    - AutoRef-31P: PCr is set at 0 ppm for 31P MRS data
    - ManualRef: Manually select peak and enter appropriate value (in ppm)
- LW button
    - Estimate the linewidth of a particular peak. To use this feature, click LW and click the top of the interest. The LW in Hz will be displayed on the spectrum.
- SNR button
    - Measure signal-to-noise ratio (SNR). Make sure the display shows the spectrum with the highest peak to measure include noise region. E.g. 1H, you can zoom between 4 to -5 ppm. Then click SNR and select the noise region. The calculated SNR is shown in the MATLAB window. This feature can also be used in "Stacked plot" mode.
- Apodization functions available and used for **display purposes only**
    - LB: line-broadening
    - GF: Gaussian broadening
    - ZF: zero-filling
    - NS: Number of scans to display/use

- H plot: display stacked plot data in horizontal plot
- V0: display stacked plot data in vertical plot based on user-defined value
- Data can be visualize either in time domain (Time) or frequency domain (Freq)
- Metabolite and water references can be displayed using either the Metabolite, Water (ECC) or Water Ref tab options
- Save As: options to save data in various formats e.g. Varian, EPS, TIFF, ASCII or SPA with or without filtering
    - Data is saved without any filterings (i.e. LB,GF) for VNMR (Varian format) and "SPA – individual spectra" formats. All other formats, the data are saved with filtering
    - ***NOTE***: To save the processed MRS data for further analysis with LCModel using the Save SPA data on the MRspa main GUI window.
- Close: Close the *SPA viewer* window

2.4 Load SPA file (Processing)

SPA files contain processed MRS data (metabolite and water reference scan for quantification if available) which were saved with MRspa. To load these types of files, you first need to change the Files Filter for selection to SPA processed file (*.spa) as shown in *Figure 7*.

You can load several SPA files (from different paths) measured with the same acquisition parameters. If the acquisition parameters does NOT match that of the first filename in the series, the "unmatched" SPA file is not loaded. This feature is useful to add, compare many SPA files.

NOTE: Do not attempt to run ECC or other processing when loading many SPA files else, the number of averages in the metabolite or water references are messed up and the metabolites concentration will be much higher after LCModel analysis. In general, simple frequency or phase correction is ok.

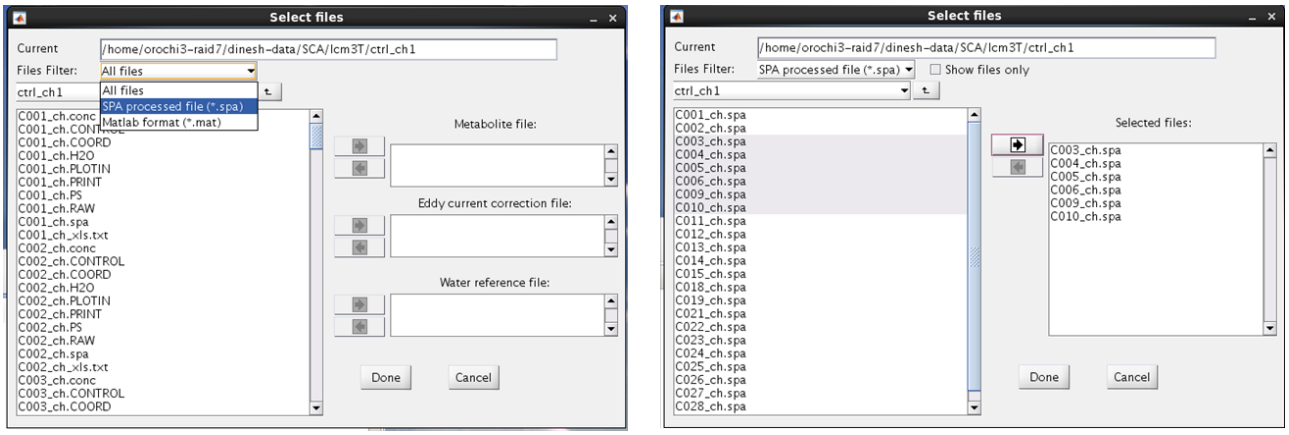

Figure 8: How to load SPA file(s). Left image: First change filterto SPA processed and then highlights SPA files, then click Done

2.5 Saving SPA file after Post-processing

After performing all required processing steps (next section), you need to save the final summed processed MRS data (metabolite and water reference scan for quantification, cerebrospinal fluid (CSF) fraction and acquisition parameters) in a single SPA file format. Use the Save SPA data button on the MRspa main GUI to save the data. All the processing steps performed on the dataset are saved into this file except if zero-order phase correction was manually performed.

NOTE: Make sure %CSF entry is not left blank to avoid a warning!

3. MRS Post-processing

The processing GUI is use to preprocess various MRS data format before running LCModel analysis. Make sure the Processing tab is active before processing and load the data as shown above.

3.1 Built-in Functions & Options

Processing functions currently available in MRspa are described below.

NOTE: After performing a correction, you need to visually inspect the MRS data in *SPA viewer* to make sure the process was successful. In most cases, using the default processing option is sufficient. These options work on Metabolite or Water scans tab (see Section 0).

