NMR spectroscopy: a methodology for assessing the concentration of cerebral metabolites Implementation at the Centre IRM-INT: acquisitions, analyses and some applications

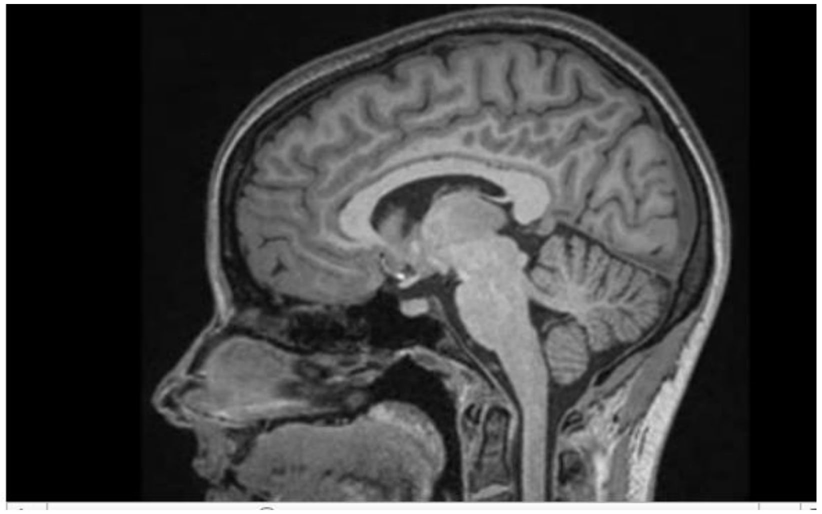
Julien Sein, Jean-Luc Anton

Réunion du REMI du 16/12/2024

Presentations and discussions on MRI spectroscopy, by experts and novices alike

Openart.ai

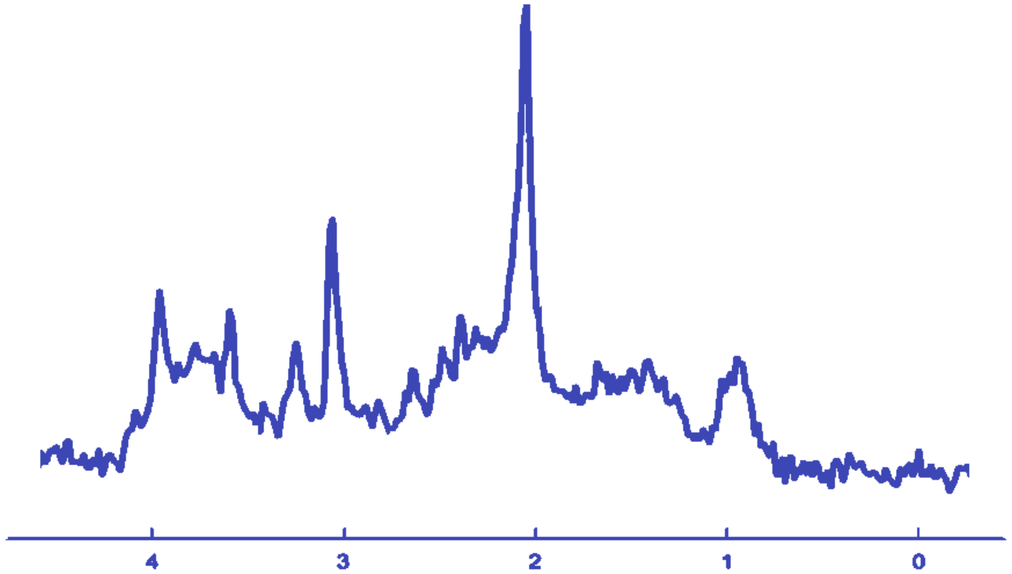
Imagerie vs Spectroscopie



T1 weighted Image, 3T

La fréquence encode l'information spatiale
(avec l'usage de gradient de champ magnétique)

Imagerie RMN =
détection du **solvant** (l'eau) par ses ^{1}H



In vivo 3T

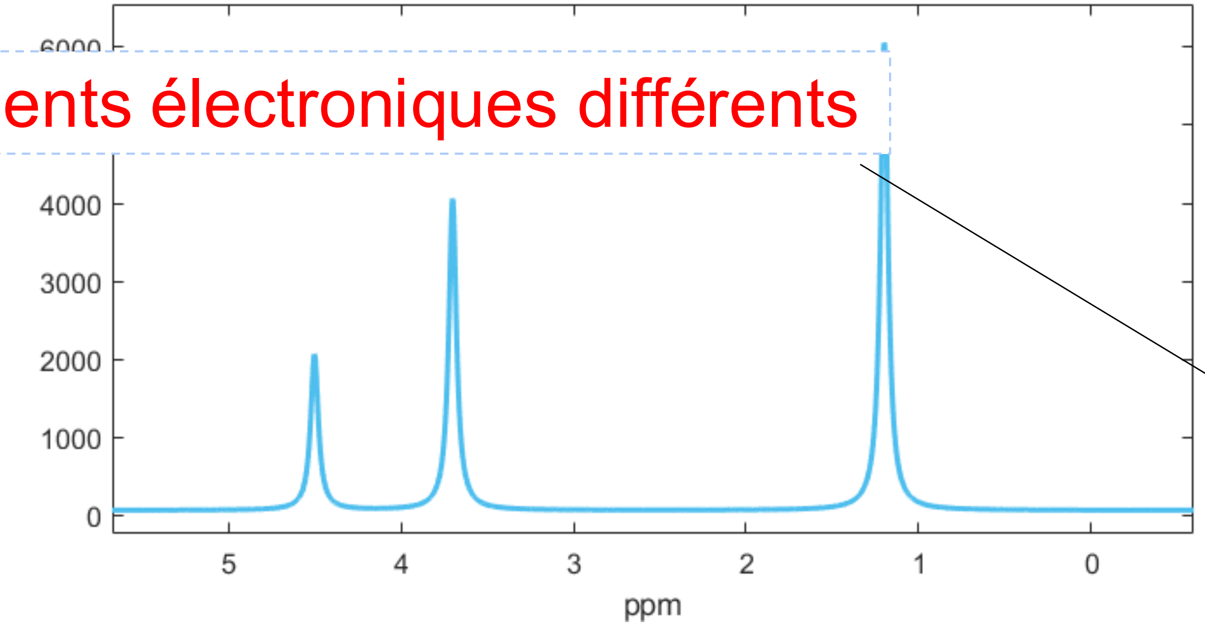
Fréquence encode l'information biochimique

Spectroscopie RMN = détection des **solutés** par les ^{1}H, ^{13}C, ^{31}P…

Présentation d'Hélène Ratiney le 16 décembre 2024 au REMI

Notion de déplacement chimique

Spectre de l'ethanol $OH\text{-}CH_2\text{-}CH_3$

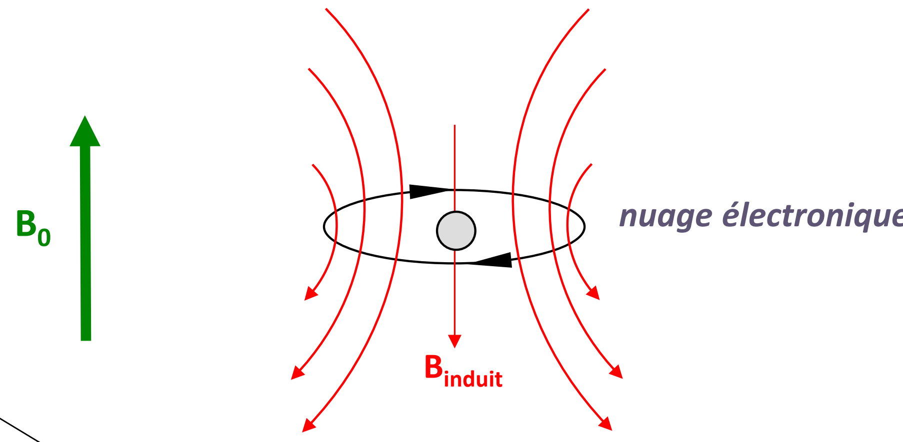


Environnements électroniques différents

En présence d'un champ magétique $B_{0,}$ les e- circulent sur leurs orbites.
Ce mvt crée un champ magnétique externe:

- qui s'additionne à B0 ➔ déblindage
- qui s'oppose à B0 ➔ blindage ou écran

Champ local au niveau des noyau = **B_0** + $B_{\text{induit par la circulation des électrons}}$



$$B_{loc} = B_0(1-\sigma)$$

Ordre de grandeur de σ ≈ 10^{-6}

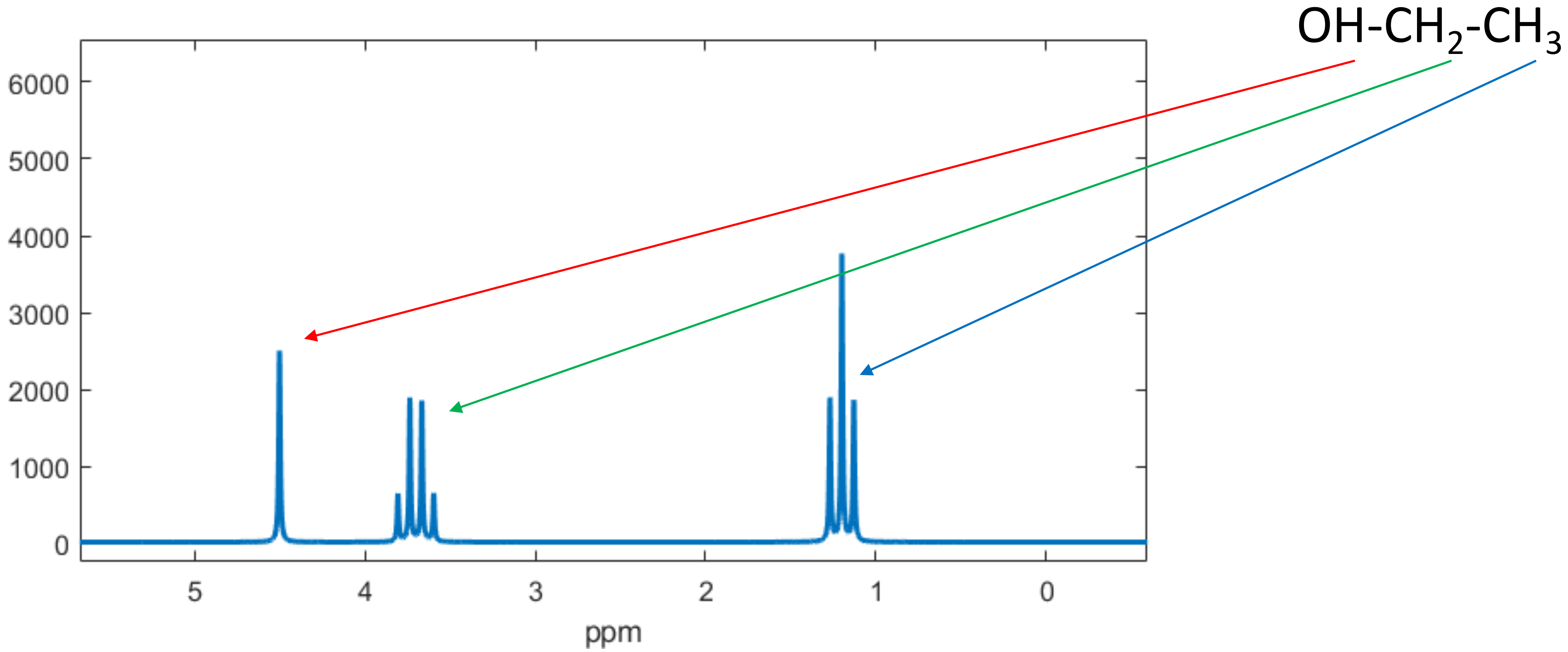
Présentation d'Hélène Ratiney le 16 décembre 2024 au REMI

Notion couplage scalaire

- interaction entre plusieurs spins à travers les liaisons chimiques

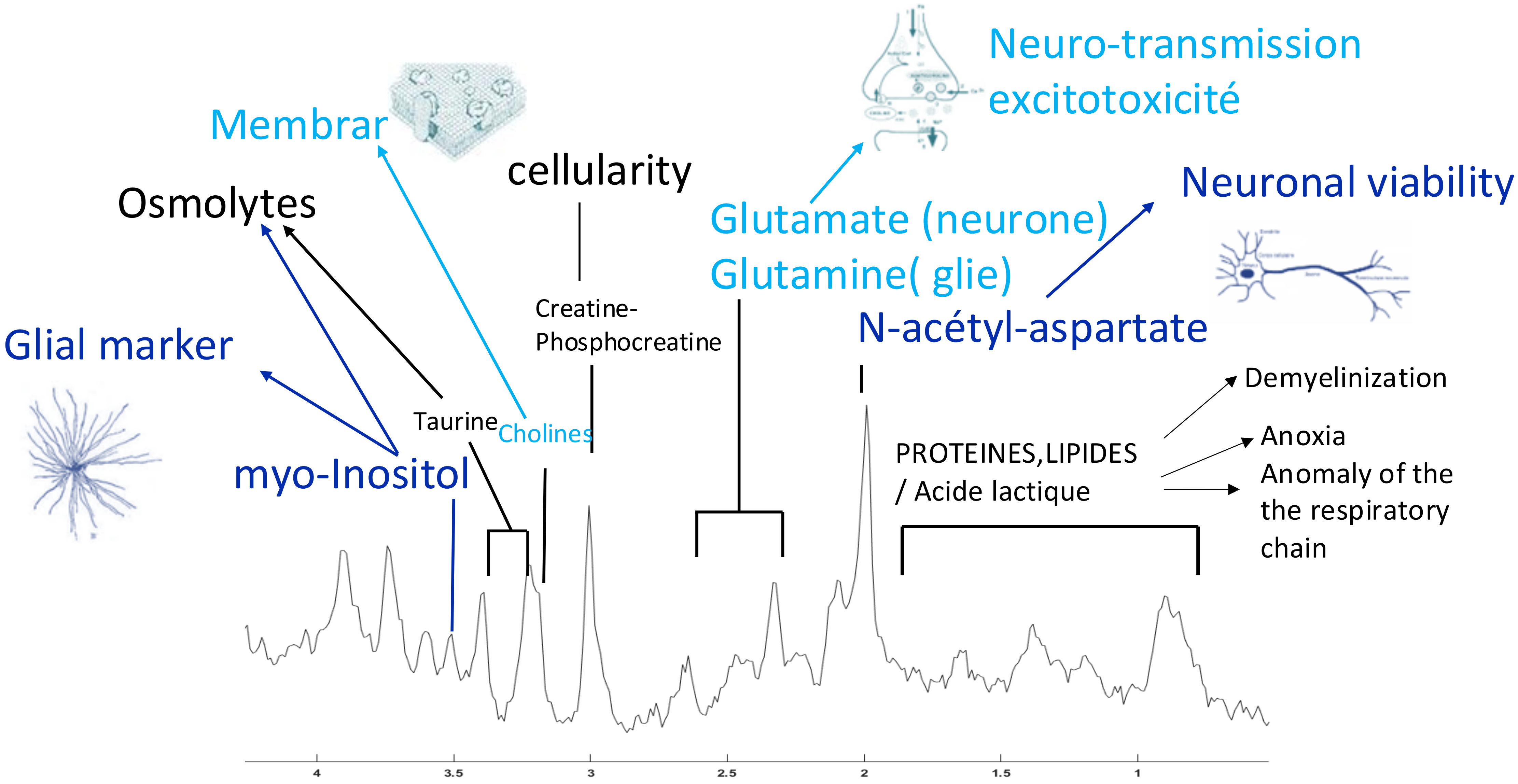
=> interaction indirecte entre deux spins nucléaires qui provient des interactions hyperfines entre les noyaux et la densité électronique locale et provoque un éclatement du signal RMN

Interactions magnétiques, transmises par l'e- à travers les liaisons chimiques demultiplication des raies de résonance



Présentation d'Hélène Ratiney le 16 décembre 2024 au REMI

La spectroscopie *in-vivo* : biopsie virtuelle non-invasive



Neuro-transmission
excitotoxicité

Membrar

cellularity

Osmolytes

Glutamate (neurone)
Glutamine(glie)

Neuronal viability

Creatine-
Phosphocreatine

N-acétyl-aspartate

Glial marker

Taurine

Cholines

myo-Inositol

PROTEINES,LIPIDES
/ Acide lactique

Demyelinization

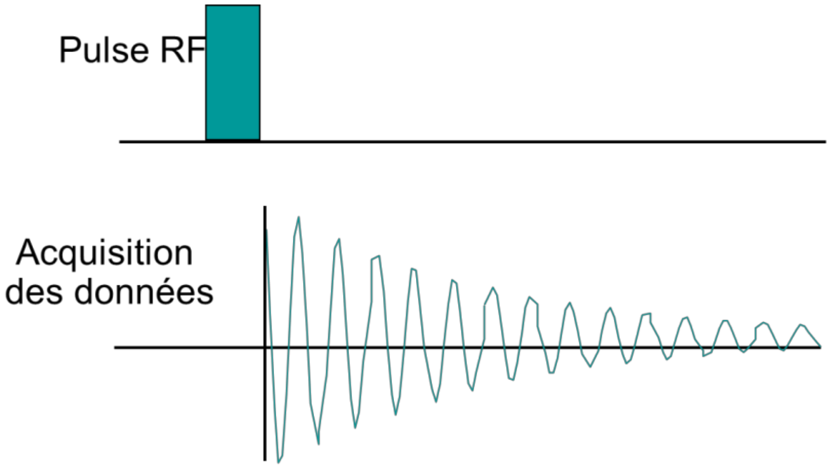
Anoxia

Anomaly of the
the respiratory
chain

Spectrum acquired with the STEAM sequence / Rat brain
TE=3ms, TR= 2500, voxel 2x2x2 mm^{3,} , 11.7T

Principe d'acquisition

Préparation – Excitation -- Détection



- ➢ l'échantillon est à l'équilibre sous l'action du champ statique B0
- ➢1 pulse RF est appliqué pour basculer l'aimantation de 90°
- ➢L'excitation RF est éteinte et le signal est détecté.

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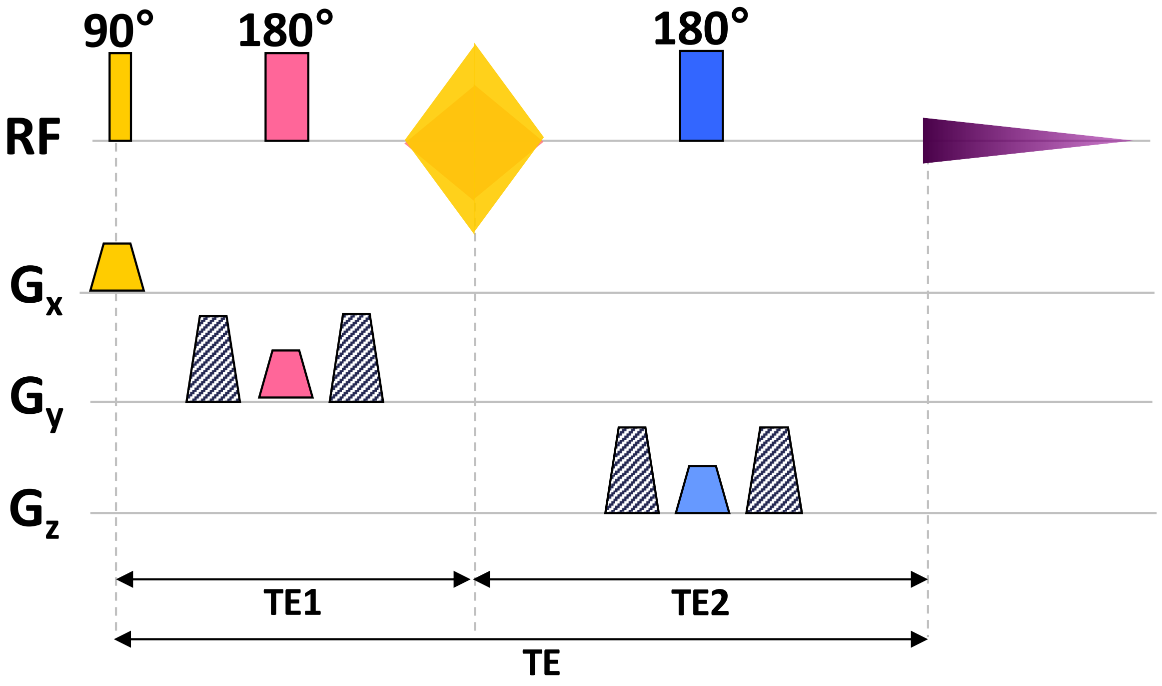
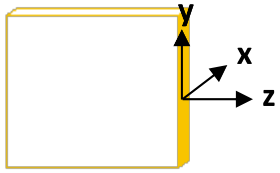
Spectroscopie localisée monovoxel

Séquence PRESS (Point RESolved Spectroscopy):





Rq : TE doit être suffisamment long pour inclure 3 pulses + gradients de dispersion

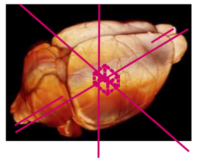
Bottomley PA. Selective volume method for performing localized NMR spectroscopy. US Patent #4,480,228 (approved 30 Oct 1984).

