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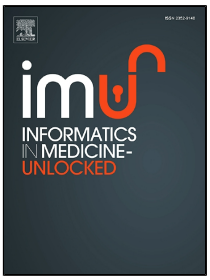

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SCSA based MATLAB pre-processing toolbox for ^{1}H MR spectroscopic water suppression and denoising

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Abstract

In vivo ^{1}H Magnetic Resonance Spectroscopy (MRS) is a useful tool in assessing neurological and metabolic disease, and to improve tumor treatment. Different pre-processing pipelines have been developed to obtain optimal results from the acquired data with sophisticated data fitting, peak suppression, and denoising protocols. We introduce a Semi-Classical Signal Analysis (SCSA) based Spectroscopy pre-processing toolbox for water suppression and data denoising, which allows researchers to perform water suppression using SCSA with phase correction and apodization filters and denoising of MRS data, and data fitting has been included as an additional feature, but it is not the main aim of the work. The fitting module can be passed on to other software. The toolbox is easy to install and to use: 1) import water unsuppressed MRS data acquired in Siemens, Philips and .mat file format and allow visualization of spectroscopy data, 2) allow pre-processing of single voxel and multi-voxel spectra, 3) perform water suppression and denoising using SCSA, 4) incorporate iterative nonlinear least squares fitting as an extra feature. This article provides information about how the above features have been included, along with details of the graphical user interface using these features in MATLAB. The code can be downloaded from https://github.com/EMANG-KAUST/GUI_spectroscopy.

Keywords

Eigenfunctions of the Schrödinger operator, magnetic resonance spectroscopy, water suppression, denoising, singular value decomposition, digital signal processing

Introduction

Magnetic Resonance Spectroscopy (MRS) aids in collecting *in vivo* tissue metabolite maps and provides quantification of metabolites for assessment of neurological and metabolic diseases. For quantification of the metabolites different fitting tools have been developed, e.g., LCModel [1], jMRUI [2], TARQUIN [3], ProFit [4], OXSA [5]. Before quantification of ^{1}H-MRS data, water suppression is usually performed using hardware based techniques like CHESS [6], WET [7], hyperbolic secant (HS) pulses [9] and variable power RF pulses with optimized relaxation (VAPOR) [8]. Different software based pre-processing techniques are further used for MRS data [10–16]. Pre-processing methods like the Hankel-Lanczos Singular Value Decomposition (HLSVD) [17] and the Hankel Lanczos squares Singular Values Decomposition with Partial Re-Orthogonalization (HLSVD-PRO) methods [17, 18] are widely used for residual water suppression in MRS data. Other methods like the Gabor transform [19, 20], Wavelet transform [19 - 22], the Fourier-based method [23], and FIR based filters (MP-FIR) [24], Advanced Method for Accurate, Robust, and Efficient Spectral fitting (AMARES) [25], Automated Quantization of Short Echo time MRS Spectra (AQSES) [26] and the semi-parametric approaches [27] are also used as water suppression filters in MRS data. *In vivo* MR spectroscopy may suffer from low signal-to-noise ratio (SNR). Therefore, many pre-processing methods were used for data denoising. These methods project the MRS data onto basis functions including Gabor [28], wavelets [29], singular value decomposition (SVD) based methods [30], [31] which have been proposed. These methods are effective in filtering noise from the signal without affecting the quantitative results. In this paper, we introduce the Semi Classical Signal Analysis (SCSA)-based MATLAB pre-processing toolbox to suppress residual water and denoise the ^{1}H MRS data. The SCSA algorithm uses squared eigenfunctions of the Schrödinger operator, which are very useful for the analysis of pulse shaped signals, as described in [32, 33]. The SCSA algorithm has been extended for denoising and residual water suppression of ^{1}H MRS/MRSI [34, 35]. The method has been tested and performs well to remove noise while preserving metabolites as compared to the SVD based method [34]. The method also provides similar performance in terms of water suppression when compared to the popular HLSVD-PRO method, but its main advantage is that it is a model-free method which works for any given shape of the residual water peak, in contrary to HLSVD, which relies on a model

function of the peak [35]. Considering all of the advantages and properties of the SCSA method as mentioned above, the algorithm is revalidated in this paper using *in vivo* data and presented in the form of a MATLAB toolbox. The toolbox is: 1. Easy to install and to use, 2. Loads water unsuppressed MRS data acquired in Siemens, Philips file format, and also from .mat files according to certain data structures, 3. Allows visualization of single voxel and multi-voxels MRS data in time and frequency domain, 4. Allows pre-processing of MRS data with phase correction (1st and 2nd order) and apodization, residual water suppression with SCSA and HLSVD-PRO and denoising using SCSA and SVD, and 5. Data fitting using the (AMARES), an advanced method for accurate, robust, and efficient spectral fitting, is included as an extra feature, but is not the main aim of the work.

Tool installation and dependencies

The SCSA-based MATLAB toolbox can be downloaded from https://github.com/EMANG-KAUST/GUI_spectroscopy. The toolbox is adapted for ^{1}H-MRS analysis. The toolbox, developed in the MATLAB platform, can be executed immediately after downloading. It includes a graphical user interface (GUI) that runs on Windows, Mac, and Linux systems, and has been tested on all MATLAB versions. A few additional requirements are the MATLAB Optimization and Signal Processing toolboxes. Reporting of bug-fixes for the toolbox can be done using GitHub's issue framework, which can be found at https://github.com/EMANG-KAUST/GUI_spectroscopy/issues. The downloaded zip file **"GUI_spectroscopy-master.zip"** needs to be extracted from the GitHub link and added as working directory in MATLAB. **"GUI_start"** should be typed in the command window of MATLAB. Then the GUI with the main window will appear on the screen. The flow diagram of the data processing unit is shown in Fig 1.