3.1.1 Eddy Current Correction (ECC)

This option performs ECC correction. Several algorithms are currently available: ECC + zero phase, ECC only, ECC2 + zero phase (default), and ECC2 only.

ECC + zero phase and ECC2 + zero phase are used to correct for both ECC and zero-order phase correction based on the phase of water reference scan. Similarly, ECC only and ECC2 only are used to only correct for ECC.

ECC2 is generally used on Siemens MRS data since very often there are phase jumps in the FID during acquisition. This algorithm corrects this issue before performing ECC.

NOTE: The ECC button is only available when a water reference for ECC is loaded.

3.1.2 Frequency Correction

This option corrects for frequency (B_0) instabilities during acquisition, most likely due to subject motion or hardware instabilities. This correction aligns the single shot spectra so that they add constructively for maximum SNR. This correction outputs "before and after" overlays, along with the frequency shift (in Hz) for individual FIDs (*Figure 9*).

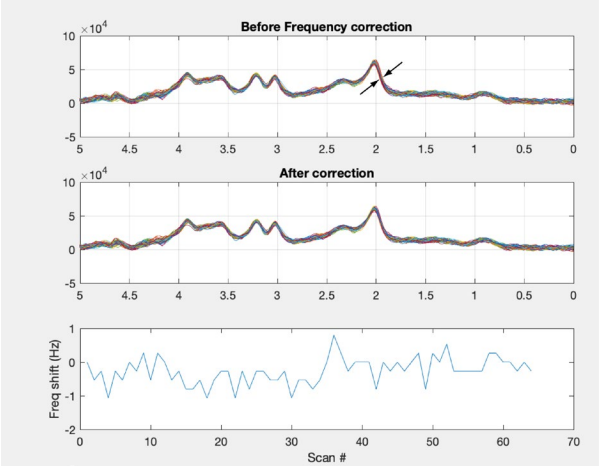

Figure 9: Frequency correction output display: top plot shows individual spectra before correction; middle plot shows data after correction and bottom plot shows the determined frequency shift.

Available frequency algorithms are:

- Amplitude: phase and Amplitude: abs

  Uses a single peak with high SNR either in phase (Amplitude: phase) or magnitude (Amplitude: abs) mode to perform correction. By default, the NAA singlet peak at 2.001 ppm is used for brain MRS.

- Least square

  This option uses least-square method to minimize the frequency difference between single shot MRS data.

- Cross-correlation (default)

  This option uses cross-correlation method to minimize the frequency difference between single shot MRS data.

- Spectral Registration

  This option does simultaneous frequency and phase corrections. Refer to Near et al. Magn Reson Med 2015 for more details.

3.1.3 Phase Correction

This option corrects for phase instabilities during acquisition, most likely due to subject motion or hardware instabilities. Single-shot spectra are required. In a similar

manner to the frequency correction output, the phase correction outputs before and after plots, with the corresponding phase correction applied for each FID (*Figure 10*).

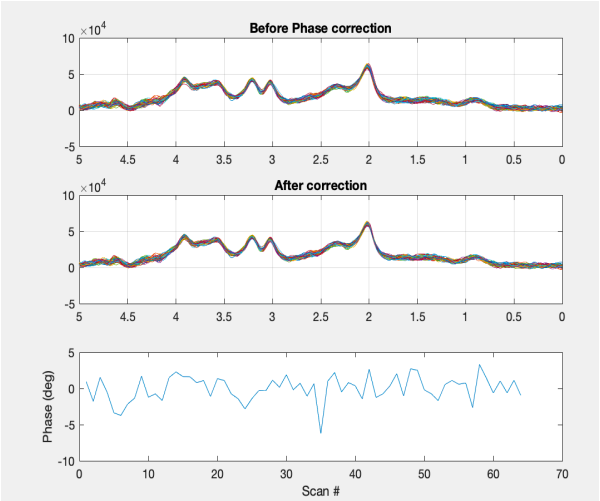

Figure 10: Phase correction output display: top plot shows individual spectra before correction; middle plot shows data after correction and bottom plot shows the determined phase difference.

Available phase algorithms for zero-order phase corrections (except where noted) are:

- Least square

  This option uses least-square method to minimize the phase difference between single shot MRS data.

- Max Intensity

  This option iteratively changes the zero-order phase of the MRS data until the real part of the spectrum is maximized. This function is useful when analyzing metabolite-cycled data i.e. without water suppression or spectrum will singlets peaks, i.e. at long echo-times.

- First 4 pts

  This option uses the first 4 points in each FID to correct for the zero-order phase of the MRS data. This function is useful when analyzing metabolite-cycled data i.e. without water suppression.

- Entropy

  This option does simultaneous zero- and first- phase corrections. Refer to Chen et al. JMR 2002 for more details.

- Cross-correlation (default)

  This option uses cross-correlation method to minimize the phase difference between single shot MRS data.

For least-square and cross-correlation algorithms, we can define additional information on the spectral range to use when performing phase correction. The + button on the MRspa main GUI is available to change the spectral range (Figure 11). By default, the chemical shift range is set from 1.9 to 3.5 ppm.

