Lecture #13
Spectral Editing

- Topics
  - Introduction
  - J-difference editing
  - Multiple quantum filtering
- Handouts and Reading assignments
  - de Graaf, Chapter 8.
  - van de Ven, 4.1, 4.2, 4.6, and 4.8

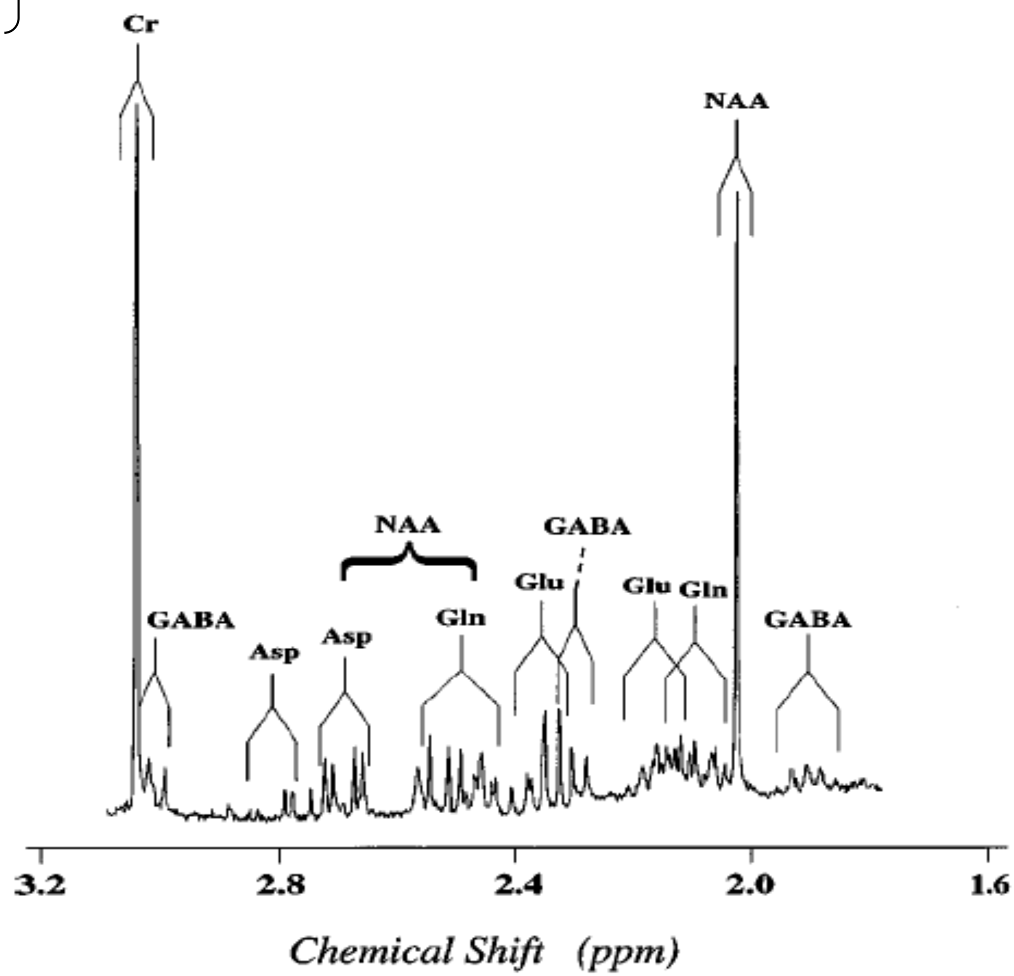
Introduction

- Even though, *in vivo* spectra are already simplified by concentration and relaxation time detection limits, there are nonetheless multiple overlapping peaks that can greatly complicate unambiguous peak assignments and quantification.
- In principle, spectral editing includes all techniques which can simplify a NMR spectrum, such as…
  - Water suppression
  - Spatial localization
  - TR/TE/TI variations
- We'll define spectral editing in the more restrictive sense of only including those techniques which utilize J coupling between spins to discriminate among metabolites.

In Vivo ^{1}H Spectrum

- We'll focus on the ^{1}H spectrum
  - ⇨ High sensitivity
  - ⇨ Small chemical shift range
  - ⇨ Same hardware as MRI

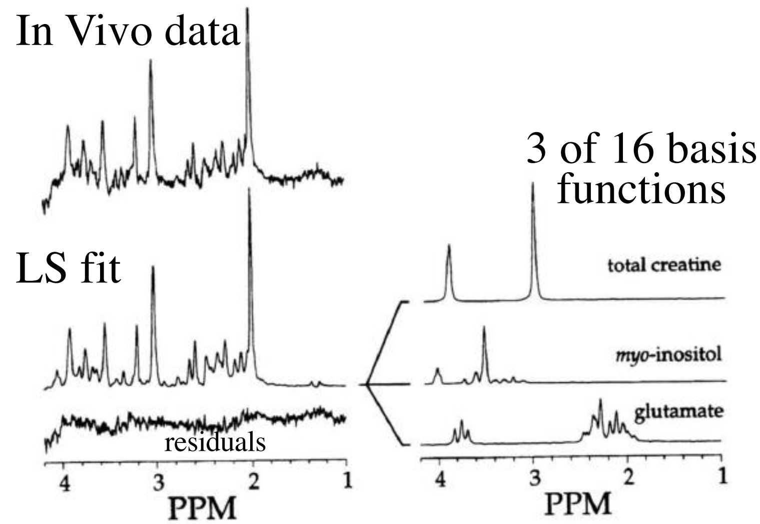
crowded ⇔ rich



Solutions

- Fit everything

e.g. least squares fit using spectra of *in vitro* metabolite solutions as basis functions (see Provencher *et al.* *MRM* 30:672-9, 1993.)

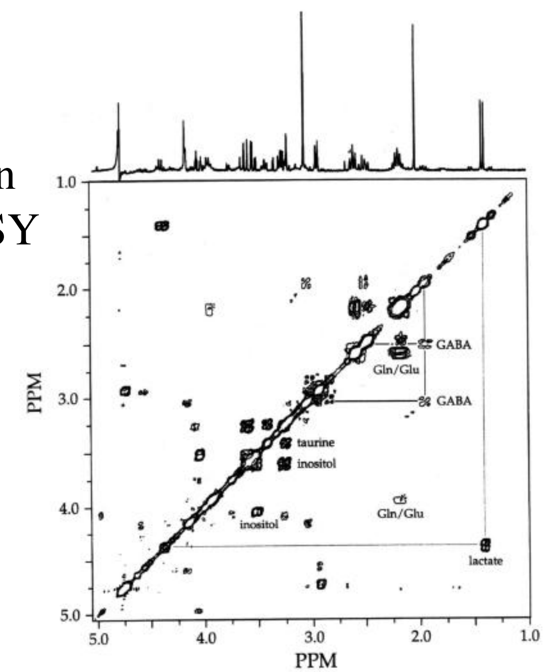


- Increase B_0

- Collect full 2D NMR spectrum

- Edit/simplify 1D NMR spectrum

Rat brain
9.4T COSY



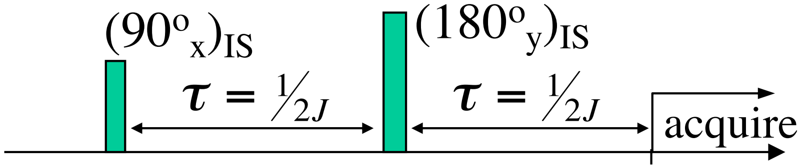
Refinements

- Strong versus weak coupling
  - In general, strong coupling requires considering the full density matrix
  - Weak coupling is appropriate to many in vivo applications (at least to a first approximation) and can be analyzed using the POF.
- Performance criteria
  - Sensitivity
  - Background discrimination

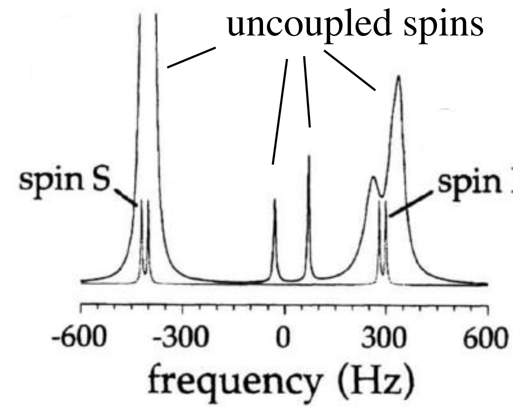
    CNR
  - Robustness to motion-artifacts (single- vs multi-shot)
  - Relaxation time considerations
- Spatial encoding - to be added later (next couple of lectures)