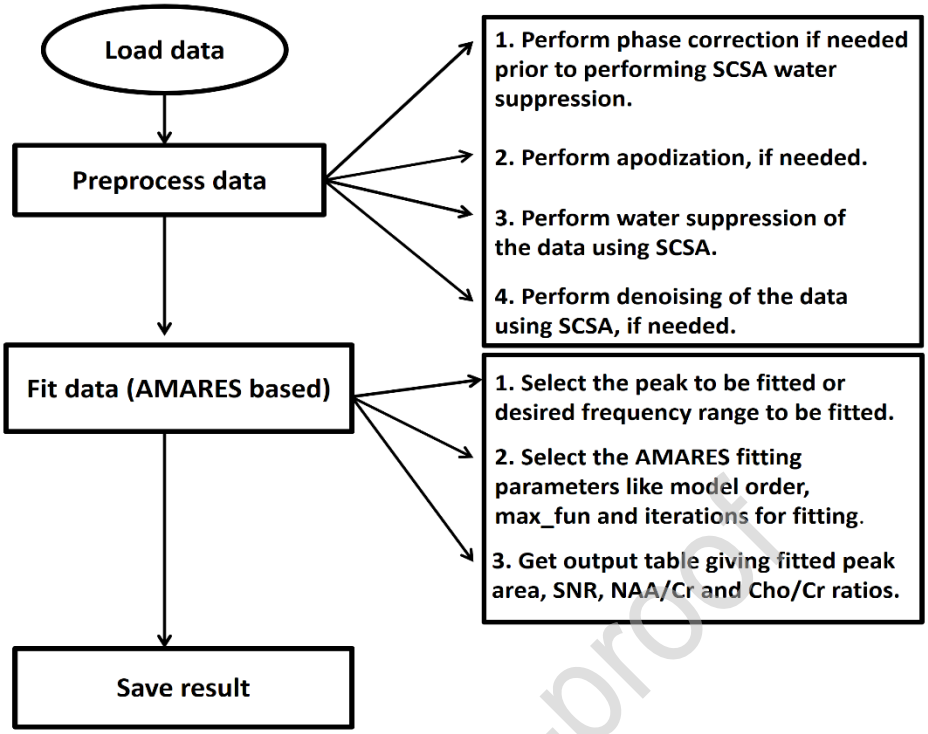

Fig 1. Flow diagram of data processing.

Importing data

This toolbox loads single voxel and multi voxel MRS data in Siemens .rda and DICOM file formats, Philips .sdat file format, and **.mat file** according to the following structure containing the variables **"complex_fid_unsuppressed"** being complex time domain single or multi voxel water unsuppressed signal, **"Fs"** being sampling frequency, and **"Tf"** being the transmitter frequency. The **"Load"** button should be clicked to load the data on the main window, shown in Fig 2. The files can be loaded from the **"Input_data"** folder corresponding to data (it can be single or multi voxel data).

Fig 2. Main GUI window.

Visualization of spectroscopy data

Spectroscopy data is visualized using the **"Preprocessing window"** and **"Fitting window"** of the GUI. The GUI works for single voxel or multi voxel ^{1}H spectroscopy data. After loading the data, the **"Preprocess"** button is activated in the main window and pressed for performing phase correction, apodization, water suppression and denoising, voxel wise. A **"Display window"** will open in parallel to the **"Preprocessing window"**. The display segment can be changed by changing the display ppm range in the **"Display Properties panel"** at the top of the **"Preprocessing window"**. The data can be displayed in the frequency domain by clicking on **"FD (real)"** for the real part, **"FD (abs)"** for the absolute part, **"FD (imag)"** for the imaginary part, and in the time domain by selecting **"TD"**. The default display range is **0.01** to **6.01** ppm, which can be changed as desired in the frequency domain. The same process can be done when the **"Fitting window"** is opened.

Pre-processing module

The **"Preprocessing window"** is shown in Fig 3. The **"Preprocessing window"** consists of a **"Display Properties panel"** discussed in the previous section. **"Zero-order phase correction"** can be used for zero-order phase correction by entering a value in the range –pi to pi or by sliding the cursor. **"First-order phase correction"** is for first-order phase correction by entering a value in the range –10 to 10 or by moving the slider inside the **"Phase correction panel"**. This can be done for individual voxels or all the voxels by clicking on the respective button in the button group inside the **"Display Properties panel"**. The **"Apodization panel"** performs apodization on the data with Exponential, Gaussian, Gaussian-Exponential and Sigmoid functions. Apodization values can be entered directly in Hz, or by using the slider. The **"Water suppress panel"** will suppress the water peak from the voxels using SCSA and HLSVD-PRO algorithms. Water suppression orders like the number of eigenfunctions for SCSA (default value: **17**) or model order for HLSVD-PRO (default value: **10**) can be entered directly, or the slider can be used. After adjusting the parameter, the **"Water suppress"** button inside the panel can be used to perform the water suppression using the desired method and parameter. The **"Denoise panel"** will perform data denoising using SCSA or the SVD based method. Denoising levels like h (default value: **1**) or model order for the SVD based method [30], [31] (default value: **3**) can be entered directly or the

slider can be used. After adjusting the parameter, the **"Denoise"** button inside the panel can be pressed to perform denoising using the selected method and parameter. Apodization, water suppression, and denoising operations can be done voxel-by-voxel, or with all the voxels, by clicking on the respective button in the button group inside the **"Display Properties panel"**. The **"Reload"** button at the top corner of the **"Preprocessing window"** can be used to reload the unsuppressed water data from the start to run the pre-processing again. Since the purpose of this toolbox is to perform the SCSA based pre-processing operation, the SCSA based algorithm for water suppression and denoising is briefly discussed in the next subsections. For comparison purposes, the SVD-based algorithm is also included in the toolbox, but will not be discussed as it is not the aim of the paper.

