Ironsmith QSM

This software has been developed for research purposes only and is not a clinical tool.

Description:

Ironsmith is an automated pipeline for creating Quantitative Susceptibility Maps (QSM)
and for extracting QSM based iron concentrations from subcortical and cortical brain regions.

Ironsmith can perform the following tasks:

a) Create QSM maps from GRE DICOM images using the MEDI Toolbox **(see section 7 for details)** .
b) Register MPR or multi-echo MPR (MEMPR) T1 images to QSM maps and then segment these into 89 ROIs **(ROI list in section 8)** using FreeSurfer.
c) Filter outlier voxels from these ROIs (QSM values larger than top 97th percentile of values), extract QSM based iron concentration, and format the output into CSV tables (MS Excel compatible).
d) Calculate SNR (magnitude image based) for each ROI as a measure of quality control for QSM and output SNR values in CSV tables (MS Excel compatible).
e) Warp QSM maps and aligned MPR/MEMPR to MNI152 1mm space for voxelwise QSM analyses.
f) Process single or multiple participants in parallel (multiple instances and nohup supported).

1) Software requirements:

a) Operating system

Unix
Any Linux distribution that supports Singularity (see point c).

Ironsmith tested on:
Red Hat Enterprise Linux Workstation release 7.8 (Maipo)

Windows 10 WSL2
Ironsmith tested on:

Ubuntu 18.04 running on Windows 10 Subsystem for Linux V2 (WSL2)
Ubuntu 16.04 running on Windows 10 Subsystem for Linux V2 (WSL2)

b) MATLAB

Ironsmith requires Matlab to run MEDI Toolbox and supports versions R2017b to R2019b.
Matlab is not needed if MEDI is not required.

c) Singularity

Ironsmith tested on Singularity versions 3.5.2 and 3.5.3
Installation guide:
https://sylabs.io/guides/3.5/admin-guide/installation.html

d) Bash UNIX shell version 4.2.46(2) or later

e) MEDI Toolbox version 01/15/2020

Ironsmith requires MEDI Toolbox if QSM maps need to be generated
Download from:
http://pre.weill.cornell.edu/mri/pages/qsm.html
MEDI Toolbox is not required if QSM maps already available
Currently only MEDI Toolbox version 01/15/2020 is supported

2) Installation:

a) Download Ironsmith QSM

Option 1: download from github

Visit https://github.com/vzachari/IronSmithQSM
Click on tags
Click on desired IronsmithQSM version (release notes are displayed by clicking the three dots `...`)
Click on source code link (zip or tar.gz) to download

NOTE: Via this download option the IronSmithQSM folder will be **IronSmithQSM-version#** *(Ex. IronSmithQSM-1.00)*.

Option 2: using git

```
git clone https://github.com/vzachari/IronSmithQSM.git && cd IronSmithQSM && git checkout v1.0
```

NOTE: `git checkout v1.0` can be replaced with a different version number. Type `git tag -l` from within the IronSmithQSM folder for a list of available versions.

b) Download QSM_Container.simg (8.8GB)

From: https://drive.google.com/file/d/1wPdd2Xa0oLV2wwpHneXZ7nlIZB3XoKFb/view?usp=sharing
Or
From: https://tinyurl.com/QSMContainer

c) Place QSM_Container.simg in IronSmithQSM/Functions

d) Download MEDI Toolbox version 01/15/2020 (~7MB)

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

e) Unzip MEDI Toolbox (typically MEDI_toolbox.zip)

f) Place MEDI_toolbox folder (folder with README.m, UPDATES.m etc) into IronSmithQSM/Functions

NOTE: Make sure the MEDI_toolbox folder in IronSmithQSM/Functions does not have another MEDI_toolbox folder in it (e.g MEDI_toolbox/MEDI_toolbox)

g) Edit IronSmithQSM/Matlab_Config.txt with the path to the matlab executable on your system.