J-Difference Editing

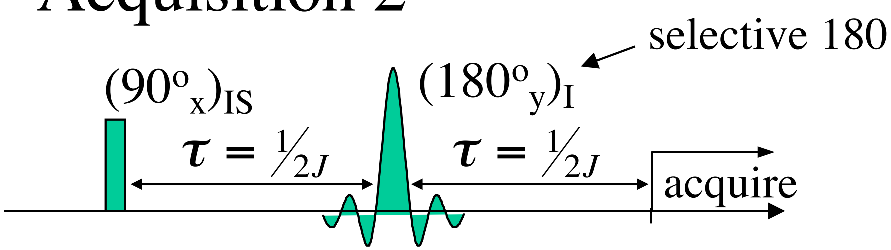
- Acquisition 1



$$\hat{I}_z \longrightarrow \hat{I}_y \longrightarrow \hat{I}_y \cos \pi J(\tfrac{1}{J}) - 2\hat{I}_x\hat{S}_z \sin \pi J(\tfrac{1}{J}) = -\hat{I}_y$$



- Acquisition 2

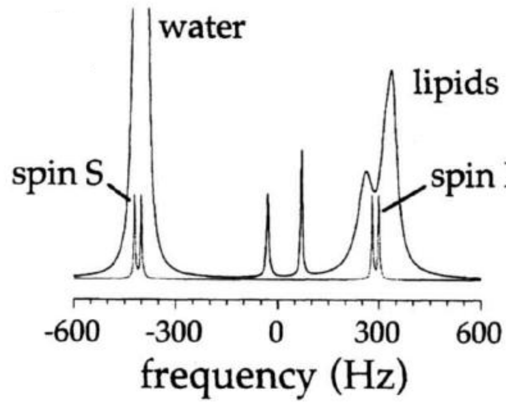


$$\hat{I}_z \longrightarrow \hat{I}_y \longrightarrow \hat{I}_y \cos \pi J(\tfrac{1}{2J} - \tfrac{1}{2J}) - 2\hat{I}_x\hat{S}_z \sin \pi J(\tfrac{1}{2J} - \tfrac{1}{2J}) = \hat{I}_y$$

