frontiers | Frontiers in Neuroimaging

TYPE Methods
PUBLISHED 18 July 2025
DOI 10.3389/fnimg.2025.1610658

OPEN ACCESS

EDITED BY
Yuhei Takado,
National Institutes for Quantum and Radiological Science and Technology (Japan), Japan

REVIEWED BY
Marcos Brioschi,
University of São Paulo, Brazil
Helge Jörn Zöllner,
Johns Hopkins Medicine, United States

*CORRESPONDENCE
Lijing Xin
✉ lijing.xin@epfl.ch

†These authors have contributed equally to this work

RECEIVED 12 April 2025
ACCEPTED 02 July 2025
PUBLISHED 18 July 2025

CITATION
Xiao Y, Kaiser A, Kockisch M, Back A, Carlet R, Liu X, Huang Z, Döring A, Widmaier M and Xin L (2025) A graphical pipeline platform for MRS data processing and analysis: MRSpecLAB.
Front. Neuroimaging 4:1610658.
doi: 10.3389/fnimg.2025.1610658

A graphical pipeline platform for MRS data processing and analysis: MRSpecLAB

Ying Xiao[1,2†], Antonia Kaiser[1†], Matthias Kockisch[1], Alex Back[3], Robin Carlet[1], Xinyu Liu[1,2], Zhiwei Huang[1], André Döring[1], Mark Widmaier[1] and Lijing Xin[1*]

[1]CIBM Center for Biomedical Imaging, Ecole Polytechnique Fédérale de Lausanne, Lausanne, Switzerland, [2]Laboratory for Functional and Metabolic Imaging, Ecole Polytechnique Fédérale de Lausanne, Lausanne, Switzerland, [3]Department of Physics, KTH Royal Institute of Technology, Stockholm, Sweden

Magnetic resonance spectroscopy (MRS) and magnetic resonance spectroscopic imaging (MRSI), are non-invasive techniques used to quantify biochemical compounds in tissue, such as choline, creatine, glutamate, glutamine, γ-aminobutyric acid, N-acetylaspartate, etc. However, reliable quantification of MRS and MRSI data is challenging due to the complex processing steps involved, often requiring advanced expertise. Existing data processing software solutions often demand MRS expertise or coding knowledge, presenting a steep learning curve for novel users. Mastering these tools typically requires a long training time, which can be a barrier for users with limited technical backgrounds. To address these challenges and create a tool that serves researchers using MRS/MRSI with a broad range of backgrounds, we developed MRSpecLAB—an open-access, user-friendly software platform for MRS and MRSI data analysis. MRSpecLAB is designed for easy installation and features an intuitive graphical pipeline editor that supports both predefined and customizable workflows. It also serves as a platform offering standardized pipelines while allowing users to integrate in-house functions for additional flexibility. Importantly, MRSpecLAB is envisioned as an open platform beyond the MRS community, bridging the gap between technical experts and practitioners. It facilitates contributions, collaboration, and the sharing of data workflows and processing methodologies for diverse MRS/MRSI applications, supporting reproducibility practices.

KEYWORDS

MRS/MRSI, 1H, X-nuclei, data processing, visualization, spectroscopy, fMRS, software tool

1 Introduction

Magnetic resonance spectroscopy (MRS) and magnetic resonance spectroscopic imaging (MRSI), are non-invasive techniques for quantifying biochemical compounds in tissues, widely used to study neurochemicals such as choline, creatine, glutamate, glutamine, γ-aminobutyric acid, N-acetylaspartate, etc. (Öz and Tkáč, 2010; Terpstra et al., 2016). ^{1}H MRS and MRSI are commonly applied (McBride et al., 1995), and advances in hardware and acquisition methods have expanded MRS applications beyond ^{1}H to include other nuclei such as deuterium (^{2}H) (Zhu et al., 2018), carbon (^{13}C) (Rothman et al., 2011; Rothman et al., 2019; Ziegs et al., 2023), and phosphorus (^{31}P) (Ren et al., 2015; Blüml et al., 1999). These innovations enable the exploration of molecular dynamics and have increased the applicability of MRS/MRSI in studying brain disorders (Martin, 2007), including epilepsy (Connelly et al., 1998),

stroke (Barker et al., 1994), Alzheimer's disease (Tedeschi et al., 1996; Schuff et al., 1997), and tumors (Negendank, 1992; Horská and Barker, 2010).

However, accurate quantification of MRS and MRSI data is not straightforward as multiple spectral preprocessing steps are required to generate high-quality, analyzable spectra (Marjańska et al., 2022). These steps generally include coil combination, frequency and phase correction, eddy current correction, removal of outlier spectra, apodization, and zero filling, etc. (Near et al., 2021). Each of these steps are essential for optimizing the SNR, minimizing artifacts and contaminations, and ensuring reliable and reproducible quantifications. Moreover, the preprocessing workflow is not uniform; different datasets, experimental setups, and applications may require specific adjustments and tailored preprocessing steps to address their unique characteristics. This variability adds to the technical complexity, making high-quality spectral processing a non-trivial task, and often requiring advanced expertise, specialized training, and in-depth knowledge of MRS principles.

Several well-established tools in the MRS community, such as FID-A (Simpson et al., 2017), FSL-MRS (Clarke et al., 2021), INSPECTOR (Gajdošík et al., 2021), Tarquin (Wilson et al., 2010), Osprey (Oeltzschner et al., 2020), and more, provide robust support for MRS data simulation, processing, and quantification. An overview and comparison of common MRS/MRSI software tools can be found in the Supplementary Section 1. These tools have significantly advanced the MRS field by offering reliable workflows and complete algorithms for spectral analysis. However, many of them are designed for in-depth analysis for users with significant knowledge about MRS data processing. For instance, the lack of intuitive graphical user interfaces (GUI) in some tools makes them less approachable, as they often rely on command-line operations or coding. Especially, a GUI-based pipeline editor is currently lacking, which would enable users to create processing workflows without requiring extensive programming skills. Additionally, some are MATLAB-based, requiring paid licenses, which may not be accessible to all users. Moreover, the setup and configuration process for some of the software or toolboxes can be time-consuming and may require users to have in-depth knowledge of their computer systems. Furthermore, most tools are designed for processing ^{1}H MRS data, and provide limited support for X-nuclei data. As MRS expands to include a broader range of nuclei and applications, the demand for software capable of handling these data types efficiently has grown, highlighting the need for more versatile, accessible, and collaborative solutions, especially for clinical applications.

To address these needs and facilitate the application of advanced MRS and MRSI techniques for clinical neuroscientists, we developed MRSpecLAB, an open-access, user-friendly, and collaborative software platform that can accommodate diverse datasets, minimize technical barriers for the wider community beyond the current MRS specialists, and facilitate the seamless sharing of functionalities and workflows in a straight-forward, plug and play manner. MRSpecLAB offers:

1 User-friendly GUI design: An intuitive graphical user interface, including a graphic pipeline editor, enables drag-and-drop workflow creation.
2 Platform character: The modular coding structure enables the straightforward development of new data processing nodes with minimal programming expertise. The customer nodes can be easily integrated into the pipeline and shared with the community.
3 Efficiency: Batch processing supports rapid, reproducible analysis of large datasets, ideal for cohort studies.
4 Open source: Free to use, with available source code to encourage community contributions.
5 Comprehensive functionality: Supports various input formats from different vendors, different sequences, X-nuclei, and MRSI.

2 Methods

MRSpecLAB was developed using Python 3 (RRID: SCR_008394), using free toolkits and libraries such as wxPython (Talbot, 2000), matplotlib (Hunter, 2007), pandas (McKinney, 2011), gswidgetkit (Sherman, n.d.), gsnodegraph (Clarke et al., 2022), suspect (Rowland et al., 2017), pyMapVBVD (pyMapVBVD CIC Methods Group, n.d.), etc. LCModel (Provencher, 2001) (RRID: SCR_014455), a widely recognized gold standard linear combination method in the MRS field for accurate metabolite quantification (Near et al., 2021), was integrated as the default fitting method to quantify metabolites. MRSpecLAB is freely available at https://github.com/MRSEPFL/MRSpecLAB, offered as both precompiled executables for Windows and Linux (via the GitHub releases) and as open-source Python code for integration into custom environments. More information about how to use the platform can be found in the user manual on GitHub: https://github.com/MRSEPFL/MRSpecLAB/blob/main/MANUAL.md.

To facilitate community-driven development, we have implemented structured issue templates on GitHub for reporting bugs and submitting feature requests. Additionally, a dedicated MRSpecLAB discussion forum will be launched on MRSHub to support user interaction, pipeline sharing, and collaborative problem-solving.

2.1 User interface

MRSpecLAB features an intuitive graphic interface designed to largely simplify the data analysis procedures for users of all expertise levels. Figure 1 provides an overview of the main window of the software:

The MRSpecLAB interface consists of several key components:

- A file import panel on the left side of the window for data input. Data can either be browsed through clicking the '+' button, or by dragging and dropping the files into the panel;
- A function button bar at the top, providing quick access to essential tools like data saving, pipeline execution, and plotting:
  - o Open the output directory;
  - o Open or change the processing pipeline in the pipeline editor;
  - o Two tick boxes for saving intermediate plots and numerical data per processing step;
  - o Change the directory of the output files;
  - o Fitting options for user defined basis sets, control files, and tissue segmentation files;
  - o Show debug options, with a tick box to save error log information;
  - o Batch mode setting;
  - o Two running modes: single arrow - run the pipeline step-by-step: double arrows - run the pipeline until the end (no in-between plots shown);
  - o Stop button to stop any ongoing process;
  - o Plotting button to set the display options for MRSI maps.