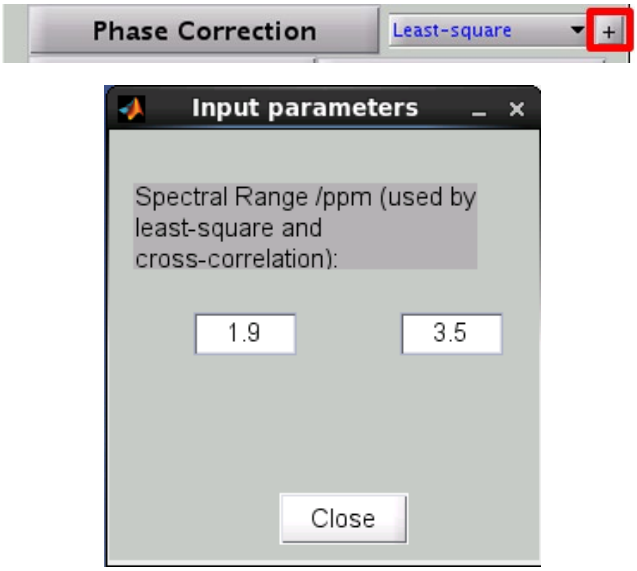

Figure 11: +sign button (red box) opens a dialog box for users to defined spectral range where phase correction will be done.

3.1.4 Remove FIDs

This option is useful to remove selected outlier individual FIDs affected maybe due to subject's motion. E.g. large water residual peak, noise only spectrum, broad linewidth. To use, click on the Remove FIDs on the MRspa main GUI. This will activate a dialog box in which you may select which FIDs to remove (*Figure 12*).

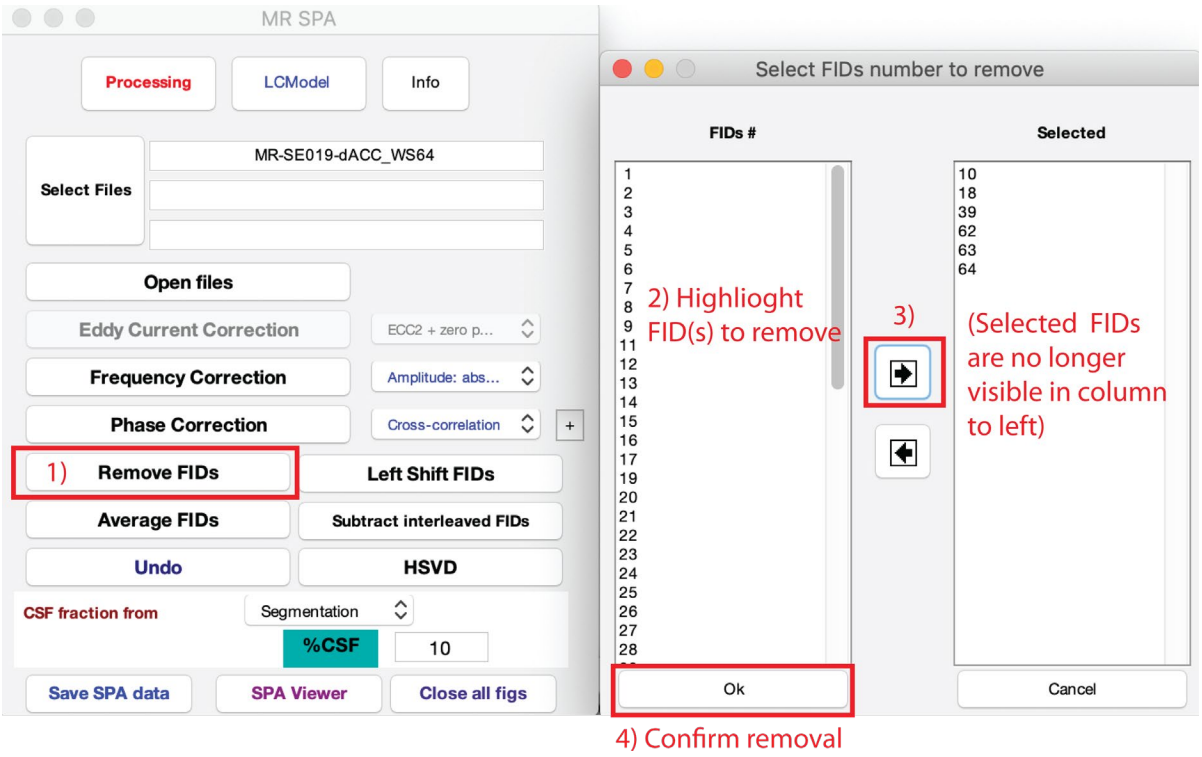

Figure 12: How to use the remove FID feature

3.1.5 Left Shift FIDs

This option removes user-defined number of points from the beginning of each individual FID; applies to both metabolite and water reference scans. This applies mostly to MRS sequences distributed by CMRR. In some cases, this step is automatically applied when the MRS data are loaded

3.1.6 Average FIDs

This option is used only if there is not enough SNR in single scans to perform scan-to-scan frequency correction. This option allows averaging of data in small blocks before frequency correction. For example, a set of 128 scans can be averaged into 32 blocks of 4 scans each, then frequency correction can be performed on these 32 blocks.

3.1.7 Subtract Interleaved FIDs

This option is used when data are acquired in an interleaved fashion, e.g. editing MRS or metabolite-cycling MRS data. Even and odd spectra will be subtracted. Only works if NS (in SPA viewer) is an even number.

