High Resolution LC-MS, TNO-DECO Tool Manual

S. Krishnan

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This document is a concise operation manual for the high resolution LC-MS, TNO-DECO tool. The tool is developed in MATLAB: the GUI and the associated functionalities. In the following sections, the operation information will be discussed. The discussion will be based from the GUI perspective.

1 The GUI

Figure 1, shows the GUI to the high resolution LC-MS, TNO-DECO tool. This GUI is available by tying the following command at the command line, or clicking the application, `lcmsdeco.exe`, in the windows explorer.

```
>>lcmsdeco
```

Four sections, marked, 1, 2, 3, 4 that respectively corresponding to data input, pre-processing, deconvolute, and results will be discussed in the following sub-sections.

1.1 Data input

Data input section is to create a new project or load existing project. New project (`button: New project`), button prompts the user to enter the name of the new project and load (`button: Load project`) the mass chromatogram files (*.cdf files) that belong to that project. The maximum number of scans edit box (`edit box: Max scan`) is automatically filled with the maximum scan number, which is defines the maximum length of the chromatogram in terms of the scan numbers, while the minimum scan number (`edit box: Min scan`) is zero (default). The user can edit the maximum scan number to any other scan number, lower than the maximum possible scan number displayed and the minimum scan number to any number greater than zero and less than the maximum scan number. The load project (`button: Load project`) is used to load existing project. All the mass chromatogram files (*.cdf files are loaded), corresponding to the project is loaded. The mass chromatogram of the selected file can be displayed with the display chromatogram button. It should however, be noted that only after the pre-processing step: binning, the chromatogram

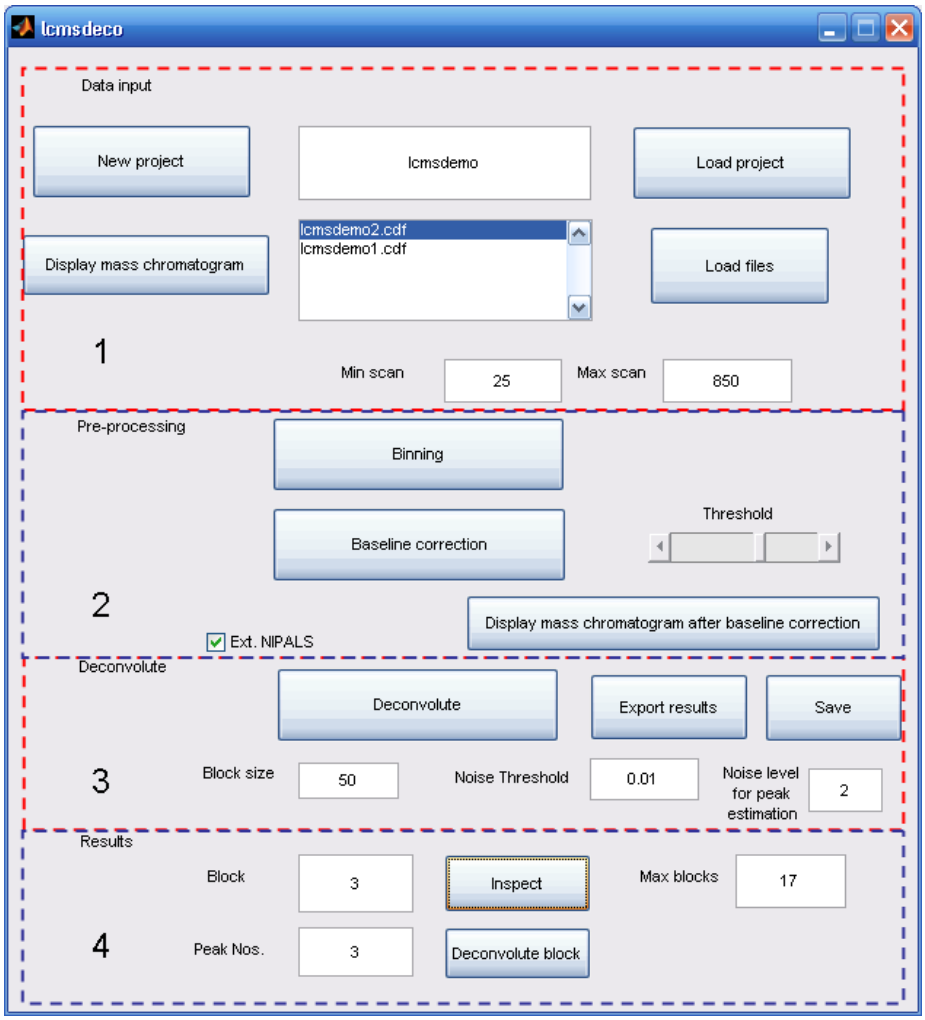

Figure 1: LC-MS TNO-DECO GUI

can be displayed. Hence, for the new project, until the binning is completed, the chromatogram cannot be displayed.

