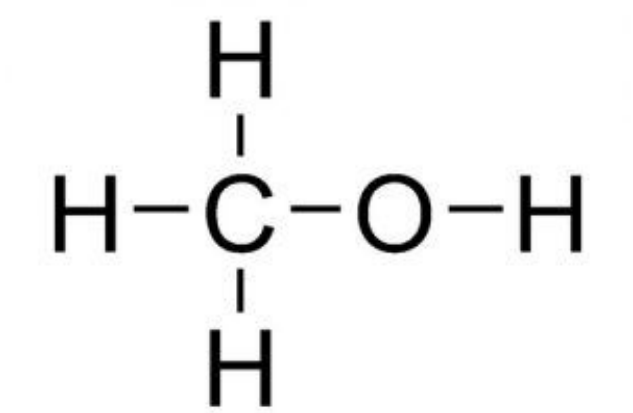
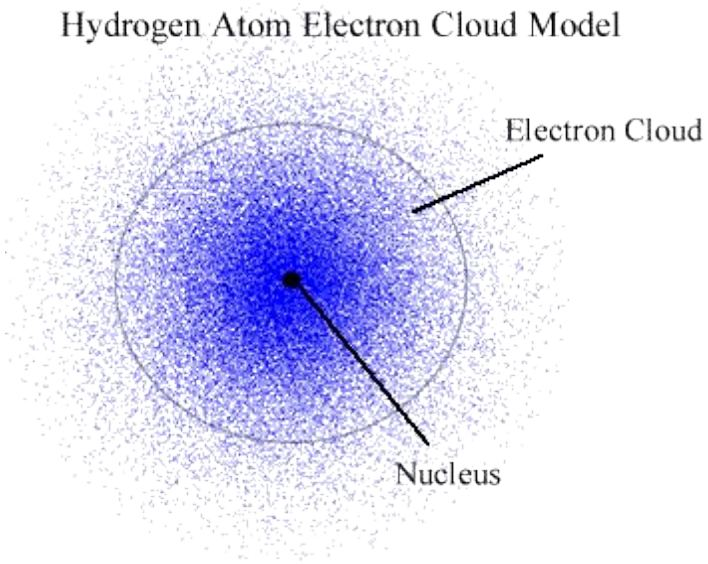
Journal Club
2/6/2020

Maria Perica

Outline

- MRS 101
- Spectral quality
- LCModel output
- Proposed updates to procedure
- Metabolites we collect





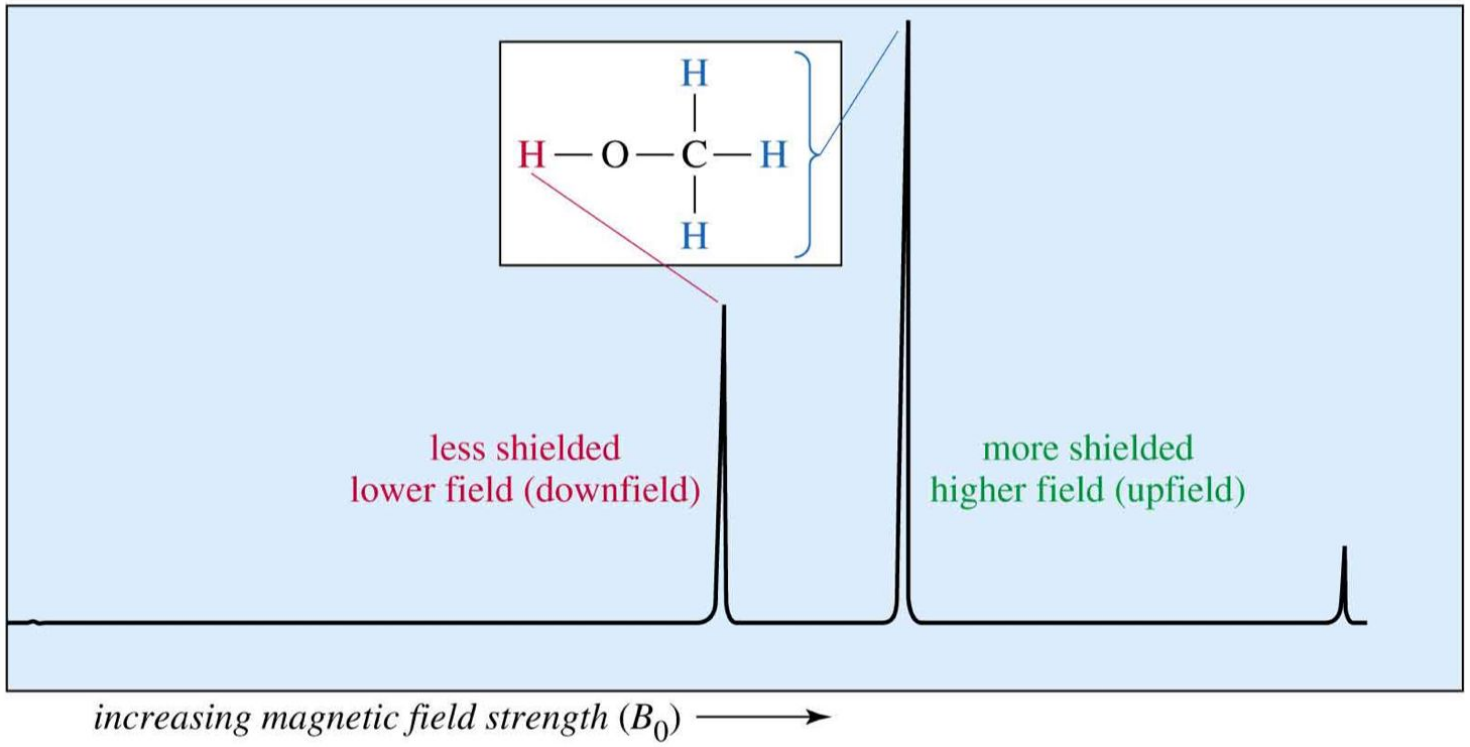
MRS aka Chemical Shift Imaging

- Measure metabolites noninvasively in vivo
  - Organic compound structure determination
  - Same principles as conventional MRI
- Magnetic field that a molecule experiences depends on chemical structure and the environment in which it is
- Slightly different effective field
- CS gives rise to the spectrum

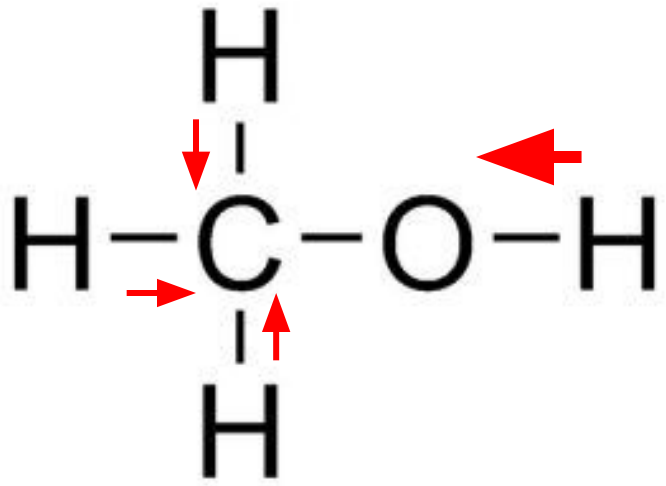
Shielding and **deshielding**: nucleus ”experiences” weaker or stronger magnetic field as a result of the electron density