- Algorithm: Edited signal = Acq2-Acq1

Example: Lactate-Lipid Discrimination

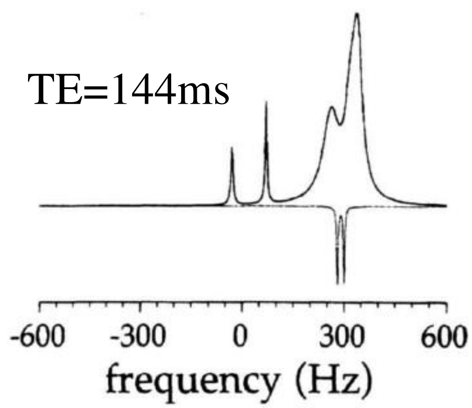
Spin echo:
Unedited spectrum



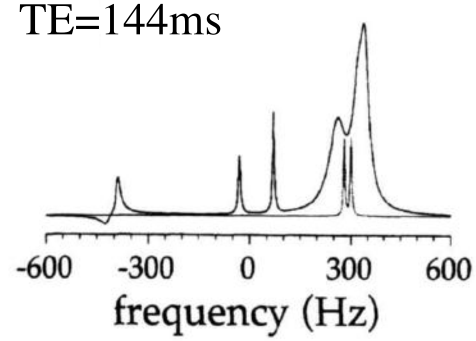
J=7 Hz

Acquisition 1:
Spin echo w/
nonselective 180

TE=144ms

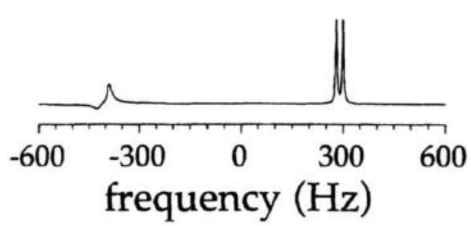


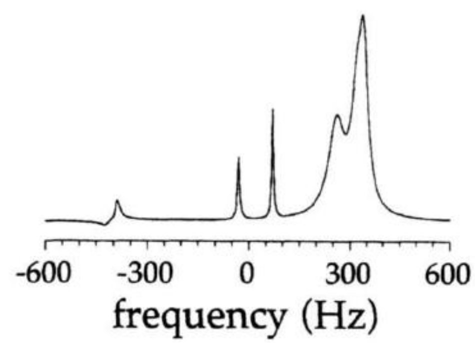
TE=144ms



Acquisition 2:
Spin echo w/
selective 180

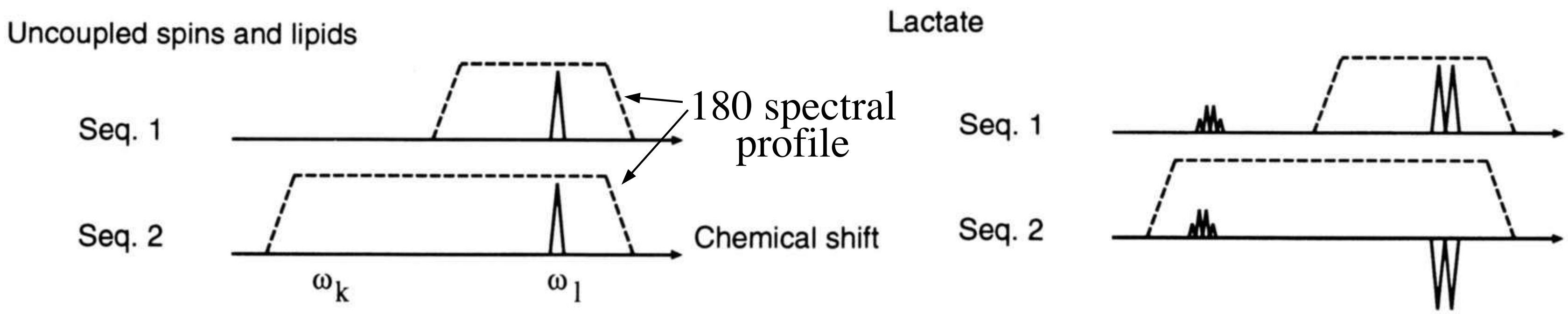
Difference
spectrum



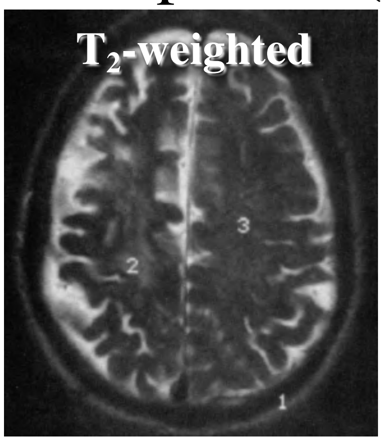


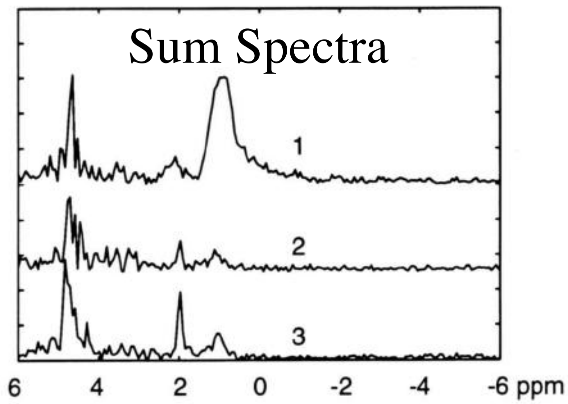
Sum
spectrum

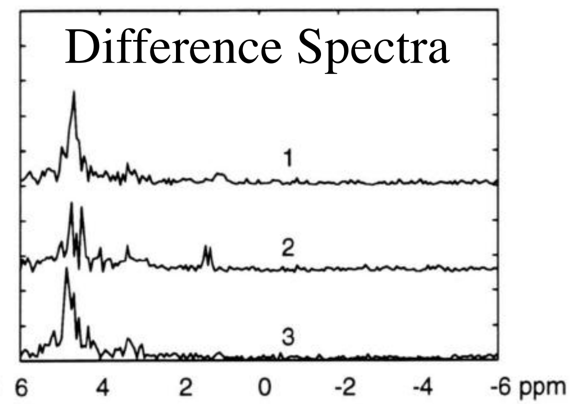
MRSI with J-editing for Lactate

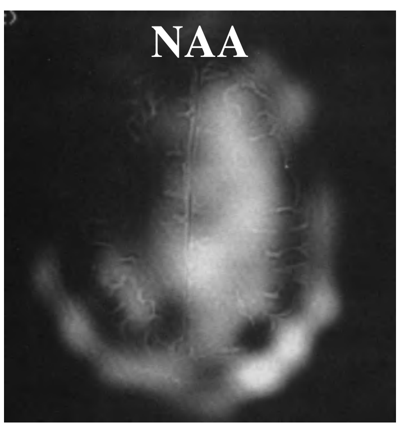


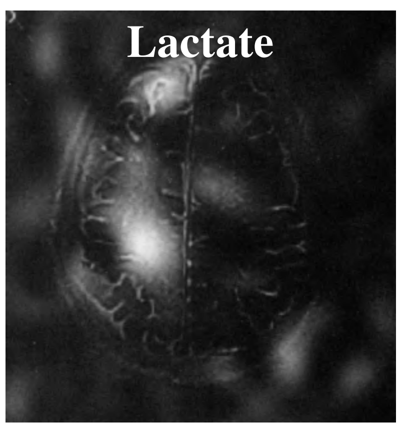
- MELAS patient (metabolic disorder with multiple strokes)

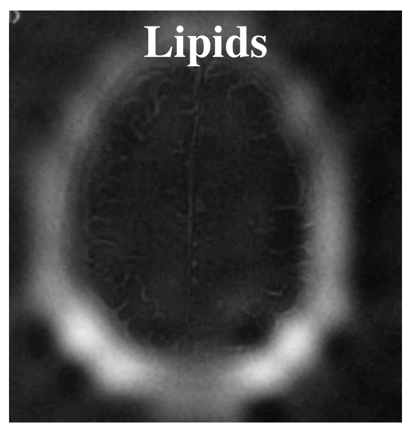




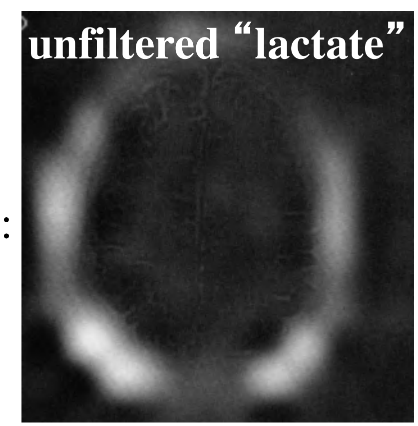








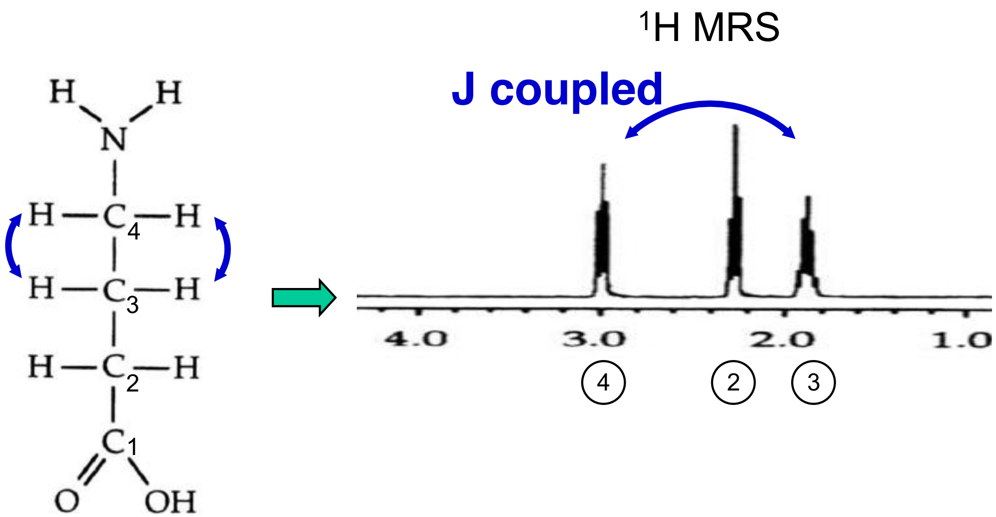
For comparison:



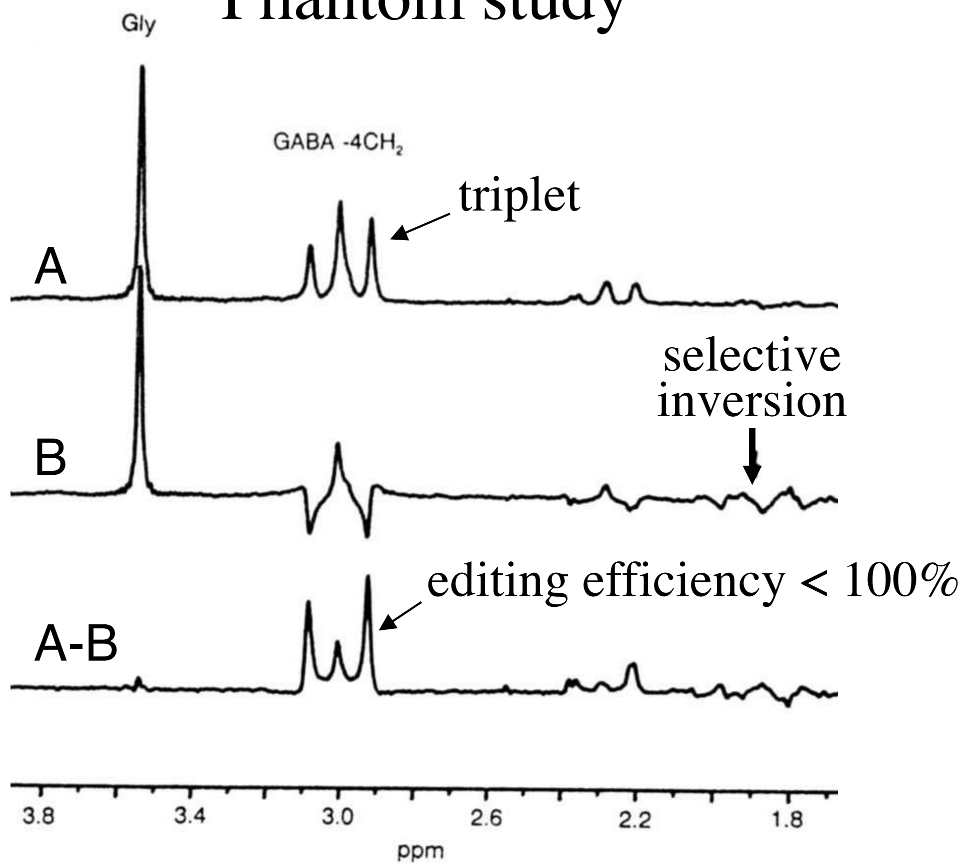
Adalsteinsson, et al, *MRM* 30:124-130, 1993.