(e.g. /usr/local/MATLAB/R2019b/bin/matlab)
Supported versions R2017b to R2019b.

h) Add the IronSmithQSM directory to $PATH

Guide: https://opensource.com/article/17/6/set-path-linux

3) Syntax:

Ironsmith [MyInputFile] [absolute path to output folder]

Example: "Ironsmith File.csv /home/data/MyAmazingExp/QSM_Analysis"

a) The output folder does not need to exist.

b) The output folder does not need to be empty but Ironsmith will skip any participant specified in MyInputFile that has a corresponding folder inside the output folder.

Ex. if S0001 is specified in MyInputFile and folder S0001 exists in output folder, S0001 will be skipped.

c) Absolute path to MyInputFile needs to be provided
(Ex. /home/data/MyAmazingExp/CSVFileVault/File.csv) if MyInputFile is not in current folder.

d) Freesurfer_Skip is a reserved folder name under output folder and may be used by Ironsmith. See section #5 on Optional features below.

4) MyInputFile format:

a) MyInputFile has to be CSV formatted (entries separated by commas ',').

b) MyInputFile can be created in Excel (MS Windows or MacOS) and saved as a CSV (Comma delimited) file or in a Unix text editor (e.g. Gedit, Atom, Emacs).

c) Each row in MyInputFile corresponds to a different participant.

see Example_File.csv in IronSmithQSM folder:

If MEDI Toolbox is required to create QSM images/maps:

Column1 = Subj (nominal subject variable e.g. S0001 or 01 or Xanthar_The_Destroyer)
Column2 = MEDI_Yes <-- this is case sensitive
Column3 =
Either absolute path to directory with MPR/MEMPR files **OR** absolute path to a single NIFTI (.nii or .nii.gz) MPR/MEMPR file
*(e.g. /home/subjects/S01/MPR **OR** /home/subjects/S01/MPR/S01_MPR.nii.gz)*

If a single NIFTI (.nii or .nii.gz) MPR/MEMPR file is provided:
File can have any name.
File can have multiple volumes, each corresponding to a different echo (RMS will be calculated).
File can have a single echo/volume.

If path to directory with MPR/MEMPR files is provided:

MPR/MEMPR files in provided folder can be:

a) DICOMS

Only MPR/MEMPR DICOMS should be present in the MPR folder if you want Ironsmith to process DICOMS. If NIFTI files exist together with DICOMS, they will be selected instead (see "b" below).

b) Multiple .nii/.nii.gz files each corresponding to a different echo (will be catenated and RMS will be calculated).

To make sure the correct files are selected, each NIFTI file needs to have _e# in the file name, where # is the echo number.
(e.g. S0001_MEMPR_e1.nii.gz, S0001_MEMPR_e2.nii.gz…)
This is the default **dcm2niix** output format for multiple echos.

c) Single .nii/nii.gz file with multiple volumes, each corresponding to a different echo (RMS will be calculated).
This single NIFTI file can have any name.

d) Single .nii/nii.gz file with a single echo/volume.
This can be rms/averaged across echos or just a single echo T1 MPRAGE.
This single NIFTI file can have any name and will be used as is.

Column4 = Absolute path to folder with QSM DICOM files
(e.g. /home/subjects/S01/QSM_Dicom)
QSM DICOM folder must include DICOMS for both GRE magnitude and phase.

Preferably only QSM DICOMS should be present in the QSM_Dicom folder. However, Ironsmith can filter out the following filetypes .nii .json .txt .nii.gz .HEAD .BRIK .hdr .img

All 4 columns need to be provided, otherwise Ironsmith will exit with errors.

If QSM maps and GRE magnitude images are already available:

Column1 = Subj (nominal subject variable e.g. S0001 or 01 or Xanthar_The_Destroyer)
Column2 = MEDI_No <-- This is case sensitive
Column3 =
Either absolute path to directory with MPR/MEMPR files **OR** absolute path to a single NIFTI (.nii or .nii.gz) MPR/MEMPR file
*(e.g. /home/subjects/S01/MPR **OR** /home/subjects/S01/MPR/S01_MPR.nii.gz)*

If a single NIFTI (.nii or .nii.gz) MPR/MEMPR file is provided:
File can have any name.
File can have multiple volumes, each corresponding to a different echo (RMS will be calculated).
File can have a single echo/volume.