3.1.8 Undo

This button undo previous processing steps, starting with the most recent one. To view all the processing steps carried out (*Figure 13*), move the mouse arrow over the Undo button.

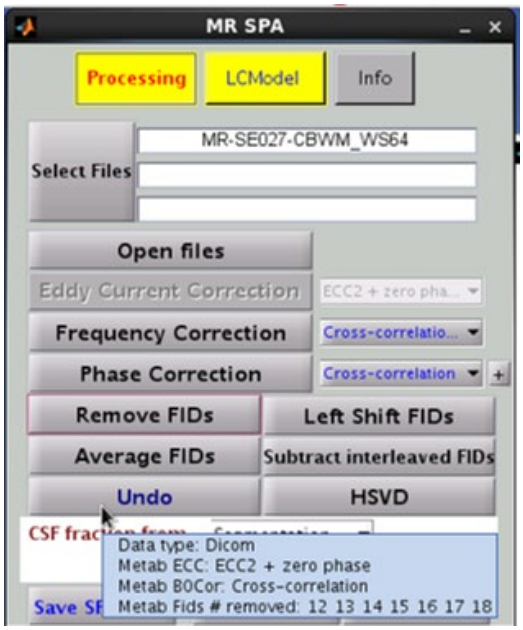

Figure 13: Undo button shows the processing steps which has so far been performed.

3.1.9 HSVD

HSVD or Hankel Singular Value Decomposition will decompose the summed spectrum into various components and specific resonances such as water residual or total creatine peak at 3.93 ppm (for macromolecule spectrum) can be removed. It is advice to process the MRS data before running this option. You have the option to save the HSVD processed spectrum into a RAW file (used by LCModel to create a basis set).

3.1.10 %CSF

The CSF voxel fraction is used to refine the concentrations of metabolites within the voxel since most metabolites are not present in CSF in appreciable amounts (lactate, glucose may be two possible exceptions). There are two ways to obtain this information

- Using water signal acquired at different echo-times, Water TEs

  In the %CSF menu, select Water TEs. The user will be prompted to select the water files and the T_2 for CSF in this VOI. A Bi-exponential fit of water data at different TEs is performed to obtain the %CSF.

- From segmentation of 3D T_1 MRI images

  In the %CSF menu, select Segmentation and enter the percent value (not fractional value) of CSF within the subject's VOI associated with the spectral data being processed. The MATLAB script to perform this task is available under request from the author.

3.1.11 SPA Viewer

This button opens, upload the global variables or reset the MRS display axes of the *SPA Viewer* window. See section 0 for more details.

3.2 Write Your Own MATLAB Code

The user have the option to write their own MATLAB script e.g. for sorting their data, for additional processing, etc. An example of how to process MEGA spectra acquired in batch of 32 averages in OFF and ON cases is shown in *Figure 14*.

```
global fidm  %variable where metab FID is stored
fid=fidm;
ct=1;
for ix=1:32:size(fid,2)
   fid_temp(:,ct)=sum(fid(:,ix:ix+31),2);
   ct=ct+1;
end
fid_off=sum(fid_temp(:,1:2:end),2);
fid_on=sum(fid_temp(:,2:2:end),2);
diff_fid=fid_on-fid_off;
clear global fidm
global fidm
fidm(:,1)=fid_off;
fidm(:,2)=fid_on;
fidm(:,3)=diff_fid;
```

Figure 14: Script to process MEGA data

3.3 Examples of Post-Processing Steps

3.3.1 Commonly used with water suppression

– ECC: ECC2+zero-order phase

- Freq Cor: cross-correlation
- Phase Cor: cross-correlation
- Freq Cor: Amplitude phase/abs using NAA peak
- AutoRef-1H

3.3.2 Commonly used with water suppression with low SNR

- Average FIDs: 4 or 8 averages
- Freq Cor: cross-correlation
- Phase Cor: cross-correlation
- Freq Cor: Amplitude phase/abs using NAA peak
- Average FIDs: all data
- ECC: ECC2+zero-order phase
- AutoRef-1H

3.3.3 Metabolite cycling data

- ECC: ECC2+zero-order phase
- Phase Cor: Max intensity
- Freq Cor: Amplitude phase/abs using water
- Subtract interleaved FIDs
- Freq Cor: Amplitude phase/abs using NAA peak
- AutoRef-1H

3.3.4 Editing (e.g. GABA editing)

- ECC: ECC2+zero-order phase
- Freq Cor: Amplitude phase/abs using tCr at 3.03 ppm
- ManualRef: tCr peak at 3.03ppm
- Sum even and odd data (external script)

4. LCModel quantification via MRspa GUI

After processing and saving the SPA files for all MRS dataset of interest, it is now time to use these as input to LCModel. To do this, select the LCModel tab in the top center of the MRspa main GUI. The lettering of LCModel will turn red when activated (*Figure 15*). LCModel analysis can be carried out on a single SPA file or multiple SPA files (i.e. in batch analysis). The workflow is from top to bottom, as described in the consecutive sub-sections below.