J-editing for GABA

GABA



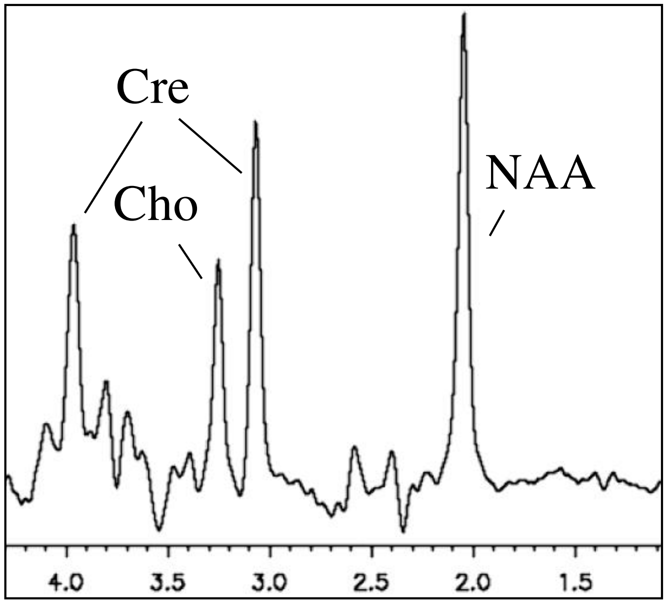
Phantom study



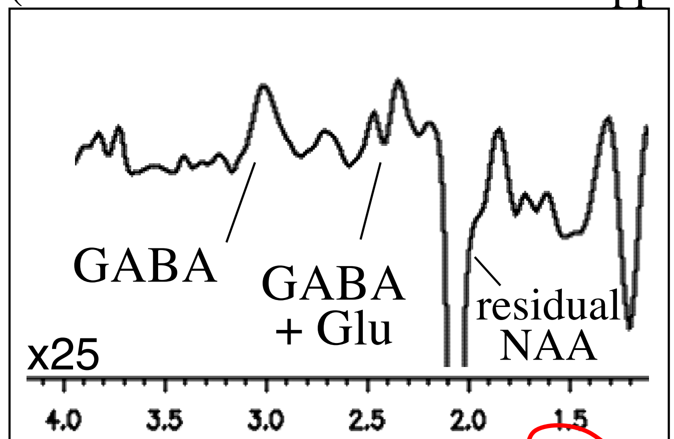
J-editing for GABA

- 3 T In Vivo Brain Spectra

Editing Off



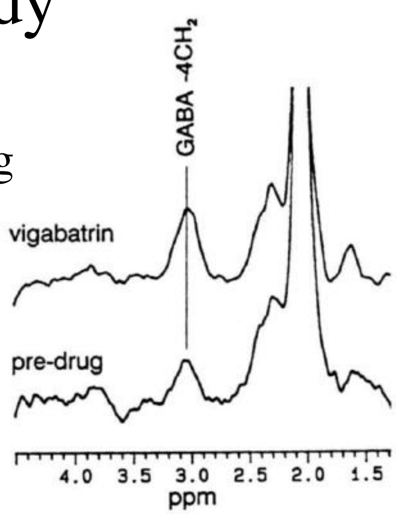
Difference spectrum
(w/ selective 180 centered at 1.9 ppm)

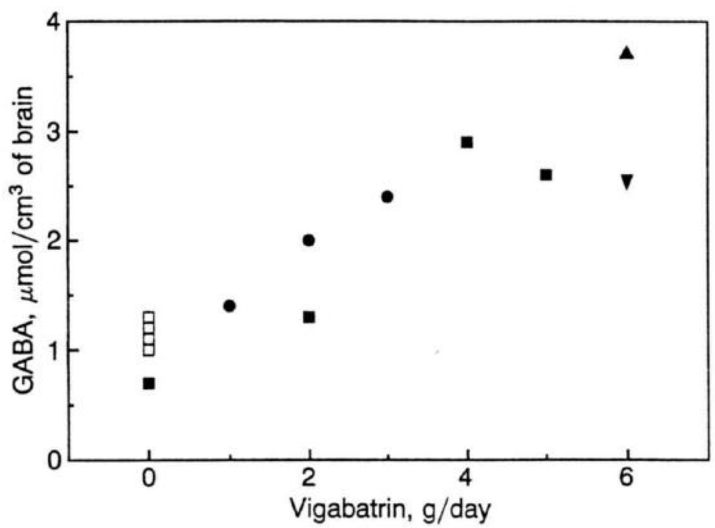


Parameters: TR/TE = 1500/68 ms, 18cc voxel, occipital lobe, 26 min acquisition, head coil

- Drug study

anti-seizure drug

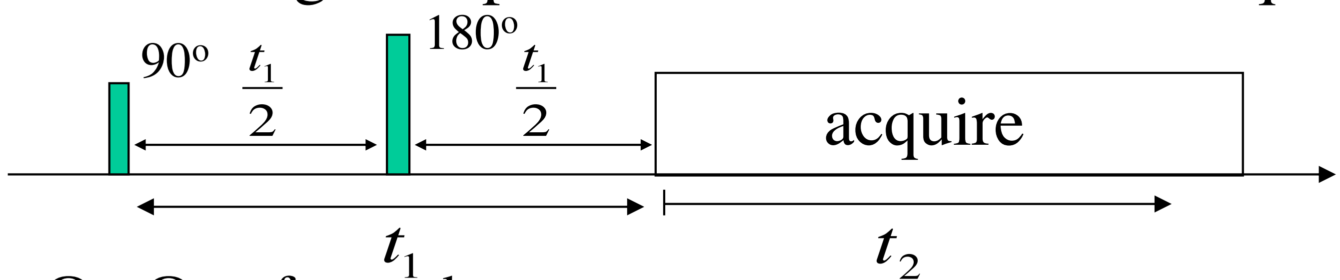




Note: quantitation complicated by some co-edited resonances

The Oversampled 2D-J Experiment

- J-difference editing is a special case of a full 2D-J acquisition



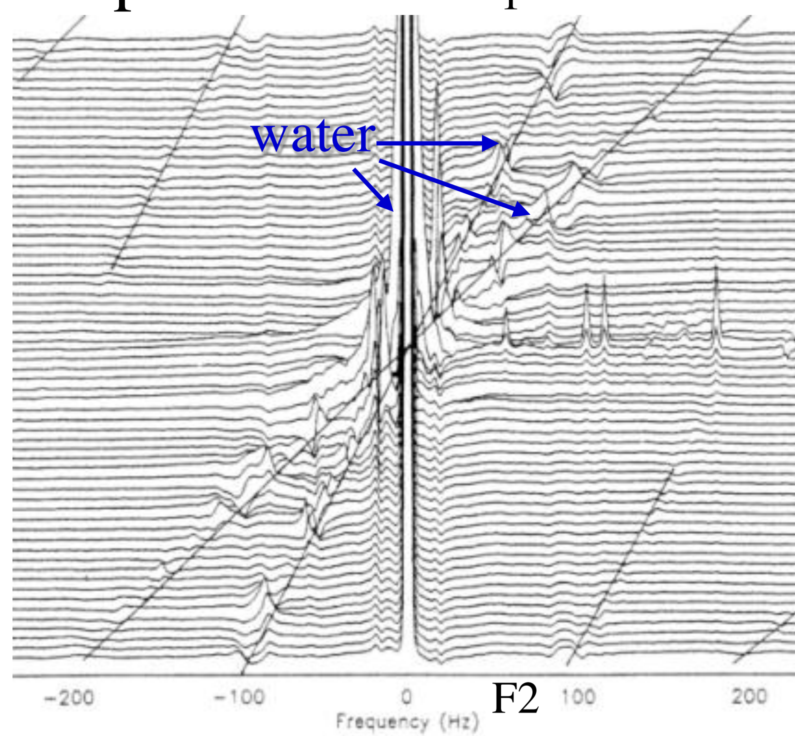
Ω_I, Ω_I refocused

$\therefore$ only J evolution during t_1

Both J and Ω evolution during t_2

- Acquire data for multiple values of t_1. 2D-FFT yield 2D-J spectrum.