Upfield and **downfield**

- More shielded stronger field must be applied



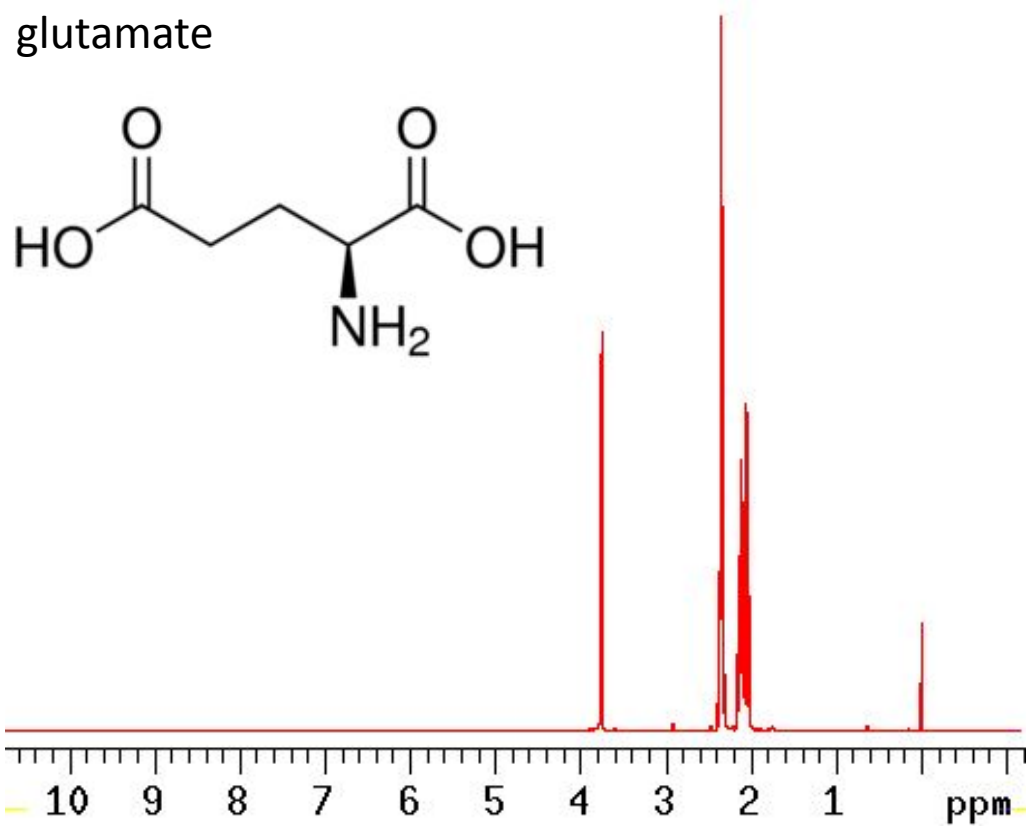
Electronegativity also influences shielding



Wade, L.G., *Organic Chemistry*, 5th Edition

From spectrum to molecule

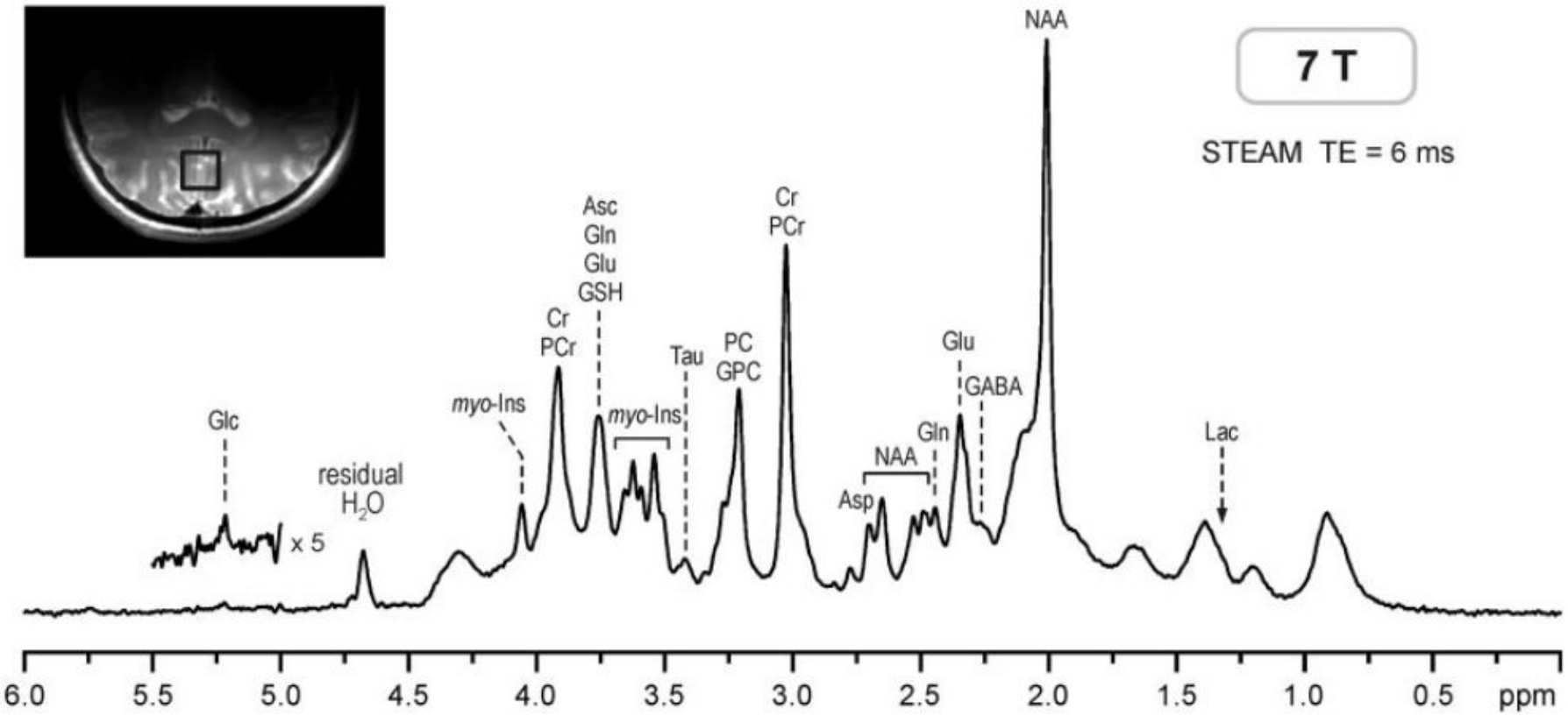
- Location of peaks shielding
- Number of peaks Number of H
- Intensity of signal Number of that type of H
- Signal splitting Number of protons on adjacent atoms
- Integral Concentration



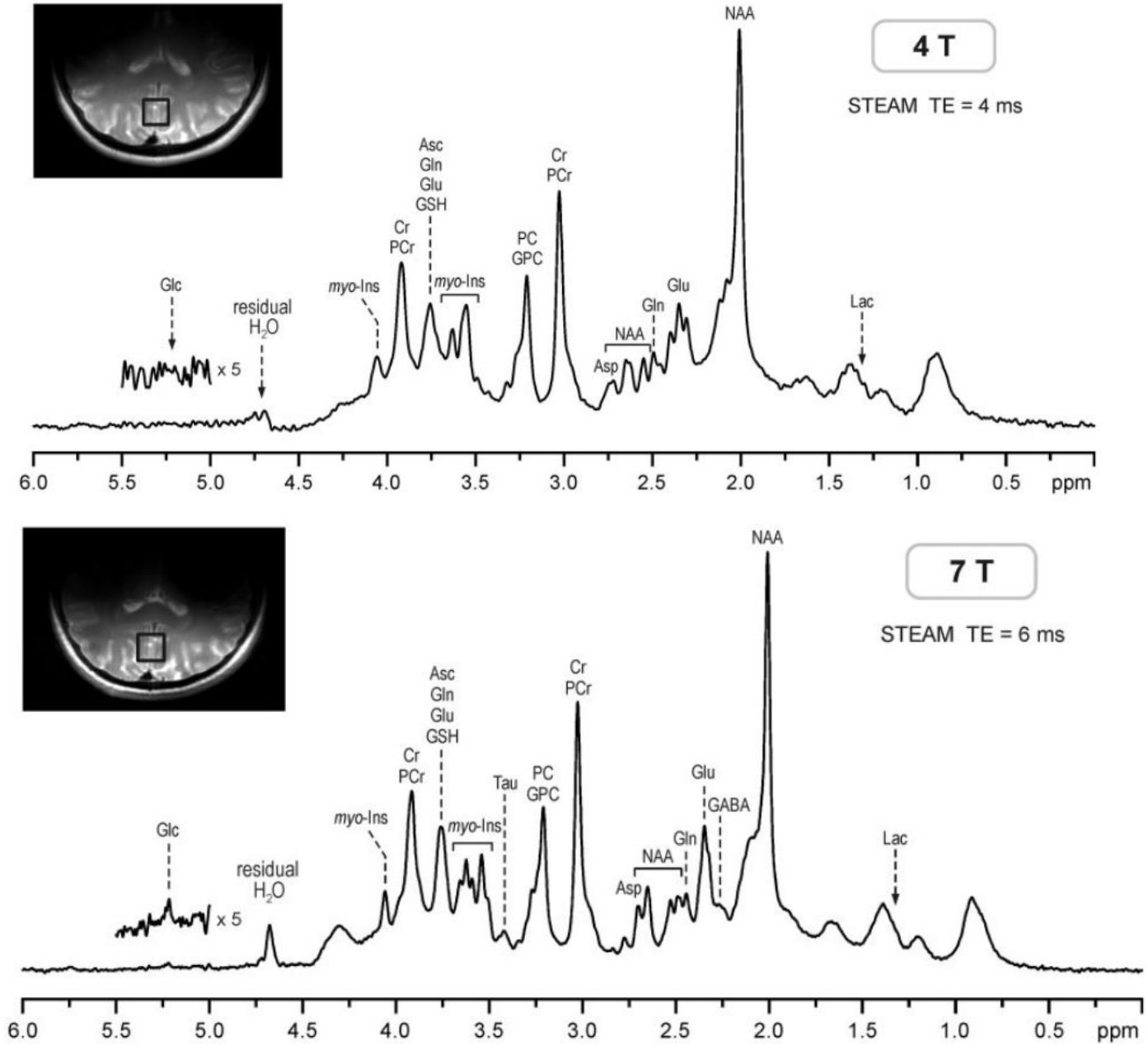
Bio-Rad Laboratories, Inc. SpectraBase; **http://spectrabase.com/**