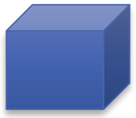
Animations Vincent Lebon

Présentation d'Hélène Ratiney le 16 décembre 2024 au REMI

Spectroscopie localisée monovoxel

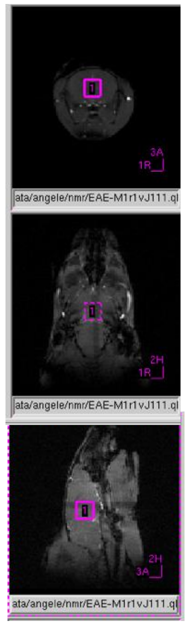
Positionnement a priori d'un voxel de plusieurs
-- mm^3 (parallélépipède) sur le petit animal
-- cm^3 sur l'homme



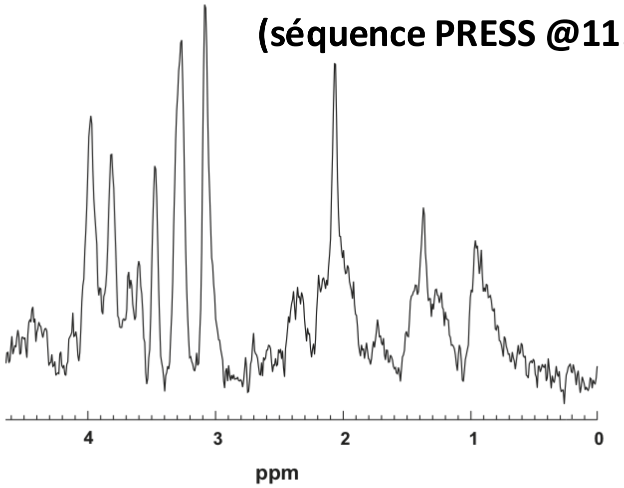


Séquences couramment utilisées en spectroscopie localisée

- **PRESS** (Point RESolved Spectroscopy): double écho de spin
- **STEAM** (Stimulated Echo Acquisition Mode): écho stimulé
- **ISIS** (Image selected in vivo spectroscopy)

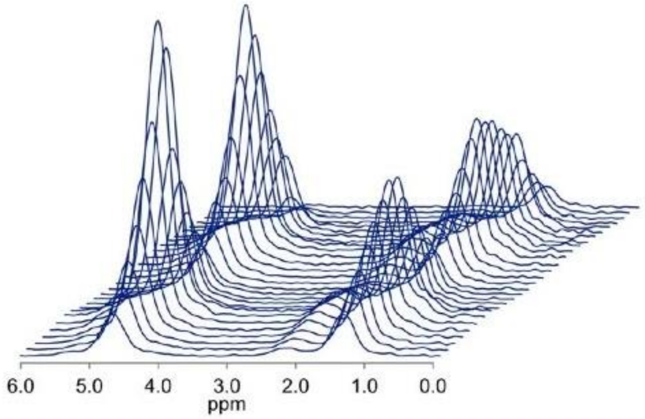


SRM^{1}H du cerveau souris
(séquence PRESS @11.75T)



(A. Viola)

SRM^{1}H du foie humain
(séquence STEAM @3T)



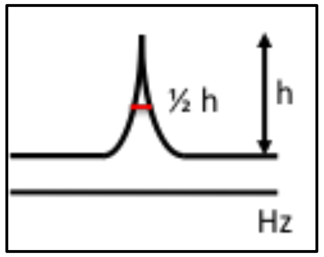
Hamilton et al, J Magn Reson Imaging, 2015

Les paramètres clé de l'acquisition (cerveau)

1) Correction des inhomogeneités de champ B0: SHIM

Procédures manuelles ou automatique(FASTMAP, MAPSHIM...)

Qualité du "Shim " → largeur à mi-hauteur du pic

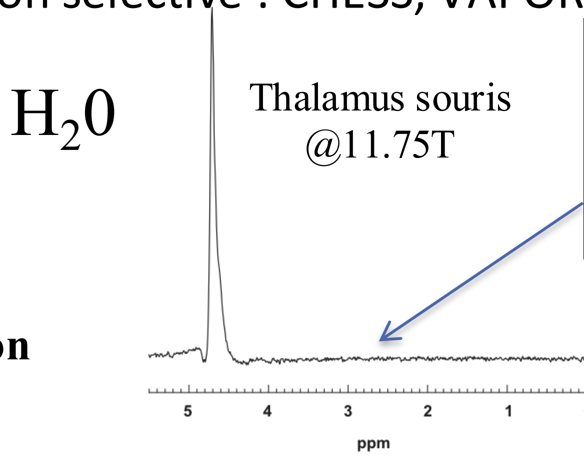


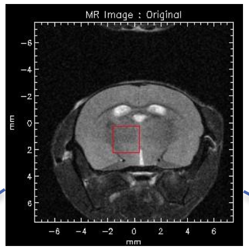
2) Suppression du pic d'eau (SRM-1H)

[H2O] dans les tissus≈ 50 M, [metabolites] metabolites observables≈ 1-12 mM

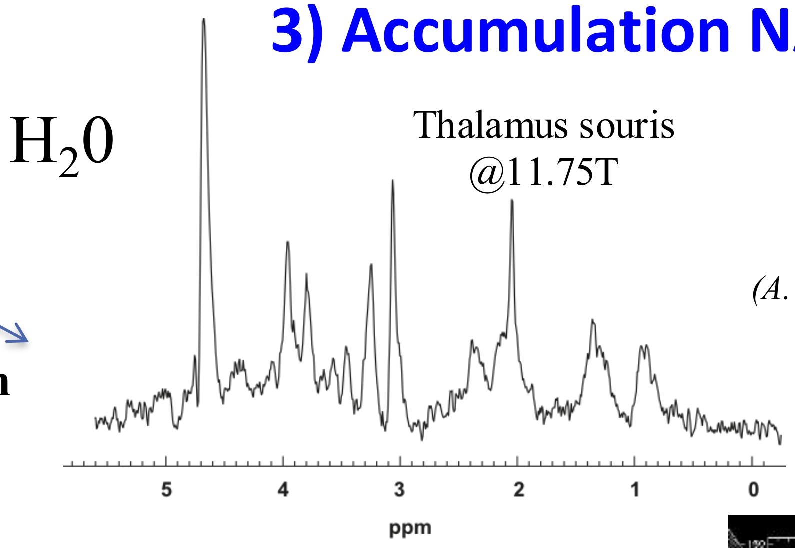
Impulsion de saturation selective : CHESS, VAPOR ...

Without saturation





with saturation

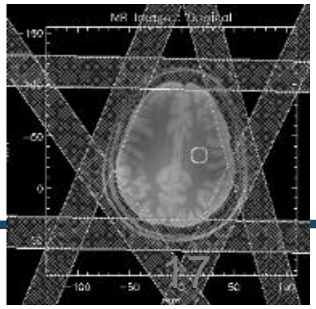


3) Accumulation NA

(A. Viola, Y. Le Fur)

4) Saturation des lipids sous cutanés (SRM-1H)

Ajout de bande de saturation OVS (Outer Volume Saturation)



Réseau d'Entraide Multicentrique en IRM

Paramètres d'acquisition clé

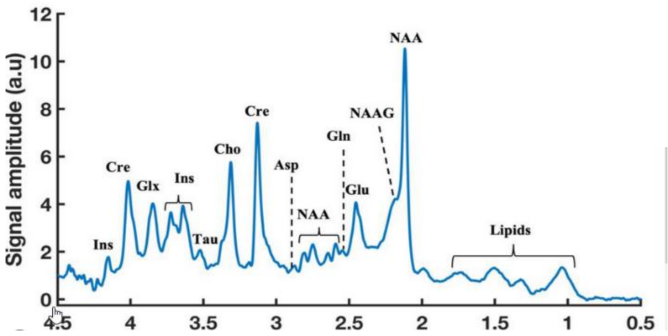
Temps d'écho TE et Temps de répétition TR

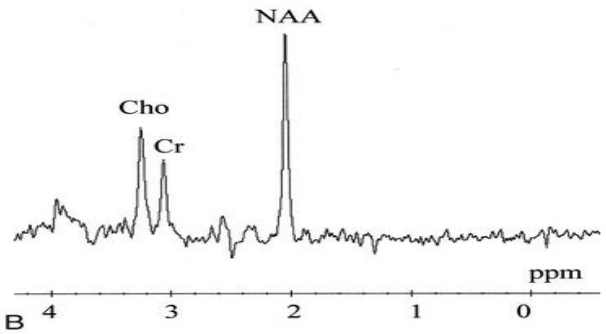
Idéalement: TR>5xT1 and TE<< T2

T1 des métabolites en général ≥ 1000 ms (proton) ≥ 1500 ms (phosphore) T1 >> T2

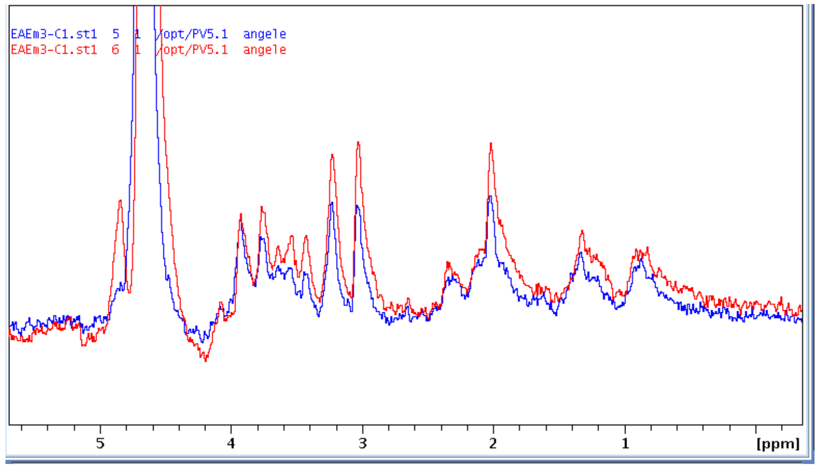
T2 metabolites ≥ 100 ms (ten ms for 31P)

Effet TE (MRS-^{1}H)



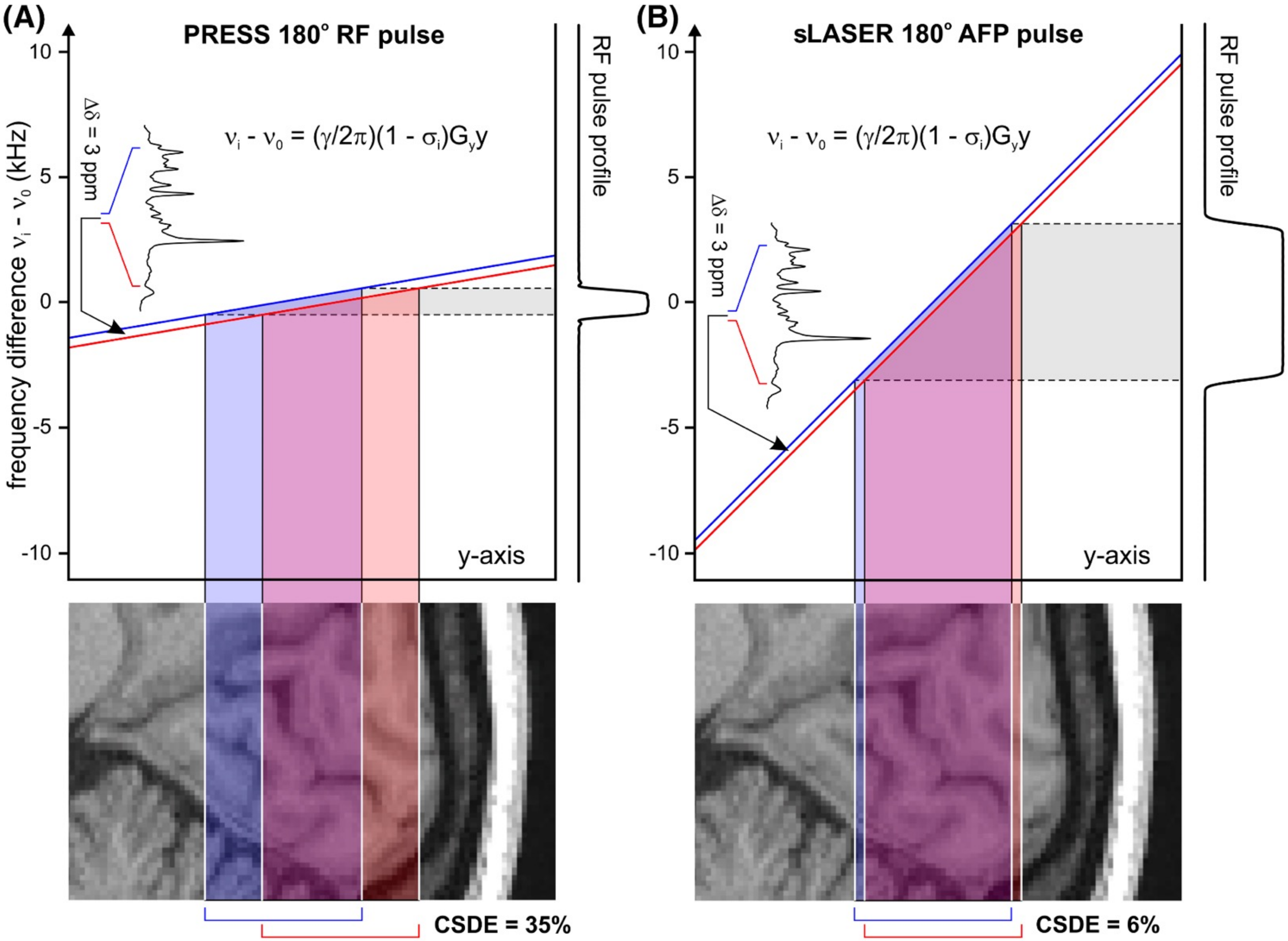


Effet du TR (SRM-^{1}H)



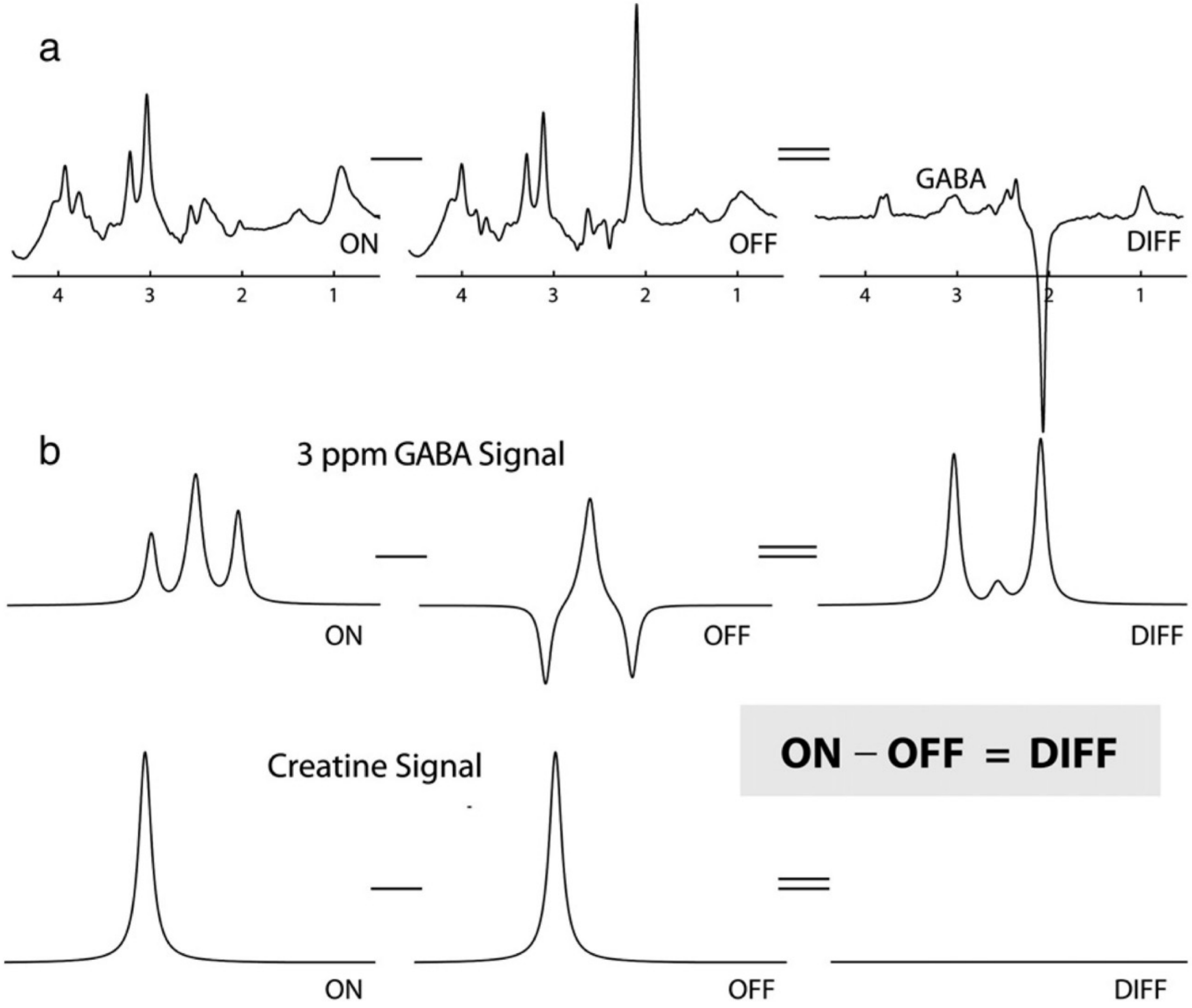
Présentation d'Hélène Ratiney le 16 décembre 2024 au REMI

Choice of sequence: Chemical Shift Displacement Error (CSDE)



Near et al. NMR Biomed (2021)

Editing metabolites: MEGA-PRESS sequence



ON − OFF = DIFF

Mullins et al, NeuroImage (2014)

Protocoles SVS implémentés au Centre IRM- INT sur la 3T Prisma

- SVS PRESS
- SVS MEGA-PRESS

Preprocessing

- Phasage
- Correction des Courant de Foucault,
- Recalage fréquentiel
- Suppression du pic d'eau résiduel (HLVD)

Analyse Quantitative

- Fonction modèle
- Estimation Paramétrique
- Connaissance A priori
- CRLBs

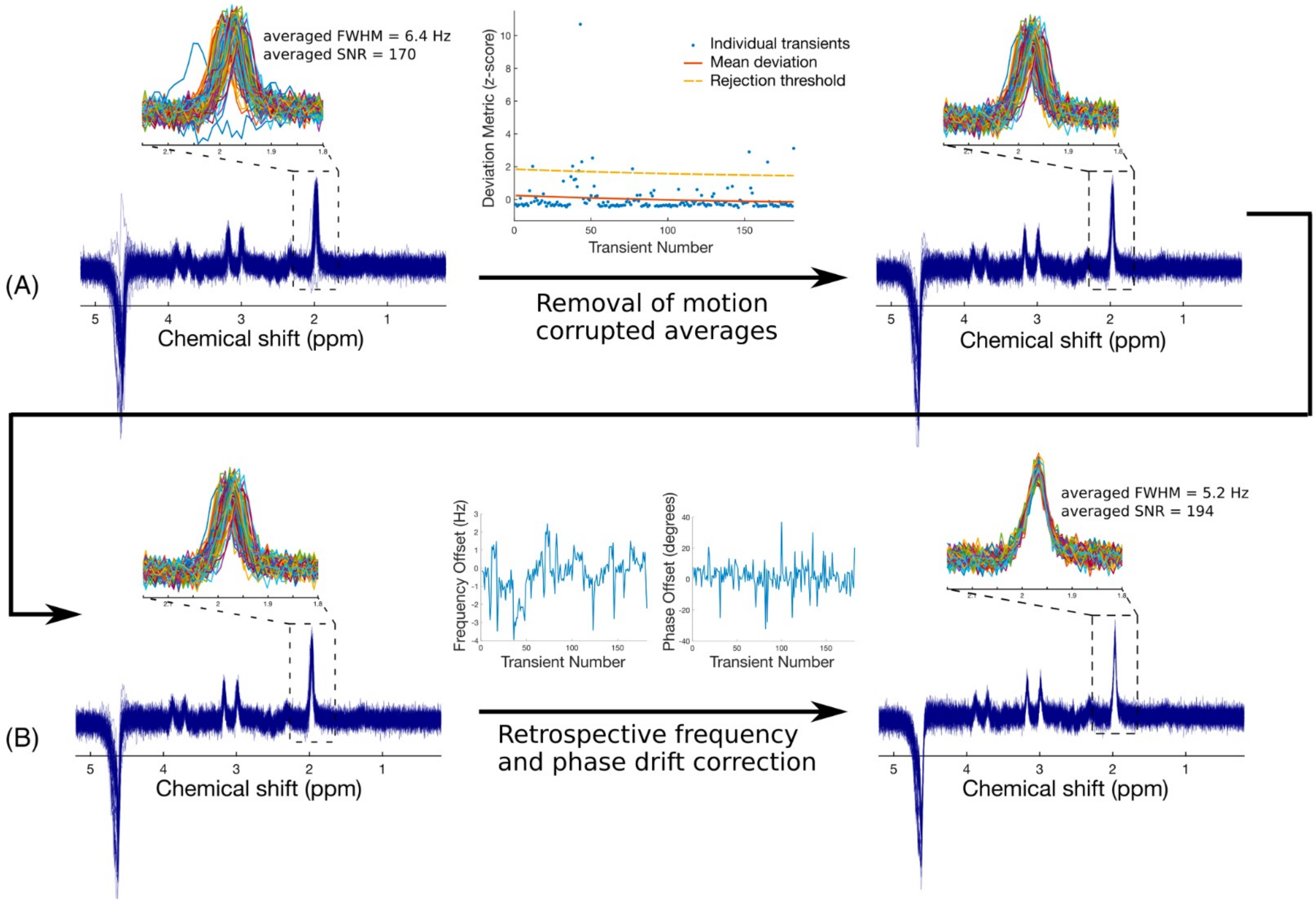
Reference/Calibration/

« Quantification Absolue»

