Magnetic Resonance Spectroscopy II: Novel Technology Developments and selected applications

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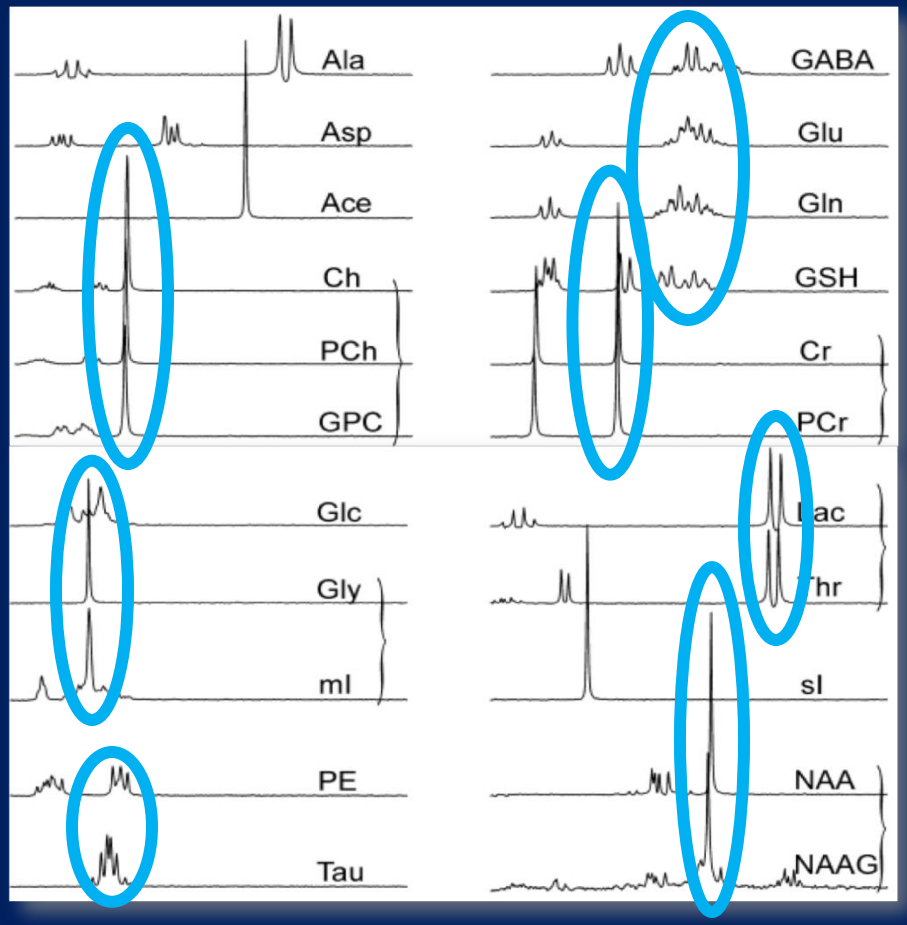
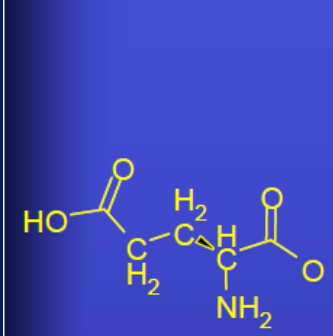
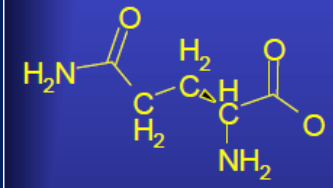
1D Spectroscopy

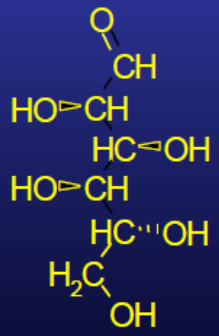
- Different metabolites share similar peaks
- Severe spectral overlap limits the amount of useful information
- Limited applicability and enthusiasm for spectroscopy

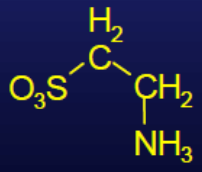


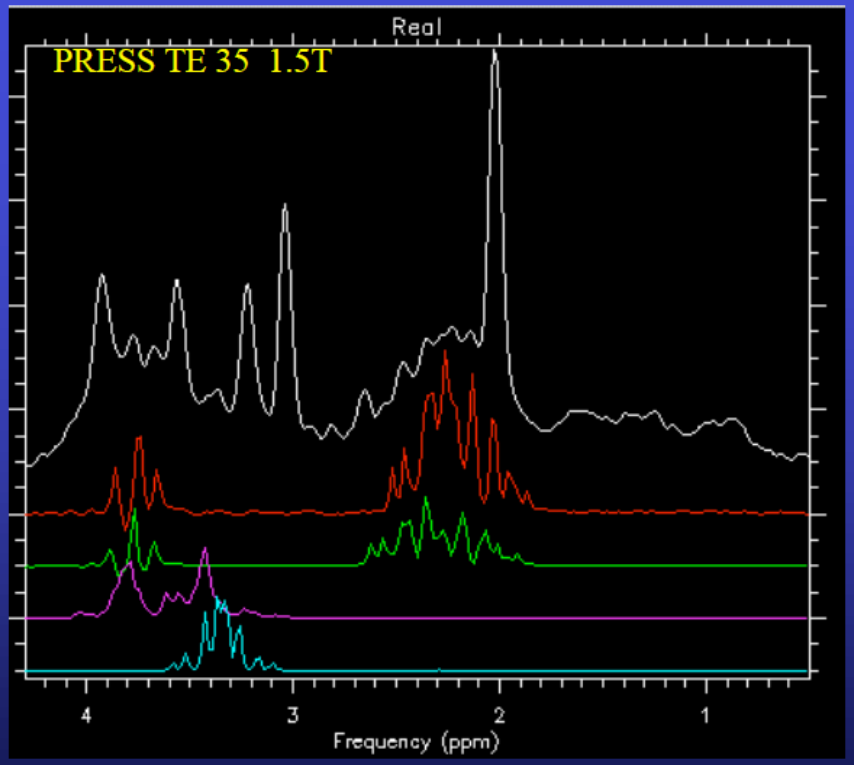
1D MRS











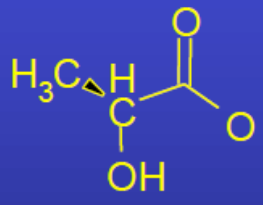
Glutamate

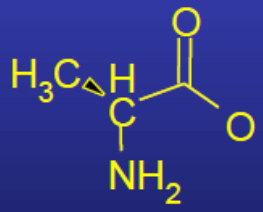
Glutamine

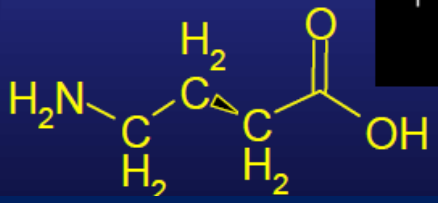
Glucose

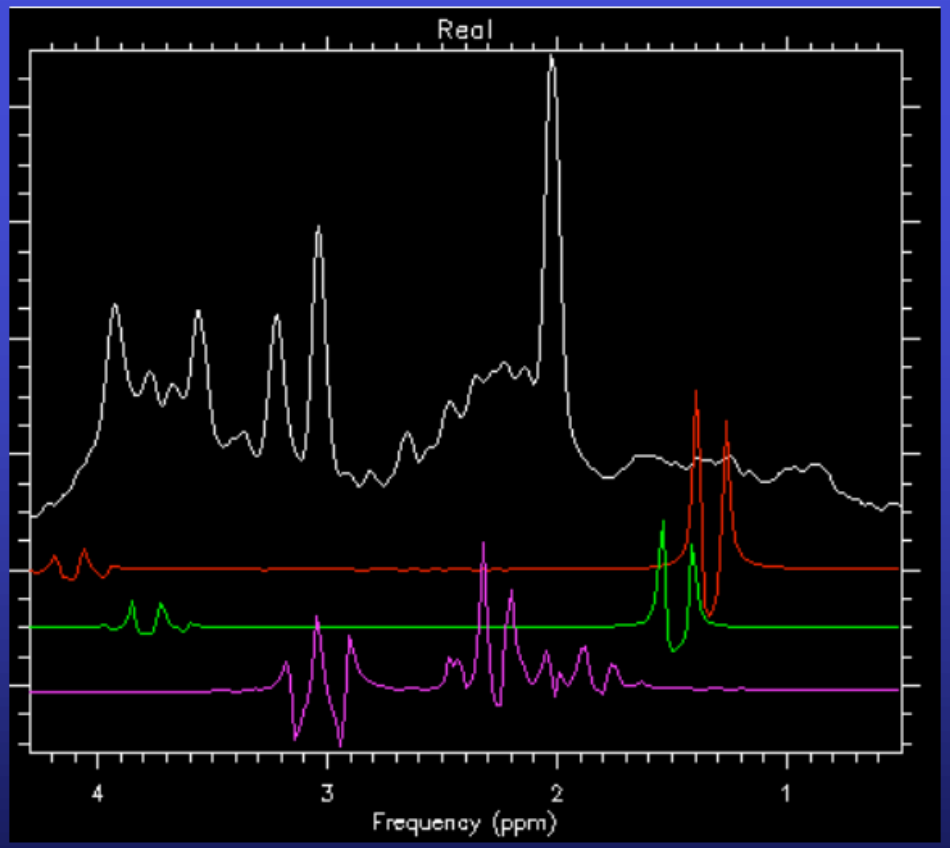
Taurine

1D MRS









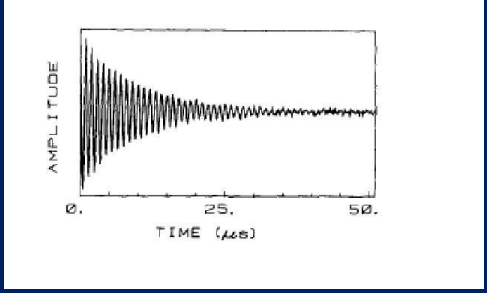
Lactate
Alanine
GABA

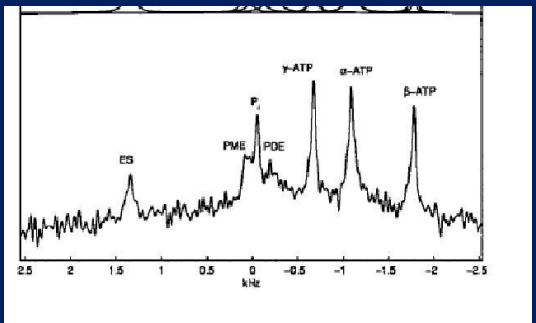
MRS allows non-invasive quantitation of metabolite concentrations > 0.5mM

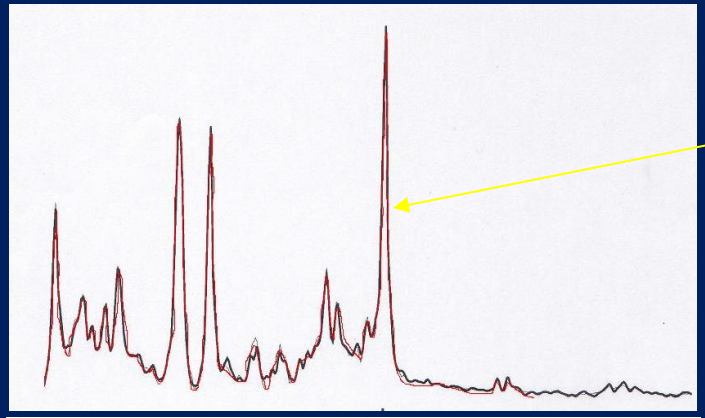
Main algorithms for 1D MRS quantitation: LC-Model and MRUI

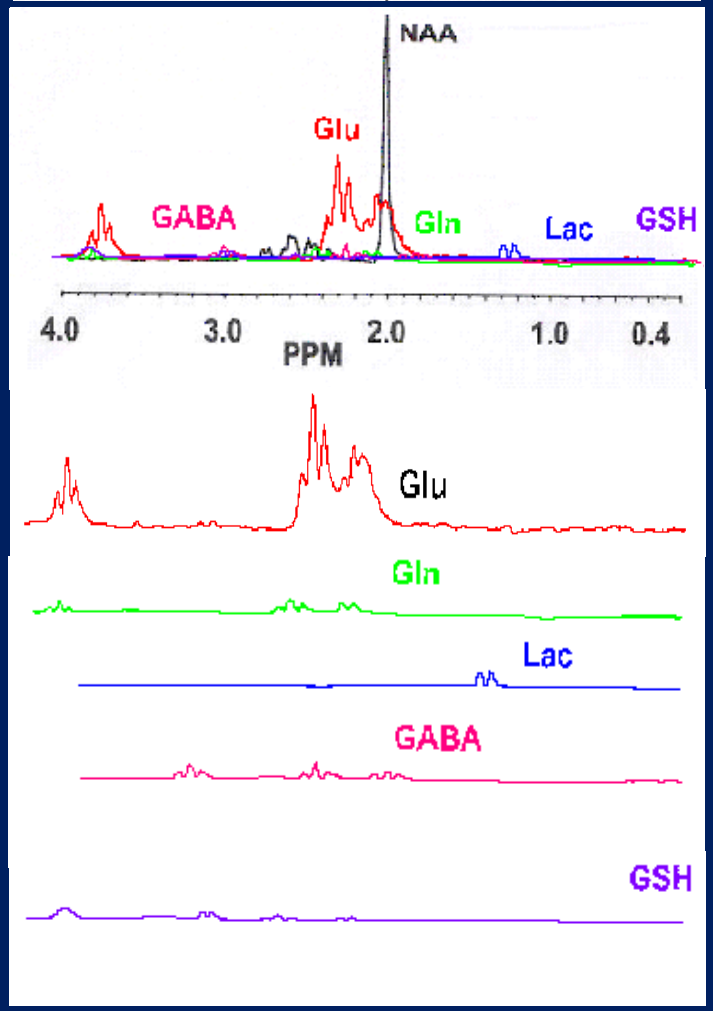
- ***MRUI: Time-domain fitting using a Graphical User Interface (***Barkhuijsen 1985)

- ***Frequency Domain fitting using Linear Combination of Basis-sets (Provencher 1993)***









LCModel Fitting

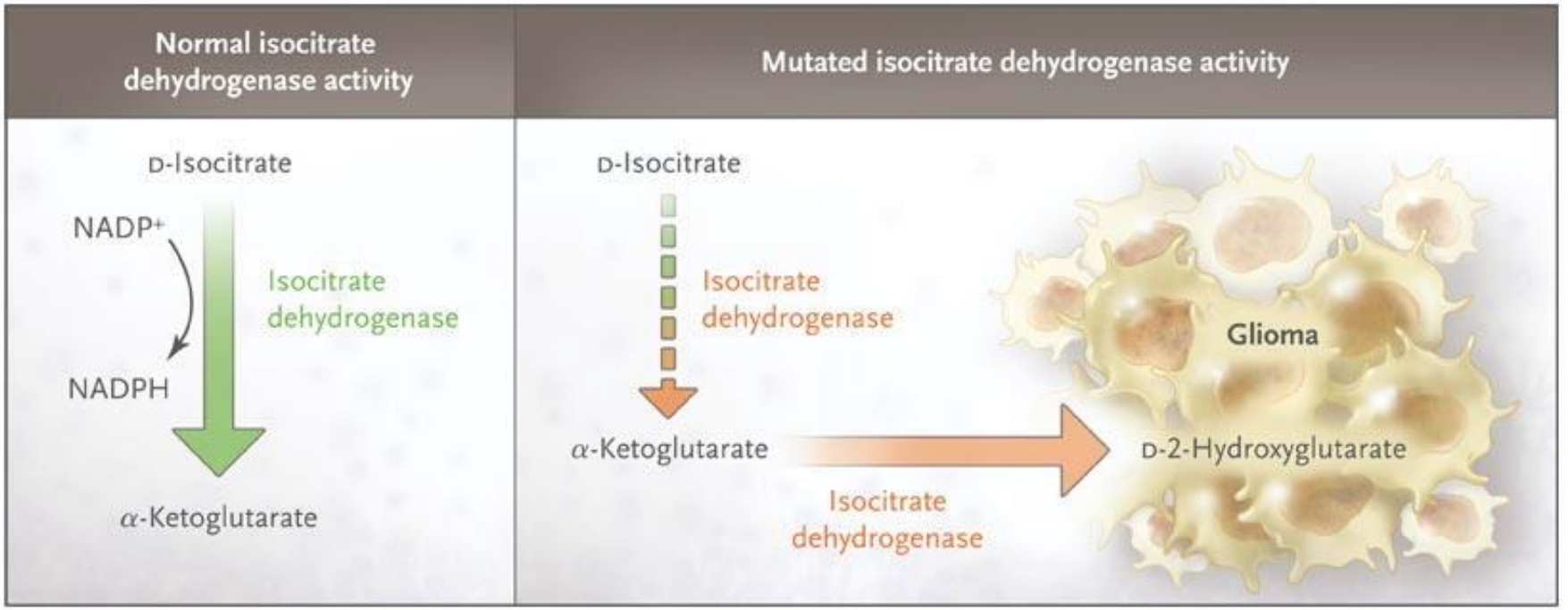
Conc.	%SD	/Cr+PCr	Metabolite
0.000	999%	0.000	Ala
3.518	*14%*	*0.452*	*+Asp*
3.821	10%	0.491	Cr
3.959	10%	0.509	PCr
2.709	17%	0.348	GABA
0.000	999%	0.000	Glc
0.000	999%	0.000	Gln
10.277	5%	1.321	Glu
1.348	3%	0.173	GPC
0.000	999%	0.000	PCh
6.427	3%	0.826	Ins
0.239	111%	0.031	Lac
10.010	2%	1.287	NAA
0.291	82%	0.037	NAAG
0.256	23%	0.033	Scyllo
2.265	17%	0.291	Tau
0.385	47%	0.049	-CrCH2
1.769	7%	0.227	Gua
1.348	3%	0.173	GPC+PCh
10.300	2%	1.324	NAA+NAAG
7.780	2%	1.000	Cr+PCr
10.277	5%	1.321	Glu+Gln
1.724	84%	0.222	Lip13a
0.000	999%	0.000	Lip13b
0.126	652%	0.016	Lip09
11.957	11%	1.537	MM09
0.000	999%	0.000	Lip20
20.740	9%	2.666	MM20
4.600	21%	0.591	MM12
13.786	12%	1.772	MM14
5.342	16%	0.687	MM17
1.724	84%	0.222	Lip13a+Lip13b
20.111	11%	2.585	MM14+Lip13a+L
12.083	9%	1.553	MM09+Lip09
20.740	9%	2.666	MM20+Lip20