Gallery of spectral quality and artifacts

Good spectrum

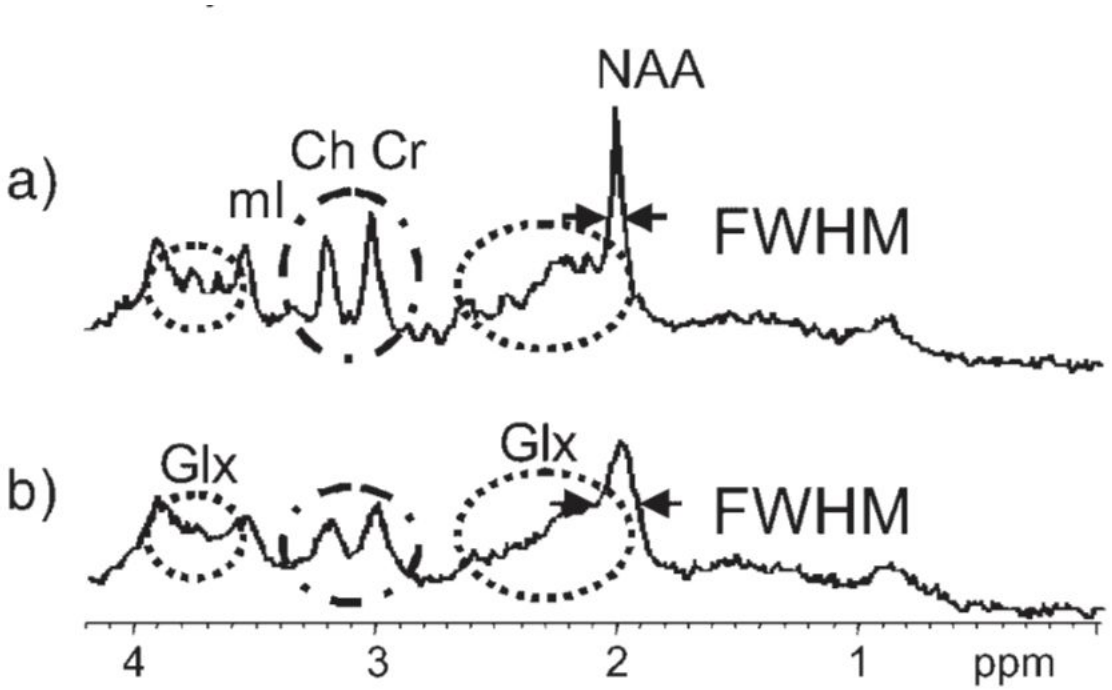


Tkac et al., 2009

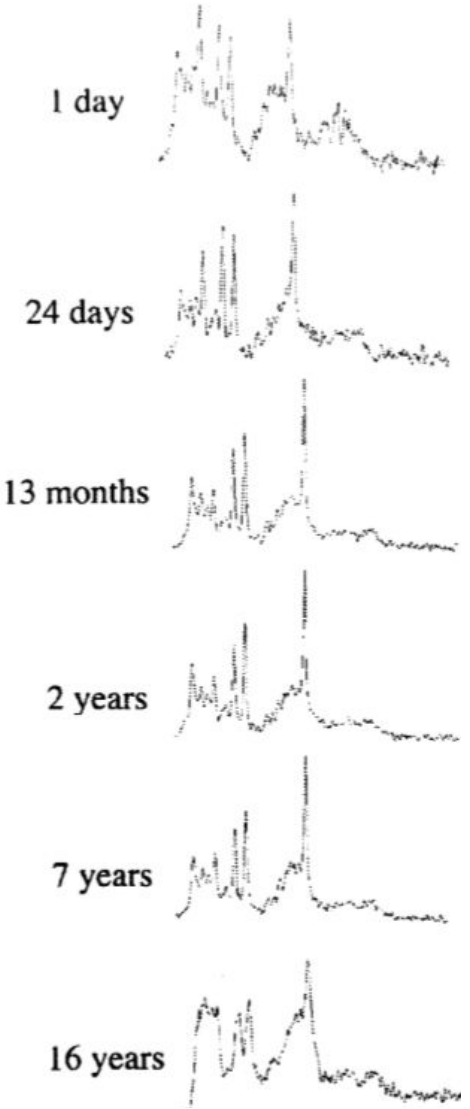


Tkac et al., 2009

Linewidth

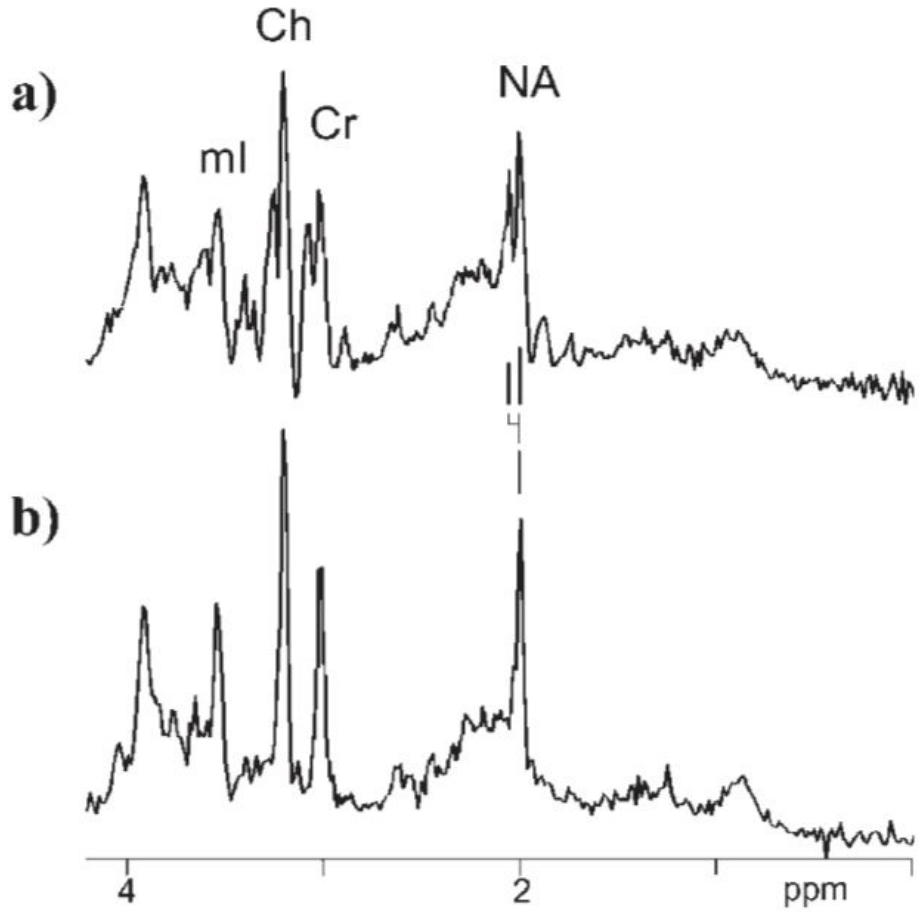


Kreis, 2004