Concentration en mM

Présentation d'Hélène Ratiney le 16 décembre 2024 au REMI

Preprocessing individual spectra



Near et al. NMR Biomed (2021)

EQUATION pour plusieurs raies de résonances: somme des signatures spectrales des métabolites

Modèle Paramétrique

∝ Concentration

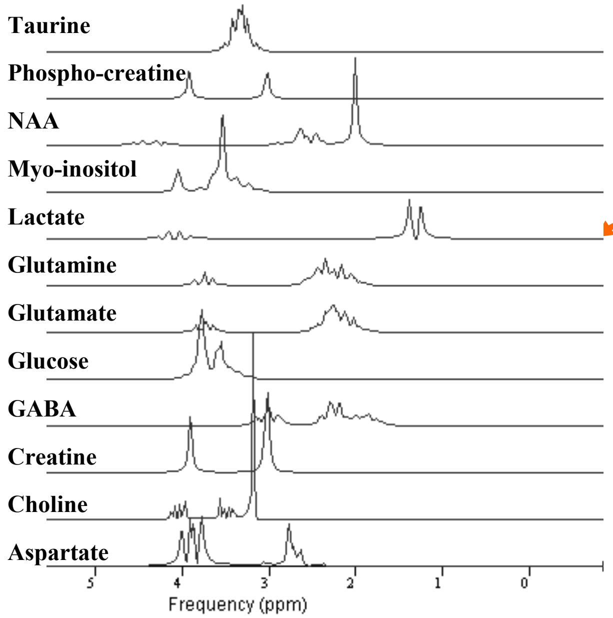
$$\hat{y}(t) = \sum_{m=1}^{M} a_m x_m(t) \exp\underbrace{\left(\Delta\alpha_m t + i2\pi\Delta f_m t\right)\exp(i\phi_0)}$$

Base de connaissance

TF

- **Pondération**
  - apodisation
  - décalage en fréquence
  - phase additionnelle

Softwares
NMR –SCOPE [*]
GAMMA
SPINACH [†]
SIMPSON
FSL-MRS



→ **Bornes de Cramér Rao pour renseigner**

[*] *D. Graveron, JMR, 1993* , [†] *H. J. Hogben, et al, J. Magn. Reson., 2011*,

Reference, calibration: obtenir une concentration absolue ?

$$[m] = \frac{A_m}{A_{ref}}[\text{ref}] \; {*}\text{correction\_factors}$$

1-Eau comme référence interne (ou Creatine)
Suppose de connaitre la concentration de l'eau dans les tissus

2- Référence externe associée au moment de l'acquisiion(in a sample)
 Difficultées si inhomogénéités B1

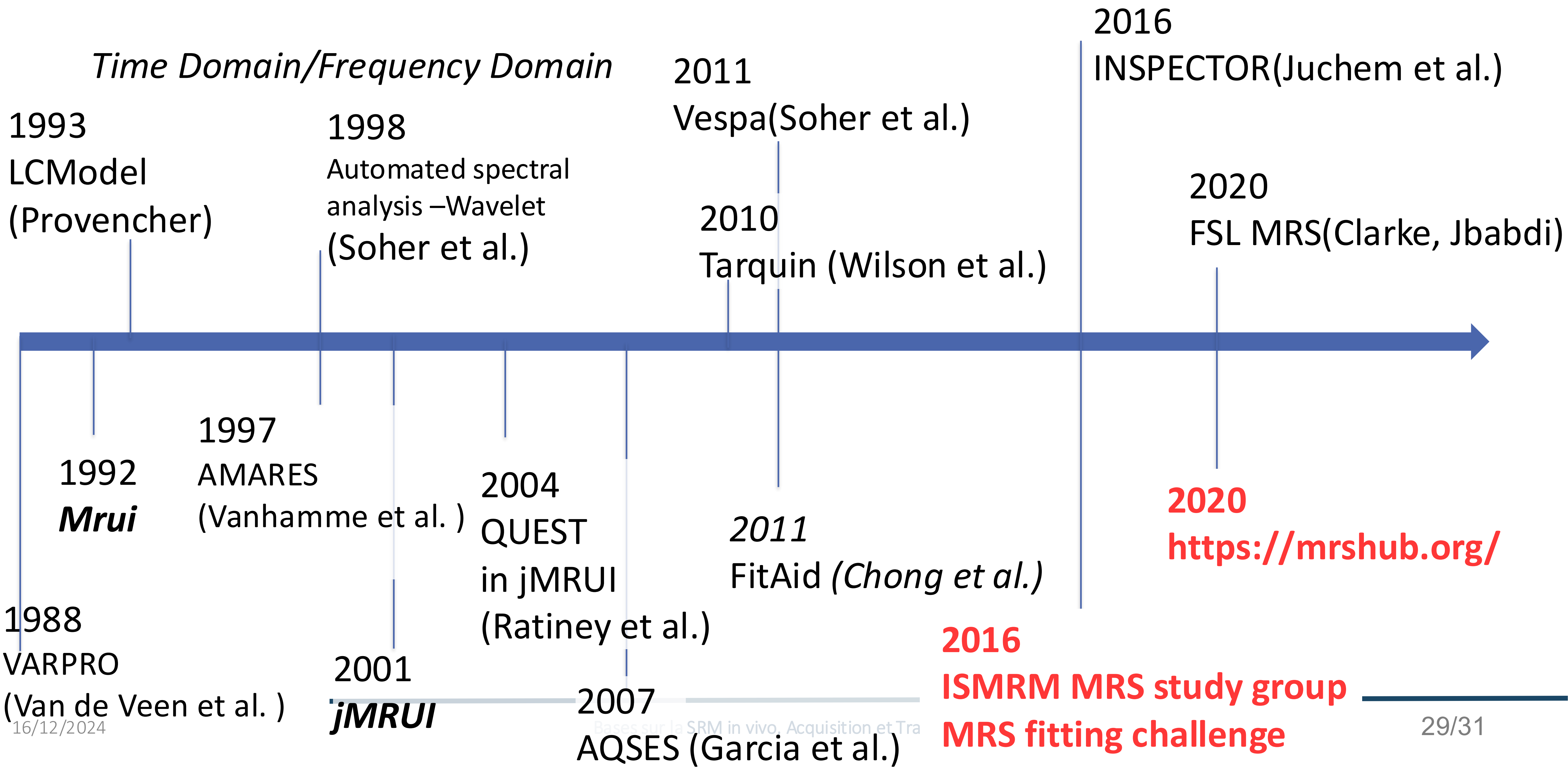
3-Reference externe avec remplacement par un fantôme
Differences possible sur la charge de l'antennte entre tissus et fantôme

T1, T2, NA,
nb of de noyau equivalent

REMI
Réseau d'Entraide Multicentrique en IRM

CREATIS

30 ans de développements



Time Domain/Frequency Domain

1993
LCModel
(Provencher)

1998
Automated spectral
analysis –Wavelet
(Soher et al.)

2011
Vespa(Soher et al.)

2010
Tarquin (Wilson et al.)

2016
INSPECTOR(Juchem et al.)

2020
FSL MRS(Clarke, Jbabdi)

1988
VARPRO
(Van de Veen et al.)

1992
Mrui

1997
AMARES
(Vanhamme et al.)

2001
jMRUI

2004
QUEST
in jMRUI
(Ratiney et al.)

2007
AQSES (Garcia et al.)

2011
FitAid *(Chong et al.)*

2016
ISMRM MRS study group
MRS fitting challenge

2020
https://mrshub.org/

Présentation d'Hélène Ratiney le 16 décembre 2024 au REMI

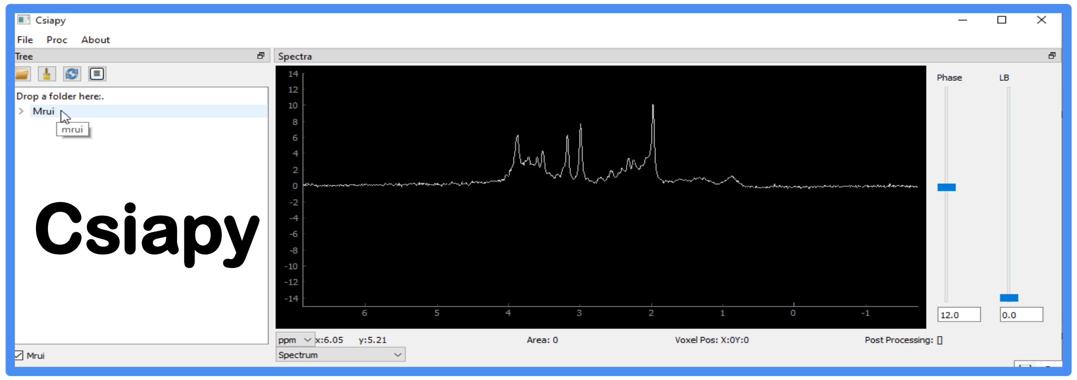
En pratique…

Lecture differents Format d'écriture, SPAR/SDAT, DAT/DCM, NII ,RAW, MRUI etc…

Visualisation

Traiter une cohorte

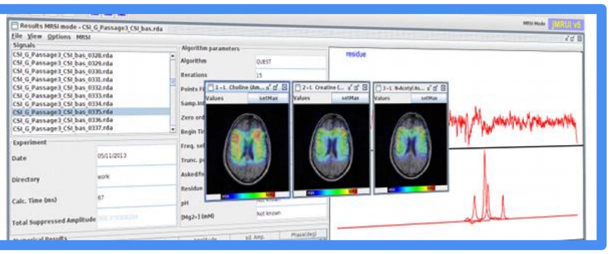
LCModel

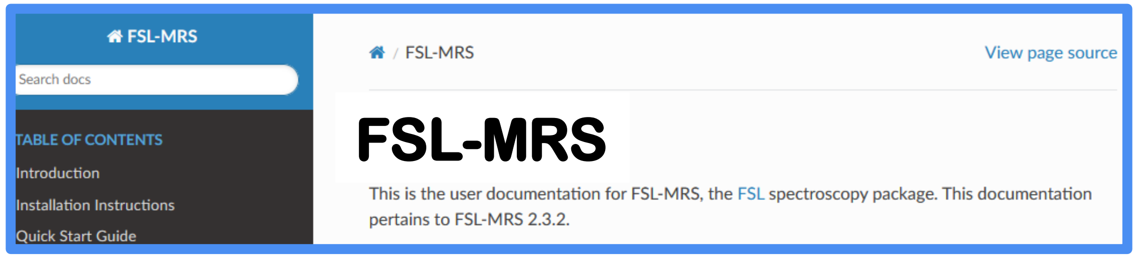


Csiapy

jMRUI

Software for the clinical and biomedical MRS





FSL-MRS

This is the user documentation for FSL-MRS, the FSL spectroscopy package. This documentation pertains to FSL-MRS 2.3.2.

VIP

VIRTUAL IMAGING PLATFORM

Matlab

Gannet

FID-A

Présentation d'Hélène Ratiney le 16 décembre 2024 au REMI

Logiciels pour traiter les données SVS PRESS

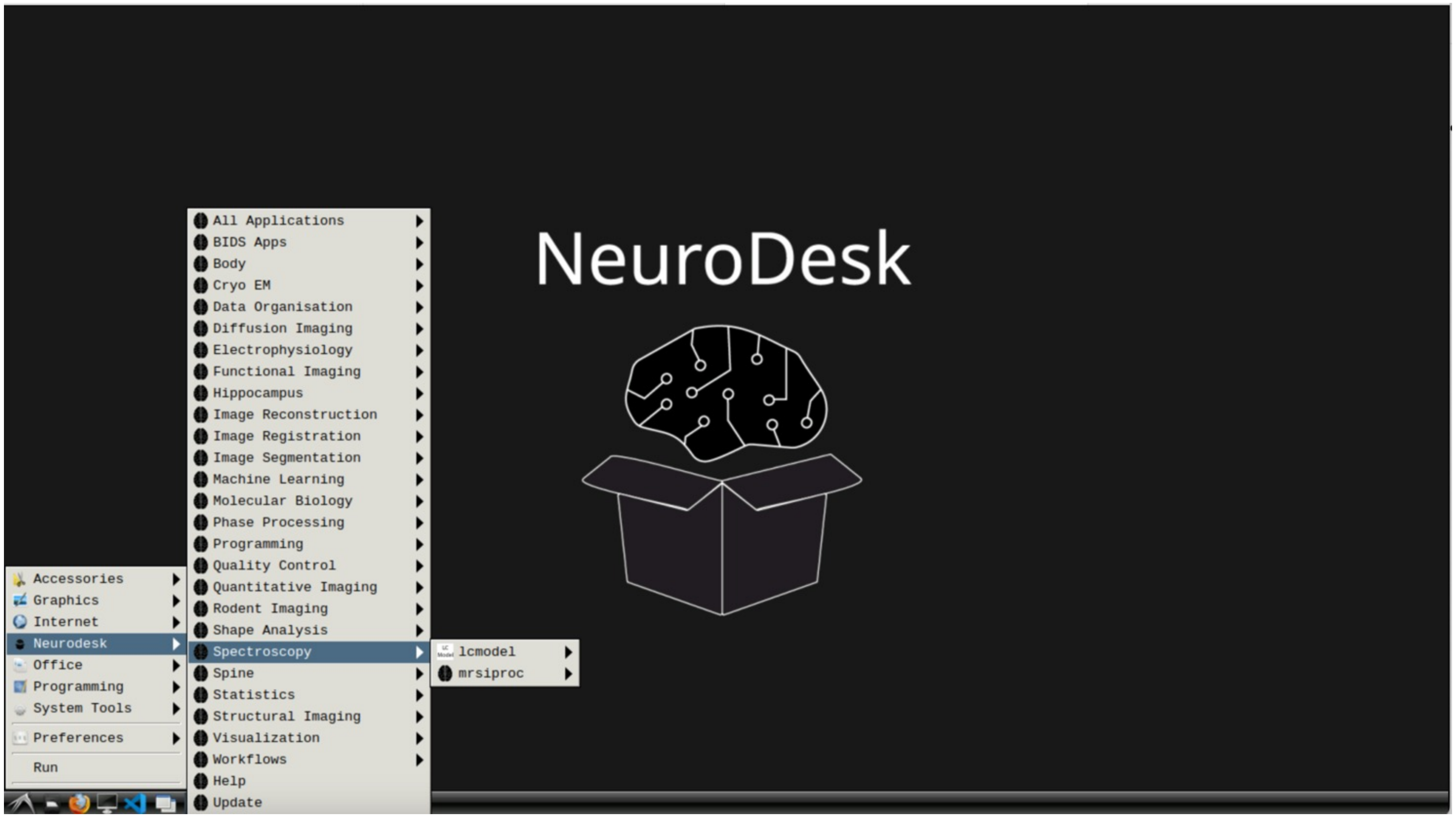
LCMODEL

OSPREY

SUSPECT

MRSPA

LCM via NeuroDesk



LCM via NeuroDesk

Below are the Control Parameters that will be used in the CONTROL file.
If necessary, you can change, add or delete these in the window below.

Click on "OK" when you are satisfied with the values below.

Click on "Restore" to cancel any changes that you have made below.

```
deltat= 8.330e-04
doecc= T
dows= T
echot= 30.00
filbas= '/home/jovyan/.lcmodel/basis-sets/3t/press_te30_3t_v3.basis'
filh2o= '/home/jovyan/.lcmodel/temp/14d-15h-40m-15s-2488pid/h2o/RAW'
filps= '/home/jovyan/.lcmodel/temp/14d-15h-40m-15s-2488pid/ps'
filraw= '/home/jovyan/.lcmodel/temp/14d-15h-40m-15s-2488pid/met/RAW'
hzpppm= 1.2324e+02
key= 210387309
nunfil= 1024
ppmend= 0.2
ppmst= 4.0
title= 'sub-1054001 (31D65B22F9) Series/Acq=11/1 (2023.01.17 14:52) svs_se_TE30_CPF_  TR/TE/NS=1500/30/128,  8.000E+00mL (M 050Y, 105kg) Projets N
```

Further restrictions for editing above:
(1) filraw, filps, etc., contain temporary filenames assigned by LCMgui. Do not change these.
(2) Each line must contain exactly one assignment; e.g., you can enter
  nomit=1
  chomit='Glyc'
but not
  nomit=1, chomit='Glyc'
(3) Do not assign a value to the same Control Parameter element twice. This is easy to see, since they are listed alphabetically.

TITLE: sub-1054001 (31D65B22F9) Series/Ac

Analyzing spectrum from: 4.0 ppm, do

BASIS file: /home/jovyan/.lcmodel/basis-sets

☑ Do eddy-current correction

☑ Do w

to directory: /home/jovya

Only for Multi-Voxel or Multi-Channel data fil sub-1054001 (31D65B22F9) Series/Acq=9/1 (2023.01.17 14:47) svs_se_TE30_CPF_ TR/TE/NS=1500/30/128, 8.400E+00mL (M 050Y, 105kg) Projets NEMO (Universite d aix Marseille) _pwc_16

Data of:

LCModel (Version 6.3-1R) Copyright: S.W. Provencher. *Ref.: Magn. Reson. Med. 30:672-679 (1993).* *14-December-2024 16:08*

```
   Conc.  %SD /Cr+PCr  Metabolite
   0.000 999%   0.000 Ala
   0.303 111% 6.3E-02 Asp
   2.901   7%   0.606 Cr
   1.889  10%   0.394 PCr
   1.480  21%   0.309 GABA
   0.000 999%   0.000 Glc
   0.699  56%   0.146 Gln
   5.146   8%   1.074 Glu
   1.669   3%   0.348 GPC
   0.000 999%   0.000 PCh
   1.404  10%   0.293 GSH
   3.679   5%   0.768 Ins
   0.788  41%   0.164 Lac
   6.928   3%   1.446 NAA
   0.316  80% 6.6E-02 NAAG
4.55E-03 832% 9.5E-04 Scyllo
   0.436  67% 9.1E-02 Tau
   0.000 999%   0.000 -CrCH2
   1.669   3%   0.348 GPC+PCh
   7.244   3%   1.512 NAA+NAAG
   4.791   2%   1.000 Cr+PCr
   5.845   9%   1.220 Glu+Gln
-------------------------------------
   0.000 999%   0.000 Lip13a
   1.247  16%   0.260 Lip13b
   0.336  45% 7.0E-02 Lip09
   7.484  16%   1.562 MM09
   0.188  56% 3.9E-02 Lip20
  11.414  16%   2.383 MM20
   0.000 999%   0.000 MM12
   9.291  21%   1.939 MM14
   3.107  37%   0.649 MM17
   1.247  16%   0.260 Lip13a+Lip13b
  10.538  19%   2.200 MM14+Lip13a+Lip13b+MM12
   7.820  15%   1.632 MM09+Lip09
  11.602  15%   2.422 MM20+Lip20
-------------------------------------
                DIAGNOSTICS
   1 info      FINOUT  9
  Doing Water-Scaling
-------------------------------------
             MISCELLANEOUS OUTPUT
 FWHM = 0.043 ppm    S/N =  30
 Data shift = 0.014 ppm
```

```
Ph:  -2 deg      -7.6 deg/ppm
----------------------------------------------
                INPUT CHANGES
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dows= T
echot= 30.00
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hzpppm= 1.2324e+02
lps= 8
ltable= 7
nunfil= 1024
ppmend= 0.2
ppmst= 4.0
savdir= '/home/jovyan/.lcmodel/saved/'
srch2o= '/neurodesktop-storage/spectro/MrSpec_NE
  MO_sub-1054001_ses-01_CPF-R_ssWS.rda'
srcraw= '/neurodesktop-storage/spectro/MrSpec_NE
  MO_sub-1054001_ses-01_CPF-R.rda'
```
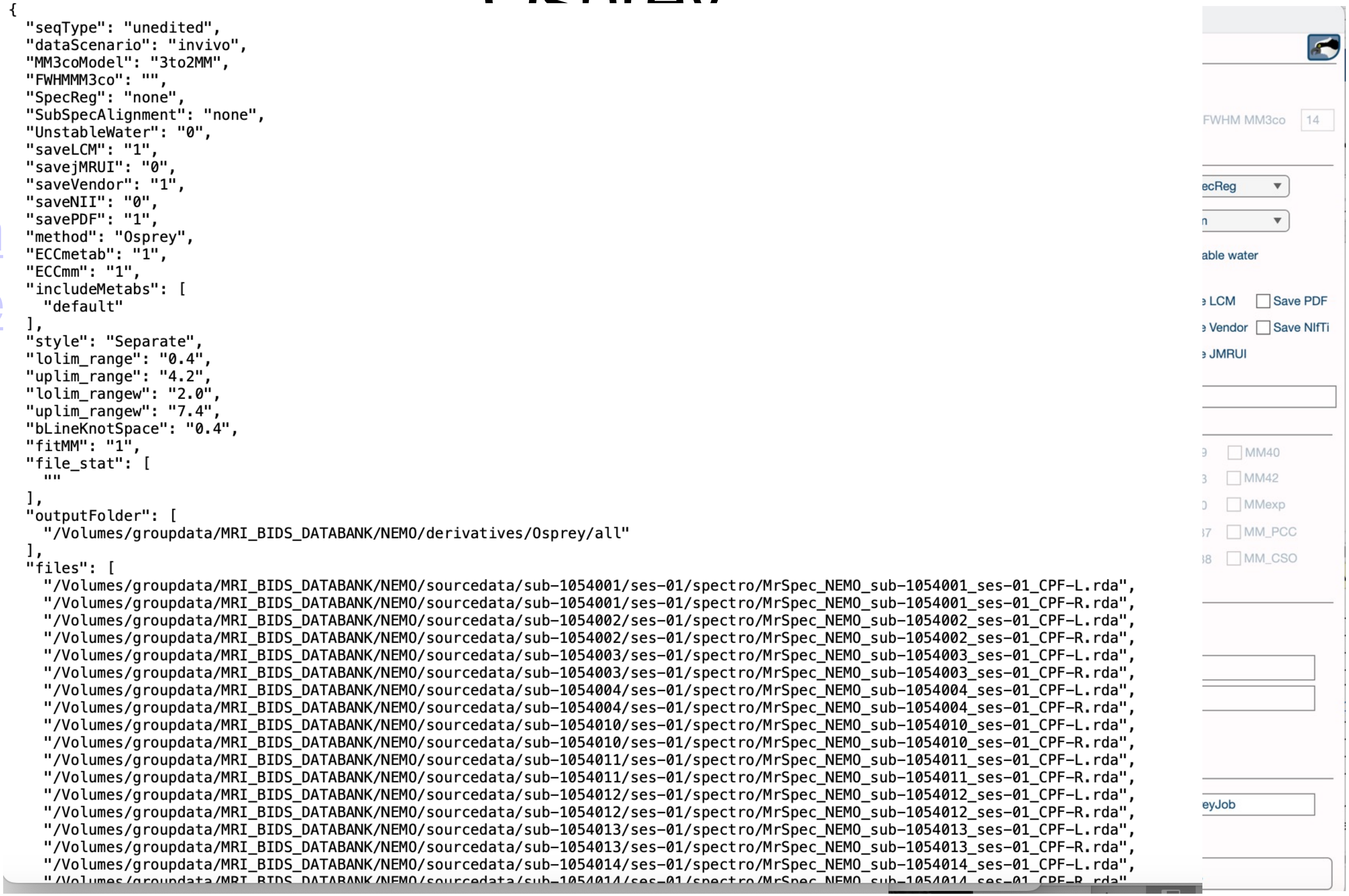

```
 LCModel (Version 6.3-1R)
 sub-1054001 (31D65B22F9) Series/Acq=9/1 (2023.01.17 14:47) svs_se_TE30_CPF_  TR/TE/NS=1500/30/128,  8.400E+00mL (M
 050Y, 105kg) Projets NEMO  (Universite d aix Marseille) _pwc_16

$$CONC 36 lines in following concentration table = NCONC+1
    Conc.  %SD /Cr+PCr  Metabolite
    0.000 999%   0.000 Ala
    0.303 111% 6.3E-02 Asp
    2.901   7%   0.606 Cr
    1.889  10%   0.394 PCr
    1.480  21%   0.309 GABA
    0.000 999%   0.000 Glc
    0.699  56%   0.146 Gln
    5.146   8%   1.074 Glu
    1.669   3%   0.348 GPC
    0.000 999%   0.000 PCh
    1.404  10%   0.293 GSH
    3.679   5%   0.768 Ins
    0.788  41%   0.164 Lac
    6.928   3%   1.446 NAA
    0.316  80% 6.6E-02 NAAG
 4.55E-03 832% 9.5E-04 Scyllo
    0.436  67% 9.1E-02 Tau
    0.000 999%   0.000 -CrCH2
    1.669   3%   0.348 GPC+PCh
    7.244   3%   1.512 NAA+NAAG
    4.791   2%   1.000 Cr+PCr
    5.845   9%   1.220 Glu+Gln
    0.000 999%   0.000 Lip13a
    1.247  16%   0.260 Lip13b
    0.336  45% 7.0E-02 Lip09
    7.484  16%   1.562 MM09
    0.188  56% 3.9E-02 Lip20
   11.414  16%   2.383 MM20
    0.000 999%   0.000 MM12
    9.291  21%   1.939 MM14
    3.107  37%   0.649 MM17
    1.247  16%   0.260 Lip13a+Lip13b
   10.538  19%   2.200 MM14+Lip13a+Lip13b+MM12
    7.820  15%   1.632 MM09+Lip09
   11.602  15%   2.422 MM20+Lip20

$$MISC  6 lines in following misc. output table
  FWHM = 0.043 ppm    S/N =  30
  Data shift = 0.014 ppm
  Ph:  -2 deg      -7.6 deg/ppm
  alphaB,S = 3.0E-02,   1.2E+01
   28 spline knots.   Ns =11(1)
  (20) 8 infls.   (13) 3 extrs.

$$DIAG  1 lines in following diagnostic table:
   1 info      FINOUT  9

$$INPU 17 lines in following table of input changes:
 deltat= 8.330e-04
 doecc= T
 dows= T
 echot= 30.00
 filbas= '/home/jovyan/.lcmodel/basis-sets/3t/pre
   ss_te30_3t_v3.basis'
 hzpppm= 1.2324e+02
 lps= 8
```