If path to directory with MPR/MEMPR files is provided:

MPR/MEMPR files in provided folder can be:

a) DICOMS

Only MPR/MEMPR DICOMS should be present in the MPR folder if you want Ironsmith to process DICOMS. If NIFTI files exist together with DICOMS, they will be selected instead (see "b" below).

b) Multiple .nii/.nii.gz files each corresponding to a different echo (will be catenated and RMS will be calculated).

To make sure the correct files are selected, each NIFTI file needs to have _e# in the file name, where # is the echo number.
(e.g. S0001_MEMPR_e1.nii.gz, S0001_MEMPR_e2.nii.gz…)
This is the default **dcm2niix** output format for multiple echos.

c) Single .nii/nii.gz file with multiple volumes, each corresponding to a different echo (RMS will be calculated).
This single NIFTI file can have any name.

d) Single .nii/nii.gz file with a single echo/volume.
This can be rms/averaged across echos or just a single echo T1 MPRAGE.
This single NIFTI file can have any name and will be used as is.

Column4 = Absolute path including filename to QSM magnitude image
(e.g. /home/subjects/S01/QSM/QSM_Magnitude.nii.gz)

Column5 = Absolute path including filename to QSM map
(e.g. /home/subjects/S01/QSM/QSM_Map.nii.gz)

All 5 columns need to be provided, otherwise Ironsmith will exit with errors.

5) Optional features:

Skipping FreeSurfer segmentation

If FreeSurfer has already run and a participant has a completed FreeSurfer recon-all -all segmentation folder, Ironsmith can skip the FreeSurfer segmentation step by doing the following:

a) Copy the FreeSurfer recon-all folder (the one containing the *label*, *mri*, *scripts*, *stats*, *surf*… folders) into **/OutputFolder/Freesurfer_Skip**, where **OutputFolder** is the one specified/to be specified in the Ironsmith command.

You can create the /OutputFolder/Freesurfer_Skip folder or Ironsmith will create it for you if you have run it at least once previously for OutputFolder.

b) Rename the recon-all folder to **Subj_FreeSurfSeg_Skull**. Subj should match the one provided in MyInputFile and should correspond to the participant you want the segmentation step skipped.

Note: if Ironsmith runs FreeSurfer it will create **Subj_FreeSurfSeg_Skull** and place it under **/OutputFolder/Subj/MPR**. This helps reduce processing time if for any reason one would like to repeat the analysis on a given participant (e.g. due to crash or errors). Just copy/move this folder over to **/OutputFolder/Freesurfer_Skip**, delete the problematic participant folder (e.g. **/OutputFolder/Subj**) and re-run Ironsmith.

Processing participants in parallel

Parallel processing can significantly increase the speed of analyses. Running the Ironsmith command with the same MyInputFile and output folder in multiple terminal windows allows for parallel processing of participants specified in MyInputFile.

For example, running three instances of Ironsmith:

Terminal 1:
Ironsmith File.csv /home/data/MyAmazingExp/QSM_Analysis

Terminal 2:
Ironsmith File.csv /home/data/MyAmazingExp/QSM_Analysis

Terminal 3:
Ironsmith File.csv /home/data/MyAmazingExp/QSM_Analysis

Terminals 1-3 will each be running a different instance of Ironsmith (each working on a different set of participants) but all instances will be working on the same group/list of participants (from **File.csv**) and in the same output folder (**/home/data/MyAmazingExp/QSM_Analysis**) and will only create a single set of group output files (see section #6 below).

Viewing output NIFTI files

If you do not have a NIFTI viewer, AFNI can be launched from within the QSM_Container.simg by using the *Ironsmith_AFNI* command. Just type *Ironsmith_AFNI* from within the folder you would like to view NIFTI files from.