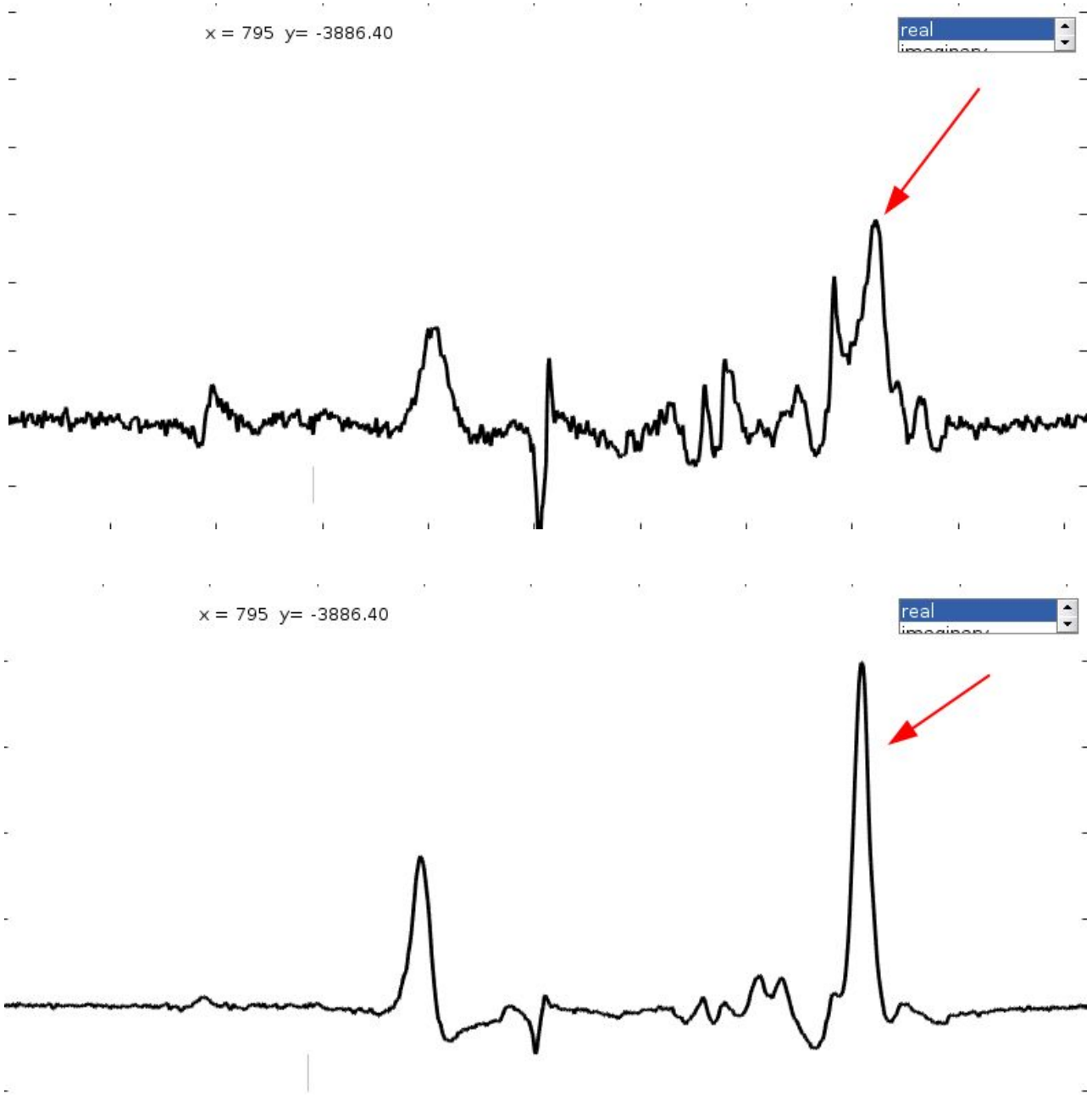
Cecil & Jones, 2001

Motion

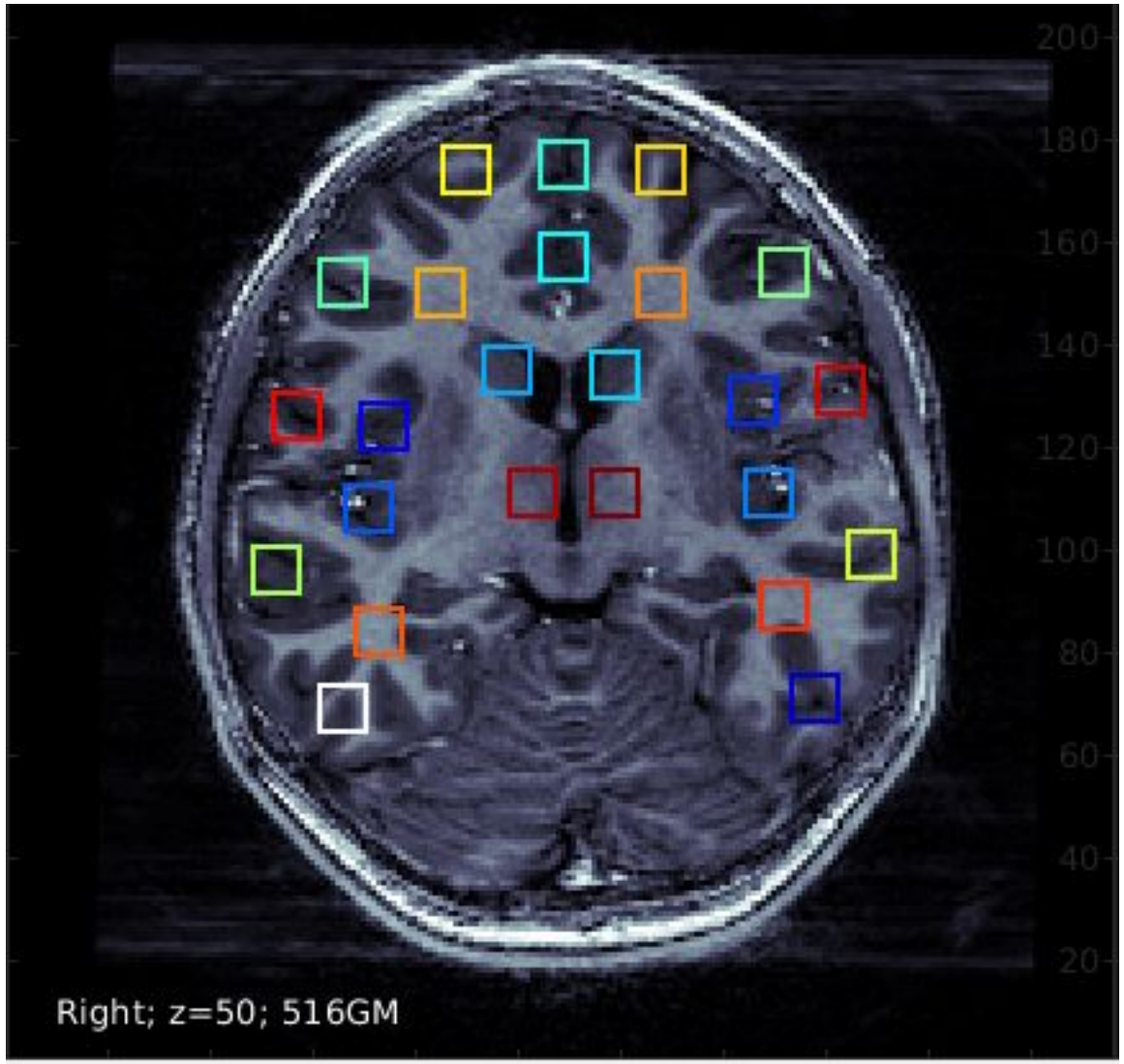


Kreis, 2004

Lipids

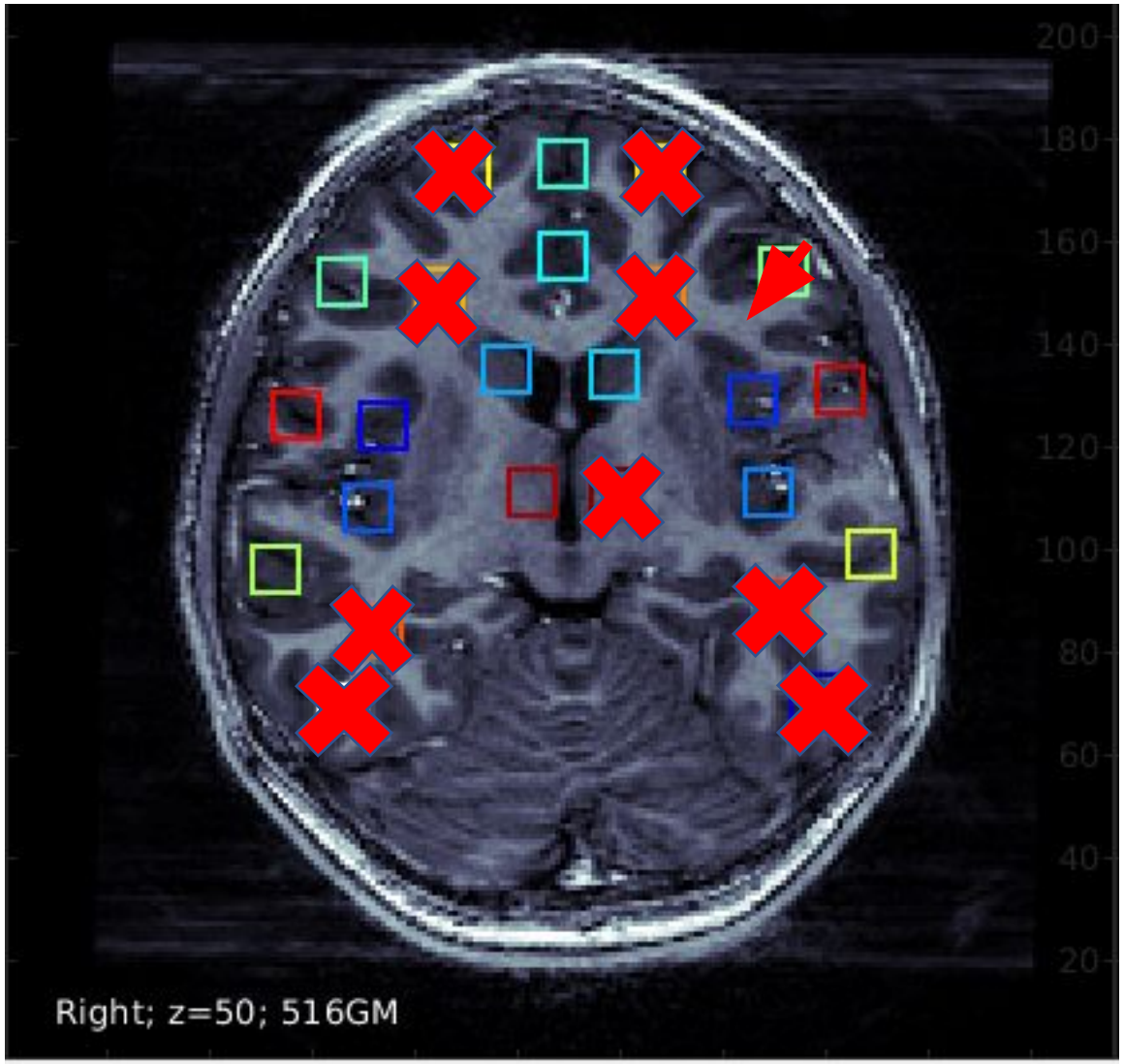


Coordinates: Before



Proposed updates

2. Remove SFG, WM voxels, one thalamus voxel