# **Chi-sep toolbox GUI Manual**

## Information

- This tool is MATLAB-based GUI software for reconstructing Quantitative Susceptibility Map (QSM) and separating positive and negative susceptibility sources (χ-separation). Separating paramagnetic (e.g., iron) and diamagnetic (e.g., myelin) susceptibility sources co-existed in a voxel provides the distributions of two sources that QSM does not provides. Magnetic susceptibility maps generated by QSM or χ-separation offer important information for research or diagnosis. An inexperienced researcher (user) can easily conduct QSM and χ-separation processing through the tool's user-friendly interface.
- The chi-sep toolbox includes the following features:
  - 1. DICOM/NIFTI/MATLAB data compatibility
  - 2. **QSMnet**: Quantitative susceptibility mapping (QSM) reconstruction algorithm based on deep neural network (QSMnet; J. Yoon et al., Neuroimage, 2018)
  - 3. χ-separation using R2' (or R2\*): magnetic susceptibility source separation algorithms based on convex optimization that share similar contrasts and optimization parameters with either MEDI+0 (Liu et al., MRM, 2018) or iLSQR (Li et al., Neuroimage, 2015) algorithms. The toolbox also provides the option to use pseudo R2 map if R2 measurement is not available (using R2' is recommended for accurate estimation).
  - 4.  $\chi$ -sepnet using R2' (or R2\*): a U-Net-based neural network that reconstructs  $\chi$ -separation using R2' and phase. In case R2 is not measured, another neural network is trained to estimate  $\chi$ -separation maps from R2\* and phase.
- Last update: Mar-18-2023

#### Reference:

- H. Shin, J. Lee, Y. H. Yun, S. H. Yoo, J. Jang, S.-H. Oh, Y. Nam, S. Jung, S. Kim, F. Masaki, W. Kim, H. J. Choi, J. Lee. χ-separation: Magnetic susceptibility source separation toward iron and myelin mapping in the brain. Neuroimage, 2021 Oct; 240:118371.
- M. Kim, H. Shin, C. Oh, H. Jeong, S. Ji, H. An, J. Kim, J. Jang, B. Bilgic, and J. Lee, "Chi-sepnet: Susceptibility source separation using deep neural network", 30th Annual Meeting of International Society of Magnetic Resonance in Medicine, 2022; 2464.
- J. Yoon, E. Gong, I. Chatnuntawech, B. Bilgic, J. Lee, W. Jung, J. Ko, H. Jung, K. Setsompop, G. Zaharchuk, E.Y. Kim, J. Pauly, J. Lee. Quantitative susceptibility mapping using deep neural network: QSMnet. Neuroimage. 2018;179:199-206.
- Chi-sep toolbox is powered by MEDI toolbox, STI Suite.
   (MEDI toolbox and STI Suite are used for phase data processing, so if you are only interested in QSMnet, χ-separation, and χ-sepnet, you don't need them.)

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Name: Affiliation: Software: Purpose:

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#### Requirements

## MATLAB toolbox

1. xiangruili/dicm2nii

(https://kr.mathworks.com/matlabcentral/fileexchange/42997-xiangruili-dicm2nii)

2. Tools for NIfTI and ANALYZE image

(https://kr.mathworks.com/matlabcentral/fileexchange/8797-tools-for-nifti-and-analyze-image)

3. Deep Learning Toolbox Converter for ONNX Model Format

(https://kr.mathworks.com/matlabcentral/fileexchange/67296-deep-learning-toolbox-converter-for-onnx-model-format)

#### QSM toolbox

1. STI Suite (Version 3.0)

(https://people.eecs.berkeley.edu/~chunlei.liu/software.html)

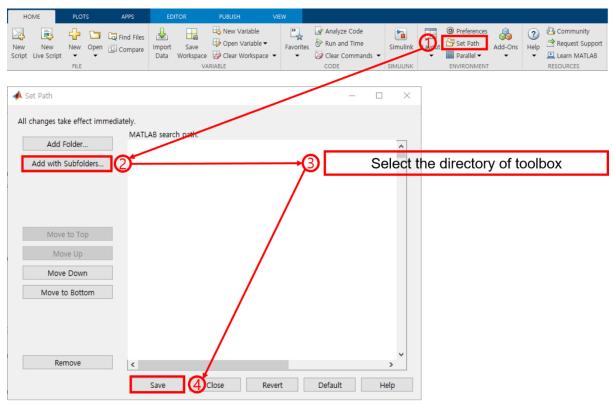
2. MEDI toolbox

(http://pre.weill.cornell.edu/mri/pages/qsm.html)

• MEDI toolbox and STI Suite are used for phase data processing, so if you are only interested in QSMnet,  $\chi$ -separation, and  $\chi$ -sepnet, you do not need to install them.