Osprey

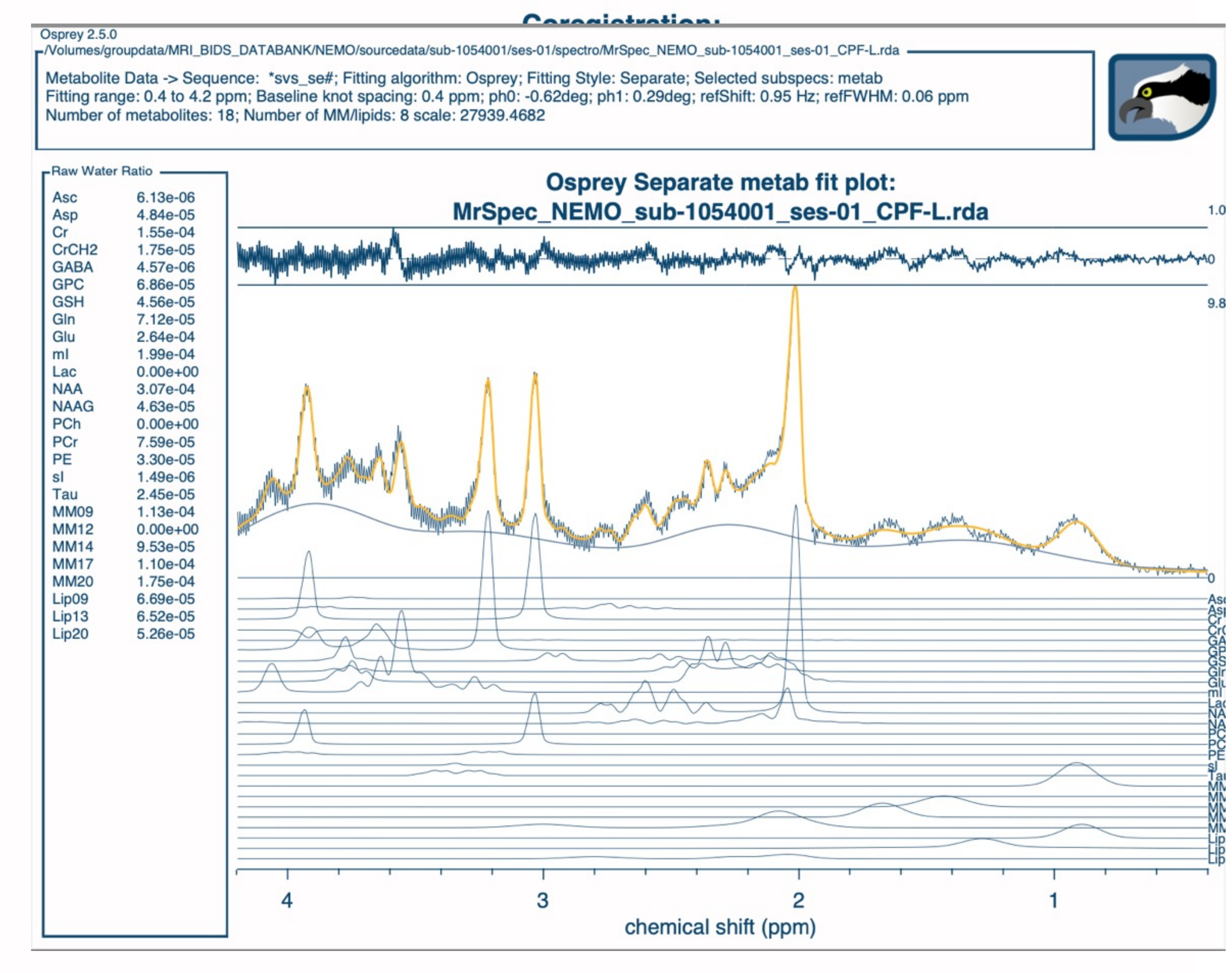
h

e



```
{
  "seqType": "unedited",
  "dataScenario": "invivo",
  "MM3coModel": "3to2MM",
  "FWHMMM3co": "",
  "SpecReg": "none",
  "SubSpecAlignment": "none",
  "UnstableWater": "0",
  "saveLCM": "1",
  "savejMRUI": "0",
  "saveVendor": "1",
  "saveNII": "0",
  "savePDF": "1",
  "method": "Osprey",
  "ECCmetab": "1",
  "ECCmm": "1",
  "includeMetabs": [
    "default"
  ],
  "style": "Separate",
  "lolim_range": "0.4",
  "uplim_range": "4.2",
  "lolim_rangew": "2.0",
  "uplim_rangew": "7.4",
  "bLineKnotSpace": "0.4",
  "fitMM": "1",
  "file_stat": [
    ""
  ],
  "outputFolder": [
    "/Volumes/groupdata/MRI_BIDS_DATABANK/NEMO/derivatives/Osprey/all"
  ],
  "files": [
    "/Volumes/groupdata/MRI_BIDS_DATABANK/NEMO/sourcedata/sub-1054001/ses-01/spectro/MrSpec_NEMO_sub-1054001_ses-01_CPF-L.rda",
    "/Volumes/groupdata/MRI_BIDS_DATABANK/NEMO/sourcedata/sub-1054001/ses-01/spectro/MrSpec_NEMO_sub-1054001_ses-01_CPF-R.rda",
    "/Volumes/groupdata/MRI_BIDS_DATABANK/NEMO/sourcedata/sub-1054002/ses-01/spectro/MrSpec_NEMO_sub-1054002_ses-01_CPF-L.rda",
    "/Volumes/groupdata/MRI_BIDS_DATABANK/NEMO/sourcedata/sub-1054002/ses-01/spectro/MrSpec_NEMO_sub-1054002_ses-01_CPF-R.rda",
    "/Volumes/groupdata/MRI_BIDS_DATABANK/NEMO/sourcedata/sub-1054003/ses-01/spectro/MrSpec_NEMO_sub-1054003_ses-01_CPF-L.rda",
    "/Volumes/groupdata/MRI_BIDS_DATABANK/NEMO/sourcedata/sub-1054003/ses-01/spectro/MrSpec_NEMO_sub-1054003_ses-01_CPF-R.rda",
    "/Volumes/groupdata/MRI_BIDS_DATABANK/NEMO/sourcedata/sub-1054004/ses-01/spectro/MrSpec_NEMO_sub-1054004_ses-01_CPF-L.rda",
    "/Volumes/groupdata/MRI_BIDS_DATABANK/NEMO/sourcedata/sub-1054004/ses-01/spectro/MrSpec_NEMO_sub-1054004_ses-01_CPF-R.rda",
    "/Volumes/groupdata/MRI_BIDS_DATABANK/NEMO/sourcedata/sub-1054010/ses-01/spectro/MrSpec_NEMO_sub-1054010_ses-01_CPF-L.rda",
    "/Volumes/groupdata/MRI_BIDS_DATABANK/NEMO/sourcedata/sub-1054010/ses-01/spectro/MrSpec_NEMO_sub-1054010_ses-01_CPF-R.rda",
    "/Volumes/groupdata/MRI_BIDS_DATABANK/NEMO/sourcedata/sub-1054011/ses-01/spectro/MrSpec_NEMO_sub-1054011_ses-01_CPF-L.rda",
    "/Volumes/groupdata/MRI_BIDS_DATABANK/NEMO/sourcedata/sub-1054011/ses-01/spectro/MrSpec_NEMO_sub-1054011_ses-01_CPF-R.rda",
    "/Volumes/groupdata/MRI_BIDS_DATABANK/NEMO/sourcedata/sub-1054012/ses-01/spectro/MrSpec_NEMO_sub-1054012_ses-01_CPF-L.rda",
    "/Volumes/groupdata/MRI_BIDS_DATABANK/NEMO/sourcedata/sub-1054012/ses-01/spectro/MrSpec_NEMO_sub-1054012_ses-01_CPF-R.rda",
    "/Volumes/groupdata/MRI_BIDS_DATABANK/NEMO/sourcedata/sub-1054013/ses-01/spectro/MrSpec_NEMO_sub-1054013_ses-01_CPF-L.rda",
    "/Volumes/groupdata/MRI_BIDS_DATABANK/NEMO/sourcedata/sub-1054013/ses-01/spectro/MrSpec_NEMO_sub-1054013_ses-01_CPF-R.rda",
    "/Volumes/groupdata/MRI_BIDS_DATABANK/NEMO/sourcedata/sub-1054014/ses-01/spectro/MrSpec_NEMO_sub-1054014_ses-01_CPF-L.rda",
    "/Volumes/groupdata/MRI_BIDS_DATABANK/NEMO/sourcedata/sub-1054014/ses-01/spectro/MrSpec_NEMO_sub-1054014_ses-01_CPF-R.rda"
```

Osprey : Résultats



Osprey 2.5.0

/Volumes/groupdata/MRI_BIDS_DATABANK/NEMO/sourcedata/sub-1054001/ses-01/spectro/MrSpec_NEMO_sub-1054001_ses-01_CPF-L.rda

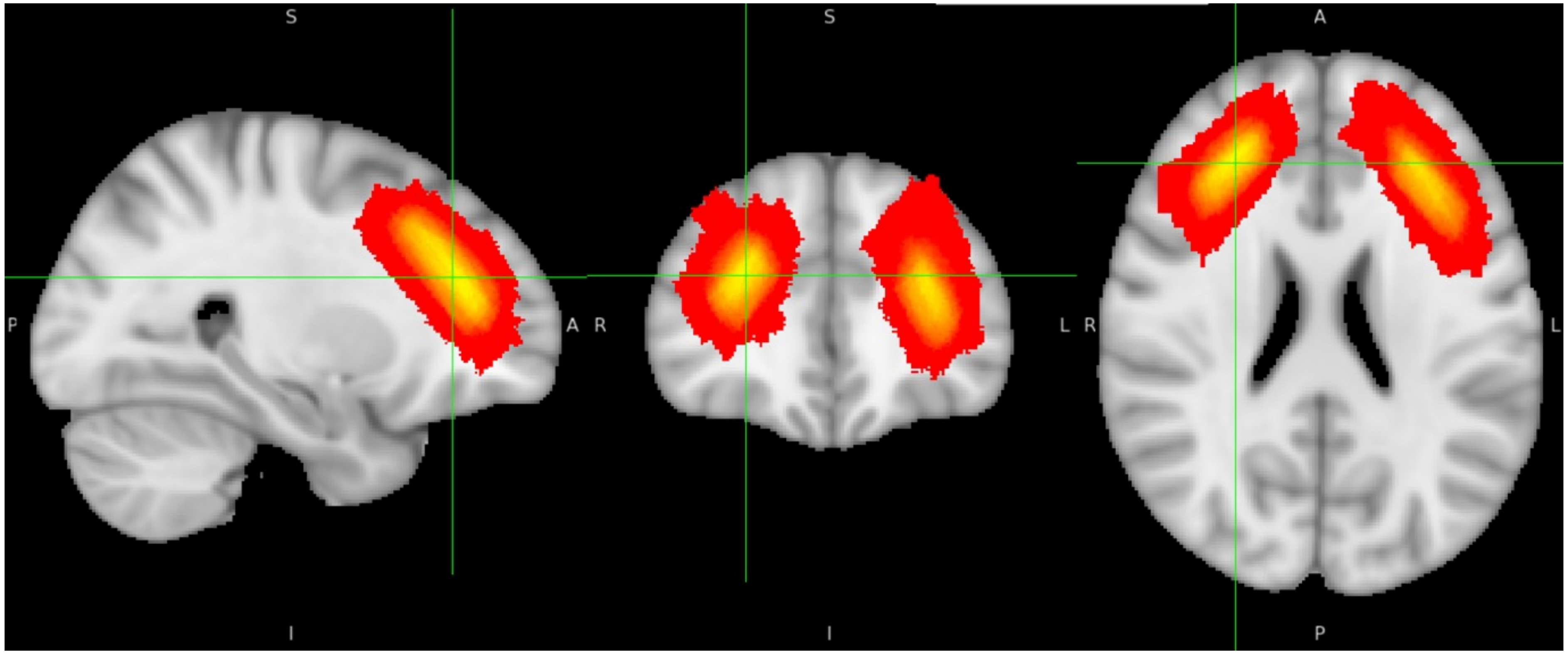
Metabolite Data -> Sequence: *svs_se#; Fitting algorithm: Osprey; Fitting Style: Separate; Selected subspecs: metab
Fitting range: 0.4 to 4.2 ppm; Baseline knot spacing: 0.4 ppm; ph0: -0.62deg; ph1: 0.29deg; refShift: 0.95 Hz; refFWHM: 0.06 ppm
Number of metabolites: 18; Number of MM/lipids: 8 scale: 27939.4682

Raw Water Ratio

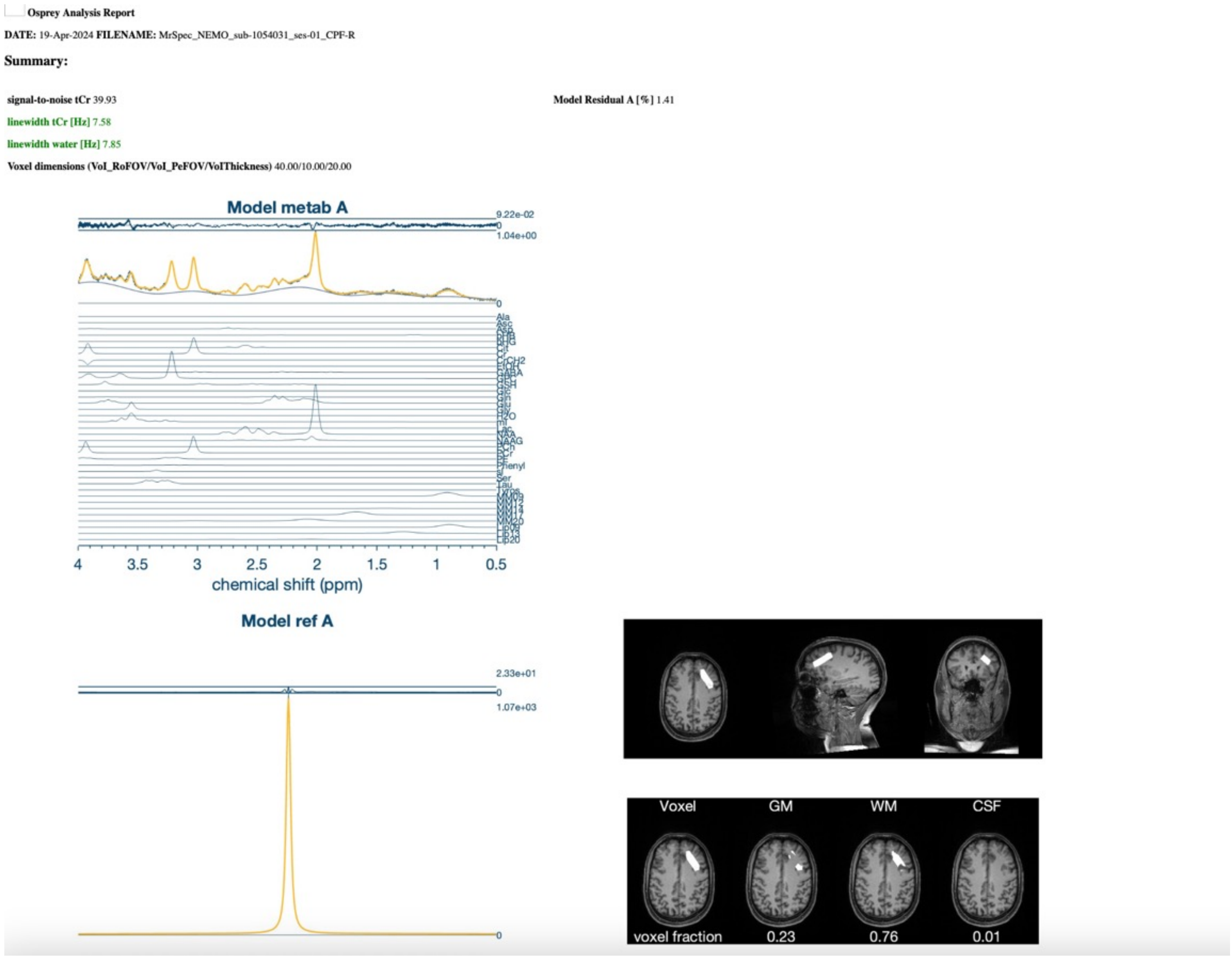
Asc	6.13e-06
Asp	4.84e-05
Cr	1.55e-04
CrCH2	1.75e-05
GABA	4.57e-06
GPC	6.86e-05
GSH	4.56e-05
Gln	7.12e-05
Glu	2.64e-04
mI	1.99e-04
Lac	0.00e+00
NAA	3.07e-04
NAAG	4.63e-05
PCh	0.00e+00
PCr	7.59e-05
PE	3.30e-05
sI	1.49e-06
Tau	2.45e-05
MM09	1.13e-04
MM12	0.00e+00
MM14	9.53e-05
MM17	1.10e-04
MM20	1.75e-04
Lip09	6.69e-05
Lip13	6.52e-05
Lip20	5.26e-05

Osprey Separate metab fit plot:
MrSpec_NEMO_sub-1054001_ses-01_CPF-L.rda

Osprey : Résultats (70 sujets, 2 voxels par sujet)