because they are too close together and not statistically independent



1. Move all peripheral voxels away from outer-volume lipids

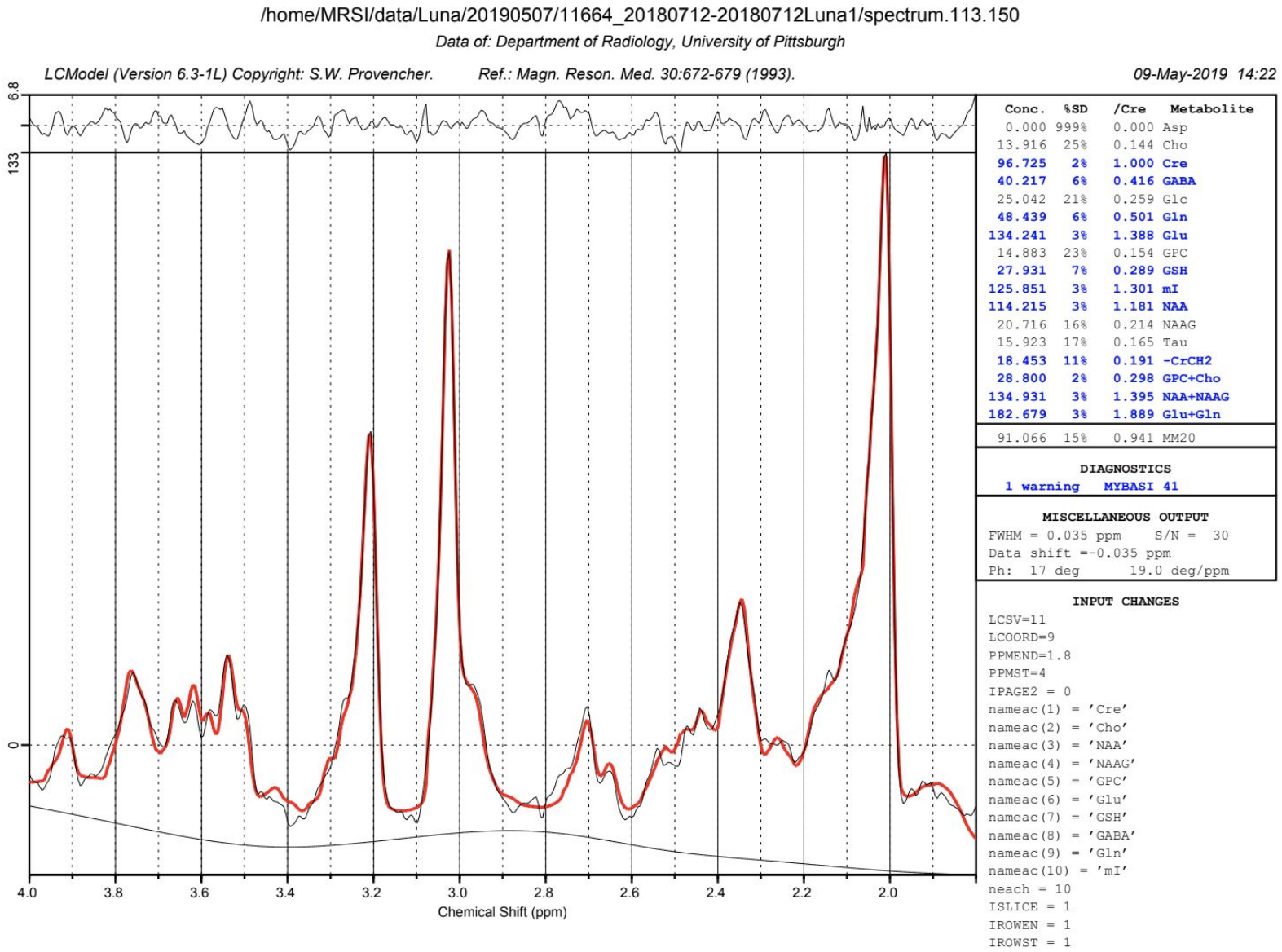
3. Remove MOG voxels because bad data quality as a result of not optimized acquisition

