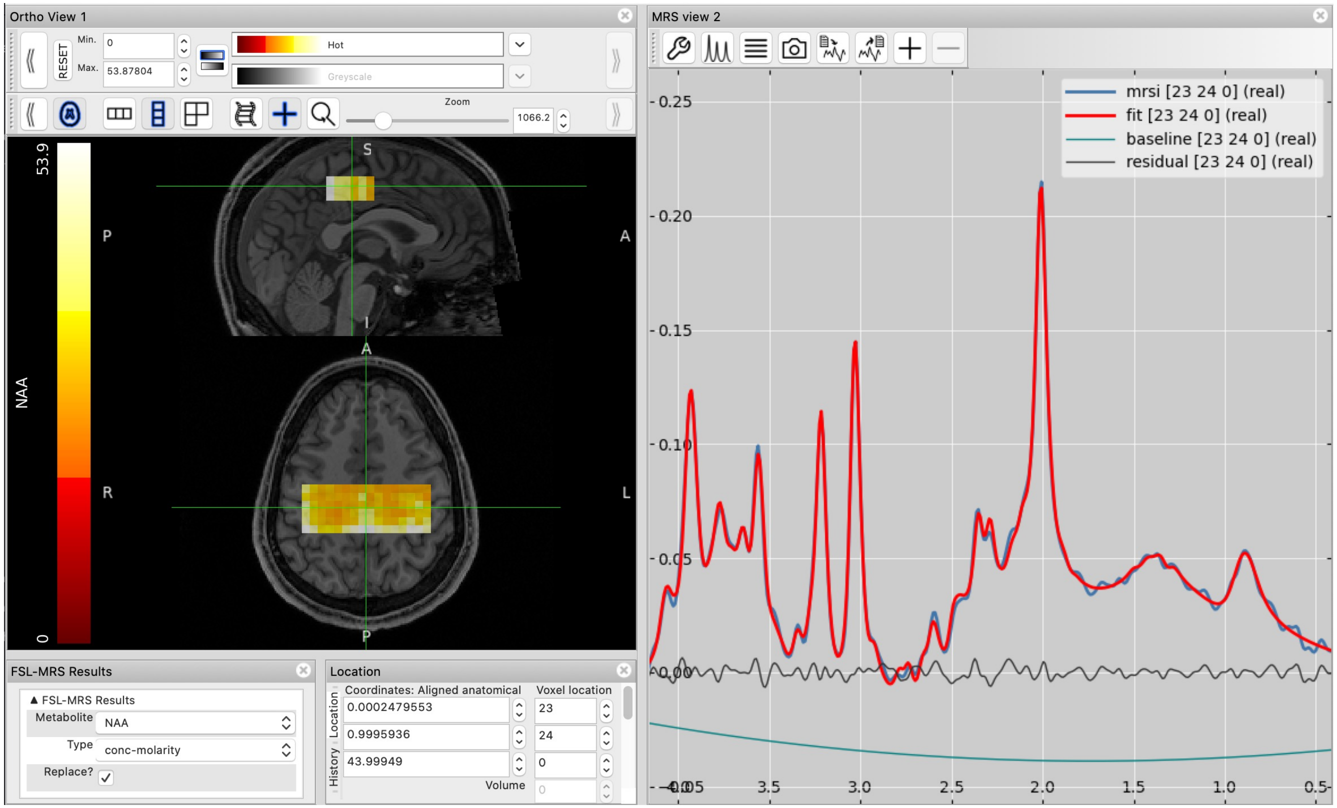
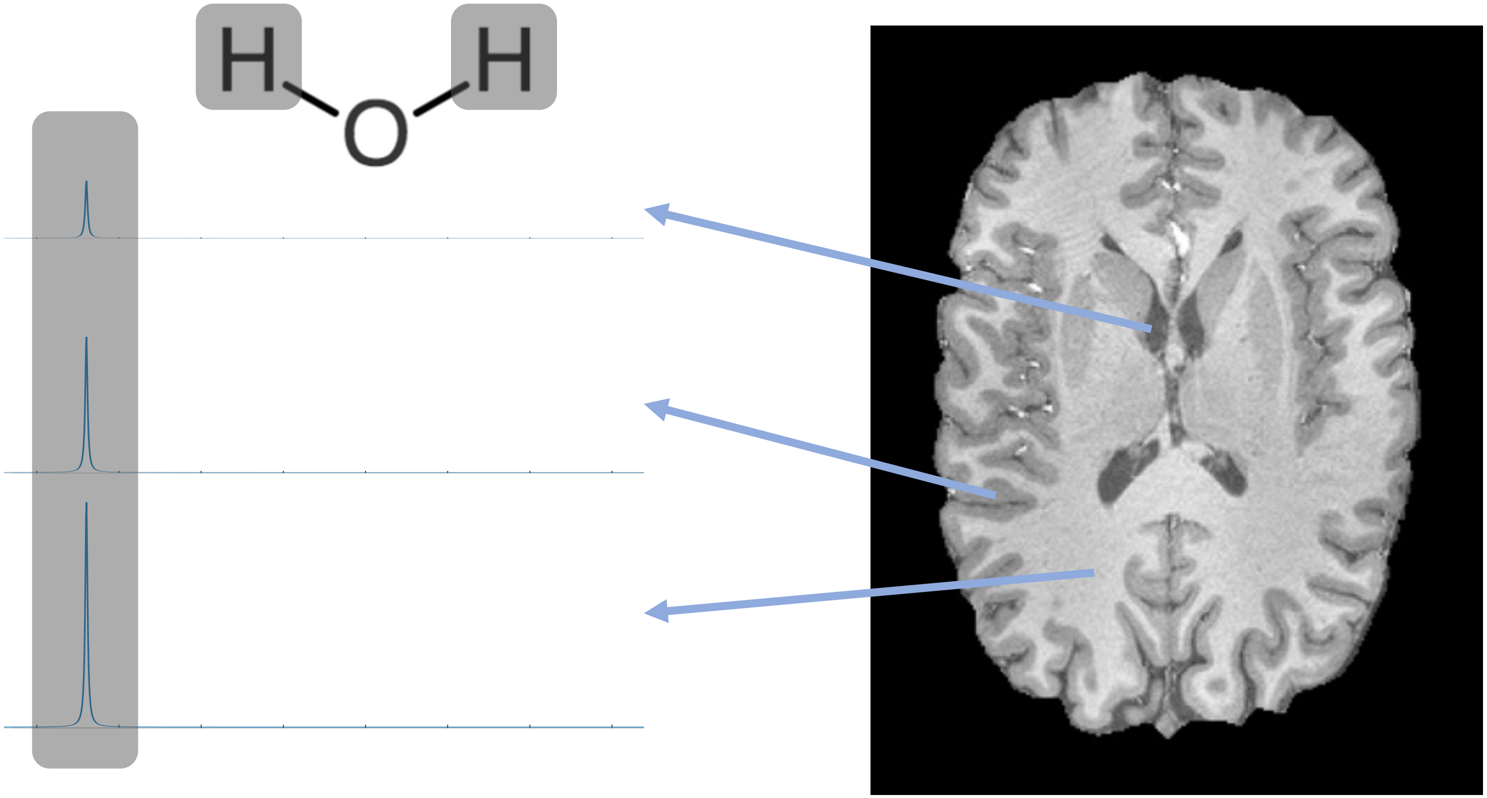
FSL-MRS – Tools for Magnetic Resonance Spectroscopy



I. Introduction to MRS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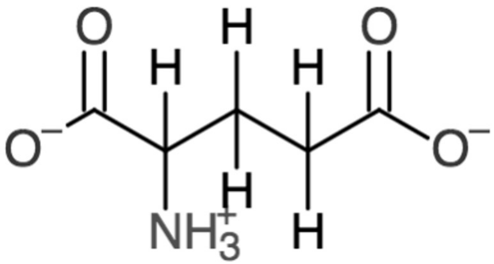
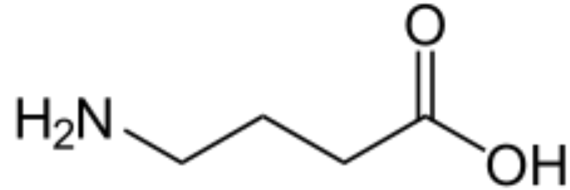
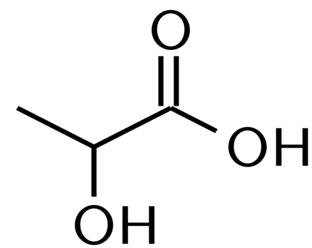