IDH1 R132H mutation and 2-HG

- **Somatic mutations of the isocitrate dehydrogenase 1 and 2 genes (IDH1 and IDH2) have recently been implicated in gliomagenesis and are found in approximately 80% of World Health Organization (WHO) grade II-III gliomas and secondary glioblastomas (WHO grade IV) in humans.**

- **Vast majority of IDH1 mutant, high-grade gliomas have evolved from lower grade lesions.**

IDH1 R132H mutation produces 2-HG

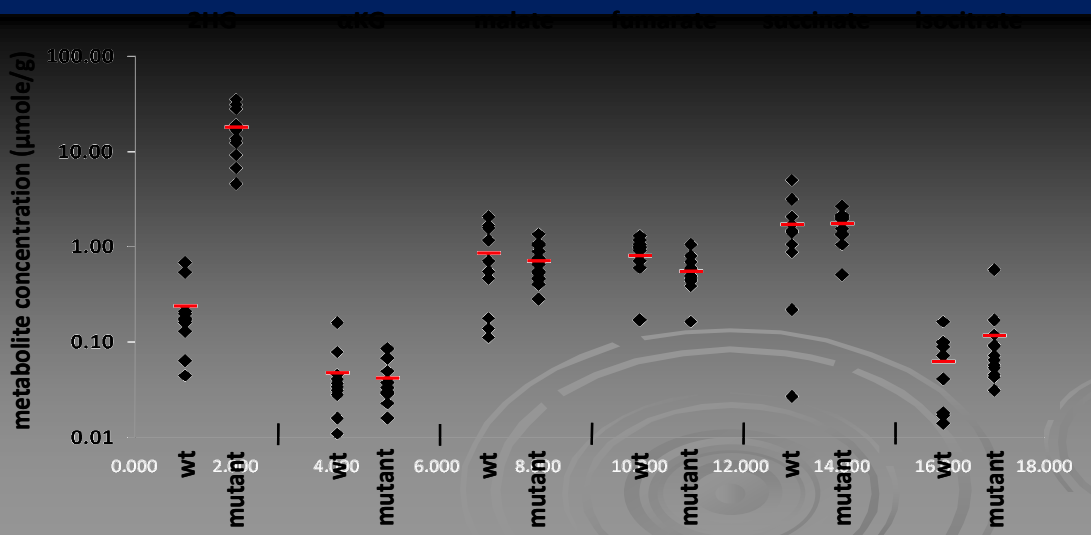


Smeitnik, J. "Metabolism, Gliomas, and IDH1," N Eng J Med 362: 1144-45, 2010

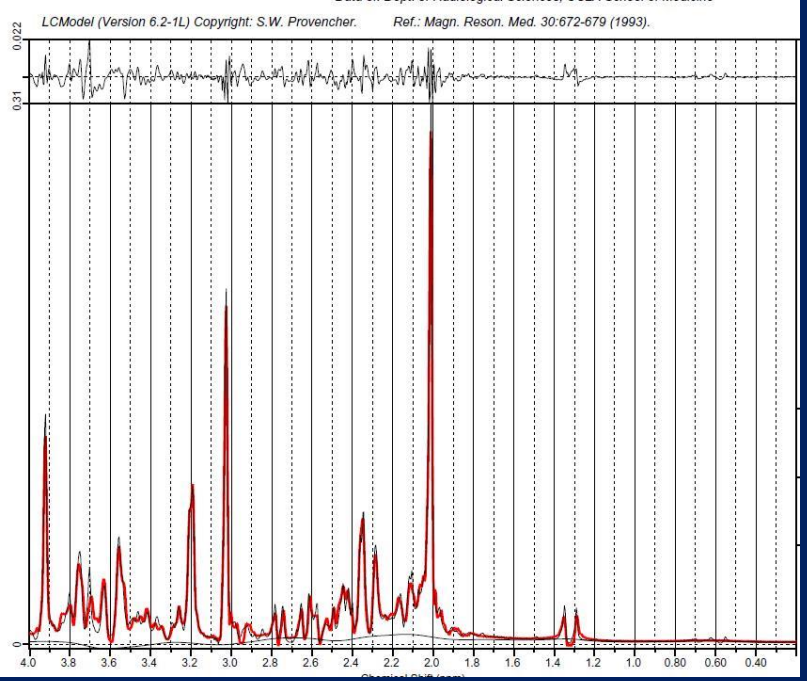
Pope et al. 2012
Andrenosi et al. 2012
Elkhaked et al. 2012
Choi et al. 2012

IDH1 R132H mutation and 2-HG

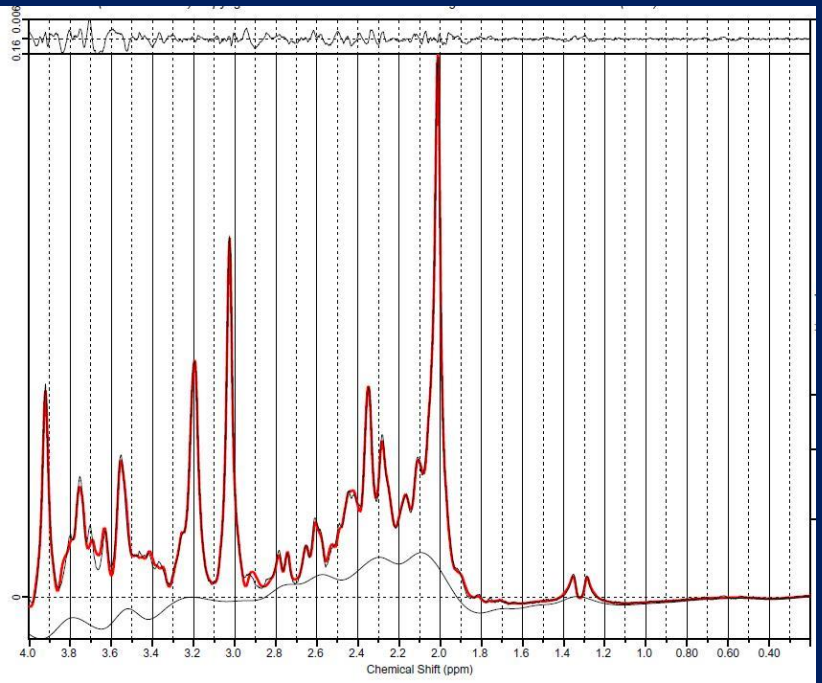
A recent work by Dang and co-workers reported a mutation observed in the isocitrate dehydrogenase1 (IDH1*)* gene, which occurs in the majority of grade II and grade III gliomas and secondary glioblastomas, resulting in significant elevation of 2HG in these tumors.



Dang et al. 2010, Nature

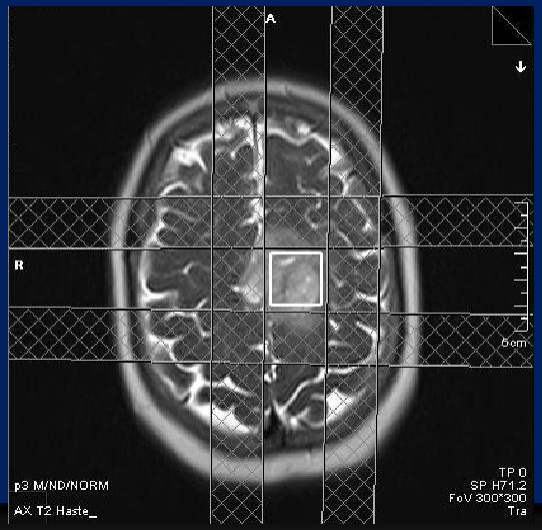


Conc.	%SD	/Cr+PCr	Metabolite
0.000	999%	0.000	Ala
0.558	28%	0.214	Asp
0.966	8%	0.371	Cr
1.642	6%	0.629	PCr
0.660	18%	0.253	GABA
1.088	13%	0.417	Glc
0.948	15%	0.363	Gln
5.411	5%	2.075	Glu
0.245	10%	9.4E-02	GPC
0.433	7%	0.166	PCh
0.815	10%	0.313	GSH
0.000	999%	0.000	2HG
2.411	5%	0.925	Ins
0.474	13%	0.182	Lac
3.534	2%	1.355	NAA
0.277	21%	0.106	NAAG
0.142	89%	5.5E-02	PE
2.48E-02	78%	9.5E-03	Scyllo
0.414	30%	0.159	Tau
0.279	29%	0.107	-CrCH2
0.678	3%	0.260	GPC+PCh
3.810	2%	1.461	NAA+NAAG
2.608	2%	1.000	Cr+PCr
6.359	5%	2.438	Glu+Gln



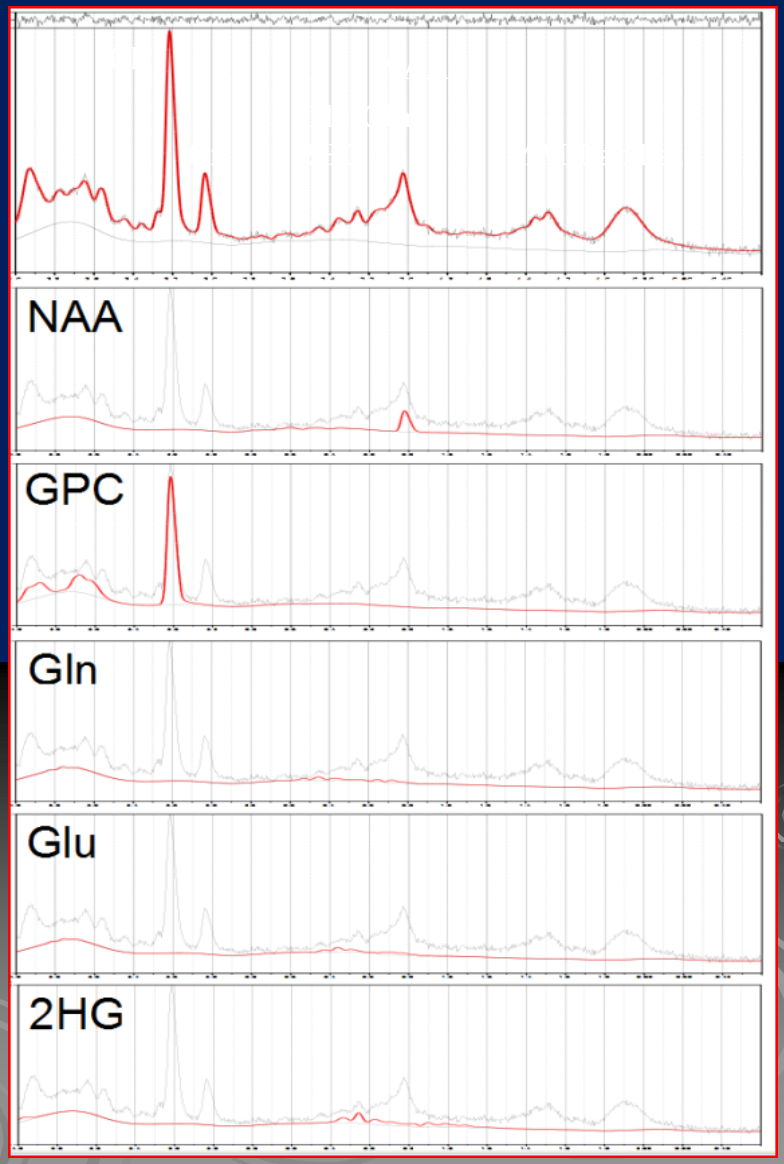
Conc.	%SD	/Cr+PCr	Metabolite
0.000	999%	0.000	Ala
0.886	14%	0.286	Asp
1.414	7%	0.457	Cr
1.680	6%	0.543	PCr
0.322	32%	0.104	GABA
1.464	8%	0.473	Glc
0.698	16%	0.226	Gln
6.218	5%	2.010	Glu
0.223	12%	7.2E-02	GPC
0.544	6%	0.176	PCh
0.952	7%	0.308	GSH
1.095	16%	0.354	2HG
2.645	4%	0.855	Ins
0.432	10%	0.140	Lac
3.598	2%	1.163	NAA
0.310	18%	0.100	NAAG
0.398	30%	0.129	PE
7.20E-02	22%	2.3E-02	Scyllo
0.415	28%	0.134	Tau
3.34E-02	181%	1.1E-02	-CrCH2
0.768	2%	0.248	GPC+PCh
3.908	2%	1.263	NAA+NAAG
3.093	2%	1.000	Cr+PCr
6.916	5%	2.236	Glu+Gln

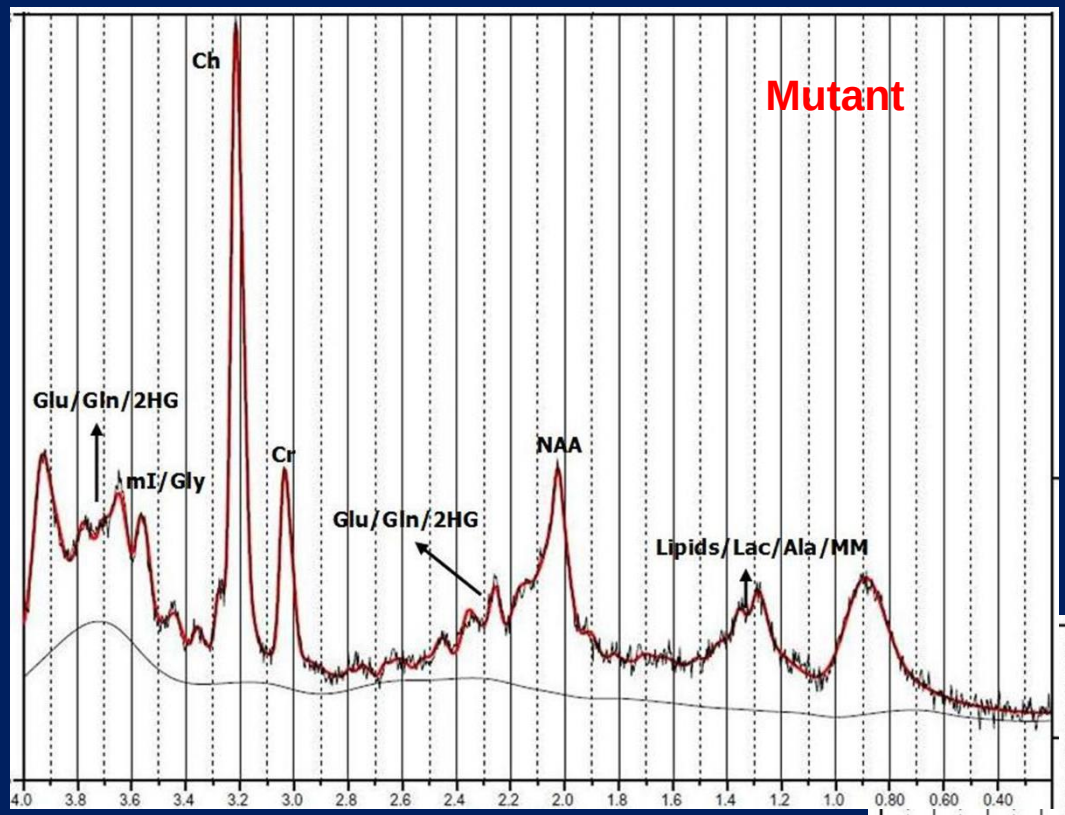
Scanner	**:**	**Siemens 3T Trio-Tim**
Coil	**:**	**12 Channel receive**
Subjects	**:**	**24 brain tumor**
Mutant Tumor	**:**	**9 (Mean age 43 years)**
Wild Tumor	**:**	**15 (Mean age 59 years)**
Tumor Grade	**:**	**14 primary GBM (grade IV), 6 oligodendroglioma (grade III), and 4 low grade (grade II)**

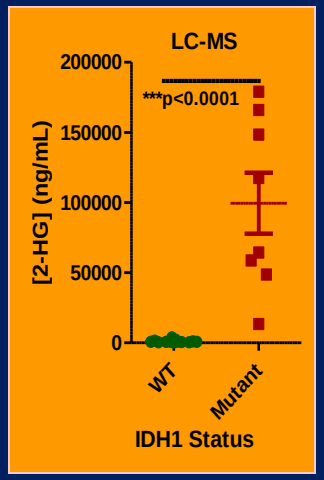


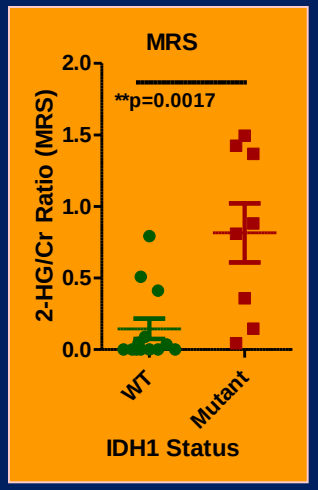
A 69 y.o. Anaplastic oligodendroglioma (WHO grade III) with *IDH1* mutation

-PRESS
-8cm^3
-2s/30ms
-128 averages









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Non-invasive detection of 2-hydroxyglutarate and other metabolites in *IDH1* mutant glioma patients using magnetic resonance spectroscopy