LCModel

1. residuals

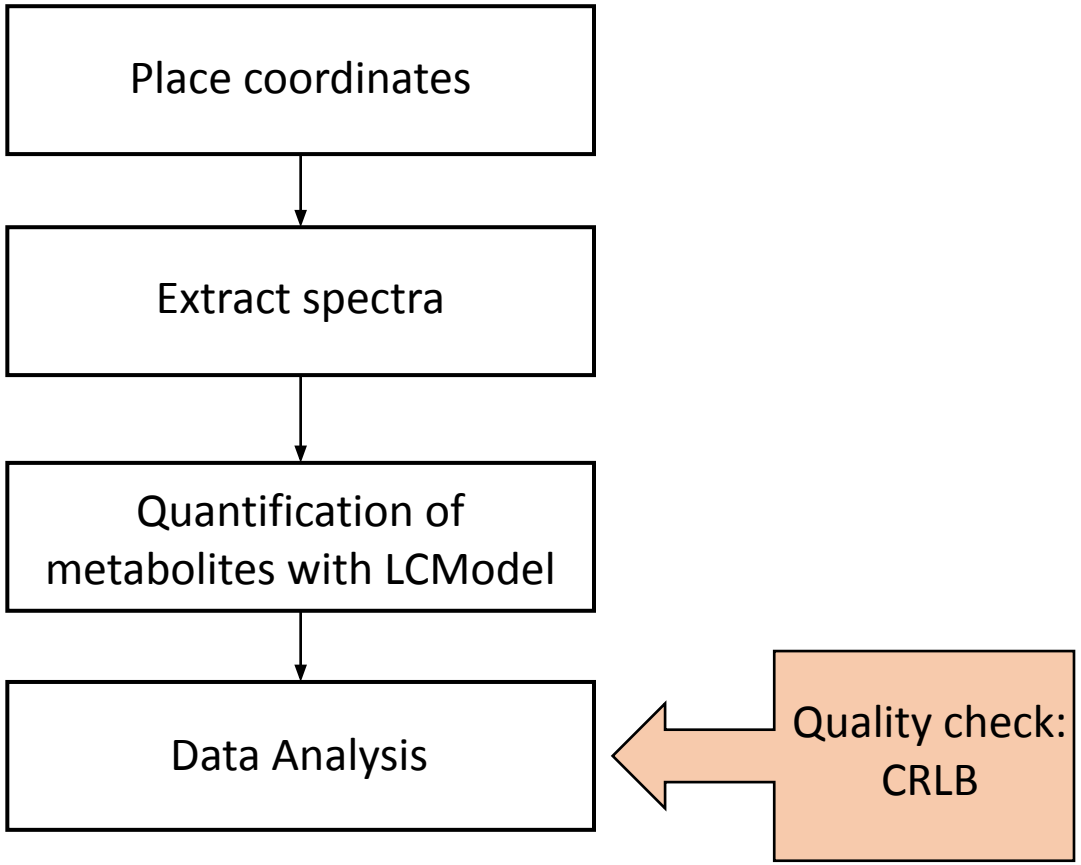
2. Model fit

3. Baseline

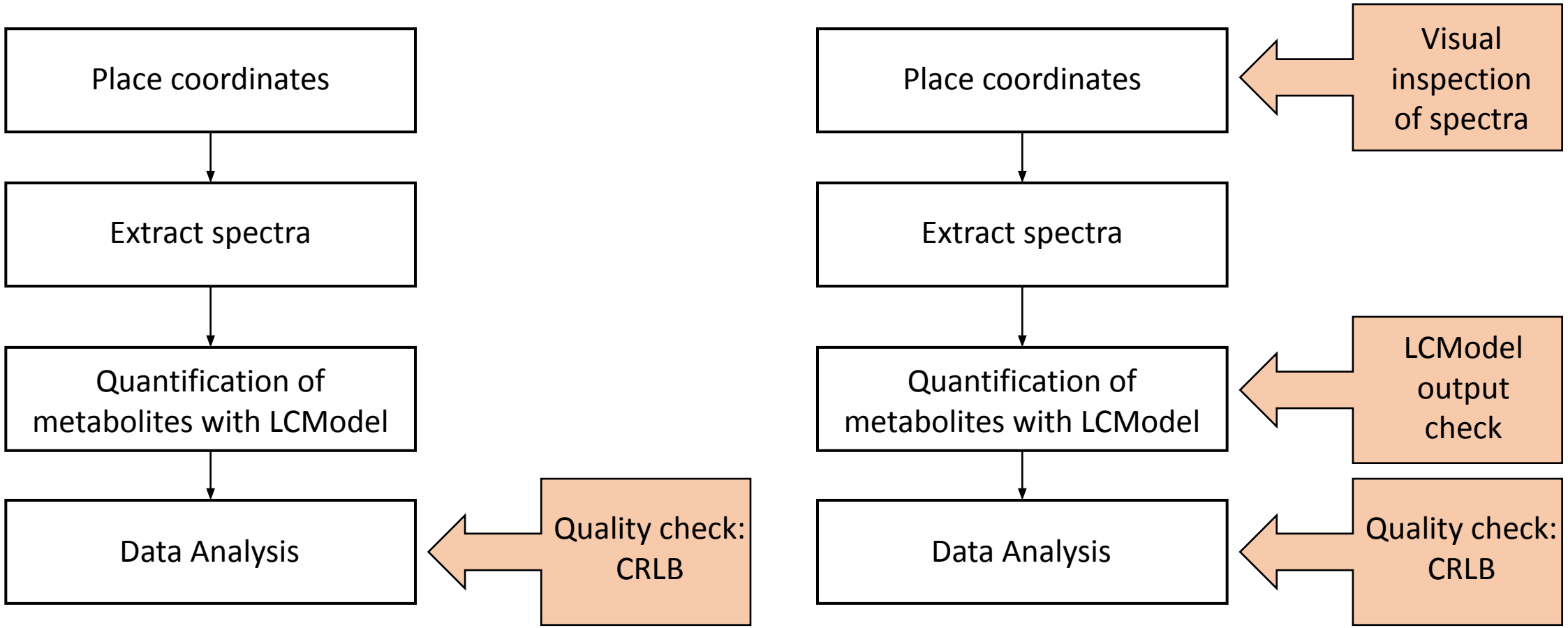


Concentration relative to Cre and CRLB

Current workflow



Updates


Place coordinates
Extract spectra
Quantification of metabolites with LCModel
Data Analysis
Quality check: CRLB
Place coordinates
Visual inspection of spectra
Extract spectra
Quantification of metabolites with LCModel
LCModel output check
Data Analysis
Quality check: CRLB

Proposed new quality check/ exclusionary criteria

Spectral inspection:

- Doubled peaks (motion)
- Lipid artifact
- Linewidth

LCModel check

- Model fit
- Baseline
- Residuals

Data

- CRLB > 20

Metabolites that we collect

- Aspartate
- Choline + GPC
- Cre
- GABA
- Glutamate
- Glutamine
- Glutathione
- Glucose
- Myoinositol
- NAA + NAAG

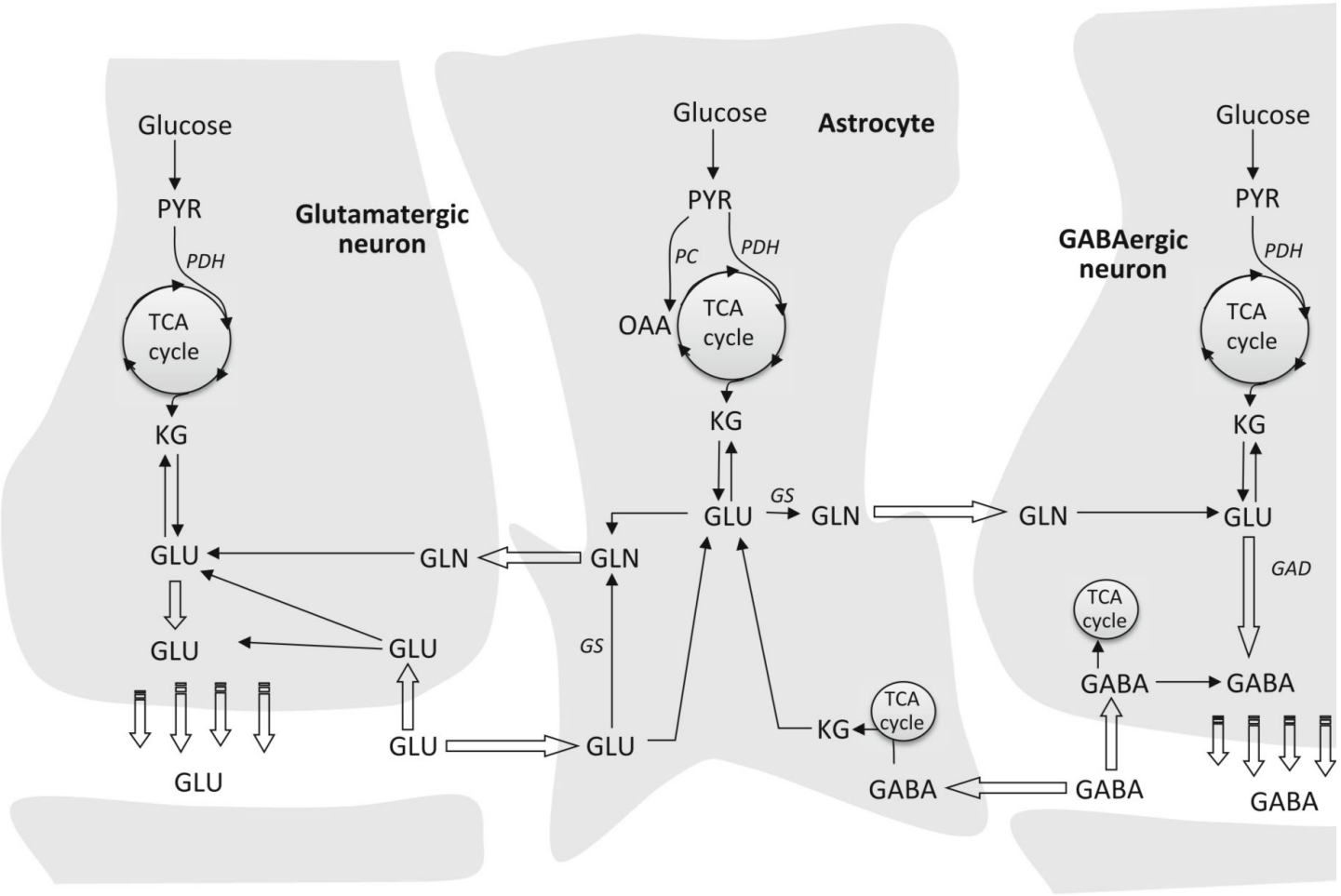
Disclaimer: we know very little about the actual biochemical roles of each of these (especially in humans), and even less about exactly what MRS picks up on