Glutamate

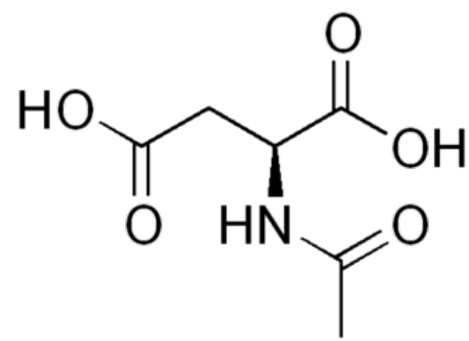
GABA

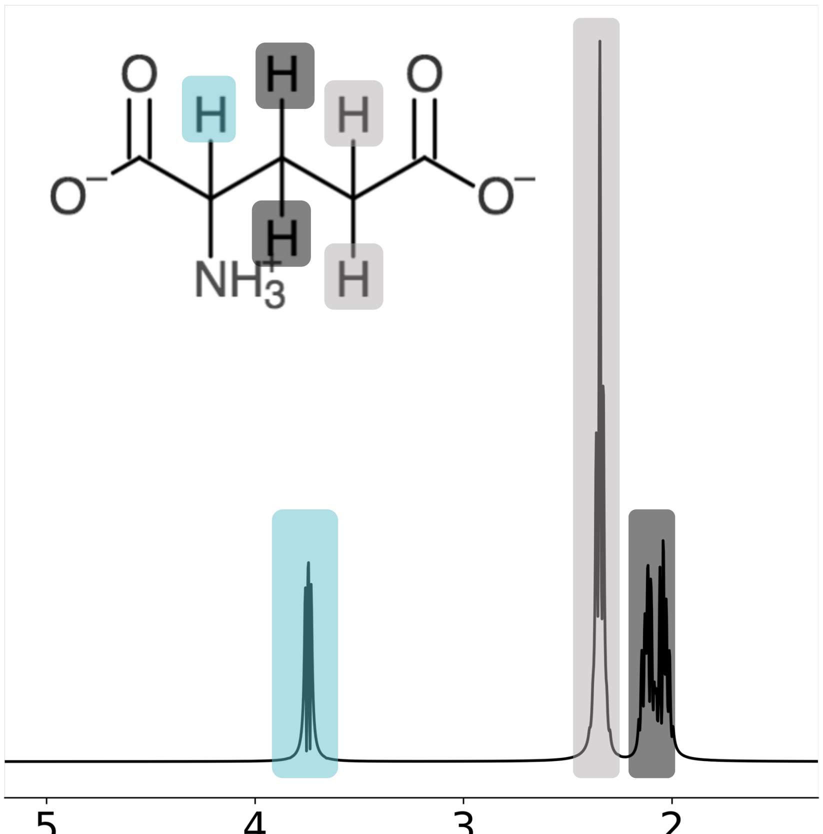


Lactate

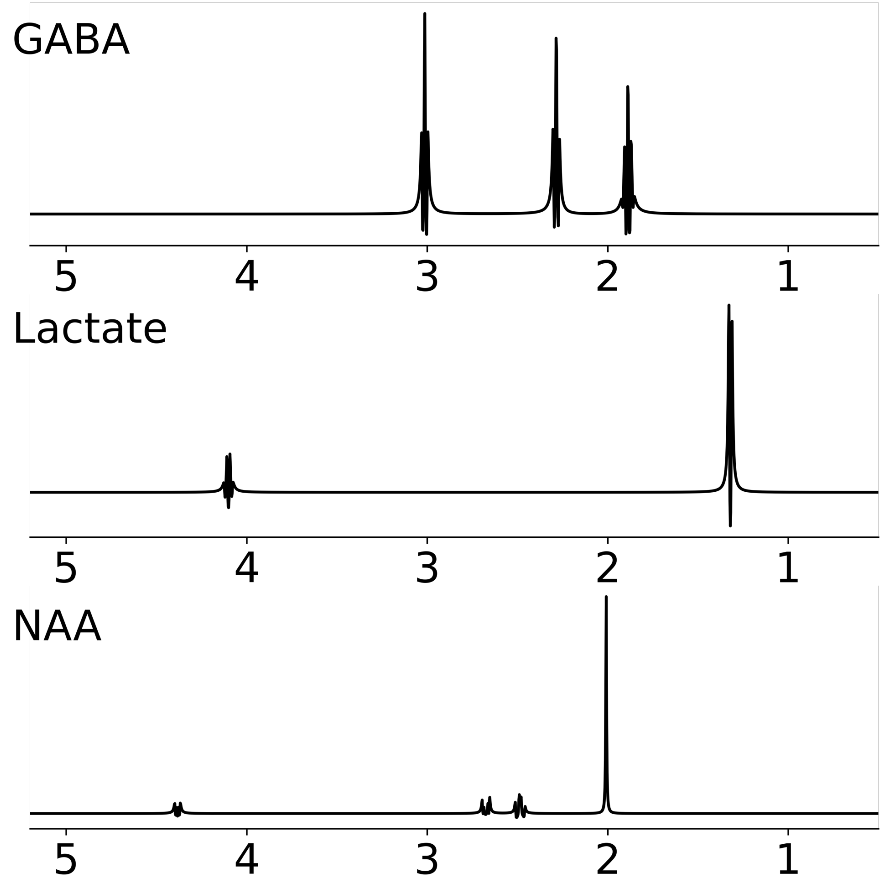


NAA

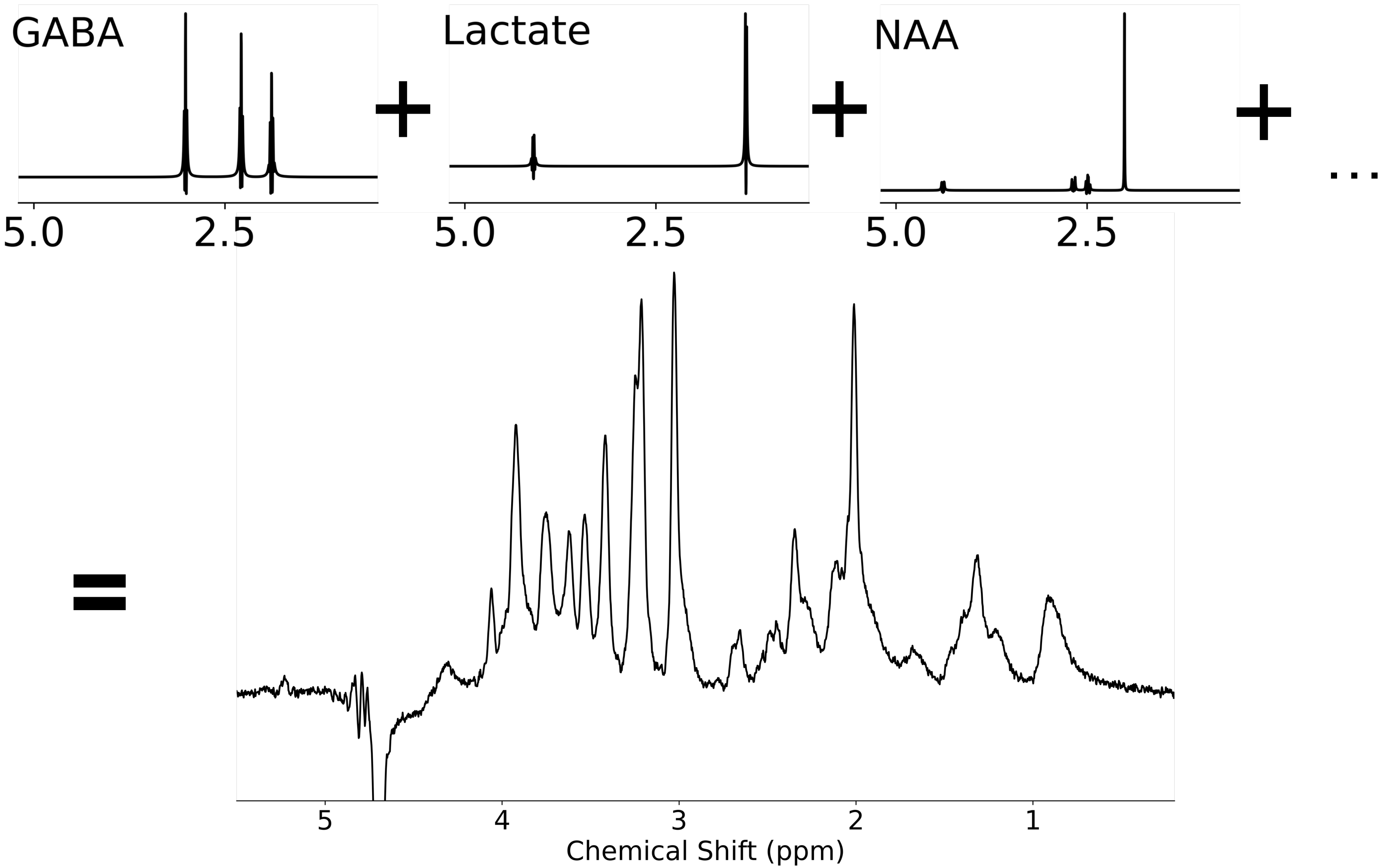


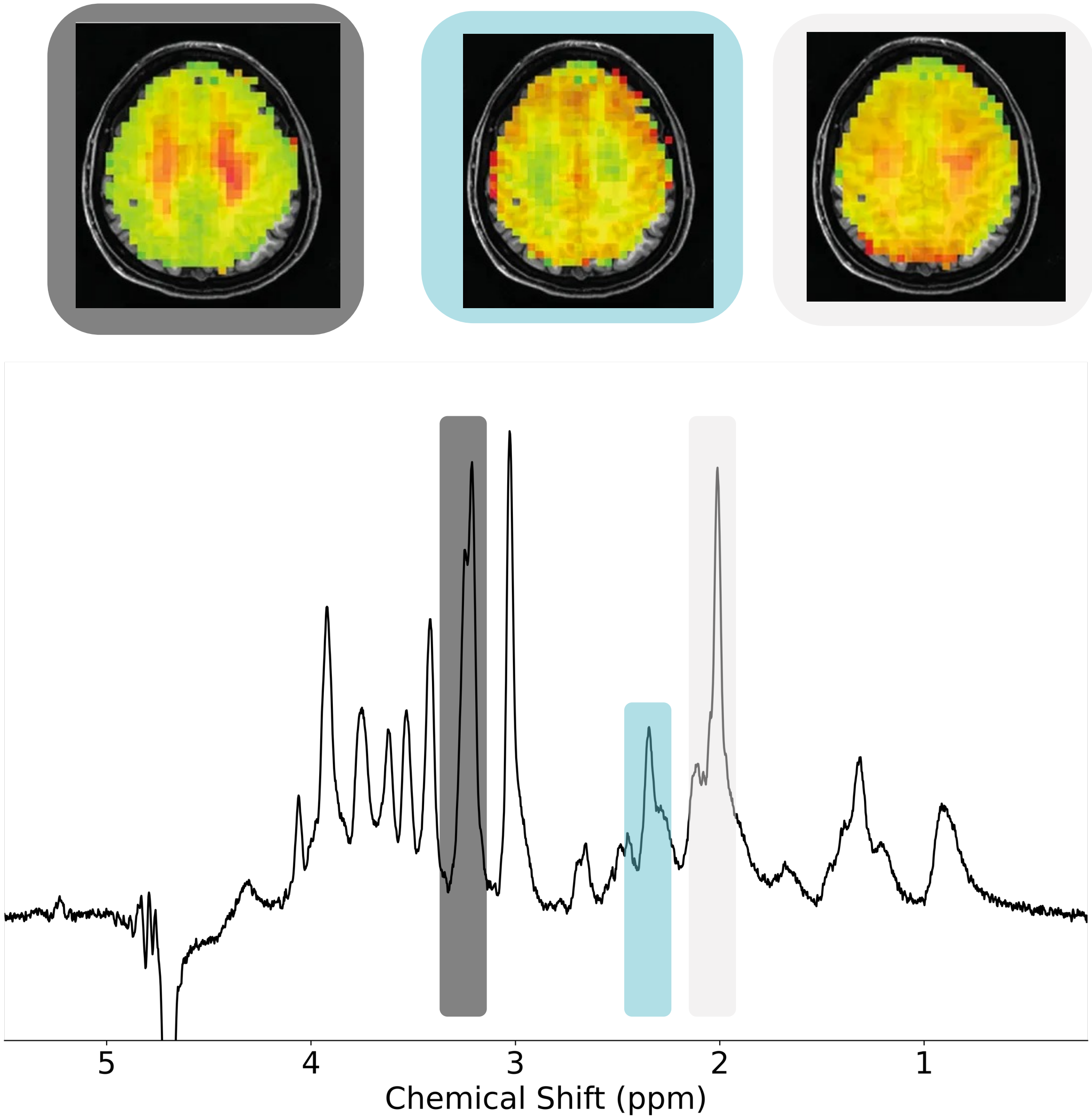


Glutamate



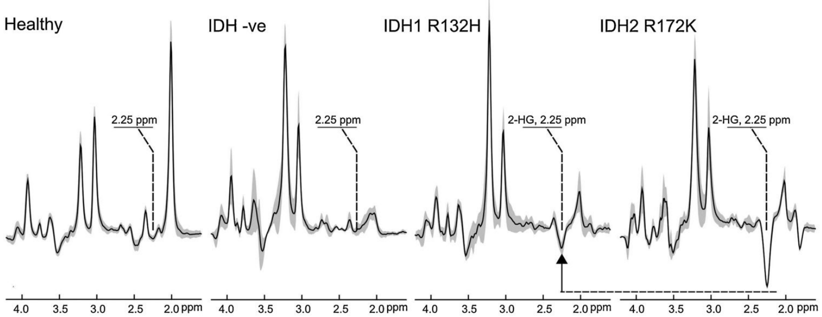
+ 15 other metabolite “fingerprints”


GABA
Lactate
NAA
5.0
2.5
5.0
2.5
5.0
2.5
...
5
4
3
2
1
Chemical Shift (ppm)


5
4
3
2
1
Chemical Shift (ppm)

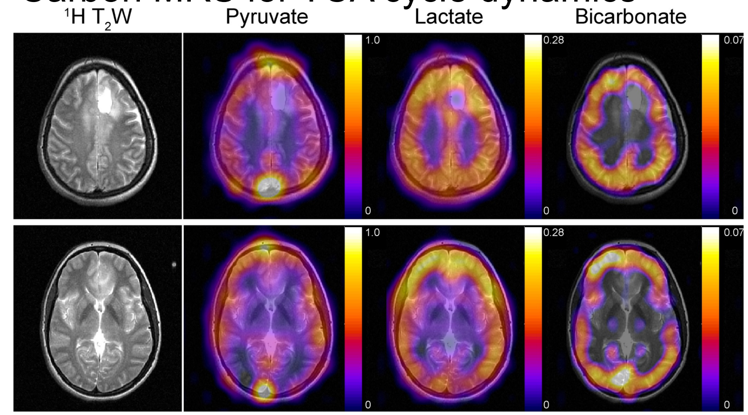
Many uses of MRS

Proton MRS for metabolic profile



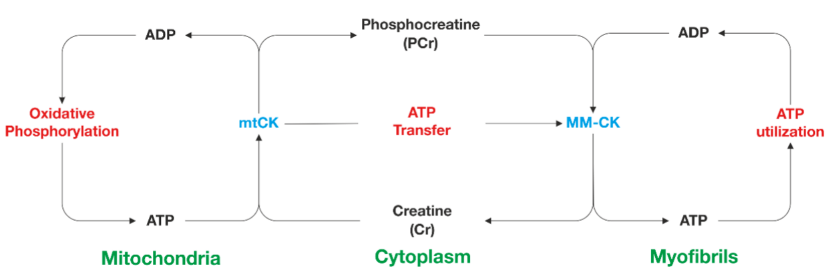
Emir et al. Cancer Res. 2016 Jan 1;76(1):43-9.

Carbon MRS for TCA cycle dynamics

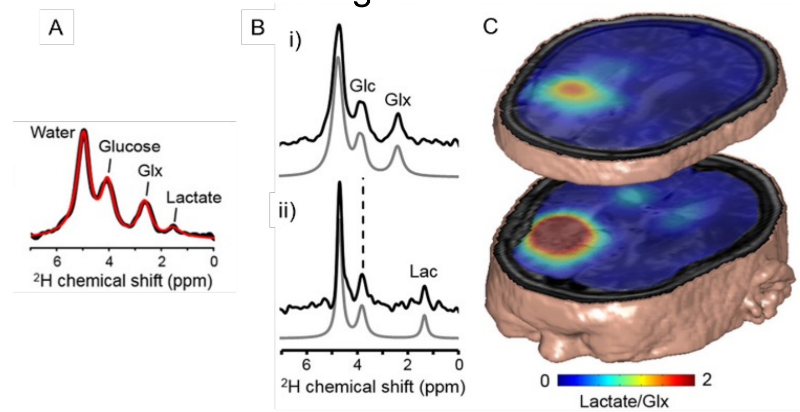


Gordon et al MRM 81(4) 2702-2709

Phosphorus MRS for oxidative phosphorylation



Deuterium MRS for glucose metabolism



Henk M. De Feyter et al. Sci Adv 2018;4:eaat7314

Visible Neurochemicals

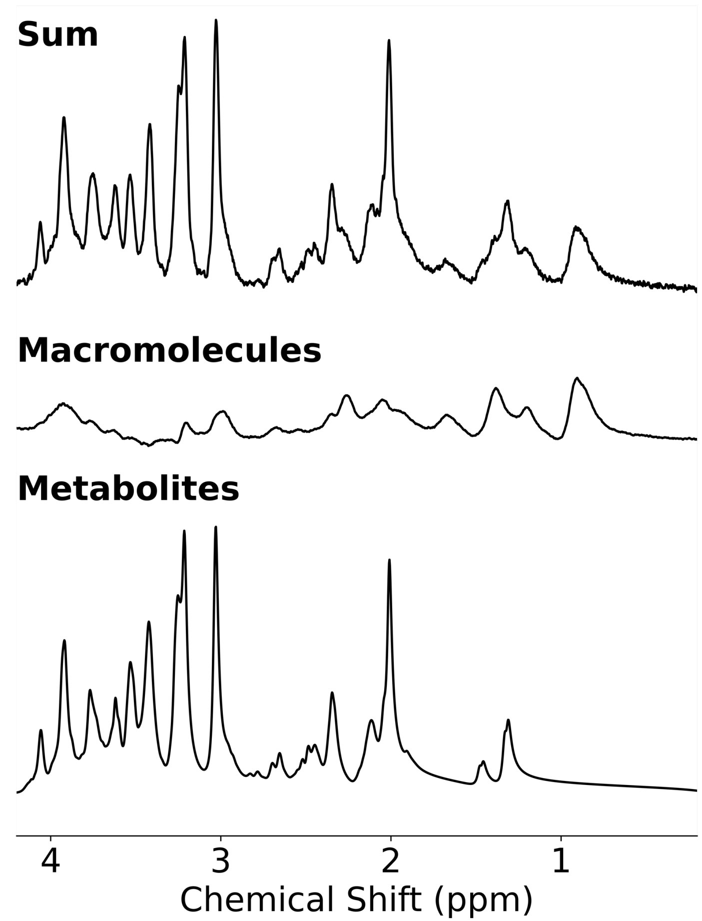
- Water ~10000 times larger
- Lipids – artefactual or pathological

✓ Metabolites with >1 mM concentration

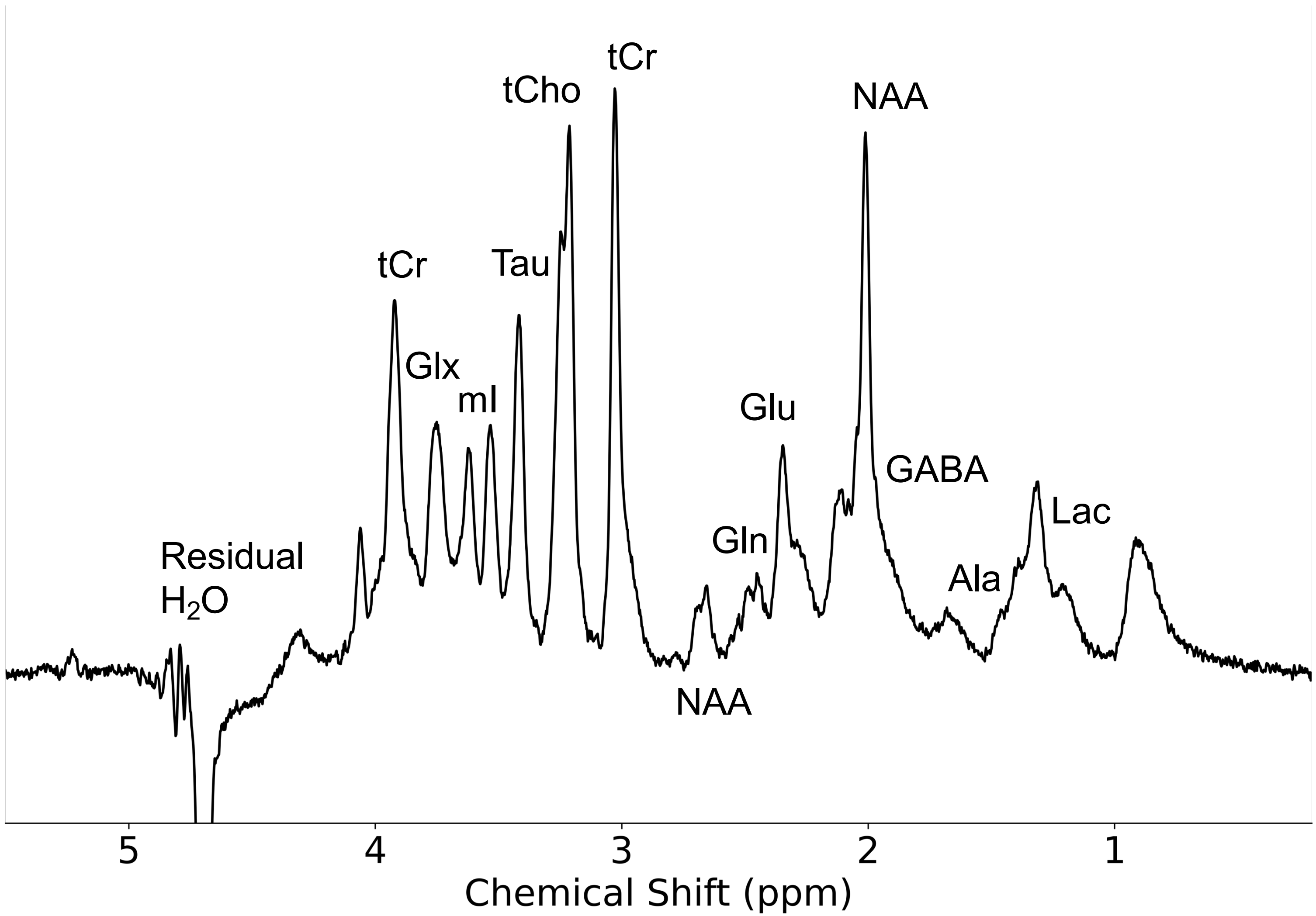
✓ "Macromolecules": amino acid residues & peptides

x Solids, proteins, bound substrates.