#### Installation and integration with support tools

## 1. Add Chi-sep toolbox path



< Set toolbox path >

- ① Click "Set Path"
- ② Click "Add with Subfolders"
- 3 Select the directory of Select the directory of "chi-sep toolbox"
- 4 Click "Save"

#### 2. Add MATLAB toolbox path

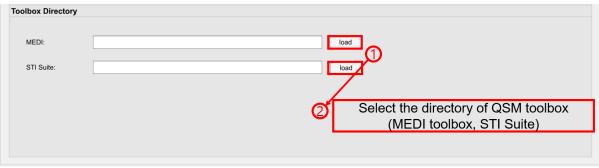
- xiangruili/dicm2nii: Add the directory path of dicm2nii in the same way as 1 (Add χ-separation tool path).
- 2 Tools for NIfTI and ANALYZE image: Add the directory path of Tools for NIfTI and ANALYZE image in the same way as 1 (Add χ-separation tool path).
- ③ Deep Learning Toolbox Converter for ONNX Model Format: Download onnxconverter Add-on, and then install it.

## 3. Add QSM toolbox path

- ① STI Suite: Add the directory path of STI Suite in the same way as 1 (Add chi-sep toolbox path).
- ② MEDI toolbox: Add the directory path of MEDI toolbox in the same way as 1 (Add chi-sep toolbox path).

Alternatively, there are two ways to add QSM toolbox path.

① Load the QSM toolbox path from the common tab of the chi-sep toolbox GUI.



< Set QSM toolbox path in χ-sep toolbox GUI >

② Write the QSM toolbox path in 'chi-sep\_toolbox\_dir/initialize/ ToolboxDirectoryFile.m'.

```
ToolboxDirectoryFile.m * +

1 - MEDIDirectory = 'your_path/MEDI_toolbox';
2 - STISuiteDirectory = 'your_path/STISuite';
3
```

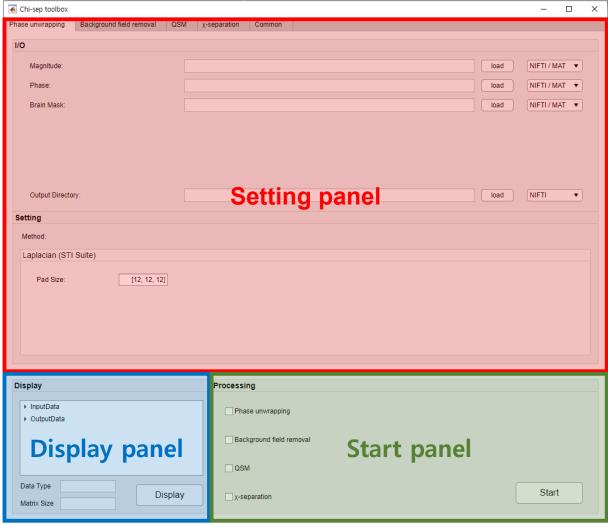
< Write the QSM toolbox path in ToolboxDirectoryFile.m >

#### 4. Open chi-sep toolbox GUI.

- Type "Chisep" in MATLAB command.
- Click "GUI for chi-separation" button.

## Information of chi-sep toolbox GUI

#### 1. Main window



< Chi-sep toolbox GUI main window >

**Setting panel**: You can set data I/O and parameters for process. This panel consist of 'Phase unwrapping', 'Background field removal', 'QSM', 'χ-separation', and 'Common' tabs.

Display panel: This panel displays briefly the data.

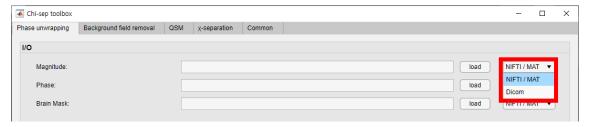
**Start panel**: You can select processes, then run it.