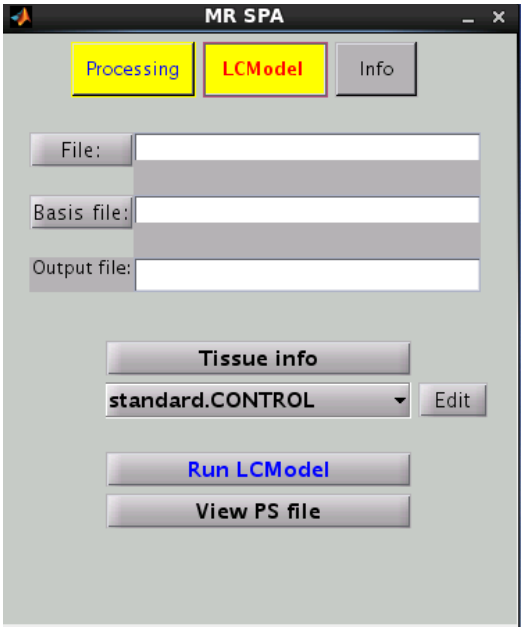

Figure 15: LCModel analysis window

4.1 Load SPA file(s)

After clicking the File: button, a directory listing will appear (*Figure 16*). Select the appropriate SPA files you wish to analyze. Note that you can navigate to different folder. When finished, click on Done in the directory search popup.

If more than one SPA file is loaded, you will be prompted to give the batch process a name (*Figure 17*). This will create a file (with .batch extension) with a path list to each of the SPA data files that were selected for analysis. Name this file in an appropriate manner for your study. The name of the saved .batch file will be shown in this file entry.

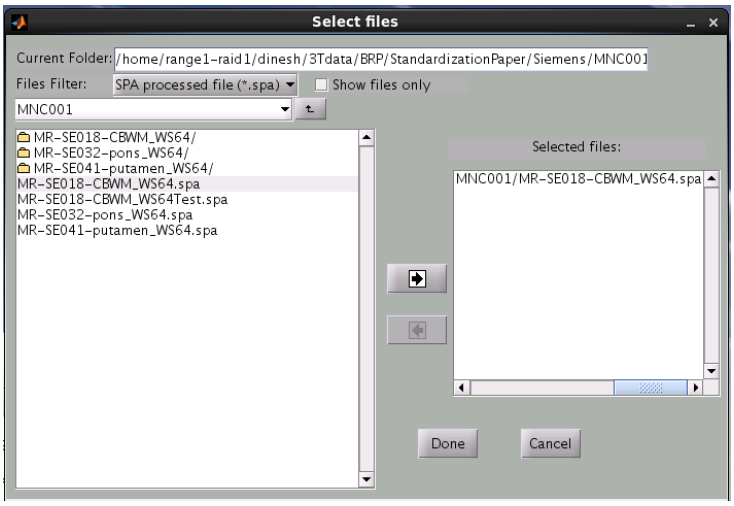

Figure 16: Single SPA file selection for analysis (i.e. in single mode).

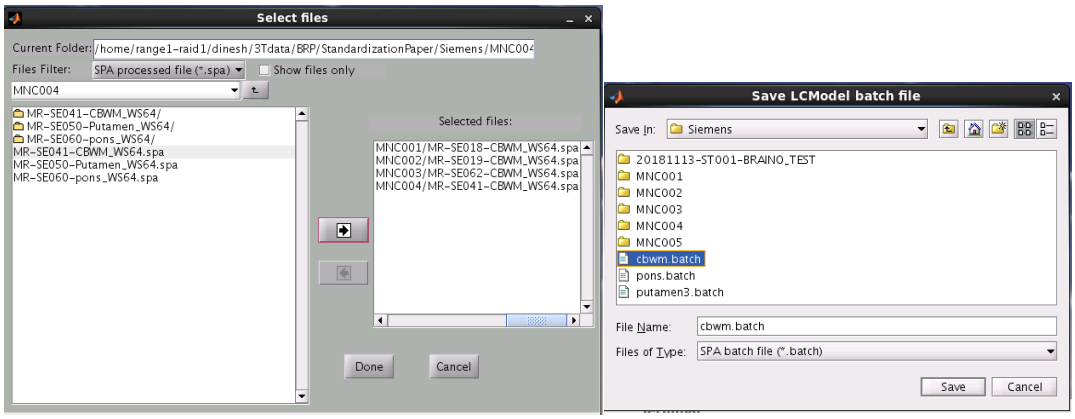

Figure 17: Multiple SPA files selection for analysis (i.e. in batch mode).

4.2 Basis File

Select the appropriate LCModel metabolite basis set (*Figure 18*) corresponding to the field strength, echo times and pulse sequence used to acquire the data that will be analyzed.

NOTE: For easy basis file selection, it is recommended to copy your .BASIS file in a directory called basis-sets located in your MRspa directory.