x Low concentration (<1 mM)



The in vivo spectrum



Metabolites

***N*-acetylaspartate (NAA)**
- **Present only in neurons (not glia)**
- **Biomarker for neuronal integrity**

Lactate (Lac)
- **Indicates anaerobic glycolysis**
- **Complex, dynamic metabolism.**
- **Tricky to monitor by MRS**

Total creatine (tCr: Cr + PCr)
- **Energy buffering**
- **Often a static reference, except in metabolic disorders**

Myo-inositol (mIns)
- **(Disputed) marker for gliosis**
- **Varied physiological uses and variations in pathology.**

Total Choline (tCho: PCho + GPC)
- **Marker of cellular proliferation, membrane turnover, inflammation.**

Glutamate (Glu) + GABA
- **Primary neurotransmitters**

Glutathione (GSH)
- **Oxidative stress in astrocytes**

See

1) Rae CD. A Guide to the Metabolic Pathways and Function of Metabolites Observed in Human Brain 1H Magnetic Resonance Spectra. Neurochem Res 2014;39:1–36

2) De Graaf RA. In Vivo NMR Spectroscopy: Principles and Techniques. Chapter 2

Equipment

✓ Same scanner

✓ Same coil hardware

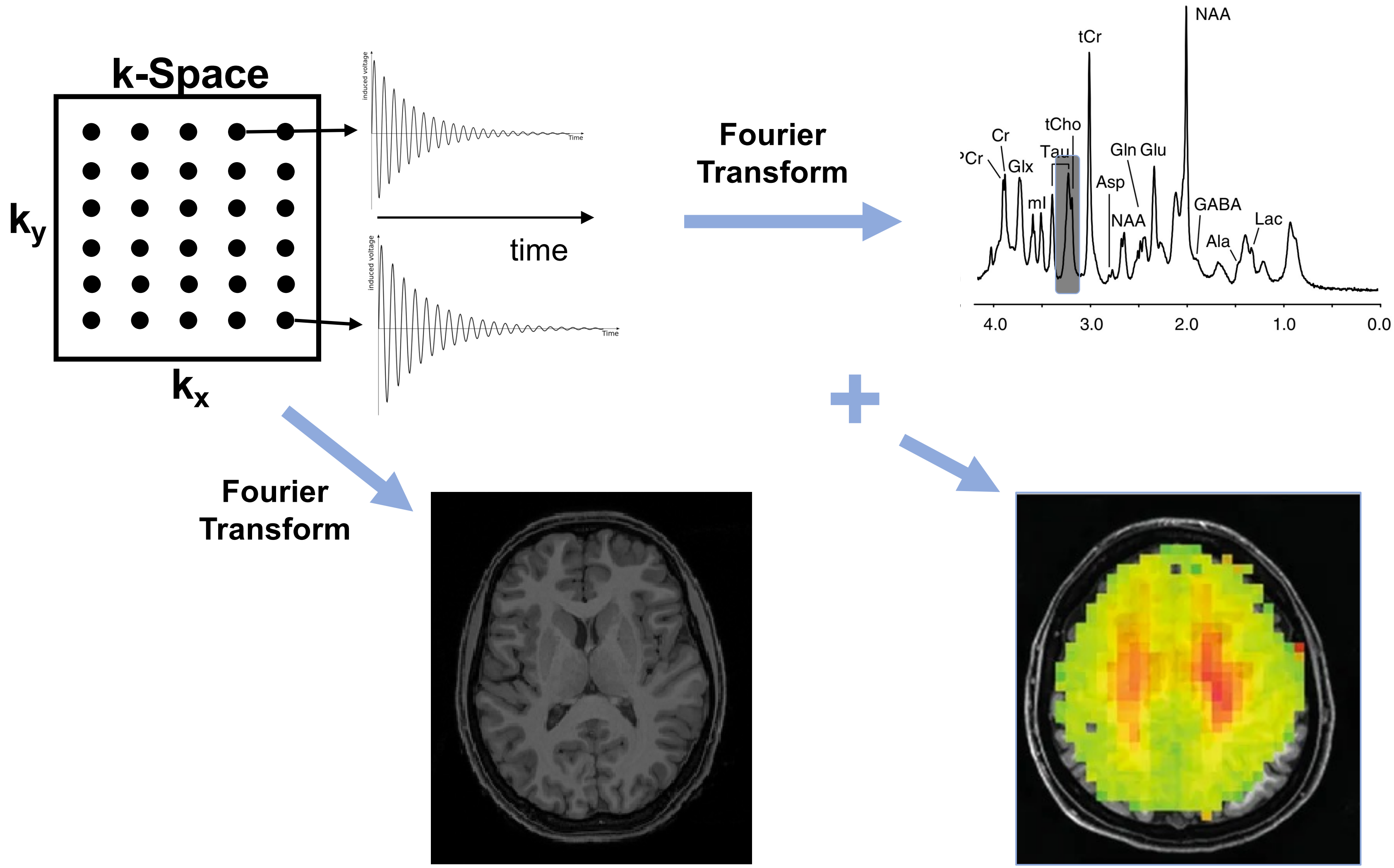
GRE
FLAIR
DWI
SWI
T1w

PRESS
STEAM
sLASER
CSI

✗ Different sequences

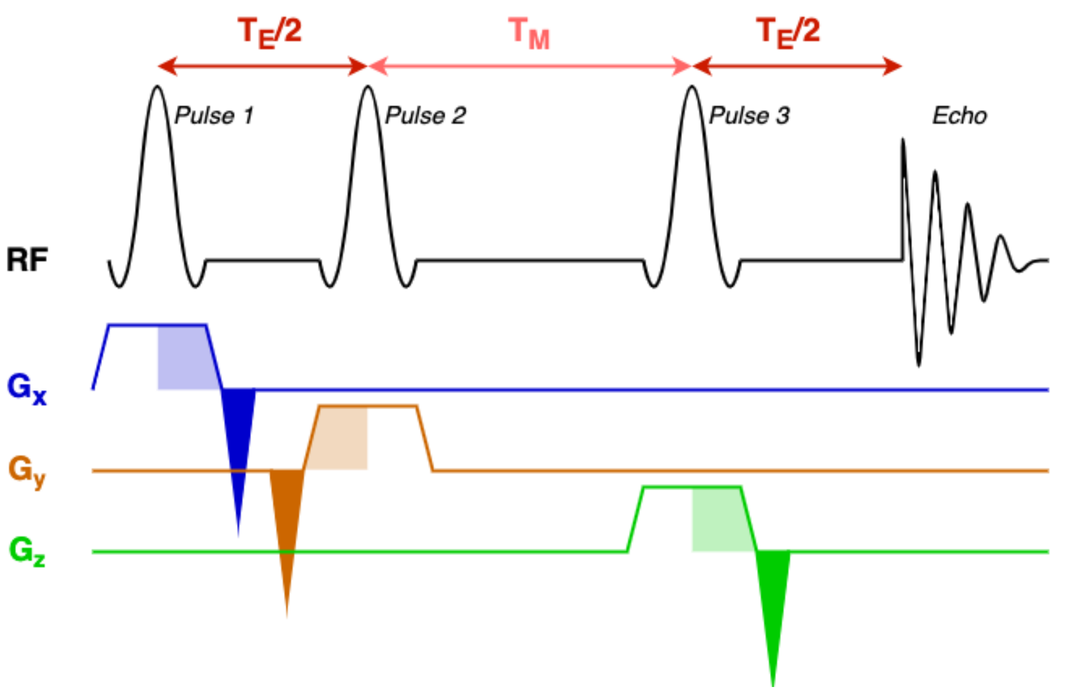
✗ Additional training

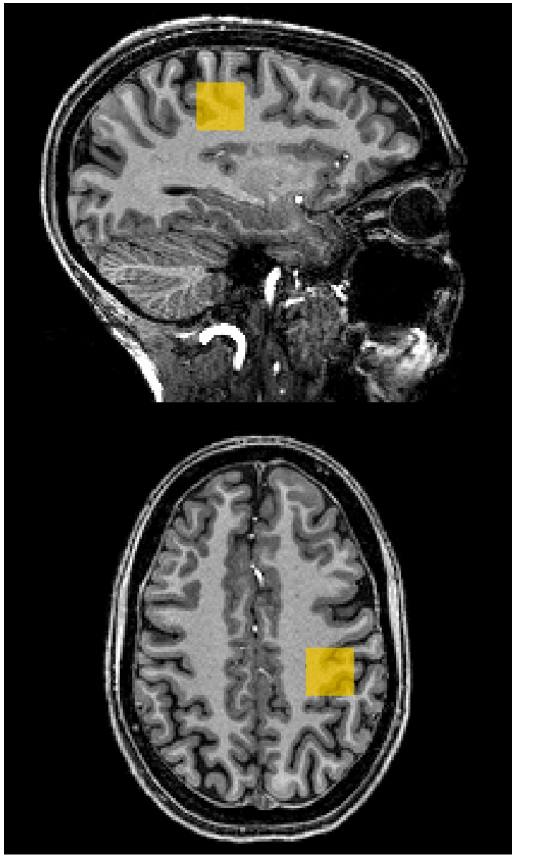
Spectroscopy pulse sequences



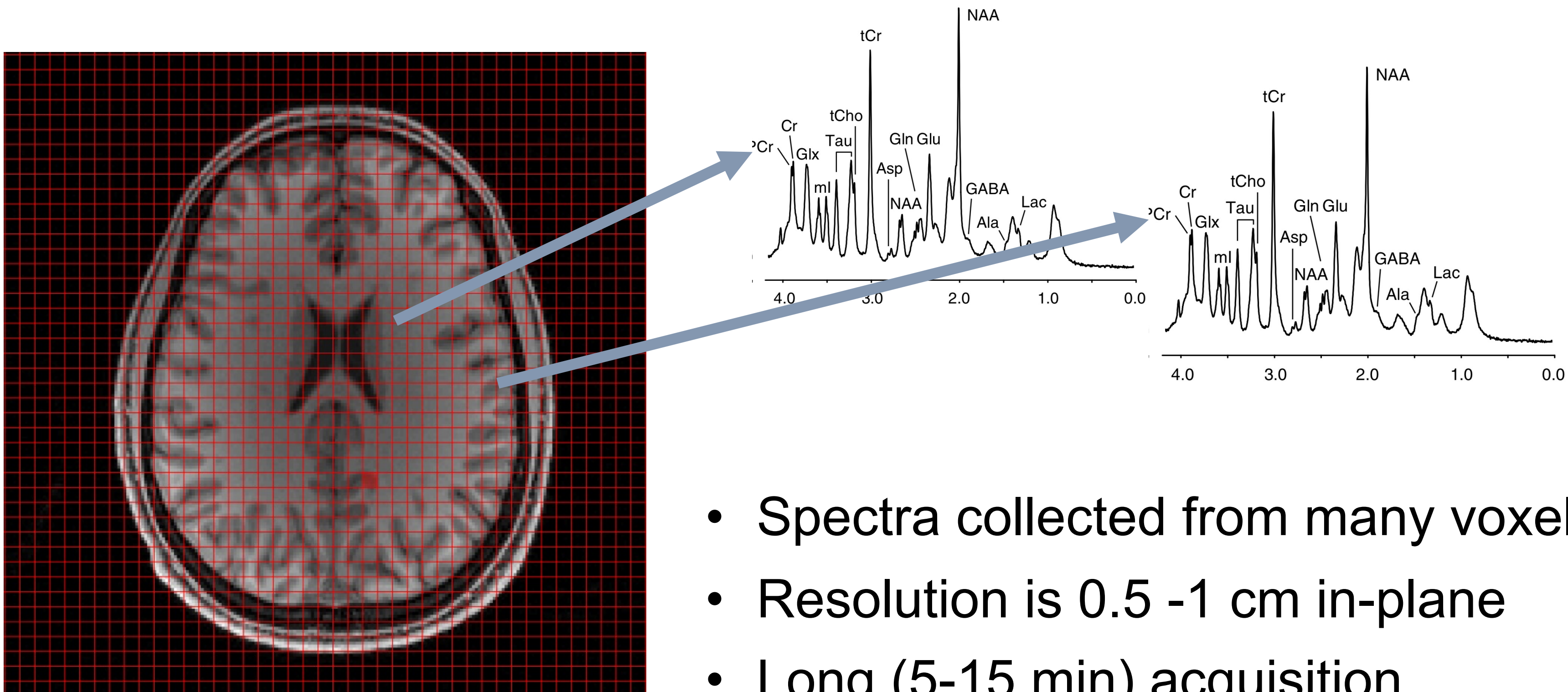
Single Voxel Spectroscopy (SVS)

- Single spectrum acquired from one volume
- 2-3 cm isotropic size, ~5 min acquisition
- Examples: PRESS, **STEAM**, Semi-LASER
- Three intersecting slice selective pulses.