1.2 Pre-processing

For the new project, there are two pre-processing steps: binning and baseline correction. The binning (`button: Binning`), will perform multiple binning procedure over all chromatogram files, included in the project. Once the binning is completed, an estimate of threshold value will be automatically updated resulting the slider of the threshold to be initialize at a certain position. The user can perform a baseline correction with the estimated threshold or with a new threshold (`move the slider: threshold`) with the baseline correction button. The button, display chromatogram after baseline correction, can be used to view the mass chromatogram after baseline correction at the current threshold value (position). It should be noted that the baseline correction, takes into effect only if the baseline correction (`button: Baseline correction`), is clicked.

1.3 Deconvolute

Deconvolution (`button: Deconvolute`), deconvolute, performs multiple file deconvolution. There are two methods of deconvolution available, namely, the MCR-ALS, and the Ext. NIPALS (Extended NIPALS). The default deconvolution method is MCR-ALS. To perform deconcolution with Ext. NIPALS, the check box has to be active, i.e tick (`check box: Ext. NIPALS`). The other parameters to be filled or edited (to change from default values) are the `block size` that defines the deconvolution window size, the `Noise threshold` that defines the value below which signals are considered to be noise signals, the `noise level for peak estimation` that defines the level of noise to be injected to the model for estimating the number of components in the mass chromatogram window (block size). For first time users, the following values should provide a good start[1], Block size: 100, Noise Threshold: 0.01, Noise level for peak estimation: 2. The deconvoluted results of the project can be saved (button: Save) and the results exported (`button: Export results`) to an excel file.

1.4 Results

The deconvolution results can be inspected per block with the inspect (`button: Inspect`). The block number to be inspected has to be entered in the block edit window. The total number of blocks available for inspection is automatically updated in the max blocks window after deconvolution. The deconvolution results are displayed corresponding deconvolution method, the MCR-ALS or Ext. NIPALS, selected by the user. The concentration profile for the block all for all the files are displayed in a single window. The size of the concentration

[1]There are some known issues with convergence. Hence, please consult the remedy section of this document for work-around solutions

profile depends on the window size and the number of mass chromatogram files in the project. For example, if the block size was set to 100 and the number of mass chromatogram files were 3, the concentration profile window is of size 300. Each of the 100 (300/3) scan numbers, shows the concentration profiles of the metabolites in the respective 3 mass chromatogram files. It should be noted that the scan number is exact only for the first mass chromatogram file, while for the remaining it is relative to the other files. Hence in the above example, if the block was chosen from 200 to 300, the scan number for the first chromatogram file begins with 200 and ends with 300, while for the second, it begins with 300 and ends with 400 (actual scan number from mass chromatogram will be 200 to 300) and for the last it begins with 500 and ends with 600 (actual scan number from mass chromatogram will be 200 to 300). The mass spectrum for each metabolite found in the block will be displayed separately in another window.

The inspect button provides the deconvolution results for the the block the user has selected. The number of peaks estimated for that block is displayed in the peak numbers edit window (`Peak Nos.`). The user can over-ride the number of peaks estimated and can either increase or decrease the peak number and re-run the deconvolution for that block with the deconvolute block (`button: Deconvolute block`). The deconvolution is then performed for the chosen block with the user provided peak numbers.

A typical LC-MS, TNO-DECO (`lcmsdeco`), work-flow (`Nos. 1-15`) for deconvoluting multiple high resolution LCMS data is depicted in Figure 2.

2 Remedy

There are some known situations that can result in either non-stop run or failure while running the tool. These situation arise because at this time of tool development, suitable exit conditions with appropriate messages have not been included into the program. Future versions of the software will correct these known problems. Some of the situations are discussed and remedies for work-around solutions are provided.

2.1 Warnings

MATLAB issues lot of warnings during the tool run. Users may discard these warnings at this moment.

