# 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.
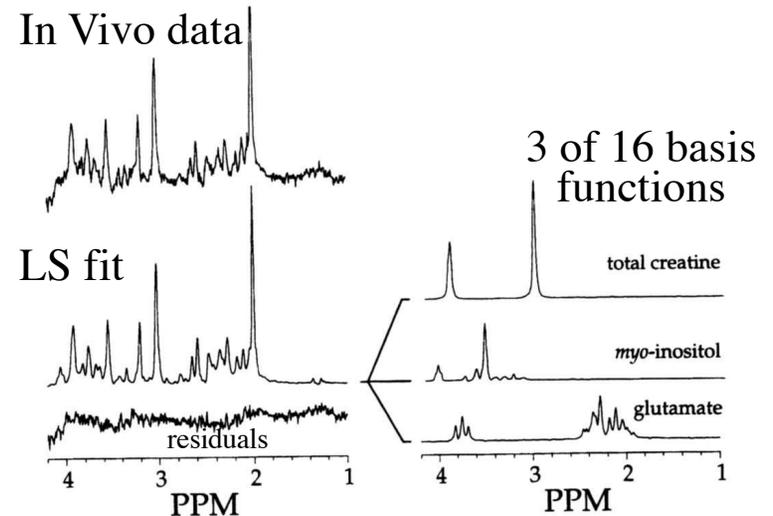
In Vivo ^{1}H Spectrum

- We'll focus on the ^{1}H spectrum

  ⇨ High sensitivity

  ⇨ Small chemical shift range

  ⇨ Same hardware as MRI

⟹   crowded ⇔ rich

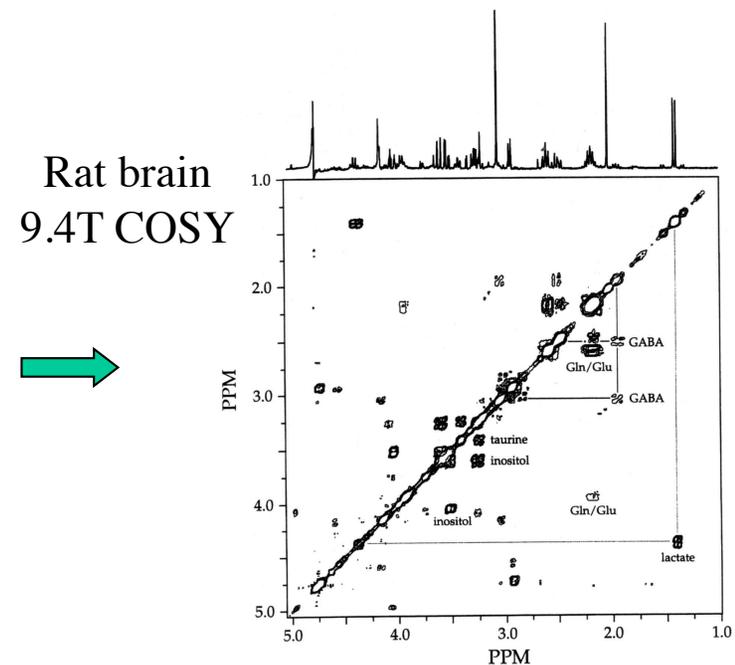Chemical Shift (ppm)
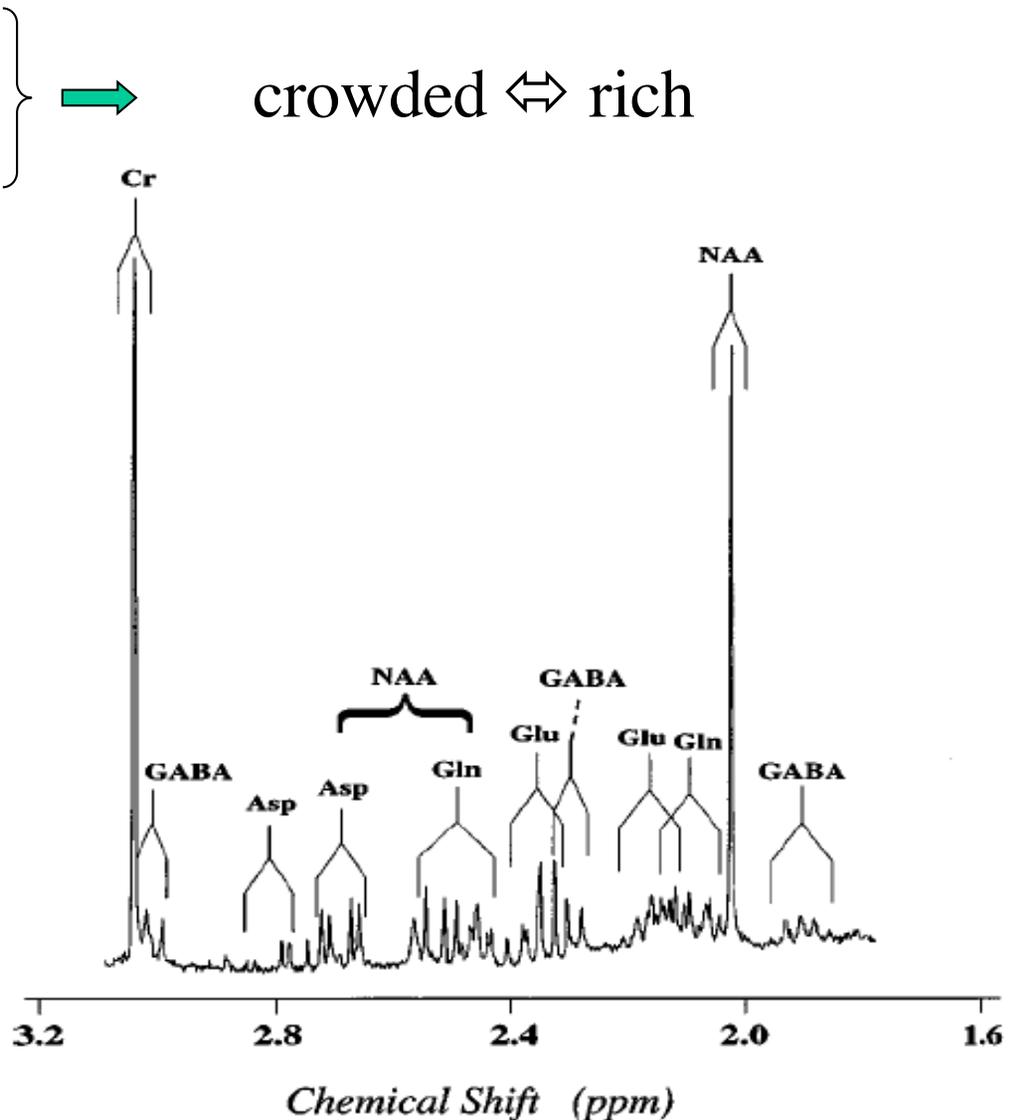
Solutions

- 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

In Vivo data

LS fit

residuals

3 of 16 basis functions

total creatine

myo-inositol

glutamate

Rat brain 9.4T COSY

GABA
Gln/Glu
GABA
taurine
inositol
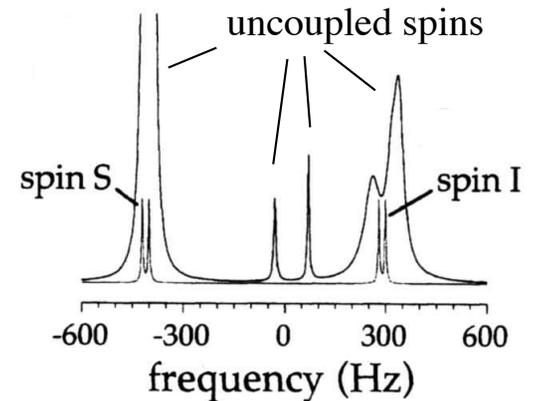Gln/Glu
inositol
lactate

4

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 $\left.\vphantom{\begin{matrix}a\\b\end{matrix}}\right\}$ CNR
  - Robustness to motion-artifacts (single- vs multi-shot)
  - Relaxation time considerations