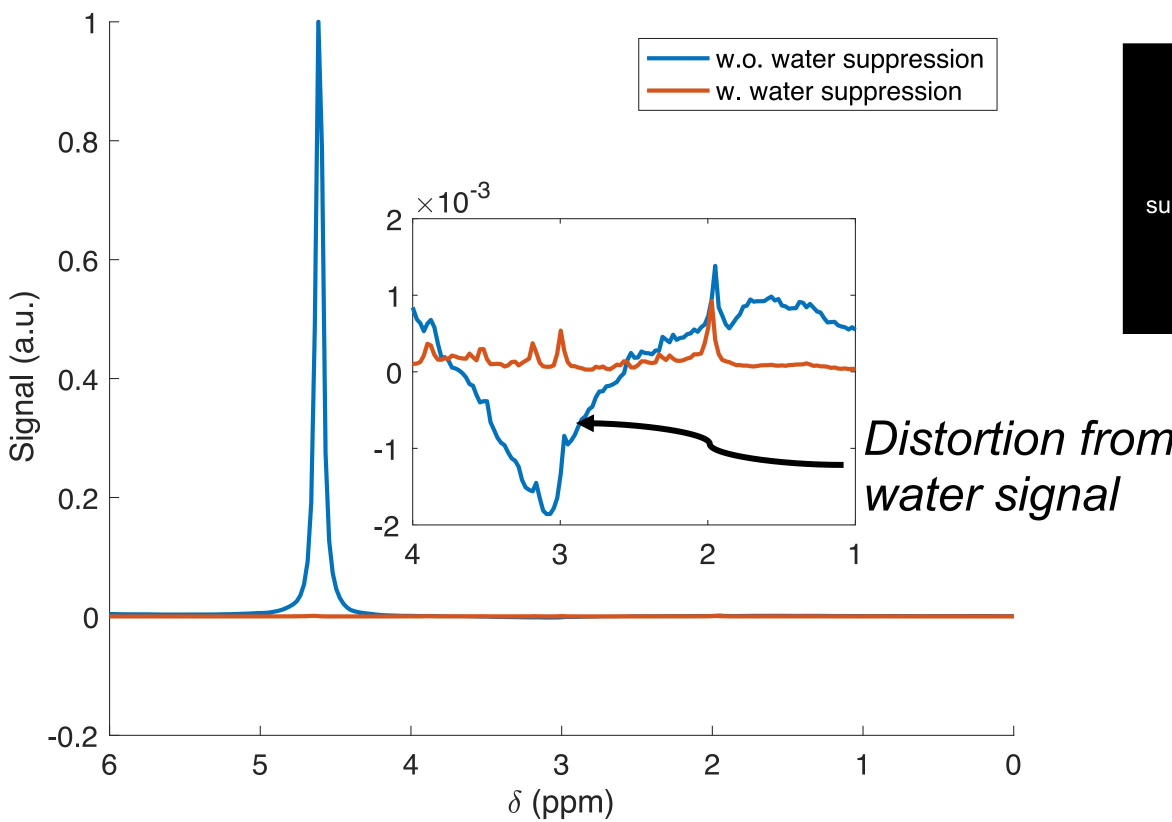
MR Spectroscopic Imaging (MRSI)

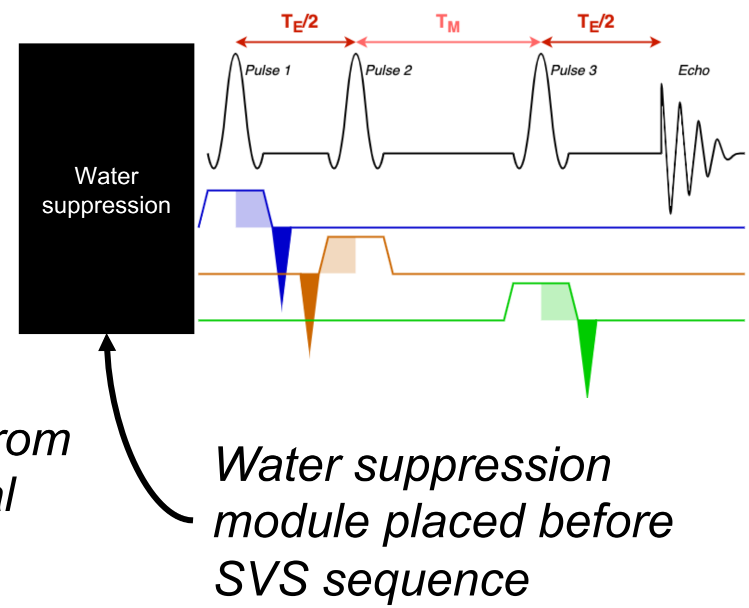


- Spectra collected from many voxels
- Resolution is 0.5 -1 cm in-plane
- Long (5-15 min) acquisition
- Examples: CSI, EPSI, CRT

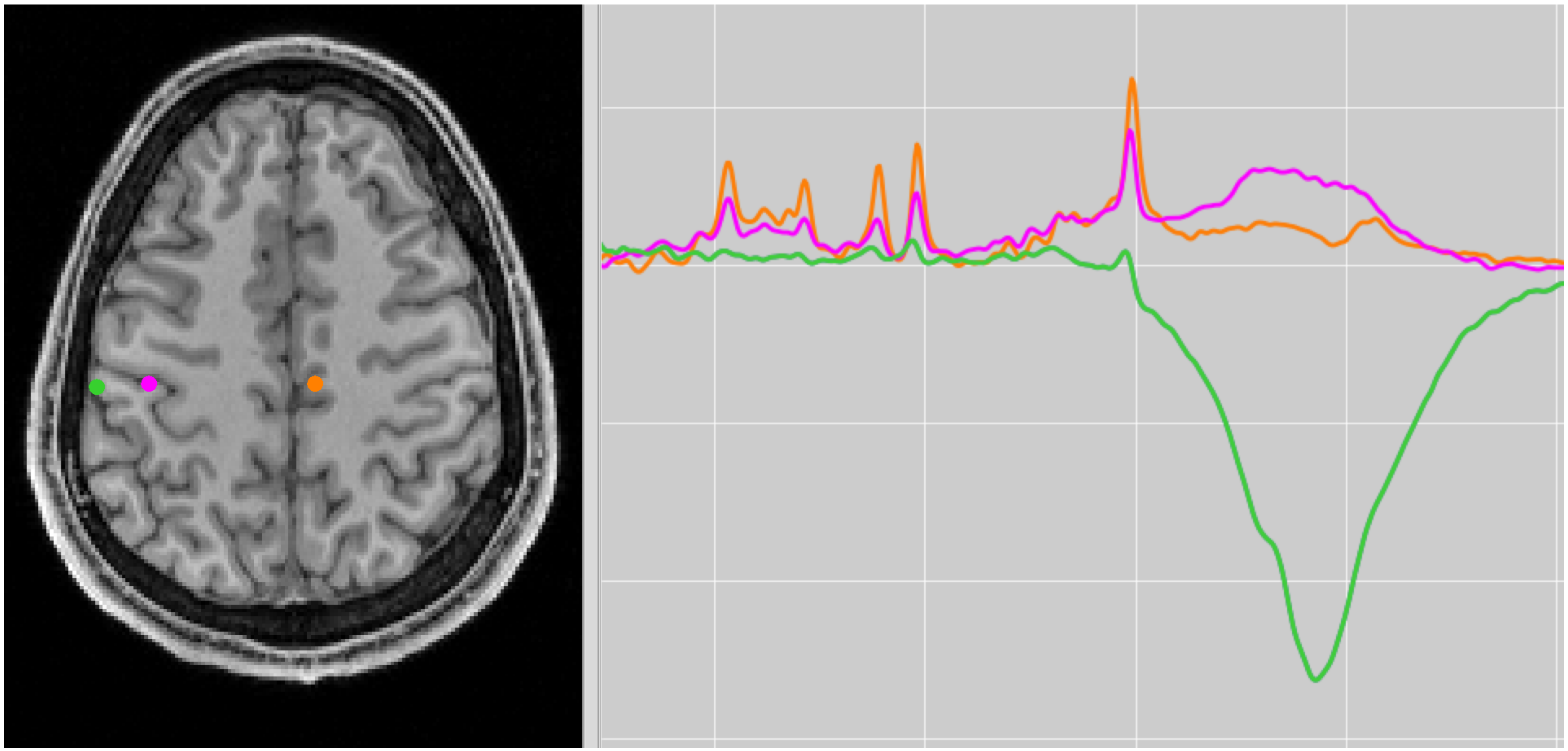
Water suppression

- Water signal >> metabolite signal
- Selective suppression used to remove water
- Reduces baseline distortion



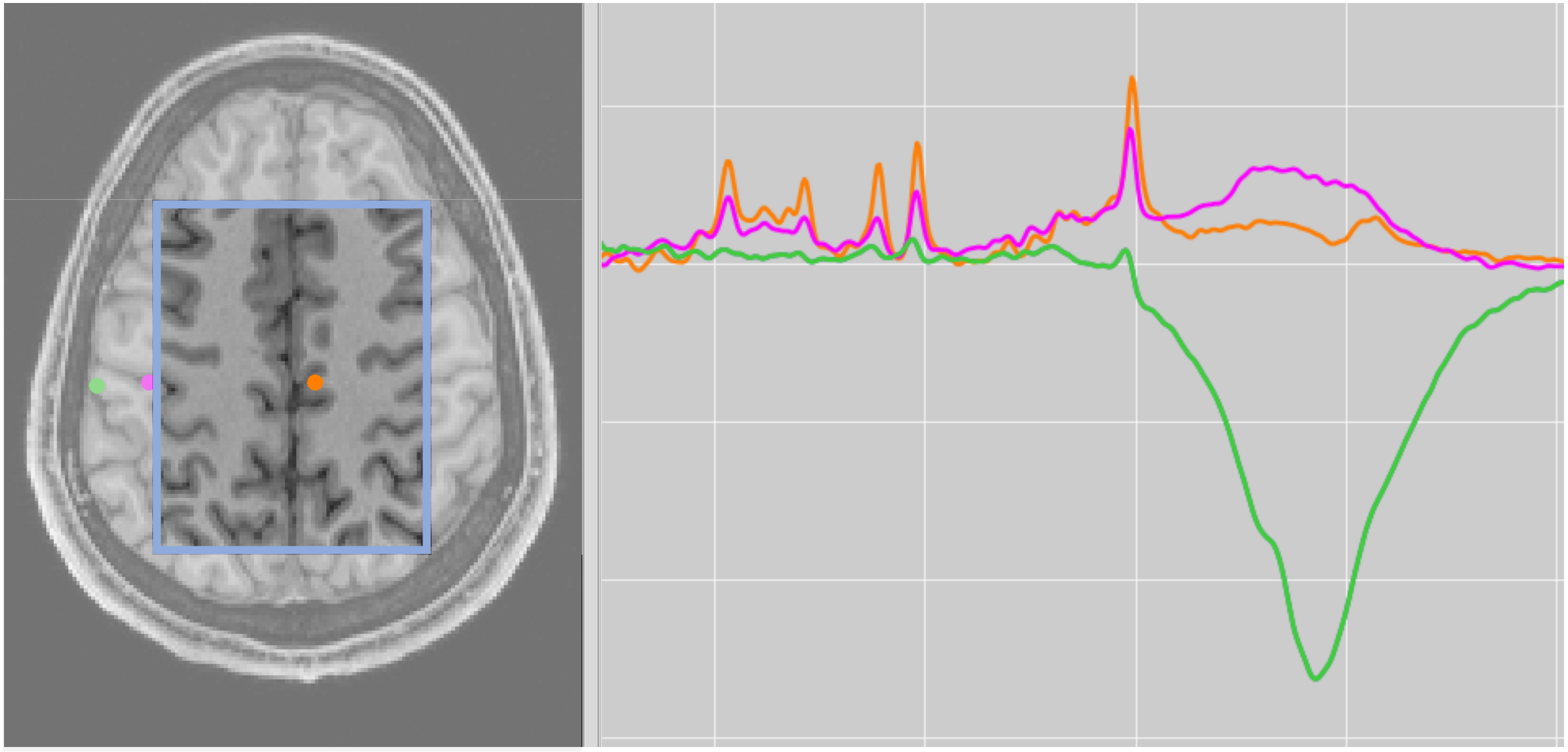


Outer volume suppression



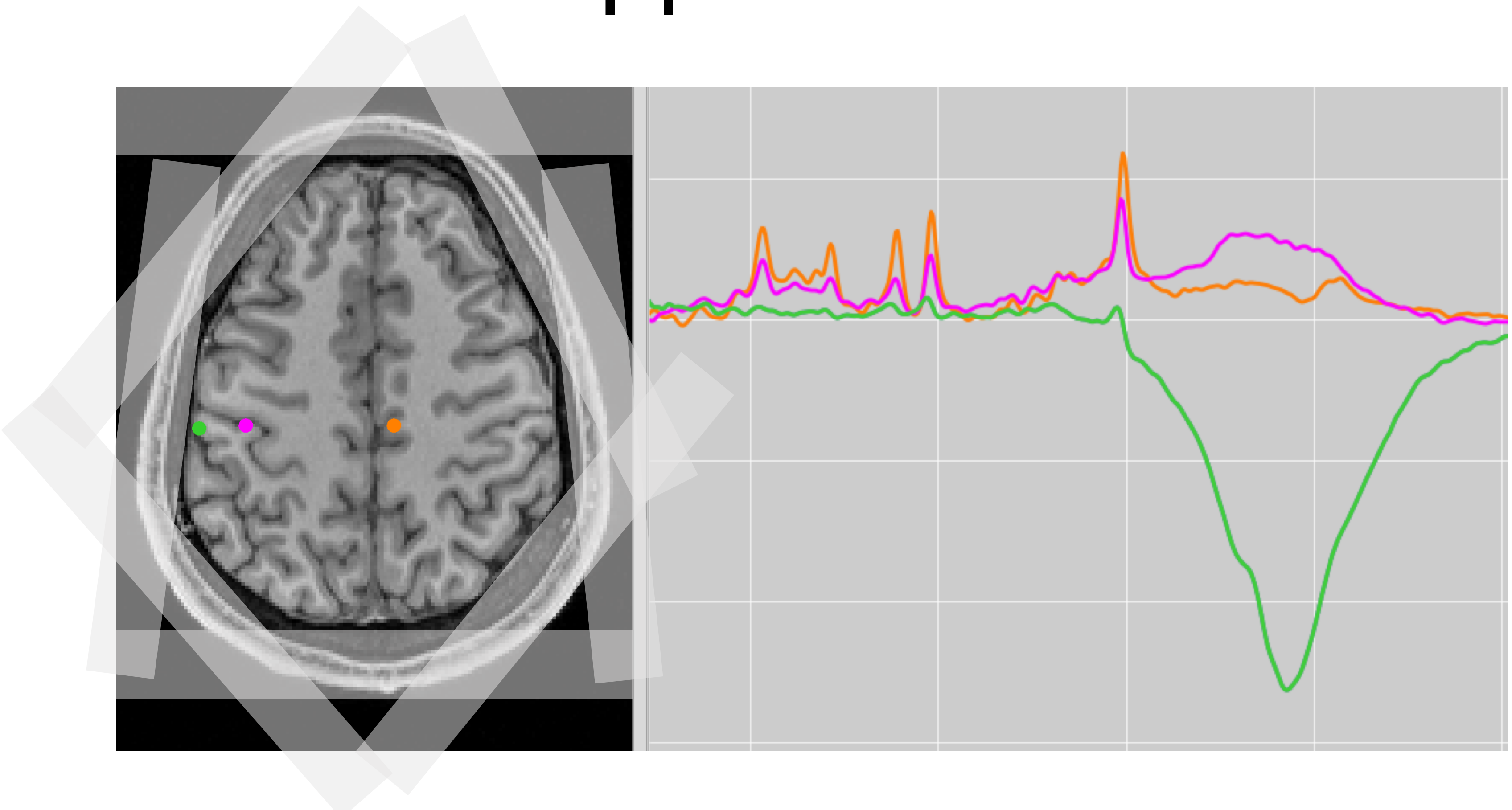
High concentration lipids present in dura and skull.

Inner volume selection



Use SVS localisation to only excite signal from brain tissue.

Outer volume suppression

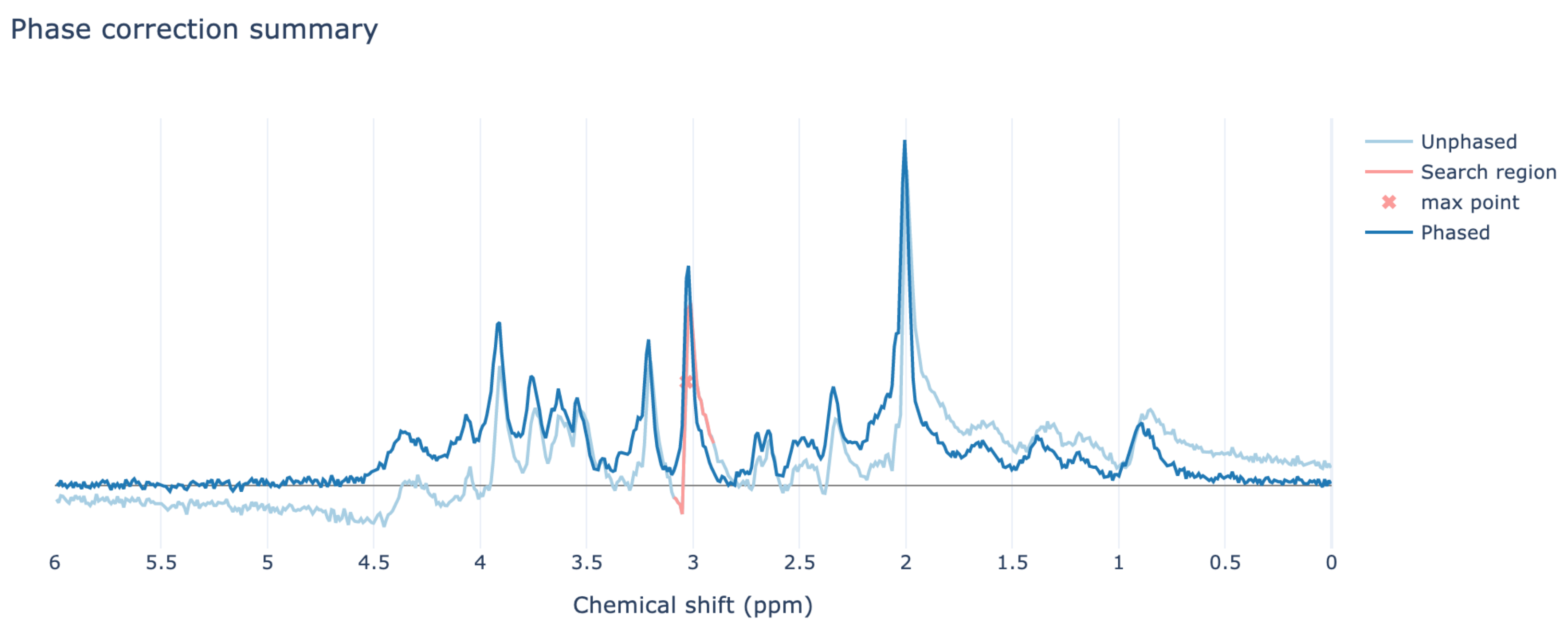


Use saturation bands to suppress signal outside brain.