Osprey : Rapport HTML



Osprey Analysis Report

DATE: 19-Apr-2024 **FILENAME:** MrSpec_NEMO_sub-1054031_ses-01_CPF-R

Summary:

signal-to-noise tCr 39.93

linewidth tCr [Hz] 7.58

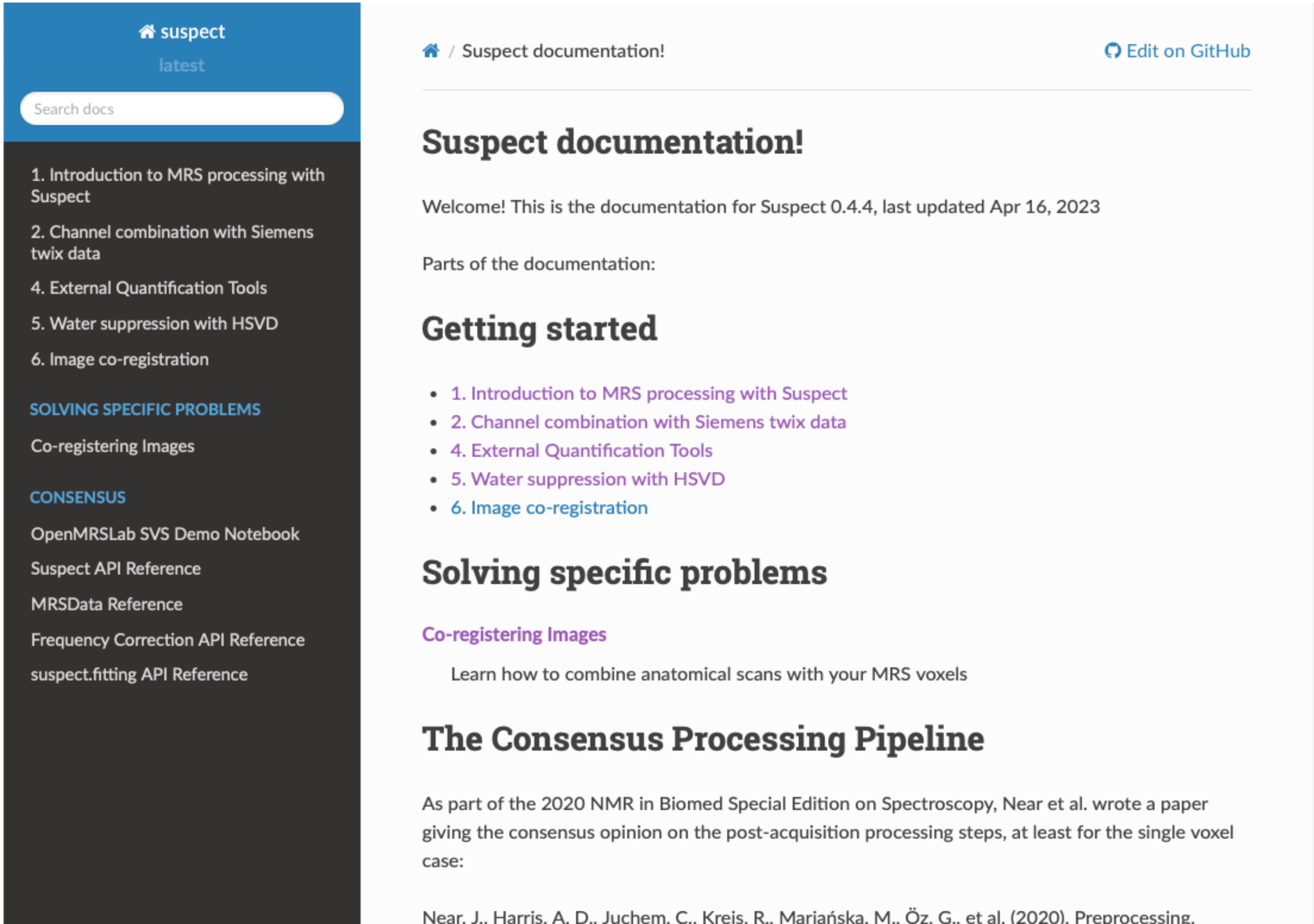
linewidth water [Hz] 7.85

Voxel dimensions (VoI_RoFOV/VoI_PeFOV/VoIThickness) 40.00/10.00/20.00

Model Residual A [%] 1.41

Processing with Suspect:

https://suspect.readthedocs.io/en/latest/index.html



Suspect documentation!

Welcome! This is the documentation for Suspect 0.4.4, last updated Apr 16, 2023

Parts of the documentation:

Getting started

- 1. Introduction to MRS processing with Suspect
- 2. Channel combination with Siemens twix data
- 4. External Quantification Tools
- 5. Water suppression with HSVD
- 6. Image co-registration

Solving specific problems

Co-registering Images

Learn how to combine anatomical scans with your MRS voxels

The Consensus Processing Pipeline

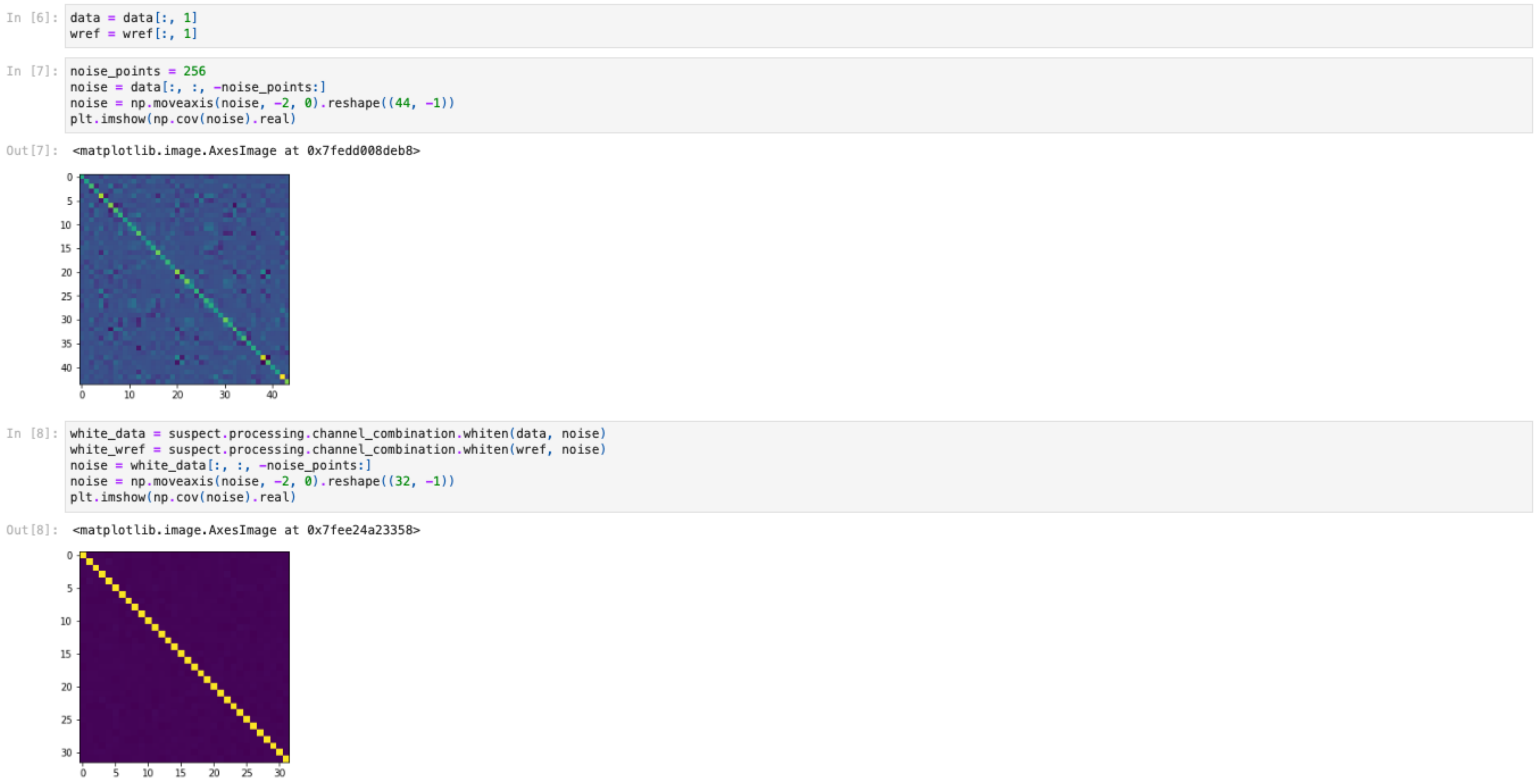
As part of the 2020 NMR in Biomed Special Edition on Spectroscopy, Near et al. wrote a paper giving the consensus opinion on the post-acquisition processing steps, at least for the single voxel case:

Near, J., Harris, A. D., Juchem, C., Kreis, R., Marjańska, M., Öz, G., et al. (2020). Preprocessing,

Preprocessing avec Suspect

- Python code
- Able to read .dat Files
- Noise pre-whitening
- Frequency correction
- Eddy current correction
- HSVD water suppression
- Segmentation and voxel tissue composition
- Fit with Tarqin
- Quality assessment

Noise prewhitening (input in .dat format)



```
In [6]: data = data[:, 1]
        wref = wref[:, 1]
```

```
In [7]: noise_points = 256
        noise = data[:, :, -noise_points:]
        noise = np.moveaxis(noise, -2, 0).reshape((44, -1))
        plt.imshow(np.cov(noise).real)

Out[7]: <matplotlib.image.AxesImage at 0x7fedd008deb8>
```

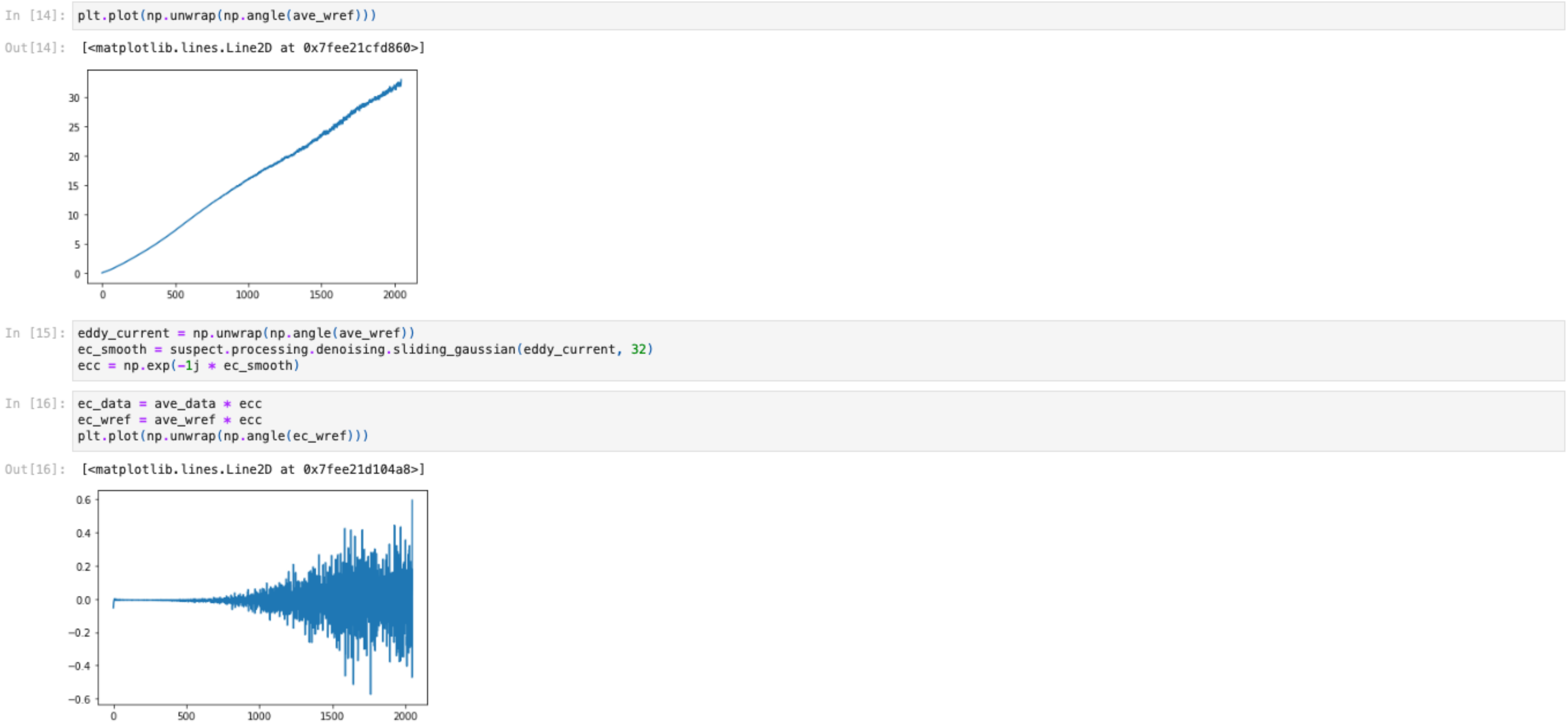
```
In [8]: white_data = suspect.processing.channel_combination.whiten(data, noise)
        white_wref = suspect.processing.channel_combination.whiten(wref, noise)
        noise = white_data[:, :, -noise_points:]
        noise = np.moveaxis(noise, -2, 0).reshape((32, -1))
        plt.imshow(np.cov(noise).real)

Out[8]: <matplotlib.image.AxesImage at 0x7fee24a23358>
```

Frequency correction

```
In [10]: spectra = cc_data.spectrum()
         frequency_slice = spectra.slice_ppm(3.5, 1.9)
         plt.imshow(spectra[:, frequency_slice].T.real, extent=[0, 128, 1.9, 3.5], aspect='auto')

Out[10]: <matplotlib.image.AxesImage at 0x7fedf07693c8>
```

```
In [11]: sr_data = suspect.processing.frequency_correction.correct_frequency_and_phase(cc_data, cc_data[0], method="sr")
         sr_wref = suspect.processing.frequency_correction.correct_frequency_and_phase(cc_wref, cc_wref[0], method="sr")

In [12]: sr_spectra = sr_data.spectrum()
         frequency_slice = sr_spectra.slice_ppm(3.5, 1.9)
         plt.imshow(sr_spectra[:, frequency_slice].T.real, extent=[0, 128, 1.9, 3.5], aspect='auto')

Out[12]: <matplotlib.image.AxesImage at 0x7fede01cabe0>
```

Eddy current Correction



```
In [14]: plt.plot(np.unwrap(np.angle(ave_wref)))

Out[14]: [<matplotlib.lines.Line2D at 0x7fee21cfd860>]
```

```
In [15]: eddy_current = np.unwrap(np.angle(ave_wref))
         ec_smooth = suspect.processing.denoising.sliding_gaussian(eddy_current, 32)
         ecc = np.exp(-1j * ec_smooth)

In [16]: ec_data = ave_data * ecc
         ec_wref = ave_wref * ecc
         plt.plot(np.unwrap(np.angle(ec_wref)))

Out[16]: [<matplotlib.lines.Line2D at 0x7fee21d104a8>]
```

Suspect : Water suppression

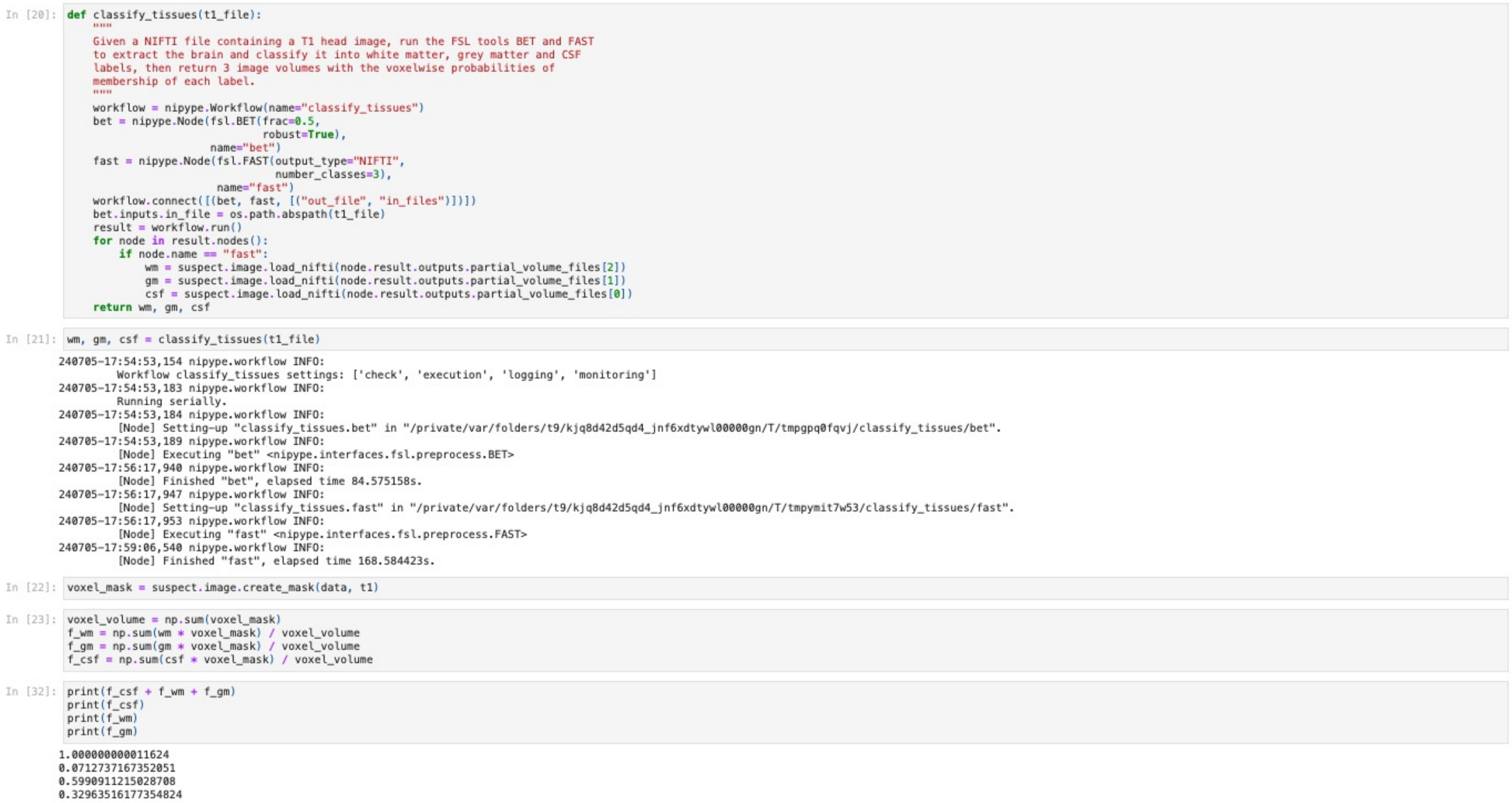
```
In [18]: components = suspect.processing.water_suppression.hsvd(ec_data, 30)
         water_components = [component for component in components if component["frequency"] < 60]
         water_fid = ec_data.inherit(suspect.processing.water_suppression.construct_fid(water_components, ec_data.time_axis()))
         plt.plot(ec_data.frequency_axis_ppm(), ec_data.spectrum().real)
         plt.plot(water_fid.frequency_axis_ppm(), water_fid.spectrum().real)
         plt.xlim([5, 0])
```

```
Out[18]: (5.0, 0.0)
```

```
In [19]: dry_data = ec_data - water_fid
         plt.plot(dry_data.frequency_axis_ppm(), dry_data.spectrum().real)
         plt.xlim(5, 0)
```

```
Out[19]: (5.0, 0.0)
```

Segmentation and tissue composition



In [20]:

```python
def classify_tissues(t1_file):
    """
    Given a NIFTI file containing a T1 head image, run the FSL tools BET and FAST
    to extract the brain and classify it into white matter, grey matter and CSF
    labels, then return 3 image volumes with the voxelwise probabilities of
    membership of each label.
    """
    workflow = nipype.Workflow(name="classify_tissues")
    bet = nipype.Node(fsl.BET(frac=0.5,
                              robust=True),
                      name="bet")
    fast = nipype.Node(fsl.FAST(output_type="NIFTI",
                                number_classes=3),
                       name="fast")
    workflow.connect([(bet, fast, [("out_file", "in_files")])])
    bet.inputs.in_file = os.path.abspath(t1_file)
    result = workflow.run()
    for node in result.nodes():
        if node.name == "fast":
            wm = suspect.image.load_nifti(node.result.outputs.partial_volume_files[2])
            gm = suspect.image.load_nifti(node.result.outputs.partial_volume_files[1])
            csf = suspect.image.load_nifti(node.result.outputs.partial_volume_files[0])
    return wm, gm, csf
```

In [21]:

```python
wm, gm, csf = classify_tissues(t1_file)
```

```
240705-17:54:53,154 nipype.workflow INFO:
	 Workflow classify_tissues settings: ['check', 'execution', 'logging', 'monitoring']
240705-17:54:53,183 nipype.workflow INFO:
	 Running serially.
240705-17:54:53,184 nipype.workflow INFO:
	 [Node] Setting-up "classify_tissues.bet" in "/private/var/folders/t9/kjq8d42d5qd4_jnf6xdtywl00000gn/T/tmpgpq0fqvj/classify_tissues/bet".
240705-17:54:53,189 nipype.workflow INFO:
	 [Node] Executing "bet" <nipype.interfaces.fsl.preprocess.BET>
240705-17:56:17,940 nipype.workflow INFO:
	 [Node] Finished "bet", elapsed time 84.575158s.
240705-17:56:17,947 nipype.workflow INFO:
	 [Node] Setting-up "classify_tissues.fast" in "/private/var/folders/t9/kjq8d42d5qd4_jnf6xdtywl00000gn/T/tmpymit7w53/classify_tissues/fast".
240705-17:56:17,953 nipype.workflow INFO:
	 [Node] Executing "fast" <nipype.interfaces.fsl.preprocess.FAST>
240705-17:59:06,540 nipype.workflow INFO:
	 [Node] Finished "fast", elapsed time 168.584423s.
```

