JÜLICH
FORSCHUNGSZENTRUM

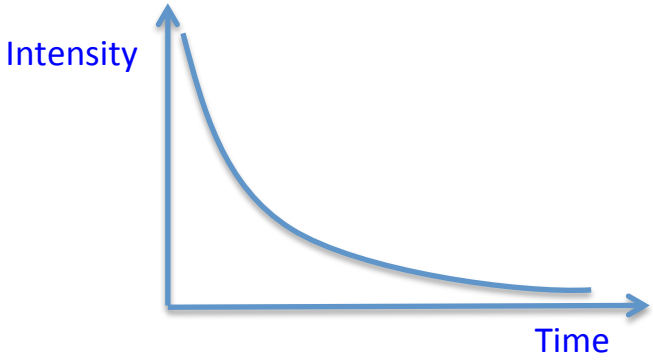
MR Spectroscopy

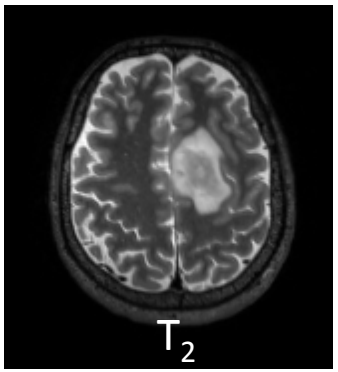
Introduction to Proton MR Spectroscopy

August 20th, 2018 | Jörg Mauler

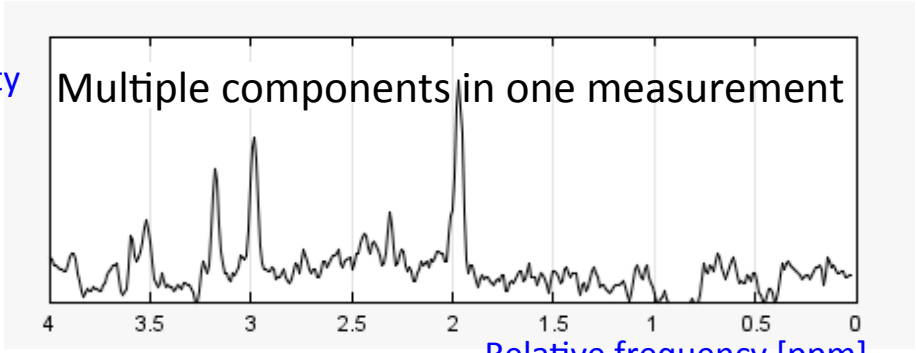
MR(I) versus MRS(I)

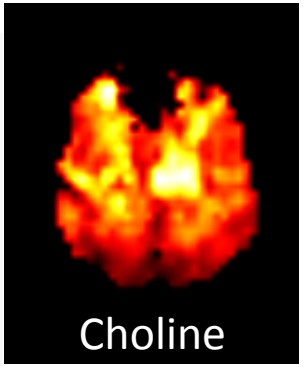
- Shared common principle, but:
  - MR(I): Relaxation/density/diffusion/… of water molecules



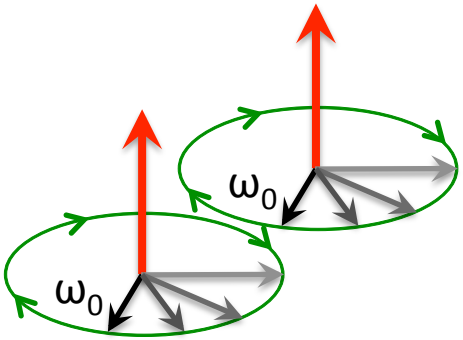


  - MRS(I): Chemical composition





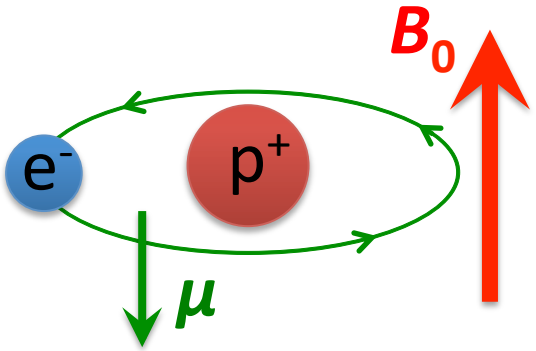
Chemical Shift



- Electrons neglected ➔ nuclei of the same kind resonate at the Larmor frequency $\omega_0 = \gamma B_0$

- Electrons included ➔ electrons e^- in the chemical environment shield the nuclei

- Electrons rotate about B_0



- Rotary motion of the e^- in the B_0 field ➔ induces magnetic moment μ
- μ has opposite orientation to B_0 ➔ lower effective field $B = B_0 (1 - \sigma)$

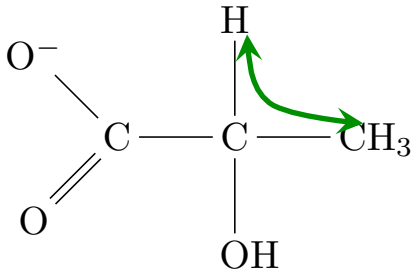
Larmor frequency $\omega_0 = \gamma B_0 (1 - \sigma)$

$$\delta\ [\text{ppm}] = \frac{\omega_0 - \omega_{\text{ref}}}{\omega_{\text{ref}}} \cdot 10^6$$

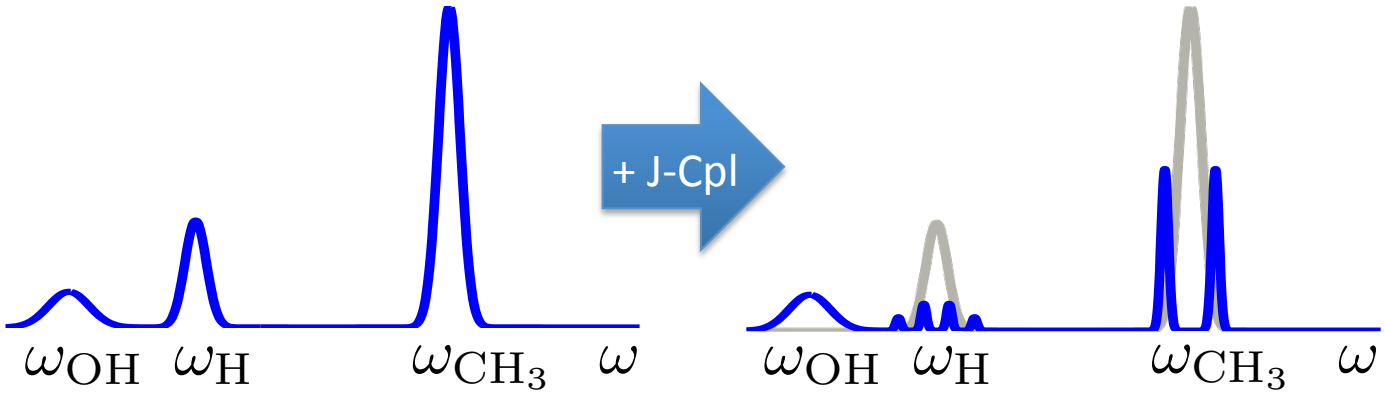
J-Coupling = Indirect Spin–Spin Coupling