- Spatial encoding - to be added later (next couple of lectures)
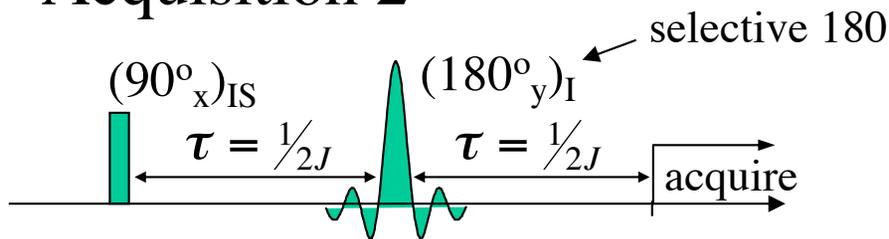
J-Difference Editing

- Acquisition 1

$(90^{\circ}{}_x)_{IS}$
$(180^{\circ}{}_y)_{IS}$
$\tau = \frac{1}{2J}$
$\tau = \frac{1}{2J}$
acquire
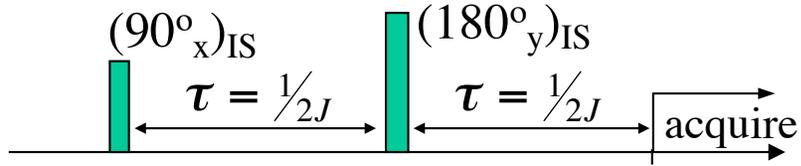
$$\hat{I}_z \longrightarrow \hat{I}_y \longrightarrow \hat{I}_y \cos \pi J(\tfrac{1}{J}) - 2\hat{I}_x \hat{S}_z \sin \pi J(\tfrac{1}{J}) = -\hat{I}_y$$
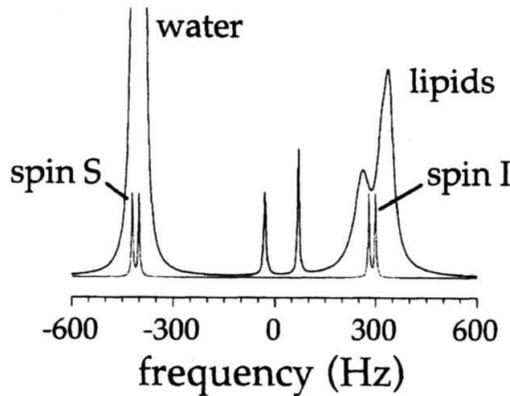
- Acquisition 2

selective 180

$(90^{\circ}{}_x)_{IS}$
$(180^{\circ}{}_y)_I$
$\tau = \frac{1}{2J}$
$\tau = \frac{1}{2J}$
acquire

$$\hat{I}_z \longrightarrow \hat{I}_y \longrightarrow \hat{I}_y \cos \pi J(\tfrac{1}{2J} - \tfrac{1}{2J}) - 2\hat{I}_x \hat{S}_z \sin \pi J(\tfrac{1}{2J} - \tfrac{1}{2J}) = \hat{I}_y$$
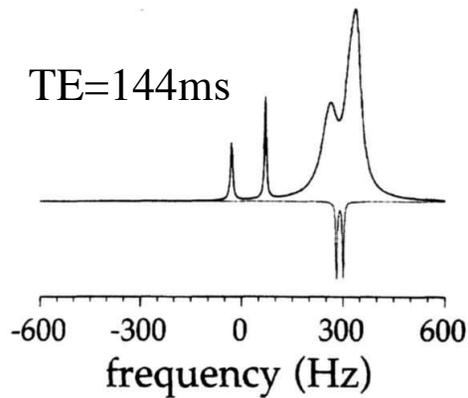
- Algorithm: Edited signal = Acq2-Acq1

6

Example: Lactate-Lipid Discrimination
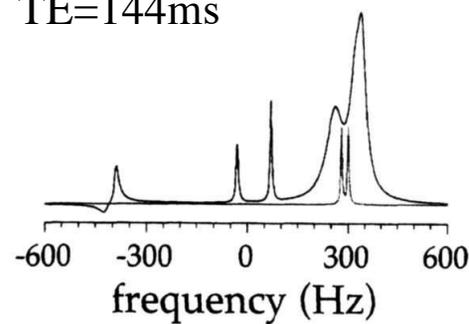
Spin echo:
Unedited spectrum

J=7 Hz

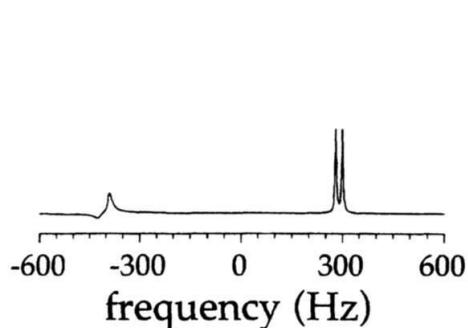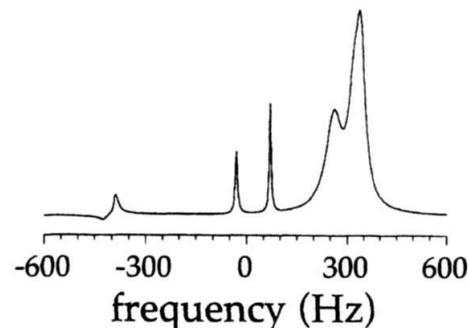Acquisition 1:
Spin echo w/
nonselective 180

Acquisition 2:
Spin echo w/
selective 180

Difference
spectrum

Sum
spectrum

MRSI with J-editing for Lactate

Uncoupled spins and lipids

Lactate

Seq. 1

Seq. 2

180 spectral profile

Chemical shift

ω_k ω_1

Seq. 1

Seq. 2
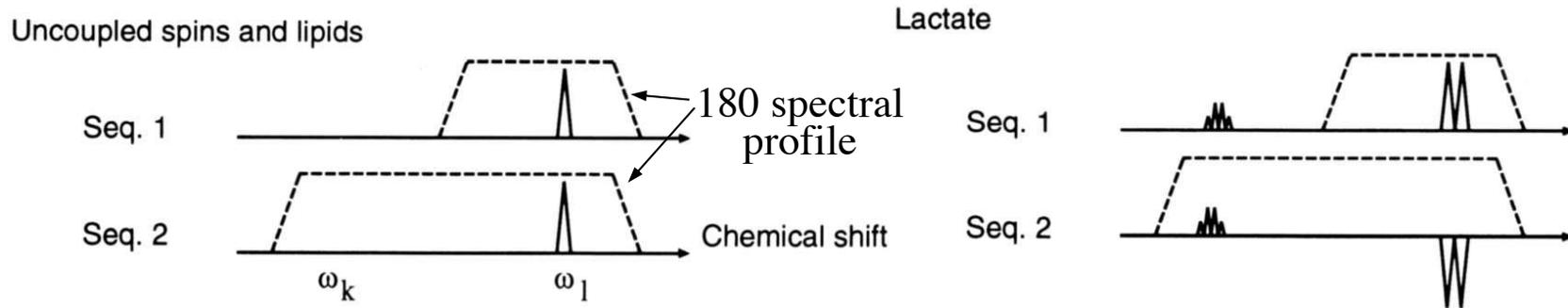
- MELAS patient (metabolic disorder with multiple strokes)

T$_2$-weighted

Sum Spectra

Difference Spectra

6 4 2 0 -2 -4 -6 ppm   6 4 2 0 -2 -4 -6 ppm

NAA

Lactate

Lipids

unfiltered "lactate"

For comparison:

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

8

J-editing for GABA

GABA

¹H MRS

J coupled

Phantom study

Gly

GABA -4CH₂

A   triplet

B   selective inversion

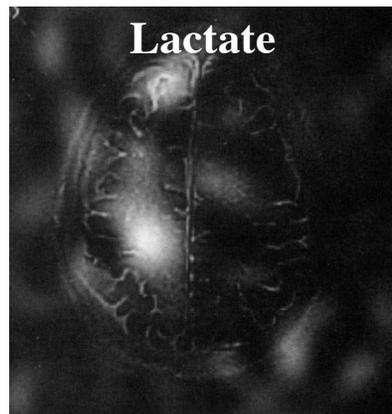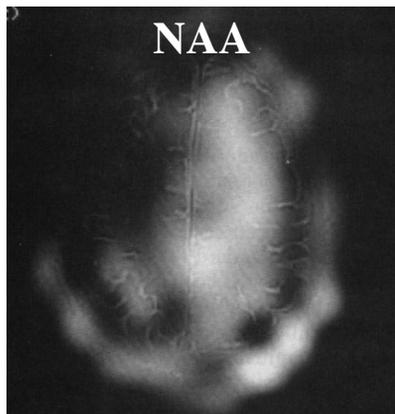A-B   editing efficiency < 100%
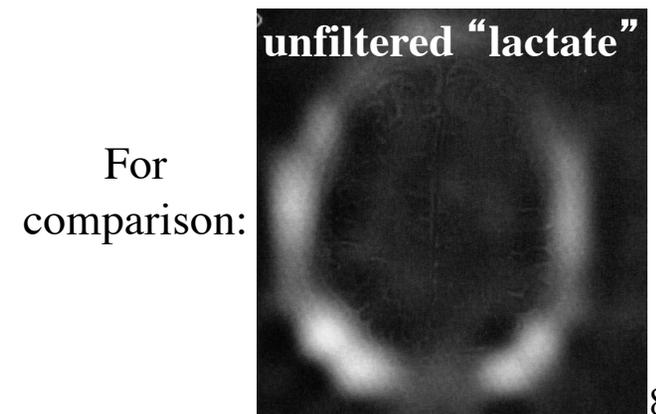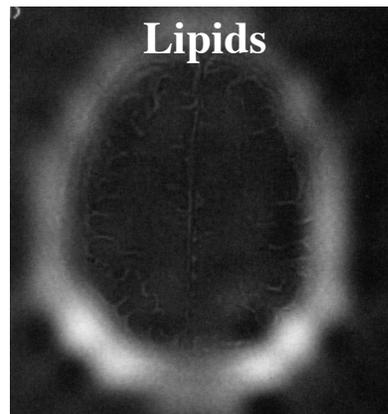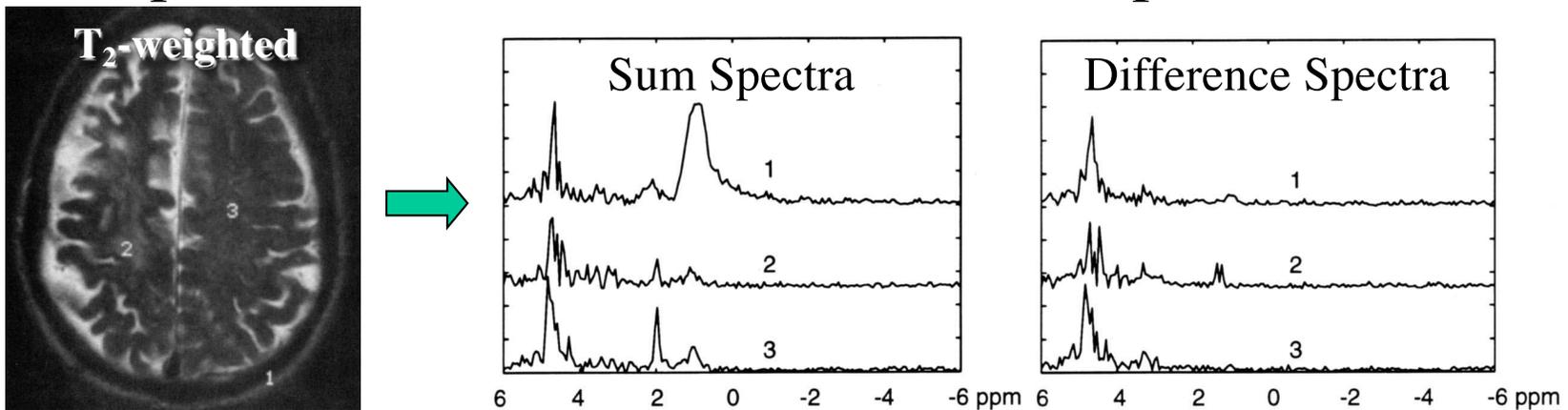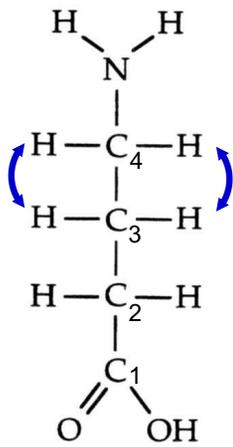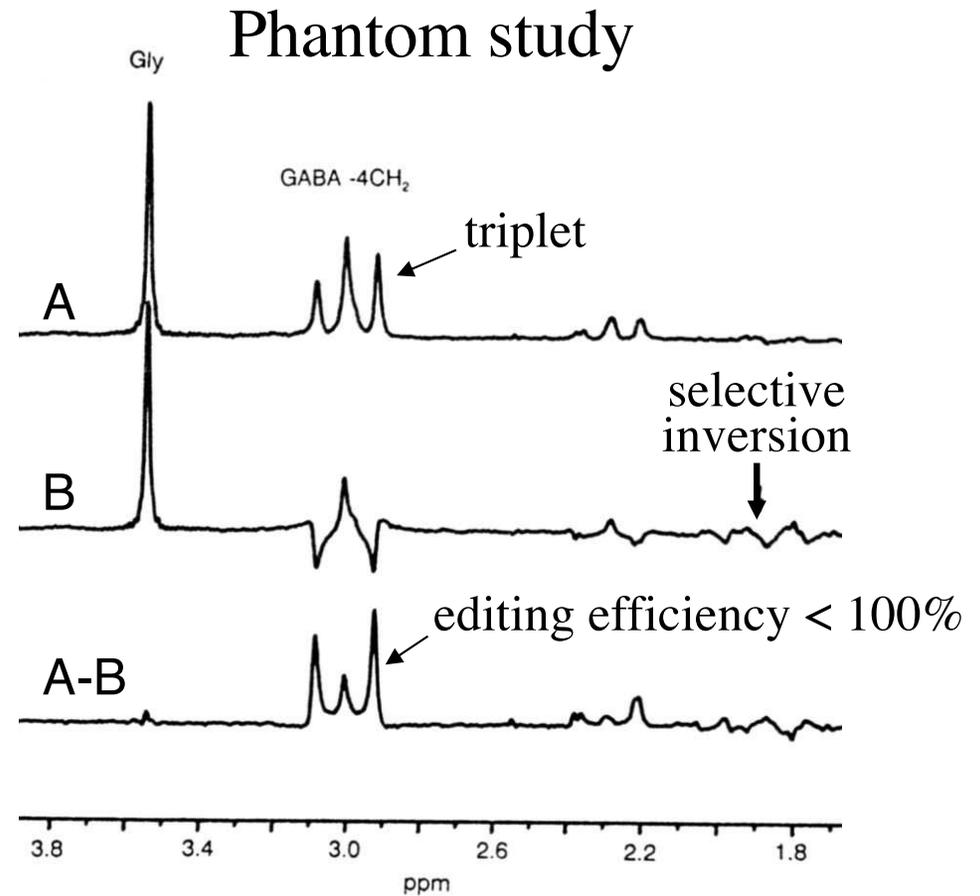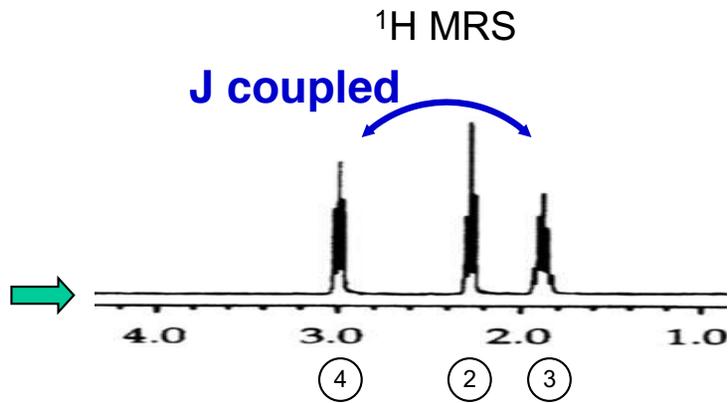
J-editing for GABA