A quick pause for questions

Up next: Pre-processing

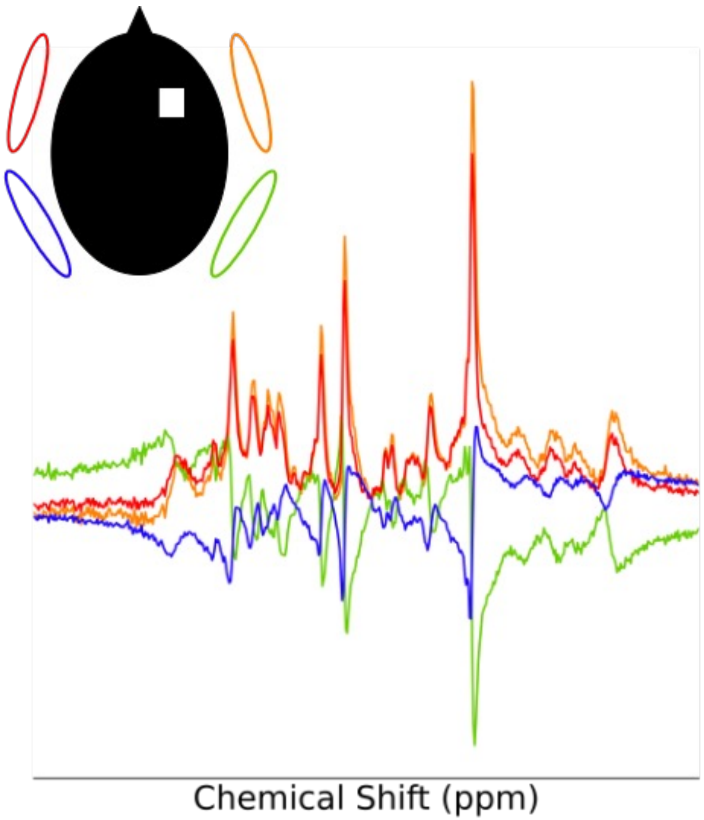
FSL-MRS – Tools for Magnetic Resonance Spectroscopy



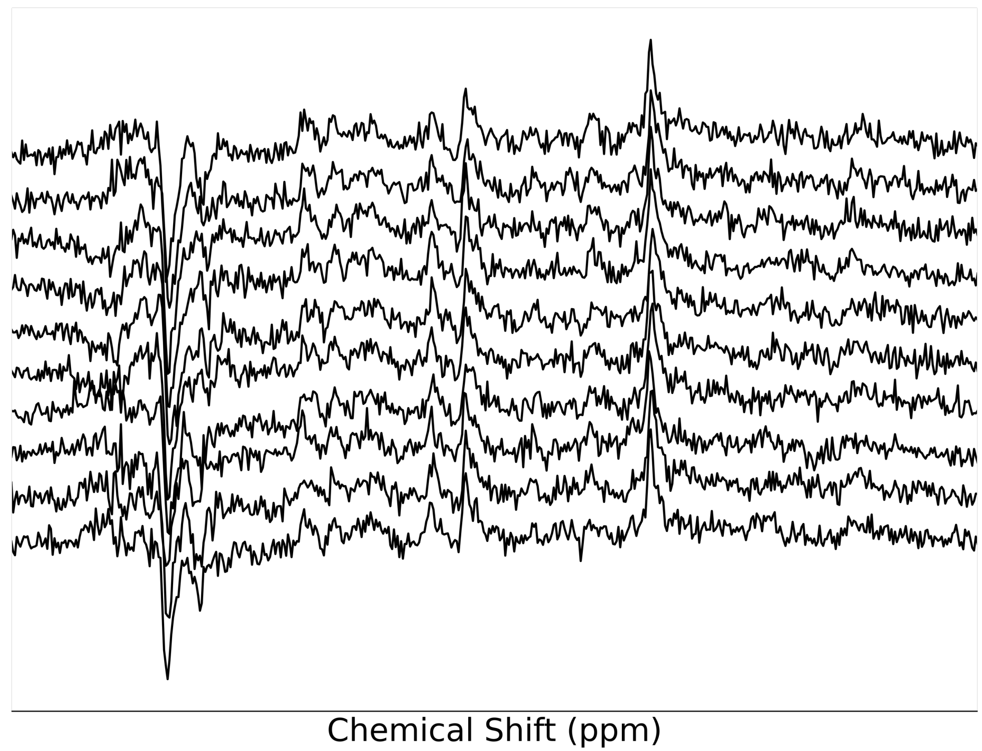
II. MRS pre-processing

SVS: before pre-processing

Uncombined coils

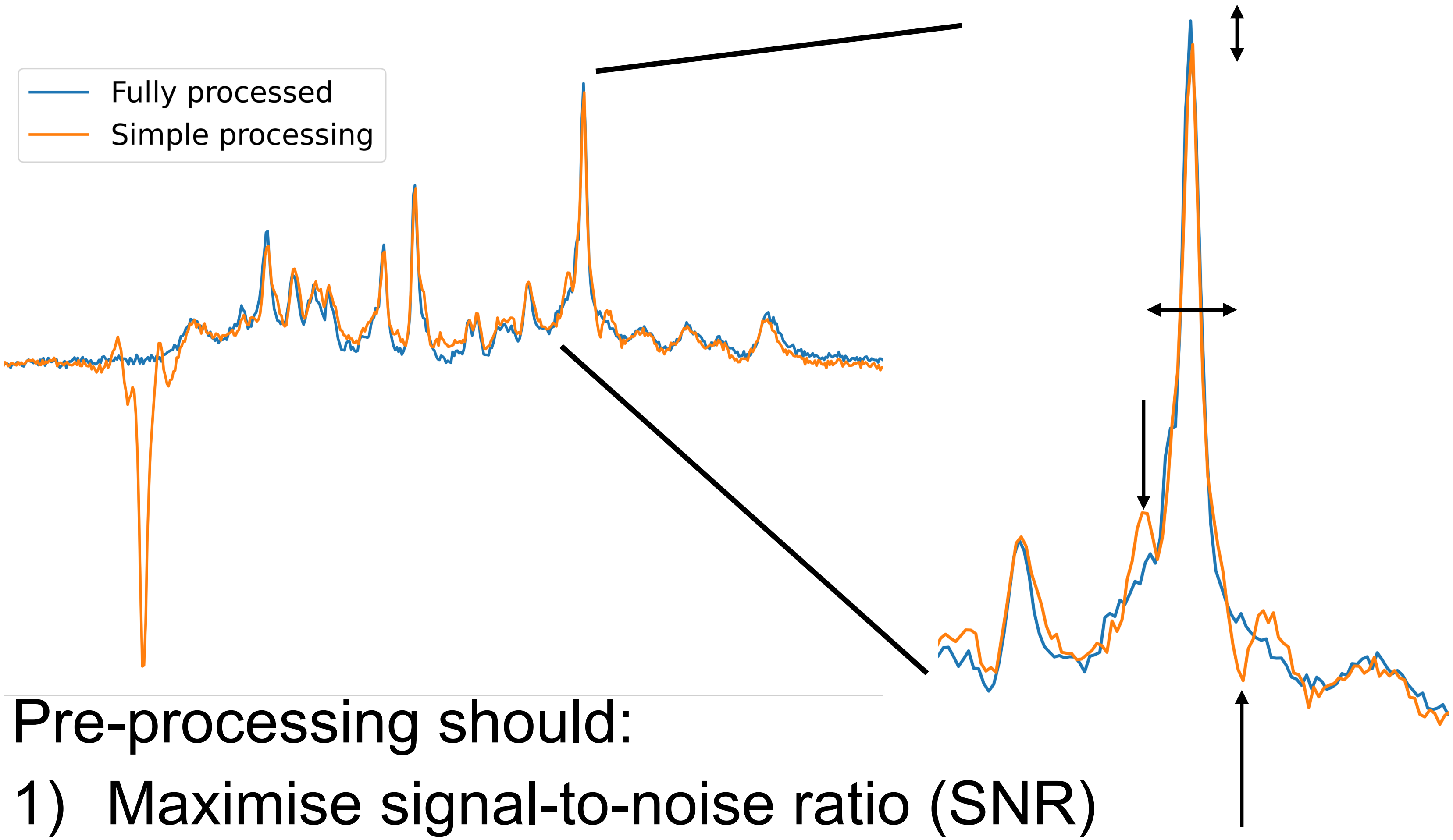


Un-averaged repeats



Data shape - $N_{\text{Time Points}} \times N_{\text{Averages}} \times N_{\text{Coils}}$

SVS: after pre-processing



Pre-processing should:

1) Maximise signal-to-noise ratio (SNR)
2) Minimise peak linewidths
3) Reduce baseline and line shape distortion

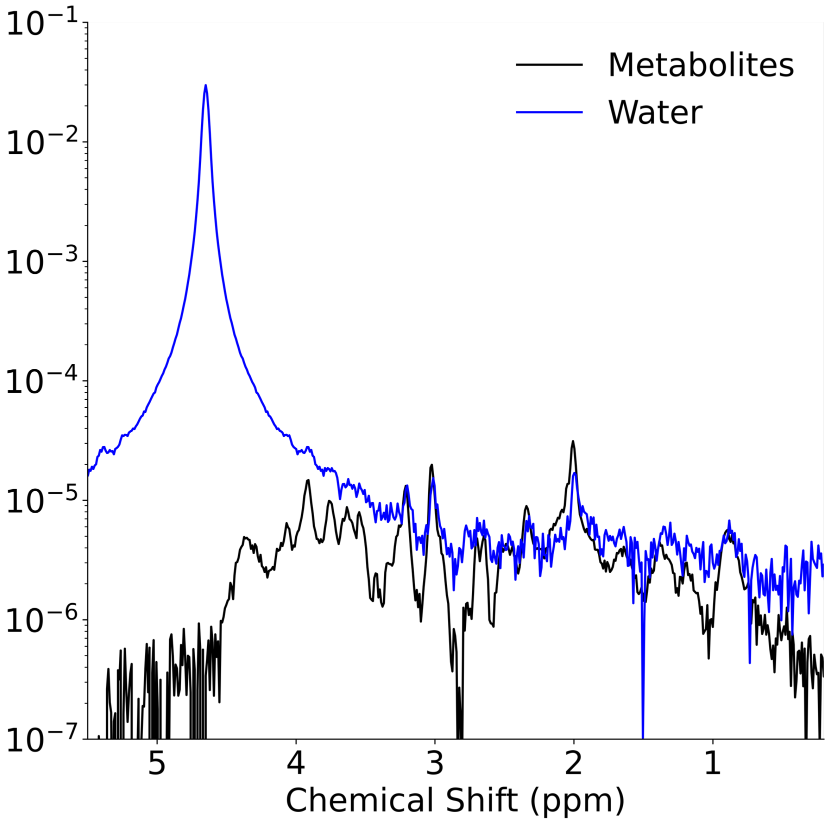
The water-reference

Very high SNR water signal experiences (almost) the same acquisition conditions.

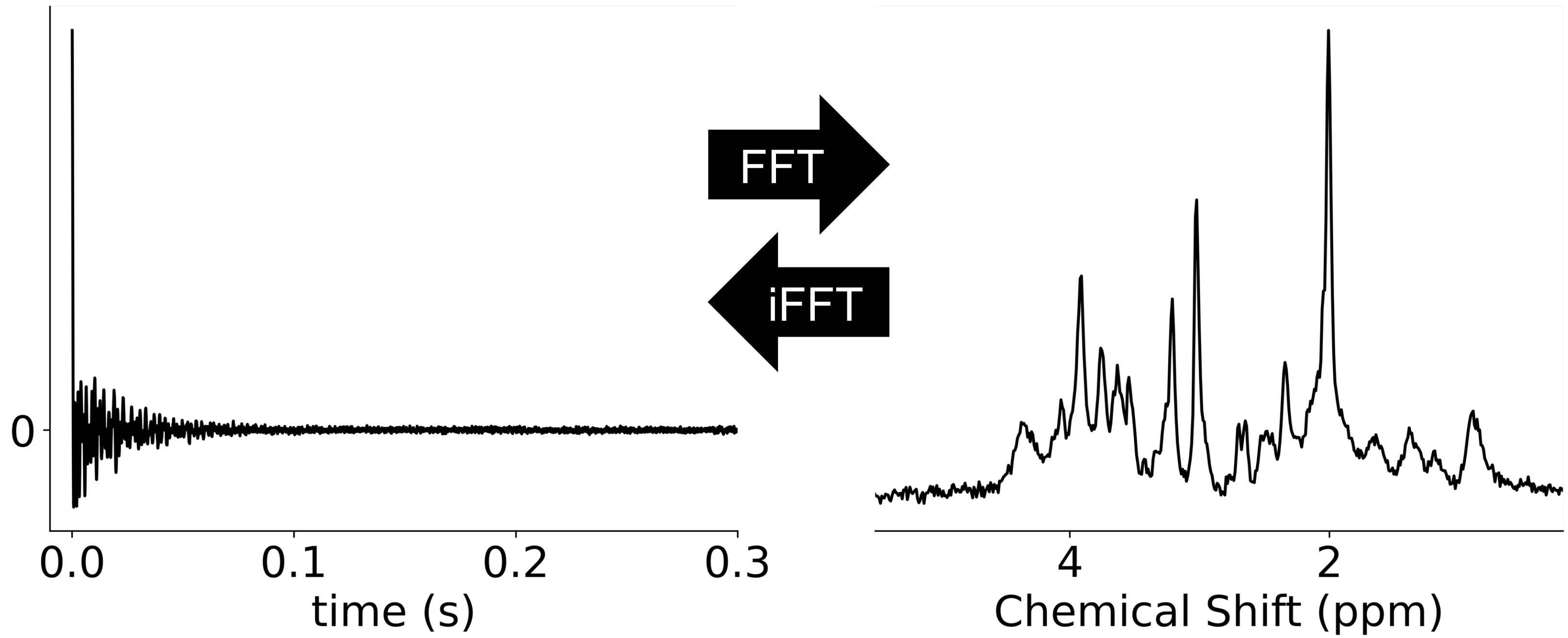
Use it for:

- coil combination,
- eddy current correction,
- (sometimes) phase and frequency correction,
- (sometimes) motion correction.