- Direct spin-spin coupling ➔ averages out to zero in liquids.
- Indirect spin-spin coupling transmitted by bonding electrons
- The more bonds ➔ the lower the amplitude of the J-coupling

Lactate

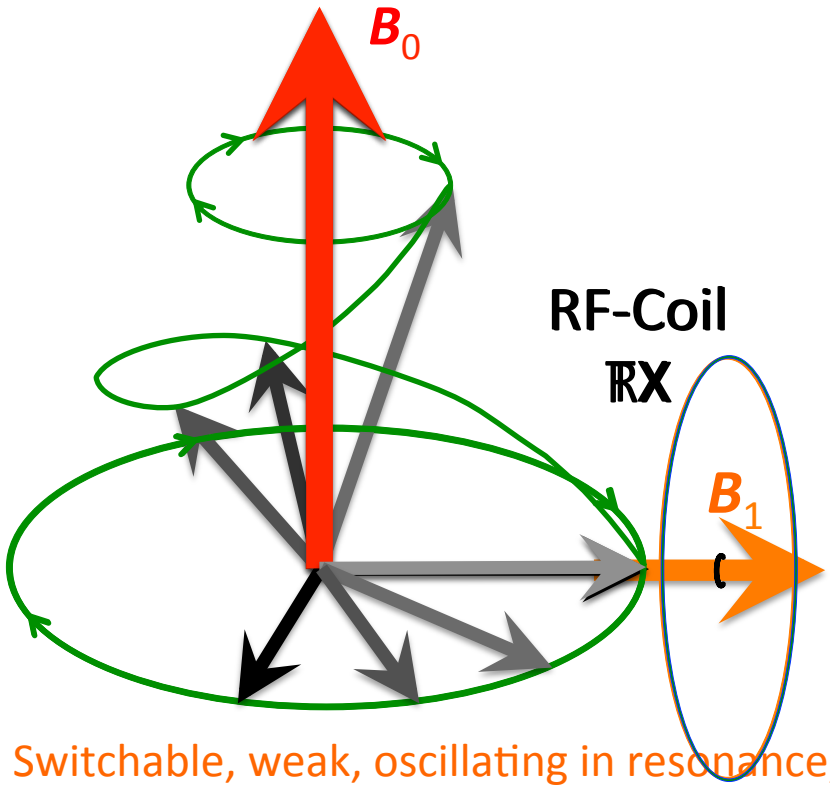


- Nucleus A coupled to a nucleus X ➔ symmetrically split spectrum, centred at the chemical shift frequency ν_A