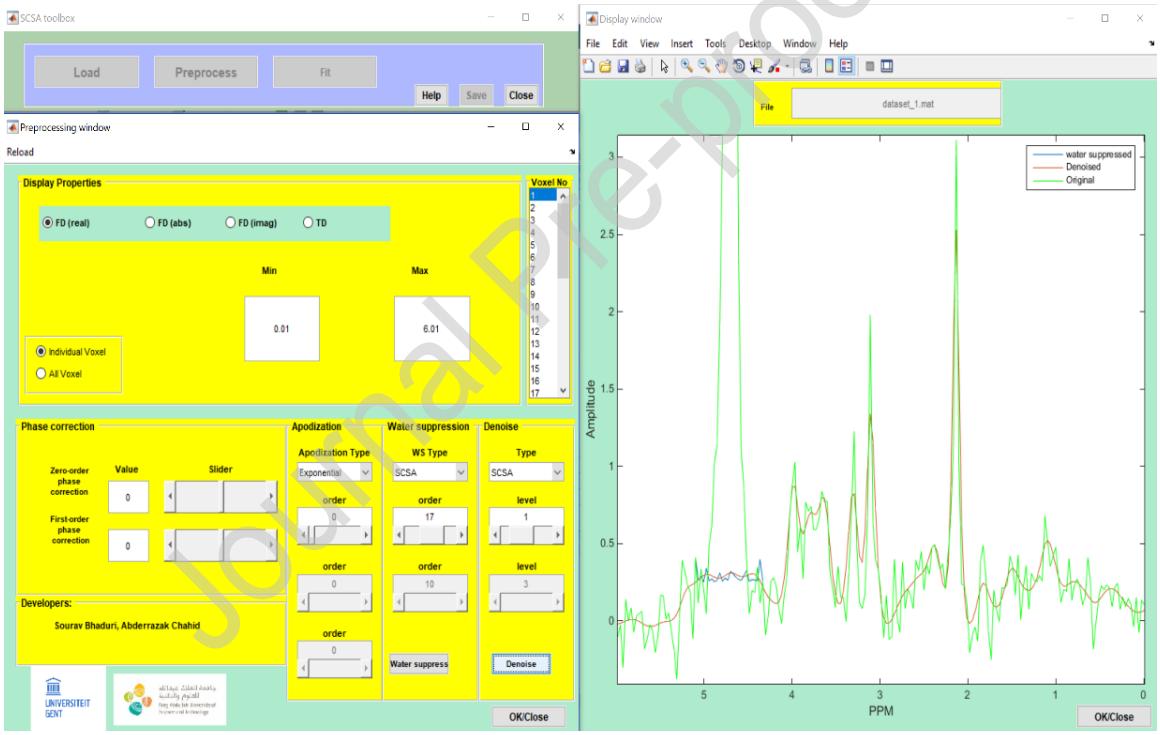

Fig 3. The "Preprocessing window" along with the "Display window" of the GUI. The figure shows the original spectrum (green) and the water suppressed spectrum (blue) and the denoised spectrum (red) in the "Display window" after the pre-processing operation.

SCSA method for signal reconstruction

The SCSA method is based on the use of the spectrum of a semi-classical Schrödinger operator $H(y)$ given by:

$$H(y) = -h^2\frac{d^2}{df^2} - y. \qquad (1)$$

The Schrödinger operator has been proposed for signal decomposition and representation in [32] and [33] where a real positive input signal $y(f)$ is approximated by $y_h(f)$ given by:

$$y_h(f) = 4h\sum_{n=1}^{N_h}\sqrt{(-\lambda_{nh})}\,\psi_{nh}^2(f), \qquad (2)$$

where $h \in R_+^*$, is called the semi-classical parameter and N_h represents the number of eigenfunctions. λ_{nh} are negative eigenvalues with $\lambda_{1h} < \lambda_{nh} < \ldots < 0$ and $\psi_{nh}(f)$ are the corresponding L^2-normalized eigenfunctions of the Schrödinger operator $H(y)$ such that :

$$H(y)\psi(f) = \lambda\ \psi(f). \qquad (3)$$

It is worth noting that the representation given by Eq.1 exactly reconstructs the signal when the semi-classical parameter h converges to a value of zero. Moreover, when the value of h decreases, the number of negative eigenvalues increases, improving the reconstruction (2) [32]. The algorithm below describes the SCSA based signal reconstruction.

- Input signal: $y(f)$
- Semi-classical parameter: h
- Output signal: $y_h(f)$
- **Step 1**: Discretize Eq.1.
- **Step 2**: Solve Eq. 3 to obtain the eigenvalues and their corresponding eigenfunctions.
- **Step3**: Select the negative eigenvalues and their corresponding eigenfunctions.
- **Step 4**: Use Eq.2 to reconstruct the output signal $y_h(f)$.