## 2. Input data

Data name	Unit	File format	Note	If select 'process',
Magnitude	-	DICOM, NIFTI, MAT	3D or 4D (multi-echo)	-
Phase	-	DICOM, NFITI, MAT	3D or 4D (multi-echo)	-
Brain mask	-	NIFTI, MAT	3D	Generated by toolbox (Brain extraction based on the BET tool from the MEDI)
Field map	Hz	NIFTI, MAT	3D	Generated by toolbox (Phase unwrapping process)
Local field	Hz	NIFTI, MAT	3D	Generated by toolbox (Background field removal process)
QSM	ppm	NIFTI, MAT	3D	Generated by toolbox (QSM process)
R2'	-	NIFTI, MAT	3D	-
R2*	-	NIFTI, MAT	3D	Generated by toolbox (Auto-Regression on Linear Operations from the MEDI: multi-echo mag is needed)

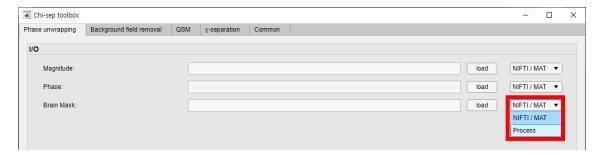
< Information of input data >

- You can specify the format of input data with the dropbox. It can be loaded as NIFTI
  or MAT with the 'NIFTI / MAT'. For Magnitude and Phase, they can be loaded as
  DICOM by selecting the 'Dicom' of the dropbox.
- The Chi-sep toolbox exclusively supports DICOM containing magnitude/phase data, requiring real/imag files to be converted to NIFTI format before they can be loaded.



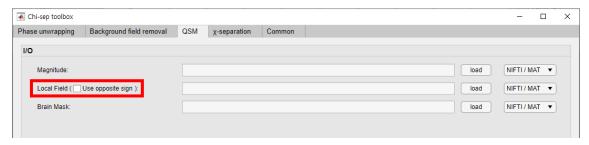
< Example: a dropbox of magnitude >

 If the 'Process' is selected, Brain mask, Field map, Local field, QSM, and R2\* can be generated.



< Example: a dropbox of brain mask >

 If the sign of QSM results is inverted or the positive and negative maps look interchanged, your input Local Field map would have opposite sign. For this, you can select the "Use opposite sign" checkbox, which will multiply -1 to the input Local Field.



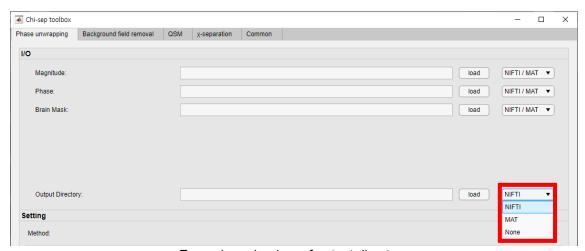
< Example: a checkbox of opposite sign >

## 3. Output data and directory

Data name	Unit	File format	Note
Field map	Hz	NIFTI, MAT	Generated by Phase unwrapping
Local field	Hz	NIFTI, MAT	Generated by Background field removal
Brain mask	-	NIFTI, MAT	Generated by Background field removal (V-SHARP)
QSM	ppm	NIFTI, MAT	Generated by QSM
χ-positive map	ppm	NIFTI, MAT	Generated by χ-separation
χ-negative map	ppm	NIFTI, MAT	Generated by χ-separation
χ-total map (pos + neg)	ppm	NIFTI, MAT	Generated by χ-separation

< Information of output data >

- You can define the format of data to save on the drop box next to the load button of the 'Output Directory'.
- If 'None' is selected, the output data is not saved.



< Example: a dropbox of output directory >

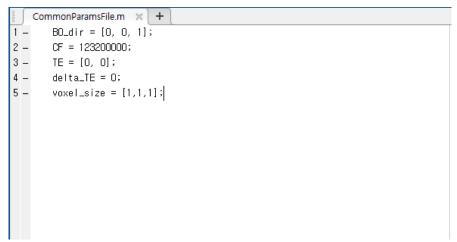
## 4. Parameters and process

- Common parameters
  - These are the six parameters of the data commonly used in various processes: B0 strength, B0 direction, central frequency (CF), echo time (TE), delta TE, and voxel size.
  - ➤ The B0 strength is automatically calculated from the CF as follows: B0 strength = CF / (42.57478 \* 1e6).
  - > There are two ways to set common parameters.
  - > The first way is to put the parameters of your data at the common tab of the setting panel.