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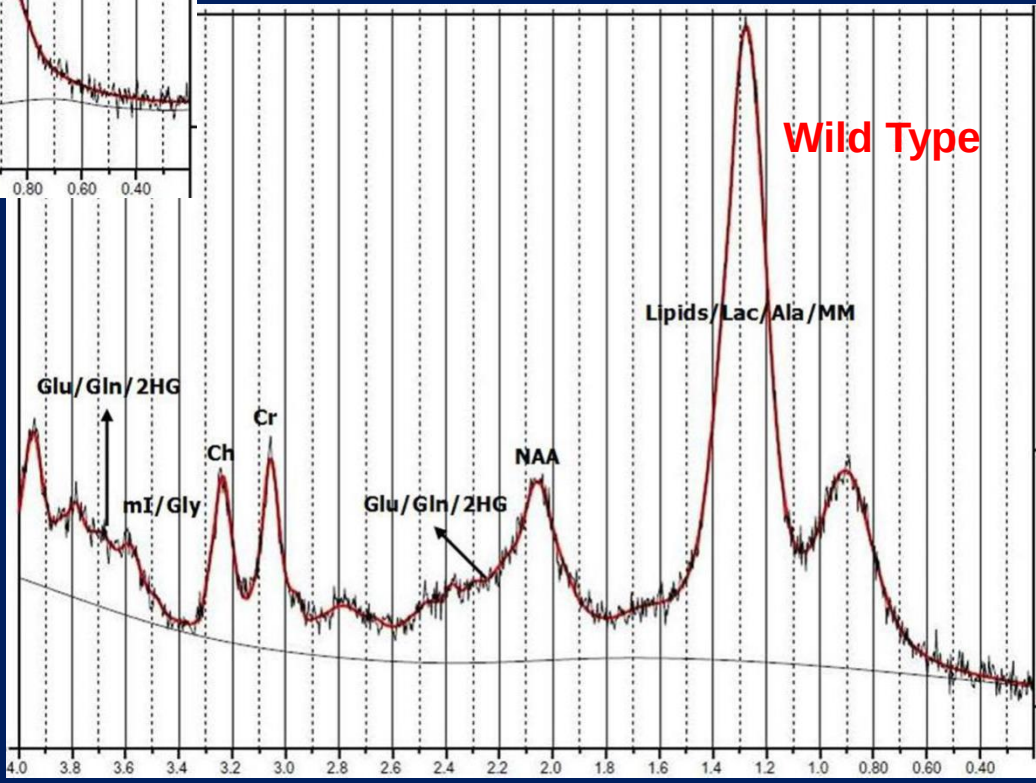


Cramer-Rao Lower Bound (CRLB) Values – 2HG MRS Peak Fitting Error Estimation

Wild Type: CRLB Values > 60 %SD (60-999%)

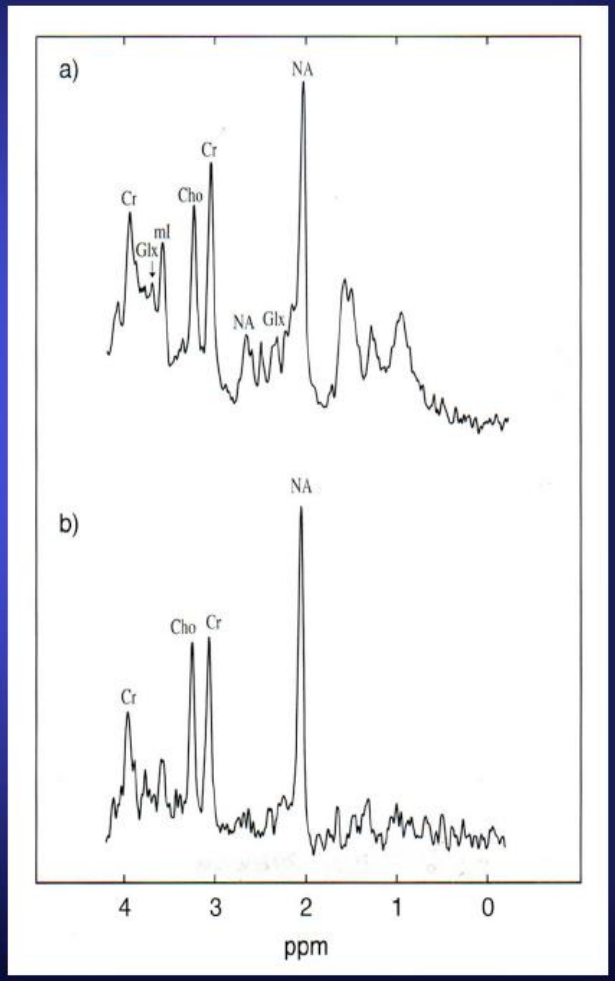
Mutant: CRLB Values < 60 %SD

Possible Solutions to Signal overlap in 1D MRS

- Subtraction-based spectral Editing sequences (GABA, Glu, Taurine, GSH, myo-inositol, etc.)
- Multiple-quantum filter MRS techniques

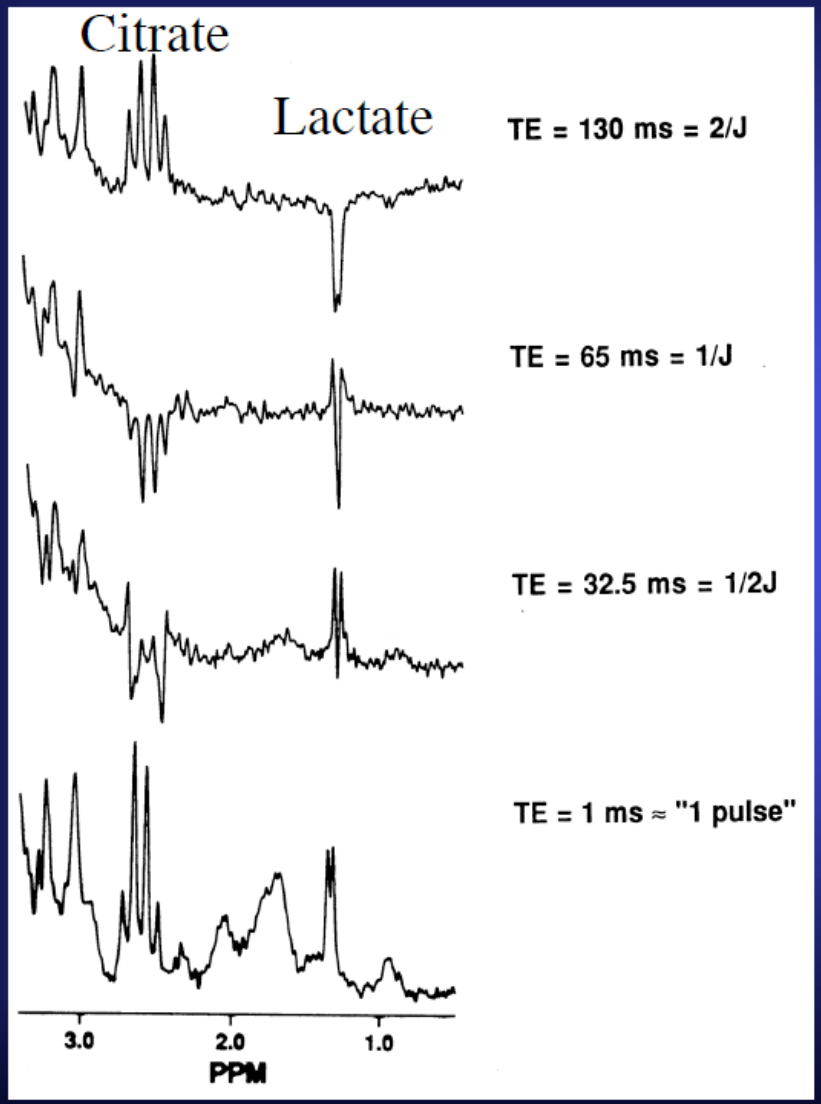
Spectral Editing Techniques I

The use of longer echo times will cause the loss of not only macromolecules such as lipids but also metabolites with shorter T2 relaxation times.



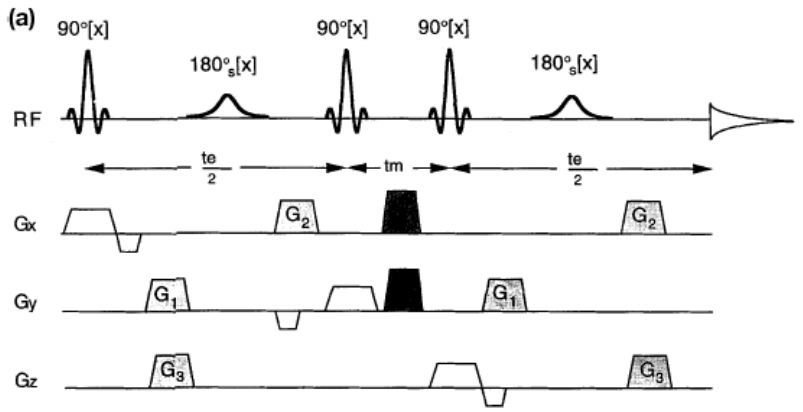
Spectral Editing Techniques II

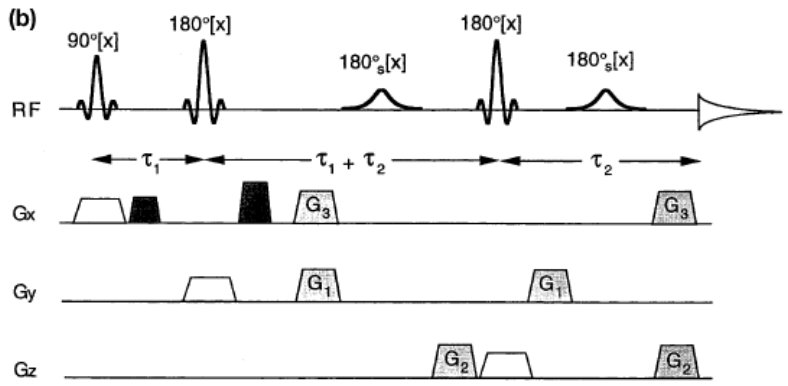
Simple editing based on J-coupling



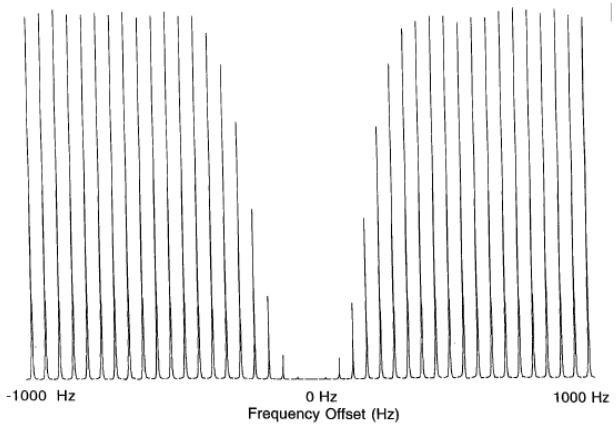
This J-modulation results in a inverted doublet at TE = 1/2 * 1/(J/2) = 1/J = 1/7Hz = 144 ms, and returning to a positive doublet at TE= 1/(J/2) = 2/J = 288 ms. Whereas the strongly coupled citrate spin system - is negative at 65 ms and has a maximum around 130ms.

MEGA Spectral Editing Techniques

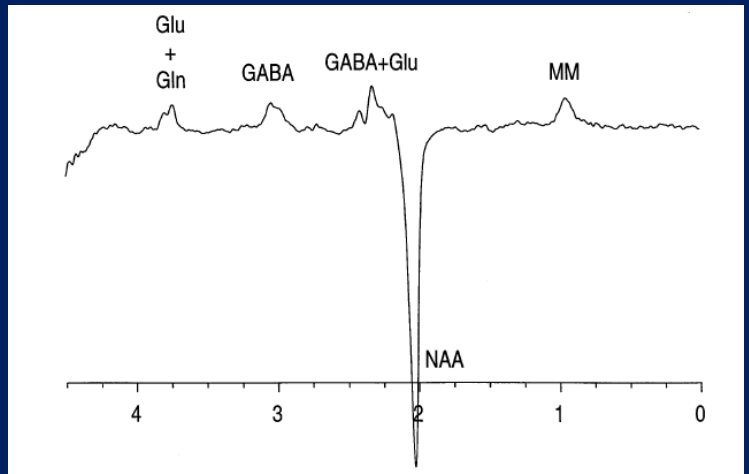




The sequence element MEGA as implemented in STEAM is shown in A. Excitation pulses and gradient waveforms for the PRESS sequence incorporating MEGA are illustrated in B. Gradients G_1, G_2 and G_3 are used for MEGA implementation in both sequences. For suppression of the water signal only, a single-banded frequency selective pulse is used



Offset characteristics of MEGA. To demonstrate that phase sensitive spectra do not exhibit phase distortion outside the bandwidth of the frequency selective pulses, the frequency of the selective pulses in MEGA was varied in 50 Hz increments (±1000 Hz) about the water resonance. Spectra were acquired without signal averaging using $TE = 32$ ms and $TR = 3$ s



An edited spectrum from a voxel in the occipital area of a human subject acquired using MEGA–PRESS (Fig. 2B). Parameters for the displayed spectrum are : $TE = 68$ ms, $TR = 3$ s, voxel size = 27 mL, NEX = 64, total acquisition time = 6.4 min

Mescher et al. NMR Biomed 1998

GABA concentrations using MEGA-PRESS-IVS in the AC and DLPFC

Region	Visit	GABA/H_20 ($x10^{-6}$ IU)	STD.	Mean CV (%)	Mean Abs Diff (%)
AC	1	4.85	0.8	13.6%	16.5%
	2	4.39	0.6		
DLPFC	1	7.62	0.2	13.4%	18.1%
	2	7.33	0.2		

IU - institutional units, STD. - Standard Deviation

J Magn Reson Imaging. 2013 August ; 38(2): 460–467. doi:10.1002/jmri.23997.

Reproducibility of Brain Spectroscopy at 7T using Conventional Localization and Spectral Editing Techniques

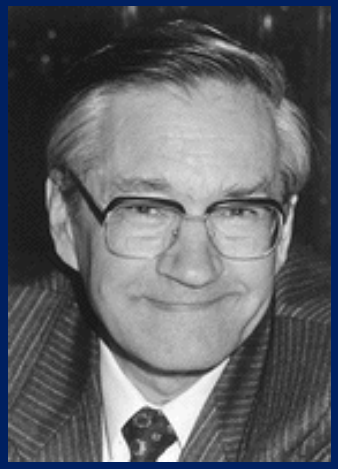
S. Andrea Wijtenburg, Ph.D.[1], **Laura M. Rowland, Ph.D.**[1], **Richard A.E. Edden, Ph.D.**[2,3], and **Peter B. Barker, D.Phil.**[2,3,*]

Possible Solutions to Signal overlap in 1D MRS

- Subtraction-based spectral Editing sequences (GABA, Glu, Taurine, GSH, myo-inositol, etc.)
- Multiple-quantum filter MRS techniques
- Adding another dimension to 1D MRS

Single-voxel localized 2D MRS : L-COSY and JPRESS

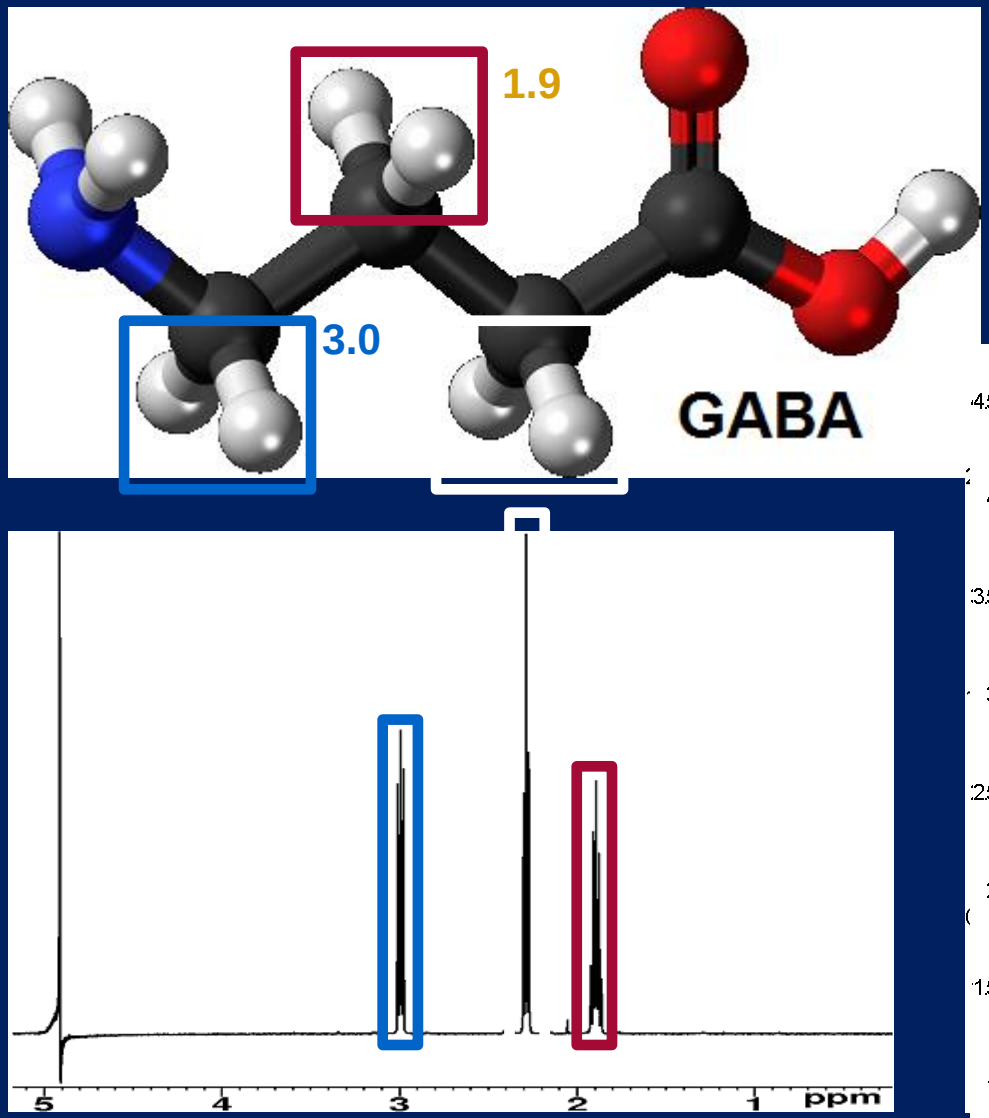
Pioneers of Two-Dimensional Nuclear *Magnetic Resonance Spectroscopy*