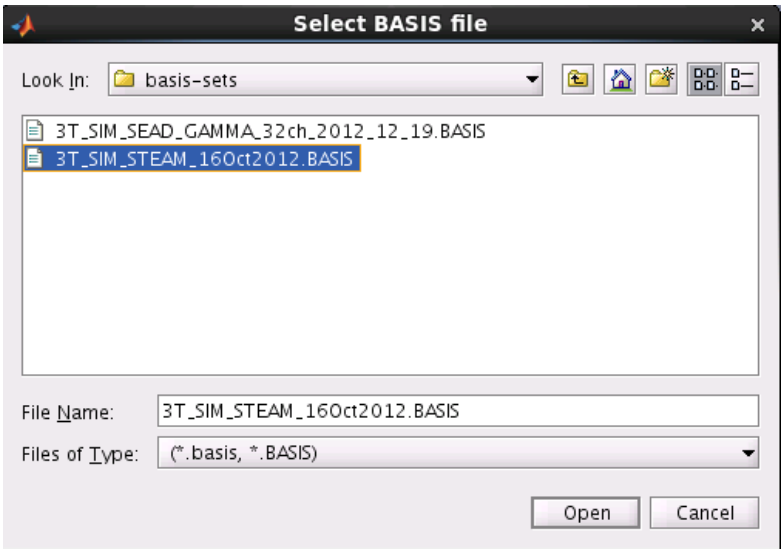

Figure 18: LCModel basis file selection

4.3 Output File

If running a single SPA file, this entry is self-generated and will assign the output filename to that of the input SPA file but the output name can be changed to whatever you want.

If more than one SPA file is input (batch mode), the output will display "Batch mode". For each dataset, the output filename will corresponds to the filename of the starting SPA file.

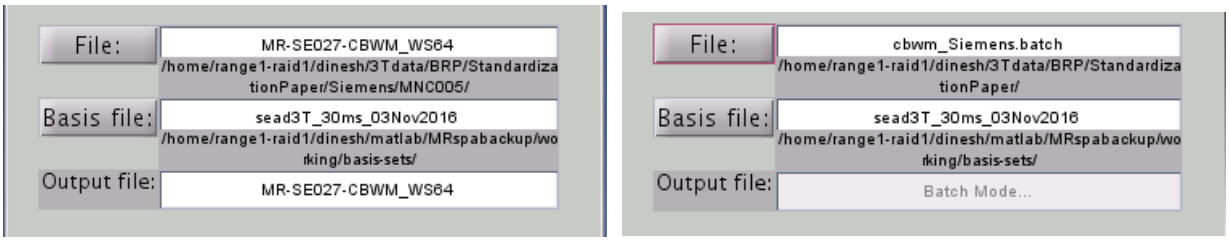

Figure 19: Output filename for single mode (left) or batch mode (right) analysis

4.4 Tissue Info

For absolute concentration, the following parameters are required: T_E, T_2 of tissue water (user defined or fitted T2 value obtained during processing step from CSF calculation), T_2 of metabolite, %CSF fraction, %water content and %CSF water content.

- Single file mode: If the SPA file contains the CSF fraction (calculated during the Processing steps), the "CSF fraction (%)" entry will display its value. Otherwise this entry will be empty and will need to be entered manually.
- Batch mode: The "CSF fraction (%)" entry is omitted in the input parameters and MRspa assume that all SPA files contain the CSF info. Another way to include the CSF fraction info is to edit the .batch file and add the CSF fraction value at the end of each line. ***NOTE***: the latter option will ignore any CSF fraction value contained in the .spa file.

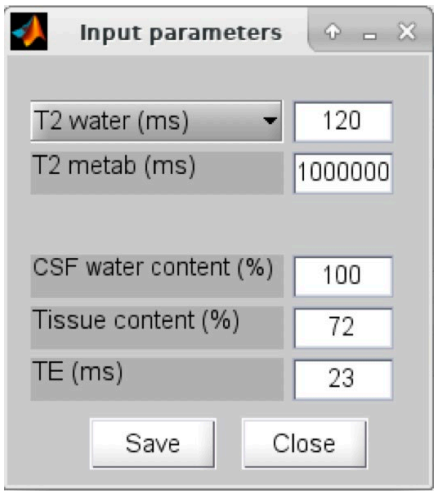

Figure 20: Tissue info input parameters

4.5 CONTROL File

Select the appropriate CONTROL file from the popup list. All .CONTROL files are located in a directory called CONTROL located in the MRspa directory. The standard.CONTROL is selected by default and should be used. The CONTROL file defines a number of parameters regarding the LCModel fit; e.g., spectral range fit, which metabolites are reported as sums, which metabolites (if any) should be omitted, etc.

4.5.1 Edit Button

Click on the Edit button to view, modify/add the input parameters for a selected CONTROL file. ***NOTE***: It is strongly advised that the user refer to the LCModel manual before considering changing any parameters in the CONTROL file.