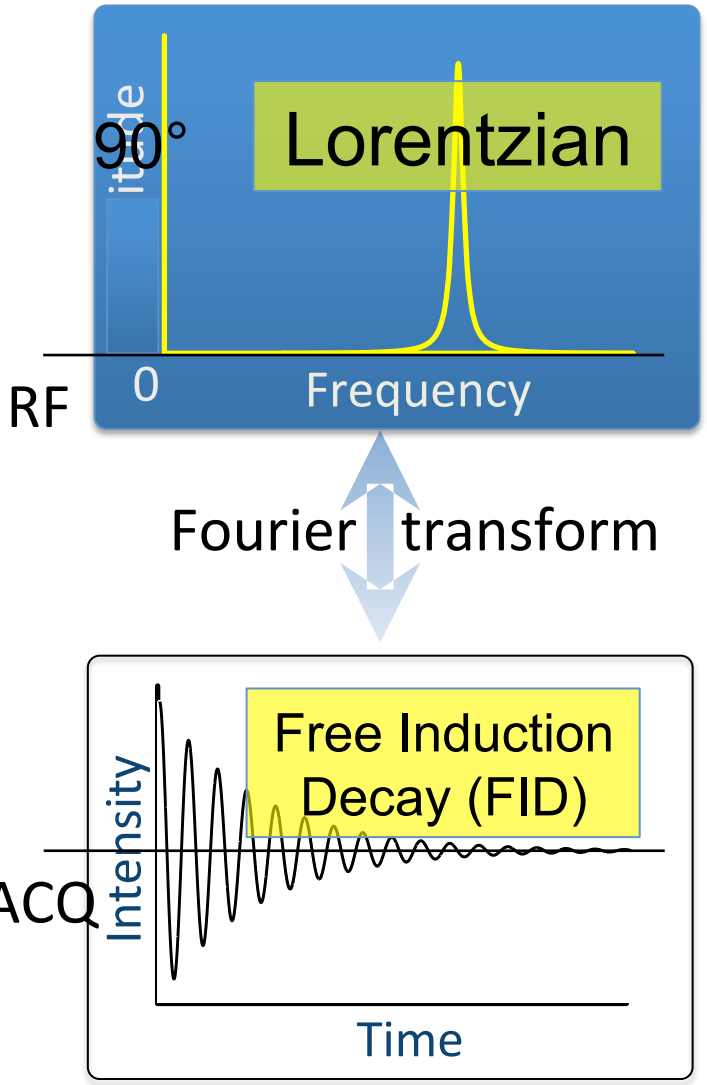


Pulse Acquire Experiment

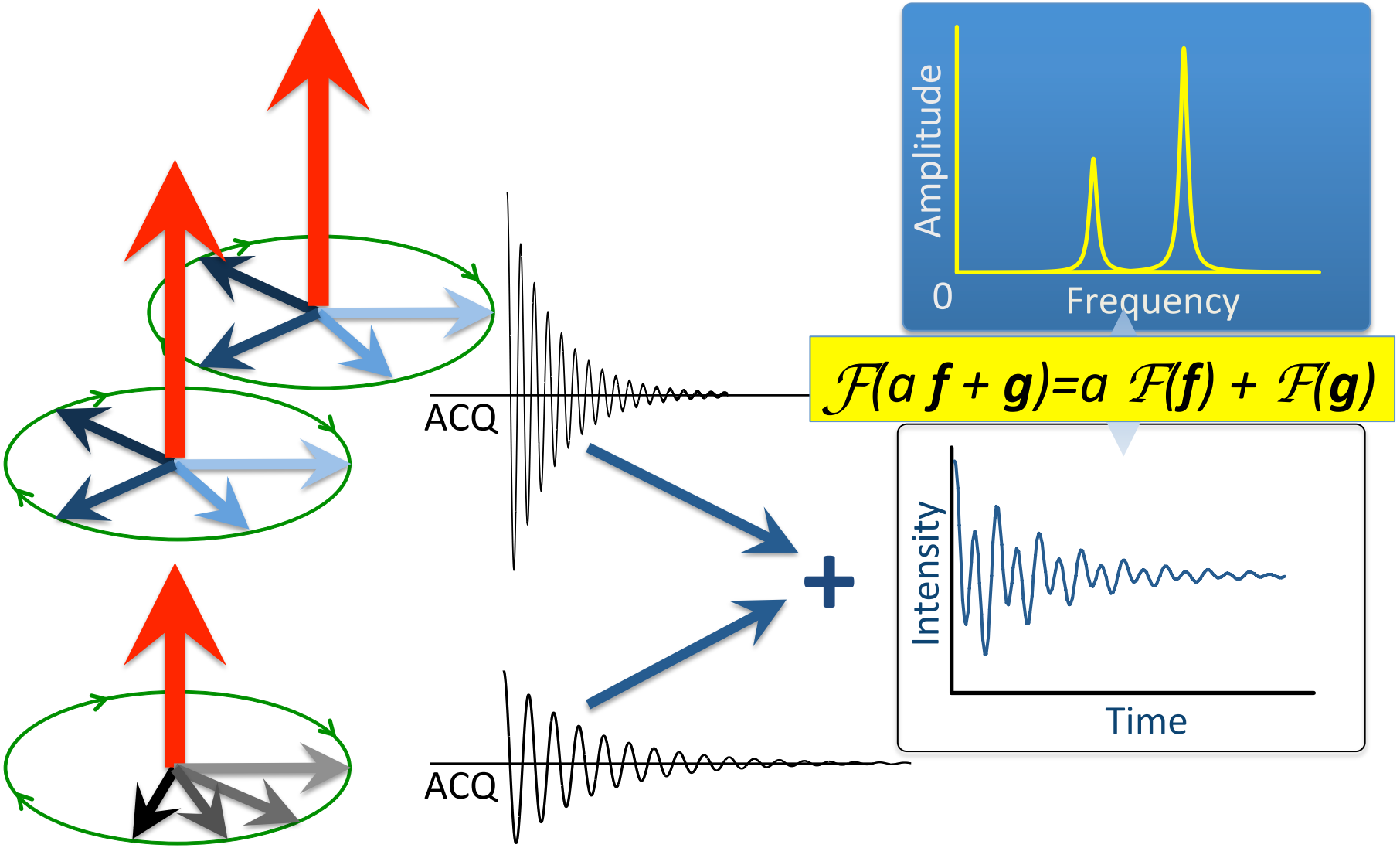
Static, strong magnetic field



Switchable, weak, oscillating in resonance, external magnetic field B_1



Pulse Acquire Experiment



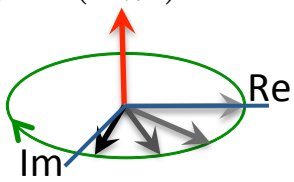
From the Raw Data to the Spectrum

- On-resonance pulse about +*y*

$$M_x = \sum_{n=1}^{N} M_{0,n} \cos(\Omega_n t) \quad \text{and} \quad M_y = -\sum_{n=1}^{N} M_{0,n} \sin(\Omega_n t)$$

- From magnetisation to complex signal

$$\boldsymbol{S} \propto \boldsymbol{M} \quad \Rightarrow \quad \boldsymbol{S}(t) = \boldsymbol{S}_x(t) + i\boldsymbol{S}_y(t)$$



- Single resonance, incl. T_2 relaxation

$$S(t) = (S_0 \cos(\Omega t) + iS_0 \sin(\Omega t))\, e^{-\frac{t}{T_2}} = S_0\, e^{i\Omega t} e^{-\frac{t}{T_2}}$$

- Zero order phase shift

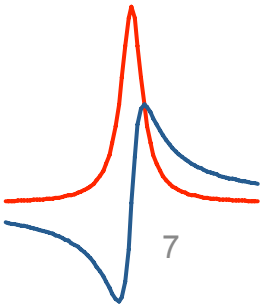
$$S_0\, e^{i(\Omega t + \phi)} e^{-\frac{t}{T_2}} \quad \Rightarrow \quad \text{introduction of} \quad \exp(i\widetilde{\phi}) \quad \text{with} \quad \phi + \widetilde{\phi} = 0$$

- Phase correction

$$\exp(i\widetilde{\phi}) S(t) = \exp(i\widetilde{\phi})\, S_0\, \exp(i\phi)\, \exp(i\Omega t - \frac{t}{T_2}) = S_0\, \exp(i\Omega t - \frac{t}{T_2})$$