- 3 T In Vivo Brain Spectra

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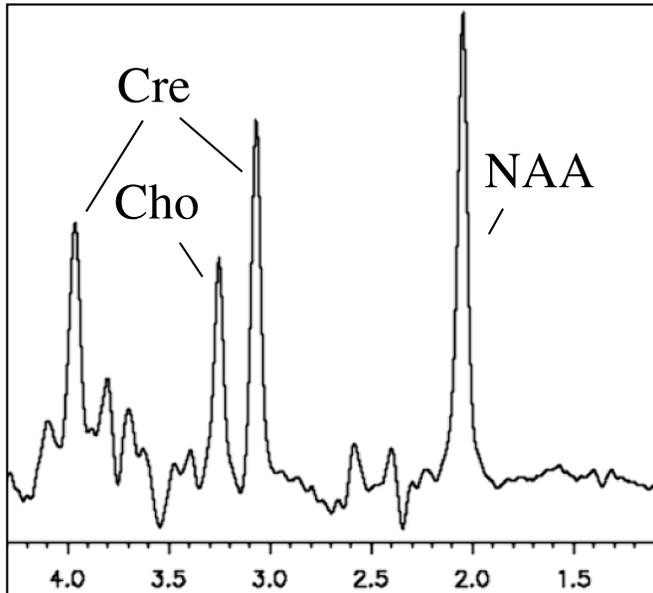
Difference spectrum
(w/ selective 180 centered at 1.9 ppm)

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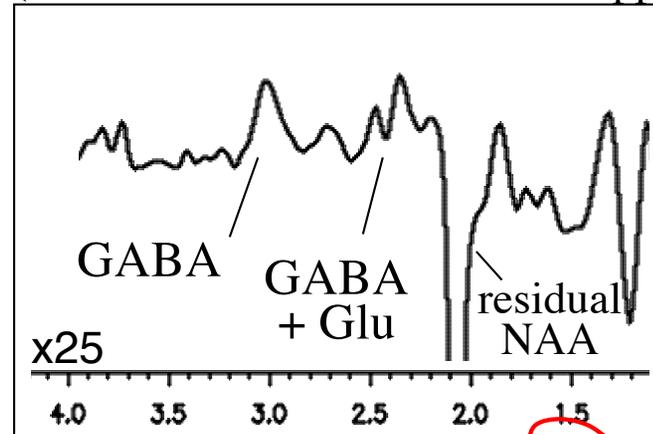
Parameters: TR/TE = 1500/68 ms, 18cc voxel,
occipital lobe, 26 min acquisition, head coil

- Drug study
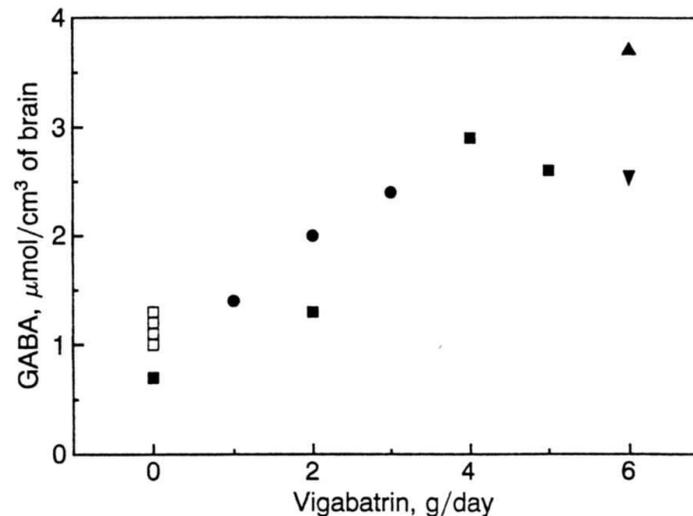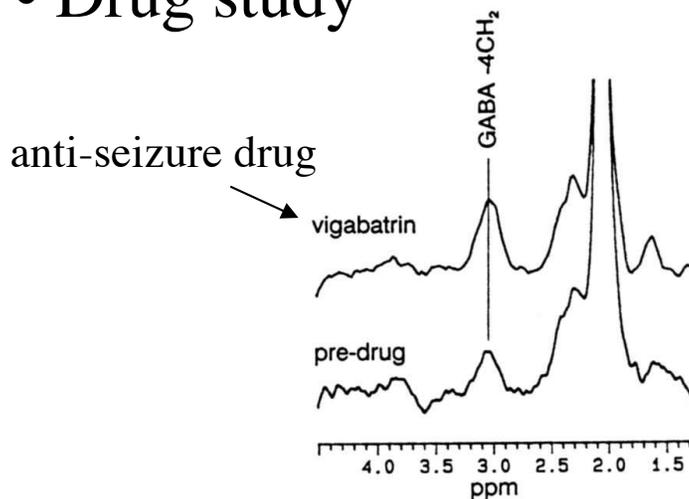
Note: quantitation
complicated by
some co-edited
resonances

The Oversampled 2D-J Experiment

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

90° $\quad \dfrac{t_1}{2}$ $\qquad$ 180° $\dfrac{t_1}{2}$

acquire

t_1

t_2

Ω_I, Ω_I refocused

$\therefore$ only J evolution during t_1

Both J and Ω evolution during t_2
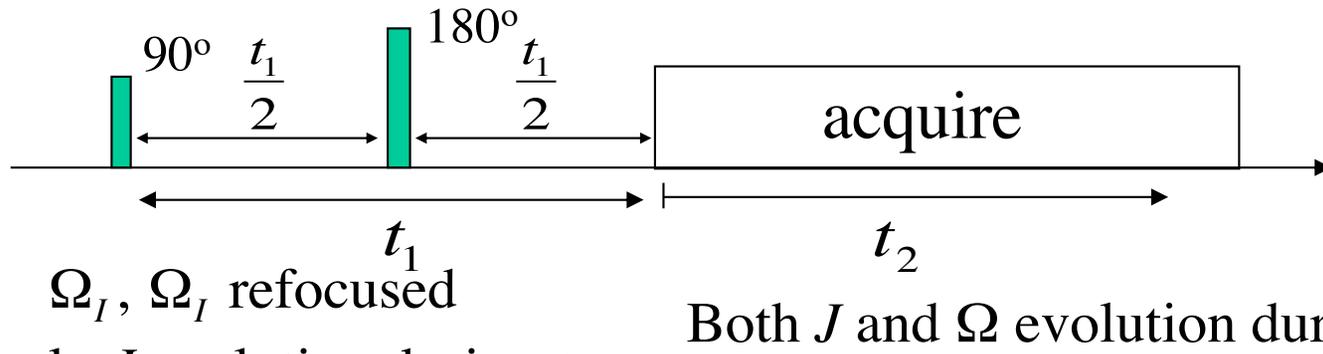
- Acquire data for multiple values of t_1. 2D-FFT yield 2D-J spectrum.

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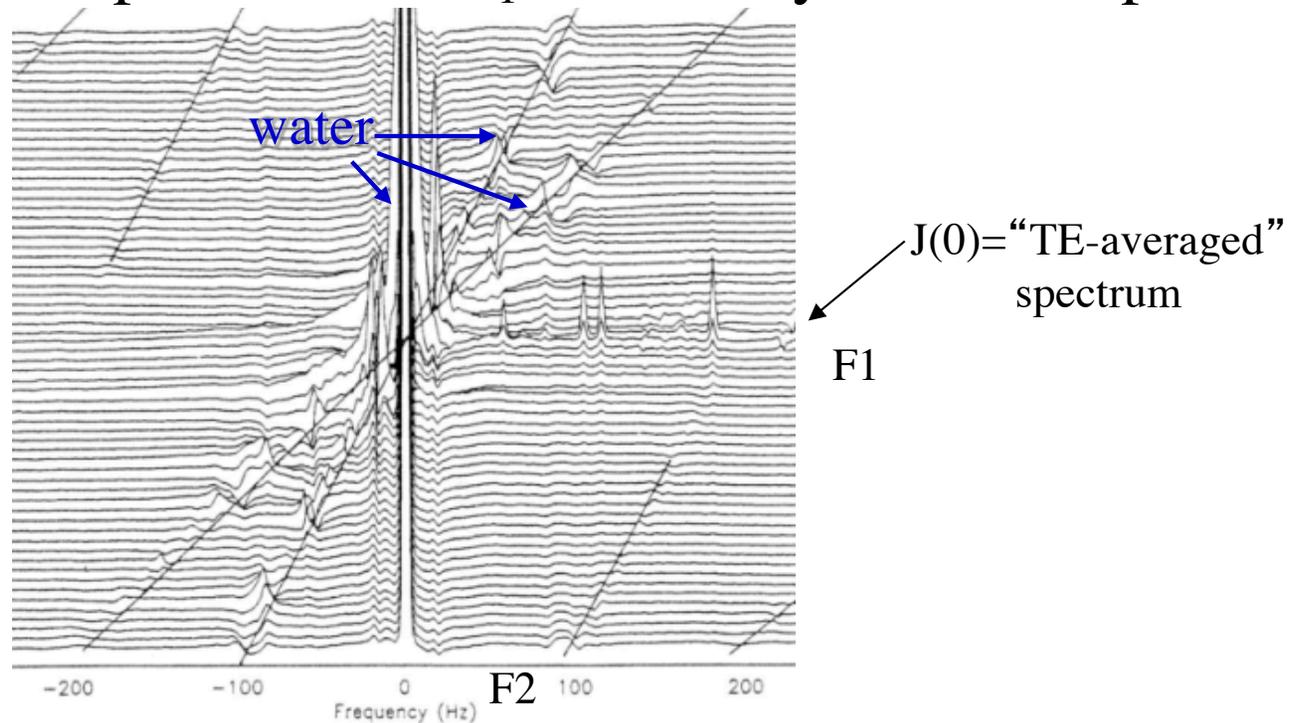
Hurd, et al., *MRM* **40**:343-347, 1998