Creatine

- Cr+PCr = tCr
- Present in both neurons and glia
- Energy metabolism
- Use of Cre as ratio denominator
  - Correct for:
  - Stationarity assumption
    - Absolute quantification studies mixed/contradictory, but most find no changes
  - Introduces more variability than absolute metabolite quantification (Li et al., 2003)
  - Metabolite-to-creatine ratios estimated by LCModel more accurate than absolute (Kanowski et al., 2004)

Glutamate and GABA

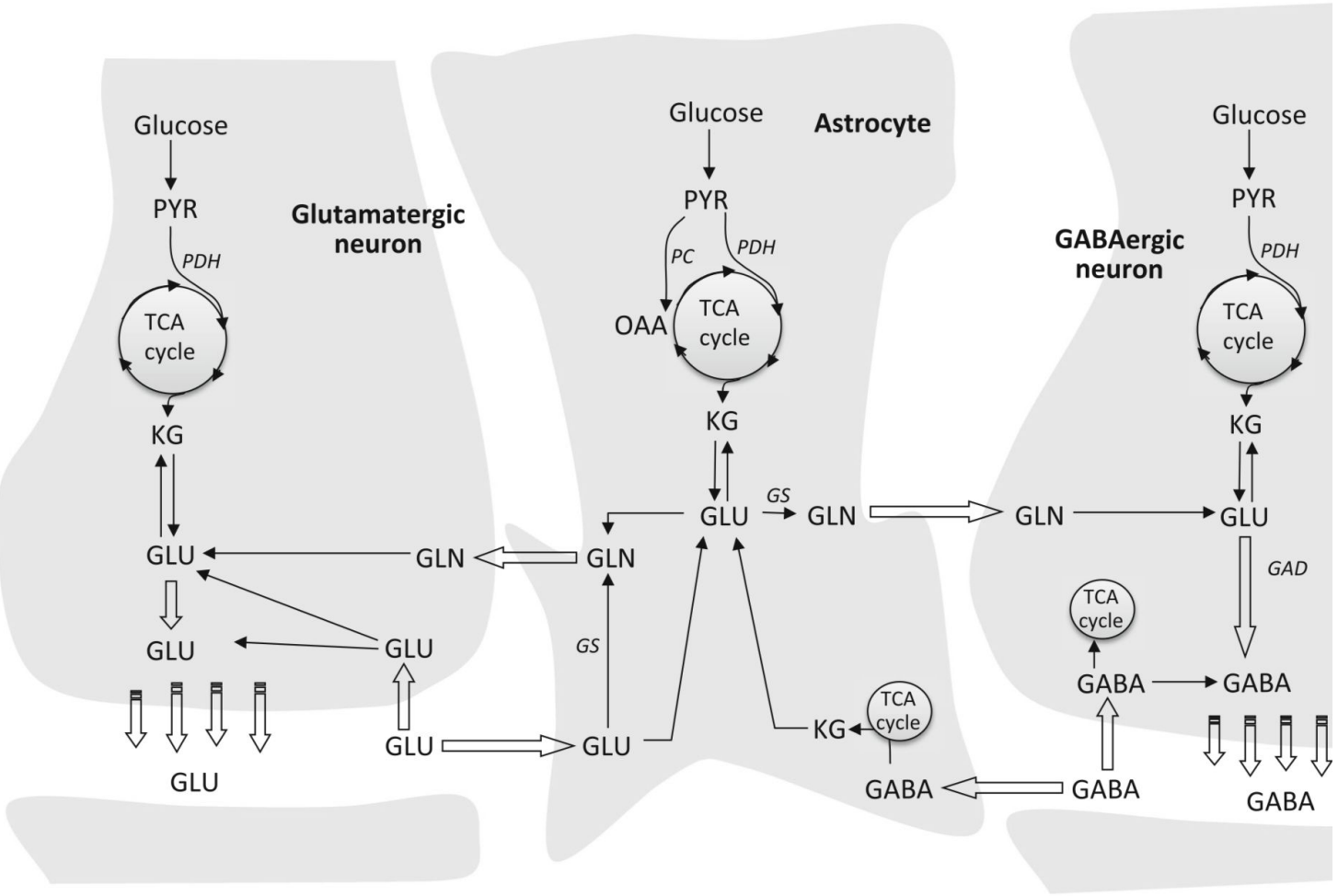
- In MRS: “Glutamate release and recycling is a major metabolic pathway that cannot be distinguished from its actions of neurotransmission.” (Rothman et al, 2002)
- Intracellular Glu: ~10mM; extracellular glu: 2 uM
- Intracellular GABA: 1 mM; extracellular GABA: 2 uM
- Exists in several metabolic pools
- Almost any pool may be available to be used as NT



Walls et al., 2015

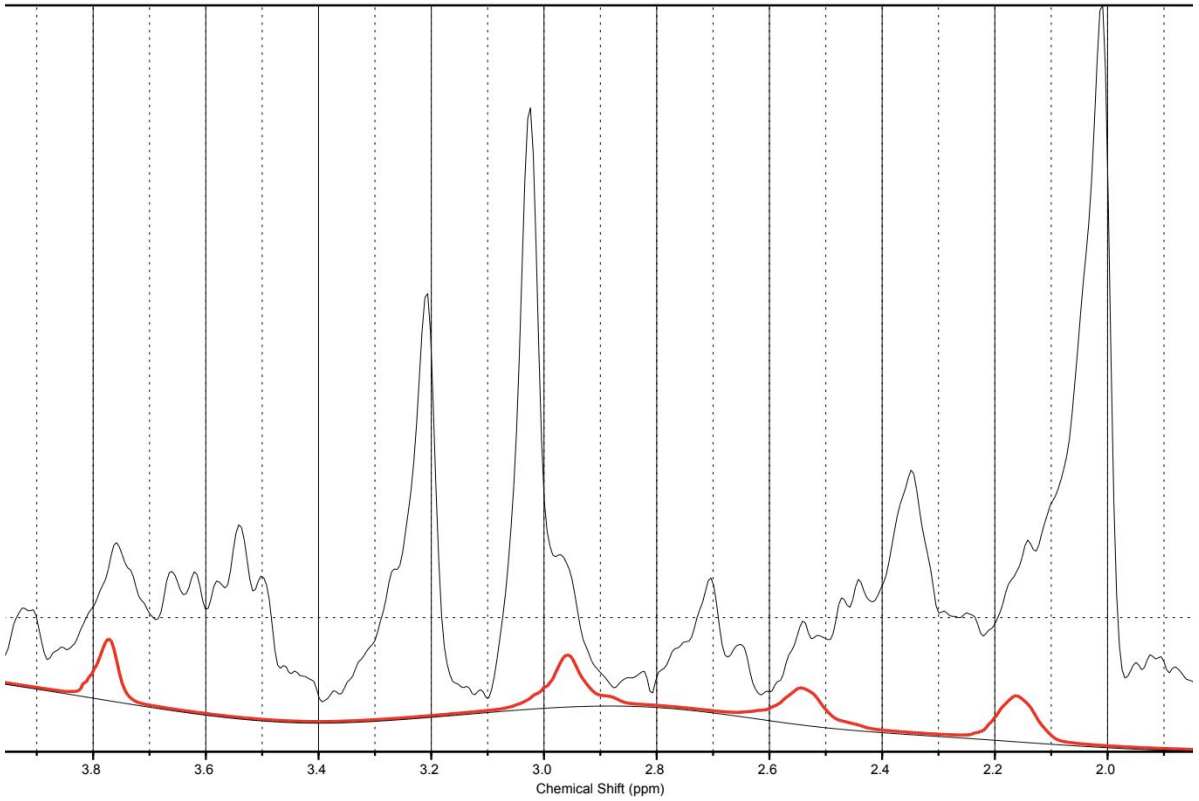
Glutamine

- Precursor to glutamate
- Glu stored as Gln in glia
- Small amounts of Gln also produced from GABA
- Glu+Gln=Glx