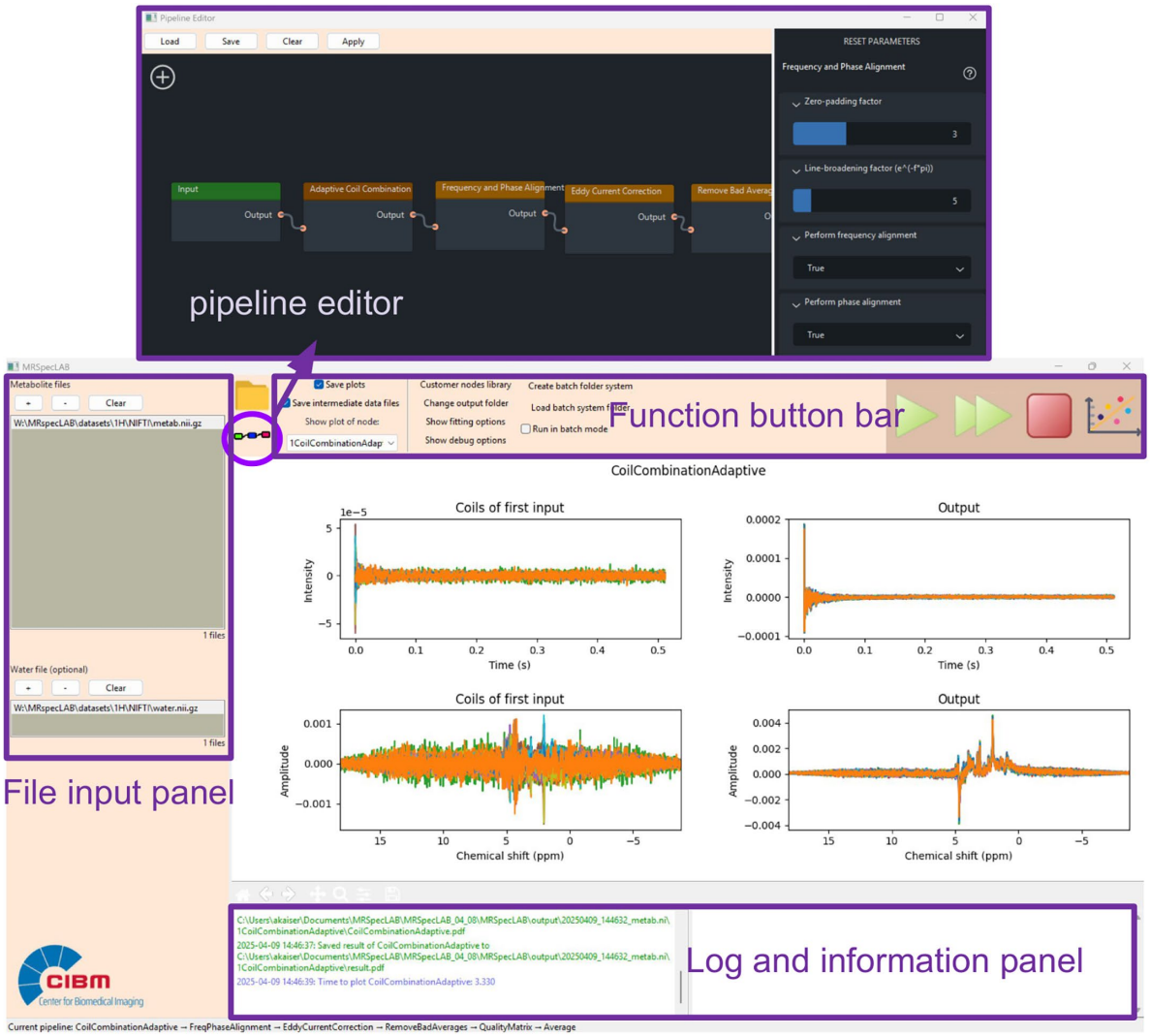

FIGURE 1
MRSpecLAB user interface, consisting of the file import panel (left), function button bar (top), the main plot panel (center), and information panels (bottom), as well as the pipeline editor (the floating window).

- A central plot panel where users can view the imported data, intermediate processed plots, fitted spectra, and metabolite maps;
- Two information panels: the bottom-left corner shows real-time updates on processing progress, while the bottom-right corner displays the quantification results extracted from the LCModel coordinate file (.COORD, a text file containing the coordinates of all fitting curves), including quantification results, SNR, and full width at half maximum (FWHM).

The graphic pipeline editor can be accessed from the function button bar, provides users with a fast and intuitive drag-and-drop functionality to build or customize their spectral processing pipelines. By clicking the "+" button within the editor, users can access a library of predefined processing functions (called "nodes" in the following) in the workflow. These nodes can be arranged in any desired order, by dropping them on the canvas and connecting them with already existing nodes. Each node in the pipeline corresponds to a specific processing step. Users can adjust the parameters of each node via the options panel on the right by clicking on the node. The pipeline can be saved as a .pipe file with the "save" button, shared, or stored for future reference, and consequently loaded into the pipeline editor with the "load" button.

2.2 Data workflow

MRSpecLAB can process MRS and MRSI data in different formats exported from the scanner, or NIfTI format (Clarke et al., 2022). The software can automatically identify the source and structure of the input data, ensuring compatibility with various data formats, by utilizing suspect (Rowland et al., 2017). Throughout the workflow, all processed data will be stored and transferred into RAW and NIfTI format. The input data can be processed with either a predefined pipeline, or the pipeline can be adapted to the users' needs by using nodes in the library, or custom-made nodes. Several predefined pipelines have been included in the current version and introduced in the section below. All example datasets, pipelines, LCModel control files, and basis-set files can be found on Zenodo: https://zenodo.org/records/15729683 (Figure 2).

2.2.1 Pre-processing nodes

MRSpecLAB is equipped with a set of built-in data processing nodes to handle essential steps in MRS analysis, which are mainly adapted from the existing package (Simpson et al., 2017) and widely used for MRS and MRSI data processing, mainly including:

1 Coil combination: Offers three ways of combining signals from multiple receiver coils, including adaptive combine (Walsh et al., 2000), S/N^2 (Hall et al., 2014), SVD (Rodgers and Robson, 2010).
2 Frequency and phase alignment: Corrects frequency drifts and phase variations across sub-spectra by referring to the median spectrum within a specified frequency range. Frequency and phase shifts are estimated via nonlinear least-squares optimization and then the correction applied to each spectrum (Near et al., 2015).
3 Apodization: Applies Lorentzian or Gaussian apodization functions.
4 Zero padding: Extends time-domain signals with zeroes to improve frequency-domain spectral resolution.
5 Eddy current correction: Compensates for spectral shape distortion induced by gradient eddy currents.
6 Bad average removal: Detects and removes motion-corrupted or outlier sub-spectra.
7 Quality metrics: Computes SNR of input metabolite spectra and full width at half maximum (FWHM) of the water peak to enable quick data quality assessment.
8 Spectral averaging: Offers three averaging modes, such as overall averaging, blocked averaging, and moving averaging for data quantification.

Detailed information about each processing node and its adjustable parameters is provided in the manual.

2.2.2 Prebuilt pipelines

To support diverse MRS applications, MRSpecLAB is equipped with several pre-built pipelines tailored to common applications. These pipelines include:

(1) Single-voxel ^{1}H MRS (designed for single voxel spectra acquisitions). The provided pipeline includes: adaptive coil combination, frequency and phase correction, eddy current correction, bad average removal, and averaging;
(2) Functional MRS (fMRS, supporting dynamic data processing and repeated metabolite quantification for functional studies). The provided pipeline includes: adaptive coil combination, frequency and phase correction, eddy current correction, blocked/moving averaging, and quantification per averaged data set;
(3) ^{31}P MRS (supports single-voxel ^{31}P MR spectra processing). The provided pipeline includes: frequency and phase correction (additional manual frequency and phase correction if necessary), averaging;
(4) ^{31}P MRSI. The provided pipeline includes: 3D Hanning weighted averaging (Pohmann and von Kienlin, 2001) and apodization;
(5) GABA-edited MRS (MEGA-editing based single-voxel acquisition). The provided pipeline includes: adaptive coil combination, frequency and phase correction, eddy current correction, bad average removal, averaging, and additional manual frequency and phase correction (optional).

2.2.3 Manual frequency adjustment and phasing

The manual frequency adjustment and phasing tool provides an easy way to fine-tune processed data before fitting. After completing the pipeline before quantification, users can access the manual frequency and phase adjustment option via a popup window. In this panel, they can adjust the spectral frequency offset by entering a value or using the slider to shift the entire spectrum along the frequency axis. This is an optional fine-tuning step that allows users to align peaks with their expected positions, ensuring the spectrum is correctly centered for further analysis.

Users can also manually input values for zero-order and first-order phasing. As users adjust, the updated spectrum is displayed in real-time in the plot panel, providing immediate visual feedback. Once the adjustments are complete, these settings will be applied to the averaged data before moving on to the fitting stage.

All manual adjustments made during processing are automatically logged in a text file saved alongside the pipeline configuration file, ensuring full traceability.

2.2.4 Spectral fitting

Spectral fitting in MRSpecLAB is realized with LCModel Version 6.3. For LCModel-based spectral fitting, a basis-set file (a collection of simulated or experimentally acquired model metabolite spectra compatible with the input data) and a control file (a text file specifying the spectral fitting parameters and options for spectral decomposition and individual metabolite concentration estimation) are needed. MRSpecLAB will attempt to identify a default basis set by matching the sequence parameters extracted from the input data header, as well as the LCModel control file.[1] Alternatively, users can supply their own basis set and LCModel control file via the "fitting options" button on the top panel before running the pipeline analysis. Once provided, the software automatically directs the processed data to the fitting procedure at the end of the pipeline.

Additionally, users can provide gray matter (GM), white matter (WM), and cerebral spinal fluid (CSF) probabilistic tissue segmentation files (probabilities between 0 and 1) to correct metabolite concentrations for water content differences, which improves quantification accuracy by accounting for voxel composition and tissue-specific relaxation effects. For this, any segmentation program can be used, which can segment a T_1-weighted anatomical scan into these three tissue components. The user can upload the tissue segmentations in the appropriate fields through the "fitting options." The voxel-specific fractions will then be calculated and used to determine the water concentrations within the voxel (Dhamala et al., 2019). The water content value will be automatically adapted into the control file for metabolite concentration analysis with LCModel.

2.2.5 Output structure

Clicking the folder icon in the function bar opens the designated output folder, where users can access intermediate results, processed

1 This list will be lively updated and expanded in the folders of https://github.com/MRSEPFL/MRSprocessing/basissets; https://github.com/MRSEPFL/MRSprocessing/controlfiles.