AFNI viewer documentation:
https://afni.nimh.nih.gov/pub/dist/edu/latest/afni_handouts/afni03_interactive.pdf

6) Outputs:

Each participant processed by Ironsmith will have a corresponding folder in **OutputFolder**. For example, if "**S0001**" is one of the participants processed, then **OutputFolder/S0001** will be created and populated with data.

a) All FreeSurfer based masks/ROIs are placed under:

S0001/QSM/FreeSurf_QSM_Masks/Cort_Mask_AL_QSM_RS_Erx1
S0001/QSM/FreeSurf_QSM_Masks/SubC_Mask_AL_QSM_RS_Erx1

b) All QSM maps/images created are placed under S0001/QSM/FreeSurf_QSM_Masks and are labelled as:

Subj_QSM_Map_FSL.nii.gz <-- Whole brain CSF, segmented from magnitude image, as the QSM reference structure (default MEDI)
Subj_QSM_Map_New_CSF_FSL.nii.gz <-- Lateral ventricles as the QSM reference structure
Subj_QSM_Map_New_WM_FSL.nii.gz <-- White matter as the QSM reference structure

c) All QSM maps warped to MNI space are placed under

S0001/QSM/FreeSurf_QSM_Masks/MNI152_QSM

d) QSM per ROI means (89 ROIs) are under **OutputFolder/Group** as follows:

Group_QSM_Mean.csv
Group_QSM_Mean_CSF.csv
Group_QSM_Mean_WM.csv
Group_QSM_ADJ_Mean.csv
Group_QSM_ADJ_Mean_CSF.csv
Group_QSM_ADJ_Mean_WM.csv
Group_QSM_SNR.csv

_Mean = Using only positive QSM voxels
_ADJ_Mean = Using only positive QSM voxels and adjusting for ROI size *(sum of all positive QSM voxels / Number of all voxels within an ROI)*
_CSF = Lateral ventricles as the QSM reference structure
_WM = White matter as the QSM reference structure

SNR is calculated as follows:
mean signal intensity of magnitude image within an ROI / standard deviation of magnitude signal outside the head (away from the frequency and phase axes).
Lastly, SNR is multiplied by the Rayleigh distribution correction factor $\sqrt{(2-\pi/2)}$.

The outside of the head mask used for SNR can be found here:
/QSM_Analysis/S0001/QSM/FreeSurf_QSM_Masks/Subj_QSM_Mag_FSL_rms_OH_Mask.nii.gz

7) Ironsmith uses the following software, provided in the form of a Singularity image:

AFNI

RW Cox. AFNI: Software for analysis and visualization of functional magnetic resonance neuroimages. Computers and Biomedical Research, 29:162-173, 1996.

RW Cox and JS Hyde. Software tools for analysis and visualization of FMRI Data. NMR in Biomedicine, 10:171-178, 1997.

S Gold, B Christian, S Arndt, G Zeien, T Cizadlo, DL Johnson, M Flaum, and NC Andreasen. Functional MRI statistical software packages: a comparative analysis. Human Brain Mapping, 6:73-84, 1998.

dcm2niix

Li, Xiangrui, et al. "The first step for neuroimaging data analysis: DICOM to NIFTI conversion." Journal of neuroscience methods 264 (2016): 47-56.

FreeSurfer

Dale, A.M., Fischl, B., Sereno, M.I., 1999. Cortical surface-based analysis. I. Segmentation and surface reconstruction. Neuroimage 9, 179-194.

Dale, A.M., Sereno, M.I., 1993. Improved localization of cortical activity by combining EEG and MEG with MRI cortical surface reconstruction: a linear approach. J Cogn Neurosci 5, 162-176.

Desikan, R.S., Segonne, F., Fischl, B., Quinn, B.T., Dickerson, B.C., Blacker, D., Buckner, R.L., Dale, A.M., Maguire, R.P., Hyman, B.T., Albert, M.S., Killiany, R.J., 2006. An automated labeling system for subdividing the human cerebral cortex on MRI scans into gyral based regions of interest. Neuroimage 31, 968-980.