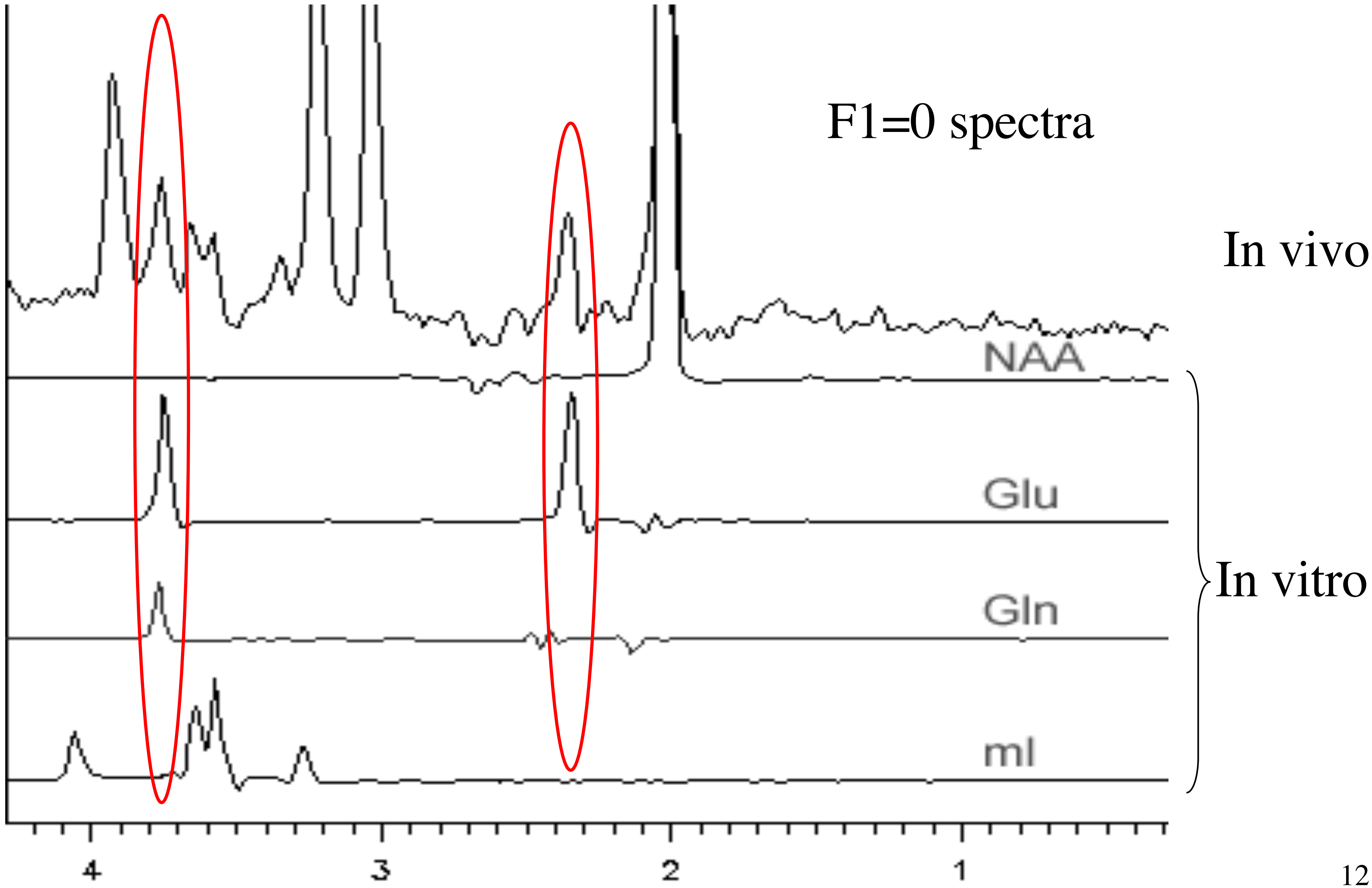
Hurd, et al., *MRM* **40**:343-347, 1998