In [22]:

```python
voxel_mask = suspect.image.create_mask(data, t1)
```

In [23]:

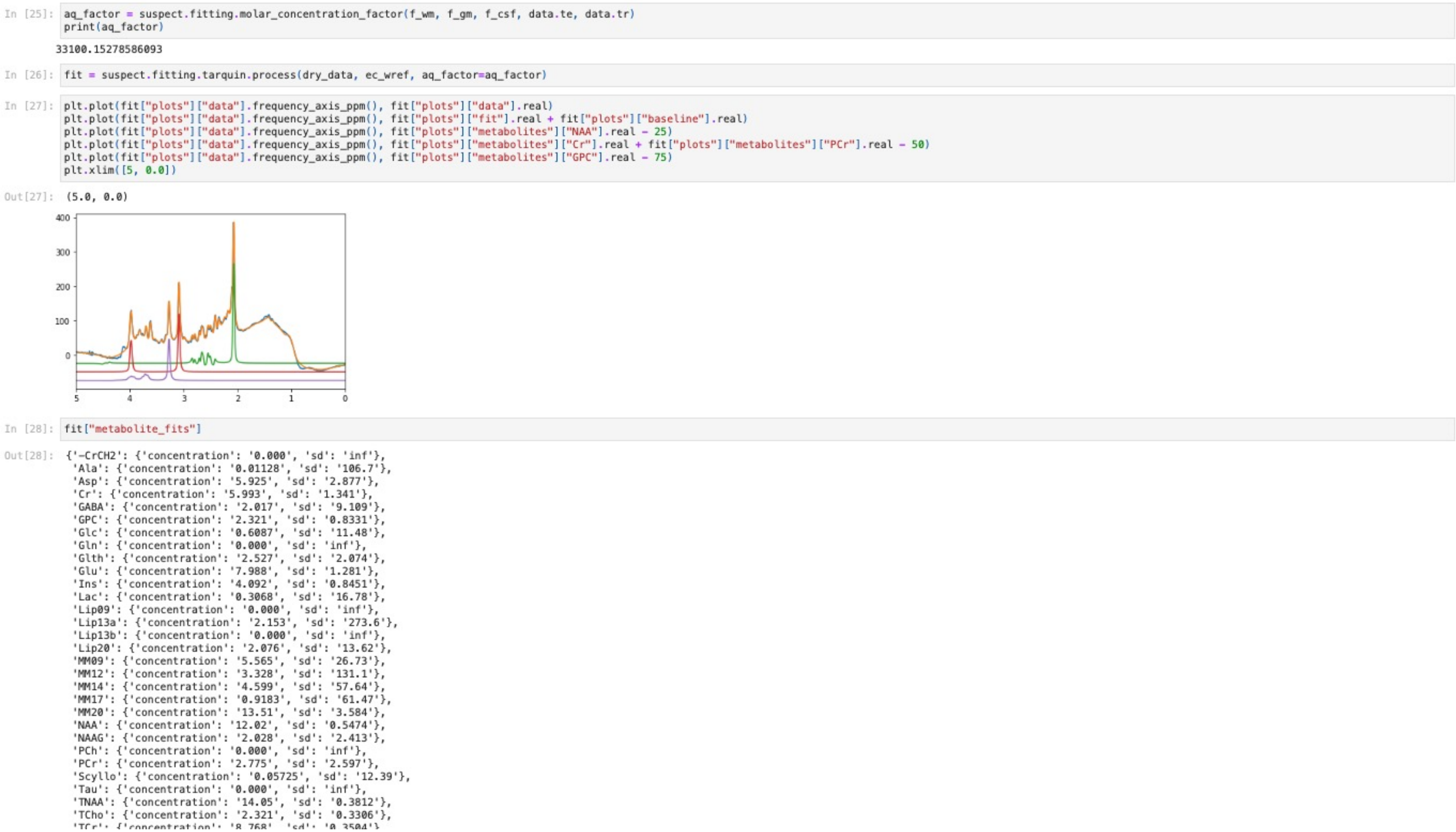
```python
voxel_volume = np.sum(voxel_mask)
f_wm = np.sum(wm * voxel_mask) / voxel_volume
f_gm = np.sum(gm * voxel_mask) / voxel_volume
f_csf = np.sum(csf * voxel_mask) / voxel_volume
```

In [32]:

```python
print(f_csf + f_wm + f_gm)
print(f_csf)
print(f_wm)
print(f_gm)
```

```
1.000000000011624
0.0712737167352051
0.5990911215028708
0.32963516177354824
```

Fit with Tarquin



```
aq_factor = suspect.fitting.molar_concentration_factor(f_wm, f_gm, f_csf, data.te, data.tr)
print(aq_factor)
```

```
33100.15278586093
```

```
fit = suspect.fitting.tarquin.process(dry_data, ec_wref, aq_factor=aq_factor)
```

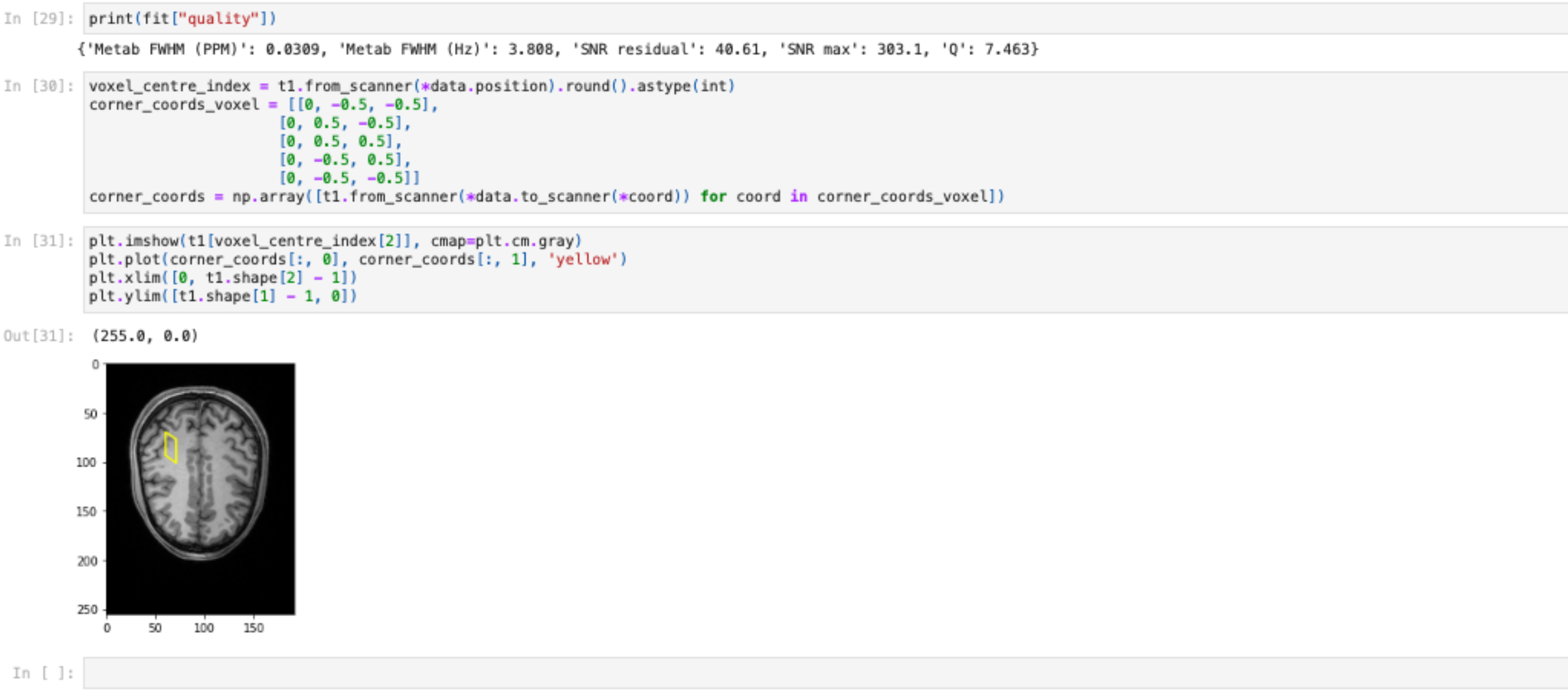
```
plt.plot(fit["plots"]["data"].frequency_axis_ppm(), fit["plots"]["data"].real)
plt.plot(fit["plots"]["data"].frequency_axis_ppm(), fit["plots"]["fit"].real + fit["plots"]["baseline"].real)
plt.plot(fit["plots"]["data"].frequency_axis_ppm(), fit["plots"]["metabolites"]["NAA"].real - 25)
plt.plot(fit["plots"]["data"].frequency_axis_ppm(), fit["plots"]["metabolites"]["Cr"].real + fit["plots"]["metabolites"]["PCr"].real - 50)
plt.plot(fit["plots"]["data"].frequency_axis_ppm(), fit["plots"]["metabolites"]["GPC"].real - 75)
plt.xlim([5, 0.0])
```

```
(5.0, 0.0)
```

```
fit["metabolite_fits"]
```

```
{'-CrCH2': {'concentration': '0.000', 'sd': 'inf'},
 'Ala': {'concentration': '0.01128', 'sd': '106.7'},
 'Asp': {'concentration': '5.925', 'sd': '2.877'},
 'Cr': {'concentration': '5.993', 'sd': '1.341'},
 'GABA': {'concentration': '2.017', 'sd': '9.109'},
 'GPC': {'concentration': '2.321', 'sd': '0.8331'},
 'Glc': {'concentration': '0.6087', 'sd': '11.48'},
 'Gln': {'concentration': '0.000', 'sd': 'inf'},
 'Glth': {'concentration': '2.527', 'sd': '2.074'},
 'Glu': {'concentration': '7.988', 'sd': '1.281'},
 'Ins': {'concentration': '4.092', 'sd': '0.8451'},
 'Lac': {'concentration': '0.3068', 'sd': '16.78'},
 'Lip09': {'concentration': '0.000', 'sd': 'inf'},
 'Lip13a': {'concentration': '2.153', 'sd': '273.6'},
 'Lip13b': {'concentration': '0.000', 'sd': 'inf'},
 'Lip20': {'concentration': '2.076', 'sd': '13.62'},
 'MM09': {'concentration': '5.565', 'sd': '26.73'},
 'MM12': {'concentration': '3.328', 'sd': '131.1'},
 'MM14': {'concentration': '4.599', 'sd': '57.64'},
 'MM17': {'concentration': '0.9183', 'sd': '61.47'},
 'MM20': {'concentration': '13.51', 'sd': '3.584'},
 'NAA': {'concentration': '12.02', 'sd': '0.5474'},
 'NAAG': {'concentration': '2.028', 'sd': '2.413'},
 'PCh': {'concentration': '0.000', 'sd': 'inf'},
 'PCr': {'concentration': '2.775', 'sd': '2.597'},
 'Scyllo': {'concentration': '0.05725', 'sd': '12.39'},
 'Tau': {'concentration': '0.000', 'sd': 'inf'},
 'TNAA': {'concentration': '14.05', 'sd': '0.3812'},
 'TCho': {'concentration': '2.321', 'sd': '0.3306'},
 'TCr': {'concentration': '8.768', 'sd': '0.3504'}
```

Quality assessment and voxel placement



```
In [29]: print(fit["quality"])

         {'Metab FWHM (PPM)': 0.0309, 'Metab FWHM (Hz)': 3.808, 'SNR residual': 40.61, 'SNR max': 303.1, 'Q': 7.463}

In [30]: voxel_centre_index = t1.from_scanner(*data.position).round().astype(int)
         corner_coords_voxel = [[0, -0.5, -0.5],
                                [0, 0.5, -0.5],
                                [0, 0.5, 0.5],
                                [0, -0.5, 0.5],
                                [0, -0.5, -0.5]]
         corner_coords = np.array([t1.from_scanner(*data.to_scanner(*coord)) for coord in corner_coords_voxel])

In [31]: plt.imshow(t1[voxel_centre_index[2]], cmap=plt.cm.gray)
         plt.plot(corner_coords[:, 0], corner_coords[:, 1], 'yellow')
         plt.xlim([0, t1.shape[2] - 1])
         plt.ylim([t1.shape[1] - 1, 0])

Out[31]: (255.0, 0.0)
```

```
In [ ]:
```

MEGA-PRESS

MEGA-PRESS sequence (C2P du CMRR)

Calibration du FA spécifique par sujet

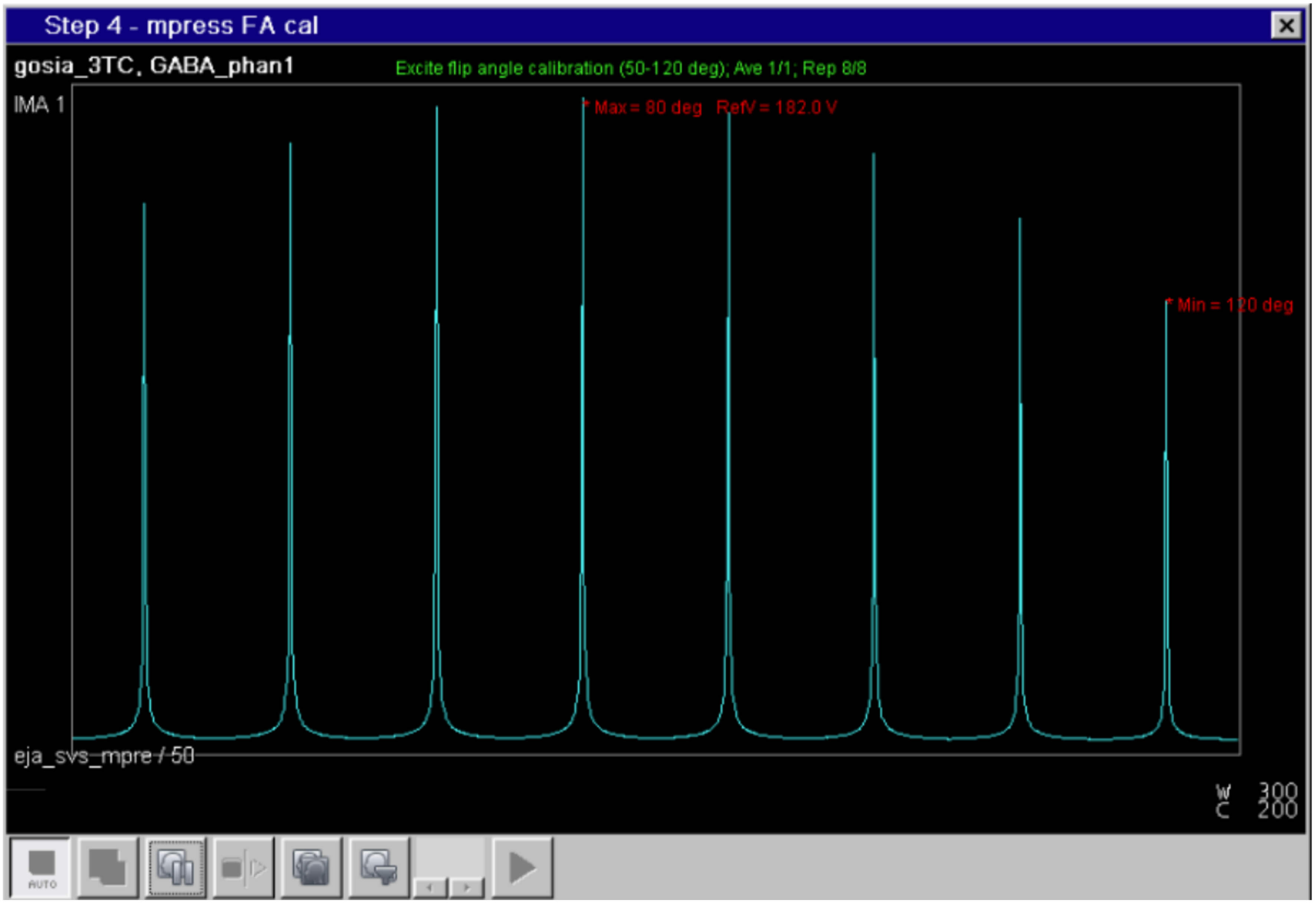
Pas de bandes de saturation

Problème avec la contamination de macromolecules qui demande de repositionner le voxel

TA= 8min27, TR/TE= 2020/68ms, 240 averages

Taille de voxel: 25 x 25 x 30mm^3, sur le sillon central.

Calibration par sujet



Step 4 - mpress FA cal

gosia_3TC, GABA_phan1

Excite flip angle calibration (50-120 deg); Ave 1/1; Rep 8/8

* Max = 80 deg RefV = 182.0 V

* Min = 120 deg

Positionnement du voxel

Protocole avec session pre et session post pour les sujets

Stratégie de postionnement du voxel?

Test du C2P AutoVOI de Minneapolis

En VE11C: utilisation de l’AutoAlign de Siemens

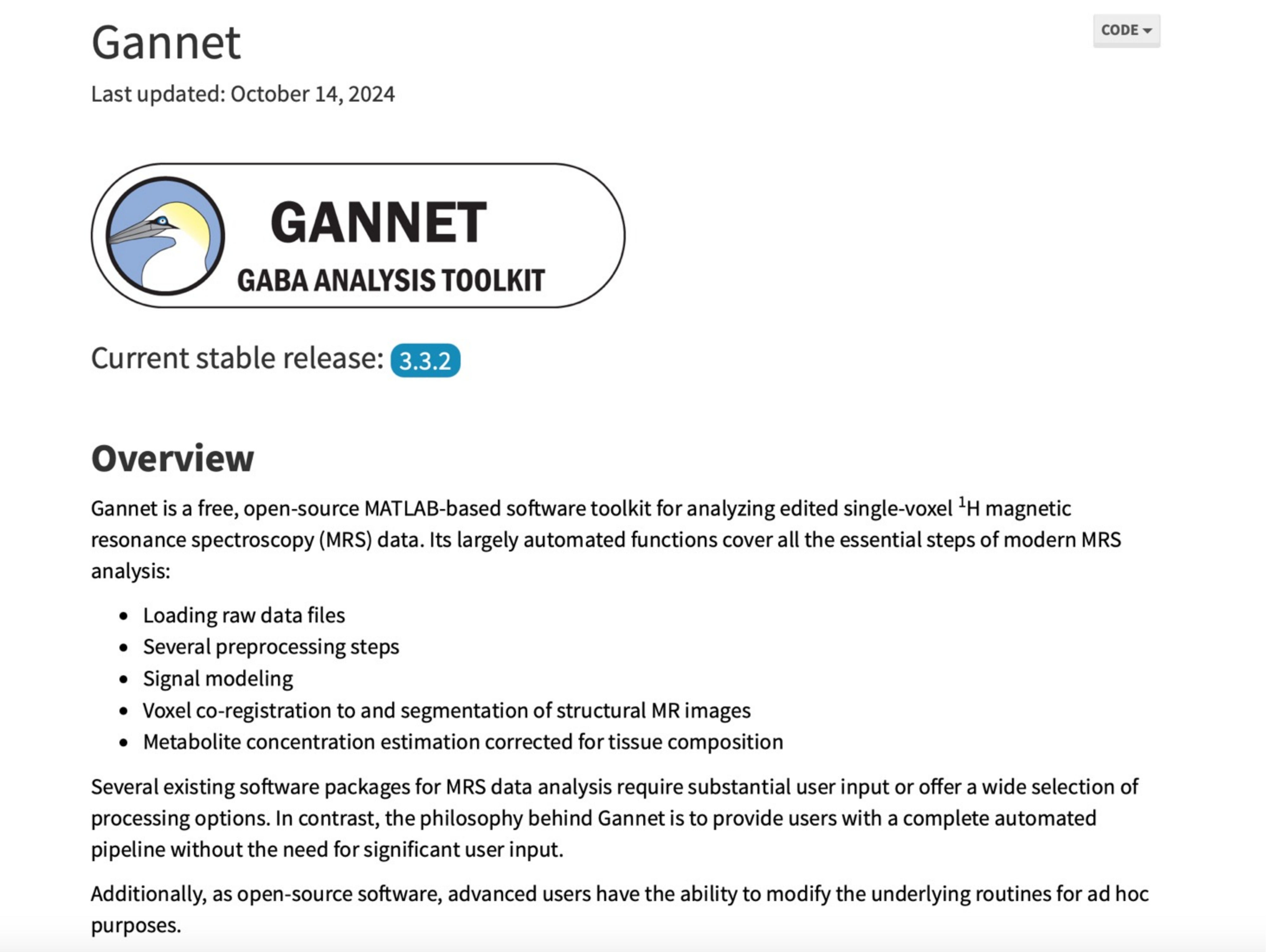
Perte de la fonctionnalité en XA60

Processing avec Gannet

https

Utilis

Utilis



Gannet

Last updated: October 14, 2024

Current stable release: 3.3.2

Overview

Gannet is a free, open-source MATLAB-based software toolkit for analyzing edited single-voxel ^{1}H magnetic resonance spectroscopy (MRS) data. Its largely automated functions cover all the essential steps of modern MRS analysis:

- Loading raw data files
- Several preprocessing steps
- Signal modeling
- Voxel co-registration to and segmentation of structural MR images
- Metabolite concentration estimation corrected for tissue composition

Several existing software packages for MRS data analysis require substantial user input or offer a wide selection of processing options. In contrast, the philosophy behind Gannet is to provide users with a complete automated pipeline without the need for significant user input.