FSL

M.W. Woolrich, S. Jbabdi, B. Patenaude, M. Chappell, S. Makni, T. Behrens, C. Beckmann, M. Jenkinson, S.M. Smith. Bayesian analysis of neuroimaging data in FSL. NeuroImage, 45:S173-86, 2009

S.M. Smith, M. Jenkinson, M.W. Woolrich, C.F. Beckmann, T.E.J. Behrens, H. Johansen-Berg, P.R. Bannister, M. De Luca, I. Drobnjak, D.E. Flitney, R. Niazy, J. Saunders, J. Vickers, Y. Zhang, N. De Stefano, J.M. Brady, and P.M. Matthews. Advances in functional and structural MR image analysis and implementation as FSL. NeuroImage, 23(S1):208-19, 2004

M. Jenkinson, C.F. Beckmann, T.E. Behrens, M.W. Woolrich, S.M. Smith. FSL. NeuroImage, 62:782-90, 2012

8) ROI List:

L_ = Left hemisphere
R_ = Right hemisphere
LR_ = Bilateral
_GM = Gray matter

LR_Frontal_Lobe_GM
LR_Parietal_Lobe_GM
LR_Occipital_Lobe_GM
LR_Temporal_Lobe_GM
L_CaudalAnteriorCingulate_GM
L_CaudalMiddleFrontal_GM
L_Cuneus_GM
L_DLPFC_GM
L_Entorhinal_GM
L_Frontal_GM

L_Fusiform_GM
L_InferiorParietal_GM
L_AngularGyrus_GM
L_InferiorTemporal_GM
L_Insula_GM
L_IsthmusCingulate_GM
L_LateralOccipital_GM
L_LateralOrbitofrontal_GM
L_Lingual_GM
L_MedialOrbitofrontal_GM
L_MiddleTemporal_GM
L_Occipital_GM_Mask
L_Parietal_GM_Mask
L_Temporal_GM_Mask
L_Parahippocampal_GM
L_Pericalcarine_GM
L_Postcentral_GM
L_PosteriorCingulate_GM
L_Precentral_GM
L_Precuneus_GM
L_RostalMiddleFrontal_GM
L_RostralAnteriorCingulate_GM
L_SuperiorFrontal_GM
L_SuperiorParietal_GM
L_SuperiorTemporal_GM
L_TransverseTemporal_GM
R_CaudalAnteriorCingulate_GM
R_CaudalMiddleFrontal_GM
R_Cuneus_GM
R_DLPFC_GM
R_Entorhinal_GM
R_Frontal_GM_Mask
R_Fusiform_GM
R_InferiorParietal_GM
R_AngularGyrus_GM
R_InferiorTemporal_GM
R_Insula_GM
R_IsthmusCingulate_GM

R_LateralOccipital_GM
R_LateralOrbitofrontal_GM
R_Lingual_GM
R_MedialOrbitofrontal_GM
R_MiddleTemporal_GM
R_Occipital_GM_Mask
R_Parietal_GM_Mask
R_Temporal_GM_Mask
R_Parahippocampal_GM
R_Pericalcarine_GM
R_Postcentral_GM
R_PosteriorCingulate_GM
R_Precentral_GM
R_Precuneus_GM
R_RostalMiddleFrontal_GM
R_RostralAnteriorCingulate_GM
R_SuperiorFrontal_GM
R_SuperiorParietal_GM
R_SuperiorTemporal_GM
R_TransverseTemporal_GM
LR_Accumbens_area
LR_Amygdala
LR_Caudate
LR_Hipp
LR_Pallidum
LR_Putamen
LR_Thalamus_Proper
L_Accumbens_area
L_Amygdala
L_Caudate
L_Hipp
L_Pallidum
L_Putamen
L_Thalamus_Proper
R_Accumbens_area
R_Amygdala
R_Caudate
R_Hipp

R_Pallidum
R_Putamen
R_Thalamus_Proper