MRS spectrum denoising

The SCSA method exploits the spectral decomposition of the input signal, which helps in separating the noise, carried by the highly oscillating eigenfunctions, from the useful information in the MRS spectrum. Therefore, the denoising performance depends on the choice of the parameter h value, which produces eigenfunctions that capture perfectly the useful information in the MRS

spectrum [34]. The optimal value of h is defined by two criteria: first, maximizing the SNR value of the noisy part. Second, conserving the area under each metabolite peak illustrated in Fig 5 and formulated in Eq 4. The combination of these two criteria is illustrated in the cost function defined as follows:

$$\min_{h} \quad g(h) = \frac{\beta}{SNR_{y_h}} + \sum_{m=1}^{M} \xi_m(f) \, \|y_h(f) - y(f)\|_2^2 \tag{4}$$

$$\text{subject to} \quad h > 0$$

where

$$\xi_m(f) = \begin{cases} 1 & if \; f \in peak_m \\ 0 & elsewhere, \end{cases} \tag{5}$$

where y is the noisy MRS spectrum, and y_h is the denoised signal using the parameter value h. M is the number of metabolite peaks and SNR_{y_h} is the Signal-to-Noise Ratio (SNR) of the output signal computed deviation of the region determined by the "*Noise location*" as shown in the Fig 4. The SCSA is used to denoise the real part of the MRS spectrum using an optimal value of h . The optimal choice of h ensures the preservation of the metabolite area, determined by Metabolite peaks location. Therefore, it helps in removing as much as possible the noise from the noisy region. The tool allows the user tuning the denoising parameter h to achieve a satisfactory denoising level as shown in Fig 5.

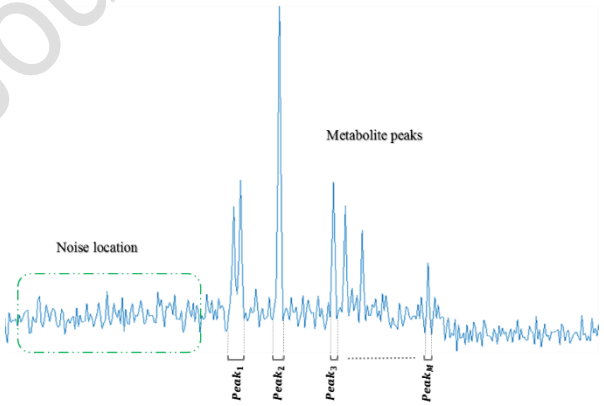

Fig 4. Determination of the metabolite peaks and noise location used in the minimization problem.

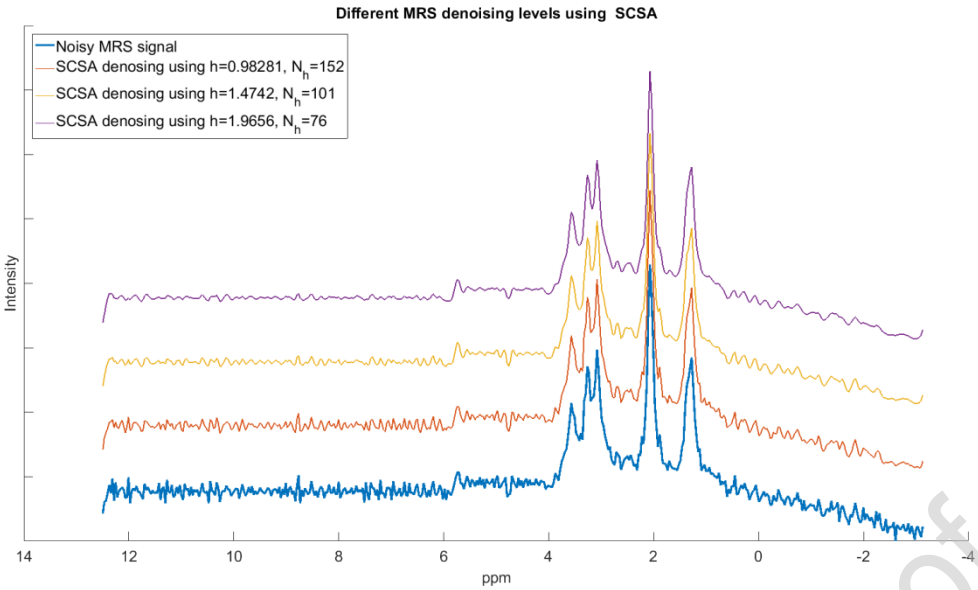

Fig 5. Different denoising levels using SCSA denoising method.

MRS water suppression

The Semi-Classical Signal Analysis (SCSA) method, is used for water suppression, utilizing the real part of the MRS spectrum. It reconstructs the water peak with a certain number of eigenfunctions determined by the optimum value of the semi-classical parameter h [35]. The SCSA reconstructs the input signal with water peak using N_{wp} number of eigenfunctions, where $N_{wp} < \frac{N}{140}$, N being the length of the input spectra [34]. The algorithm below describes the main steps of the MRS water suppression using the SCSA method.

- Input: MRS spectrum $y(f)$
- parameters: N_{wp}
- Output: Suppressed water MRS signal $\hat{y}(f)$
- **Step 1**: Water peak $y_p(f)$ estimation using N_{wp} negative eigenvalues/eigenfunctions.
- **Step 2**: Water peak refinement $\hat{y}_p(f)$ by choosing the eigenfunctions, which contribute to the water peak and do not affect the metabolites.
- **Step 3**: water peak suppression: $\hat{y}(f) = y(f) - \hat{y}_p(f)$
- **Step 4**: Reducing the water residue of $\hat{y}(f)$ by applying the SCSA, only on the water residue part, in a closed loop till achieving the desired reduction.

Fig 6 shows an example of water suppression results. The tool allows the user to tune the number of eigenfunctions, called model order N_{wp} , used for water peak estimation.