Process identically to preserve scaling

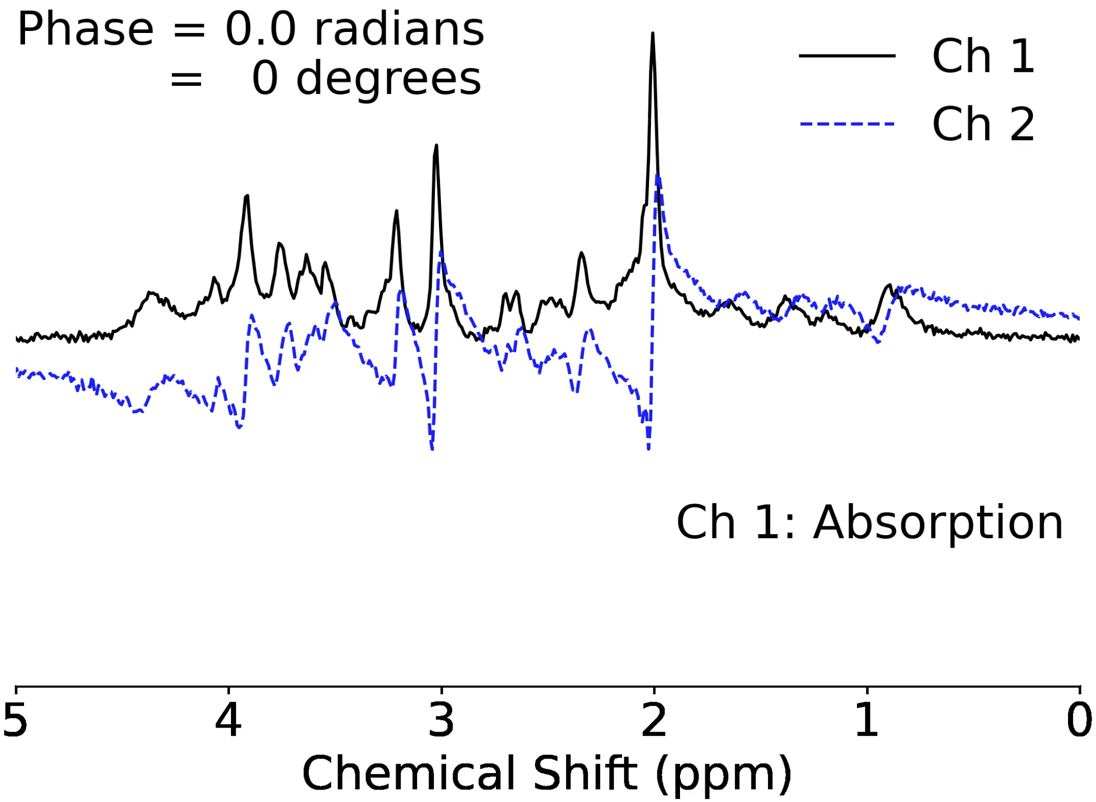


Time domain & frequency domain



Conversion between domains via (inverse) Fast Fourier Transform.

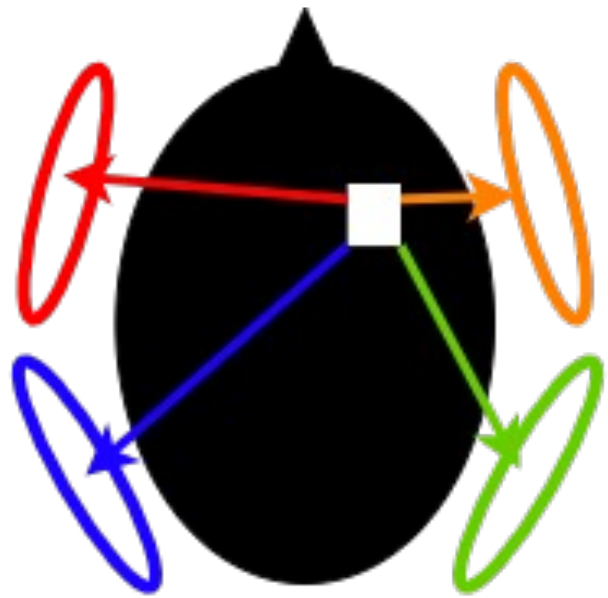
Complex MRS Data



MRS data has two channels:

- Stored as complex data,
- Quadrature relationship (90-degree phase offset).

Coil combination



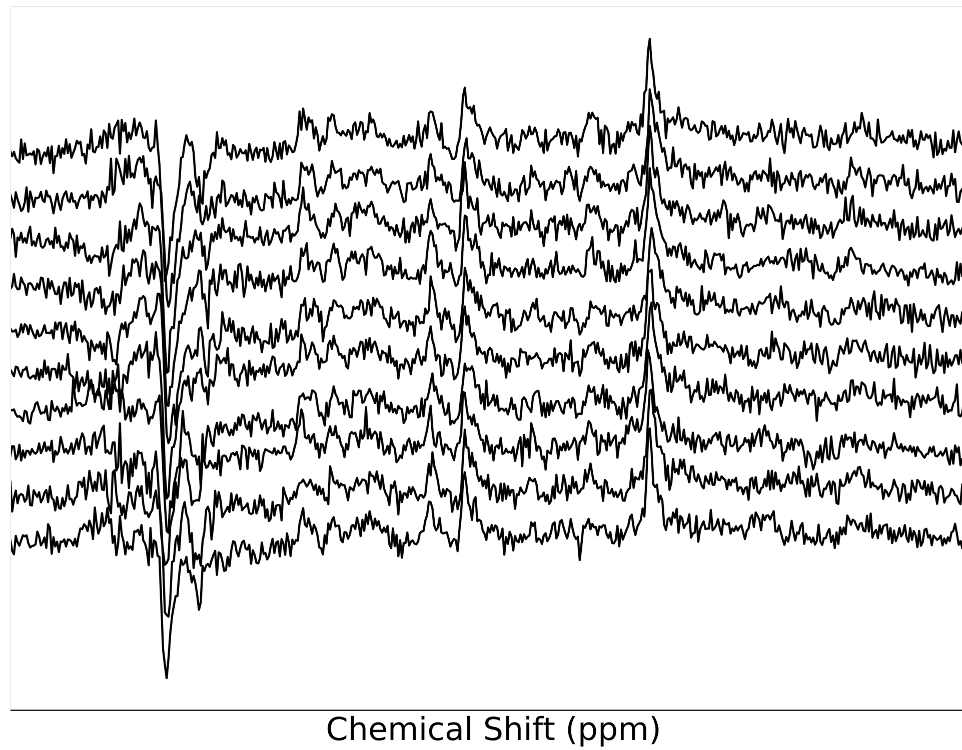
Combine signals with unknown amplitude + phase weighting. Either:

1. Fit water reference to derive complex weights.
2. Explicit rank = 1 problem, use first principal component of stacked multi-coil data.

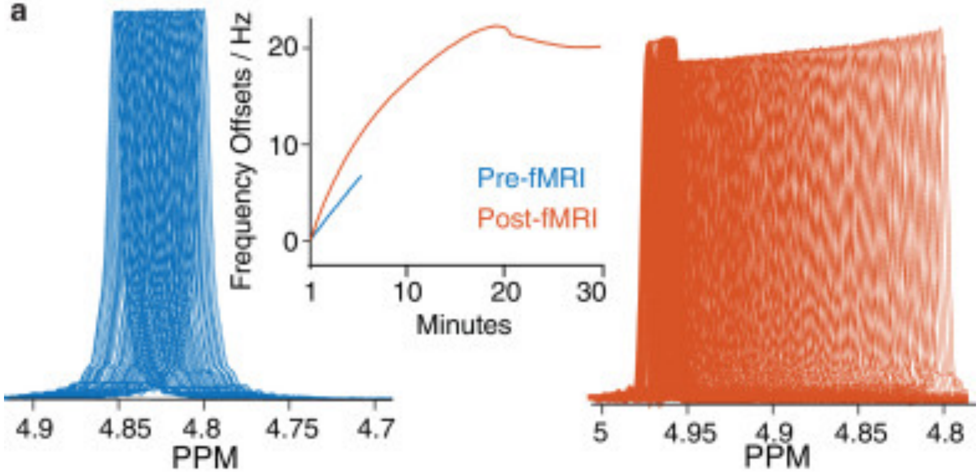
Combining repeated scans

Combine tens to hundreds of scans for sufficient SNR.

<u>BUT</u> hardware drift and physiological motion causes frequency and phase shifts.



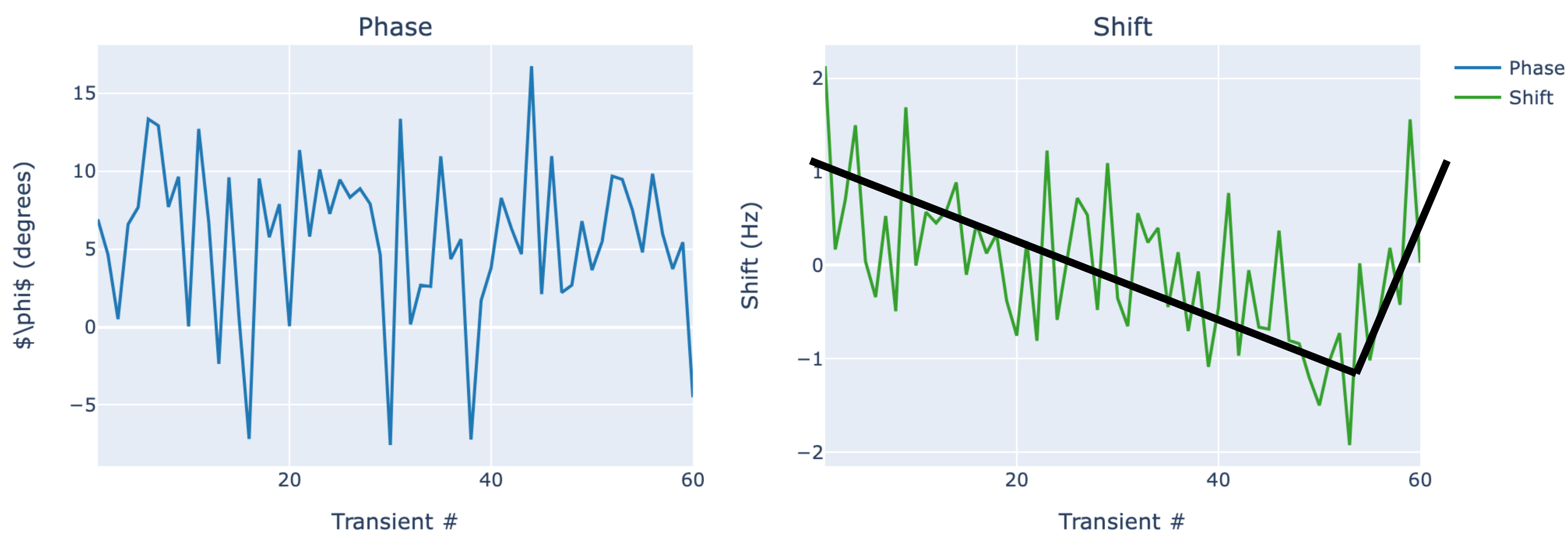
Combining repeated scans: alignment

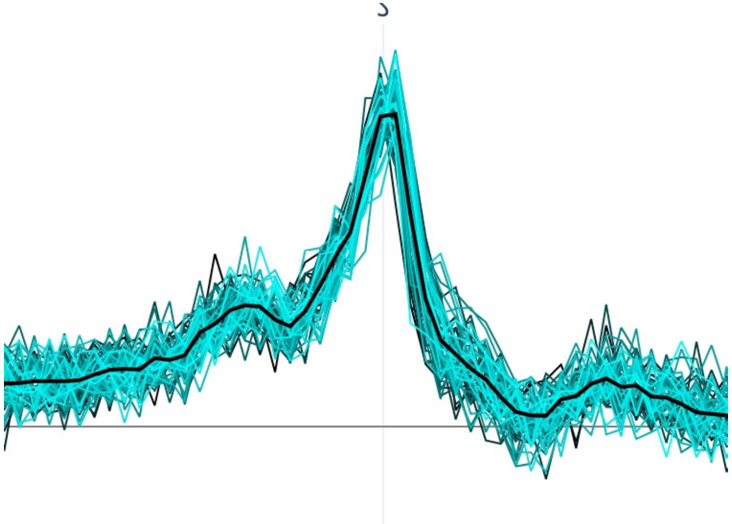


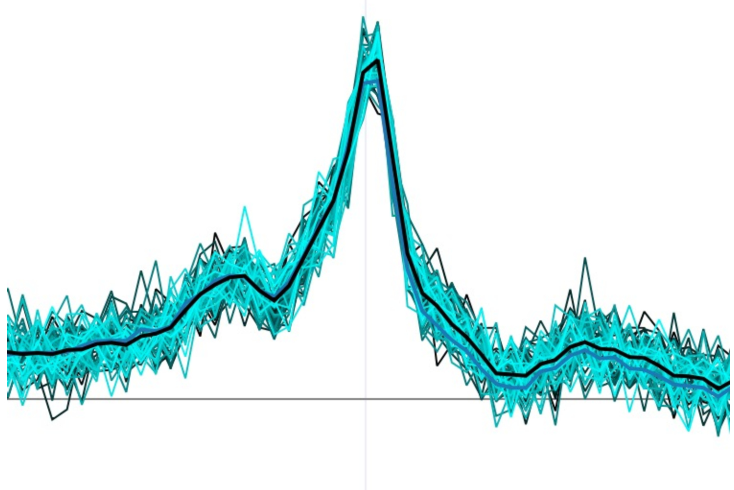
Hui et al. NeuroImage. 241, November 2021, 118430.