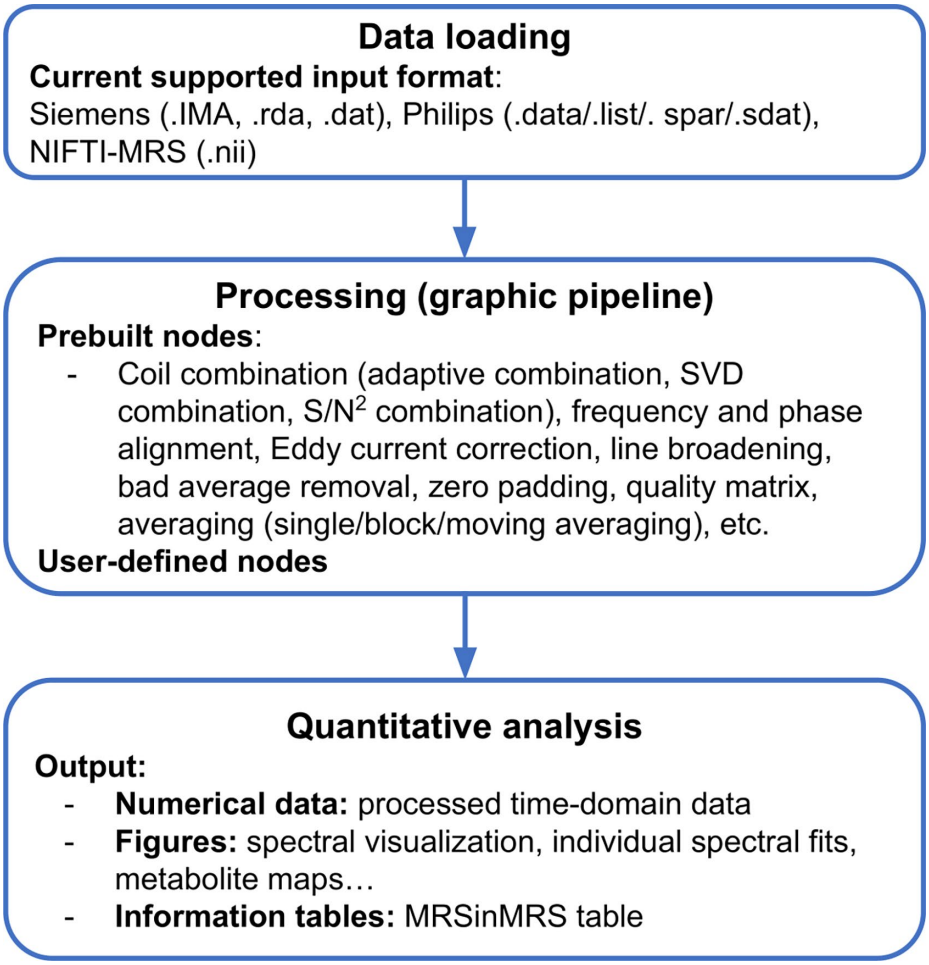

FIGURE 2
MRSpecLAB data workflow: from raw data to processed data and quantification results.

data, and LCModel fitting outcomes. The output of the autorun analysis is systematically organized within a default output directory, though users can select a custom directory using the "change output folder" button. If the "save intermediate data files" option is selected, the processed raw data will be saved as ASCII files (.RAW) and NIfTI-MRS files (.nii). The processing pipeline consists of multiple sequential steps; the results of each step are stored in a dedicated subfolder, containing processed spectra, and diagnostic plots (.PDF). LCModel fitting results are saved in a separate LCModel folder. Additionally, each run generates an MRSinMRS table (Lin et al., 2021) based on REMY tool (Susnjar et al., 2025), a standardized format for reporting MRS acquisition parameters, and processing procedures, ensuring consistency and reproducibility in research. Finally, a .pipe file will be created, which saves the pipeline used in the current processing. Details about the output files and its structure are provided in the Supplementary Section 9.

2.2.6 Self-defined processing nodes

To create a custom node that can be included into the pipeline, a developer can write a Python class that defines the functionality of the node. This class should follow the predefined framework provided by MRSpecLAB, specifying the adjustable parameters, and the processing. This file should be placed in the designated folder within the MRSpecLAB directory, which can be visible in the "Custom node library" on the function bars after re-launching MRSpecLAB. To use a custom node, open the pipeline editor, and the new node can be dragged and dropped into the canvas as prebuilt nodes, and connected with the other nodes. Users can then adjust the node's parameters (if configured) as needed.

2.3 Batch processing

MRSpecLAB now features a batch processing mode to facilitate efficient analysis of multiple MRS datasets. This mode includes three key functionalities:

(1) Make batch folder system

- This function creates a structured batch folder system in a user-specified directory.
- The user is prompted to enter the study name and define the number of participants.

The generated folder structure follows this format:

```
STUDY_NAME/
├── STUDY_NAME.control
├── STUDY_NAME.basis
├── PARTICIPANT_1/
│   ├── < FILENAME>_metabolite (required)
│   ├── < FILENAME>_water_reference (optional)
│   ├── tissue_segmentation_files/ (optional)
│   │   ├── WM_prob.nii
│   │   ├── GM_prob.nii
│   │   └── CSF_prob.nii
├── PARTICIPANT_2/
│   ├── (same structure)
│   └──...
```

- o The control and basis files, required for processing, are placed in the main study folder.
- o The user is responsible for manually placing the necessary files into the corresponding participant folders.

(2) Load batch folder system

- o This function allows users to load an existing batch folder structure for processing.
- o The tool automatically checks whether the required files (.control, .basis, and metabolite files) are present.
- o It also verifies that the provided metabolite file types match the supported input formats (as specified in the methods section).
- o Missing or incorrectly placed files trigger warnings.

(3) Run batch mode (checkbox option)

- o Enabling this option allows MRSpecLAB to automatically process all participants within the loaded batch folder structure.
- o The tool sequentially applies the same processing pipeline to each participant, ensuring consistency.
- o If optional files (e.g., tissue segmentation files or water references) are provided, they are included in the workflow.
- o Any errors, missing files, or incompatibilities are flagged before processing begins to ensure data integrity.During batch processing, MRSpecLAB attempts to catch and handle errors gracefully, allowing the remaining datasets to continue processing. While not all edge cases can be anticipated, common failure modes have been addressed to ensure stable batch execution under typical use conditions.

3 Results

We demonstrate the provided pre-defined pipelines along with example datasets in detail. The .pipe files, .control files, and basis sets along with example datasets are available on the Zenodo repository: https://zenodo.org/records/15729683.

3.1 Application 1: processing and quantification of single voxel ^{1}H MRS data

Here, we demonstrate the workflow for single-voxel spectroscopy (svs) ^{1}H MRS data processing.

3.1.1 Data input

The example dataset included water-suppressed data acquired using the STEAM sequence (TE/TR = 4.5/4000 ms, bandwidth = 4 kHz, voxel size = 30 × 30 × 30 mm^3, 32 averages) and unsuppressed water data obtained using the same sequence and parameters, from the human parietal lobe on a Siemens Terra. X 7 T scanner with a 1TX / 32RX Head Coil (Nova Medical). The input data were both in Siemens raw data format (.dat).

3.1.2 Spectral processing pipeline construction and outcome

Here the default pipeline as described above was used. The first step involved adaptive coil combination, as the raw data consisted of individual signals from multiple channels, optimizing the SNR based on the water reference data. After coil combination, the data underwent the alignment of individual transients within the dataset. The frequency and phase alignment procedure uses the N-acetylaspartate (NAA) peak at 2.02 ppm as the reference for short-TE ^{1}H MRS data by minimizing spectral differences within this region between each input spectrum and the median spectrum (Near et al., 2015). Next, eddy current correction was performed using the water reference spectra to correct for eddy current artifacts. Next, the similarity of each transient was assessed using the root-mean-squared (RMS) value of its difference from the mean of all transients, and any outliers were deleted. Finally, all remaining transients were averaged together and sent to LCModel for fitting and spectral quantification.

Figure 3 illustrates the workflow for executing the defined pipeline to obtain the quantification results. A more detailed demonstration of this application case, including step-by-step processing and visual outputs, can be found in Supplementary Section 2. An example control file for short-TE svs ^{1}H MR spectral fitting is provided in Supplementary Section 3.

3.2 Application 2: processing and quantification of fMRS data

The fMRS processing pipeline builds on the processing steps detailed in Application 1, and introduces the spectral averaging techniques. Spectral averaging is critical in fMRS data processing, as it enhances the SNR, which is essential for detecting the subtle metabolic changes associated with functional brain activity. MRSpecLAB provides several flexible averaging options, such as block averaging, and moving averaging, enabling users to tailor the process to their specific experimental conditions.

3.2.1 Data input

^{1}H-MR spectra were acquired using semi-adiabatic spin-echo full-intensity-acquired localization (sSPECIAL) (Mekle et al., 2009) (TR/TE = 4000/16 ms, bandwidth = 4 kHz, 4,096 data points) from the dmACC (128 measurements, 16 per block, voxel size = 20 × 20 × 25 mm^3) on a 7 T Siemens Terra. X MR system (Siemens Medical Solutions, Erlangen, Germany) using 1TX / 32RX Head Coil (Nova Medical). The commonly used symbol digit matching task (SDMT) was utilized in the MRI (Forn et al., 2009). During repeated MRS scans, participants were presented with a table of numbers and their corresponding symbols. The participants were then asked to match a novel set of symbols to