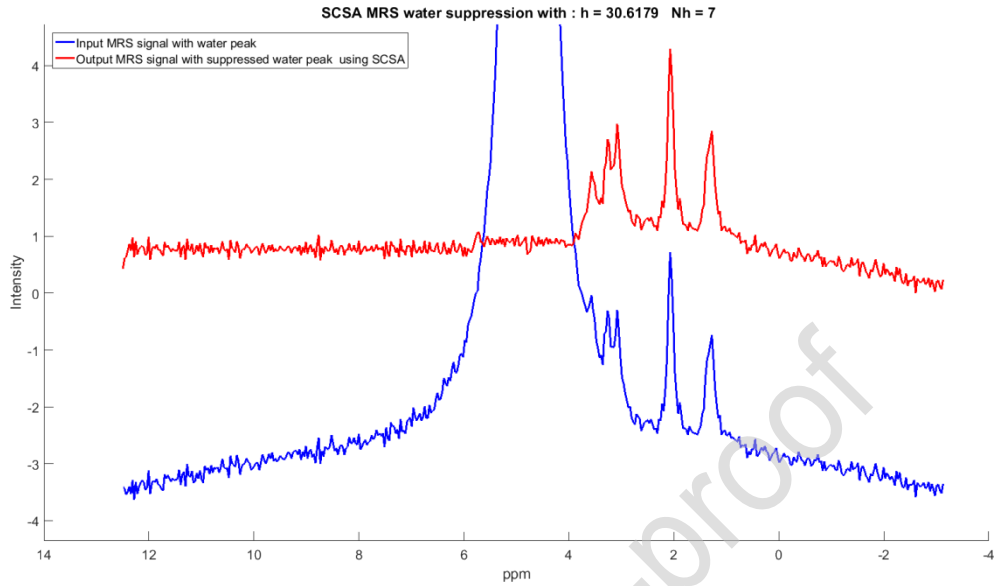

Fig 6. Water suppression using SCSA.

Fitting module (Additional feature for validation)

The advanced method for accurate, robust and efficient spectral fitting (AMARES) [25], which is a time-domain fitting algorithm incorporating prior knowledge, has been used in the toolbox. Our fitting module comprises of initial peak information estimation using the HLSVD-PRO algorithm [17,18] for estimating the peak amplitudes, damping factors, and frequencies which are optimized further using the AMARES algorithm with non-linear least square time domain fitting. The fitting model for the AMARES can be changed between Lorentz, Gauss, and Voigt. The **"Fitting window"** is shown in Fig 7. Inside the **"Fitting range panel"** in Fig 7, the desired start and end frequency of the peaks to be fitted can be given and input model order (**"order"**) for the initial HLSVD-PRO fitting is set to **15** as the default value. For the AMARES algorithm, the defaults value for the maximum number of function evaluations (**"max_fun"**) is set to **50,** and the default number of iterations (**"iterations"**) is set to **50**. These values can be changed in the **"Fitting range panel"**. The peak to be fitted can be set in the **"Metabolite panel"** where the **"Metabolite Type"** can be set between NAA, Lactate, Creatine, Choline, Myo, the default being NAA. The peak can also be selected inside the **"Fitting range panel"** by putting the desired start and end

frequency range in ppm. The fitting model of the peak can be selected inside the **"Metabolite panel"** where the **"Fitting Model"** can be set between Lorentz, Gauss, and Voigt, the default being Lorentz. Finally, the fitting can be performed by clicking on the **"Fit button"** inside the **"Fitting range panel"**. The user will be asked to wait until the fitting is completed and after the fitting operation, the output variables of interest (fitted peak area, SNR, NAA/Cr and Cho/Cr, error in fitting (Cramér-Rao bound in % of quantified peak amplitude)) will be generated in the first five columns of a table right beside the **"Metabolite panel"**.

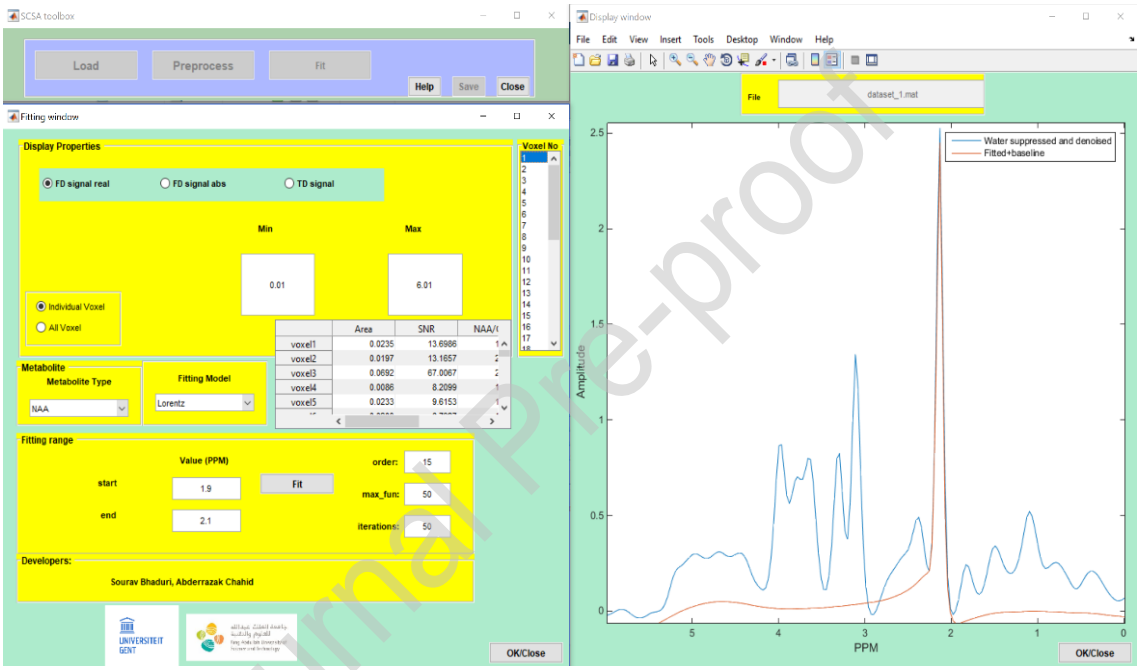

Fig 7. "Fitting window" along with the "Display window" of the GUI. The figure shows the denoised spectrum (blue) and fitted peak (red) in the spectrum in the "Display window" along with the output table inside the "Fitting window" after the fitting operation.