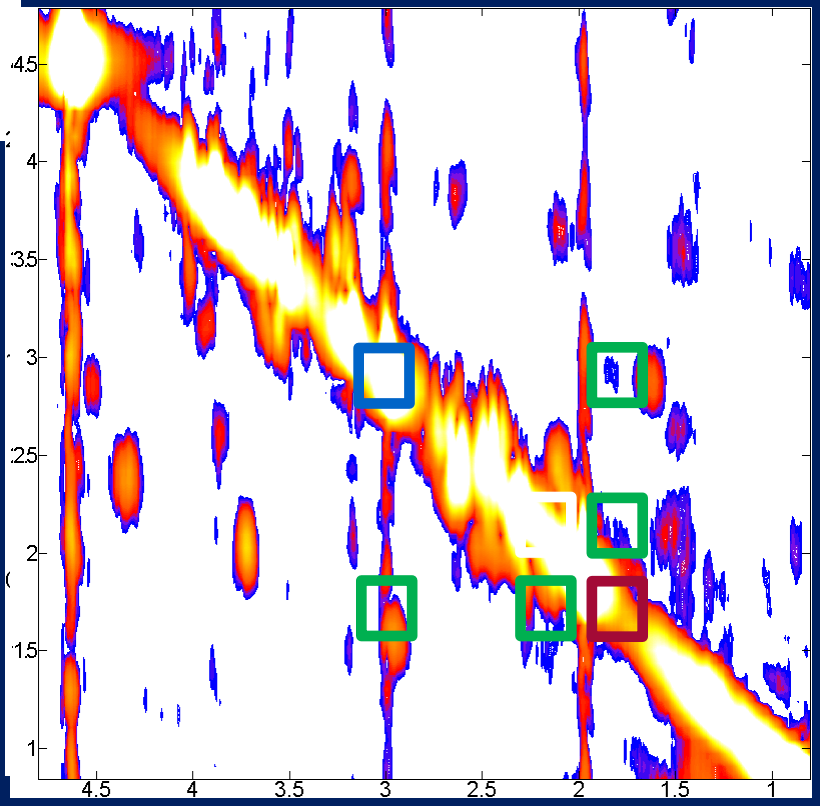


Richard R. Ernst
1991 Nobel Prize

Kurt Wüthrich
2002 Nobel Prize

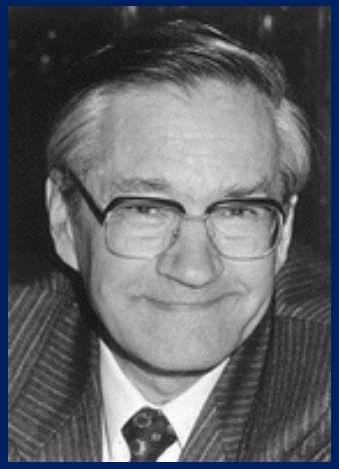
Why 2D Spectroscopy?





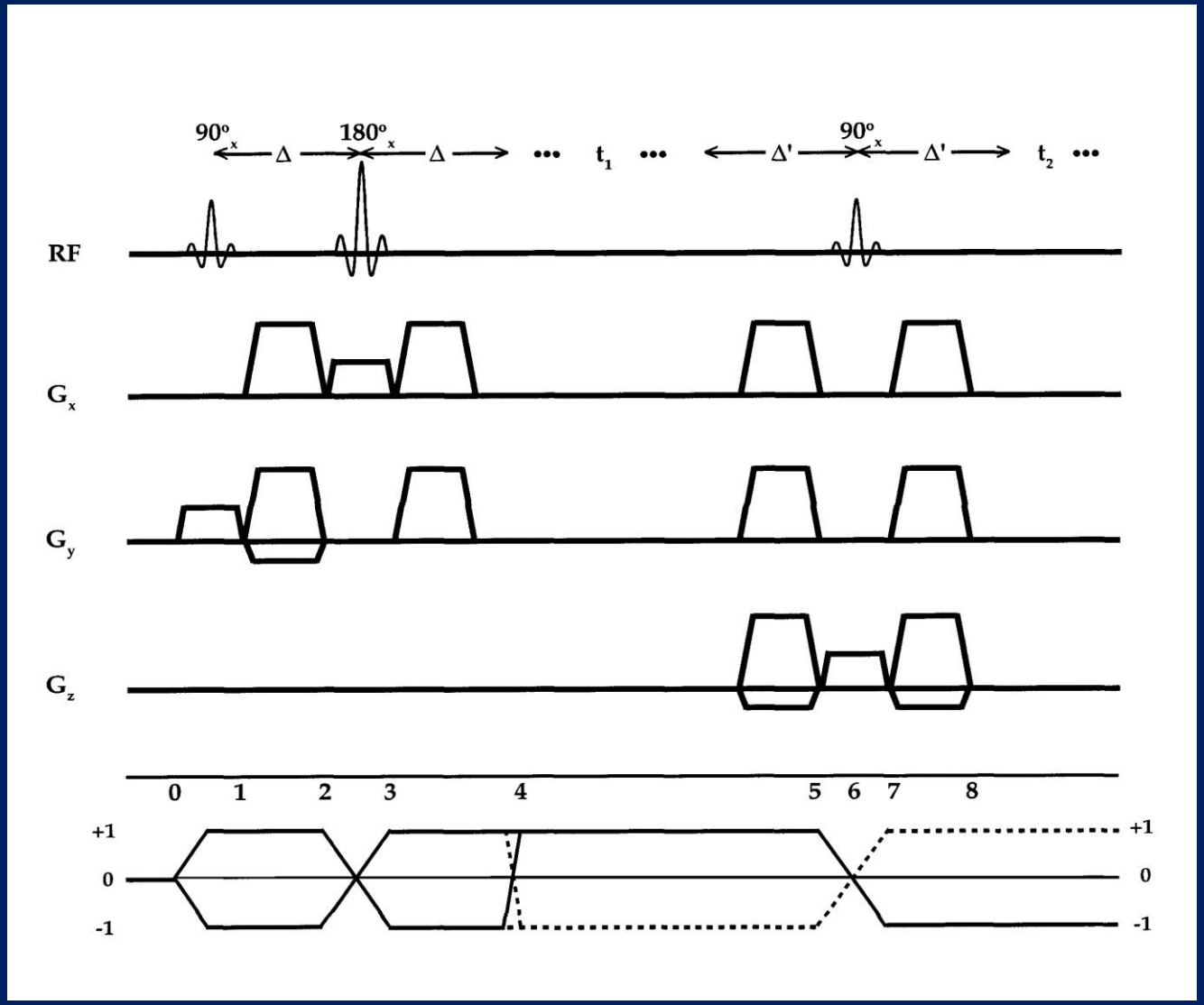
Verma et al. ISMRM 2014

A quote from Nobel laureate Richard Ernst



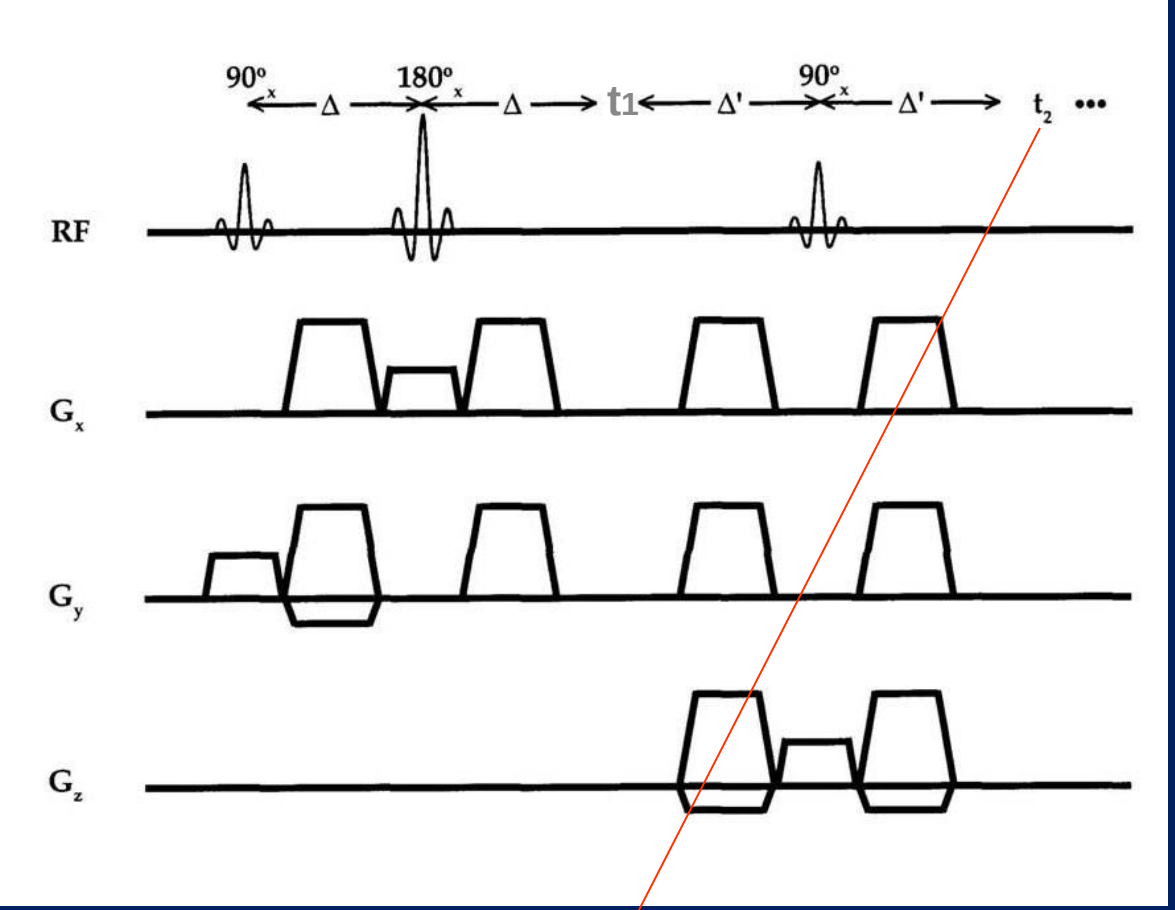
"One-dimensional spectra that are rendered inscrutable because of severe overlap may be unravelled by separating interactions of different physical origins, e.g. chemical shift and couplings, thus making it possible to spread the signals in a second frequency dimension much like opening a Venetian blind."

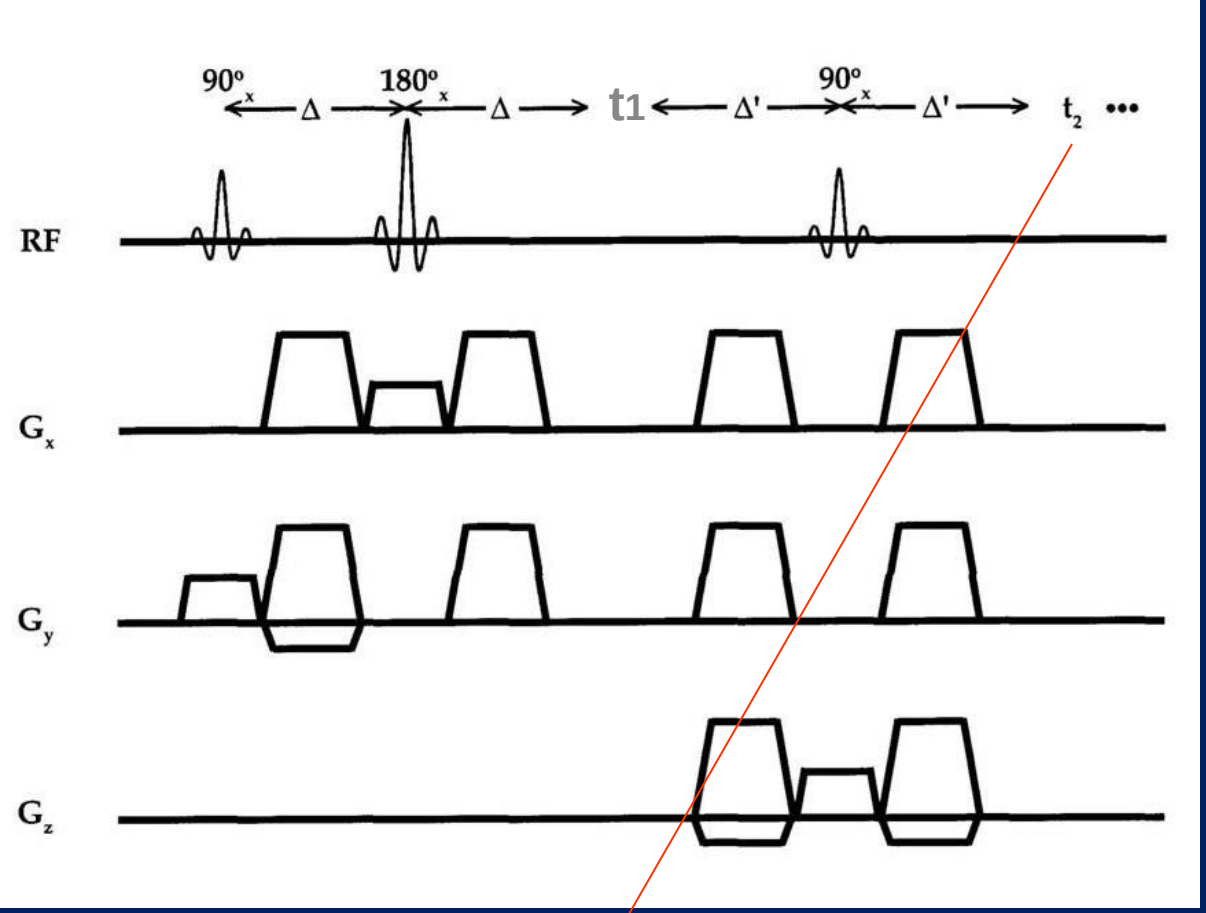
Localized 2D Correlated Spectroscopy (L- COSY)

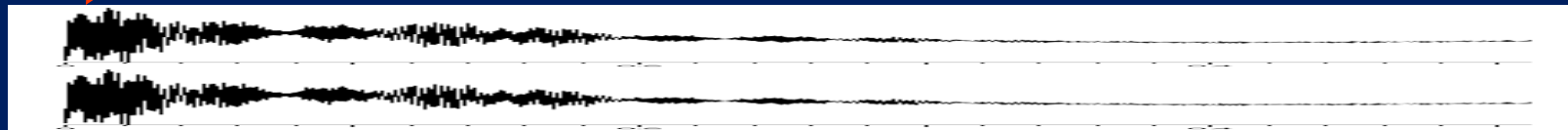


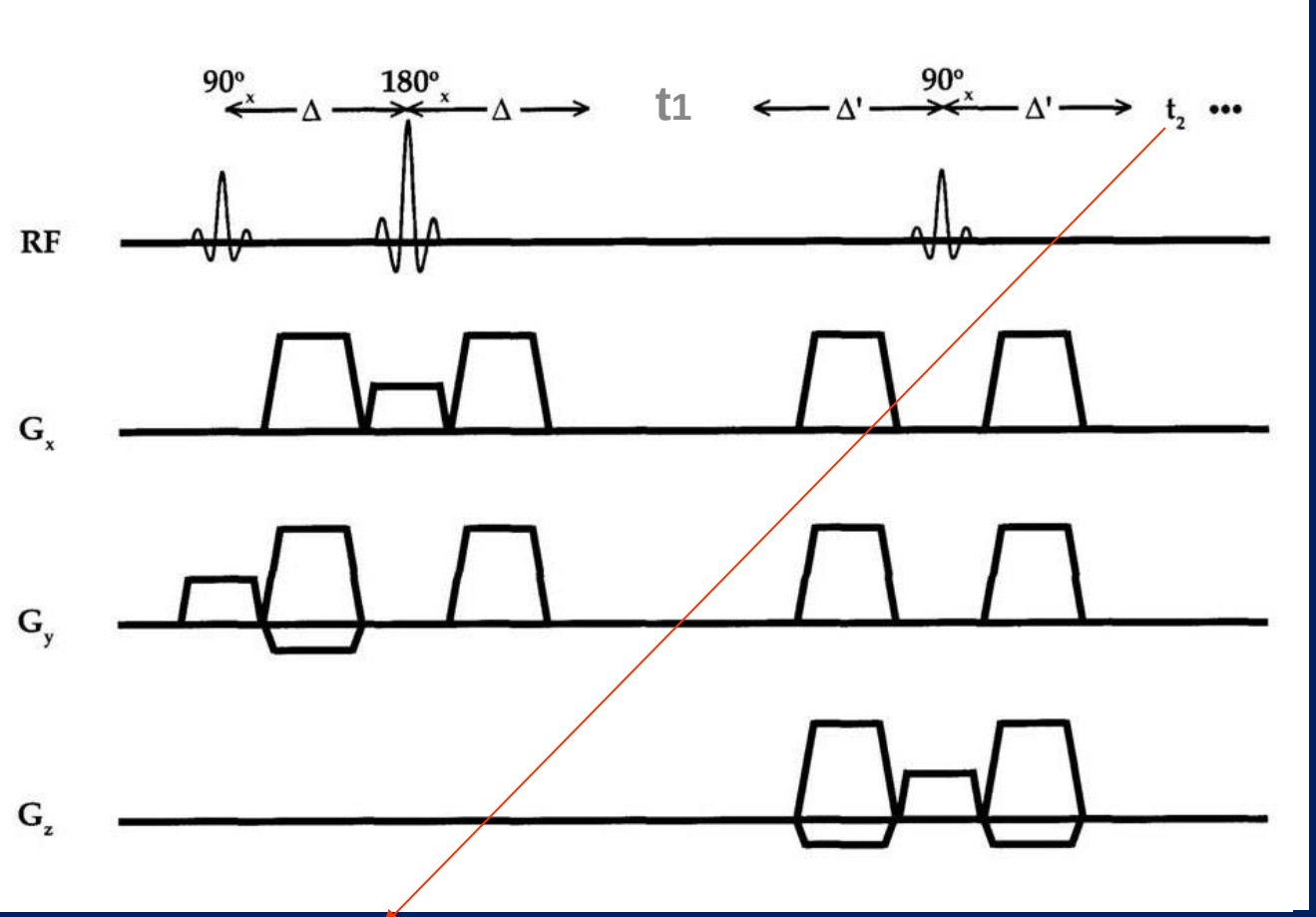
- *Based on a spin-echo and a coherence-transfer-echo*
  Hahn (1952) / Maudsley, Wokaun and Ernst (1978)