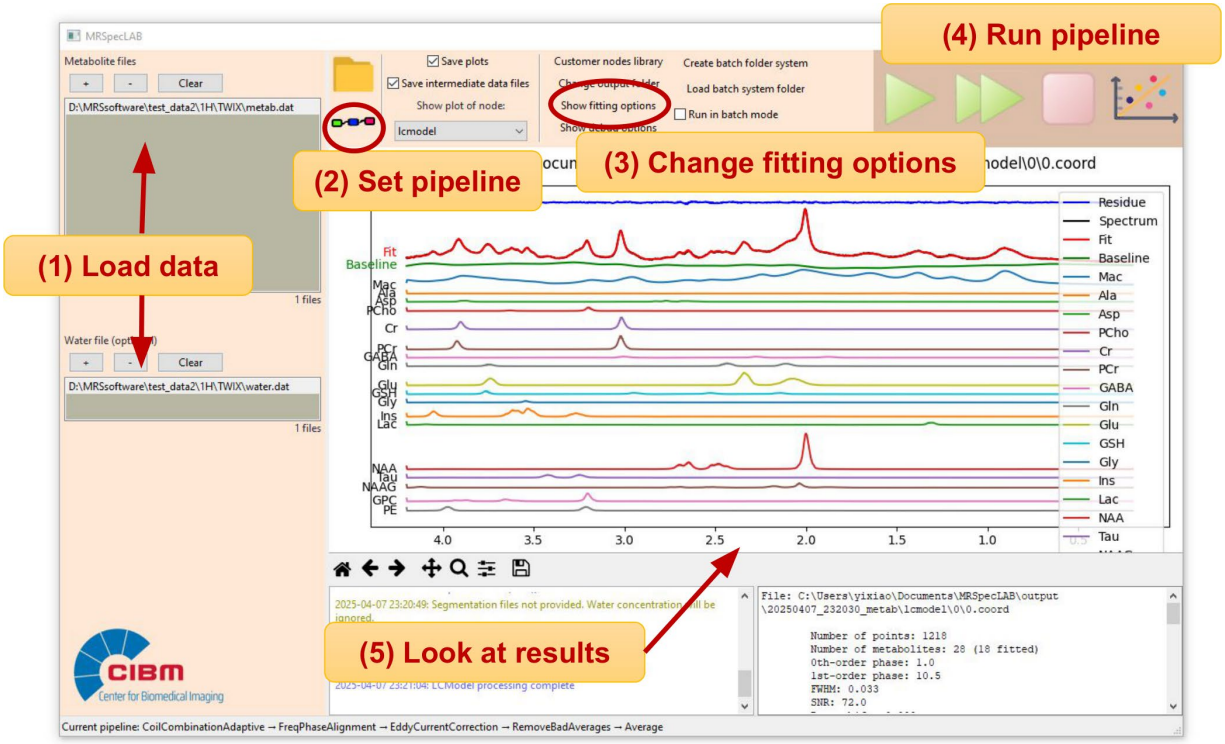

FIGURE 3
Workflow of using MRSpecLAB to process ^{1}H MRS data and obtain quantification results. Users follow these steps: (1) Load the water-suppressed data in the top section and the unsuppressed water data in the bottom section. (2) Open the pipeline editor to load, review or modify the processing pipeline as needed. (3) Change the fitting options for LCModel if desired: Add the .basis, and .control file (Supplementary Section 3), tissue segmentation files. (4) Click the "run step-by-step" or "run" button to execute the pipeline and perform spectral fitting. (5) View the fitted individual spectra in the central plot panel and examine the numerical results in the information panel.

their associated numbers in the active condition. In the rest condition, the table was empty and participants were instructed to read the number on the screen. These conditions were presented in 8 blocks (4 active, 4 rest), each 128 s, with 64 stimuli randomly presented for 2 s each.

To validate the functionality and highlight the effectiveness of the averaging techniques, we processed this example dataset using both blocked and moving averaging methods. The detailed information and output files can be found in Supplementary Section 4. By serving as a practical reference, these results guide users in applying and optimizing these techniques for their own datasets.

3.2.2 Blocked averaging

In contrast to overall averaging used in Application 1, where all transients are averaged together to maximize SNR for a single quantification result across the entire dataset, MRSpecLAB also supports block-based averaging, which divides the data into smaller time segments and averages within each block, allowing users to study metabolic changes over specific time windows, such as rest and active states.

For block averaging, MRSpecLAB provides three key parameters to control the process, as shown in the right panel of Figure 4: (1) number of measurements in an experimental block: This defines the original number of transients within each block of raw data, representing the unaveraged input for that block; (2) number of averages to produce per block: This specifies the desired number of averaged spectra per block. For example, if a block contains 16 transients, setting this parameter to 4 will produce 4 averaged spectra by averaging every 4 transients together; (3) number of block types: this determines the distinct experimental conditions (e.g., rest vs. active) to be processed separately. Each block type is treated independently.

The block averaging process involves grouping the transients within each block based on the defined number of measurements. Transients within each block are averaged according to the specified number of averages per block, effectively reducing the total number of spectra while enhancing SNR. Users can tune this parameter and try to make a balance between data quality and temporal resolution for experiments with multiple experimental conditions.

After the averaging process, each averaged spectrum was fitted and quantified. The software automatically generates outputs for each averaged spectrum, including metabolite concentrations, fit diagnostics, and spectral fits. These results are organized into distinct directories corresponding to the block types and averaging configurations, enabling users to easily access and analyze condition-specific results.

3.2.3 Moving averaging

For experiments requiring dynamic quantification, such as task-related fMRS studies or if dynamics within blocks want to be investigated, a "moving averaging" node is available. This approach calculates the average over a sliding window, maintaining temporal

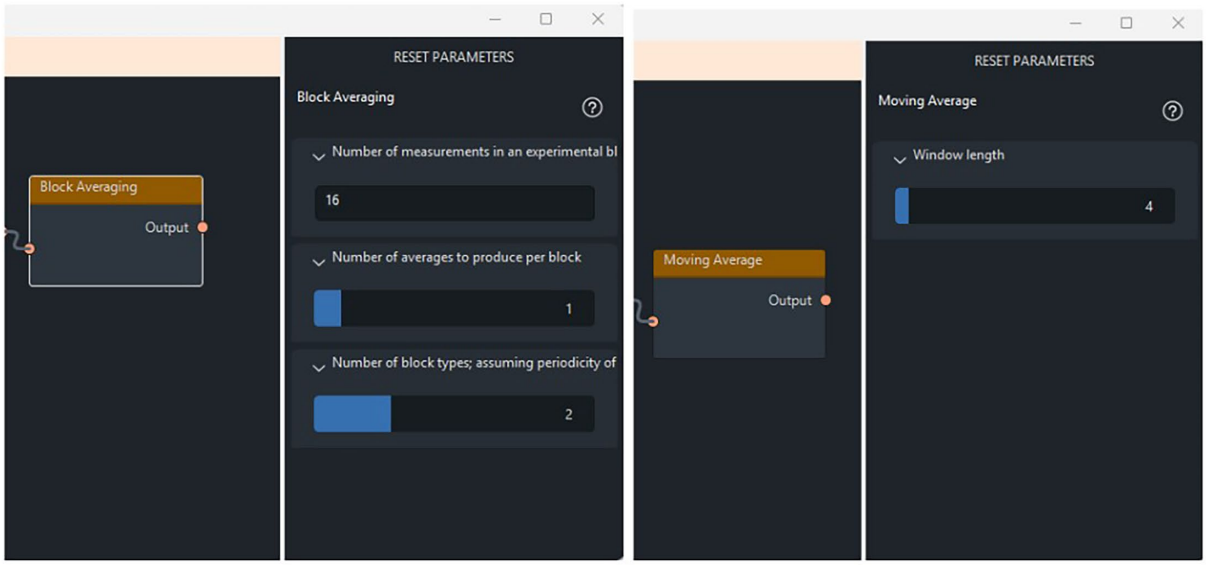

FIGURE 4
Integrating block/moving averaging into the processing pipeline for fMRS. On the right panel, the user can adjust several parameters of the function, such as the number of measurements in an experimental block, the number of averages per block, and the number of block types. **(left side)** In this dataset, two block types (rest and active) were considered, with each state including 16 transients. To generate the averaged dataset, 1 average per block was generated, resulting in 8 blocks for fitting. **(right side)** The window length of 4 is defined to average every 4 consecutive transients together, with the window advancing by 1 transient at each step.

resolution while improving SNR. This is particularly useful for capturing transient metabolic fluctuations without sacrificing data quality.

For moving averaging, MRSpecLAB provides a parameter called "window length," which defines the number of transients within the sliding window used for averaging, as shown in Figure 4. For instance, setting a window length of 5 means that every 5 consecutive transients are averaged together, with the window advancing by 1 transient at each step. This method applies the moving average by sliding the defined kernel across the dataset, averaging the transients within the window at each step. The process is repeated until the entire dataset is processed, producing a series of averaged spectra. As with blocked averaging, LCModel is employed to analyze each spectrum generated through the moving averaging process.

3.2.4 Comparison of spectral quality metrics between MRSpecLAB and FID-A

To assess the consistency between MRSpecLAB and other existing toolboxes in processing MRS data, spectral quality metrics—SNR and water linewidth, were evaluated for 24 participants' data. The dataset acquired under the protocol described in Application 2. The raw input data were identical for both tools, provided in Siemens TWIX format, and underwent the same preprocessing steps: water-signal-based coil combination, frequency and phase alignment, eddy current correction, outlier average removal, and signal averaging.

Figure 5 presents a Bland–Altman analysis comparing SNR and water linewidth estimates between MRSpecLAB and FID-A. The SNR was calculated as the peak height of the NAA signal at 2.02 ppm divided by the RMS noise in the 0.2–0.5 ppm region, while water linewidth was determined as the full width at FWHM of the unsuppressed water peak, measured in Hz. The analysis revealed a mean bias (MRSpecLAB - FID-A) of 34 for SNR and −0.29 Hz for water linewidth, indicating only minimal differences between the two methods. These small biases suggest a high level of consistency and no significant systematic over- or underestimation by either tool. The differences were evenly distributed across the measurement range with no clear trend. These results confirm that MRSpecLAB and FID-A provide closely aligned estimates for both metrics, supporting their comparability in spectral processing.

Additionally, detailed comparisons of the individual post-processed spectra, and quantification results for several metabolites (e.g., tNAA, tCr, and Glu), are presented in Supplementary Section 5.

3.3 Application 3: single-voxel ^{31}P MRS data processing

In addition to supporting ^{1}H MRS data, MRSpecLAB is also equipped to process X-nuclei data, including ^{31}P MR spectra.

3.3.1 Data input

MR experiments were performed on a 7 T/68 cm MR scanner (Siemens Medical Solutions, Erlangen, Germany) with an in-house-built ^{1}H quadrature surface coil (10-cm diameter) and a single-loop ^{31}P coil (7-cm diameter) for the coverage of the human occipital lobe. B_0 field inhomogeneity was optimized in a voxel of interest (VOI) ($50 \times 30 \times 40$ mm^3). Localized ^{31}P MR spectra were acquired using a 3D-ISIS sequence (TR/TE = 3000/0.35 ms, voxel-size = $55 \times 20 \times 25$ mm^3, averages/block = 16/6, bandwidth = 6 kHz, number of points = 2048).