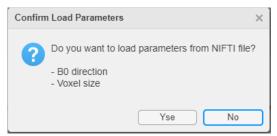
< A common tab of chi-sep toolbox GUI >

The second way is to write them in 'chi-sep\_toolbox\_dir/initialize/ CommonParamsFile.m' before running the tool.



< CommonParamsFile.m >

Additionally, you can load them that exist in the header file when data with extension of NIFTI or Dicom is loaded.



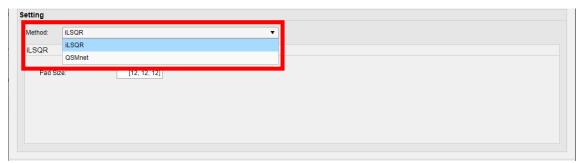
< A dialog asking whether to load the parameters existing in the header file >

#### Processes

Process name	Method	Note
Phase	Laplacian-based	
Unwrapping	method	-
Background Field Removal	V-SHARP	Generate QSM mask
QSM	iLSQR, QSMnet	You can select the reference tissue in QSMnet method
χ-separation	$\chi$ -separation <sub>L1</sub> , $\chi$ -separation <sub>SA</sub> , $\chi$ -sepnet	When you don't have R2, You can create pseudo R2 filled with nominal values for χ-separation methods. Also, you can run χ-sepnet trained by R2*.

< methods of processes >

- By controlling the drop box for Method, you can select the methods of process in the activated tab.
- ➤ A panel of the selected method appears and then you can put the parameters of the process.
- $\gt$  Since the processing time of  $\chi$ -separation<sub>L1</sub> and  $\chi$ -separation<sub>SA</sub> is much longer than that of deep learning-based methods for  $\chi$ -separation, it is recommended to use the network method if you want to see the results quickly.
- $\triangleright$  Warning: Deep learning (QSMnet and χ-sepnet) is designed for 1 mm isotropic voxel size. Too different resolution can result in artifacts.



< Example: a dropbox of QSM method >

## Usage of chi-sep toolbox GUI

1. For whole processing from phase processing to  $\chi$ -separation (R2' version)

#### **Exercise**

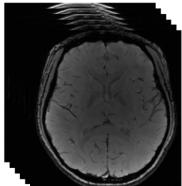
ullet Perform whole processing implemented in the tool with one run from phase processing to  $\chi$ -separation.

(MEDI toolbox and STI Suite are required for full processing.)

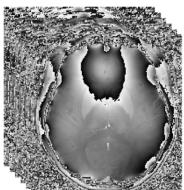
#### Input data

- Multi-echo GRE magnitude (4D: x, y, z, echo time)
- Multi-echo GRE phase (4D: x, y, z, echo time)
- R2prime (3D)

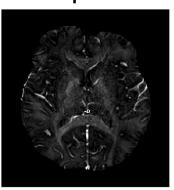
Magnitude



**Phase** 



R2prime

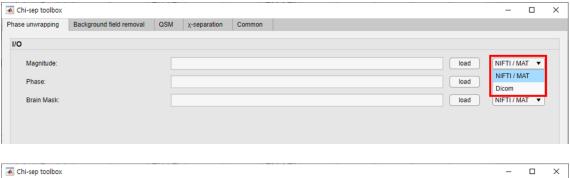


#### **Processes**

- Phase unwrapping: Laplacian-based method (STI Suite)
- Background field removal: V-SHARP
- QSM: iLSQR or QSMnet
- χ-separation: χ-separation or χ-sepnet
  - ① Execute chi-sep toolbox GUI.
  - > Type "Chisep" in MATLAB command.
  - $\triangleright$  Click "GUI for  $\chi$ -separation" button.

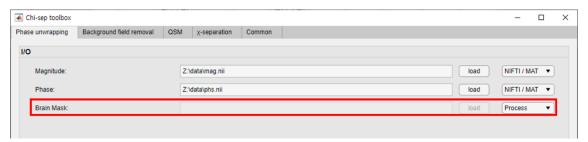
#### ② Load input data.

- Set the dropbox to 'NIFTI / MAT' if the magnitude and phase are NIfTI or MAT files, or 'Dicom' if they are DICOM in Phase unwrapping tab.
- > Then press the load button to select a NIfTI or MAT file or a Dicom directory to load the data.





Set dropbox of Brain Mask to 'Process' in Phase unwrapping tab.