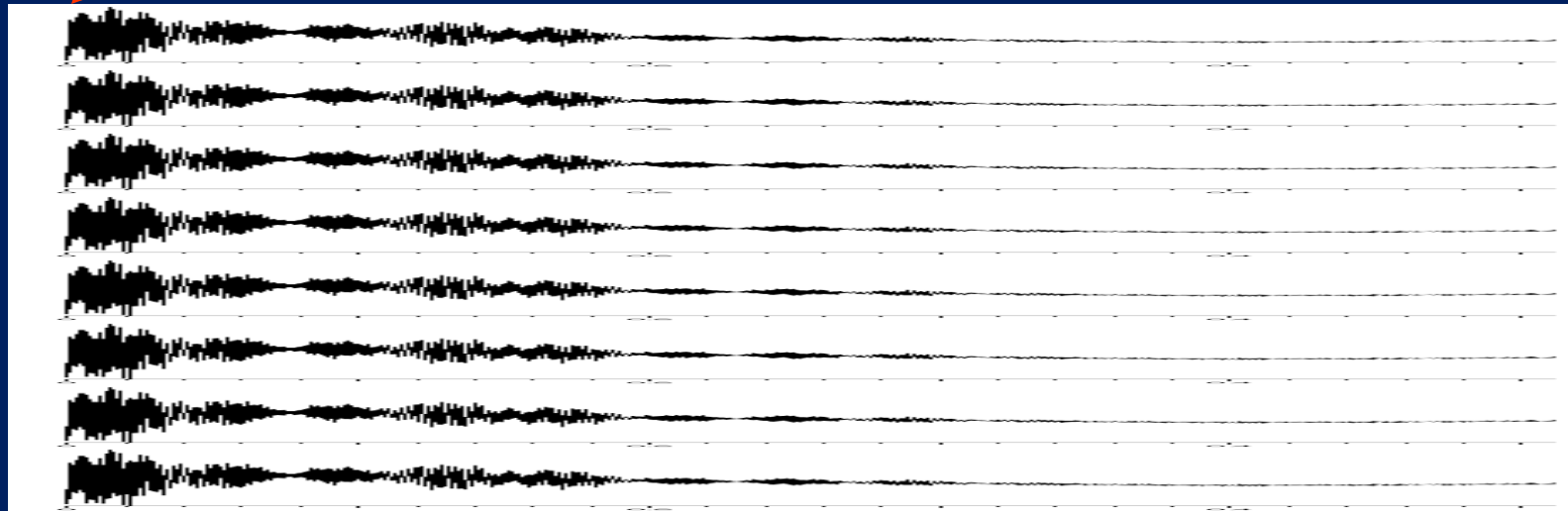
Thomas et al. (MRM2001)