J(0)="TE-averaged" spectrum

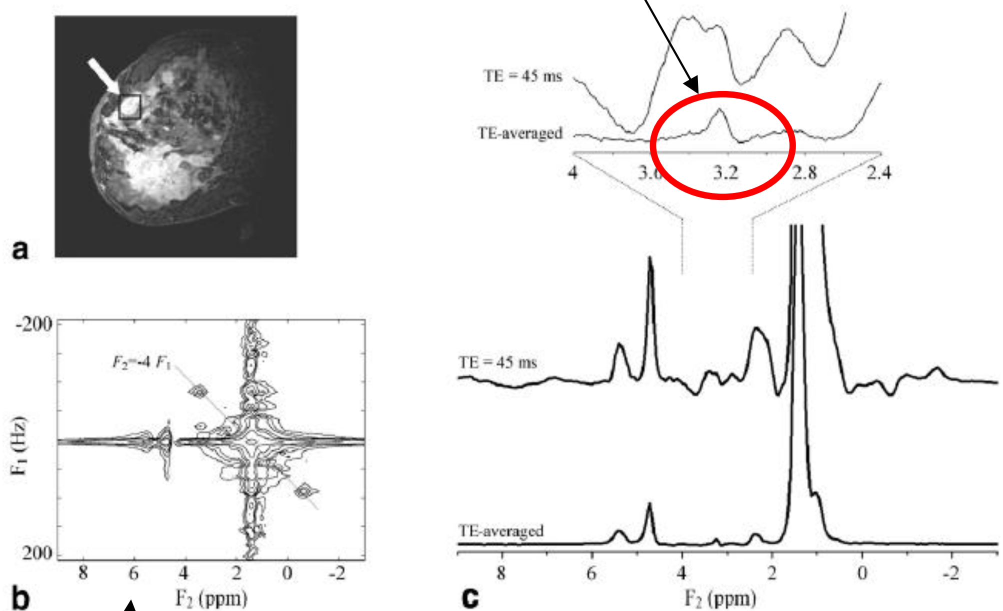
F1

3 T "TE-averaged" Normal Gray Matter Spectrum

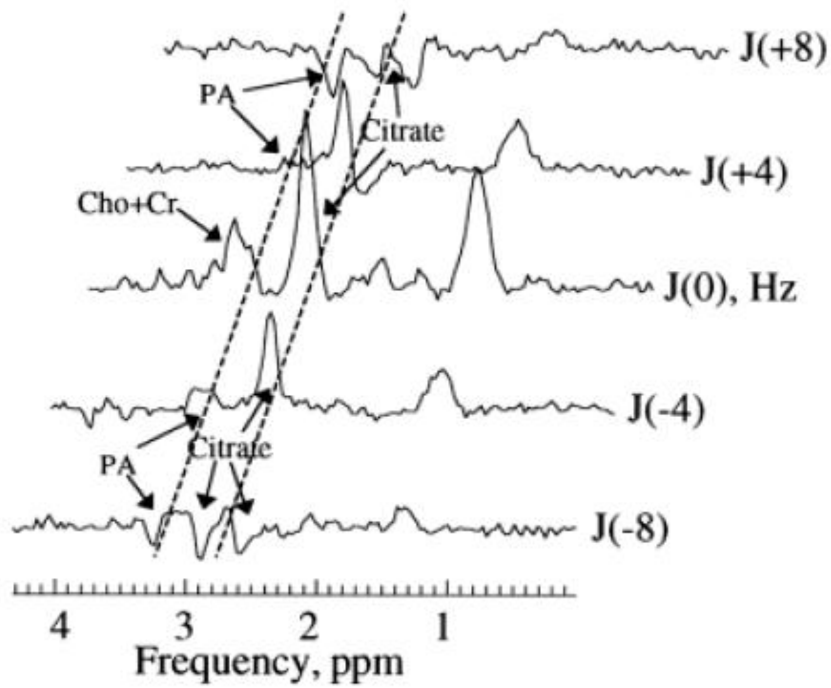


The Oversampled 2D-J Experiment

elevated choline



Breast cancer



Prostate

2D-J spectrum

Summary: J-editing

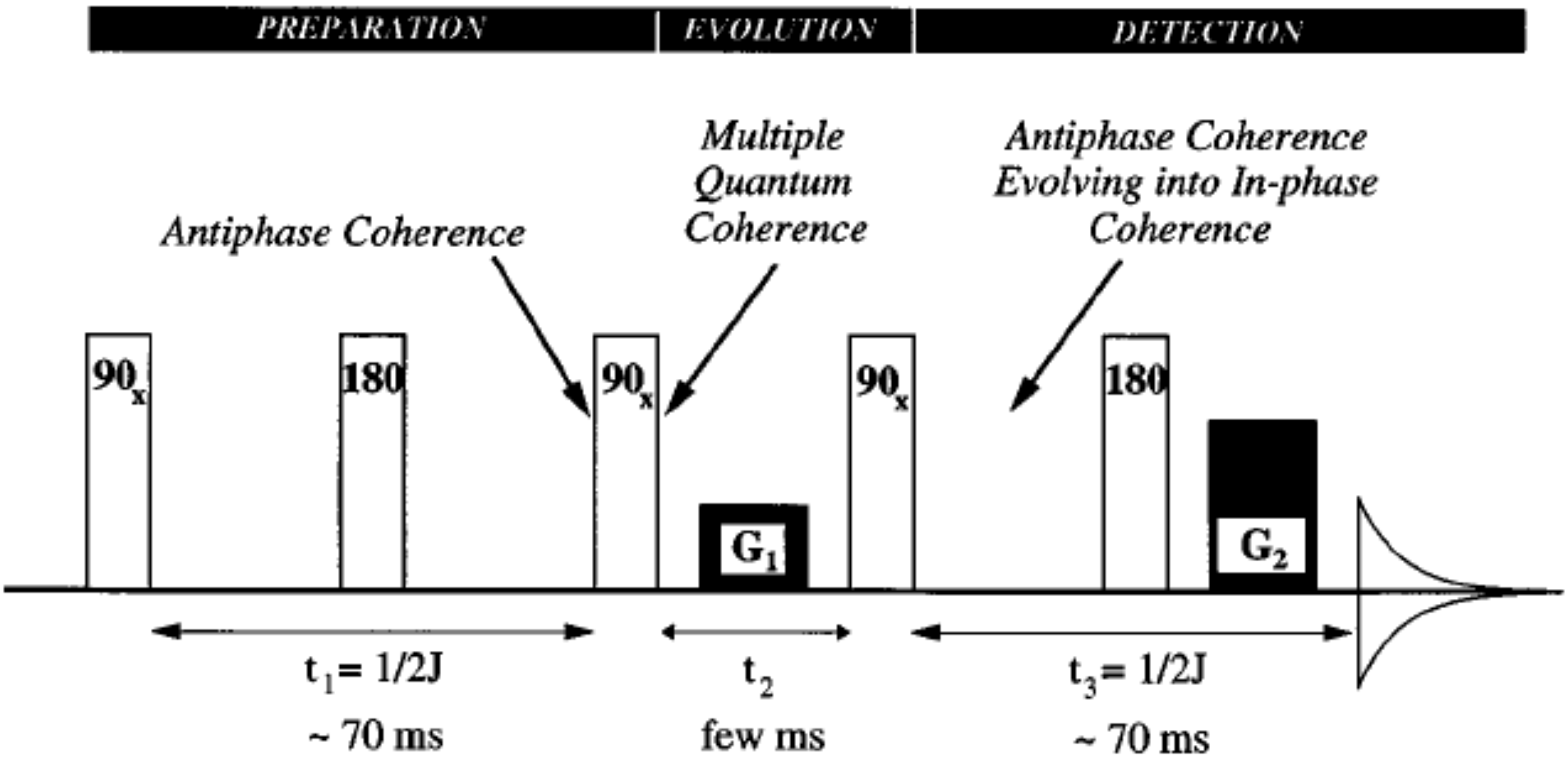
- Positives
  - Simple, robust
  - High sensitivity
  - High specificity
- Negatives
  - Subtraction artifacts due to …

    … motion

    … hardware instabilities

    … minor differences in spin dynamics between pulse sequences (e.g. slice profiles)

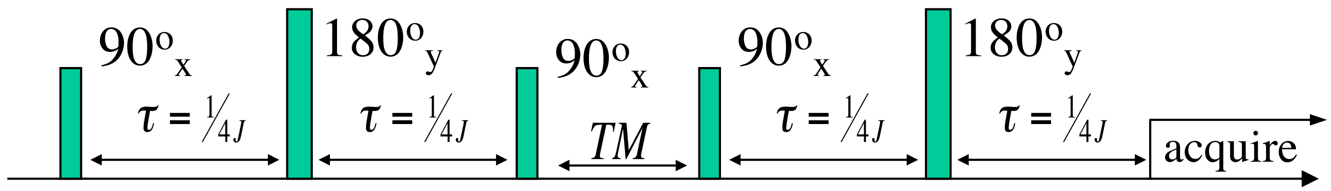
Generic Multiple-Quantum Filter



- 180s used to refocus chemical shift
- Selection of coherences via phase cycling or use of gradients

DQ Filter - POF

- Consider a three spin system where *I* and *S* are J-coupled and *R* is an uncoupled spin we wish to suppress (for now, assume *TM* is very short).



$$\hat{I}_z + \hat{S}_z + \hat{R}_z$$

$$-\underbrace{(2\hat{I}_x\hat{S}_z + 2\hat{I}_z\hat{S}_x)}_{\text{antiphase}} + \hat{R}_y$$

$$-\underbrace{(2\hat{I}_x\hat{S}_y + 2\hat{I}_y\hat{S}_x)}_{\widehat{DQ}_y} - \hat{R}_z$$

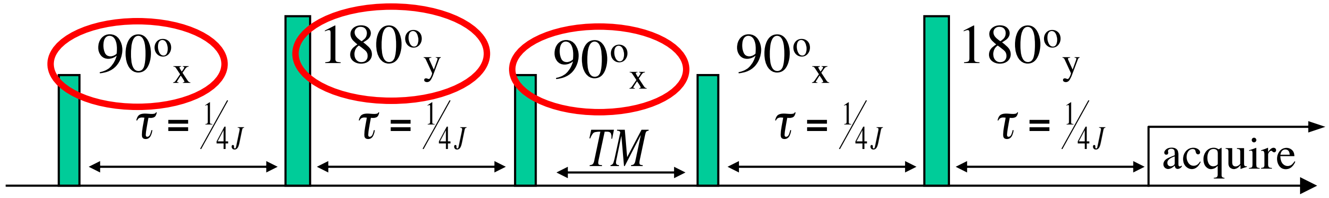
assuming TM is very short

$$\underbrace{(2\hat{I}_x\hat{S}_z + 2\hat{I}_z\hat{S}_x)}_{\text{antiphase}} - \hat{R}_y$$

$$\hat{I}_y + \hat{S}_y - \hat{R}_y$$

Only problem is that we haven't really filtered out anything!

Phase Cycling



- One solution: cycle the phases of the first three RF pulses

  Example of a 4-cycle experiment

Experiment (1st three pulses)	$\hat{\sigma}$ after readout pulse	$\hat{\sigma}$ at data acquisition
$90^\circ_x - \tau - 180^\circ_y - \tau - 90^\circ_x - \cdots$	$(2\hat{I}_x\hat{S}_z + 2\hat{I}_z\hat{S}_x) - \hat{R}_y$	$\hat{I}_y + \hat{S}_y - \hat{R}_y$
$90^\circ_y - \tau - 180^\circ_{-x} - \tau - 90^\circ_y - \cdots$	$-(2\hat{I}_x\hat{S}_z + 2\hat{I}_z\hat{S}_x) - \hat{R}_y$	$-\hat{I}_y - \hat{S}_y - \hat{R}_y$
$90^\circ_{-x} - \tau - 180^\circ_{-y} - \tau - 90^\circ_{-x} - \cdots$	$(2\hat{I}_x\hat{S}_z + 2\hat{I}_z\hat{S}_x) - \hat{R}_y$	$\hat{I}_y + \hat{S}_y - \hat{R}_y$
$90^\circ_{-y} - \tau - 180^\circ_x - \tau - 90^\circ_{-y} - \cdots$	$-(2\hat{I}_x\hat{S}_z + 2\hat{I}_z\hat{S}_x) - \hat{R}_y$	$-\hat{I}_y - \hat{S}_y - \hat{R}_y$

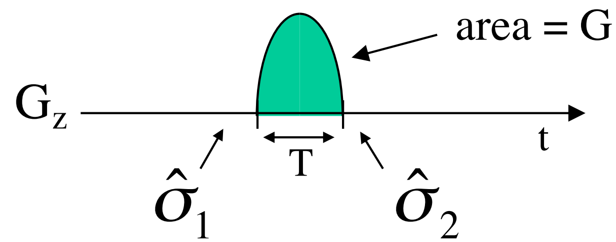
filter = (1)-(2)+(3)-(4)

- Problem: no longer single-shot editing

Gradients

- Consider the effect of the application of a gradient pulse on $\hat{\sigma}$.

  Assume the gradient is a z gradient:



  The gradient adds to B_0 such that $\hat{H}$ becomes a function of position.