2.2 Non-stop run

Non-stop run is a situation in which the user will notice that the current deconvolution block does not stop to produce the completion message (message: Deconvolution completed). This can happen during the project deconvolution run (button: Deconvolution), where all blocks are deconvoluted one after another without user intervention (situation-1). This can also happen when the user initiates the deconvolution of the block (button: Deconvolution block) of

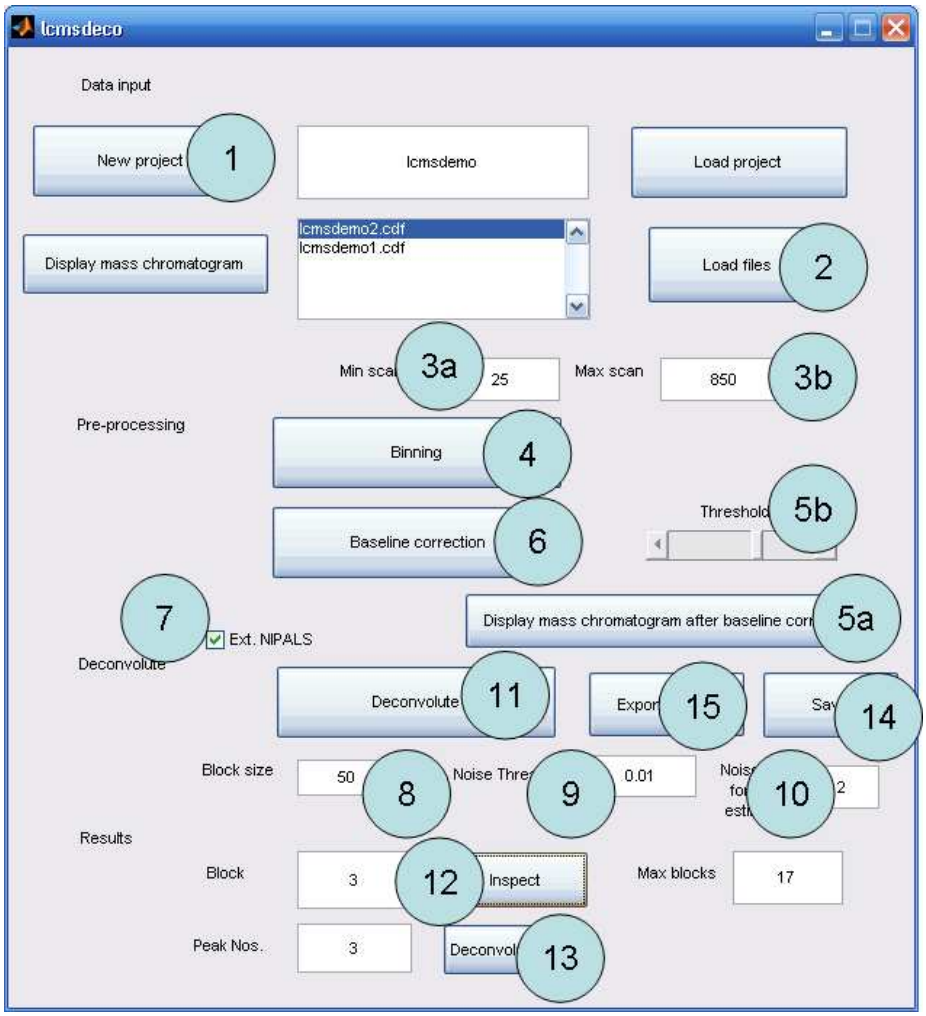

Figure 2: A typical LCMSDECO work-flow

his choice (situation-2). In both situations, the user will notice the following example of a no-stop message scrolling in the screen without any noticeable change.

```
Warning: Rank deficient, rank = 1,  tol =   4.1707e-015.
> In deco_als990>als99 at 67
  In deco_als990 at 18
  In deco_fixspectra at 19
  In deco_deconvoluteblock at 23
  In deco_deconvolutelcms at 31
  In lcmsdeco>deconvolution_Callback at 222
  In gui_mainfcn at 96
  In lcmsdeco at 42
  In @(hObject,eventdata)lcmsdeco('deconvolution_Callback',
  hObject,eventdata,guidata(hObject))
```

The following are the suggested actions and remedies to the known problem.

1. Exit the program. This can be done with close application button (X) available at the top-right corner of the command window.
2. Situation-1: Start the tool again (>> lcmsdeco) and load the project. Change the block size (edit box: block size) from the current value to either to a larger window size or a smaller size.
3. Situation-2: Start the tool again (>> lcmsdeco) and load the project. Change the peak number (edit Peak Nos.) to a value either higher or lower than the current value. In case the situation prevails, edit the noise threshold value (edit box: Noise Threshold) to suitable lower or higher values.

2.3 Failed run

Fail run is a situation in which the tool fails to proceed further and displays MATLAB specific fail messages. At this moment, only one fail situation is known. This situation happens when the user initiates the deconvolution of the block (button: Deconvolution block) of his choice. An example of this fail situation is as follows,

```
??? Index exceeds matrix dimensions.

Error in ==> deco_pcarep at 12
u=u(:,1:nf);
```

The following are the suggested actions and remedies to the known problem.

1. Deconvolute the block (button: Deconvolution block) with lower number of peaks (edit box: Peak Nos.) or noise threshold value (edit box: Noise Threshold) .