J(0)="TE-averaged" spectrum

F1

F2

-200 $\qquad$ -100 $\qquad$ 0 $\qquad$ 100 $\qquad$ 200

Frequency (Hz)

11

3 T "TE-averaged" Normal Gray Matter Spectrum

F1=0 spectra

In vivo

NAA

Glu

Gln

ml

In vitro
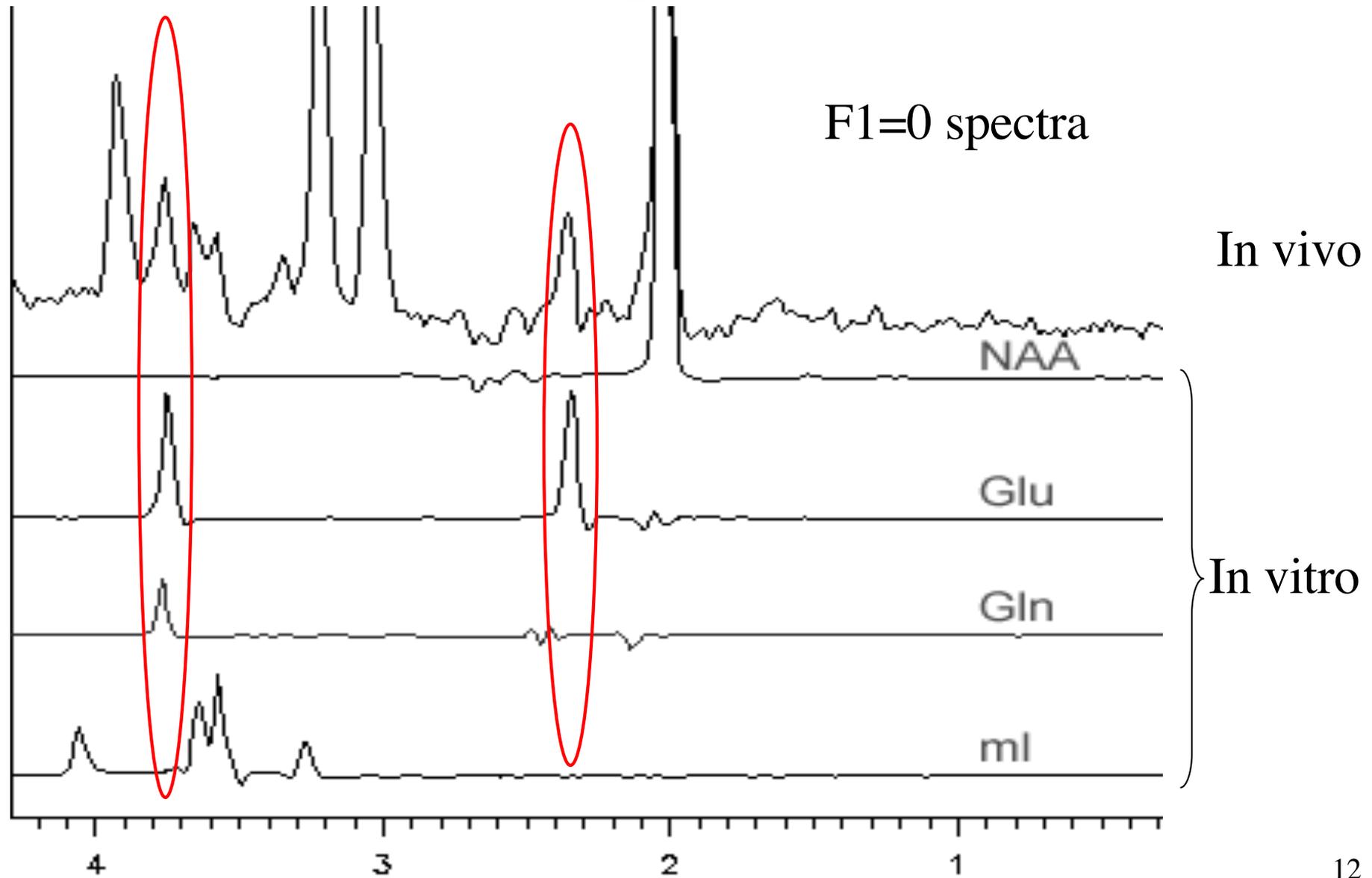
The Oversampled 2D-J Experiment

elevated choline
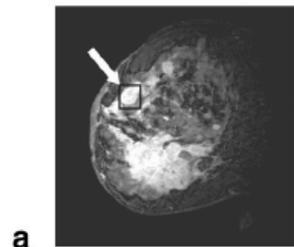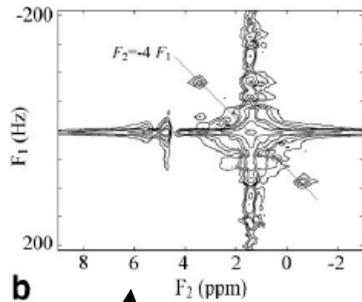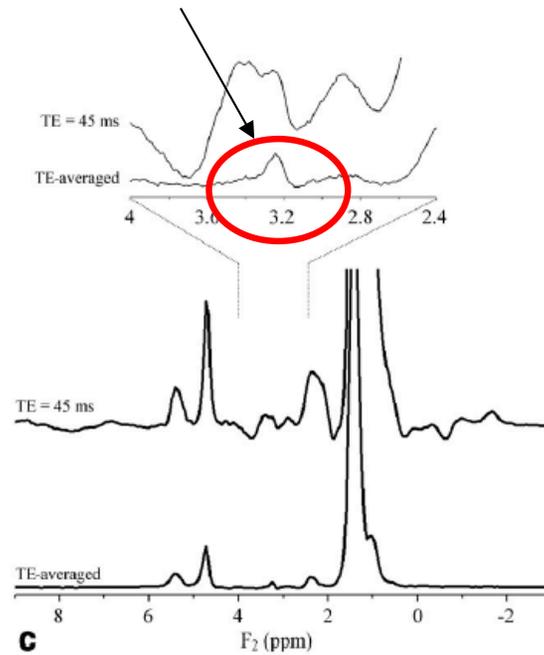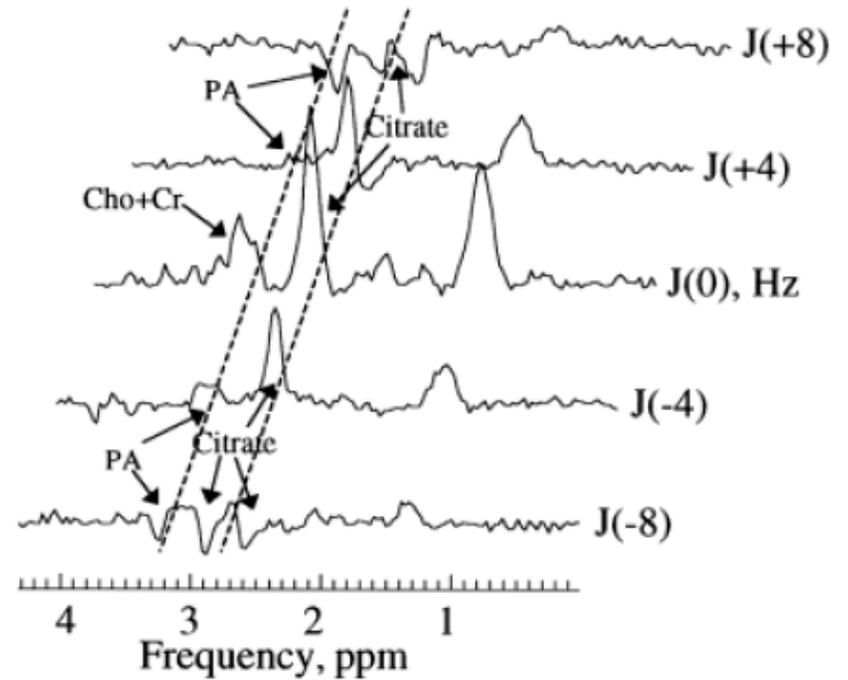
Breast cancer