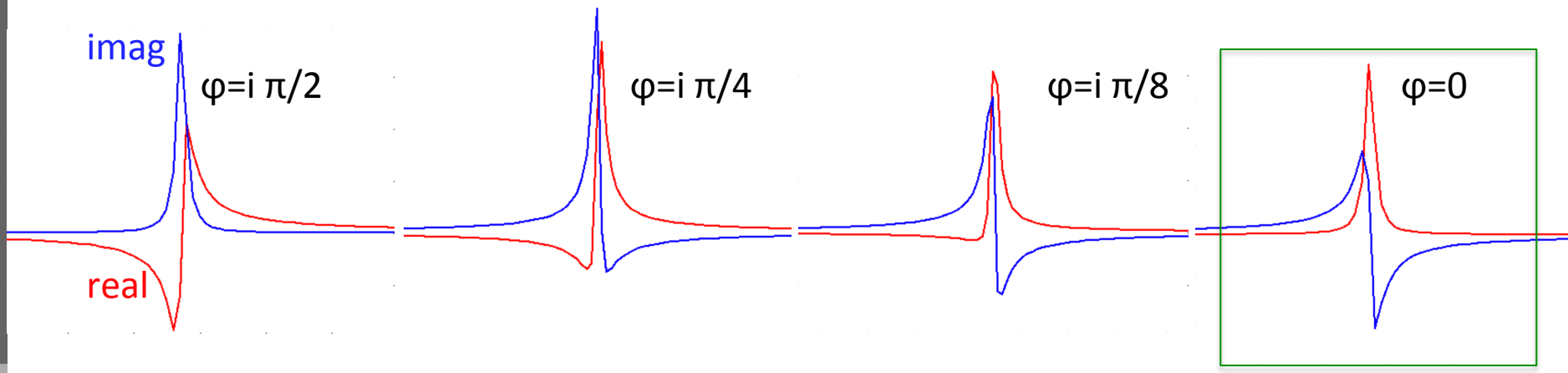
- Fourier transform ➔Lorentzian

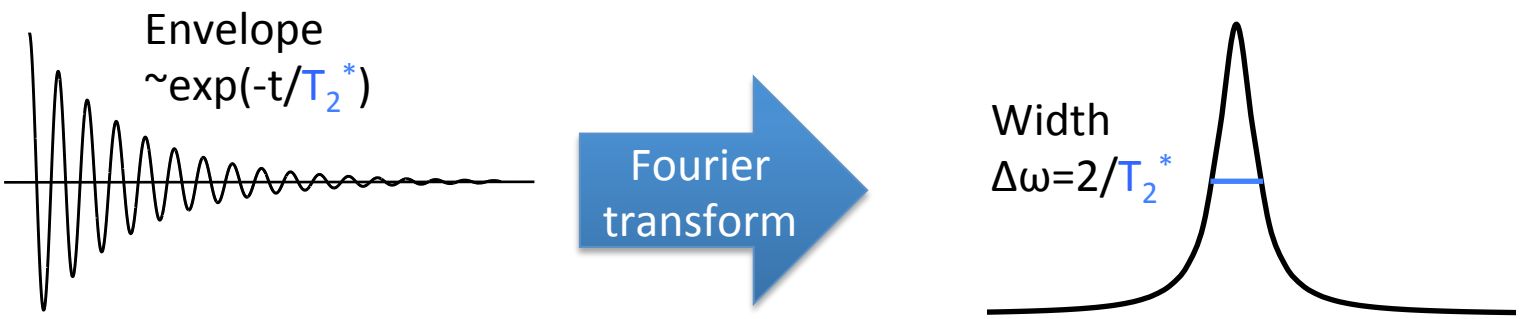
$$\mathcal{F}\{S_0 \exp(i\Omega t - \frac{t}{T_2})\} = S_0 \left(\frac{1}{\frac{1}{T_2} + i(\Omega - \Omega_0)} \right)$$



Lineshape

$$\mathcal{F}\{S_0 \exp(i\Omega t - \frac{t}{T_2})\} = S_0 \left(\frac{1}{\frac{1}{T_2} + i(\Omega - \Omega_0)} \right) = S_0 \left(\underbrace{\frac{\frac{1}{T_2^2}}{\frac{1}{T_2} + (\Omega - \Omega_0)^2}}_{\text{real}} - \underbrace{i \frac{(\Omega - \Omega_0)}{\frac{1}{T_2^2} + (\Omega - \Omega_0)^2}}_{\text{imag}} \right)$$





Data Processing – Analysis of the Spectrum

- Human subjects, H^+-MRS: up to 20 metabolites in the brain

N-Acetyl-Aspartate	Myo-inositol	Ascorbic acid
Total choline	Scyllo-inositol	Glutathione
Phosporylethalonamine	Glutamate	Taurine
Creatine	Glutamine	Aspartate
Glucose	γ-Amino-butyric acid	Acetate
Lactate	N-acetyl-aspartyl-glutamate	Homo-carnosine
Lipids	Glycine	Macro-molecules

- Neurotransmitters (+precursors), second messengers, energy metabolites, membrane turnover, osmoregulation, protein synthesis, anti-oxidants

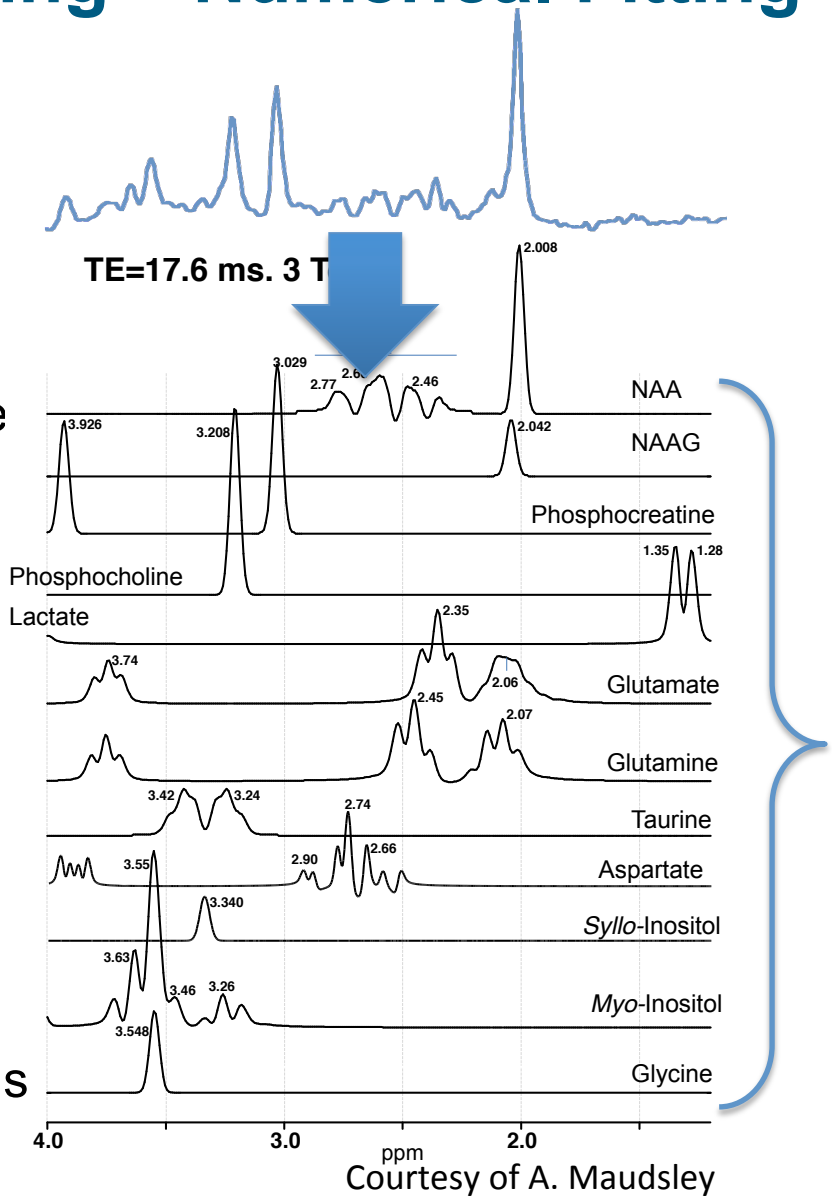
- Distinguishable and quantifiable by using numerical fitting algorithms
  - Time domain data
  - Frequency domain data (LCModel, Tarquin, jMRUI)