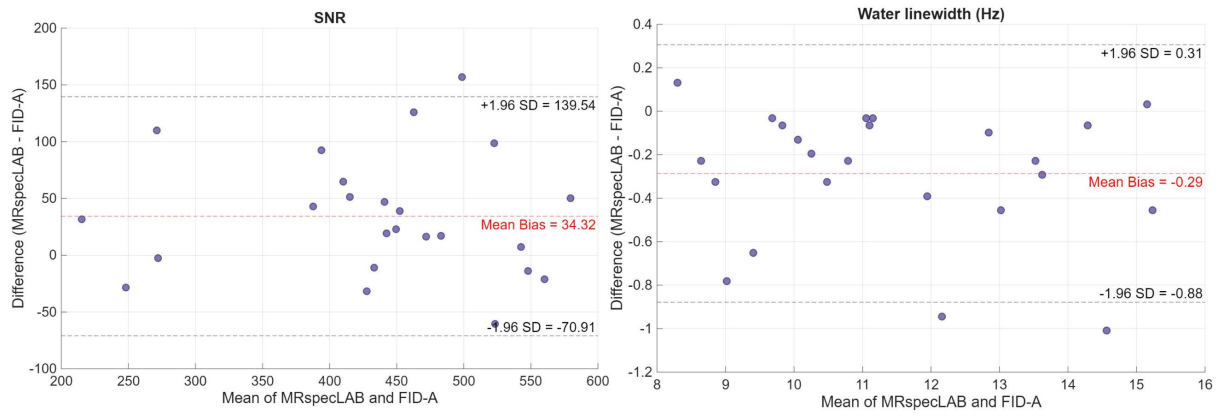

FIGURE 5
Bland–Altman analysis between post-processed spectral quality metrics (SNR and water linewidth) obtained from FID-A and MRSpecLAB for five participants. The input data consisted of 128 transients for each participant, acquired using the protocol outlined in Application 2. Identical raw data in TWIX format were processed by both FID-A and MRSpecLAB, following the same preprocessing pipeline: coil combination based on the water signal, frequency and phase alignment, bad average removal, eddy current correction, and signal averaging. SNR was calculated from the NAA peak at 2.02 ppm divided by the RMS noise from 0.2–0.5 ppm, and the linewidth (in Hz) was measured from processed water spectra for all participants. Each point represents one participant and is labeled accordingly. The x-axis shows the mean of the two methods, and the y-axis shows the difference (MRSpecLAB – FID-A). The red dashed line represents the mean bias, while the black dashed lines indicate the limits of agreement (±1.96 SD).

The processing pipeline used was described above. A surface coil was utilized in this experiment, so no coil combination was needed (Provencher, 2001). P frequency and phase correction were applied using an entropy-minimization strategy (Chen et al., 2002). The individual spectral fitting can be obtained in the end as shown in Figure 6. Supplementary Section 6 provides a more detailed demonstration of this application case, including step-by-step processing and visual outputs.

3.4 Application 4: ^{31}P MRSI data processing and metabolite mapping

MRSpecLAB also provides the plotting tools specifically designed for visualizing the concentration spatial distribution in multivoxel data. Here is an example for processing, quantifying, and visualizing the ^{31}P CSI-FID data.

3.4.1 Data input, processing, and fitting

The input data is acquired by a ^{31}P CSI-FID sequence with the following parameters: FOV = 200 × 200 × 80 mm^3, matrix size = 16 × 16 × 8, TE/TR = 2.3/260 ms, flip angle = 33°, bandwidth = 6 kHz, vector size = 1,024, 160 averages. The dataset is in Siemens .rda format, and is processed by applying the Hanning filter using the node named 3D Hanning filter (window size = 16 × 16 × 8), the phase correction, and the line broadening CSI (Gaussian, 5 Hz) to the averaged spectra to enhance the SNR. The step-by-step processing, visual outputs, and fitting, can be found in Supplementary Section 7.

The ^{31}P MR spectra are subsequently analyzed by LCModel on a voxel-by-voxel basis using the provided basis set. This basis set includes key phosphorus-containing compounds such as phosphocreatine (PCr), intracellular and extracellular inorganic phosphate (Pi), diphosphates (NAD, UDPG), triphosphates (α-, β-, and γ-ATP), phosphoethanolamine (PE), phosphocholine (PC), glycerophosphoethanolamine (GPE), and glycerophosphocholine (GPC). The basis set and the control files used in the fitting process can be found on the Zenodo repository. For each voxel, the output is stored in a dedicated subfolder named according to its 3D spatial coordinates.

3.4.2 Metabolite concentration map visualization

MRSpecLAB has a built-in plotting tool designed for generating metabolite maps, which can be accessed via the plotting button located in the top right corner of the panel. Clicking on the plotting button can launch the visualization parameter interface (Figure 6). By using this tool, users can visualize the spatial distribution of metabolite concentrations once the output data is available.

A selection list will display the available metabolites, allowing users to choose one for generating a corresponding 2D spatial concentration map. Users can specify the map orientation and select the slice number they wish to visualize. Additionally, there is an option to choose a reference metabolite. When a reference is selected, only pixels where the CRLB (Cramér-Rao Lower Bound) values for both the reference and selected metabolites fall below the threshold will be displayed, ensuring reliable data visualization. Furthermore, once a reference metabolite is chosen, users can opt to display a relative concentration map, which represents the ratio of the selected metabolite to the reference metabolite. To enhance visualization, users can also customize the colorbar scale, adjusting it for optimal contrast and clarity in the displayed maps.

Moreover, the brain masks can be calculated from the corresponding anatomical images. When the anatomical image is selected, MRSpecLAB interpolates the metabolite maps to the image resolution. If no mask is provided, the raw metabolic concentration matrix will be shown without any interpolation. Users should ensure that the anatomical input is properly aligned with the MRSI volume. Here, the corresponding 3D ^{1}H anatomical images acquired using a

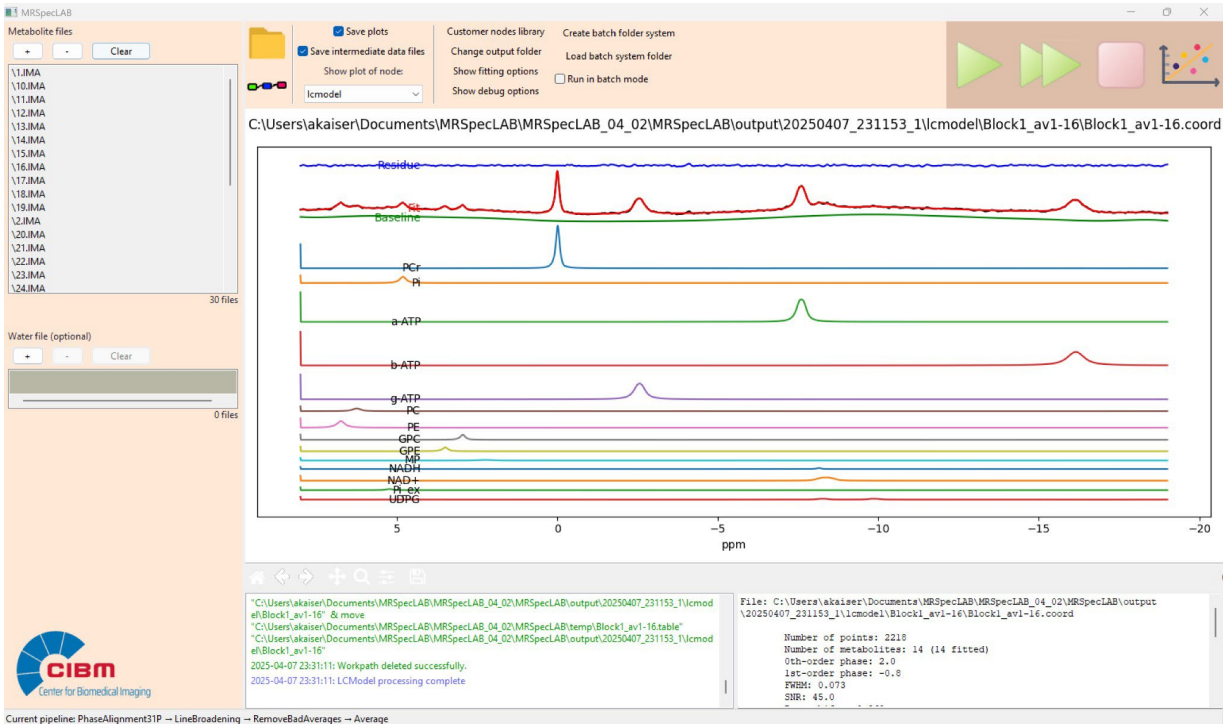

FIGURE 6
Example fitting result for a single-voxel ^{31}P MR spectra (3D-ISIS, TR/TE = 3000/0.35 ms, voxel size = 55 × 20 × 25 mm3, averages/block = 16/6, bandwidth = 6 kHz, number of points = 2048).

GRE sequence (TE/TR = 2.82/6.50 ms, $\alpha = 4°$, 1 mm^3 isotropic resolution) were loaded. After selecting the orientation of the anatomical image and the corresponding slice number, the plotting tool can generate a brain mask and apply it to the map based on the chosen image. Figure 7 illustrates one slice of the NAD$^+$ maps derived from this workflow.

3.5 Application 5: spectral-editing for GABA measurement

Mescher–Garwood (MEGA) J-difference editing (Mescher et al., 1998; Mullins et al., 2014; Mikkelsen et al., 2019) is a common method used for the detection of the resolved GABA signal at 3.0 ppm, which is usually difficult to measure due to its overlap with other intensive metabolite resonances. The processing of MEGA data often requires subtraction of two sub-spectra to obtain the resolved GABA signal. In MRSpecLAB, the MEGA data is handled the same way as svs ^{1}H data, given that the combination of sub-spectra in the sequence is direct averaging. The alignment between edit-on and edit-off spectra is critical in MEGA-editing to obtain a resolved GABA peak.

3.5.1 Data input

Here, we processed an example dataset acquired using MEGA-sSPECIAL sequence (Lim and Xin, 2022) with the following parameters: TE/TR = 80/4000 ms, bandwidth = 4 kHz, voxel size = 30 × 30 × 20 mm^3, 32 acquisitions with 4 sub-spectra each (two additional scans are for 1D-ISIS module in the sSPECIAL).

3.5.2 Processing and quantification

The processing steps follow a similar set to those in Application 1, including adaptive coil combination, frequency and phase correction, eddy current correction, bad average removal, and averaging. One example of the fitting result is shown in Figure 8.

3.6 Application 6: development of custom processing nodes and self-defined pipelines

Each custom node should be implemented as a Python class, adhering to a predefined framework. This framework includes essential components such as the basic information (e.g., label, author, and description), parameter definitions, and core processing functionality. Developers can develop and share new nodes using this structure, seamlessly integrating them into MRSpecLAB. To create a new custom node, follow these steps (Figure 9): (1) node's information definition: provide metadata such as the node's label, author, and description to identify and describe the node within the pipeline editor; (2) key parameter definition: specify adjustable parameters that will appear in the right panel when the node is selected in the pipeline editor; (3) processing function: implement the process method to define how the node processes input data; (4) visualization (optional): Implement the plot method to generate diagnostic plots of both input and processed data. These plots will be displayed in the main window of the software upon completion of the processing step; (5) register the node: use api. RegisterNode to add the node to the library, making it accessible via the GUI.