2D-J spectrum

Prostate

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
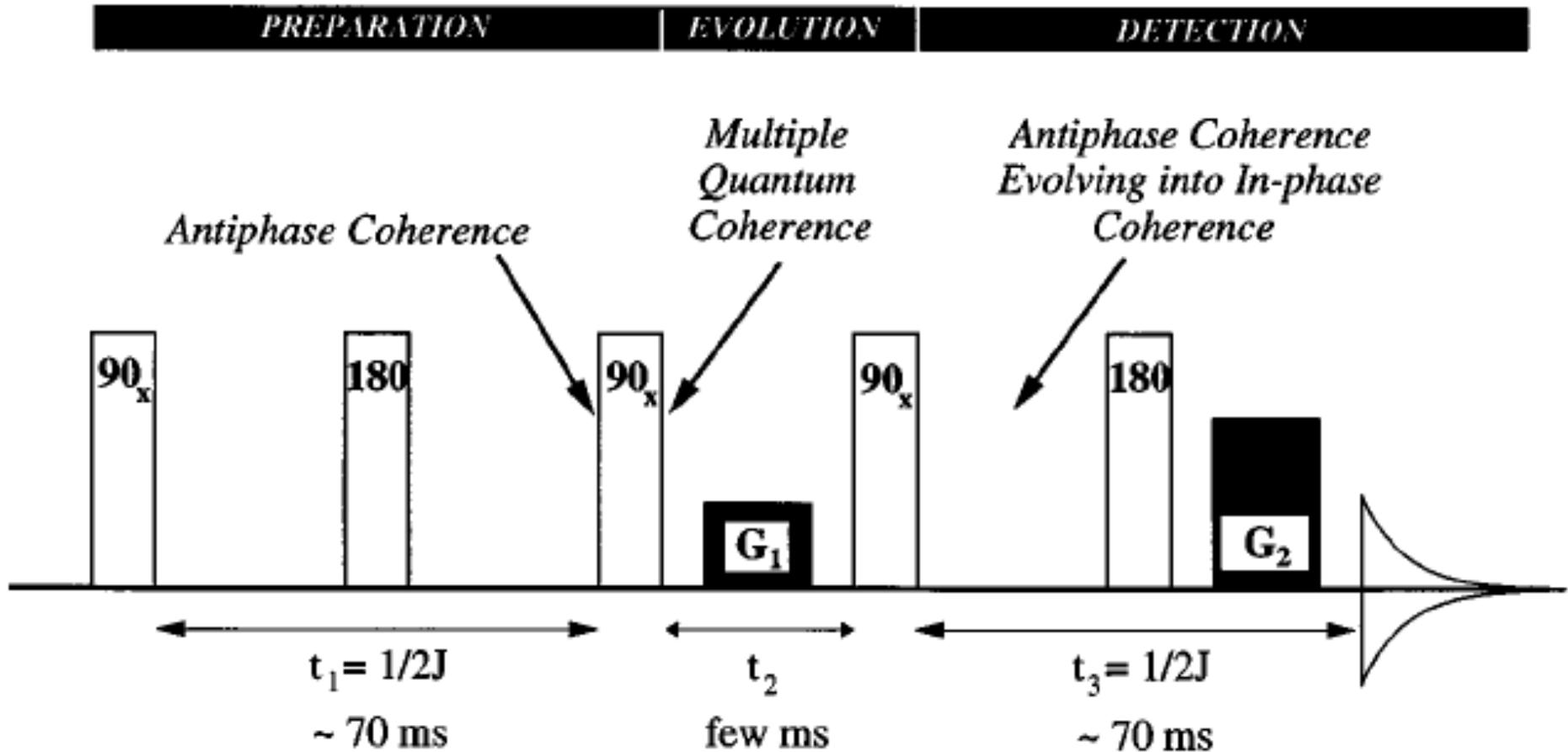
- 180s used to refocus chemical shift

- 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).

$90^o{}_x$ $180^o{}_y$ $90^o{}_x$ $90^o{}_x$ $180^o{}_y$

$\tau = \frac{1}{4J}$ $\tau = \frac{1}{4J}$ TM $\tau = \frac{1}{4J}$ $\tau = \frac{1}{4J}$ acquire

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

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

$\underbrace{\qquad\qquad\qquad}$
antiphase

assuming TM is very short

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

$\underbrace{\qquad\qquad\qquad}$
$\widehat{DQ}_y$

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

$\underbrace{\qquad\qquad\qquad}$
antiphase

$\hat{I}_y + \hat{S}_y - \hat{R}_y$
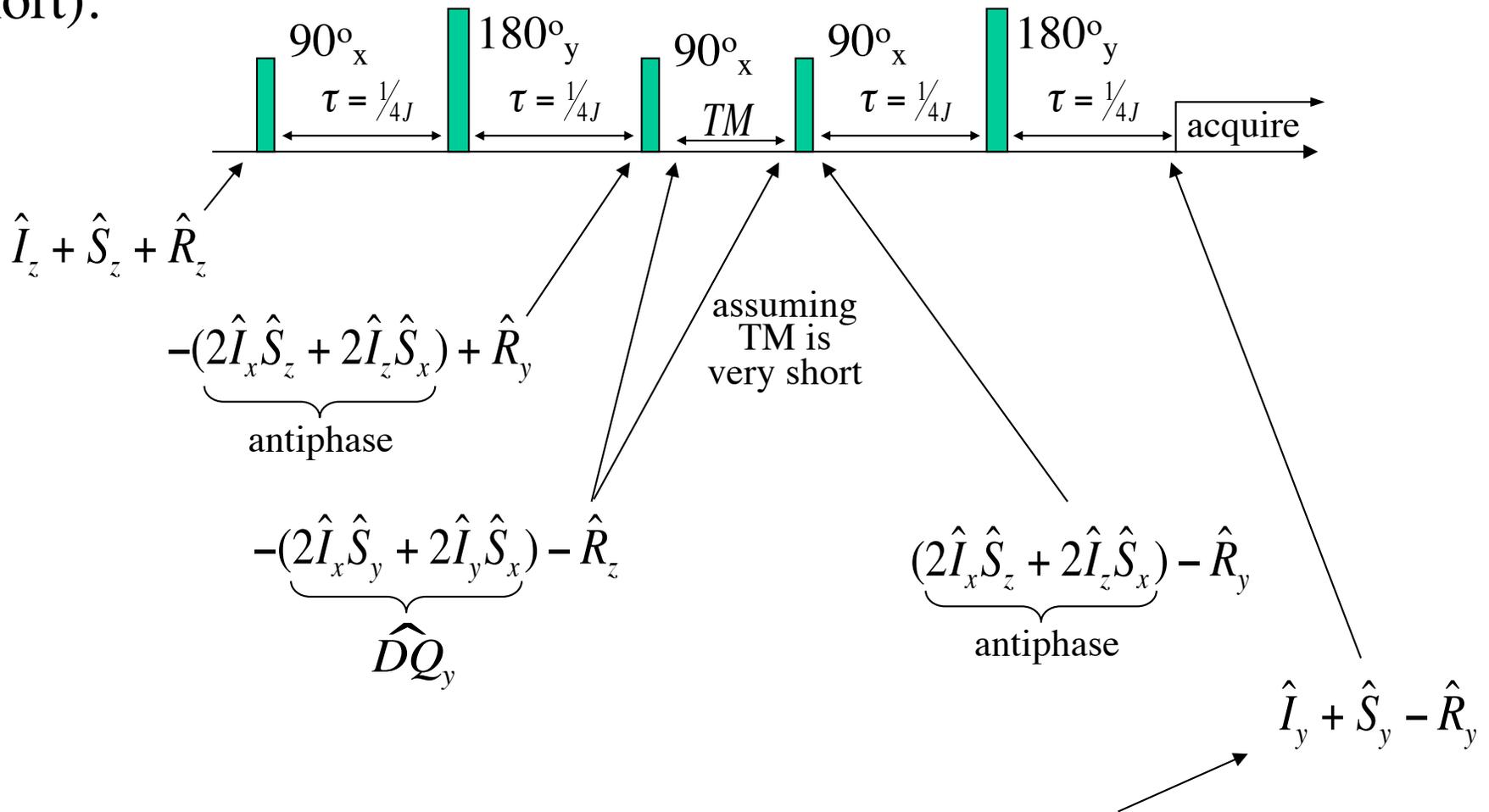
Only problem is that we haven't really filtered out anything!