Data Processing – Numerical Fitting

Measured spectrum

Decomposition into a linear combination of the spectra of the pure compounds

Unspecific macromolecular baseline contributions
➔ polynomial functions

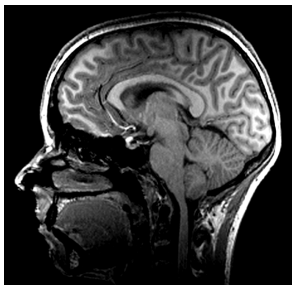


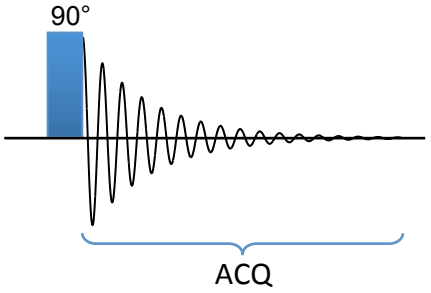
Courtesy of A. Maudsley

Basis spectra

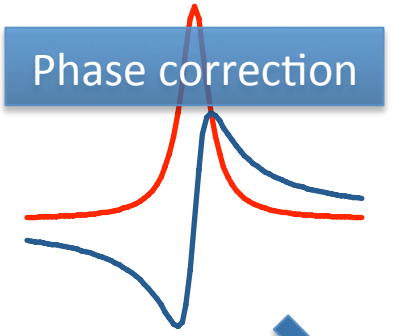
- Complete
- Simulated
- (Measured)

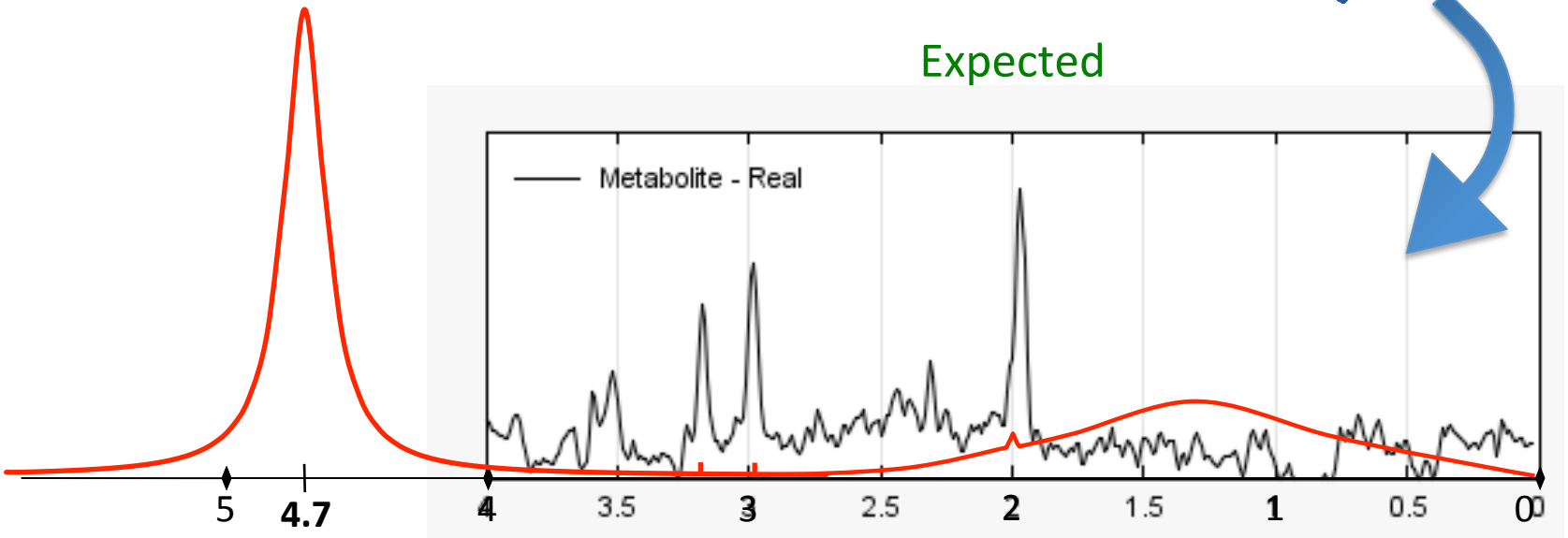
First Experiment





Fourier transform



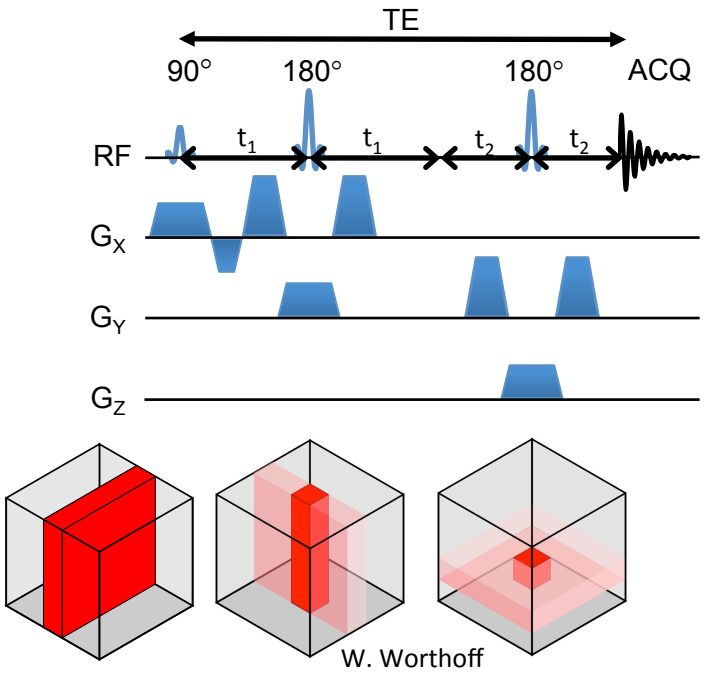


Spectrum almost useless because of the water and lipid signal

Spatial Localisation

- Signal acquisition only from relevant areas
  - Assignment of signals to their tissue of origin
  - Less contamination with extra-cranial lipids (+dedicated lipid suppr.)
- Restriction to smaller volume ➔ better B_0 homogeneity ➔ LW narrower