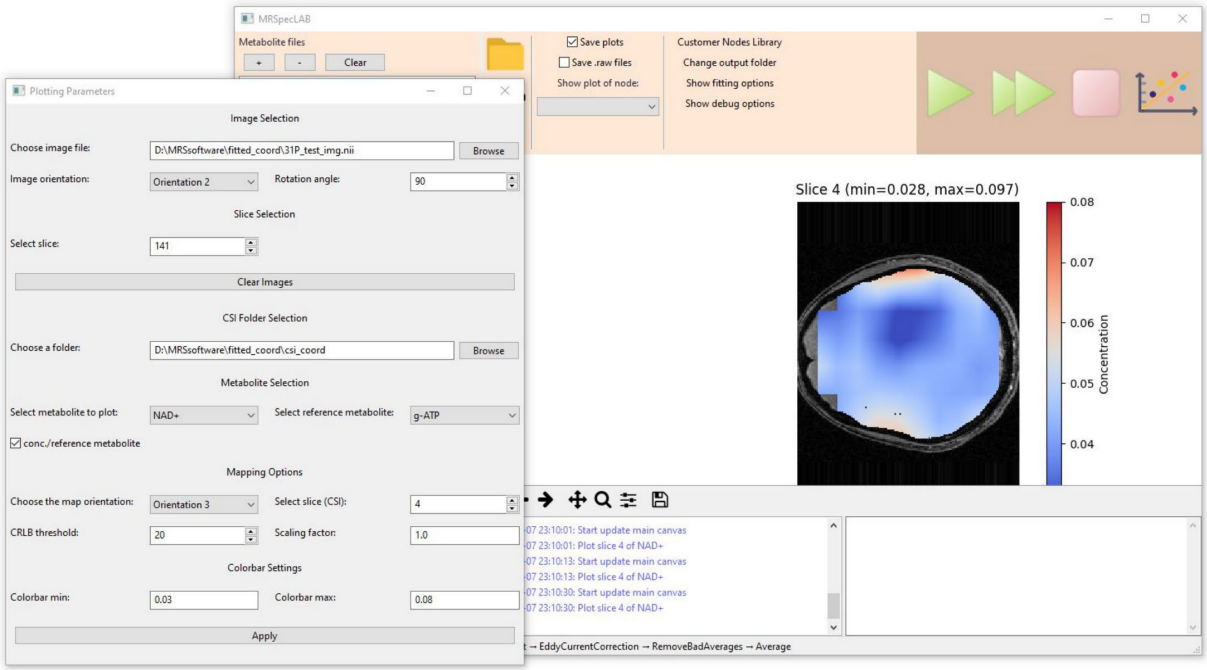

FIGURE 7
Application for processing and quantifying ^{31}P CSI-FID data (rda format, FOV = 200 × 200 × 80 mm3, matrix size = 16 × 16 × 8, TE/TR = 2.3/260 ms, flip angle = 33°, bandwidth = 6 kHz, vector size = 1,024, 160 averages). Corresponding 3D ^{1}H anatomical images were acquired using a GRE sequence (TE/TR = 2.82/6.50 ms, α = 4°, 1 mm3 isotropic resolution). The selected 2D concentration maps can be visualized using the implemented plotting tool based on spectral fitting results.

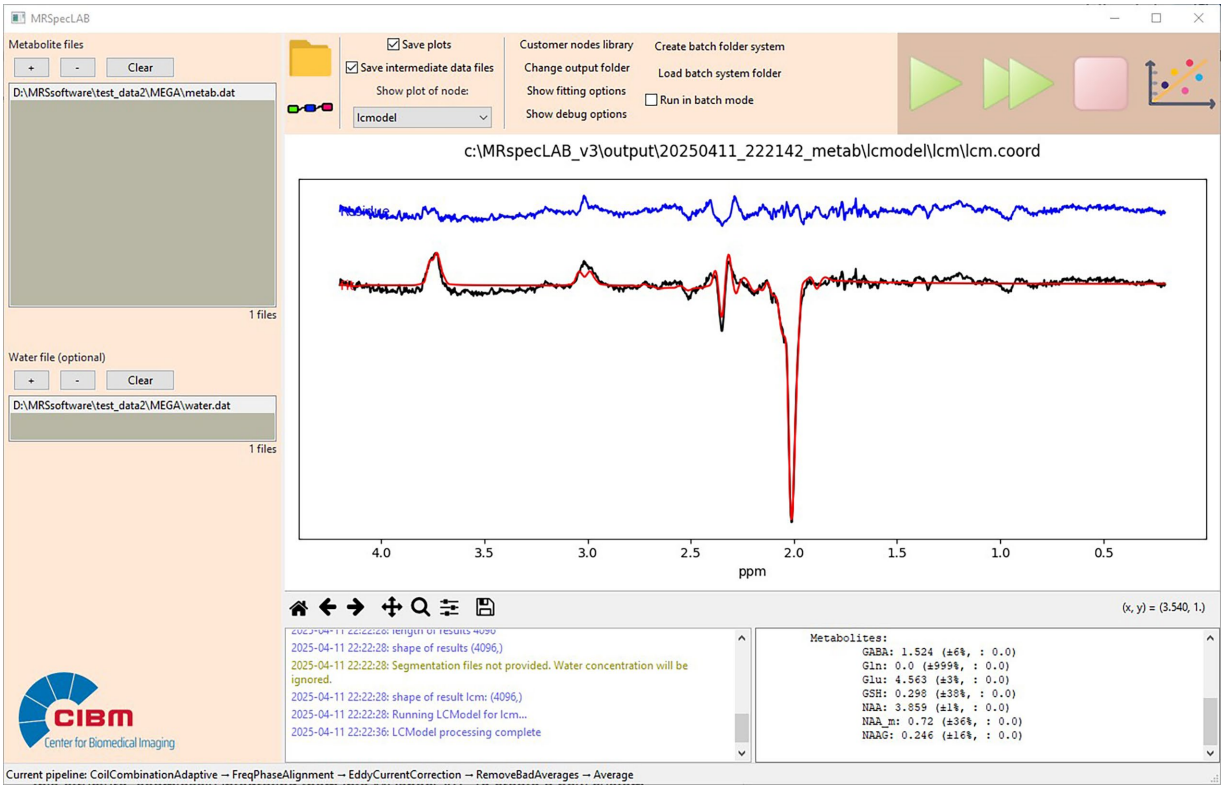

FIGURE 8
Example fitting result for an edited GABA sequence (MEGA-sSPECIAL, TE/TR = 80/4000 ms, bandwidth = 4 kHz, voxel size = 30 × 30 × 20 mm^3, 32 acquisitions).

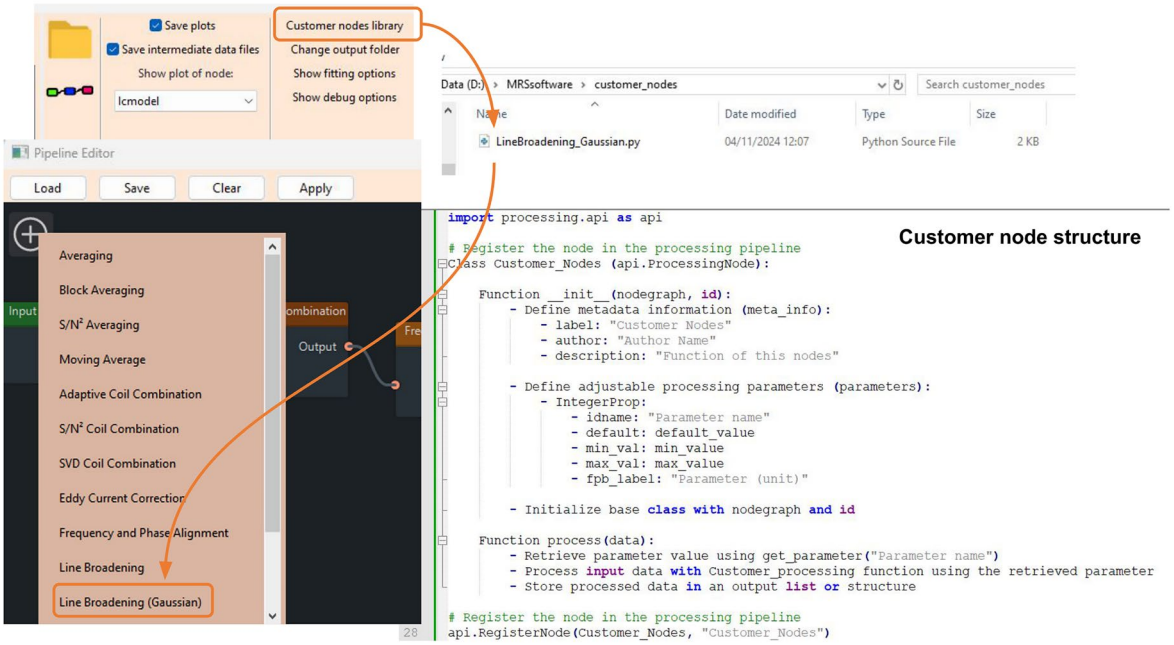

FIGURE 9
Adding custom nodes. In the main window, users can select a custom node library, which loads all available custom nodes within the chosen directory. The new nodes appear on the list with the prebuilt nodes and can be easily added to the pipeline diagram using a drag-and-drop action. Each custom node is structured as a Python class, with a predefined framework provided.

An example code for creating a custom node can be found in Supplementary Section 8. For users seeking to utilize a pipeline beyond the prebuilt options, the first step is to load all required external processing node scripts into the custom node library. After relaunching, open the pipeline editor and load an existing .pipe file to configure a specific pipeline. Additionally, a GitHub repository is available where all existing nodes are stored, and developers can contribute their nodes via push requests. Submitted nodes undergo validation before being added to the library for non-developer users.

4 Discussion

MRspecLAB is designed as a collaborative platform that bridges the gap between the MRS technical experts, neuroscientists, and clinicians. It aims to build the workflows that span from raw data to clinical or neuroscientific interpretation, to support the interdisciplinary collaboration between those focused on the technical aspects of MRS and those applying it. MRSpecLAB offers a comprehensive, user-friendly solution with a visual pipeline builder, support for MRSI, various nuclei, and edited MRS, as well as compatibility with the NIfTI format. To highlight its capabilities in context, we have included a comparative overview of widely used MRS software tools in the Supplementary Section 1 to summarize the key features of MRSpecLAB and others.