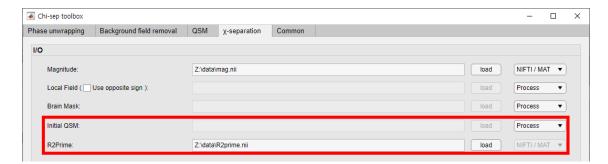
> Set dropbox of Field map to 'Process' in Background field removal tab.



Set dropbox of Local field to 'Process' in QSM unwrapping tab.



 $\triangleright$  Set dropbox of Initial QSM to 'Process' and load R2' in  $\chi$ -separation tab.



3 Set dropbox of output directory to 'NIFTI' and load output directory.



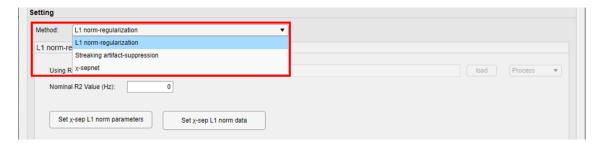
**④** Put common parameters of your data.



- **⑤** Set method of each process.
- > Keep the Laplacian method in Phase unwrapping tab.
- ➤ Keep the V-SHARP method in Background field removal tab.
- > On the QSM tab, select either the iLSQR method or the QSMnet method.



 $\triangleright$  On the χ-separation tab, select either the L1, SA or χ-sepnet method.

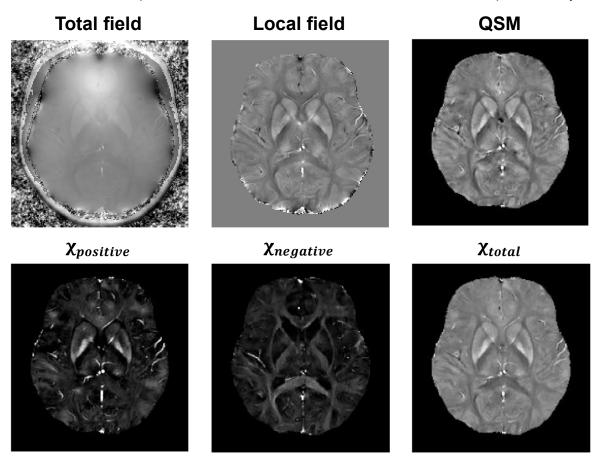


## 6 Run processing

- Check all processes in start panel.
- Press the start button.



When all processes are finished, the results are saved to the output directory.



#### 2. For whole processing from phase processing to $\chi$ -separation (R2\* version)

#### **Exercise**

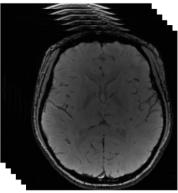
 Perform whole processing implemented in the tool with one run from phase processing to χ-separation.

(MEDI toolbox and STI Suite are required for full processing.)

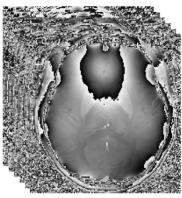
### Input data

- Multi-echo GRE magnitude (4D: x, y, z, echo time)
- Multi-echo GRE phase (4D: x, y, z, echo time)





Phase



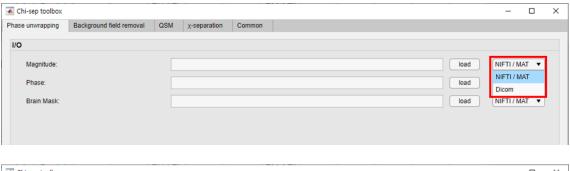
• Perform all processes implemented in the tool with one run using only multi-echo GRE data.

#### **Processes**

- Phase unwrapping: Laplacian-based method (STI Suite)
- Background field removal: V-SHARP
- QSM: iLSQR or QSMnet
- $\chi$ -separation:  $\chi$ -separation or  $\chi$ -sepnet
  - ① Execute chi-sep toolbox GUI.
  - > Type "Chisep" in MATLAB command.
  - $\triangleright$  Click "GUI for  $\chi$ -separation" button.

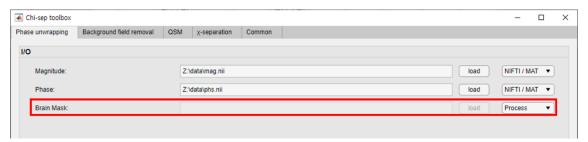
#### ② Load input data.

- Set the dropbox to 'NIFTI / MAT' if the magnitude and phase are NIfTI or MAT files, or 'Dicom' if they are DICOM in Phase unwrapping tab.
- > Then press the load button to select a NIfTI or MAT file or a Dicom directory to load the data.