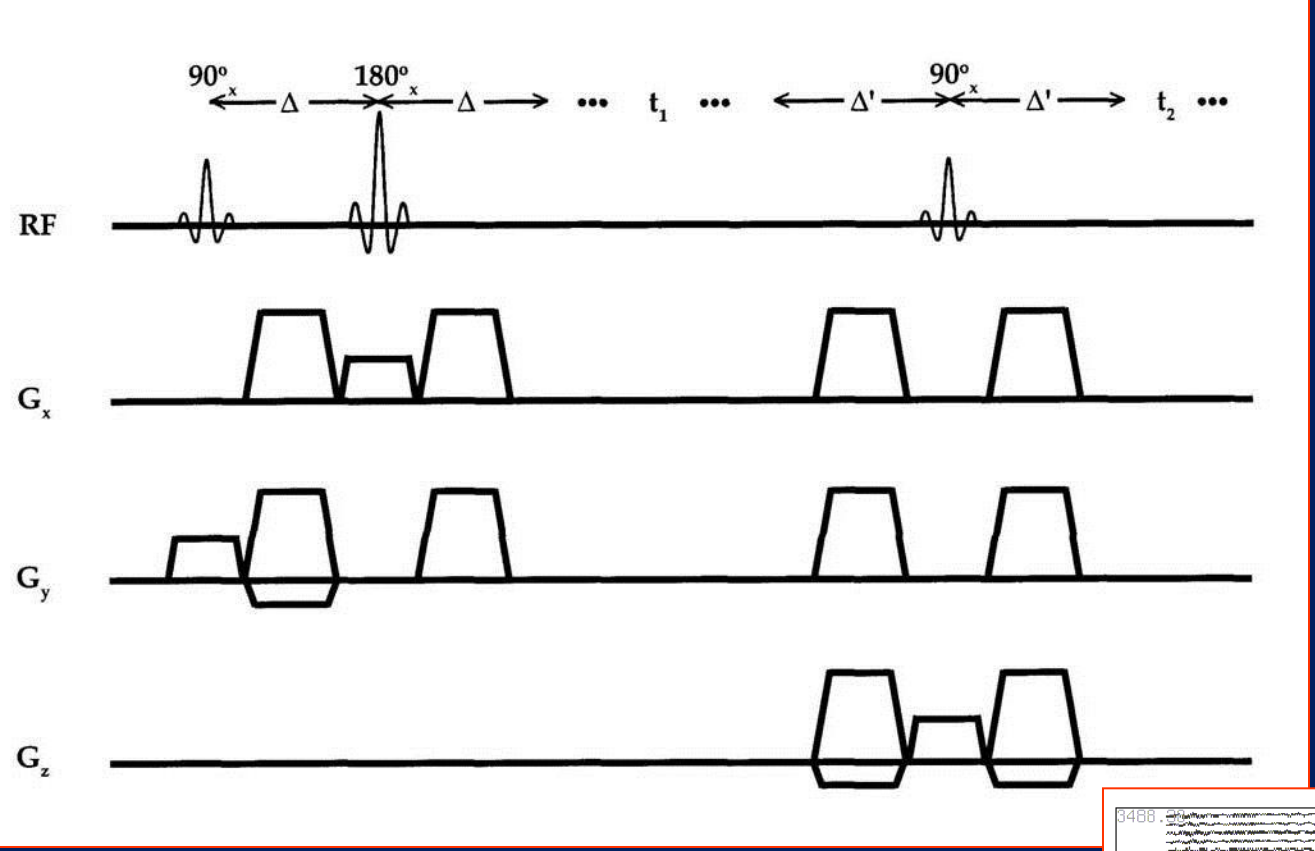

90°x
Δ
180°x
Δ
t1
Δ'
90°x
Δ'
t2
•••
RF
Gx
Gy
Gz


90°x
Δ
180°x
Δ
t1
Δ'
90°x
Δ'
t2
•••
RF
Gx
Gy
Gz

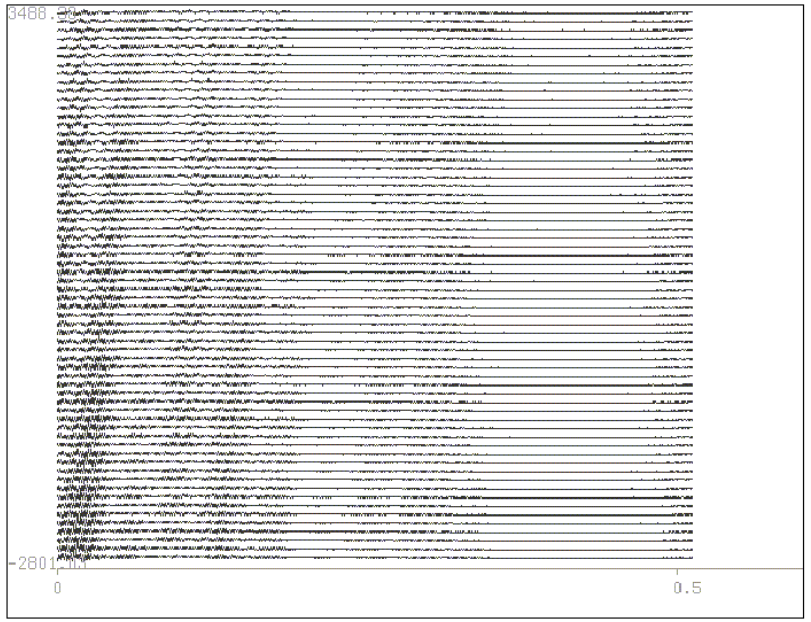


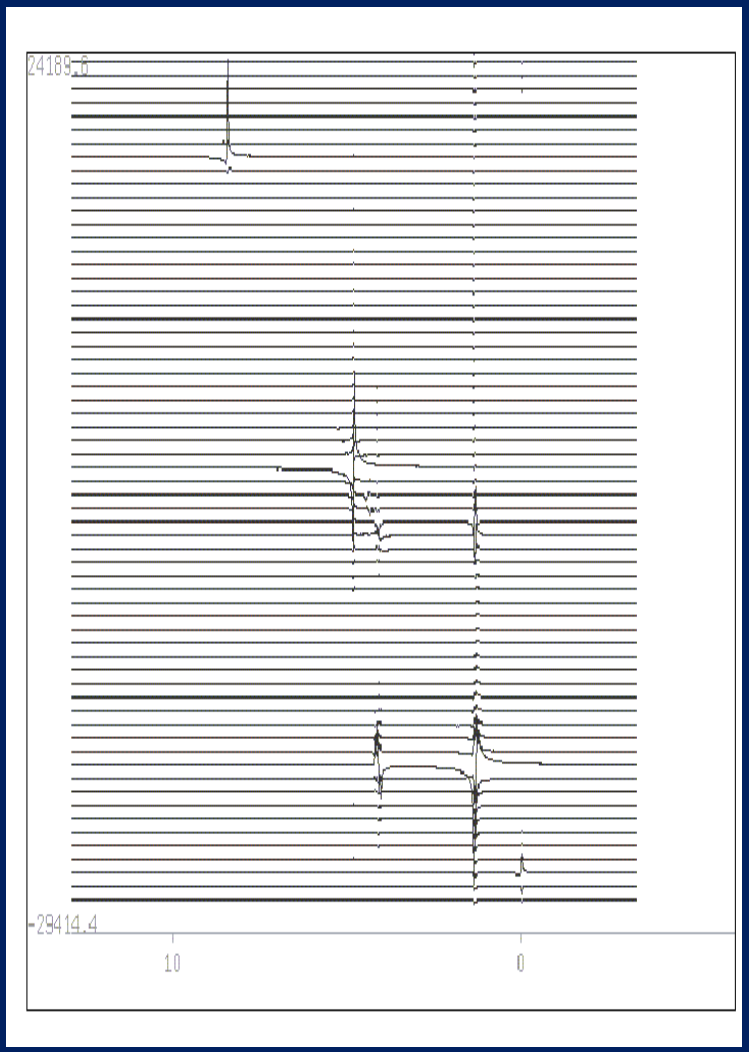

90°x
Δ
180°x
Δ
t1
Δ'
90°x
Δ'
t2
•••
RF
Gx
Gy
Gz



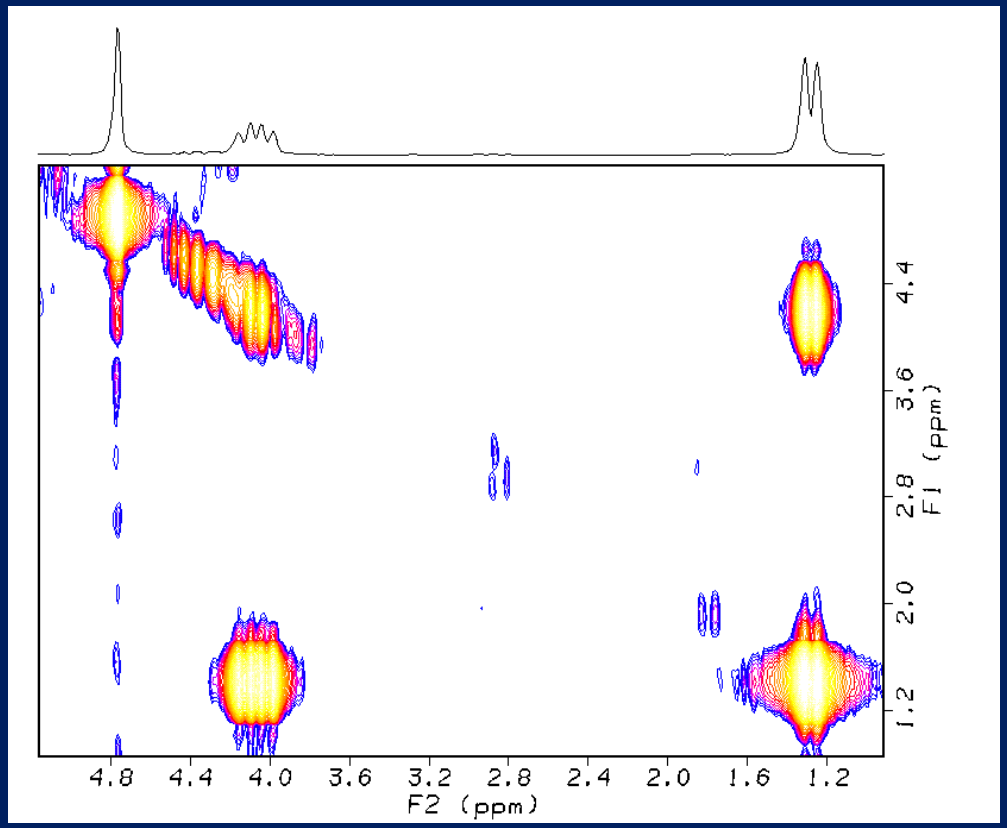


Previous process is repeated until we have 64 or 96 or 128 FIDs as shown below





F1



F2

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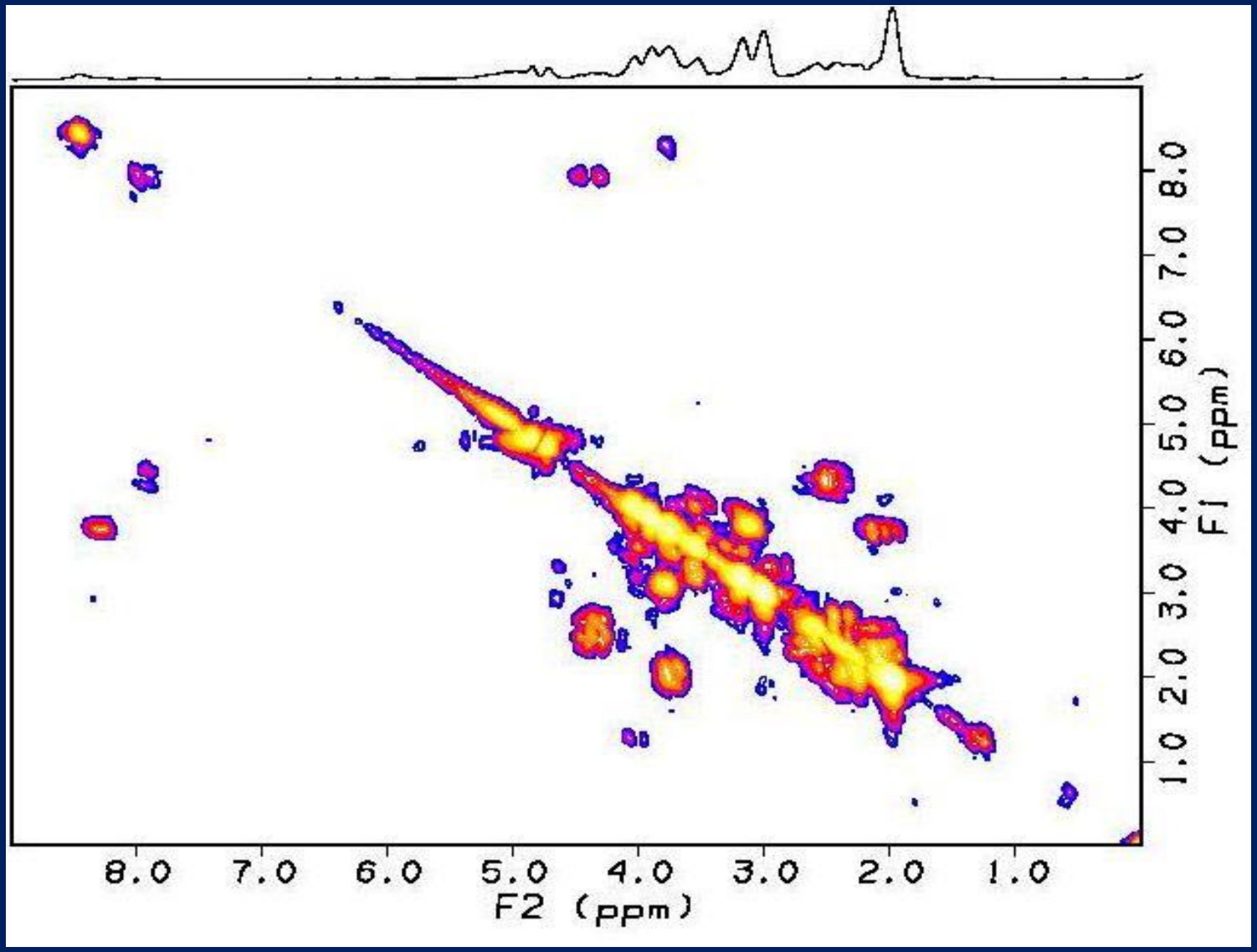
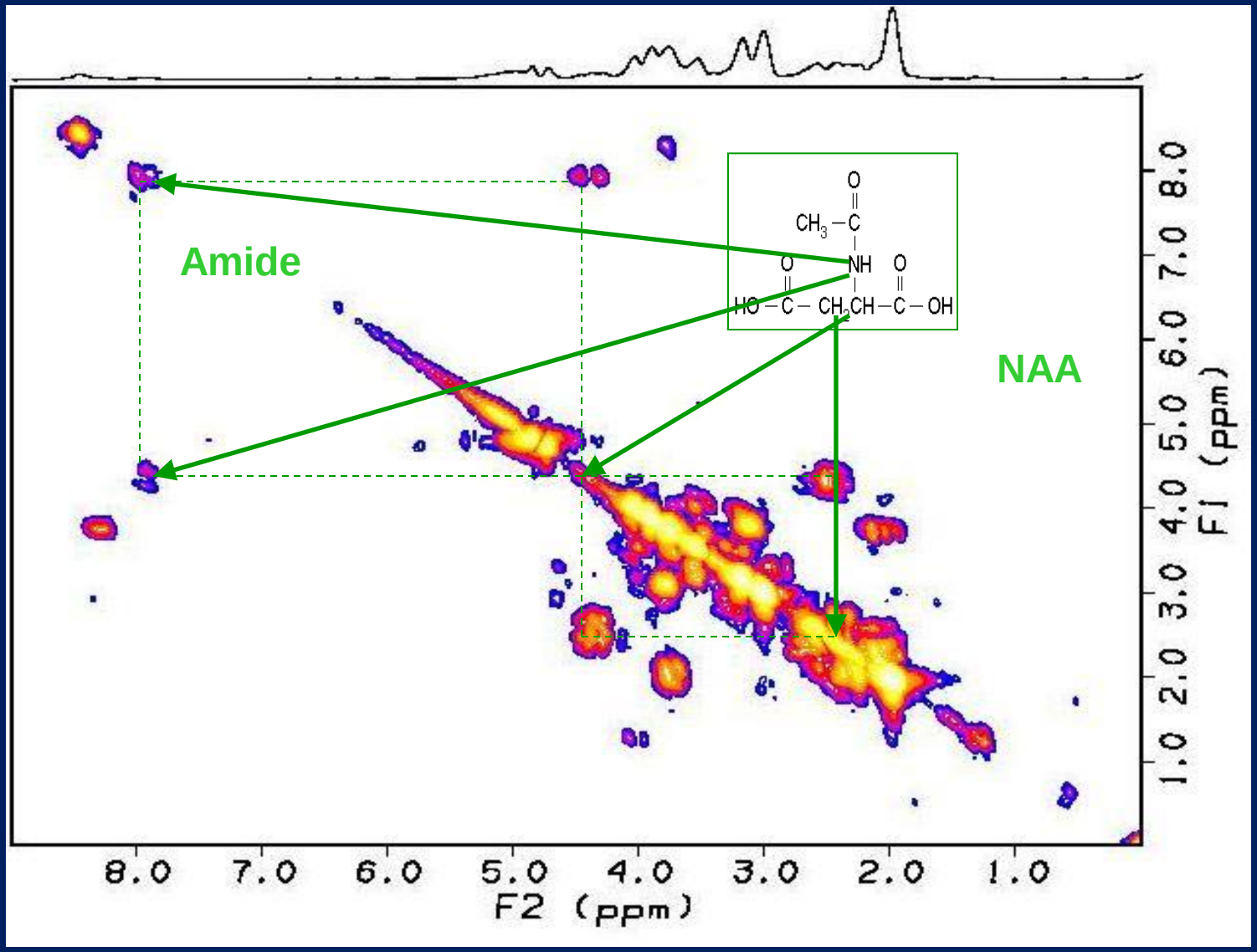
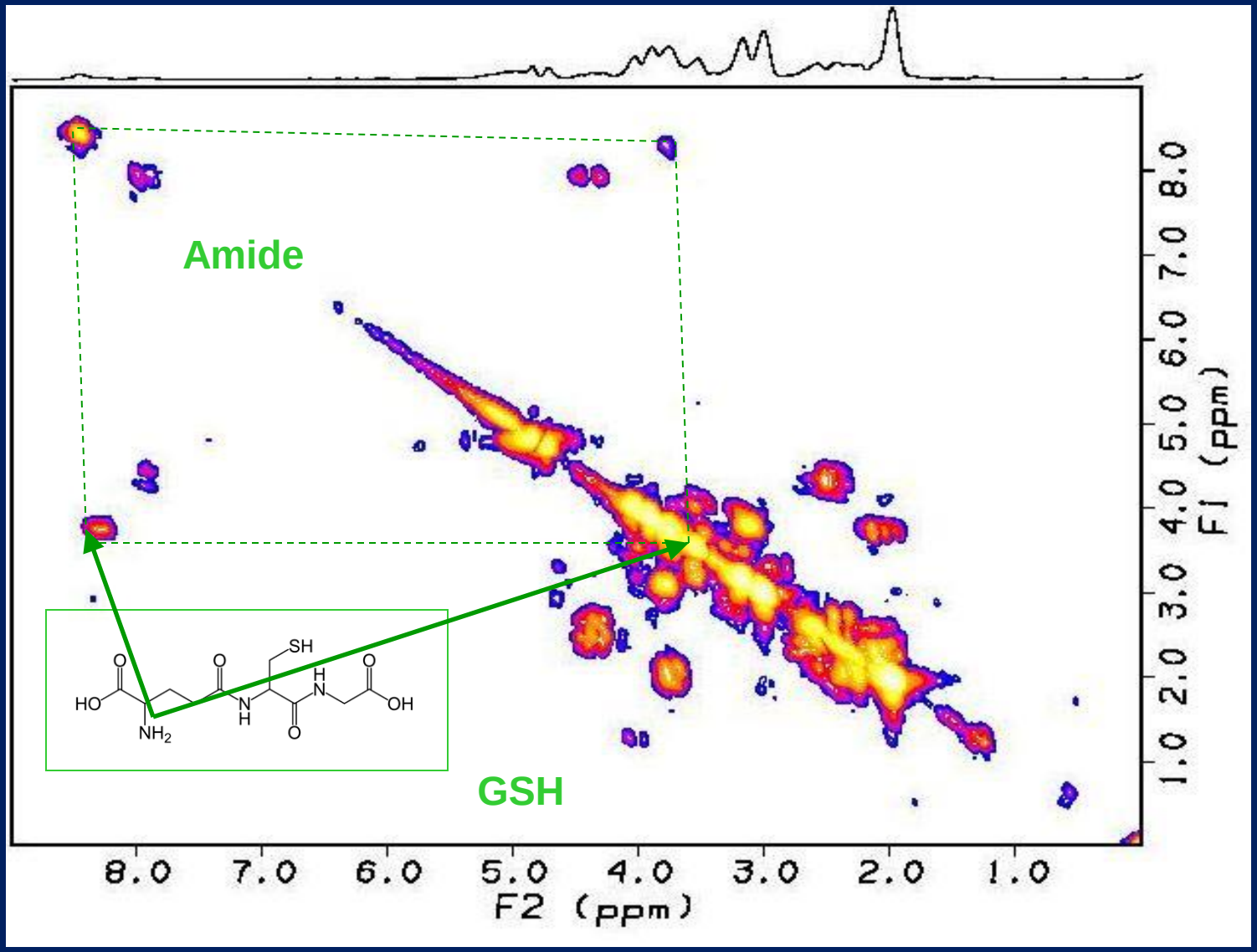
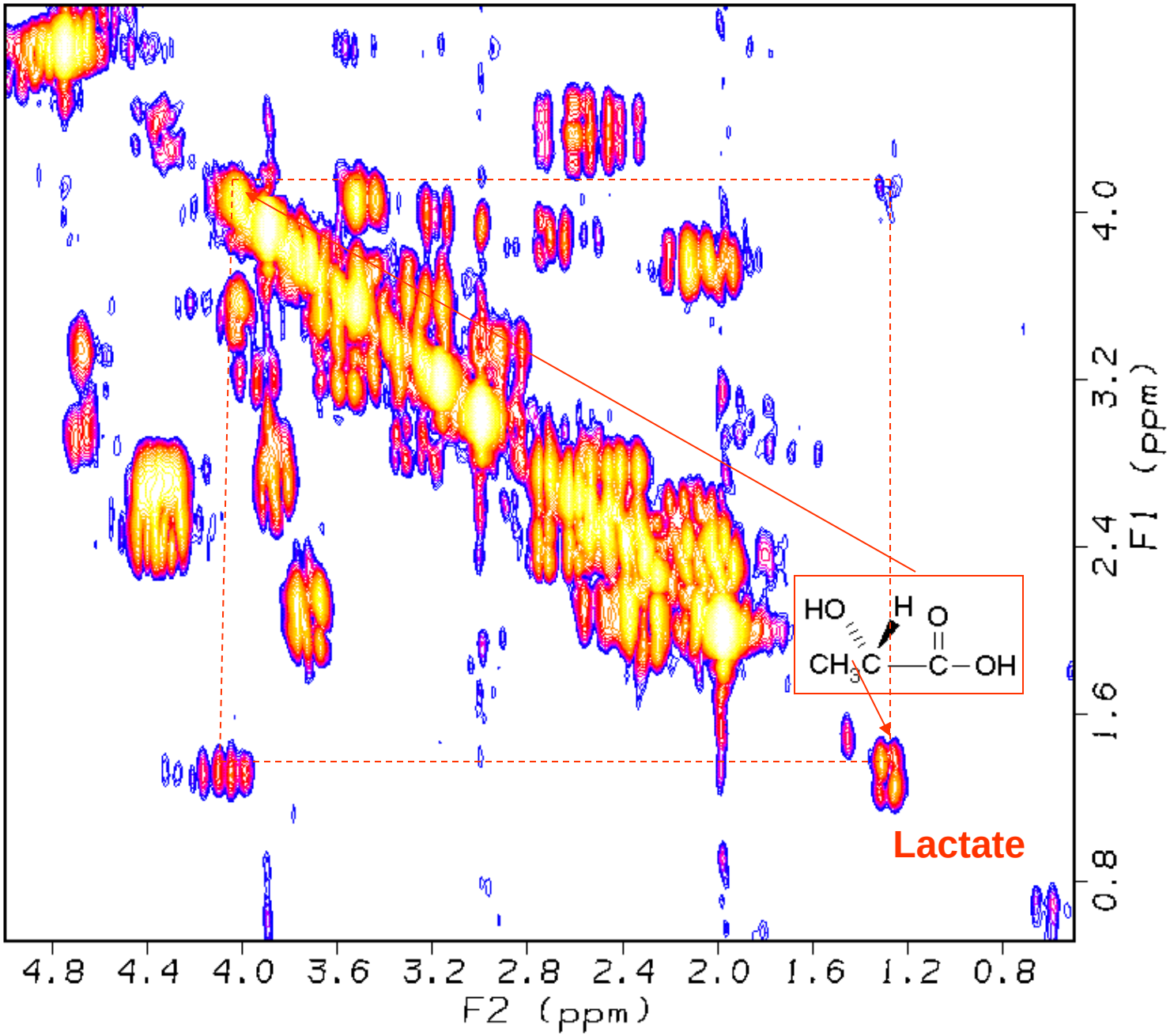
Brain Phantom 3T MRI/MRS Scanner




Amide
NAA
O
CH3 – C
O NH O
HO – C – CH2CH – C – OH
8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0
F2 (ppm)
1.0 2.0 3.0 4.0 5.0 6.0 7.0 8.0
F1 (ppm)


Amide
GSH
HO
O
NH2
O
N
H
SH
H
N
O
O
OH
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
F2 (ppm)
F1 (ppm)

2D MRS – Gray Matter Metabolites



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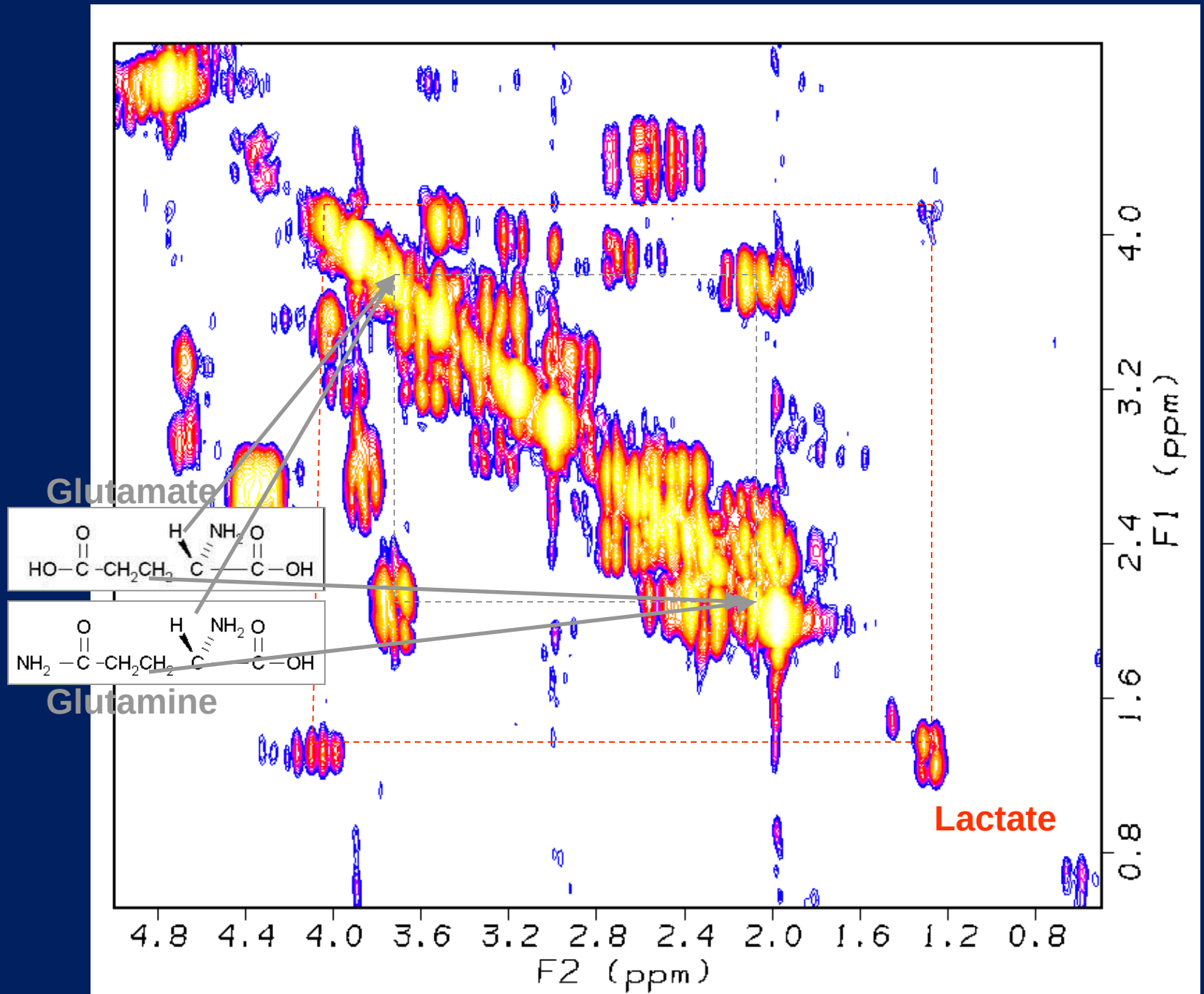
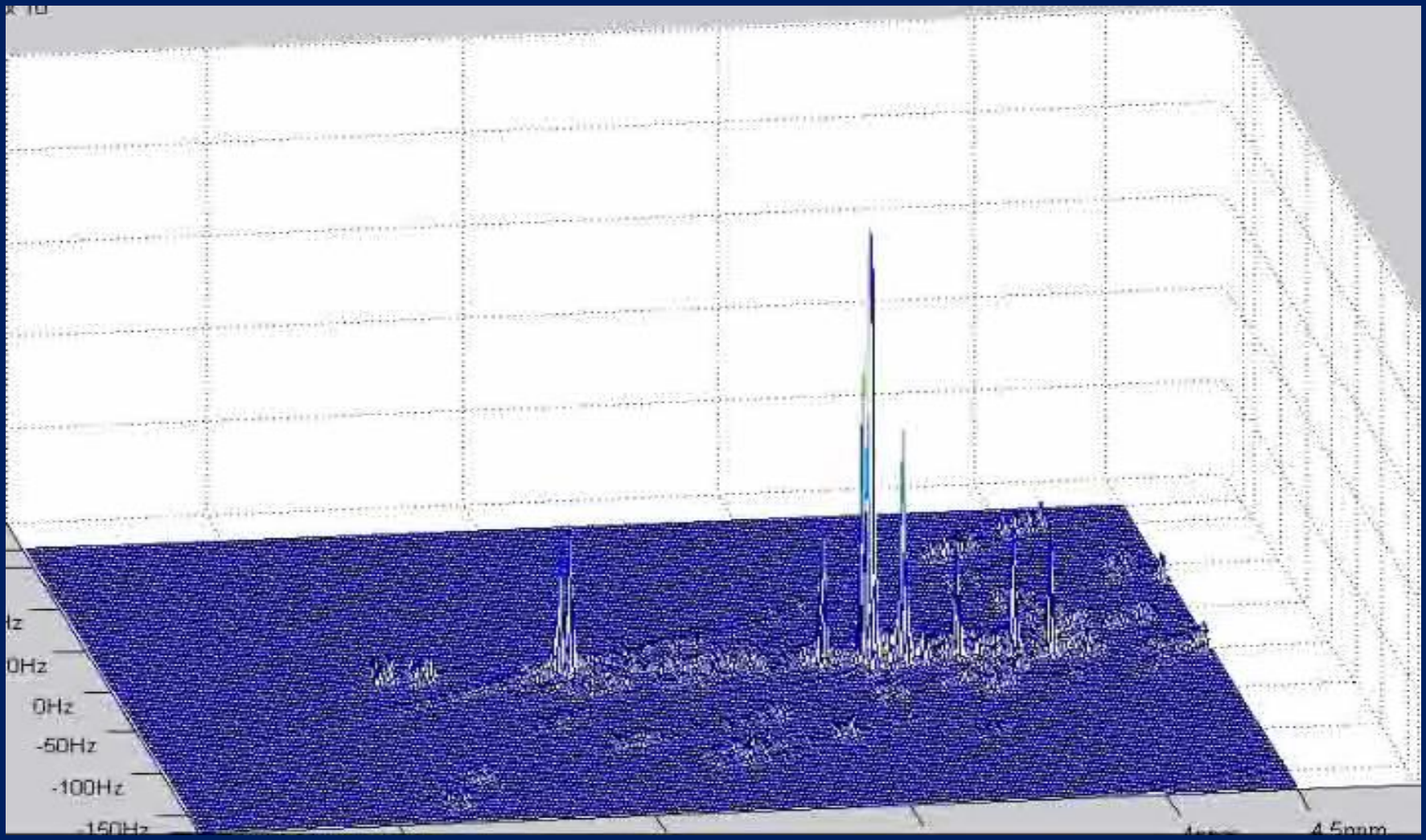
2D MRS – Gray Matter Metabolites