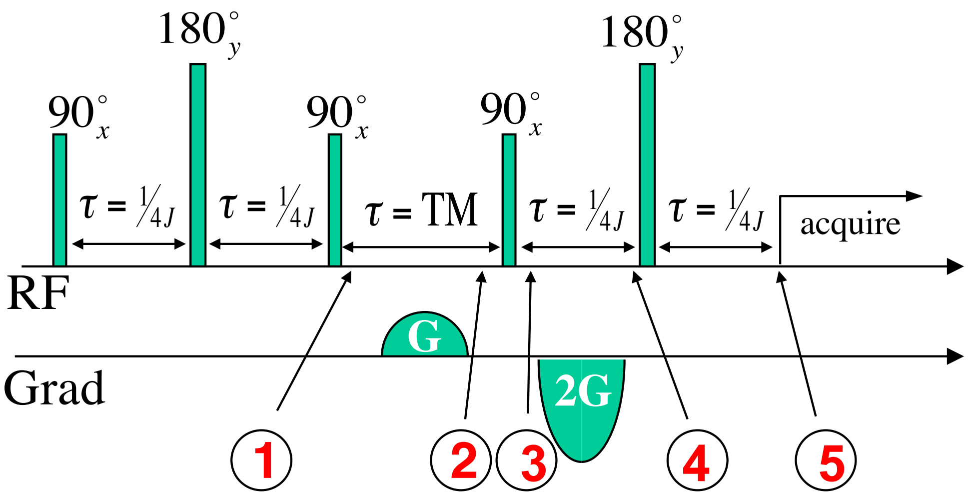
$$\hat{H}_G = -\gamma z \hat{I}_z \int_0^T G_z(t)\,dt \quad \Rightarrow \quad \hat{\sigma}_1 \xrightarrow{\hat{I}_z(zGT)} \hat{\sigma}_2$$

- Example: $\hat{\sigma}_1 = \hat{I}_y$ and gradient area such that π rads per unit z.

$$\hat{I}_y \xrightarrow{\hat{I}_z(\pi z)} \hat{I}_y \cos \pi z + \hat{I}_x \sin \pi z$$

…to get the total coherence, we would then need to integrate over z.

DQ Filtering with Gradients



$\hat\sigma$ at various points in time (ignoring chemical shift terms) is …

① $-2\hat I_x\hat S_y - 2\hat I_y\hat S_x \xrightarrow{\hat I_z(\pi z)} \xrightarrow{\hat S_z(\pi z)} (-2\hat I_x\hat S_y - 2\hat I_y\hat S_x)\cos 2\pi z + (-2\hat I_x\hat S_x + 2\hat I_y\hat S_y)\sin 2\pi z$ ②

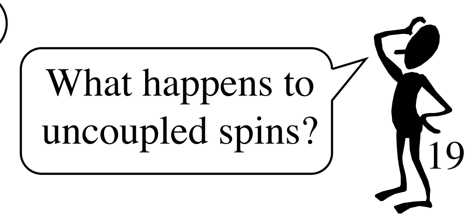
$\xrightarrow{\hat I_x(\pi/2)} \xrightarrow{\hat S_x(\pi/2)} (2\hat I_x\hat S_z + 2\hat I_z\hat S_x)\cos 2\pi z + (\underbrace{-2\hat I_x\hat S_x + 2\hat I_z\hat S_z})\sin 2\pi z$ ③

This term involves unobservable MQ coherences and can be ignored (we are going to apply no more 90s so it will never evolve into transverse magnetization).

③ $\xrightarrow{\hat I_z(-2\pi z)} \xrightarrow{\hat S_z(-2\pi z)} \underbrace{(2\hat I_x\hat S_z + 2\hat I_z\hat S_x)\cos^2 2\pi z + (\hat I_y + \hat S_y)\sin 2\pi z\cos 2\pi z}$

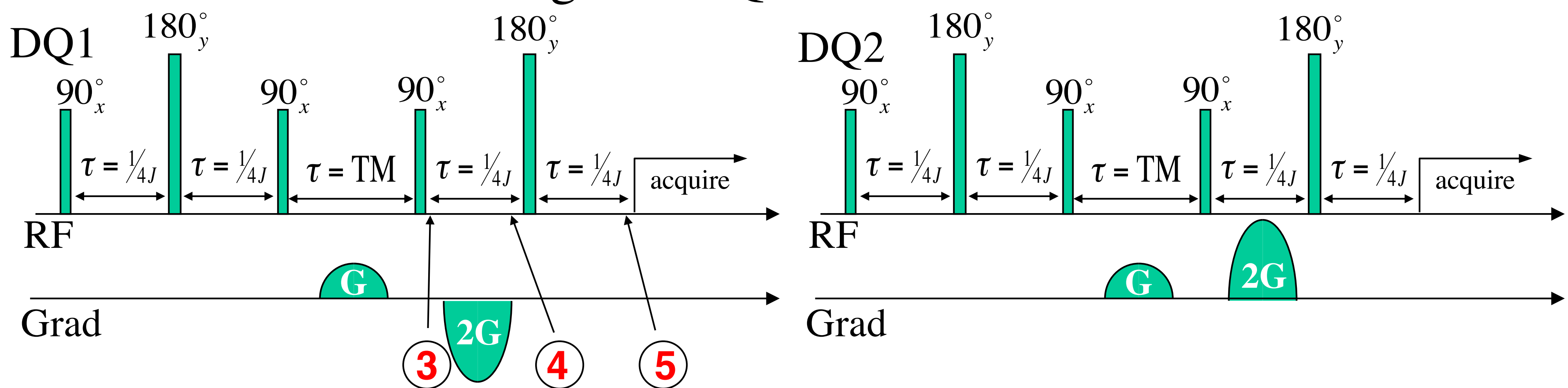
Integrating over z… $\frac{1}{2}(2\hat I_x\hat S_z + 2\hat I_z\hat S_x)$ ④

⑤ $\frac{1}{2}(\hat I_y + \hat S_y)$ … a single-shot filter with 50% yield.



DQ Filtering with Gradients

- Consider the following two DQ filters…



DQ1:

3

$$(2\hat{I}_x\hat{S}_z + 2\hat{I}_z\hat{S}_x)\cos 2\pi z \xrightarrow{\hat{I}_z(-2\pi z)+\hat{S}_z(-2\pi z)} \underbrace{(2\hat{I}_x\hat{S}_z + 2\hat{I}_z\hat{S}_x)\cos^2 2\pi z + (\hat{I}_y + \hat{S}_y)\sin 2\pi z\cos 2\pi z}$$

4

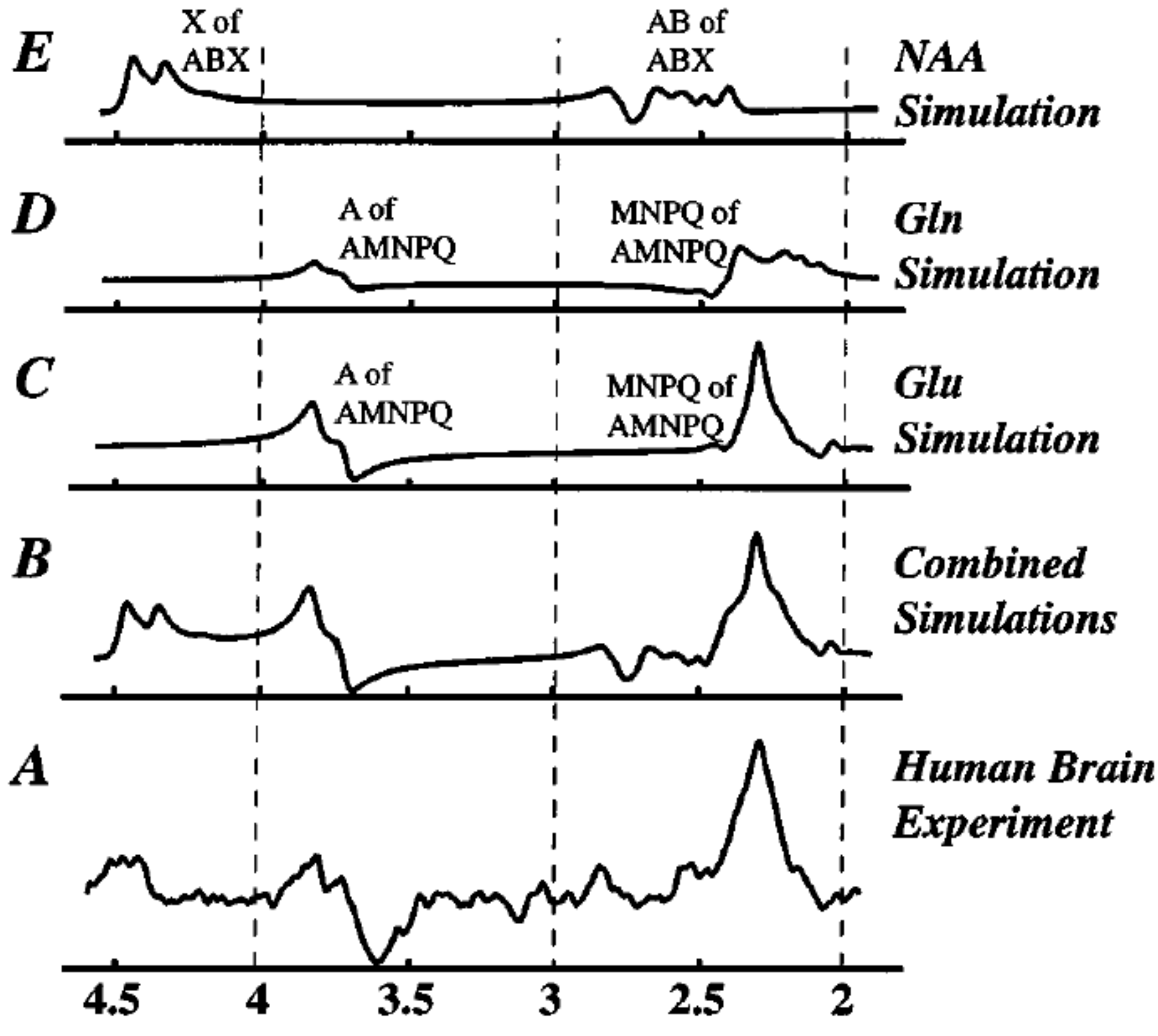
Integrating over z… $\frac{1}{2}(2\hat{I}_x\hat{S}_z + 2\hat{I}_z\hat{S}_x) \longrightarrow \frac{1}{2}(\hat{I}_y + \hat{S}_y)$ 5