Output module

After fitting, the **"save"** button will be activated in the main window to save the fitting results in a **.mat** format. The output file will be created as the **"main file name_output.mat**" in the **"Output_data"** folder. The output global variables of interest are the following: **"data_value.FID_TD"** - Time domain output water suppressed and denoised signal, **"data_value.FID_FD"** - Frequency domain output water suppressed and denoised signal, **"data_value.fit_TD"** - Time domain output fitted water suppressed and denoised signal,

"data_value.fit_FD" - Frequency domain output fitted water suppressed and denoised signal, **"data_value.peak_area"** - fitted peak areas, **"data_value.snr"** - output SNR, **"data_value.NAA_Cr"** - NAA/Cr ratio, **"data_value.Cho_Cr"** - Cho/Cr ratio. For extracting the values mentioned above, global variable **data_value** can be accessed via command window in MATLAB. An output excel file will be created as the **"main file name_output.csv**". The output variables of interest (fitted peak area, SNR, NAA/Cr, Cho/Cr, and error in fitting (Cramér-Rao bound in percentage of quantified peak amplitude)) will be stored in the first five columns of the excel file. For analyzing another data **"Load button"** needs to be clicked again. A new data can be loaded or previously saved data can also be loaded to do a reprocessing or further processing.

Results

Our toolbox is a MRS data pre-processing toolbox, which uses the SCSA [32] algorithm for residual water suppression and denoising instead of the HLSVD-PRO [17,18] algorithm which is used in other popular tools like jMRUI [2], TARQUIN [3]. However, we have compared our tool with the HLSVD-PRO (used in jMRUI [2], TARQUIN [3] packages) for validation purposes. Two *in vivo* datasets (dataset 1 and dataset 2, also provided along with the toolbox) are used. The first one is 2D MRSI data with a resolution of 16×16, obtained using the Chemical Shift Imaging sequence from ten healthy volunteers with echo time of 35 ms, repetition time of 2 s, a field of view of 100 (AP) ×100 (RL) mm^2, ADC bandwidth of 2000 Hz with 512 acquired data points, No. of averages (NEX) being 2. Forty *in vivo* MRS spectra, selected from the dataset containing data from four voxels (two from the center and two at the edges of FOV) across all the ten volunteers is used for the validation of SCSA as a water suppression algorithm and evaluate its performance with respect to HLSVD-PRO. The second dataset contains single voxel water suppressed *in* vivo MR spectroscopy data from the frontal lobe region of a healthy volunteer, using the same echo and repetition time as above, ADC bandwidth of 2500 Hz with 1024 acquired data points. The voxel dimensions are 20 × 20 × 20 mm^3. NEX ranges from 2 to 16. This dataset is used for validating the SCSA based denoising algorithm and its performance with respect to the SVD based denoising [30], [31]. All these datasets are collected from a 3T Siemens research scanner at Ghent University Hospital. This validation study was approved by the Ethical Committee of the Ghent University Hospital. In Fig 8, the absorption spectrum after phase correction containing big water signal from the first dataset is shown; the SCSA based water suppression result on the spectrum of Fig 8a is

shown in Fig 8b. Similarly, the HLSVD-PRO based water suppression result is shown in Fig 8c. NAA/Cr and Cho/Cr ratios computed using the AMARES fitting from the first dataset for the SCSA and HLSVD-PRO methods are displayed in the boxplot in Fig 8d and Fig 8e, respectively. The number of eigenfunctions for SCSA was chosen to be **13** and model order parameter for HLSVD-PRO was chosen to be **10**. This model order provided optimum residual water suppression [36]. From all these figures, it can be seen that the performances of both methods are similar in terms of residual water suppression. The calculated metabolites ratios are also found to be in accordance with the literature [37]. For the validation of the noise algorithm, the second dataset (water suppressed using SCSA) is denoised using both SCSA (with denoising parameter = **1.6**) and SVD (with denoising parameter=**3**) (Fig 9) and then quantified using AMARES fitting. The computed NAA/Cr and Cho/Cr ratios along with the SNR (calculated as the ratio of NAA peak area and noise standard deviation) before and after denoising are reported in Table 1. It can be seen that the SCSA achieves an efficient MRS signal denoising while preserving the metabolite peaks when compared with the SVD results. It is to be noted that the SCSA algorithm for water suppression and denoising has already been validated in previous published papers, where different signal types including simulated data under different noise conditions, *in vitro* and *in vivo* data were considered to check the efficiency of the method [34, 35]. In this paper, we re-validated the algorithm in the form of a MATLAB toolbox with two different sets of *in vivo* data made available freely to the users to further investigate the method. The *in vivo* datasets present a more realistic scenario in terms of metabolite peaks and spectral/spatial features to perform the validation.

Table 1: *In vivo* dataset 2 result table showing the SNR values and metabolite ratios before and after using denoising using both SCSA and SVD.