Set dropbox of Brain Mask to 'Process' in Phase unwrapping tab.



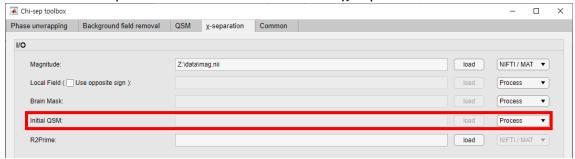
> Set dropbox of Field map to 'Process' in Background field removal tab.



> Set dropbox of Local field to 'Process' in QSM unwrapping tab.



 $\triangleright$  Set dropbox of Initial QSM to 'Process' in  $\chi$ -separation tab.



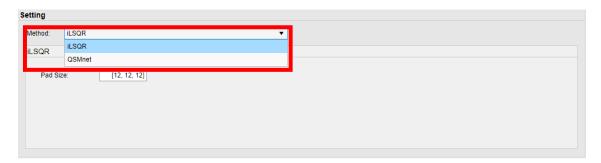
3 Set dropbox of output directory to 'NIFTI' and load output directory.



**④** Put common parameters of your data.



- **⑤** Set method of each process.
- > Keep the Laplacian method in Phase unwrapping tab.
- ➤ Keep the V-SHARP method in Background field removal tab.
- > On the QSM tab, select either the iLSQR method or the QSMnet method.



- $\triangleright$  On the χ-separation tab, select either the L1, SA or χ-sepnet method.
- Check Using R2Star (at the same time, dropbox of R2prime is set to 'None').
- $\triangleright$  If you selected the L1 or SA method, enter a nominal value for the pseudo R2 map, and if you selected χ-sepnet, enter a relaxation metric value in Dr blank. (default: 137).
- > Set dropbox of R2Star to 'Process' (available if multi-echo magnitude is given).



Or

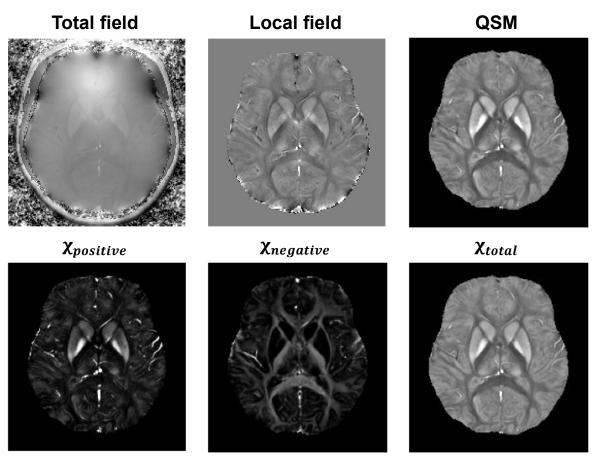


## 6 Run processing

- Check all processes in start panel.
- Press the start button.



> When all processes are finished, the results are saved to the output directory.



## 3. For phase processing

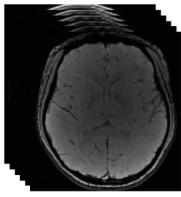
#### **Exercise**

Perform phase processing from phase to local field map.
 (MEDI toolbox and STI Suite are required for processing.)

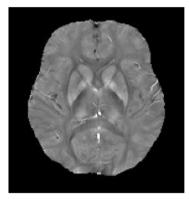
## Input data

- Multi-echo GRE magnitude (4D: x, y, z, echo time)
- Multi-echo GRE phase (4D: x, y, z, echo time)

Magnitude



Local field

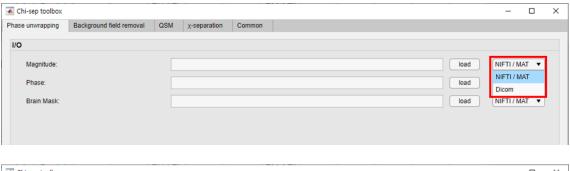


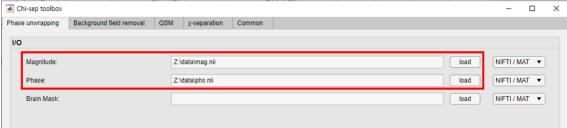
#### **Processes**

- Phase unwrapping: Laplacian-based method (STI Suite)
- Background field removal: V-SHARP
  - ① Execute chi-sep toolbox GUI.
  - > Type "Chisep" in MATLAB command.
  - $\triangleright$  Click "GUI for  $\chi$ -separation" button.