Additionally, as open-source software, advanced users have the ability to modify the underlying routines for ad hoc purposes.

Processing avec Gannet

MRS '},
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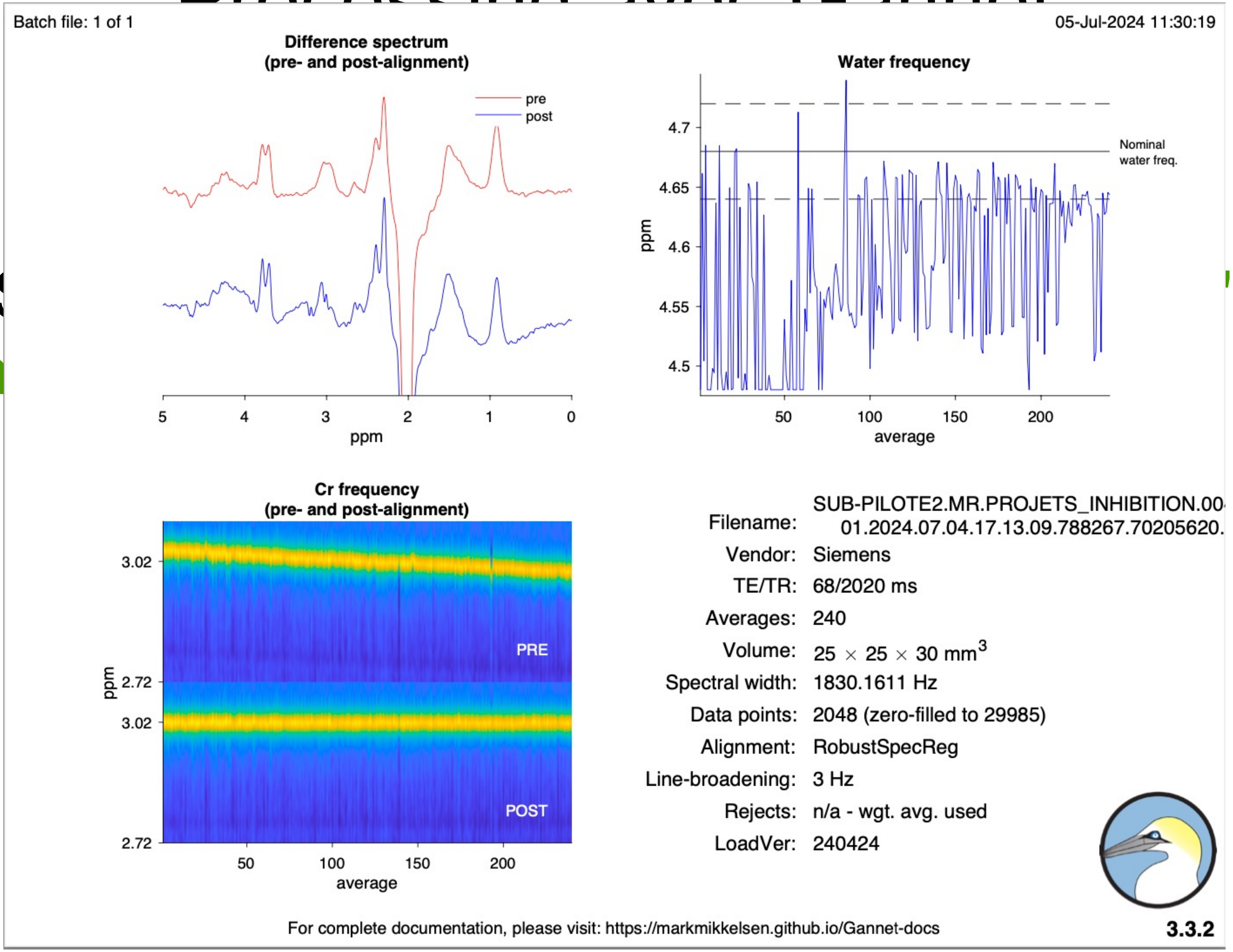

Filename:	SUB-PILOTE2.MR.PROJETS_INHIBITION.00 01.2024.07.04.17.13.09.788267.70205620.
Vendor:	Siemens
TE/TR:	68/2020 ms
Averages:	240
Volume:	25 × 25 × 30 mm^3
Spectral width:	1830.1611 Hz
Data points:	2048 (zero-filled to 29985)
Alignment:	RobustSpecReg
Line-broadening:	3 Hz
Rejects:	n/a - wgt. avg. used
LoadVer:	240424

For complete documentation, please visit: https://markmikkelsen.github.io/Gannet-docs

Processing avec Gannet

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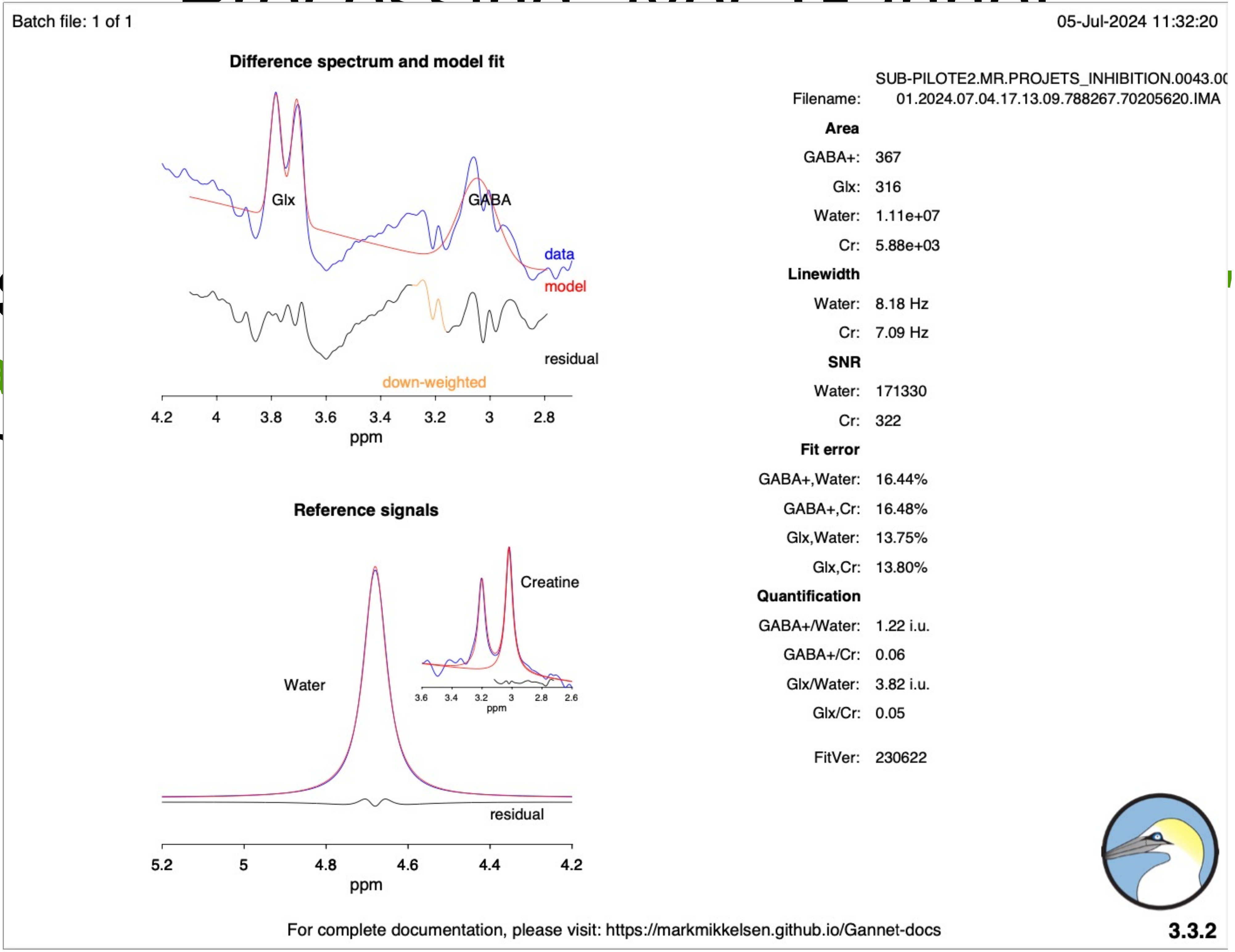

Batch file: 1 of 1

05-Jul-2024 11:32:20

Filename: SUB-PILOTE2.MR.PROJETS_INHIBITION.0043.0
01.2024.07.04.17.13.09.788267.70205620.IMA

Area

GABA+: 367

Glx: 316

Water: 1.11e+07

Cr: 5.88e+03

Linewidth

Water: 8.18 Hz

Cr: 7.09 Hz

SNR

Water: 171330

Cr: 322

Fit error

GABA+,Water: 16.44%

GABA+,Cr: 16.48%

Glx,Water: 13.75%

Glx,Cr: 13.80%

Quantification

GABA+/Water: 1.22 i.u.

GABA+/Cr: 0.06

Glx/Water: 3.82 i.u.

Glx/Cr: 0.05

FitVer: 230622

For complete documentation, please visit: https://markmikkelsen.github.io/Gannet-docs

3.3.2

Processing avec Gannet

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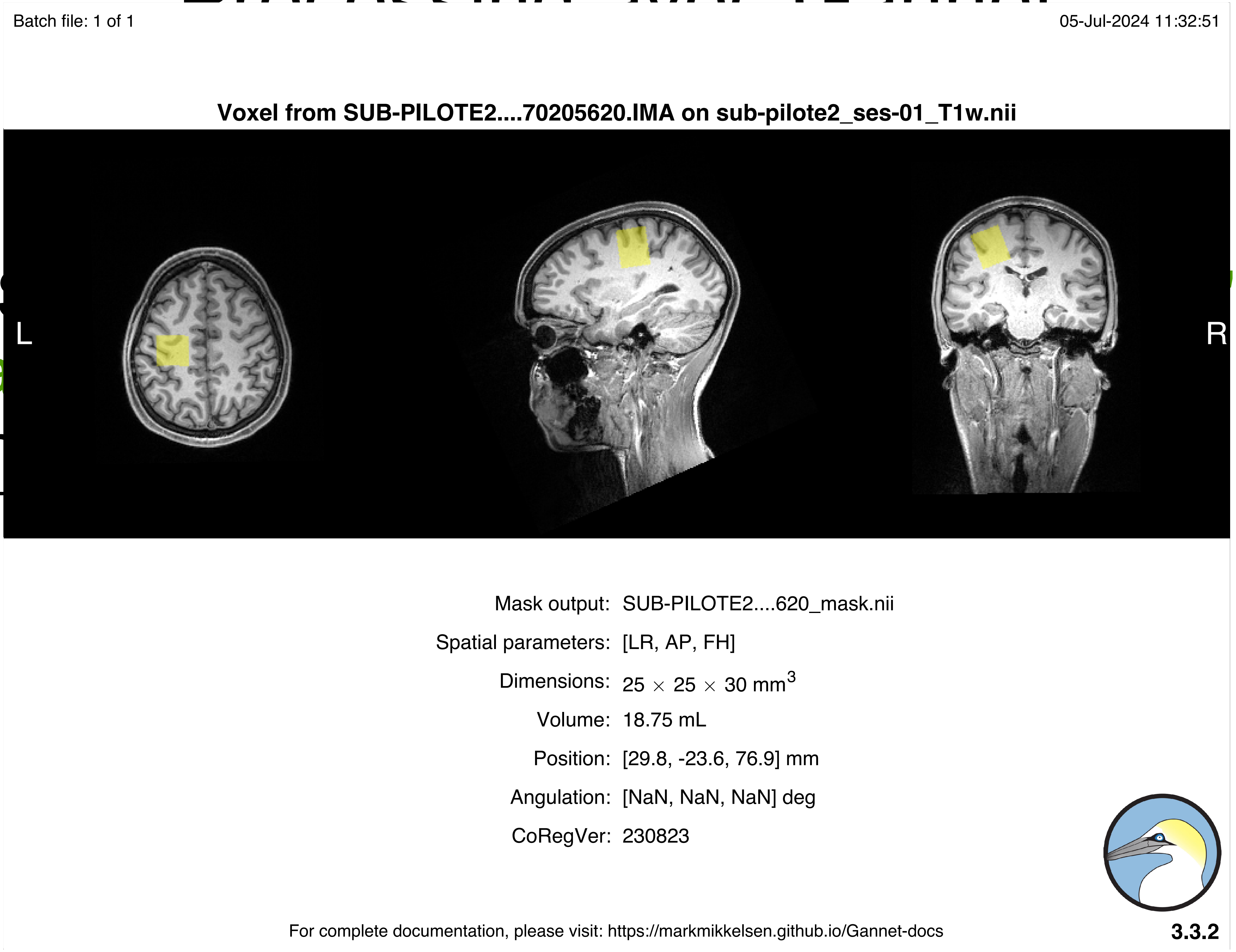

Batch file: 1 of 1

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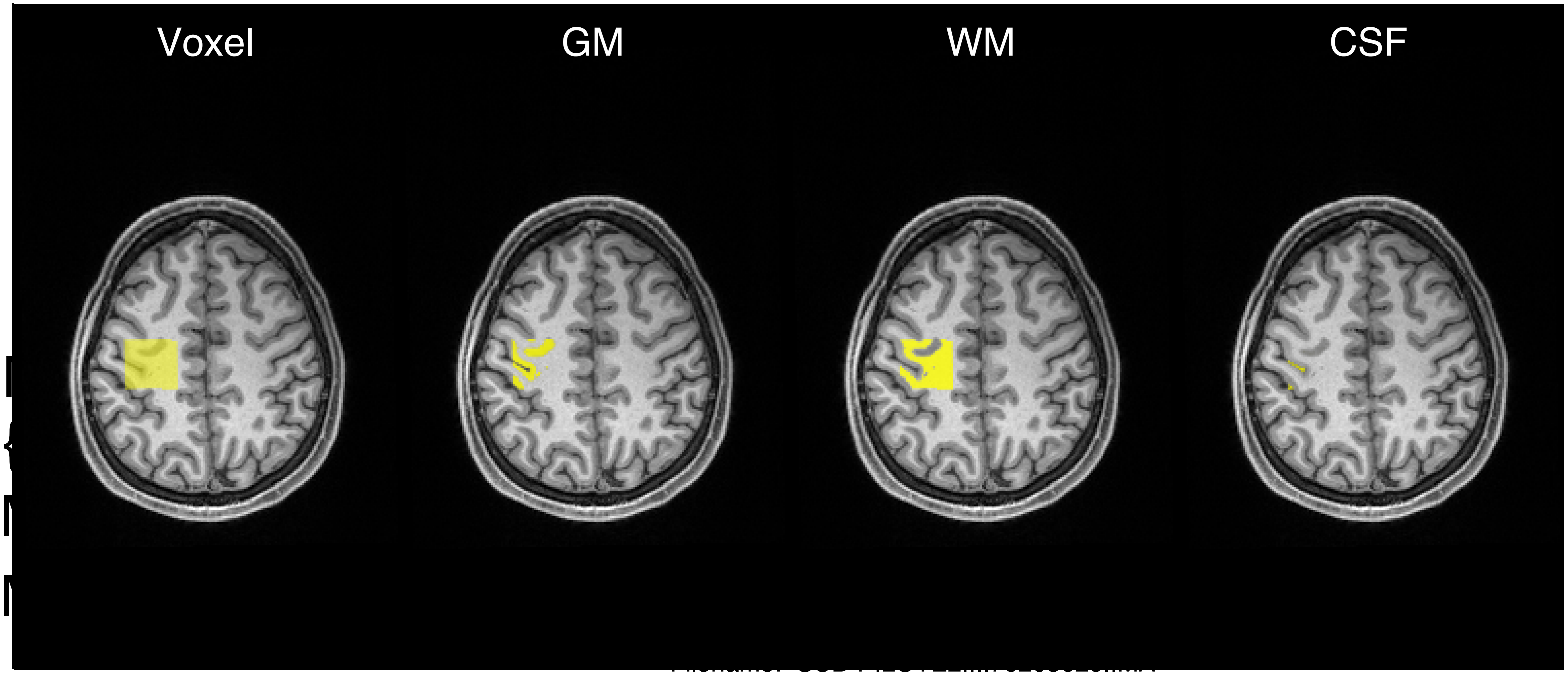
Voxel from SUB-PILOTE2....70205620.IMA on sub-pilote2_ses-01_T1w.nii

Mask output: SUB-PILOTE2....620_mask.nii
Spatial parameters: [LR, AP, FH]
Dimensions: 25 × 25 × 30 mm^3
Volume: 18.75 mL
Position: [29.8, -23.6, 76.9] mm
Angulation: [NaN, NaN, NaN] deg
CoRegVer: 230823

For complete documentation, please visit: https://markmikkelsen.github.io/Gannet-docs

Voxel from SUB-PILOTE2....70205620.IMA on sub-pilote2_ses-01_T1w.nii



Anatomical image: sub-pilote2_ses-01_T1w.nii

GABA+/Water (CSF-corrected): 1.29 i.u.

Glx/Water (CSF-corrected): 4.06 i.u.

GM voxel fraction: 0.30

WM voxel fraction: 0.64

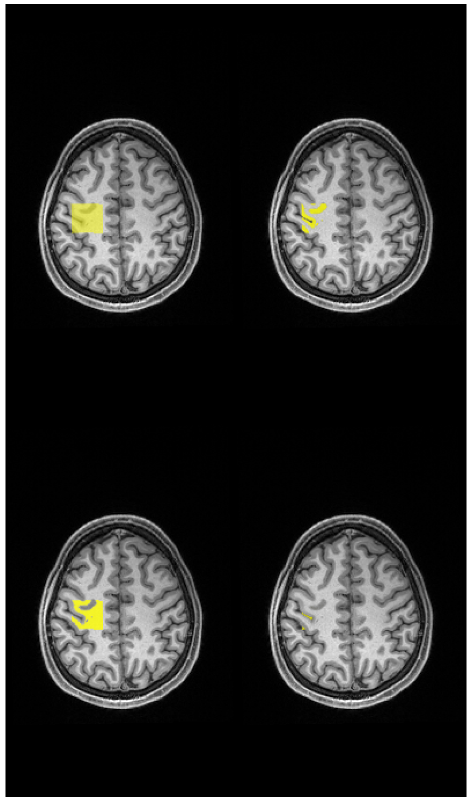
CSF voxel fraction: 0.06

SegmentVer: 230729

For complete documentation, please visit: https://markmikkelsen.github.io/Gannet-docs

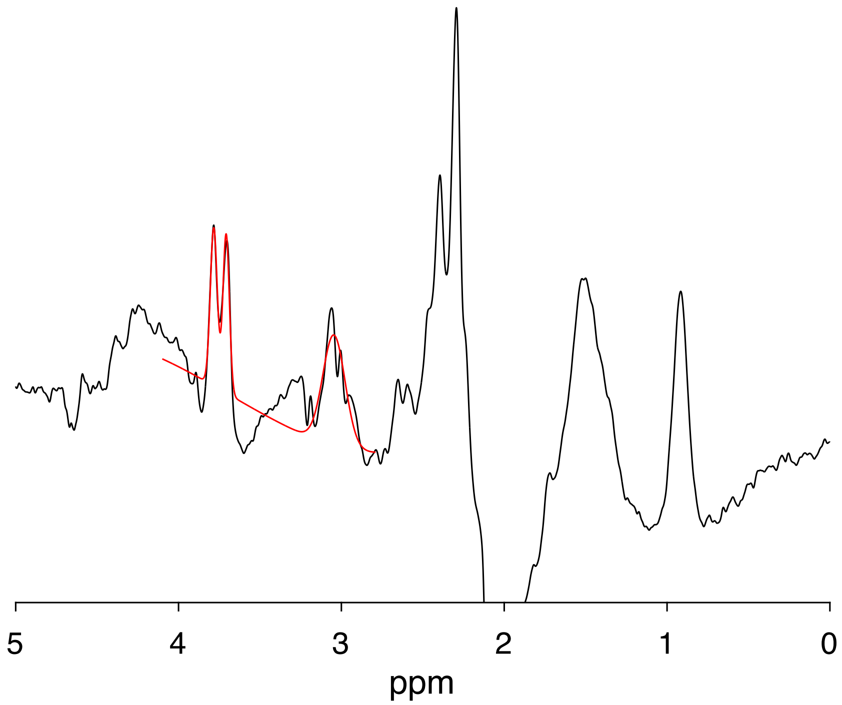
3.3.2

Voxel from SUB-PILOTE2....70205620.IMA on sub-pilote2_ses-01_T1w.nii



Filename:	SUB-PILOTE2....70205620.IMA
Anatomical image:	sub-pilote2_ses-01_T1w.nii
Relaxation-, tissue-corrected (Gasparovic et al. method)	
GABA+/Water:	1.96 i.u.
Glx/Water:	6.15 i.u.
Relaxation-, tissue-, alpha-corrected (Harris et al. method)	
GABA+/Water (α = 0.5):	2.06 i.u.
Glx/Water (α = 0.5):	6.45 i.u.
Relaxation-, tissue-, alpha-corrected; group-average-normalized (Harris et al. method)	
GABA+/Water (α = 0.5):	1.36 i.u.
Glx/Water (α = 0.5):	4.26 i.u.
QuantifyVer:	230621

Difference spectrum and model fit

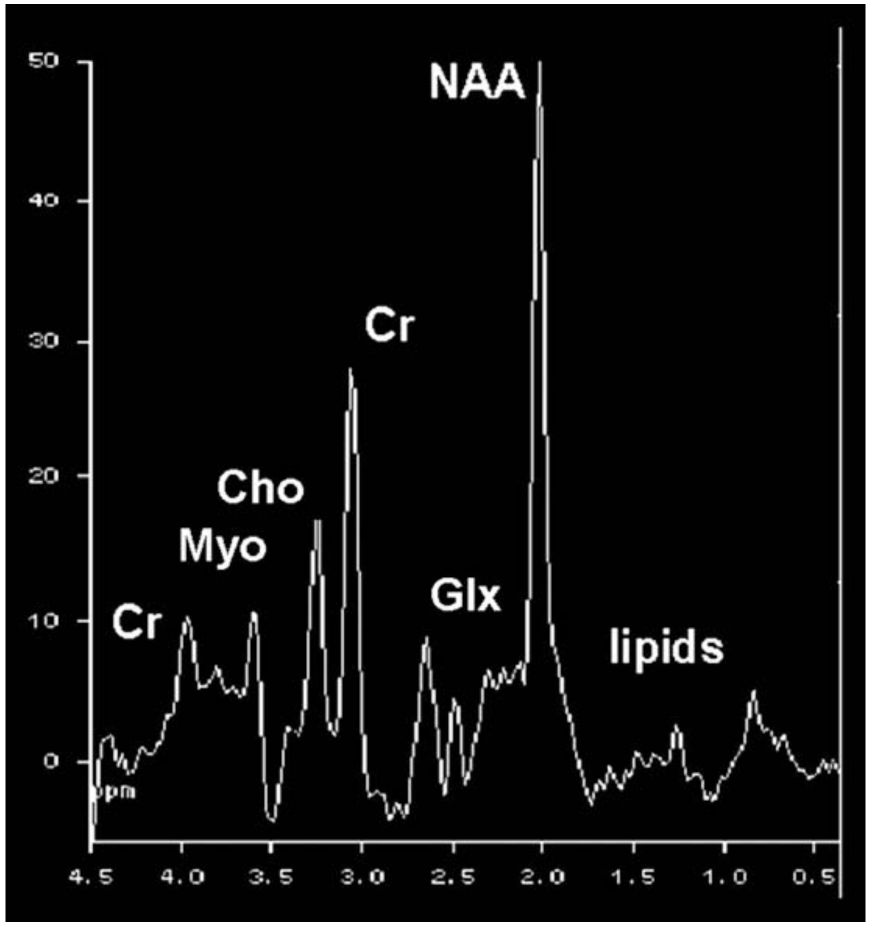


For complete documentation, please visit: https://markmikkelsen.github.io/Gannet-docs

3.3.2

Now…
Jean-Luc
Anton!