DQ2:

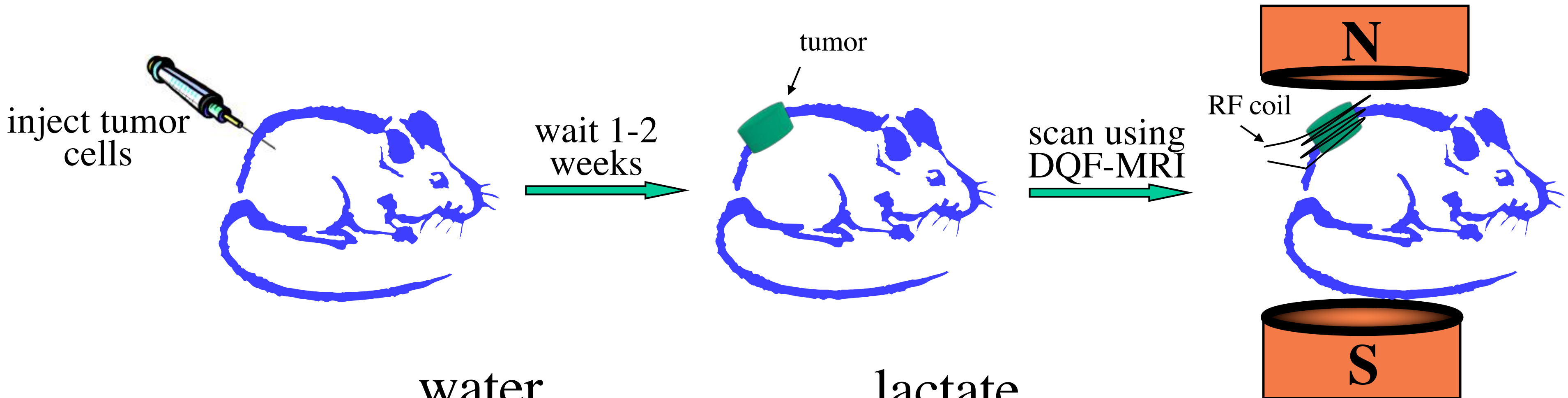
$$(2\hat{I}_x\hat{S}_z + 2\hat{I}_z\hat{S}_x)\cos 2\pi z \xrightarrow{\hat{I}_z(2\pi z)+\hat{S}_z(2\pi z)} \underbrace{(2\hat{I}_x\hat{S}_z + 2\hat{I}_z\hat{S}_x)\cos^2 2\pi z - (\hat{I}_y + \hat{S}_y)\sin 2\pi z\cos 2\pi z}$$

Integrating over z… $\frac{1}{2}(2\hat{I}_x\hat{S}_z + 2\hat{I}_z\hat{S}_x) \longrightarrow \frac{1}{2}(\hat{I}_y + \hat{S}_y)$

Example: Glutamate DQF

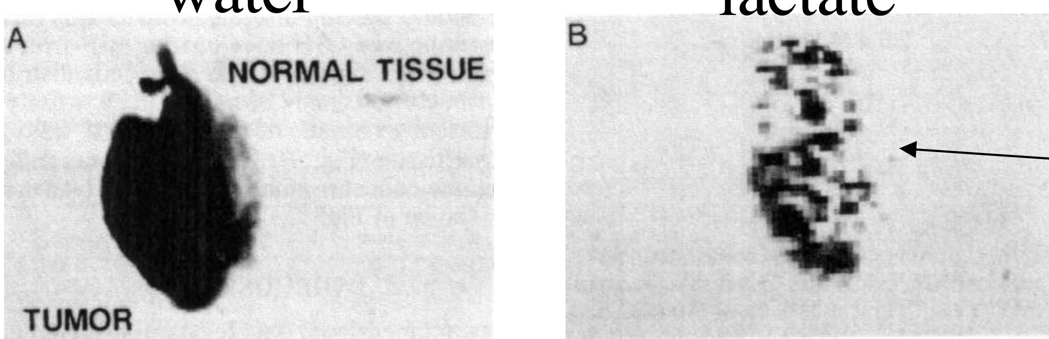


Lactate Imaging using a DQF



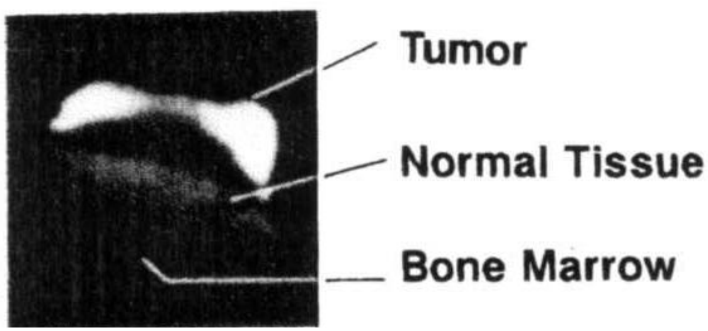
Live mouse

water | lactate

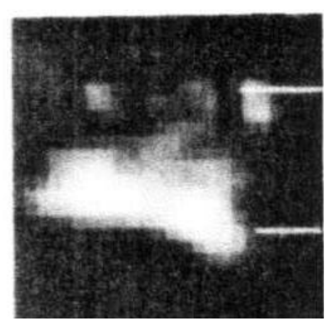


Heterogeneous lactate distribution within tumor

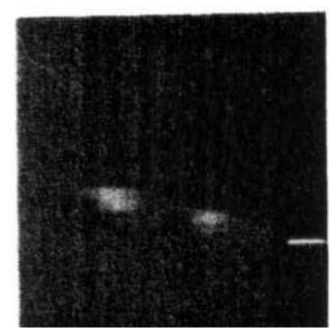
Mouse died during study



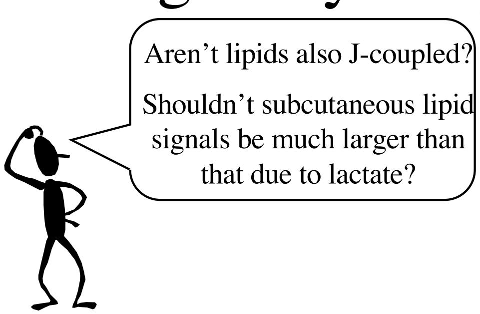
water



lactate



lipid



Summary

- Wide variety of spectral editing techniques available
- Optimum choice depends on application
- Some factors to consider:
  - Required quantitative accuracy
    - Absolute versus relative quantitation
    - Sensitivity
  - Robustness
    - B_0 inhomogeneity
    - B_1 inhomogeneity
    - Patient motion

Next Lecture: In vivo MRS-detectable metabolites