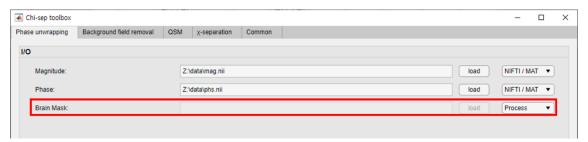
#### ② Load input data.

- > Set the dropbox to 'NIFTI / MAT' if the magnitude and phase are NIfTI or MAT files, or 'Dicom' if they are DICOM in Phase unwrapping tab.
- > Then press the load button to select a NIfTI or MAT file or a Dicom directory to load the data.





Set dropbox of Brain Mask to 'Process' in Phase unwrapping tab.



> Set dropbox of Field map to 'Process' in Background field removal tab.



3 Set dropbox of output directory to 'NIFTI' and load output directory.



4 Put common parameters of your data.



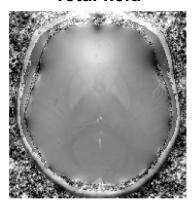
- **⑤** Set method of each process.
- Keep the Laplacian method in Phase unwrapping tab.
- > Keep the V-SHARP method in Background field removal tab.
- **6** Run processing
- Check Phase unwrapping and Background field removal in start panel.
- Press the start button.

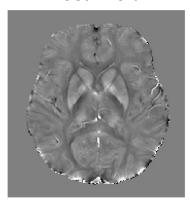


When all processes are finished, the results are saved to the output directory.

## **Total field**

Local field





## 4. For QSMnet and $\chi$ -separation (R2' version)

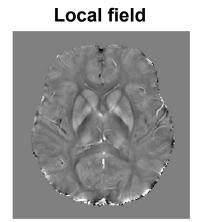
#### **Exercise**

• Perform to  $\chi$ -separation (R2' version). (Because it only uses QSMnet and  $\chi$ -separation, you don't need the MEDI Toolbox and STI Suite.)

## Input data

- Multi-echo GRE magnitude (4D: x, y, z, echo time)
- Local field map (3D)
- R2prime (3D)
- Brain mask (3D)

Magnitude



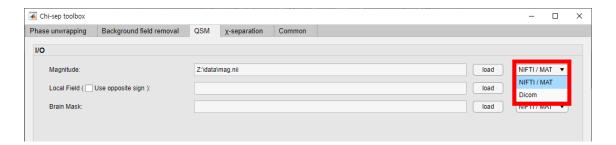


#### **Processes**

- QSM: QSMnet
- χ-separation: χ-separation or χ-sepnet
  - ① Execute chi-sep toolbox GUI.
  - > Type "Chisep" in MATLAB command.
  - > Click "GUI for χ-separation" button.

#### ② Load input data.

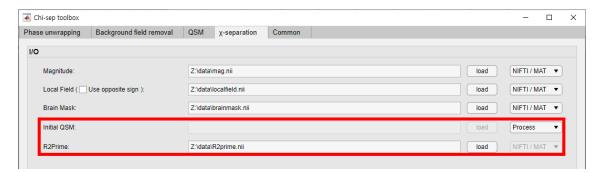
- Set the dropbox to 'NIFTI / MAT' if the magnitude is NIfTI or MAT files, or 'Dicom' if they are DICOM in QSM tab.
- > Then press the load button to select a NIfTI or MAT file or a Dicom directory to load the data.



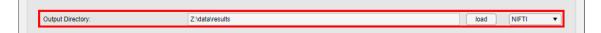
Set the dropbox for local field map and brain mask to 'NIFTI / MAT', then press the Load button to select the NIfTI or MAT file you want to load data from.



 $\triangleright$  Set dropbox of Initial QSM to 'Process' and load R2' in  $\chi$ -separation tab.



3 Set dropbox of output directory to 'NIFTI' and load output directory.



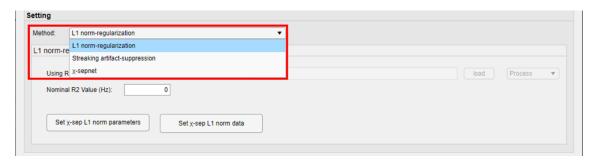
**④** Put common parameters of your data.