Magnetic resonance spectroscopy of the brain (Soares & Law)

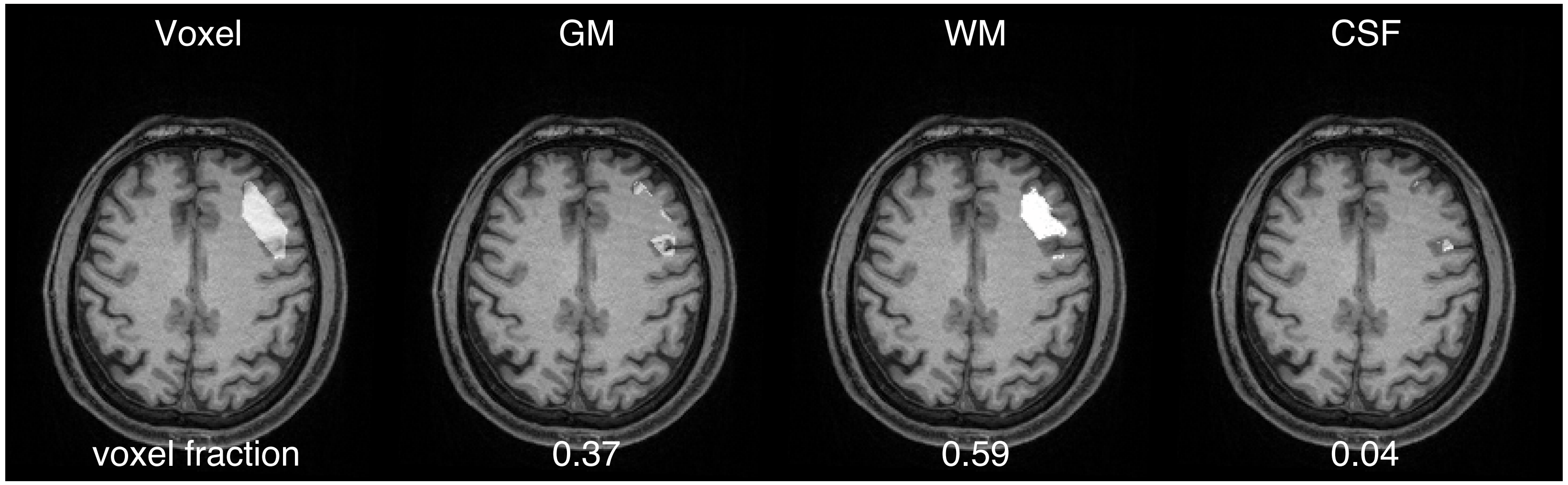


- N-acetylaspartate (NAA) ≈ marker of neuronal density and viability
- Choline (Cho) ≈ metabolic marker of membrane density and integrit
- Creatine (Cr) ≈ marker of "energy metabolism'
- Glx (Glutamate + Glutamine) : Glutamate is an excitatory neurotransmitter
- Lactate ≈ brain ischaemia, hypoxia, seizures, metabolic disorders, macrophage accumulation (areas of acute inflammation)
- Myo ≈ glial proliferation or increase in glial cell size (inflammation)

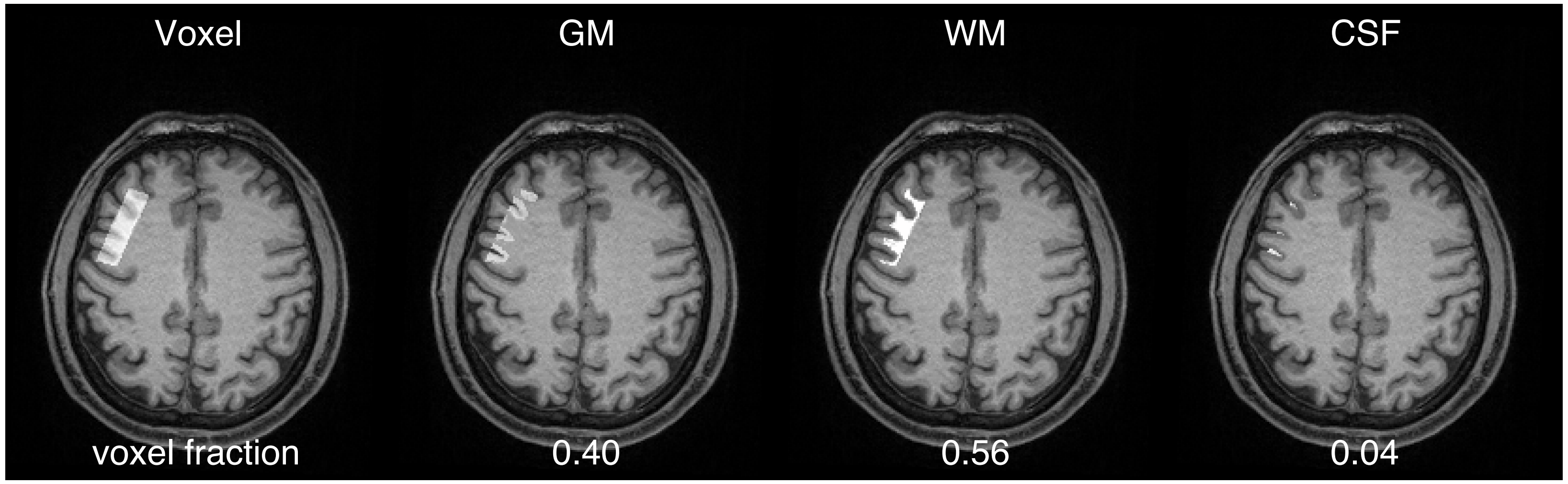
- Gamma-aminobutyric acid (GABA) : inhibitory neurotransmitter
  → peak confused with Glx: requires edited analysis (with On & Off spectra)

NEMO project: Bipolarity & Neuro-development

Right - DLPFC
10 x 40 x 20 mm3



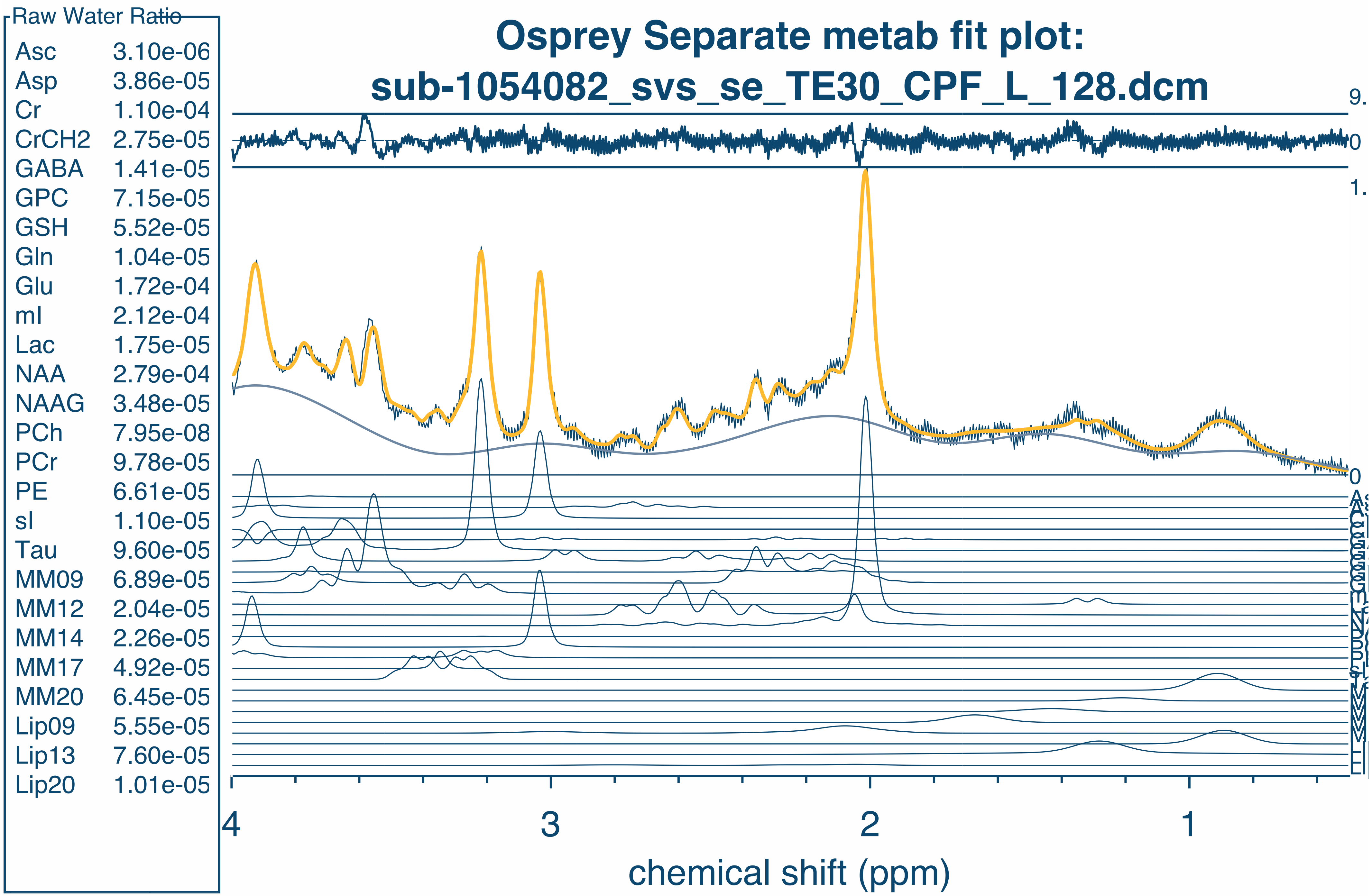
Left - DLPFC
10 x 40 x 20 mm3



128 simple spectra (non-edited analysis): TA = 3’20” **x 2 voxels**

Neurodevelopmental classification of bipolar → **NAA and Glx (Glutamate + Glutamine)**
Neurodevelopmental bipolar patients appear to respond less well to lithium treatment
→**Myo-Inositol & Lactate**

NEMO project: Bipolarity & Neuro-development



Osprey Separate metab fit plot:
sub-1054082_svs_se_TE30_CPF_L_128.dcm

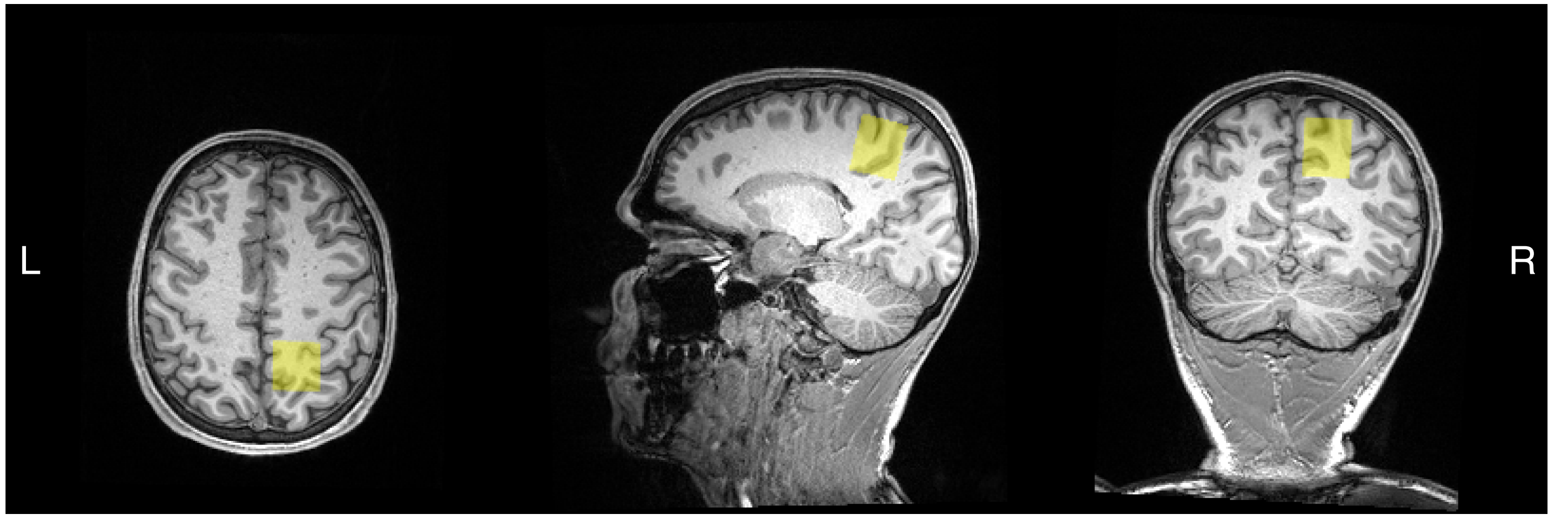
Raw Water Ratio

Asc	3.10e-06
Asp	3.86e-05
Cr	1.10e-04
CrCH2	2.75e-05
GABA	1.41e-05
GPC	7.15e-05
GSH	5.52e-05
Gln	1.04e-05
Glu	1.72e-04
mI	2.12e-04
Lac	1.75e-05
NAA	2.79e-04
NAAG	3.48e-05
PCh	7.95e-08
PCr	9.78e-05
PE	6.61e-05
sI	1.10e-05
Tau	9.60e-05
MM09	6.89e-05
MM12	2.04e-05
MM14	2.26e-05
MM17	4.92e-05
MM20	6.45e-05
Lip09	5.55e-05
Lip13	7.60e-05
Lip20	1.01e-05

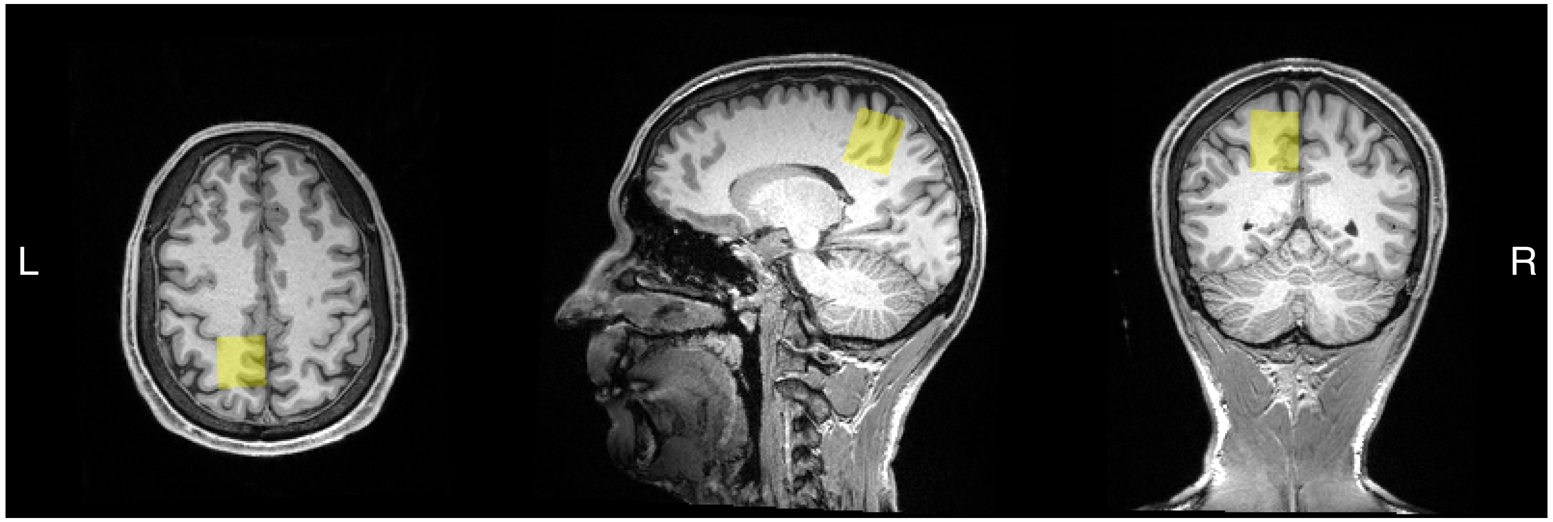
Neurodevelopmental variables ←→ quantification of certain metabolites

PhantomPain project: Phantom pain in amputees & proprioceptive treatment

Right - M1-S1 (leg)
25 x 25 x 30 mm3



Left - M1-S1 (leg)
25 x 25 x 30 mm3



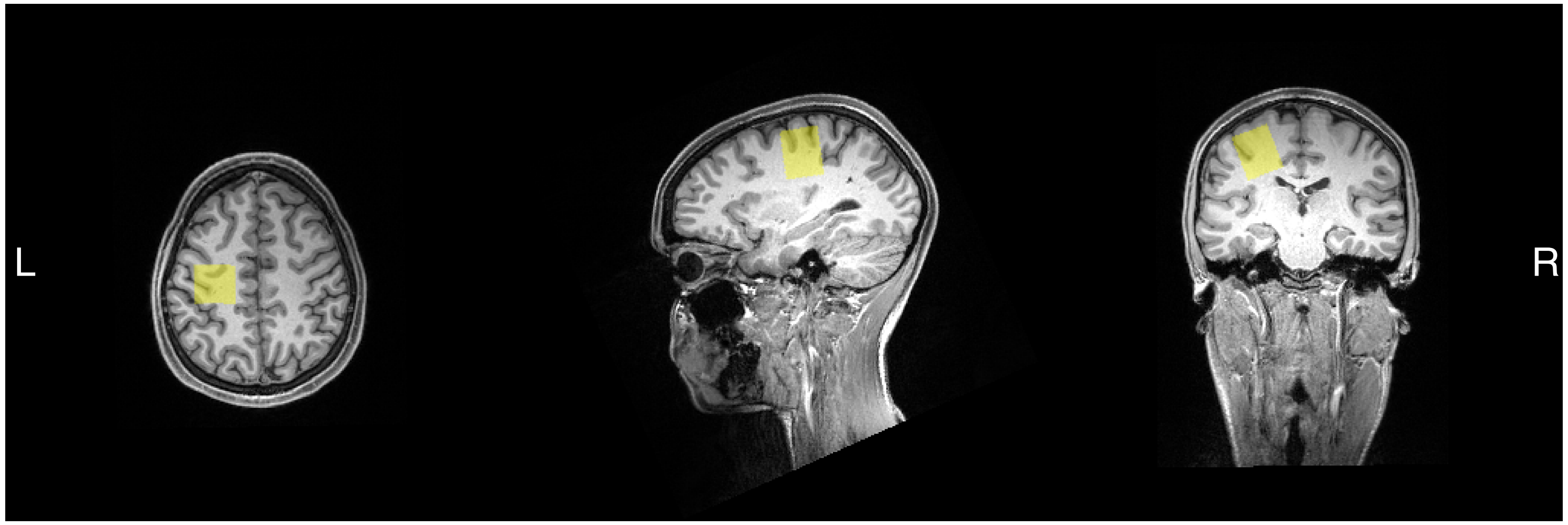
120 spectra x 2 (On & Off) (edited analysis): TA = 8’27” x 2 voxels

Reactivation of the sensory-motor loop: excitation/inhibition balance

→Glx (Glutamate + Glutamine) & GABA

Inhibition project: Motor Inhibition (Go-NoGo / Forced Choice)

Left - M1-S1 (hand)
25 x 25 x 30 mm3



128 simple spectra (non-edited analysis): TA = 4’26”

excitation → Glx (Glutamate + Glutamine)

120 spectra x 2 (On & Off) (edited analysis): TA = 8’27”

inhibition → GABA