	SNR			NAA/Cr			Cho/Cr		
	Before	After SCSA	After SVD	Before	After SCSA	After SVD	Before	After SCSA	After SVD
NEX=2	6	19	14	1.37	1.39	1.34	0.95	0.93	0.95
NEX=4	9	23	21	1.37	1.31	1.27	0.95	0.94	0.95
NEX=8	15	87	46	1.39	1.35	1.33	0.91	0.91	0.94
NEX=16	23	97	50	1.4	1.38	1.33	0.91	0.91	0.93

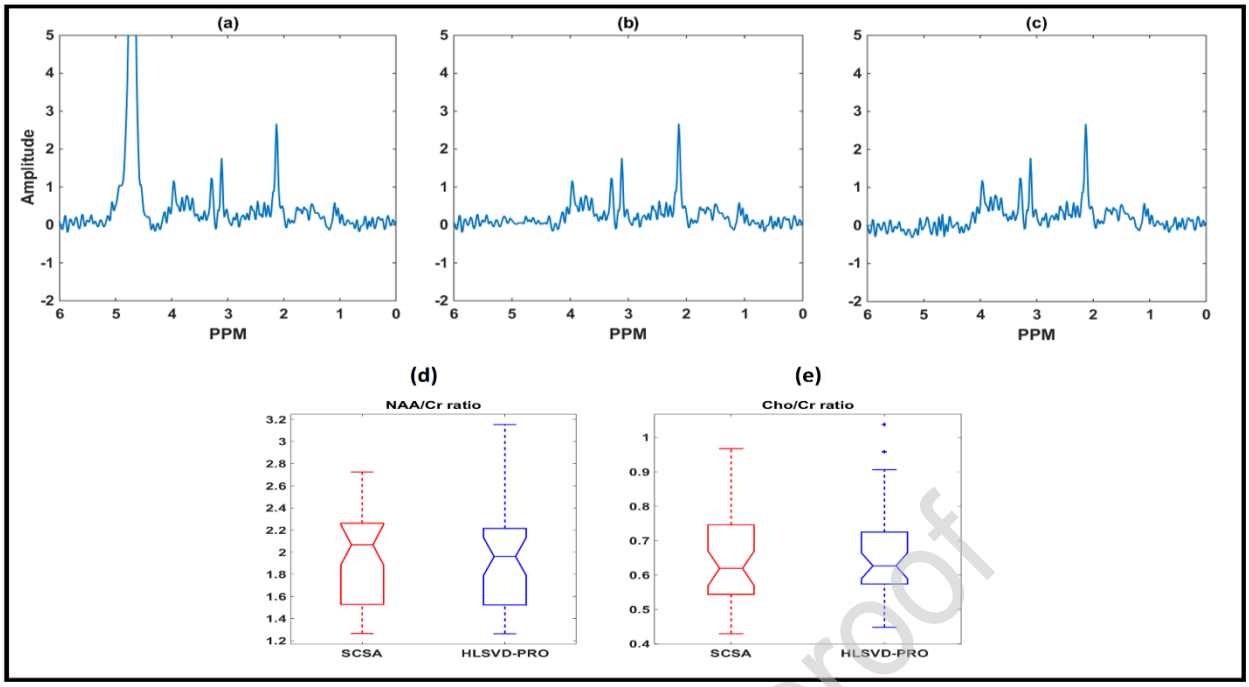

Fig 8. ***In vivo*** **dataset 1 water suppression results. Results are evaluated using selected 40 MRS spectra.**

(a) Absorption spectrum after phase correction with big water signal from dataset 1. The SCSA based residual water suppression result on the spectrum of Fig (a) is shown in blue in Fig (b). Similarly, the HLSVD-PRO based residual water suppression result is shown in blue in Fig (c). NAA/Cr metabolite ratio after residual water removal using SCSA (red) and HLSVD-PRO (blue) in Fig (d) and Cho/Cr metabolite ratio in Fig (e).

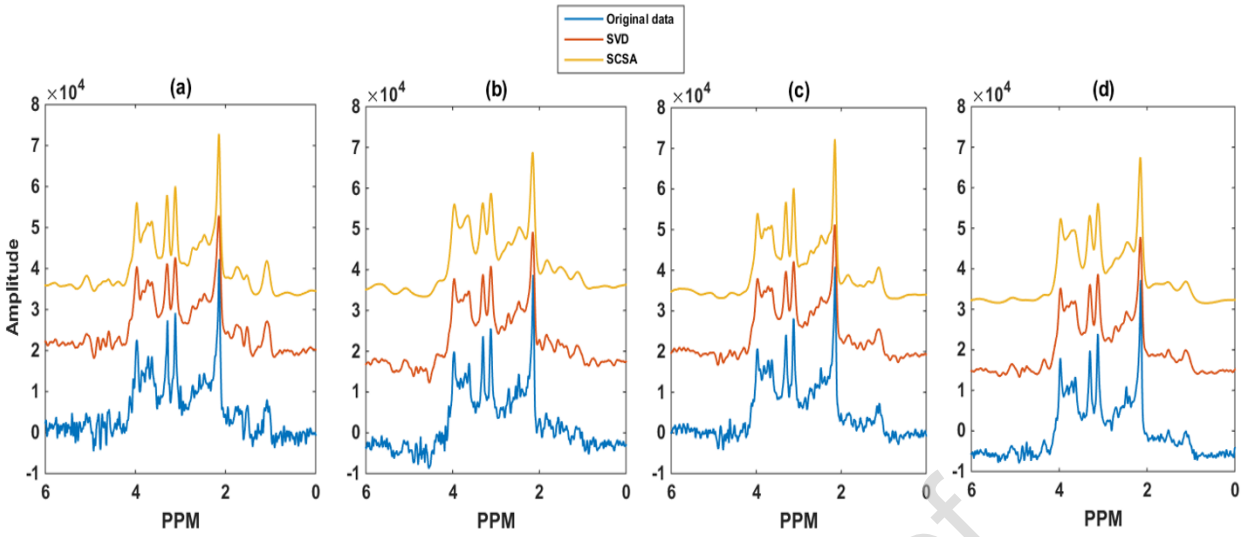

Fig 9. *In vivo* dataset 2 denoising results.