- **⑤** Set method of each process.
- On the QSM tab, select the QSMnet method.



 $\triangleright$  On the  $\chi$ -separation tab, select either the L1, SA or  $\chi$ -separation.

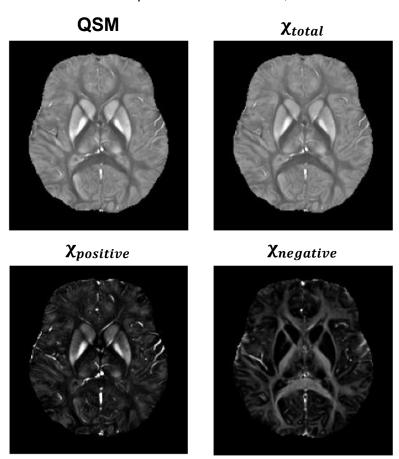


## 6 Run processing

- $\triangleright$  Check QSM and χ-separation in start panel.
- Press the start button.



When all processes are finished, the results are saved to the output directory.



## 5. For QSMnet and $\chi$ -separation (R2\* version)

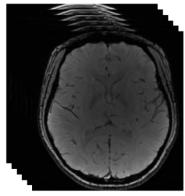
#### **Exercise**

• Perform to  $\chi$ -separation (R2\* version). (Because it only uses QSMnet and  $\chi$ -separation, you don't need the MEDI Toolbox and STI Suite.)

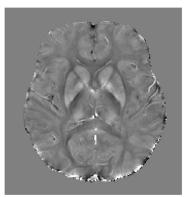
## Input data

- Multi-echo GRE magnitude (4D: x, y, z, echo time)
- Local field map (3D)
- Brain mask (3D)

Magnitude



Local field

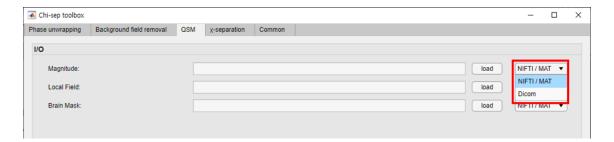


#### **Processes**

- QSM: QSMnet
- $\chi$ -separation:  $\chi$ -separation or  $\chi$ -sepnet
  - ① Execute chi-sep toolbox GUI.
  - > Type "Chisep" in MATLAB command.
  - > Click "GUI for χ-separation" button.

#### ② Load input data.

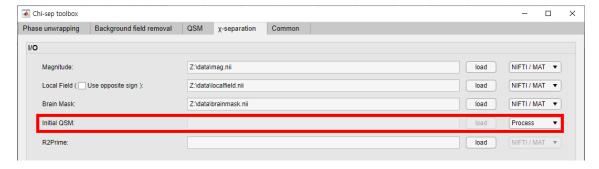
- > Set the dropbox to 'NIFTI / MAT' if the magnitude is NIfTI or MAT files, or 'Dicom' if they are DICOM in QSM tab.
- > Then press the load button to select a NIfTI or MAT file or a Dicom directory to load the data.



> Set the dropbox for local field map and brain mask to 'NIFTI / MAT', then press the Load button to select the NIfTI or MAT file you want to load data from.



 $\triangleright$  Set dropbox of Initial QSM to 'Process' in  $\chi$ -separation tab.



3 Set dropbox of output directory to 'NIFTI' and load output directory.



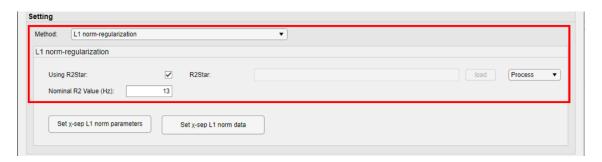
Put common parameters of your data.



- **⑤** Set method of each process.
- On the QSM tab, select the QSMnet method.



- $\triangleright$  On the  $\chi$ -separation tab, select either the L1, SA or  $\chi$ -separation method.
- ➤ Check Using R2Star (at the same time, dropbox of R2prime is set to 'None').
- $\triangleright$  If you selected the L1 or SA method, enter a nominal value for the pseudo R2 map, and if you selected χ-sepnet, enter a relaxation metric value in Dr blank. (default: 137).
- > Set dropbox of R2Star to 'Process' (available if multi-echo magnitude is given).



Or



## 6 Run processing

- $\triangleright$  Check QSM and χ-separation in start panel.
- Press the start button.



When all processes are finished, the results are saved to the output directory.