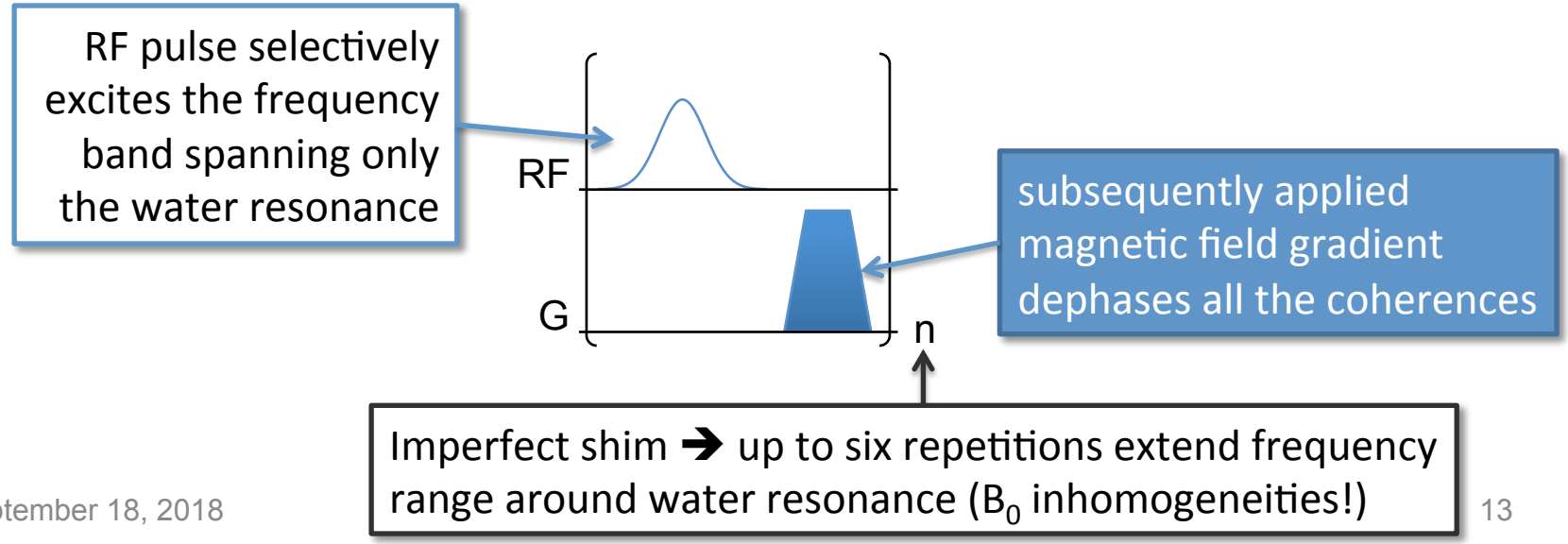
- Selectively refocus the magnetisation from the voxel under investigation
- Example: Point Resolved Spectroscopy (PRESS)
- Spin echo from the magnetisation located in the cuboid formed by the intersection of three slices
- Signal intensity high
- Minimum echo time long



Water Suppression, CHESS

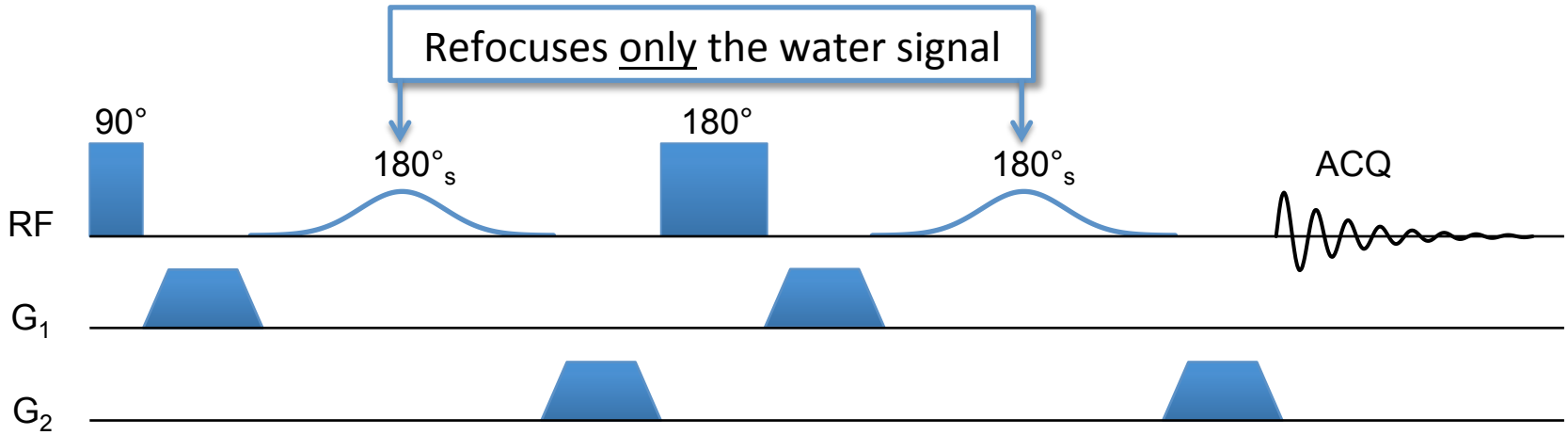
- Most abundant fraction of molecules: water
- Dominating signal at 4.7 ppm from the two H atoms of water
- Water suppression by exploiting
  - Relaxation, chemical shift, scalar coupling
  - Frequency selective excitation and re-focusing

- Example: Chemical shift selective (CHESS) water suppression



Water Suppression, MEGA (Mescher-Garwood)

- Excitation-based water suppr.: reappearing magnetisation due to T1 relax.
- Solution: frequency selective refocusing pulses
  - Water resonance experiences two refocusing pulses between two equal magnetic field gradients ➔ ***dephasing***
  - Metabolites: only one 180° pulse ➔ ***refocusing***

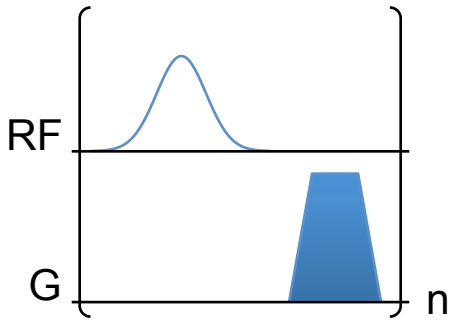


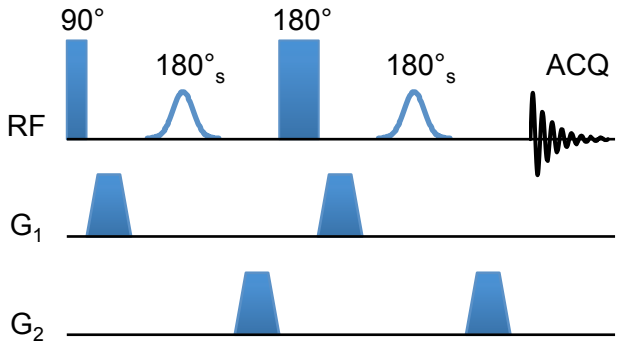
- Metabolites: Flip, dephasing (G_1), 180 pulse, rephasing (G_1), echo
- Water: Flip, dephasing (G_1), 180s pulse, 180 pulse, dephasing (G_1)

Water Suppression, CHESS vs. MEGA

- CHESS, excitation-based water suppression,
  - Drawback: reappearing magnetisation due to T1 relaxation
  - Advantage: short echo time