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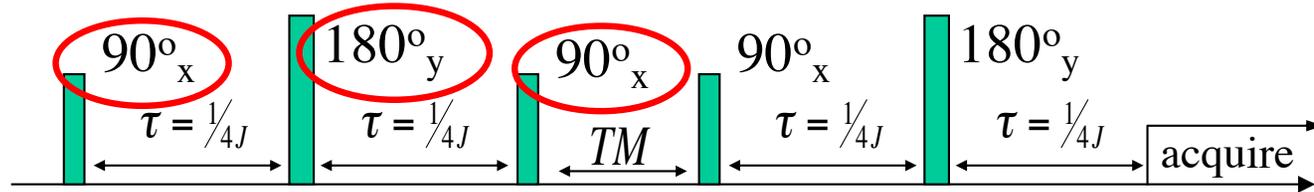
- One solution: cycle the phases of the first three RF pulses

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:

  G$_z$ area = G

  $\hat{\sigma}_1$ T $\hat{\sigma}_2$

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

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

- 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

180°_y

90°_x 90°_x 90°_x 180°_y

$\tau = \frac{1}{4J}$ $\tau = \frac{1}{4J}$ $\tau = TM$ $\tau = \frac{1}{4J}$ $\tau = \frac{1}{4J}$ acquire

RF

G

2G

Grad

① ② ③ ④ ⑤
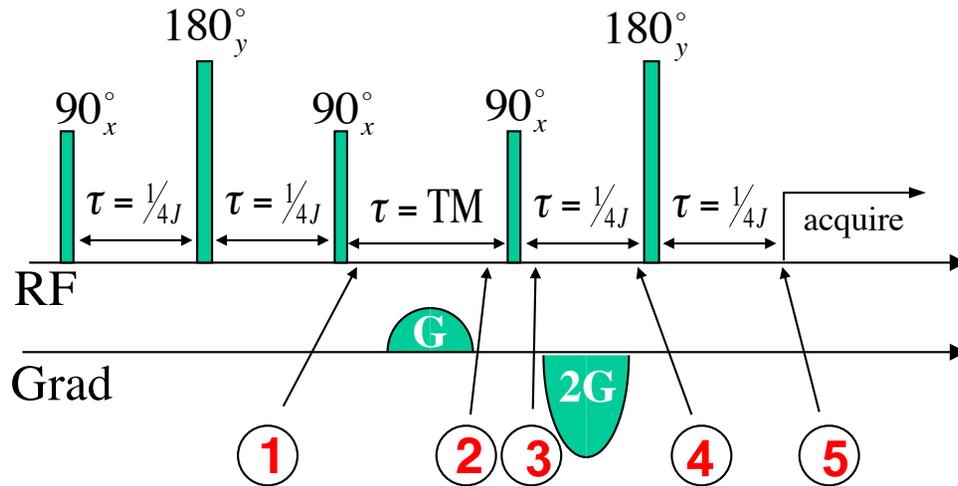
$\hat{\sigma}$ at various points in time (ignoring chemical shift terms) is …

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.

What happens to uncoupled spins?

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DQ Filtering with Gradients

- Consider the following two DQ filters…

DQ1

90°_x 180°_y 90°_x 90°_x 180°_y

$\tau = \frac{1}{4J}$ $\tau = \frac{1}{4J}$ $\tau = TM$ $\tau = \frac{1}{4J}$ $\tau = \frac{1}{4J}$ acquire

RF

Grad   **G**   **2G**

③   ④   ⑤

DQ2

90°_x 180°_y 90°_x 90°_x 180°_y

$\tau = \frac{1}{4J}$ $\tau = \frac{1}{4J}$ $\tau = TM$ $\tau = \frac{1}{4J}$ $\tau = \frac{1}{4J}$ acquire

RF

Grad   **G**   **2G**

DQ1:

③

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

④

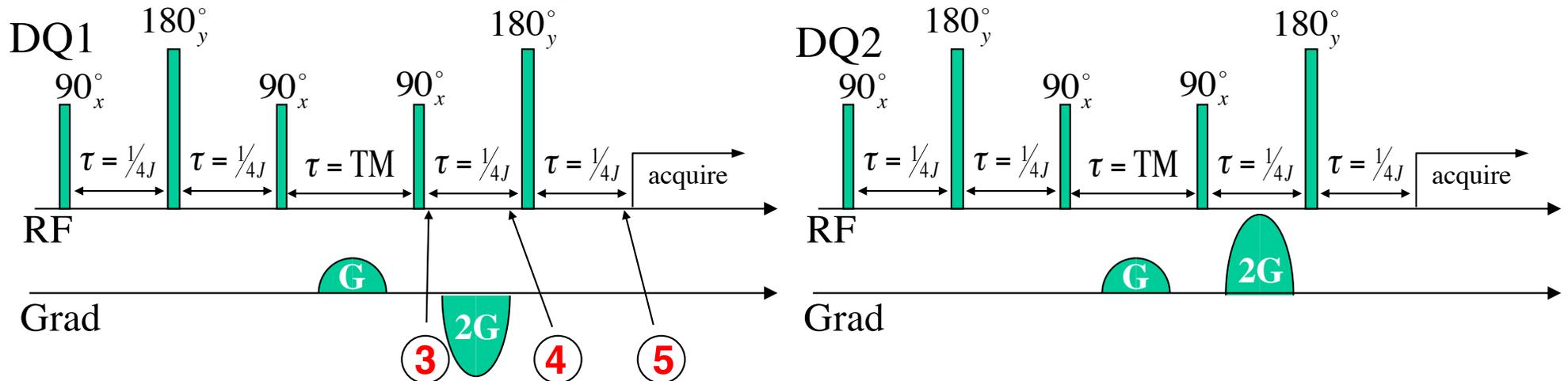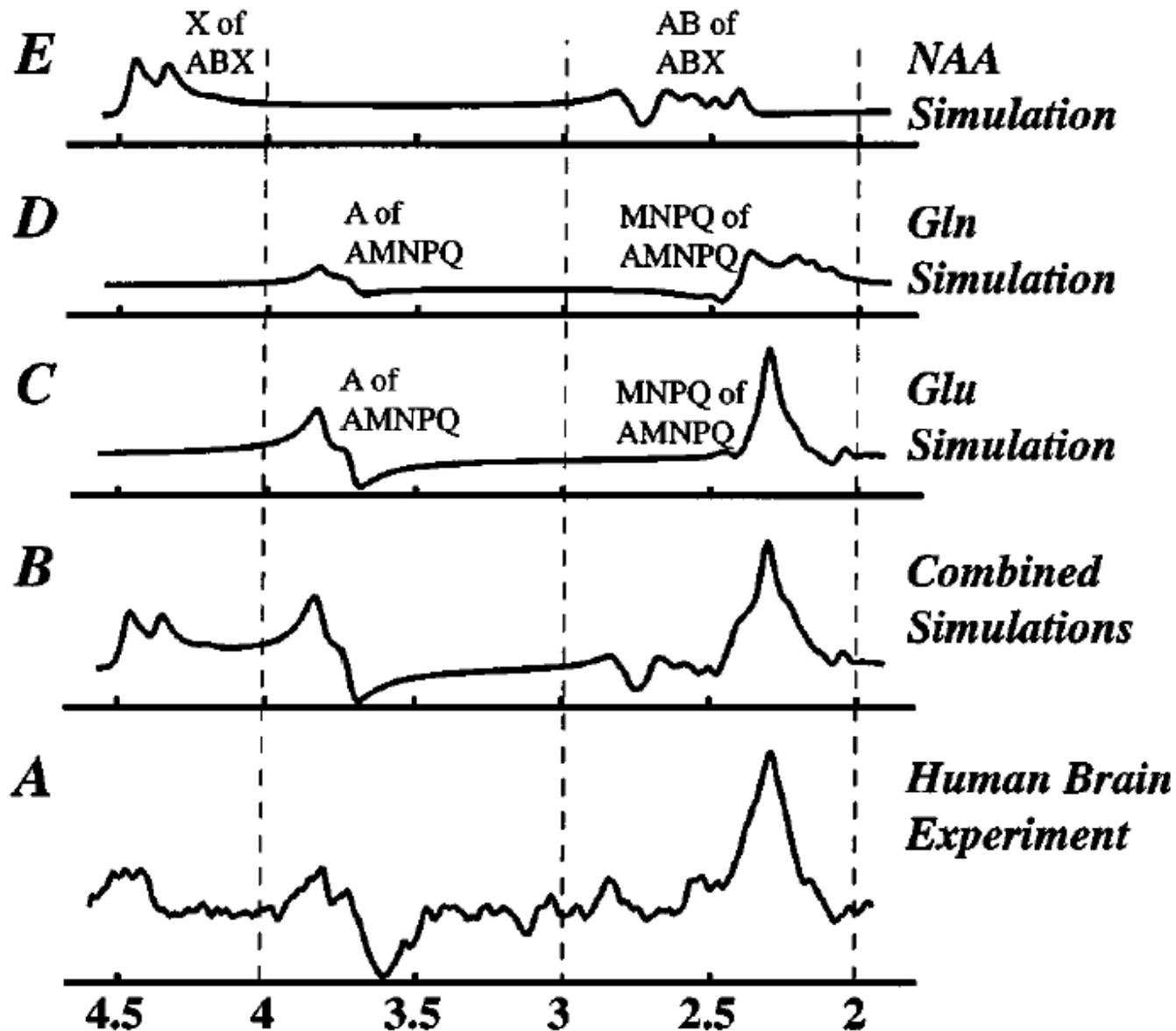Integrating over z… $\frac{1}{2}(2\hat{I}_x\hat{S}_z + 2\hat{I}_z\hat{S}_x) \longrightarrow \frac{1}{2}(\hat{I}_y + \hat{S}_y)$ ⑤
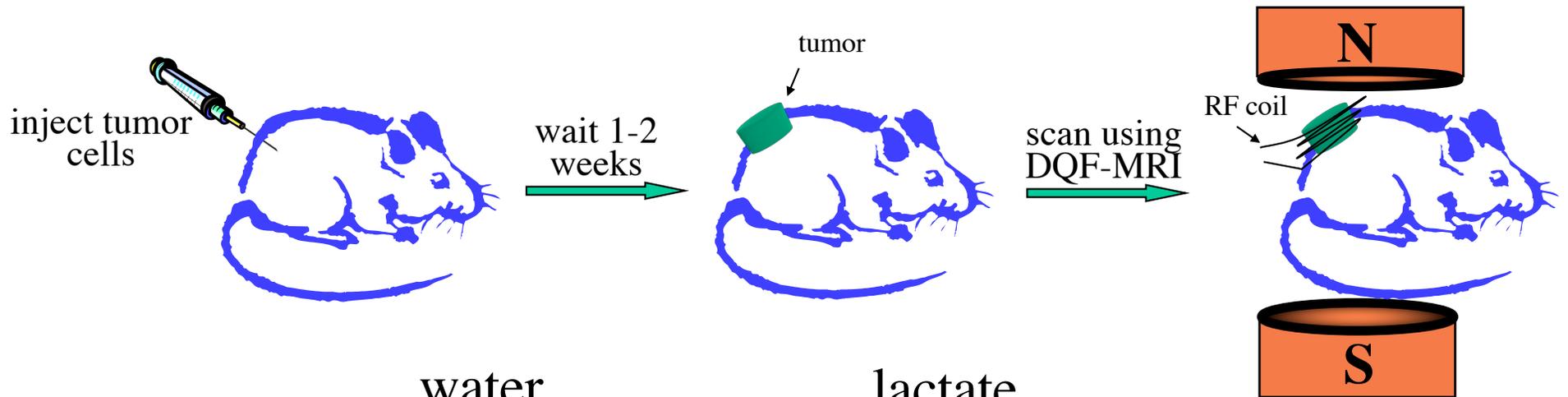
DQ2:

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

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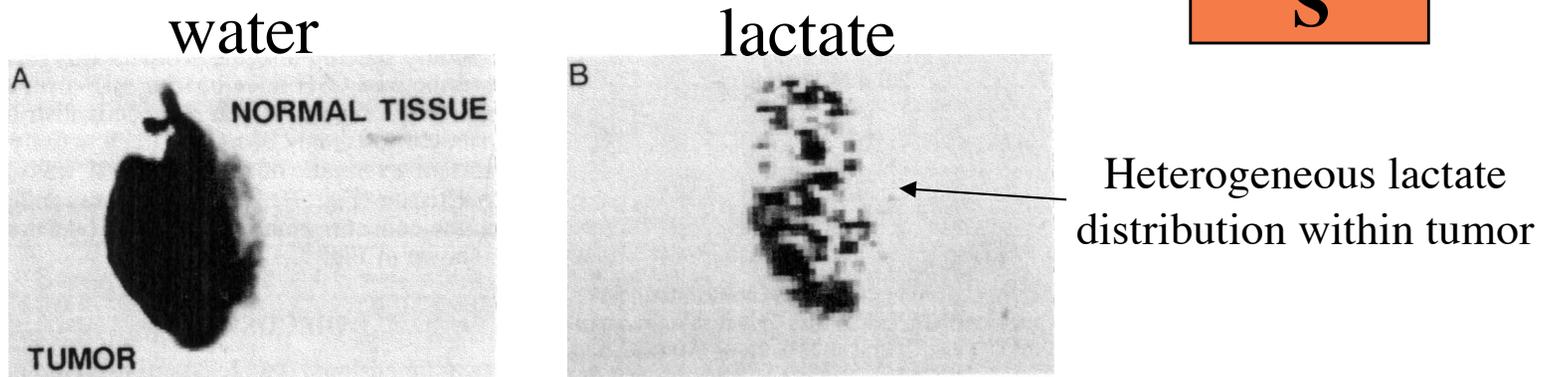
Example: Glutamate DQF

Lactate Imaging using a DQF

inject tumor cells

wait 1-2 weeks

tumor

scan using DQF-MRI

N

S

RF coil

Live mouse

water

lactate

A   NORMAL TISSUE

TUMOR

B

Heterogeneous lactate distribution within tumor

Mouse died during study

Aren't lipids also J-coupled?

Shouldn't subcutaneous lipid signals be much larger than that due to lactate?

Tumor

Normal Tissue

Bone Marrow

water

lactate

lipid

22
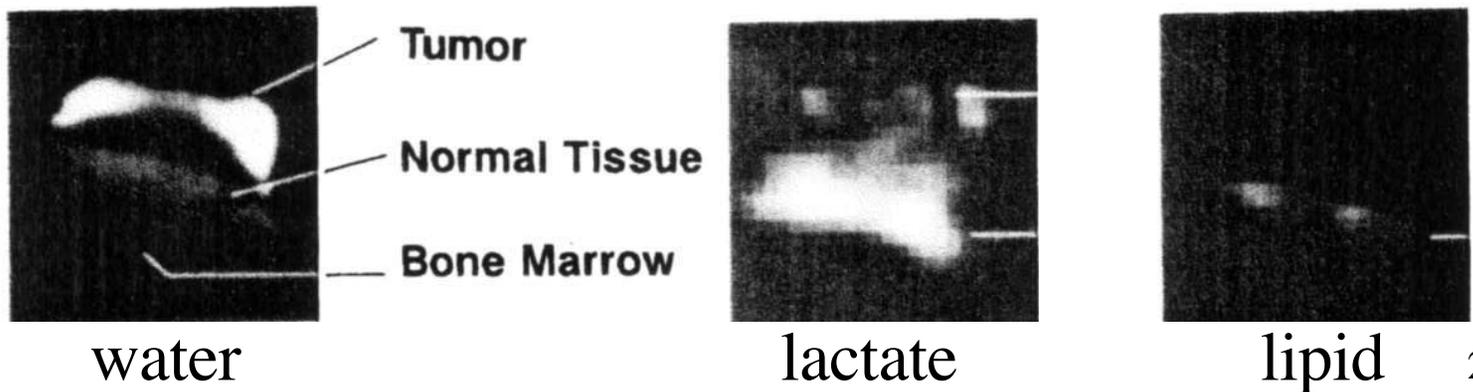
Summary

- 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