Small shifts (approx.) corrected by shifting and phasing individual spectra

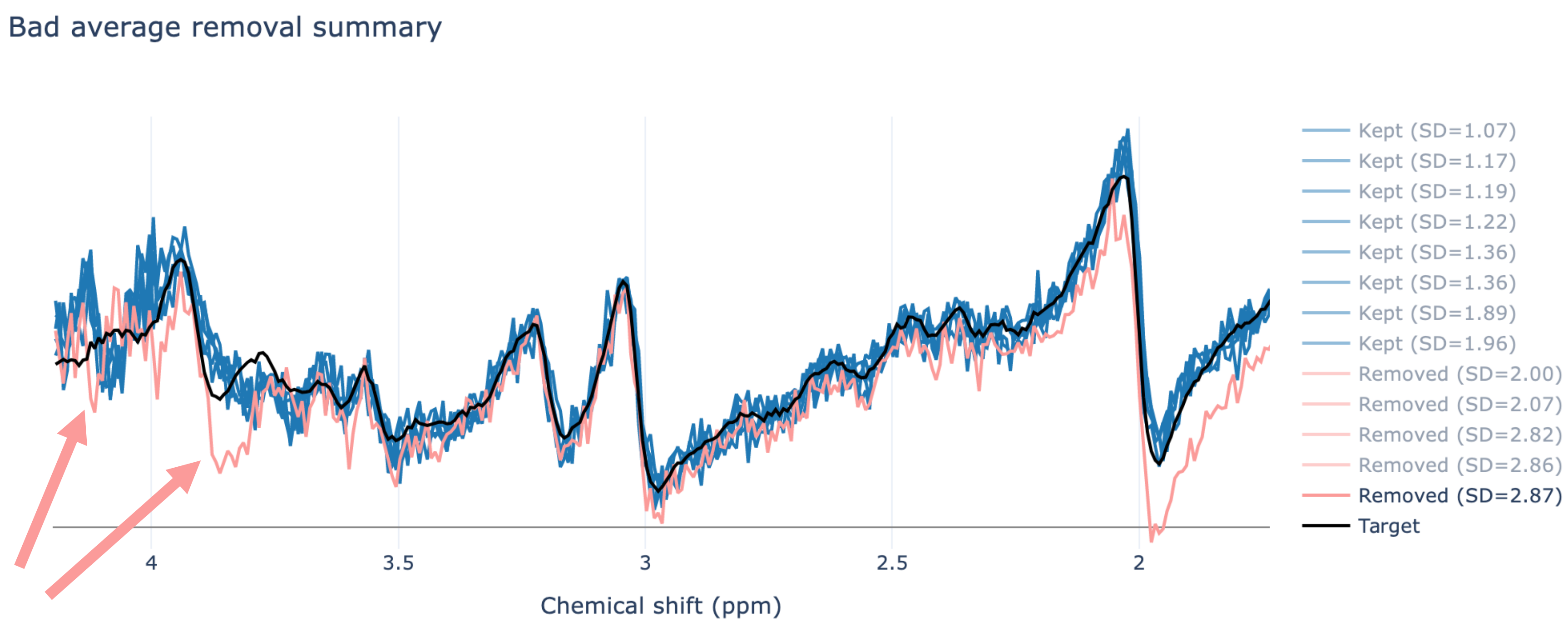
Combining repeated scans: alignment







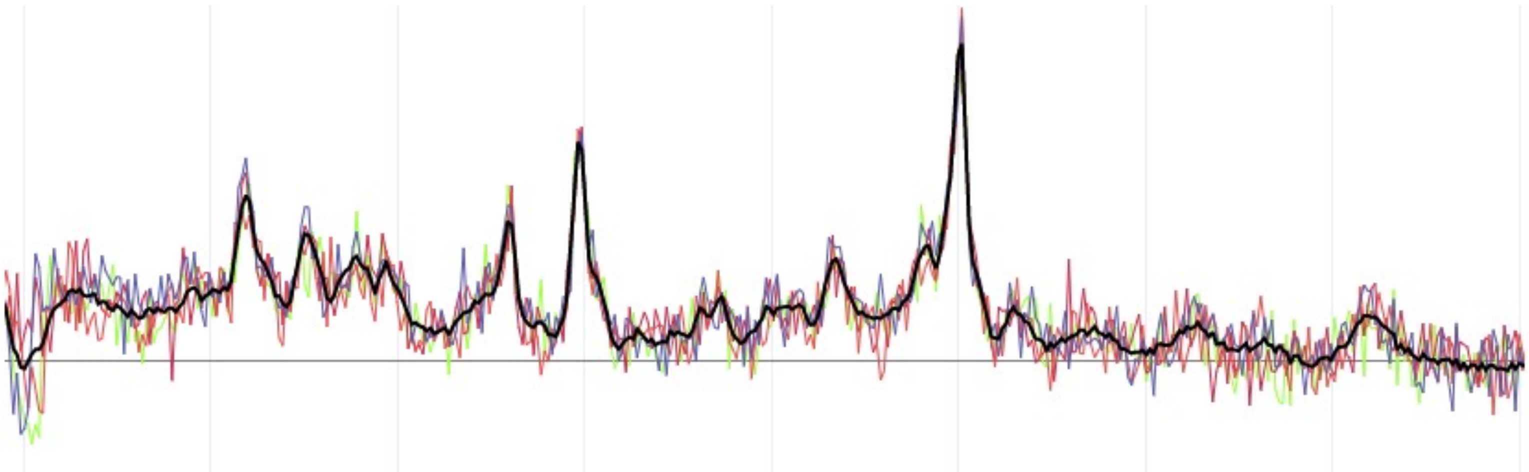
Combining repeated scans: outlier removal



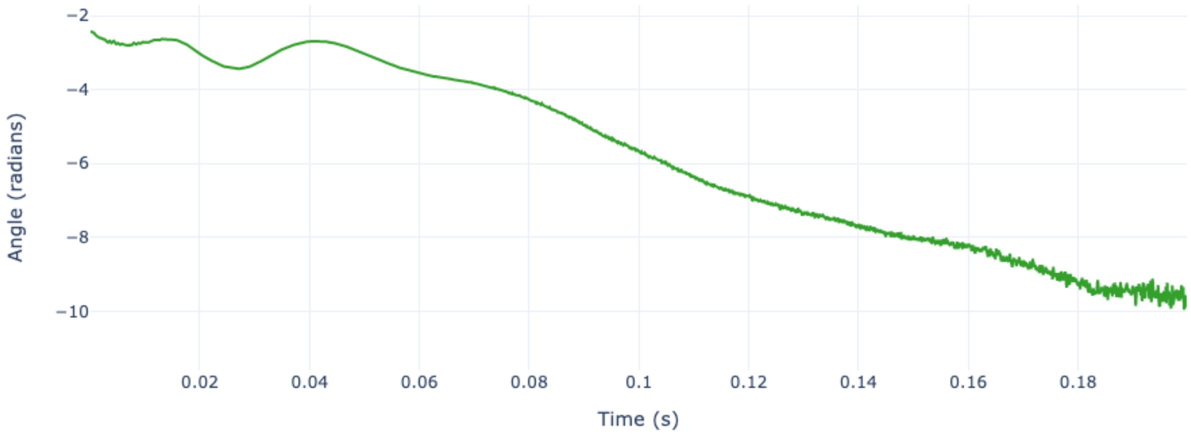
Gross motion leads to an incorrectly positioned voxel, severely degraded shim, or both. Exclude!

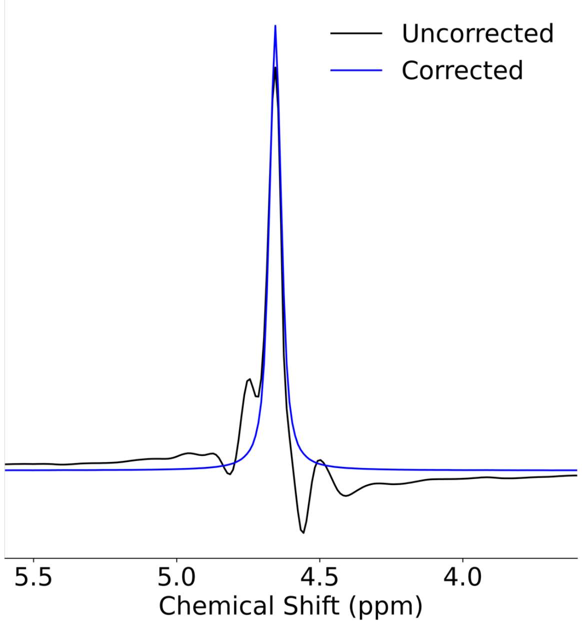
Combining repeated scans: averaging

Combine by taking the mean to preserve scaling



Eddy currents



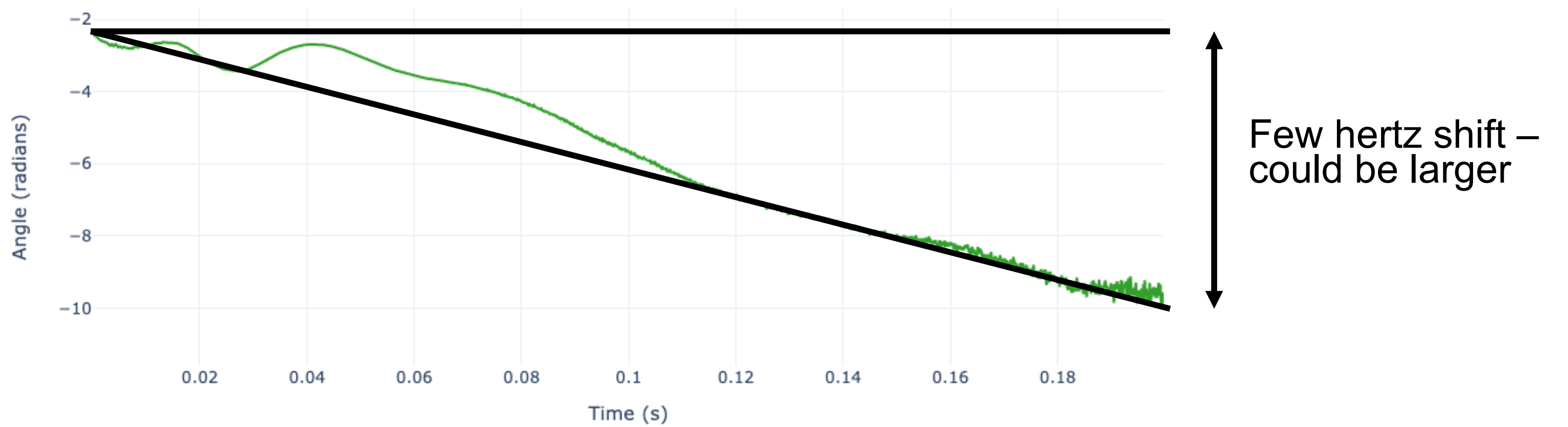


Eddy currents = time-dependent magnetic field.

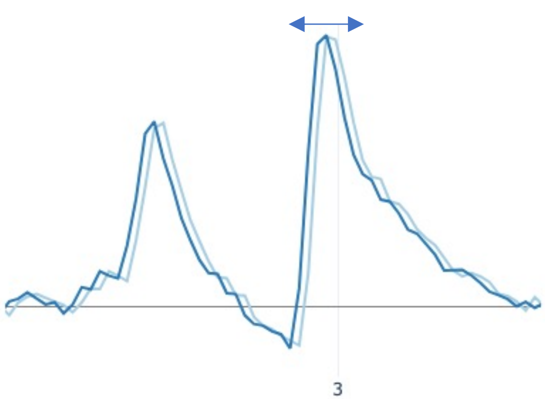
- Easily seen in phase of FID.
- Produces anti-symmetric side peaks in spectrum.
- Corrected by subtracting water reference phase

Dealing with global frequency shifts

Fitting relies on 'fingerprints' with known frequencies. Therefore, eliminate large global shifts.



ECC or incorrect identification of water frequency on scanner can introduce shifts.



Residual water removal

Large residual water peak can distort baseline.

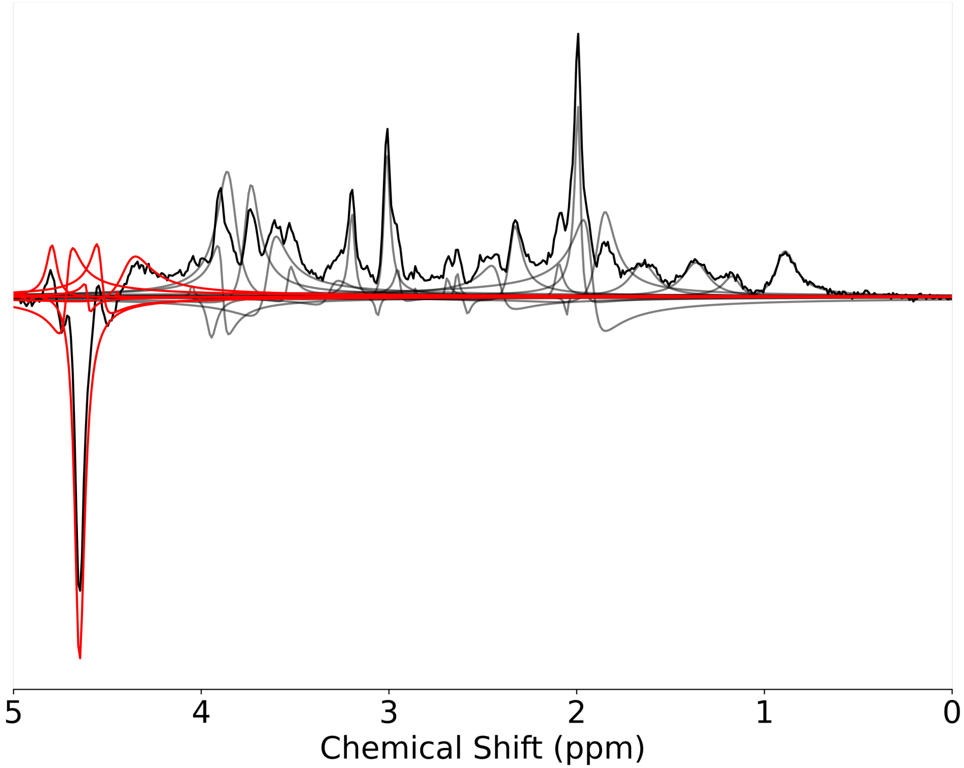
Data-driven fitting approach used to identify and remove residual peak.

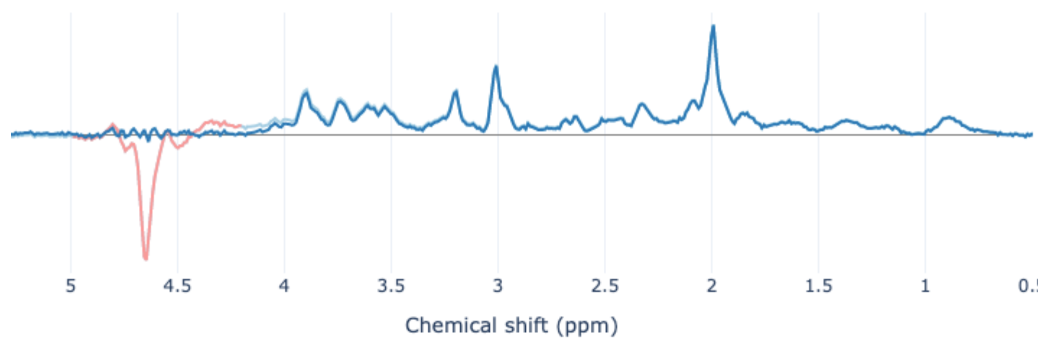
FID formed into Hankel matrix representation.

$$H = \begin{bmatrix} s[1] & \cdots & s[K] \\ s[2] & \cdots & s[K+1] \\ \cdots & \cdots & \cdots \\ s[M-K+1] & \cdots & s[M] \end{bmatrix}.$$

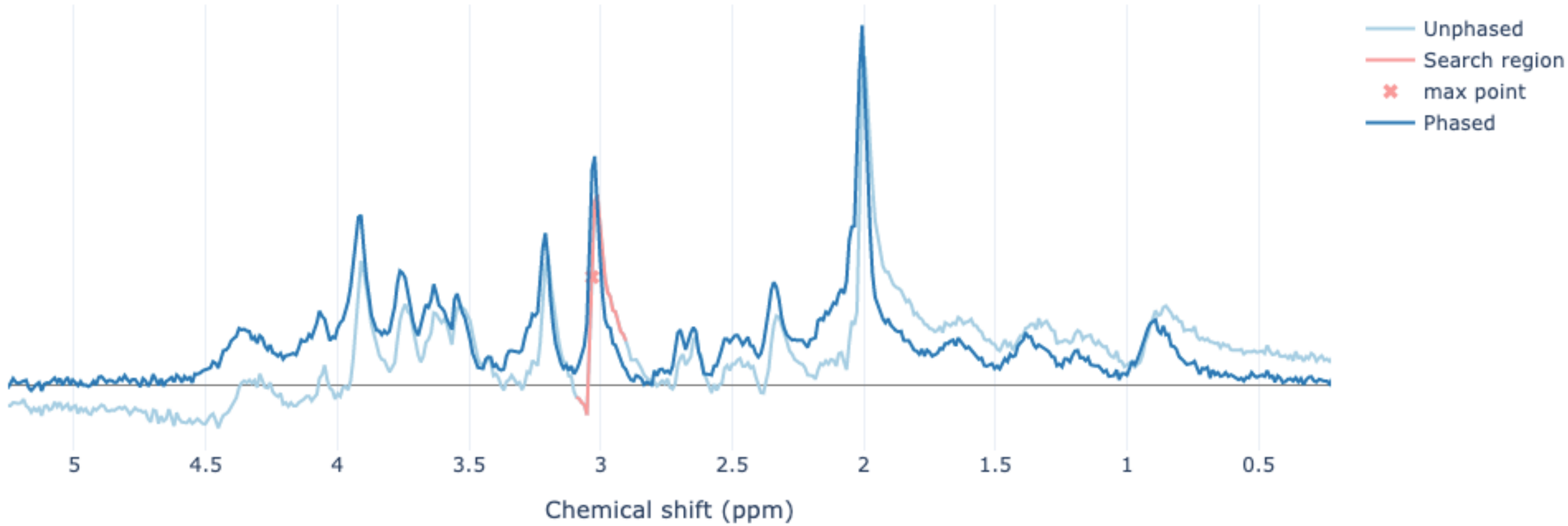
Then SVD used to identify peak components.