Its modular design empowers users to create specific processing pipelines, where each processing step is defined as an independent node that can be easily tuned and rearranged (drag-drop-connect) in a graphic interface to meet the needs of the specific datasets. The user-developed nodes can be shared across the research community and seamlessly integrated into the graphical pipeline editor by others. This allows users to focus their efforts on refining and optimizing data processing workflows, rather than spending time navigating or modifying complex code.

MRSpecLAB can be freely downloaded as a compiled executable and can be run directly on Windows or Linux without the need for any installation steps or environment configuration (available via GitHub releases). It supports a wide range of data formats from vendors and software versions. It also supports the NIfTI-MRS format (Clarke et al., 2022), which has been proposed as a standard spectroscopy data format, eliminating the need for manual format conversions. Data processed in MRSpecLAB can be exported in ASCII and NIfTI formats compatible with other widely used packages, ensuring compatibility with other software packages, and thereby allowing researchers to integrate their analyses with other established tools.

MRSpecLAB offers an intuitive interface and graphical drag-and-drop pipeline editor, making MRS/MRSI research accessible to a broad user base. Even users with minimal experience in MRS/MRSI data processing can easily analyze their data. Its user-friendly design provides a streamlined workflow, enabling students, clinicians, and researchers to engage with MRS/MRSI data analysis efficiently. With the potential of supporting a comprehensive range of spectral processing tasks, including X-nuclei datasets, MRSpecLAB is well-suited for both routine and advanced MRS/MRSI research. The pipeline files together with the data can be shared with publications to facilitate research reproducibility.

Processing and quantification of MRS data by MRSpecLAB has been validated by comparison with FID-A combined with LCModel. The results indicate that MRSpecLAB achieves comparable metabolite concentration estimates and spectral quality metrics, supporting the reliability for automated spectral preprocessing using

MRSpecLAB. Predefined pipelines in MRSpecLAB have been optimized based on expert-recommended workflows (Near et al., 2021), ensuring accurate and reproducible analysis. It should be noted, however, that validation was performed on healthy control datasets, and the tool has not yet been systematically tested on data from clinical populations or pathological cases. Pipelines specifically adapted to disease-related spectra have not been developed or shared to date, but could be created and integrated either by the development team or by users within the community.

While independent validation is a key consideration for software tools, MRSpecLAB poses specific challenges in this regard. Unlike script-based toolkits such as FID-A, MRSpecLAB is a node-based, interactive environment that relies on user-defined pipeline construction. As such, blind or masked comparisons are not feasible, since users are inherently aware of the interface and workflow they are interacting with. Additionally, once a pipeline is defined using the available nodes and parameter settings, the execution is deterministic — applying the same pipeline to the same dataset will yield the same results, regardless of the user. Thus, potential variability or bias is not introduced at the level of software execution but rather at the level of user-defined processing strategy. This source of variability is intrinsic to flexible data processing tools, underscores the importance of clear documentation and transparent sharing of processing pipelines, and should be addressed by promoting best practices and detailed and standardized pipeline sharing within the community.

A key strength of MRSpecLAB is its modular and adaptable design. Its architecture allows users to customize workflows to suit their specific datasets, with each processing step defined as an independent node that can be easily rearranged and adjusted. Users can also develop and integrate new nodes within the provided framework, facilitating expansion without requiring extensive programming skills. Additionally, custom modules and pipelines can be shared within the research community, fostering innovation and encouraging collaborative development of advanced MRS/MRSI processing methods. We recommend that developers carefully validate their custom implementations, ideally by testing them on multiple datasets or cross-validating with established tools if possible. To support safe sharing, we will maintain a dedicated folder on the GitHub repository for community-submitted custom nodes. Submissions to this folder will be reviewed and validated by the core development team prior to sharing, helping to safeguard reproducibility and correctness.

One current limitation of MRSpecLAB is the lack of support for DICOM export and integration with PACS systems, which limits its use in clinical workflows. As the tool matures, enabling compatibility with clinical infrastructure, such as its integration within the Siemens open-recon framework, will be a key focus to facilitate translational applications and broader clinical adoption. MRSpecLAB currently supports several commonly used input formats, including Siemens .dat, .ima, and .dcm files; Philips .sdat/.spar; .rda; and NIfTI/NIfTI-MRS .nii/.nii.gz files. While this covers a wide range of use cases, data from other vendors or formats not directly supported can be converted externally using tools such as spec2nii prior to import. We plan to integrate automated conversion using spec2nii in a future release to streamline this process further. After each processing step, MRSpecLAB saves both the .raw and .nii versions of the dataset, enabling seamless export to other platforms that support these formats.

MRSpecLAB has been primarily tested with 7 T Siemens data, with confirmed compatibility for Philips and GE scanners via NIfTI-MRS imports. To support broader adoption, example datasets, basis sets, and pipeline configurations for these vendors are available through our Zenodo repository. The software architecture supports lower field strengths (e.g., 3 T and 1.5 T), while preconfigured pipelines for these settings are not yet included. Users are encouraged to create and share such pipelines via the GitHub repository to promote collaboration and expand the applications. One additional limitation might be the reliance on LCModel for spectral fitting, which, although robust, may limit flexibility for users who wish to employ alternative quantification methods. Incorporating plug-ins to interface with other popular software like FSL, SPM, Osprey may be a direction for future development. However, MRSpecLAB allows to save the intermediate processed data in .nii format, which could be read into any other fitting program afterwards, if needed, and additionally, fitting algorithms could be implemented as a customized node. As an open-source platform, MRSpecLAB continues to evolve based on user feedback and contributions from the research community. Future development plans include integrating additional processing nodes and expanding support for more experimental modalities, such as (Tedeschi et al., 1996) C, and ^{2}H MRS and ^{31}P MR fingerprinting. B_0 inhomogeneity correction, especially at 7 T, is not yet implemented but is also planned as a future enhancement to improve MRSI processing accuracy. We also aim to improve user experience by adding interactive features, such as MRSI voxel selection, the co-registration of the MRI and metabolic maps, etc., to streamline data inspection and analysis. Community-driven enhancements will play a vital role in extending the software's capabilities, with MRS researchers contributing new nodes, sharing processing pipelines, and neuroscientists and clinical scientists offering usability feedback.

5 Conclusion

MRSpecLAB is a collaborative platform for MRS processing, designed to bridge the gap between technical experts and application-driven users in MRS/MRSI research, clinical applications, and education. Its intuitive graphical interface and modular pipeline editor enable experienced users to develop and share advanced functions while allowing other users to seamlessly integrate them into their workflows. With robust support for both proton and X-nuclei single-voxel and MRSI datasets, MRSpecLAB serves as a dynamic platform for knowledge exchange, innovation, the advancement of MRS methodologies, bridging MRS methods with clinical applications and enhancing the value of MRS in clinical and neuroscience research.

Data availability statement

The original contributions presented in the study are included in the article/Supplementary material, further inquiries can be directed to the corresponding author/s.

Ethics statement

The studies involving humans were approved by Commission cantonale d'éthique de la recherche sur l'être humain CER-VD. The studies were conducted in accordance with the local legislation and

institutional requirements. The participants provided their written informed consent to participate in this study.

Author contributions

YX: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Software, Validation, Visualization, Writing – original draft, Writing – review & editing, Project administration. AK: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Project administration, Validation, Visualization, Writing – original draft, Writing – review & editing, Resources, Supervision. MK: Software, Writing – original draft. AB: Software, Validation, Writing – original draft, Investigation. RC: Software, Writing – original draft. XL: Resources, Validation, Writing – original draft. ZH: Resources, Validation, Writing – original draft. AD: Resources, Validation, Writing – original draft. MW: Resources, Validation, Writing – original draft. LX: Conceptualization, Funding acquisition, Project administration, Supervision, Writing – original draft, Validation.

Funding

The author(s) declare that financial support was received for the research and/or publication of this article. The study was supported by Swiss National Science Foundation (grant no. 320030_189064 and 213769).

Acknowledgments

We acknowledge the MRI Platform of the FCBG (Fondation Campus Biotech Geneva) and the CIBM Center for Biomedical Imaging for providing expertise and resources to conduct this study. We acknowledge Yan Li (UCSF) and Anouk Schrantee (Amsterdam UMC) for providing the testing datasets. We also acknowledge the support from the Swiss National Science Foundation (grant no. 320030_189064 and 213769).

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Generative AI statement

The authors declare that no Gen AI was used in the creation of this manuscript.

Publisher's note

Supplementary material

The Supplementary material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fnimg.2025.1610658/full#supplementary-material

References

Barker, P. B., Gillard, J. H., Van Zijl, P. C., Soher, B. J., Hanley, D. F., Agildere, A. M., et al. (1994). Acute stroke: evaluation with serial proton MR spectroscopic imaging. *Radiology* 192, 723–732. doi: 10.1148/radiology.192.3.8058940

Blüml, S., Seymour, K. J., and Ross, B. D. (1999). Developmental changes in choline- and ethanolamine-containing compounds measured with proton-decoupled 31P MRS in in vivo human brain. *Magn. Reson. Med.* 42, 643–654. doi: 10.1002/(sici)1522-2594(199910)42:4<643::aid-mrm5>3.0.co;2-n

Chen, L., Weng, Z., Goh, L., and Garland, M. (2002). An efficient algorithm for automatic phase correction of NMR spectra based on entropy minimization. *J. Magn. Reson.* 158, 164–168. doi: 10.1016/S1090-7807(02)00069-1

Clarke, W. T., Bell, T. K., Emir, U. E., Mikkelsen, M., Oeltzschner, G., Shamaei, A., et al. (2022). NIfTI-MRS: a standard data format for magnetic resonance spectroscopy. *Magn. Reson. Med.* 88, 2358–2370. doi: 10.1002/mrm.29418

Clarke, W. T., Stagg, C. J., and Jbabdi, S. (2021). FSL-MRS: an end-to-end spectroscopy analysis package. *Magn. Reson. Med.* 85, 2950–2964. doi: 10.1002/mrm.28630

Connelly, A., Van Paesschen, W., Porter, D. A., Johnson, C. L., Duncan, J. S., and Gadian, D. G. (1998). Proton magnetic resonance spectroscopy in MRI-negative temporal lobe epilepsy. *Neurology* 51, 61–66. doi: 10.1212/WNL.51.1.61

Dhamala, E., Abdelkefi, I., Nguyen, M., Hennessy, T. J., Nadeau, H., and Near, J. (2019). Validation of in vivo MRS measures of metabolite concentrations in the human brain. *NMR Biomed.* 32:e4058. doi: 10.1002/nbm.4058