- MEGA, refocusing-based
  - Drawback: longer minimum TE (required by the introduction of these 180° pulses) ➔ vulnerability to T2 relaxation
  - Advantage: less sensitive to T1 relaxation

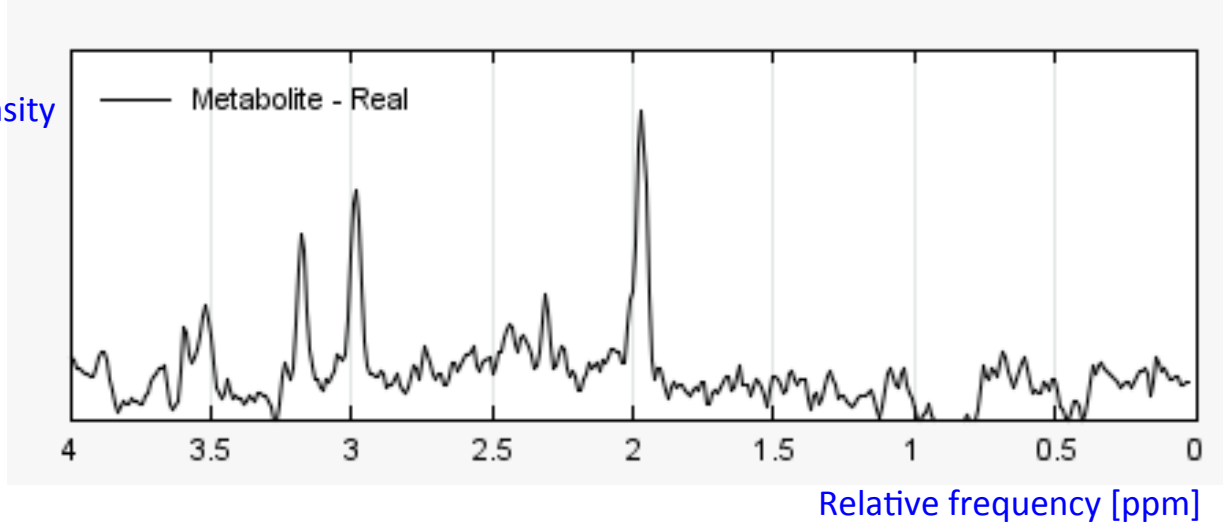




Complete MRS Experiment

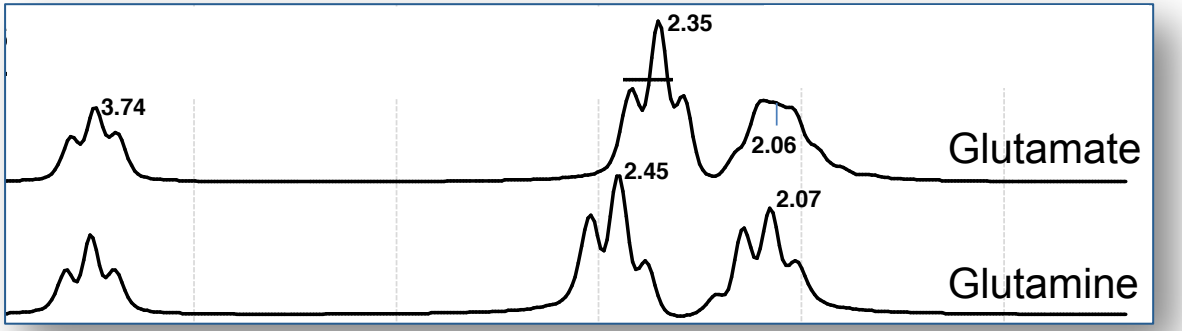
- PRESS with water suppression
- Fourier transform
- Phase correction
- Spectrum

Obtained



Advanced Techniques – Spectral Editing

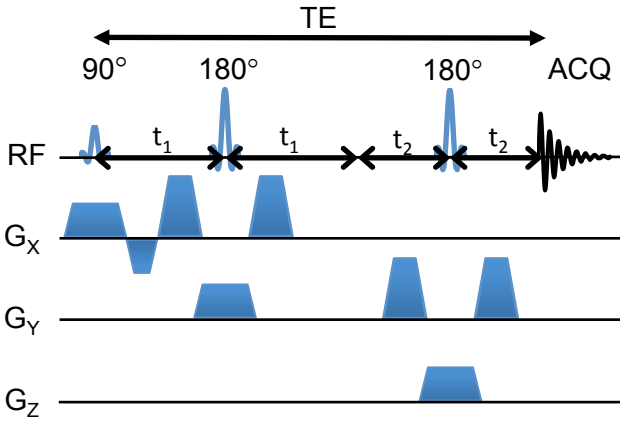
- MRS, so far shown: wide range of metabolites
- Metabolites may be difficult to be measured
  a) Low SNR ➔ increase number of acquisitions
  b) Overlap with peaks of other metabolites

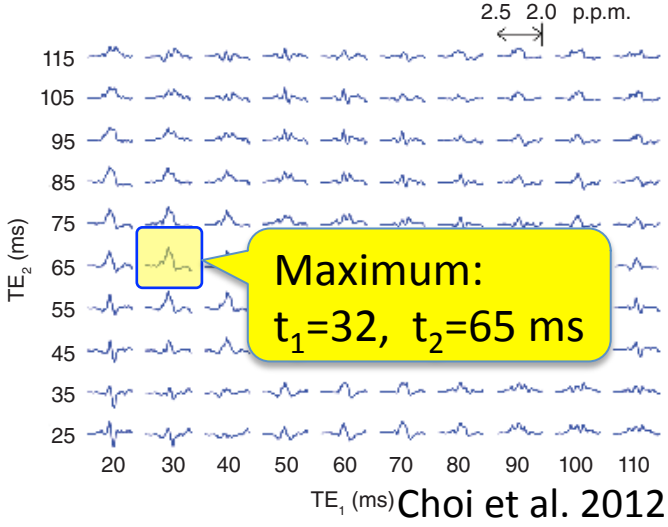


➔ Solution: editing pulse sequences (and/or higher field strength)
  - Separation of overlapping resonances
  - Tailored echo times, pulses, … such that specific resonance evolve

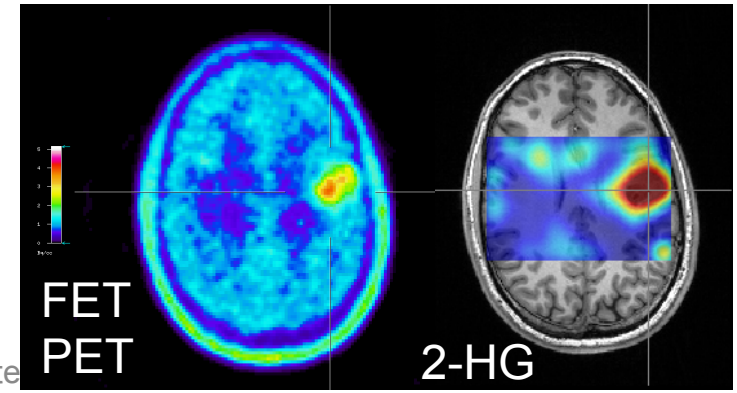
Spectral Editing: 2-Hydroxy-glutarate (2-HG)