(a) The original data before denoising with (NEX=2), SCSA and HLSVD-PRO denoised spectra, (b) original data before denoising with (NEX=4), SCSA and HLSVD-PRO denoised spectra, (c) original data before denoising with (NEX=8), SCSA and HLSVD-PRO denoised spectra, (d) original data before denoising with (NEX=16), SCSA and HLSVD-PRO denoised spectra.

Discussion

In previous papers [34, 35], the application and development of the SCSA algorithm for the purpose of ^{1}H MRS water suppression and denoising were explained separately along with the results obtained using *in vivo* data. But in this paper, the two algorithms were applied simultaneously on new *in vivo* datasets using a newly developed user interactive toolbox, incorporating the above mentioned algorithms along with some additional features for data processing. In this work, we showed that SCSA based water suppression and denoising algorithms applied together using this toolbox, suppressed the water peak efficiently and enhanced the SNR at the same time, while preserving the metabolite information. Data fitting and quantification have been included as an extra feature in this toolbox but can be performed by other sophisticated toolboxes or software by arranging the output variables generated from our toolbox into the specific format required by other software. Toolboxes like ProFit [4], OXSA [5] can provide very good prior-knowledge based fitting results with ^{1}H MRS/MRSI data. The recently developed OXSA [5] toolbox uses the (AMARES) [25] algorithm for the purpose of data fitting. However,

these toolboxes do not provide dedicated pre-processing features like manual phase correction, apodization, residual water suppression and denoising, but are only dedicated towards data fitting and quantification. The main focus of our work is not fitting, but to provide an open source user interactive platform for ^{1}H MRS data pre-processing. Most of the popular open source software packages like jMRUI [2], TARQUIN [3] utilize the HLSVD-PRO algorithm [17,18] to perform water suppression and SVD/Cadzow based denoising [30], [31], [38]. Thus for comparison purposes, instead of loading the data in those software, we incorporated the HLSVD-PRO and SVD based denoising in our toolbox to make a direct comparison and validation of the SCSA. The users can also pre-process their data with these algorithms using our toolbox for comparison purposes. It permits the users to specify pre-processing parameters at each stage and test the performance of different algorithms on their data in order to choose the best suited pre-processing pipeline. But the main objective of the work is to introduce the SCSA pre-processing algorithm, to showcase its effectiveness in ^{1}H MRS/MRSI water suppression and denoising. jMRUI software uses a Java-based graphical user interface (GUI) to analyze the time-domain MRS data and runs on PCs with Windows, Linux and Unix platforms. In comparison to LCModel software [1], jMRUI requires user interaction and processes the time-domain MRS/MRSI (^{1}H) single voxel and multiple voxel data [2]. The LCModel on the other hand, is a non-iterative, automatic, commercial software for ^{1}H MRS data analysis in the frequency domain with minimal user input [1], run in the Unix environment. The newly proposed toolbox can also be applied to single and multi-voxel ^{1}H MRS/MRSI data and can be run on PCs with Windows, Mac and Linux platforms. Like jMRUI, this toolbox is user interactive and also processes the time domain data with HLSVD-PRO based water suppression, SVD/Cadzow based denoising and AMARES based fitting. But, the SCSA algorithm based water suppression and denoising is applied on frequency domain data. Hence the toolbox operates in both time domain and frequency domain modes. The GUI must be run in MATLAB with the signal processing and optimization toolboxes. Data in Siemens, Philips file format and .mat files can be loaded and processed. The toolbox allows the visualization of a localized single and multi-voxel MRS data. In this implementation, pre-processing methods based on SCSA and SVD algorithms to perform water suppression and denoising along with phase correction and apodization were used. From the validation section, it can be seen that the SCSA performs comparably to HLSVD-PRO based residual water suppression (used in jMRUI [2], TARQUIN [3] packages) with superior performance in terms of denoising as compared to the SVD

where it effectively reduces the noise in the MRS data while preserving the metabolite peaks. The SCSA algorithm for water suppression and denoising has been validated before in previous published papers, where simulated data with different SNR values, *in vitro* and *in vivo* ^{1}H MRS/MRSI data were considered to check the efficiency of the method [34, 35]. The algorithm was revalidated in this paper in the form of a MATLAB toolbox with two different sets of *in vivo* data made available freely to the users. We chose the *in vivo* data because it presents realistic metabolite peak shapes and spectral/spatial artifacts to be considered while performing the validation. All the datasets used for the validation have been included in the package.

Conclusion

An ergonomic user interactive toolbox is developed to visualize and pre-process single or multi-voxel ^{1}H MR spectroscopy data in MATLAB. Many features are embedded in this toolbox: MRS visualization, phase correction and apodization, SCSA and HLSVD based residual water suppression, SCSA based denoising, fitting pipeline based on the AMARES algorithm (as extra feature). This toolbox will help researchers pre-process MRS data using the SCSA toolbox and export the results.

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Conflict of interest statement: Manuscript "SCSA based MATLAB pre-processing toolbox for 1H MR spectroscopic water suppression and denoising"

No conflict of interest exists in the submission of this manuscript and the manuscript is approved for publication by all authors. The work described has not been published elsewhere.

Highlights: Manuscript "SCSA based MATLAB pre-processing toolbox for 1H MR spectroscopic water suppression and denoising"

1. A new Semi-Classical Signal Analysis based Spectroscopy pre-processing toolbox is proposed.
2. The toolbox allows for the MRS water suppression and data denoising.
3. The installation and use of the proposed toolbox are explained.
4. Details of the graphical user interface of the toolbox in MATLAB is also provided.