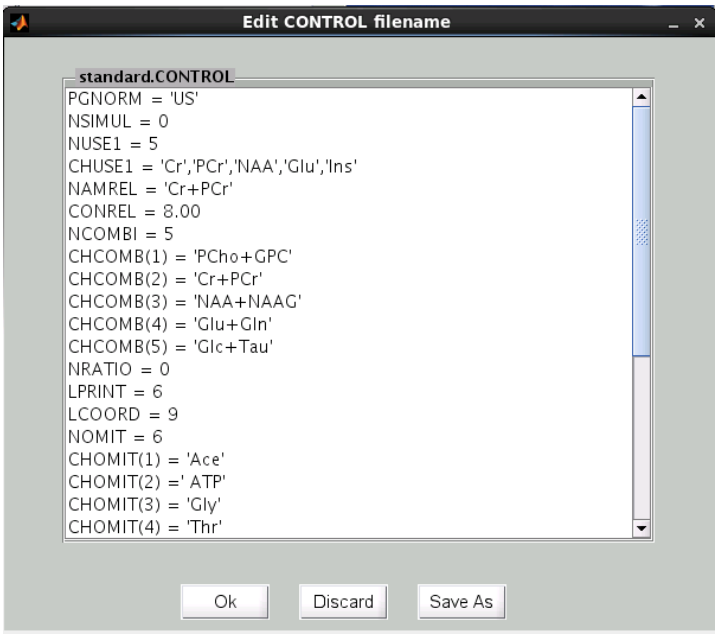

Figure 21: Edit a CONTROL file

4.5.2 Ok Button

This will save any changes made **in memory** ONLY and these changes will apply only for the current LCModel analysis. If changes are noticed, you will see the **Modified** text displayed next to the CONTROL option (*Figure 22*). To reload or reset the control file, reselect the CONTROL file from the popup menu list.

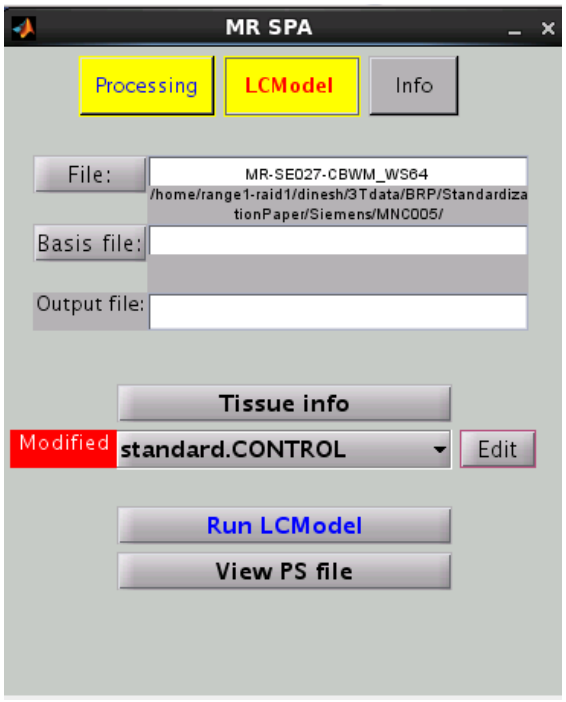

Figure 22: Temporary modified CONTROL file

4.5.3 Discard Button

Discard any changes made to the CONTROL file and use the previous parameters that are in memory.

4.5.4 Save As Button

This option will save the modified parameters in a new CONTROL file. The user will be prompted to enter the new CONTROL filename.

4.6 Run LCModel

This button will execute LCModel only after these required files (RAW, .CONTROL and/or .H2O) are successfully created. If LCModel fails, a message will display the error codes corresponding to the problem. Refer to the LCModel manual for further help. If run in batch mode, the datasets will be fitted sequentially.

When LCModel is analyzing/fitting the MRS data, the user will see these messages on the MATLAB terminal as shown in *Figure 23*. When the fit was successful, the metabolites concentration and respective Cramer-Rao Lower Bound (CRLB) will be displayed (*Figure 24*) in addition to showing the fitted spectrum (*Figure 25*).

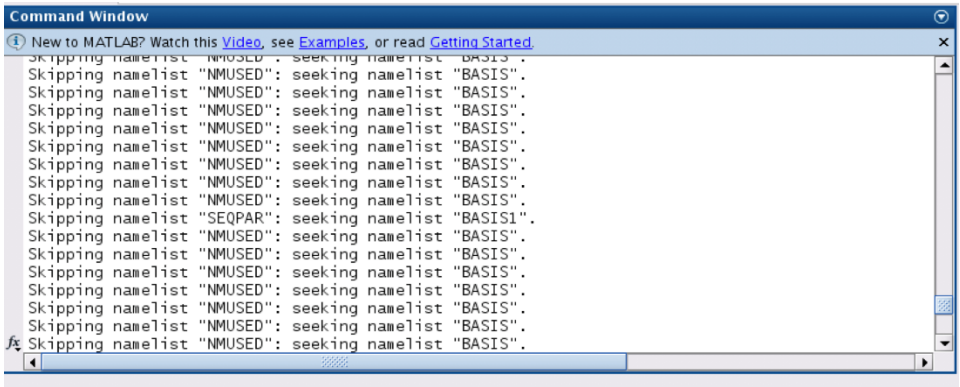

Figure 23: Output observed when LCModel is running

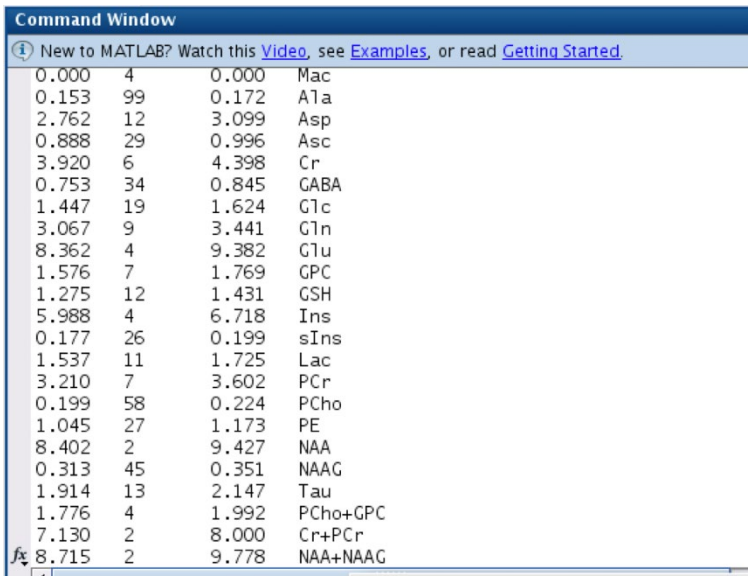

Figure 24: After LCModel analysis has successfully run, the concentration and CRLB are displayed in the terminal.