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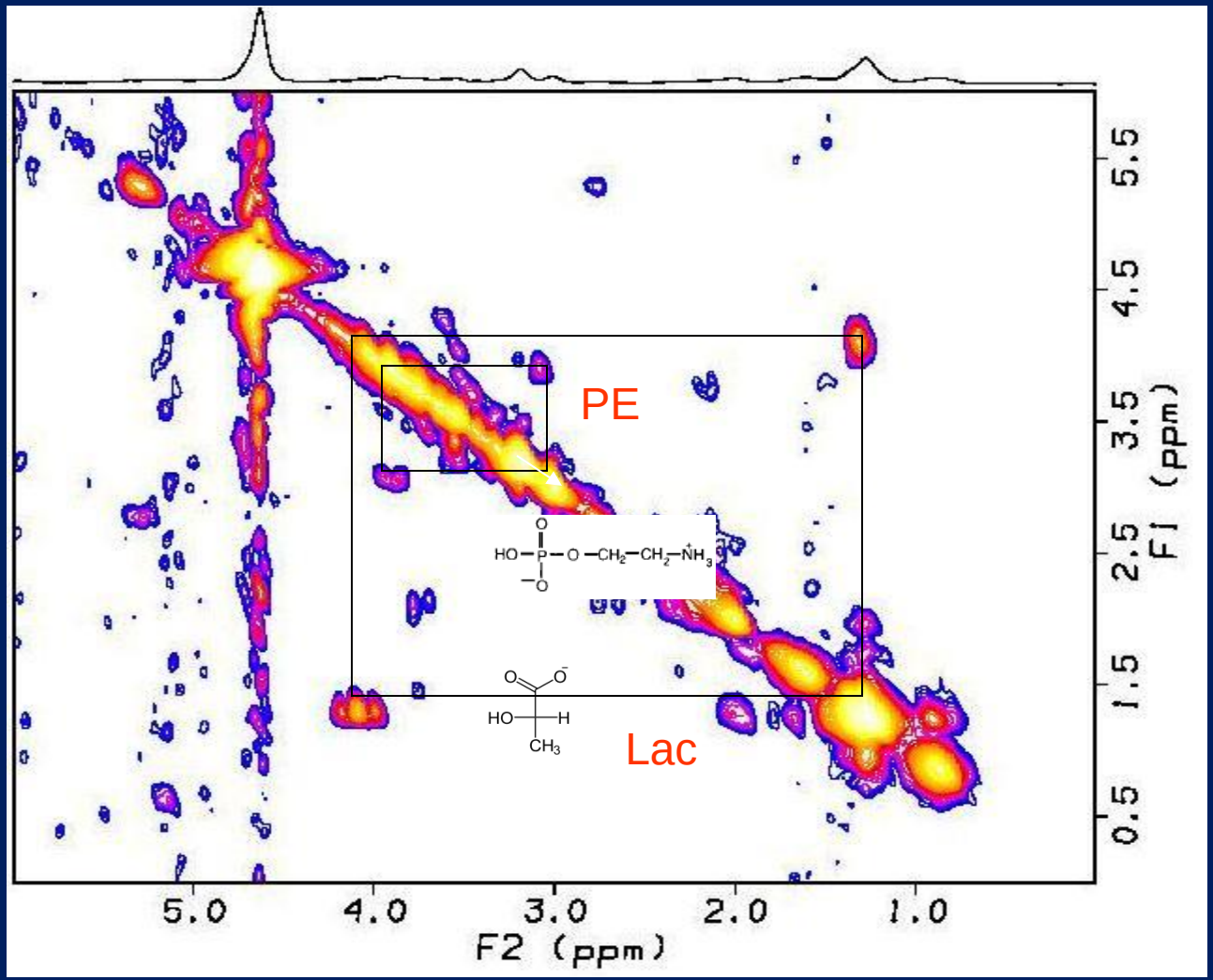
A 2D L-COSY spectrum of Brain Tumor *in vivo*

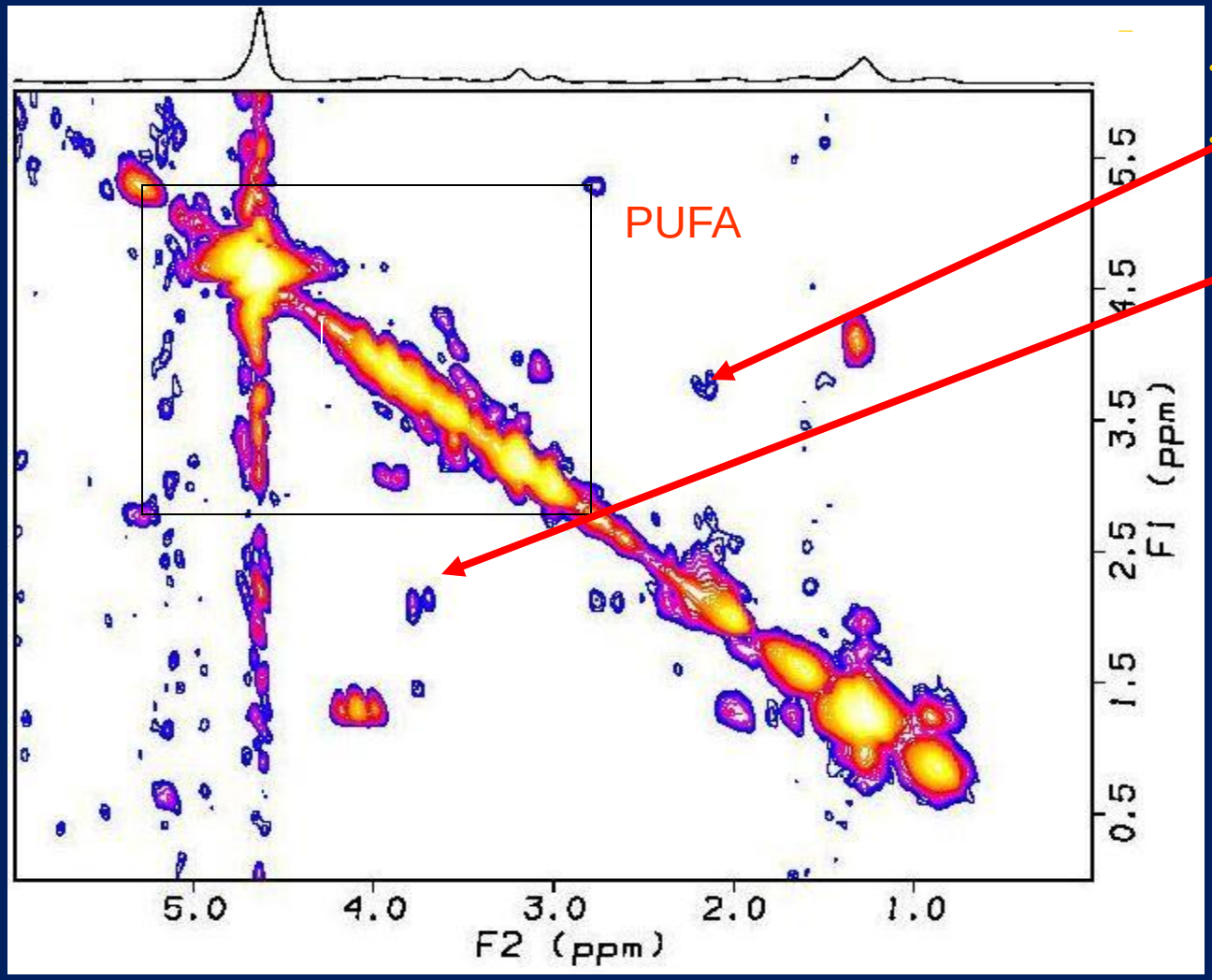


- 3T MRI Scanner
-TR/TE=2s/30ms
-26 minutes
3x3x3cm^3
-96 t_1 incr.
-8NEX/ Δt_1

Thomas et al. (2010)

A 60 yo male diagnosed with GBM

A 2D L-COSY spectrum of Brain Tumor *in vivo*

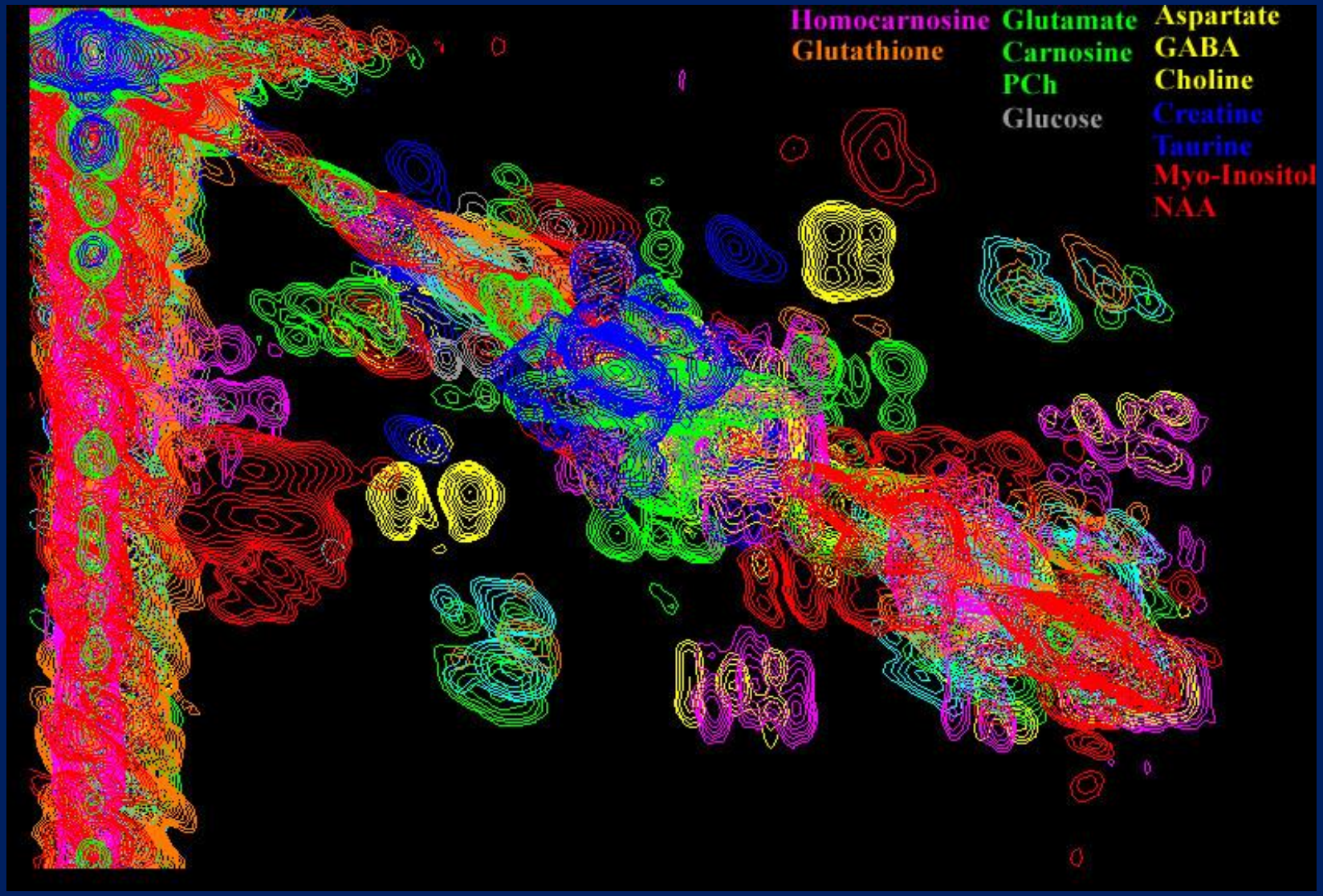


- Visible Peaks:
  - Cross Peaks:
    - Methine to methylene (C2 to C3/C4) + Glu/Gln
    - Methylene to methine (C3/C4 to C2) + Glu/Gln

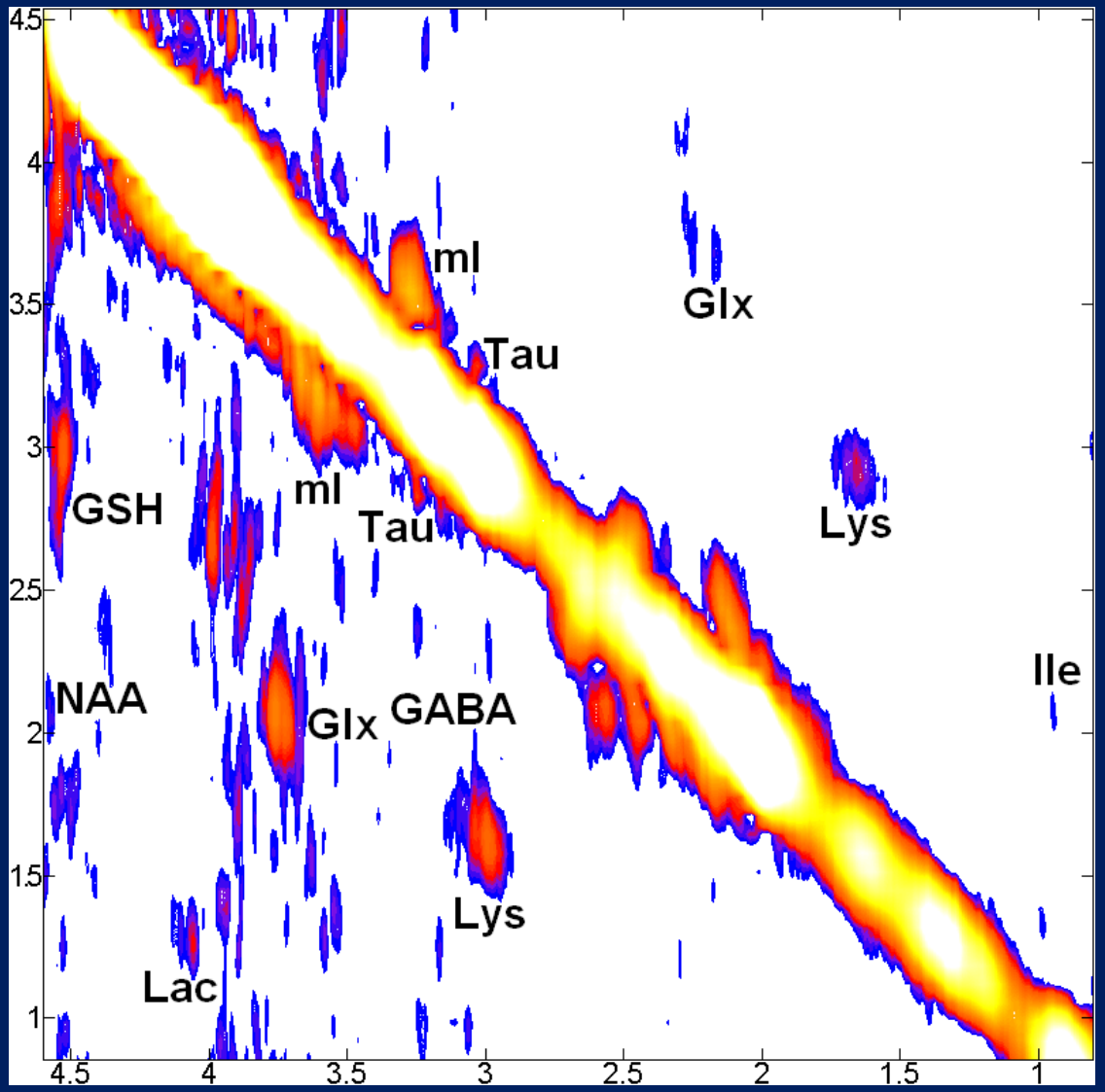
- 3T MRI Scanner
-TR/TE=2s/30ms
-26 minutes
3x3x3cm^3
-96 t_1 incr.
-8NEX/ Δ t_1

Thomas et al. (2010)
Poptani (1999)