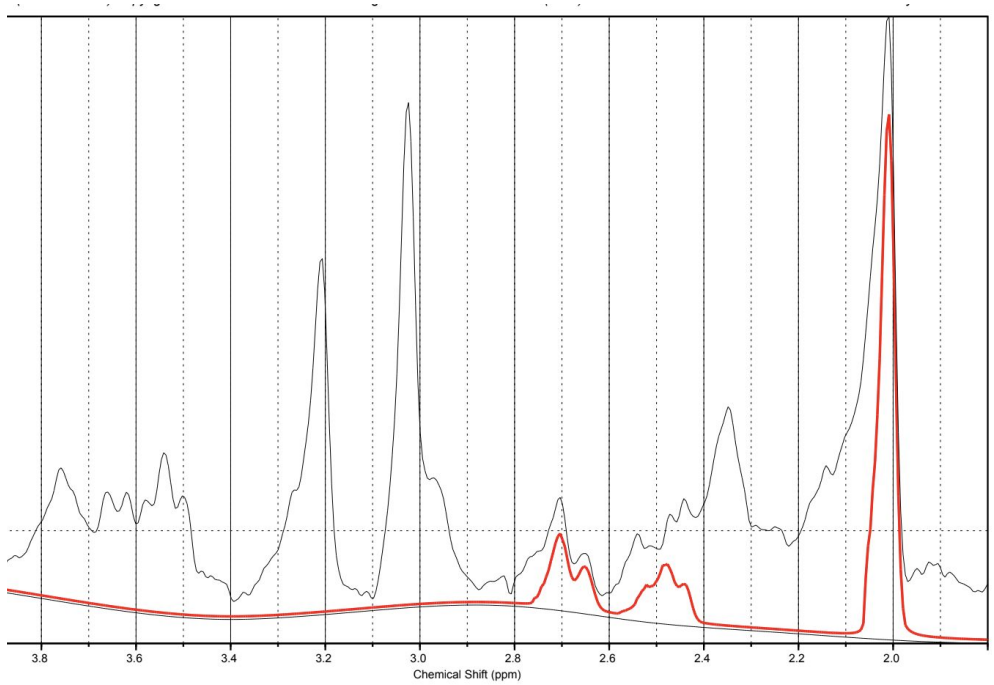
Glutathione

- Synthesized from glutamate
- Antioxidant, mitochondrial functions
- Generally elevated by stress
- Problematic to measure even at ultra-high field (14T)

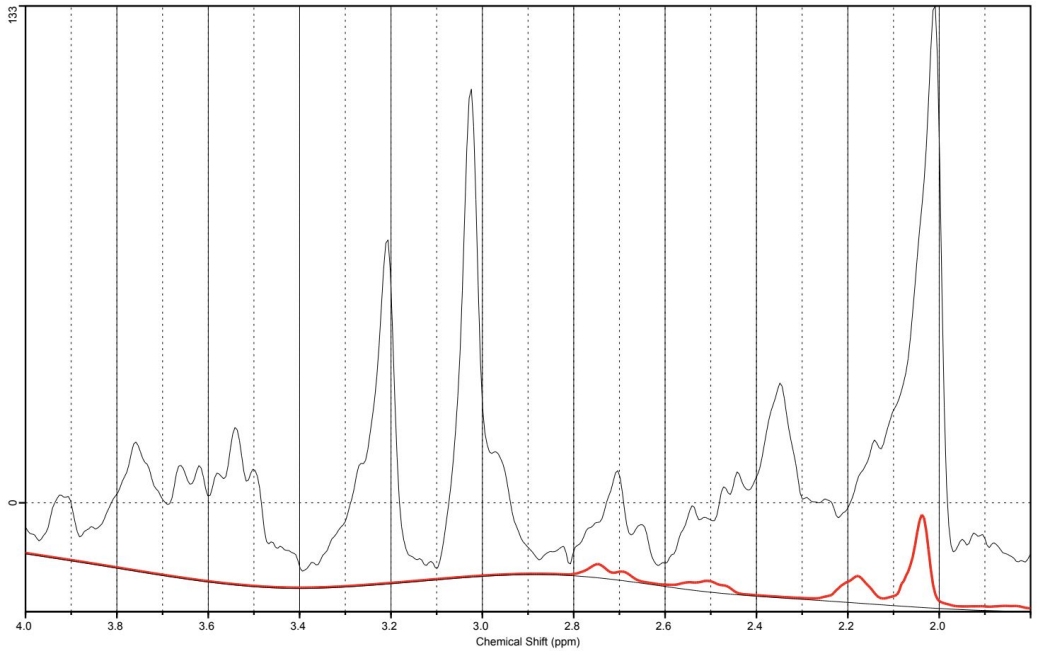


NAA + NAAG

- Role of NAA unclear; neuronal marker
  - Decreases with age
- NAAG can act as a transmitter; correlates with cognitive ability (Rahn et al., 2012)
- Separate measures likely unreliable (conversation with Victor, 2020)



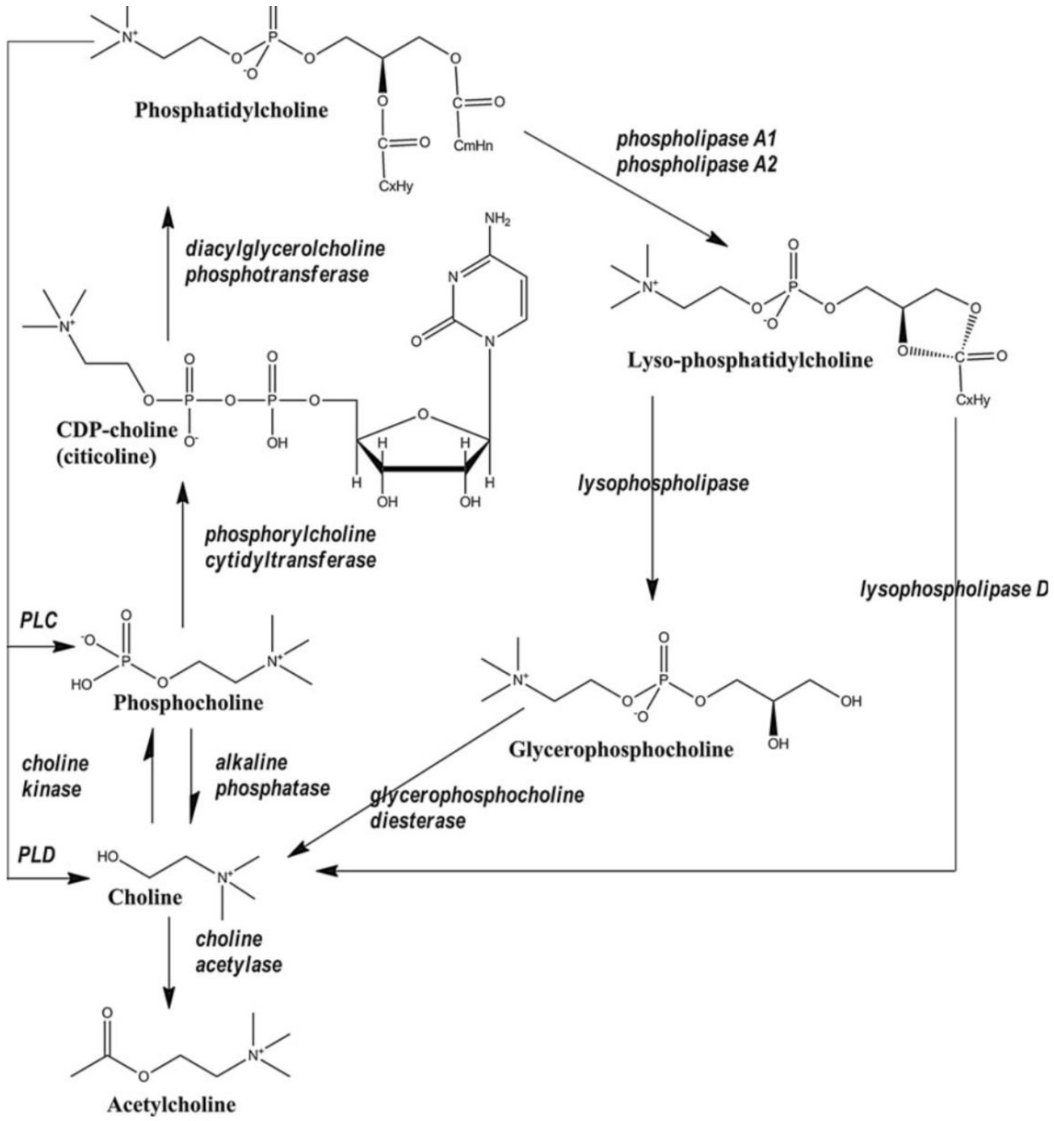
NAA



NAAG

Choline + GPC

- Role of Cho somewhat unclear
  - Membrane composition changes
- Cho correlated with acetylcholine
- Cho/PCho + GPC
  - Separate measures unreliable



Rae, 2014

Aspartate

- Amino acid
- Excitatory??
  - ¯_(ツ)_/¯
  - NMDA receptor agonist
  - Previously thought of as possibly excitatory NT, but recent evidence suggests otherwise (Herring et al., 2015)

Glucose

- Energy supply
- Levels of brain glucose related to levels of blood glucose more than to rate of brain glucose use (Rae, 2014)

Myoinositol

- Sugar synthesized from glucose
- Located mainly in glia
- Role:
  - membrane composition
  - second-messenger signaling pathways

Taurine

- Amino acid
- Role:
  - Osmoregulation
  - modulation of transmitter action via calcium