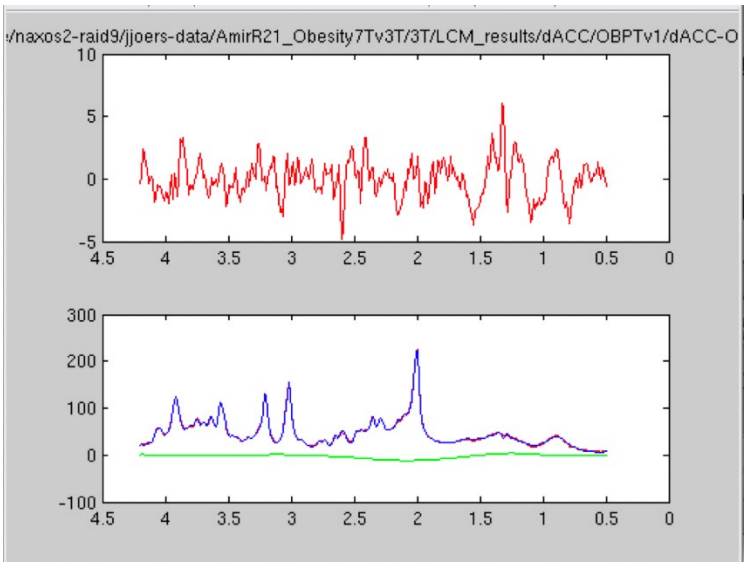

Figure 25: Output of the fitted data: top plot is the residual and bottom plot contains the input (red), fitted (blue) and spline baseline (green) after fitting.

4.6.1 LCModel Output Files

After running LCModel, each SPA file will have the following files associated with it:

File extension	Comments
conc	Column-wise text file with metabolite concentrations and CRLBs
CONTROL	CONTROL file used when running LCModel analysis
COORD	X-Y coordinates of spectra of each pure component metabolite used in the fit
H2O	Raw water spectral data
PLOTIN	Some spectral information the region of the spectral fit (#of points, ppm range)
PRINT	All of the useful LCModel output during analysis: concentrations, metabolite correlations, etc
PS	A postscript image of the LCModel fits and resulting metabolite concentrations
RAW	Raw metabolite spectral data

4.7 View PS file – *Single File Mode*

View the output postscript (PS) file generated by LCModel. This option is only available in single file mode analysis. In batch mode, the button is replaced with the Metab Conc Table button (next section). ***NOTE***: make sure to exit the viewer in order to continue using MATLAB.

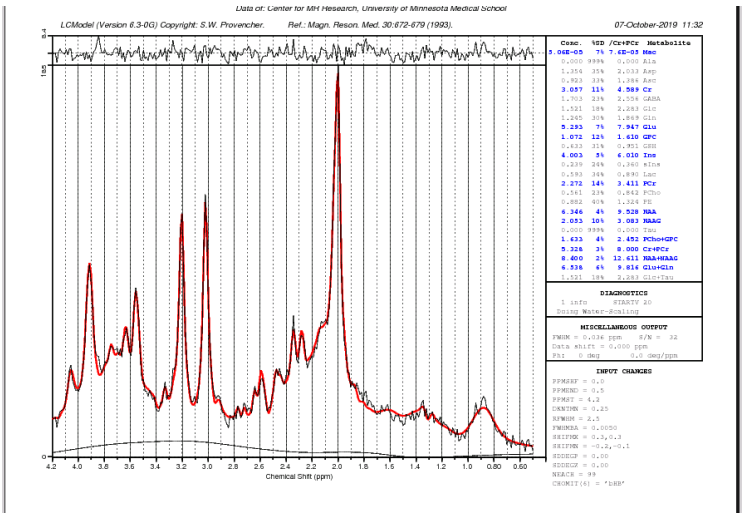

Figure 26: PS display

4.8 Metab Conc Table – *Batch Mode*

This button is only visible when analyzing MRS data in batch mode. This option generates two tables from all datasets and contains data on abs concentration and CRLB. These tables are saved as:

- *Filename*_conc.txt: Row-wise output file with metabolite concentrations and CRLBs
- *Filename*_xls.txt: Column-wise output file with metabolite concentrations and CRLBs

Where *filename* is the name of the batch file (see Section 4.3 above) and these files are located in the same directory where the .batch file was saved. These tables can be imported directly into Excel as a text file.

NOTE: For statistics work, *Filename*_xls.txt file is probably easiest to work with, since importing them into excel allows for easier data manipulation/calculation.

Figure 27: "Metab Conc Table" buttons is displayed in batch mode