Forn, C., Belloch, V., Bustamante, J. C., Garbin, G., Parcet-Ibars, M. À., Sanjuan, A., et al. (2009). A symbol digit modalities test version suitable for functional MRI studies. *Neurosci. Lett.* 456, 11–14. doi: 10.1016/j.neulet.2009.03.081

Gajdošík, M., Landheer, K., Swanberg, K. M., and Juchem, C. (2021). INSPECTOR: free software for magnetic resonance spectroscopy data inspection, processing, simulation and analysis. *Sci. Rep.* 11:2094. doi: 10.1038/s41598-021-81193-9

Hall, E. L., Stephenson, M. C., Price, D., and Morris, P. G. (2014). Methodology for improved detection of low concentration metabolites in MRS: optimised combination of signals from multi-element coil arrays. *NeuroImage* 86, 35–42. doi: 10.1016/j.neuroimage.2013.04.077

Horská, A., and Barker, P. B. (2010). Imaging of brain tumors: MR spectroscopy and metabolic imaging. *Neuroimaging Clin. N. Am.* 20, 293–310. doi: 10.1016/j.nic.2010.04.003

Hunter, J. D. (2007). Matplotlib: a 2D graphics environment. *Comput. Sci. Eng.* 9, 90–95. doi: 10.1109/MCSE.2007.55

Lim, S. I., and Xin, L. (2022). Γ-aminobutyric acid measurement in the human brain at 7 T: short echo-time or Mescher–Garwood editing. *NMR Biomed.* 35:e4706. doi: 10.1002/nbm.4706

Lin, A, Andronesi, O, Bogner, W, Choi, I-Y, Coello, E, Cudalbu, C, et al. (2021). Minimum Reporting Standards for in vivo Magnetic Resonance Spectroscopy (MRSinMRS): Experts' consensus recommendations. *NMR in Biomedicine* 34:e4484.

Marjańska, M., Deelchand, D. K., and Kreis, R.2016 ISMRM MRS Study Group Fitting Challenge Team (2022). Results and interpretation of a fitting challenge for MR spectroscopy set up by the MRS study group of ISMRM. *Magn. Reson. Med.* 87, 11–32. doi: 10.1002/mrm.28942

Martin, W. W. (2007). MR spectroscopy in neurodegenerative disease. *Mol. Imaging Biol.* 9, 196–203. doi: 10.1007/s11307-007-0087-2

McBride, D. Q., Miller, B. L., Nikas, D. L., Buchthal, S., Chang, L., Chiang, F., et al. (1995). Analysis of brain tumors using 1H magnetic resonance spectroscopy. *Surg. Neurol.* 44, 137–144. doi: 10.1016/0090-3019(95)00139-5

McKinney, W. (2011). *Pandas: a foundational Python library for data analysis and statistics*. Python for high performance and scientific computing, No. 14, pp. 1–9.

Mekle, R., Mlynárik, V., Gambarota, G., Hergt, M., Krueger, G., and Gruetter, R. (2009). MR spectroscopy of the human brain with enhanced signal intensity at ultrashort echo times on a clinical platform at 3T and 7T. *Magn. Reson. Med.* 61, 1279–1285. doi: 10.1002/mrm.21961

Mescher, M., Merkle, H., Kirsch, J., Garwood, M., and Gruetter, A. R. (1998). Simultaneous in vivo spectral editing and water suppression. *NMR Biomed.* 11, 266–272. doi: 10.1002/(SICI)1099-1492(199810)11:6<266::AID-NBM530>3.0.CO;2-J

Mikkelsen, M., Rimbault, D. L., Barker, P. B., Bhattacharyya, P. K., Brix, M. K., Buur, P. F., et al. (2019). Big GABA II: water-referenced edited MR spectroscopy at 25 research sites. *NeuroImage* 191, 537–548. doi: 10.1016/j.neuroimage.2019.02.059

Mullins, P. G., McGonigle, D. J., O'Gorman, R. L., Puts, N. A., Vidyasagar, R., Evans, C. J., et al. (2014). Current practice in the use of MEGA-PRESS spectroscopy for the detection of GABA. *NeuroImage* 86, 43–52. doi: 10.1016/j.neuroimage.2012.12.004

Near, J., Edden, R., Evans, C. J., Paquin, R., Harris, A., and Jezzard, P. (2015). Frequency and phase drift correction of magnetic resonance spectroscopy data by spectral registration in the time domain. *Magn. Reson. Med.* 73, 44–50. doi: 10.1002/mrm.25094

Near, J., Harris, A. D., Juchem, C., Kreis, R., Marjańska, M., Öz, G., et al. (2021). Preprocessing, analysis and quantification in single-voxel magnetic resonance spectroscopy: experts' consensus recommendations. *NMR Biomed.* 34:e4257. doi: 10.1002/nbm.4257

Negendank, W. (1992). Studies of human tumors by MRS: a review. *NMR Biomed.* 5, 303–324. doi: 10.1002/nbm.1940050518

Oeltzschner, G., Zöllner, H. J., Hui, S. C., Mikkelsen, M., Saleh, M. G., Tapper, S., et al. (2020). Osprey: open-source processing, reconstruction & estimation of magnetic resonance spectroscopy data. *J. Neurosci. Methods* 343:108827. doi: 10.1016/j.jneumeth.2020.108827

Öz, G., and Tkáč, I. (2010). Short-echo, single-shot, full-intensity ^{1}H MRS for neurochemical profiling at 4T: validation in the cerebellum and brainstem. *Magn. Reson. Med.* 65, 901–910. doi: 10.1002/mrm.22708

Pohmann, R., and von Kienlin, M. (2001). Accurate phosphorus metabolite images of the human heart by 3D acquisition-weighted CSI. *Magn. Reson. Med.* 45, 817–826. doi: 10.1002/mrm.1110

Provencher, S. W. (2001). Automatic quantification of localized in vivo 1H spectra with LCModel. *NMR Biomed.* 14, 260–264. doi: 10.1002/nbm.698

pyMapVBVD CIC Methods Group. (n.d.). Available online at: https://github.com/CIC-methods/pyMapVBVD.

Ren, J., Sherry, A. D., and Malloy, C. R. (2015). 31P-MRS of healthy human brain: ATP synthesis, metabolite concentrations, pH, and T1 relaxation times. *NMR Biomed.* 28, 1455–1462. doi: 10.1002/nbm.3384

Rodgers, C. T., and Robson, M. D. (2010). Receive array magnetic resonance spectroscopy: whitened singular value decomposition (WSVD) gives optimal Bayesian solution. *Magn. Reson. Med.* 63, 881–891. doi: 10.1002/mrm.22230

Rothman, D. L., De Feyter, H. M., de Graaf, R. A., Mason, G. F., and Behar, K. L. (2011). 13C MRS studies of neuroenergetics and neurotransmitter cycling in humans. *NMR Biomed.* 24, 943–957. doi: 10.1002/nbm.1772

Rothman, D. L., de Graaf, R. A., Hyder, F., Mason, G. F., Behar, K. L., and De Feyter, H. M. (2019). In vivo 13C and 1H-[13C] MRS studies of neuroenergetics and neurotransmitter cycling, applications to neurological and psychiatric disease and brain cancer. *NMR Biomed.* 32:e4172. doi: 10.1002/nbm.4172

Rowland, B., S J, L. S., and Lin, A. (2017). OpenMRSLab: an open-source software repository for magnetic resonance spectroscopy data analysis tools. *Proc. Int. Soc. Magn. Reson. Med.* 25, 687–688.

Schuff, N., Amend, D., Ezekiel, F., Steinman, S. K., Tanabe, J., Norman, D., et al. (1997). Changes of hippocampal N-acetyl aspartate and volume in Alzheimer's disease: a proton MR spectroscopic imaging and MRI study. *Neurology* 49, 1513–1521. doi: 10.1212/WNL.49.6.1513

Sherman, G. (n.d.). Available online at: https://github.com/g-sherman/gswidgetkit.

Simpson, R., Devenyi, G. A., Jezzard, P., Hennessy, T. J., and Near, J. (2017). Advanced processing and simulation of MRS data using the FID appliance (FID-A)—an open source, MATLAB-based toolkit. *Magn. Reson. Med.* 77, 23–33. doi: 10.1002/mrm.26091

Susnjar, A, Kaiser, A, Simicic, D, Nossa, G, Lin, A, Oeltzschner, G, et al. (2025). Reproducibility Made Easy: A Tool for Methodological Transparency and Efficient Standardized Reporting Based on the Proposed MRSinMRS Consensus. *NMR in Biomedicine* 38:e70039.

Talbot, H. (2000). *WxPython, a GUI toolkit*. Linux J. No. 5–es. Available online at: https://www.wxpython.org/.

Tedeschi, G., Bertolino, A., Lundbom, N., Bonavita, S., Patronas, N. J., Duyn, J. H., et al. (1996). Cortical and subcortical chemical pathology in Alzheimer's disease as assessed by multislice proton magnetic resonance spectroscopic imaging. *Neurology* 47, 696–704. doi: 10.1212/WNL.47.3.696

Terpstra, M., Cheong, I., Lyu, T., Deelchand, D. K., Emir, U. E., Bednařík, P., et al. (2016). Test-retest reproducibility of neurochemical profiles with short-echo, single-voxel MR spectroscopy at 3T and 7T. *Magn. Reson. Med.* 76, 1083–1091. doi: 10.1002/mrm.26022

Walsh, D. O., Gmitro, A. F., and Marcellin, M. W. (2000). Adaptive reconstruction of phased array MR imagery. *Magn. Reson. Med.* 43, 682–690. doi: 10.1002/(SICI)1522-2594(200005)43:5<682::AID-MRM10>3.0.CO;2-G

Wilson, M., Reynolds, G., Kauppinen, R. A., Arvanitis, T. N., and Peet, A. (2010). A constrained least-square approach to the automated quantitation of in vivo 1H MRS data. *Magn. Reson. Med.* 65, 1–12. doi: 10.1002/mrm.22579

Zhu, X. H., Lu, M., and Chen, W. (2018). Quantitative imaging of brain energy metabolisms and neuroenergetics using in vivo X-nuclear 2H, 17O and 31P MRS at ultra-high field. *J. Magn. Reson.* 292, 155–170. doi: 10.1016/j.jmr.2018.05.005

Ziegs, T., Ruhm, L., Wright, A., and Henning, A. (2023). Mapping of glutamate metabolism using 1H FID-MRSI after oral administration of [1-13C] Glc at 9.4 T. *NeuroImage* 270:119940. doi: 10.1016/j.neuroimage.2023.119940