Peaks in water frequency range removed.





Phase correction: 0th order



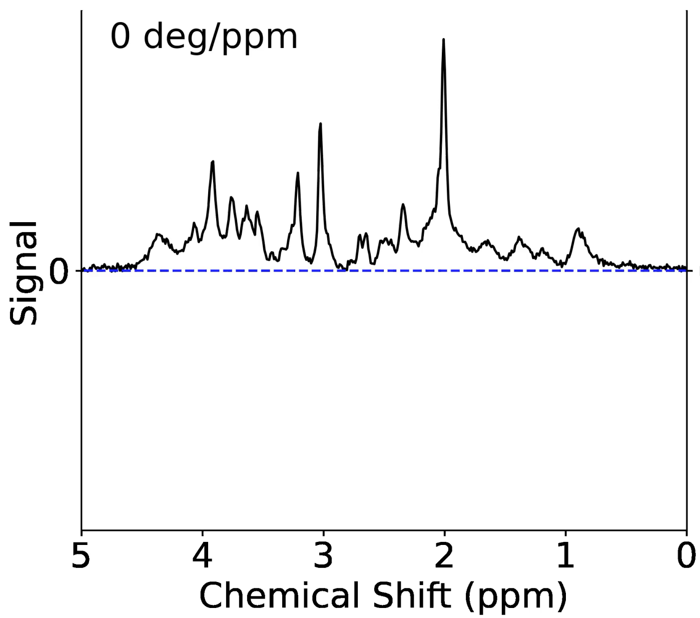
<u>Zero-order phase = uniform phase term</u>

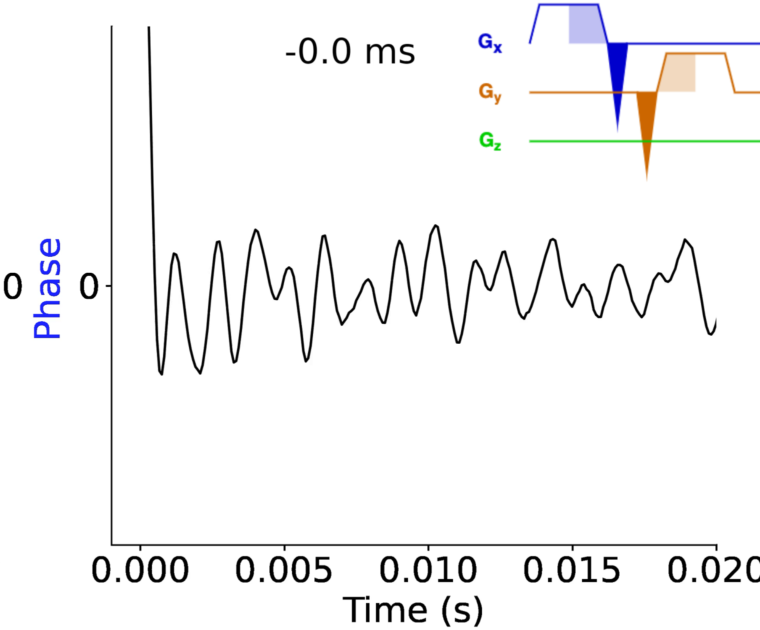
Correct using complex scalar term $e^{j\phi_0}$

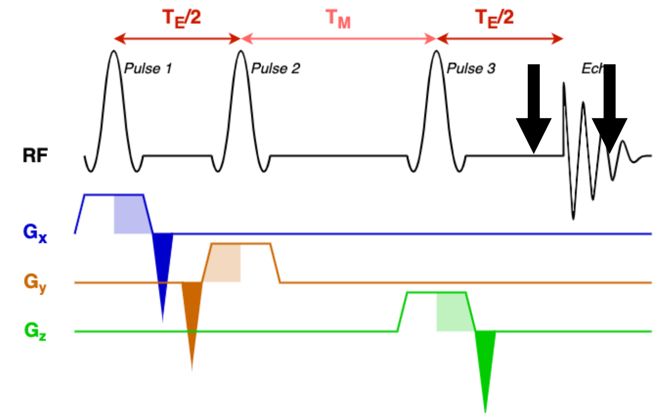
Target purely ‘absorption’ real spectrum for:

1) visualisation and 2) fitting initialisation

Phase correction: 1st order





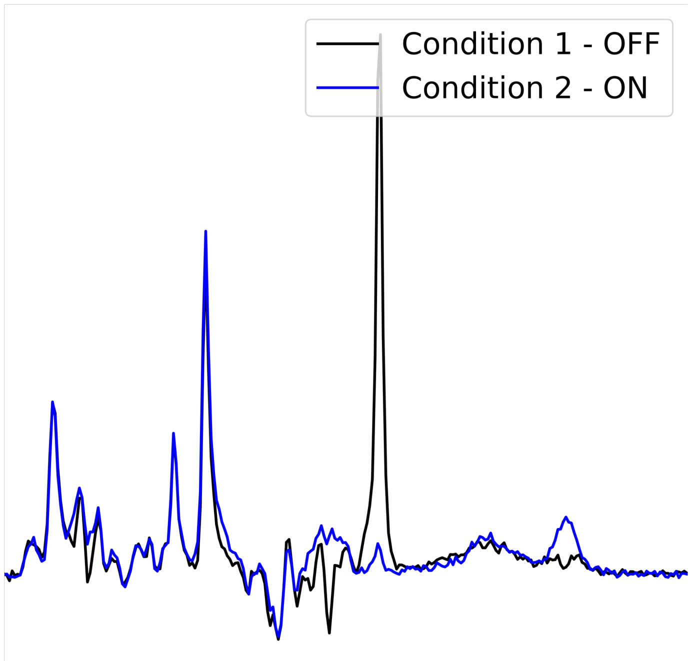


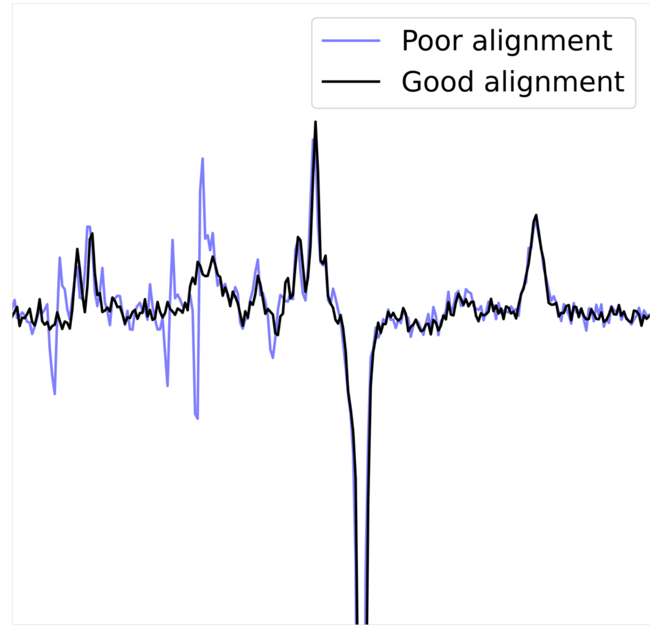
First-order phase - phase term linear with frequency

Correction applies complex vector $e^{2\pi j\omega\phi_1}$

Equivalent to time shift in time domain.

Alignment of edited spectra





Spectral editing dynamically alters spectrum.

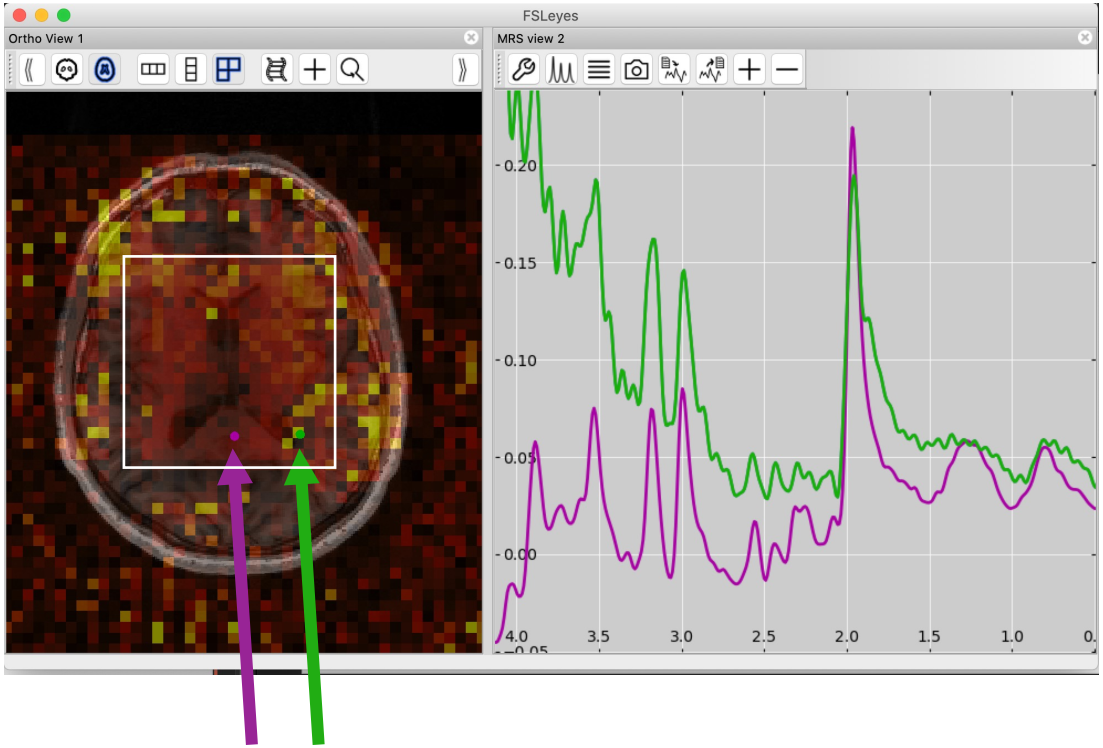
Requires alignment of two spectra based on partial similarity.

MRSI Pre-processing

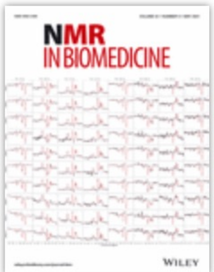
All FSL-MRS pre-processing tools can be applied per voxel.

Planned features:

- Lipid removal
- Phase correction
- Motion correction



MRS Resources



Volume 34, Issue 5

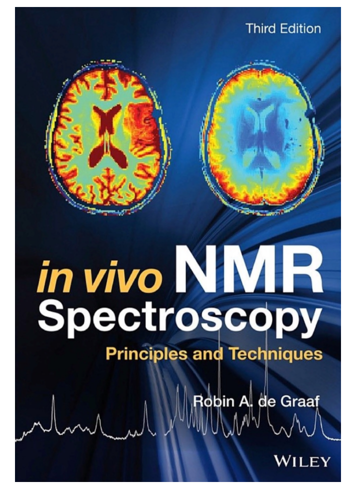
Special Issue: Advanced methodology for in vivo magnetic resonance spectroscopy

May 2021

Issue Edited by: **In-Young Choi, Roland Kreis**

NMR in Biomedicine special issue on MRS methods

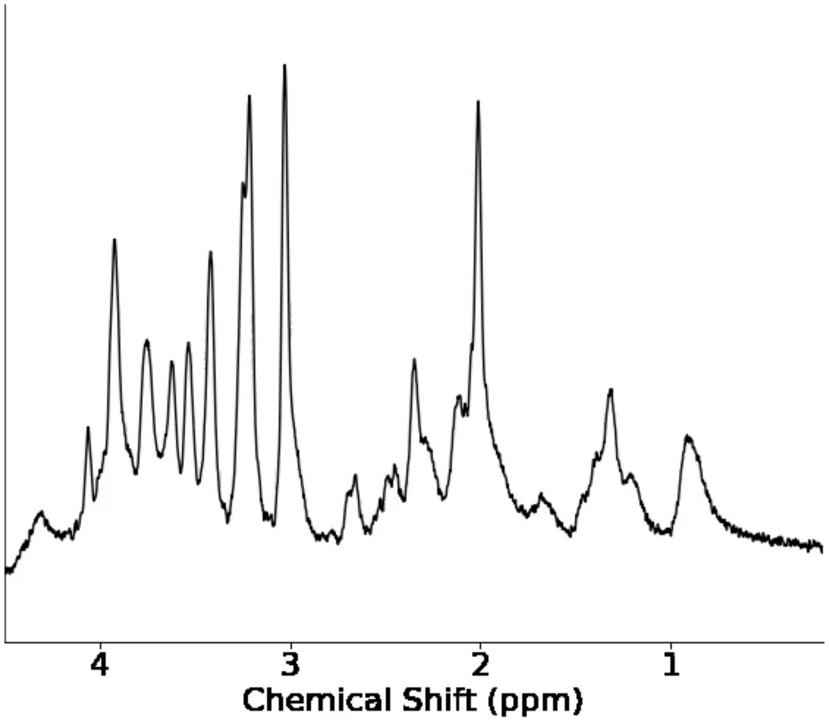
Robin de Graaf
YouTube channel & book
youtube.com/c/BasicsOfInVivoNMR



MRSHub

MRS online community.
Ask a question in the friendly forums!

Up next: Fitting + FSL-MRS



Metab	unscale	CRLB	%CRLB	/Cr+PC
Ace	0.04	0.007	20.1	0.14
Ala	0.04	0.004	8.1	0.17
Asp	0.09	0.008	8.2	0.36
Cho	0	0.001	999	0
Cr	0.13	0.006	4.1	0.52
GABA	0.03	0.006	21.4	0.11
GPC	0.04	0.004	8.5	0.17
GSH	0.07	0.003	3.7	0.27
Glc	0.14	0.004	3.1	0.55
Gln	0.11	0.005	4.6	0.41
Glu	0.25	0.005	1.9	0.96
Gly	0.11	0.008	6.9	0.43
Ins	0.21	0.004	1.8	0.8
Lac	0.12	0.003	2.8	0.48
MM_WT_	0.39	0.011	2.9	1.52
NAA	0.18	0.003	1.5	0.7
NAAG	0.03	0.002	7.1	0.1
PCho	0.02	0.004	20.6	0.07
PCr	0.12	0.006	4.6	0.48
PE	0.07	0.007	9.6	0.27
Tau	0.28	0.004	1.3	1.11
sIns	0.02	0.007	37.5	0.07
Cr+PCr	0.26	0.003	1.1	1