- IDH-1/2 mutation relevant for prognosis of gliomas
- PRESS sequence, Quantum mechanical simulations
- Maximise resonance at 2.25 ppm under variation of t_1, t_2





Choi et al. 2012

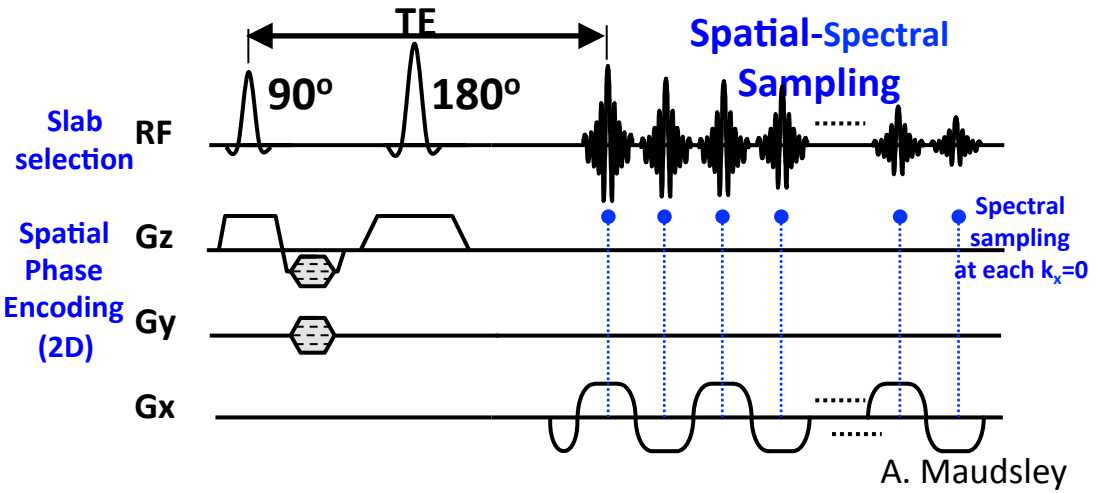


Courtesy of D. Tse

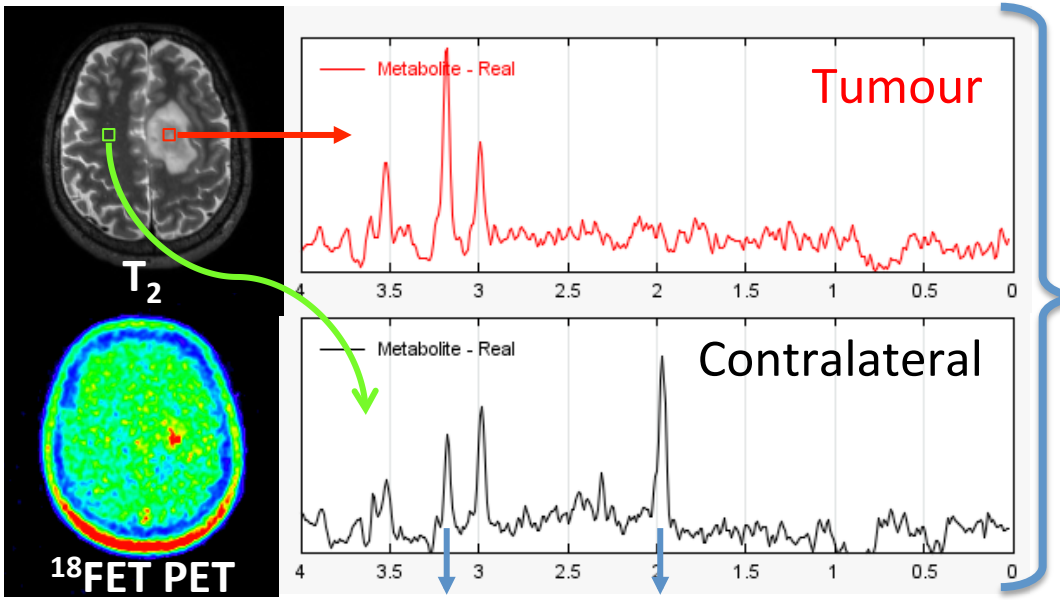
- Data acquisition in 2D matrix
- Numerical fitting with basis spectra
- Smoothing

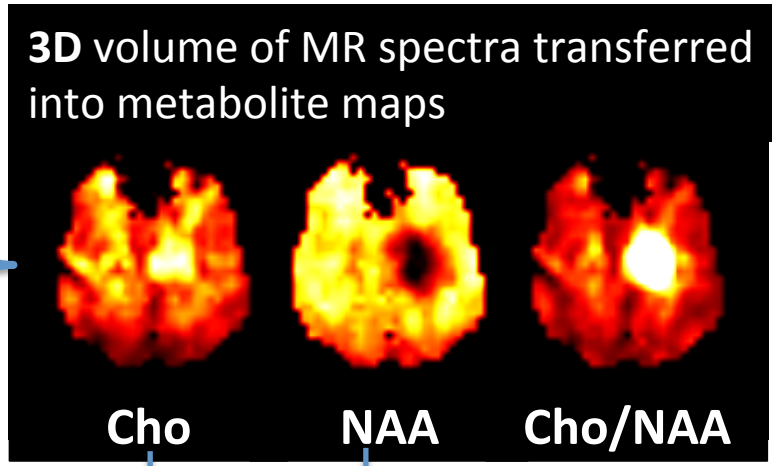
Advanced Techniques – 3D Spatial Resolution

- EPI read out
- 50 x 50 x 18 Voxel
- Vol 0.3 cm^3 each vxl
- TE=17 ms
- TR=1000-2000
- Acq time: ~16 min



A. Maudsley





Summary

- Chemical shift: shielding by the electrons shifts the Larmor frequency: $\omega_0 = \gamma B_0 (1 - \sigma)$, $\delta\,[\mathrm{ppm}] = \frac{\omega_0 - \omega_{\mathrm{ref}}}{\omega_{\mathrm{ref}}} \cdot 10^6$
- J-Coupling: transmitted by bonding electrons, splitting of the peaks
- Data processing:
  - FT, phase adjustment, numerical fitting of basis spectra
- Spatial localisation technique: PRESS
- Water suppression: CHESS, MEGA
- Spectral editing
- Full brain 3D spectroscopic imaging by using spatial-spectral sampling

Thank you for your attention !