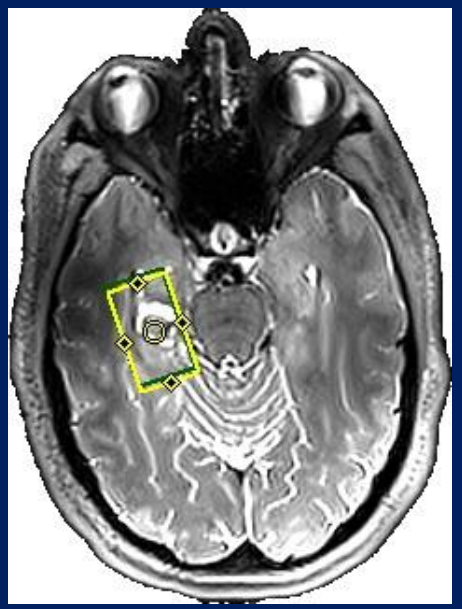
A 60 yo male diagnosed with GBM



7T 2D L-COSY of Temporal Lobe Ganglioma



- Temporal Lobe
- 20x35x25 mm^3



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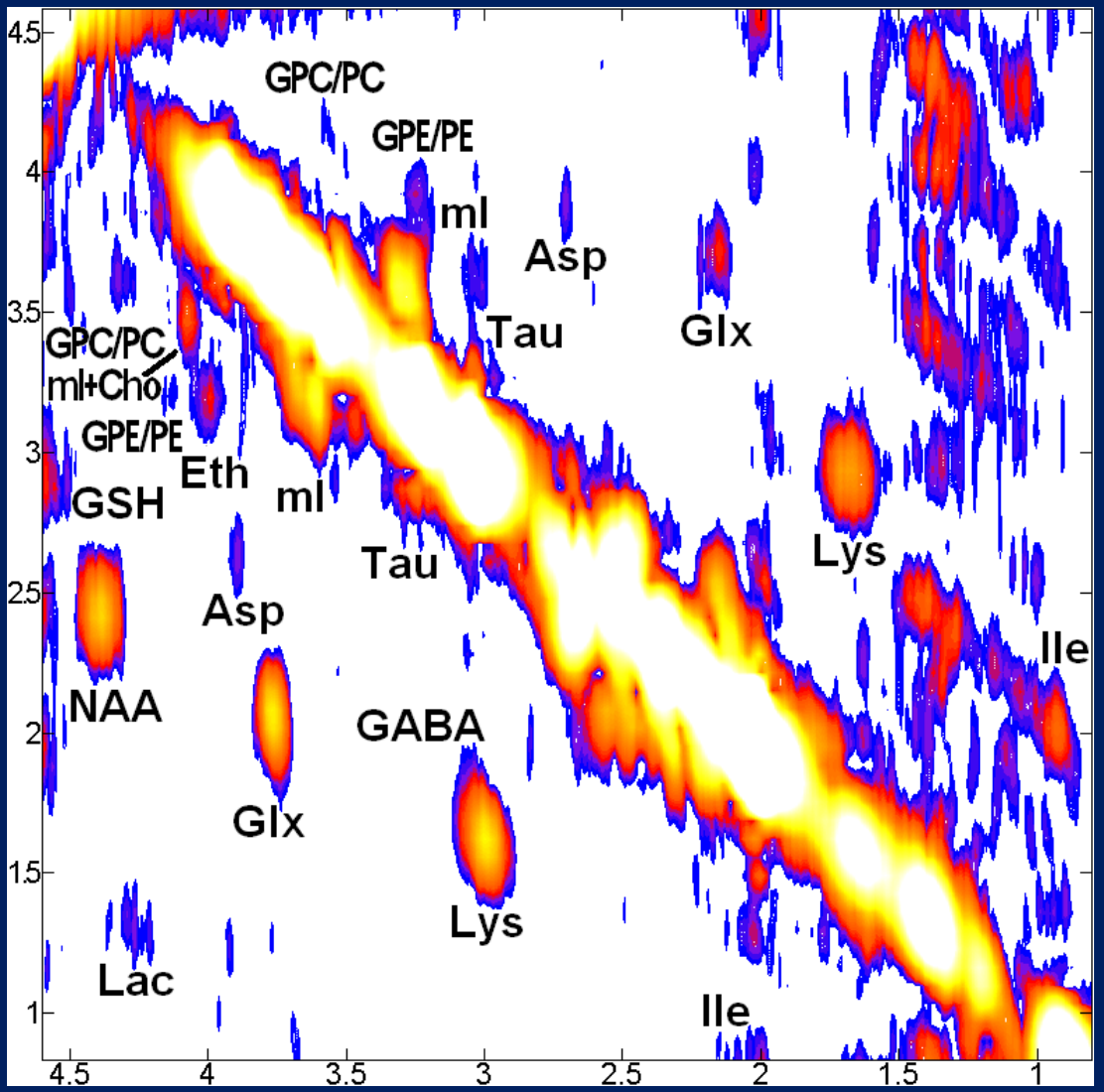
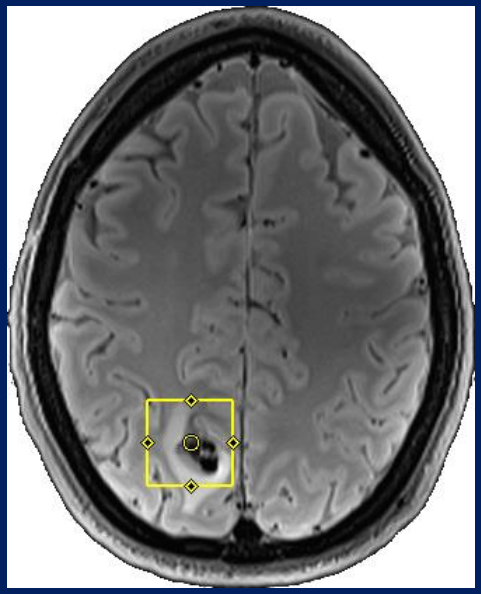
Verma et al. ISMRM 2014

7T 2D L-COSY of Occipital Lobe Low Grade



- Superior Occipital Lobe
- 25x25x25 mm^3



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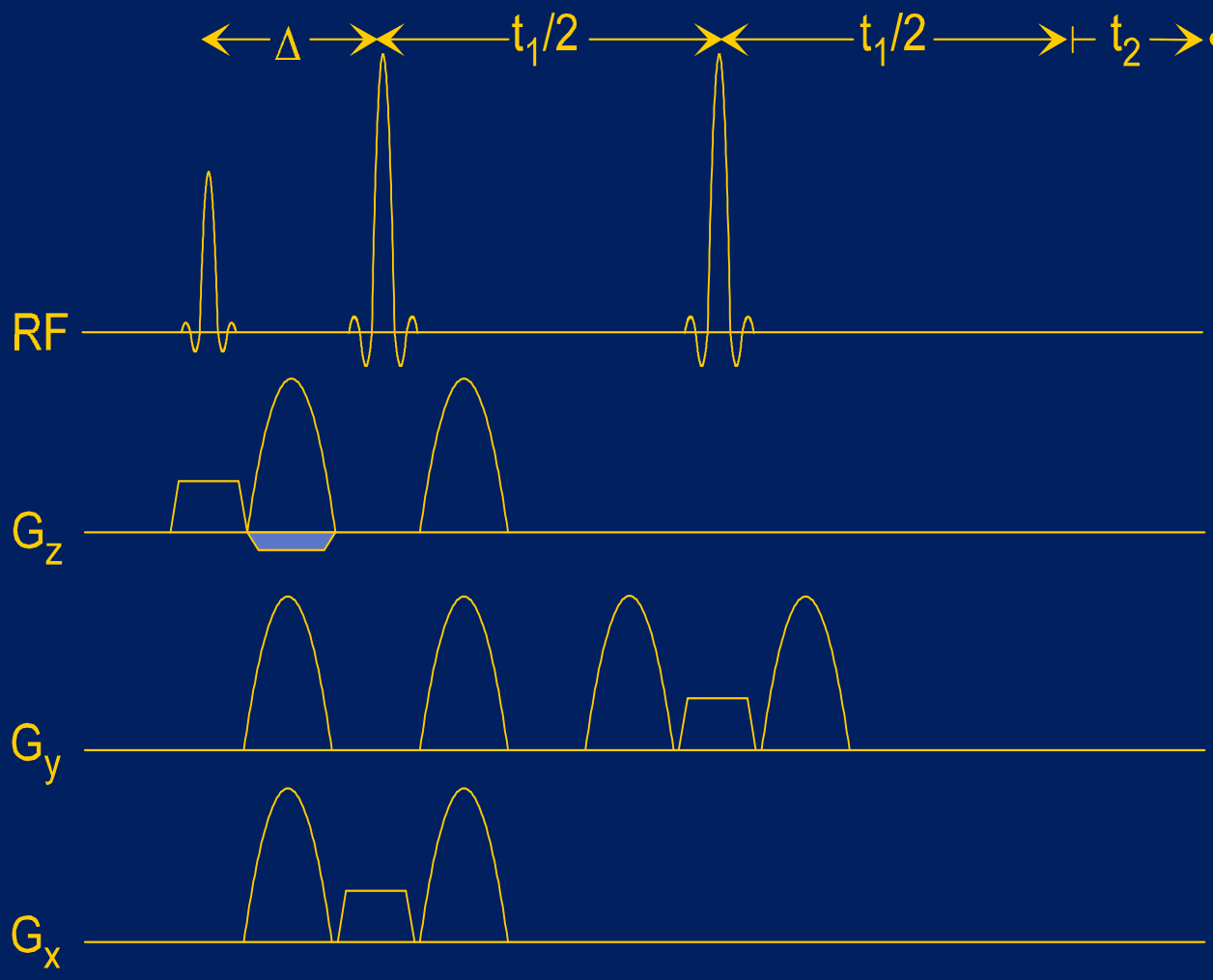
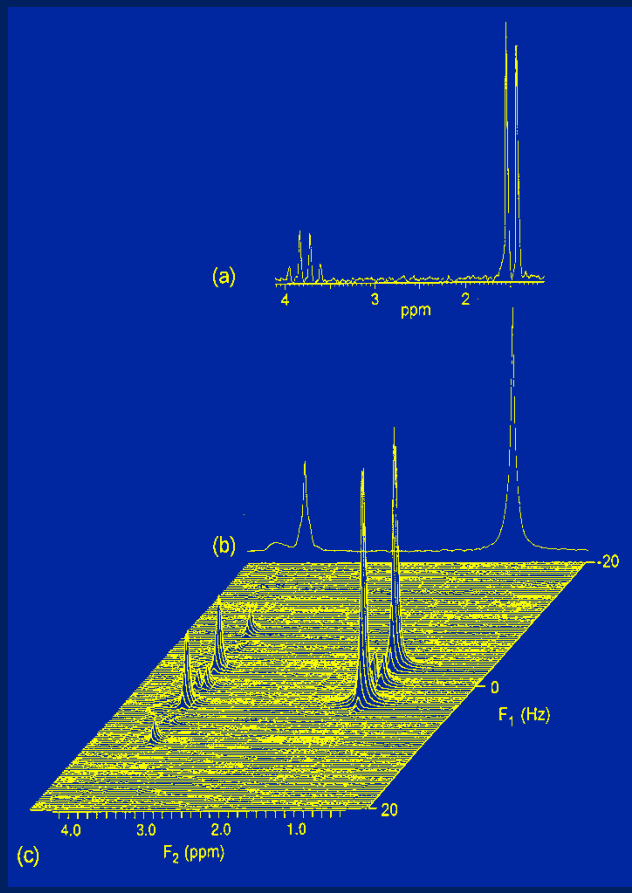
Leading Innovation >>>

Verma et al. ISMRM 2014

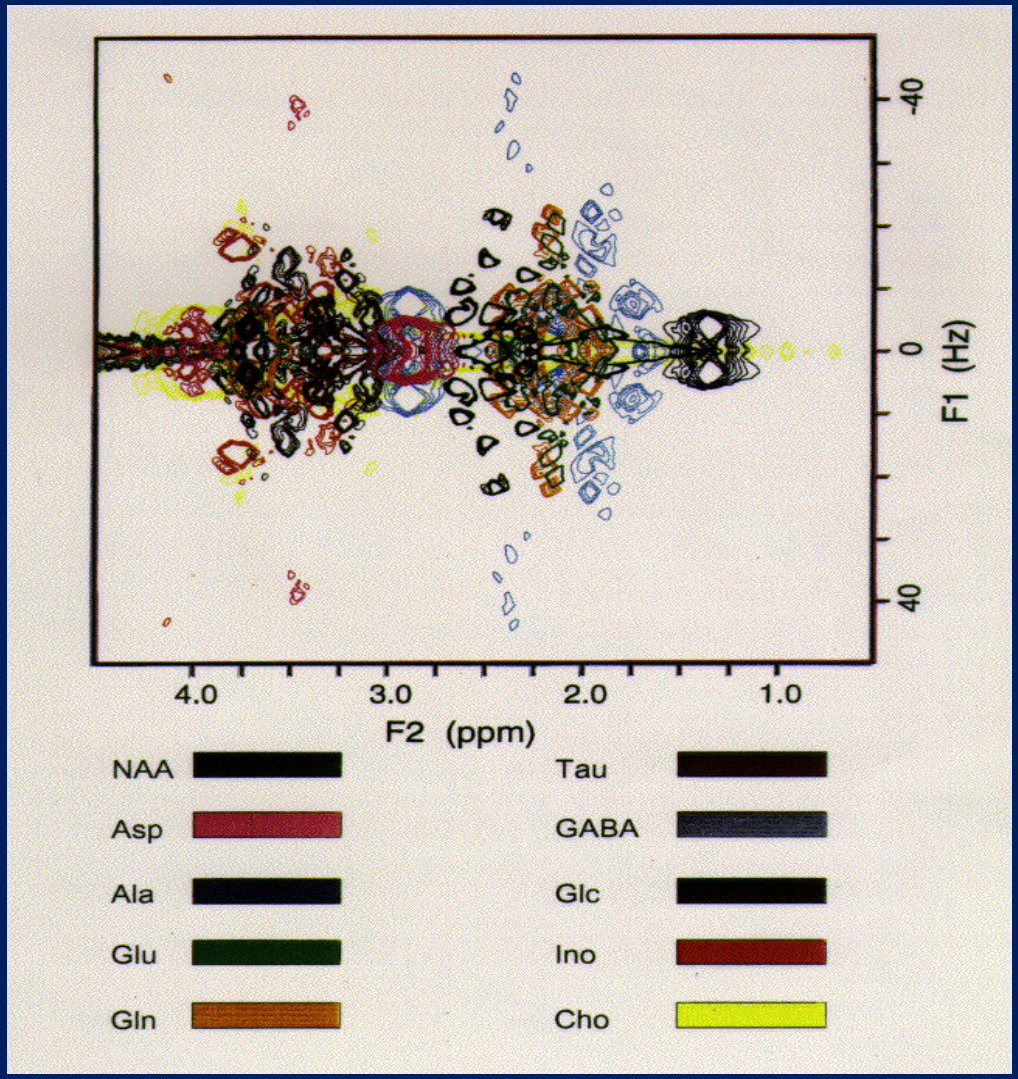
Localized 2D *J*-Resolved MRS:JPRESS





Ryner, Sorenson and Thomas, JMR (1995) & MRI (1996)

2D J-Resolved Composite Spectrum of Various Metabolites



- GE 1.5T MRI/MRS scanner

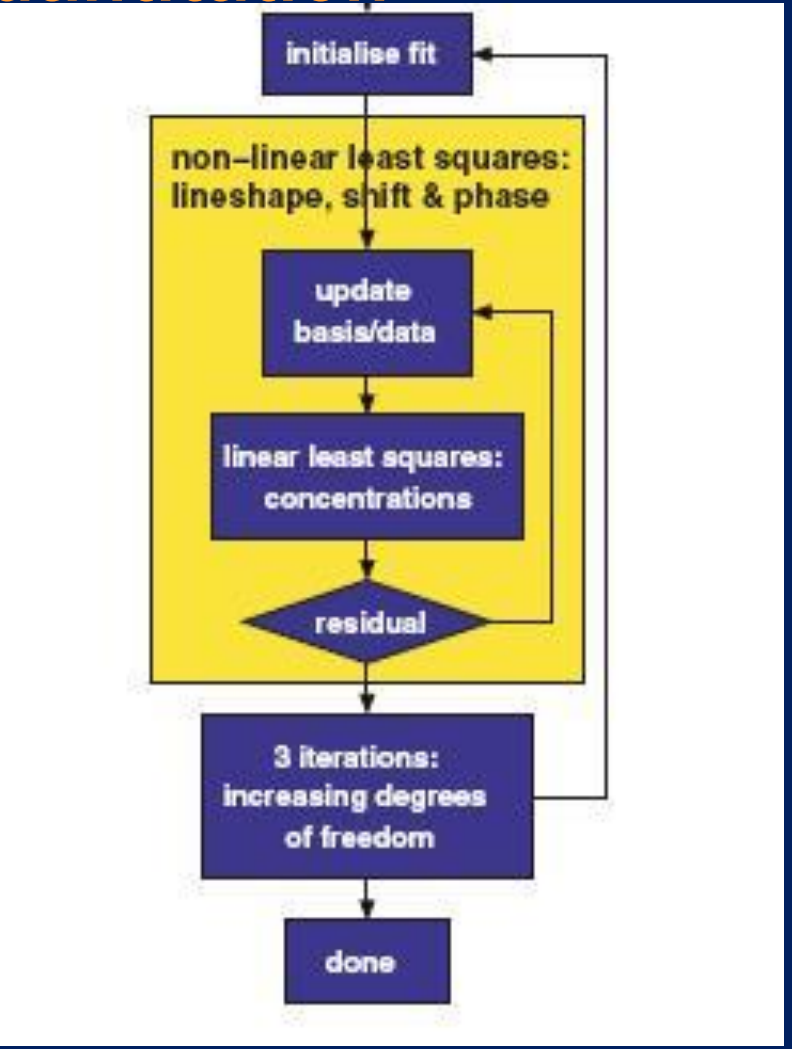
- Quadrature Head MR coil

- N-Acetyl Aspartate
-Choline
-Glutamine/Glutamate
-Myo-inositol
-Glucose
-GABA
-Taurine
-Aspartate
-Alanine

Absolute Quantitation of 2D MRS– Metabolic Assay

2D JPRESS/L-COSY Quantitation

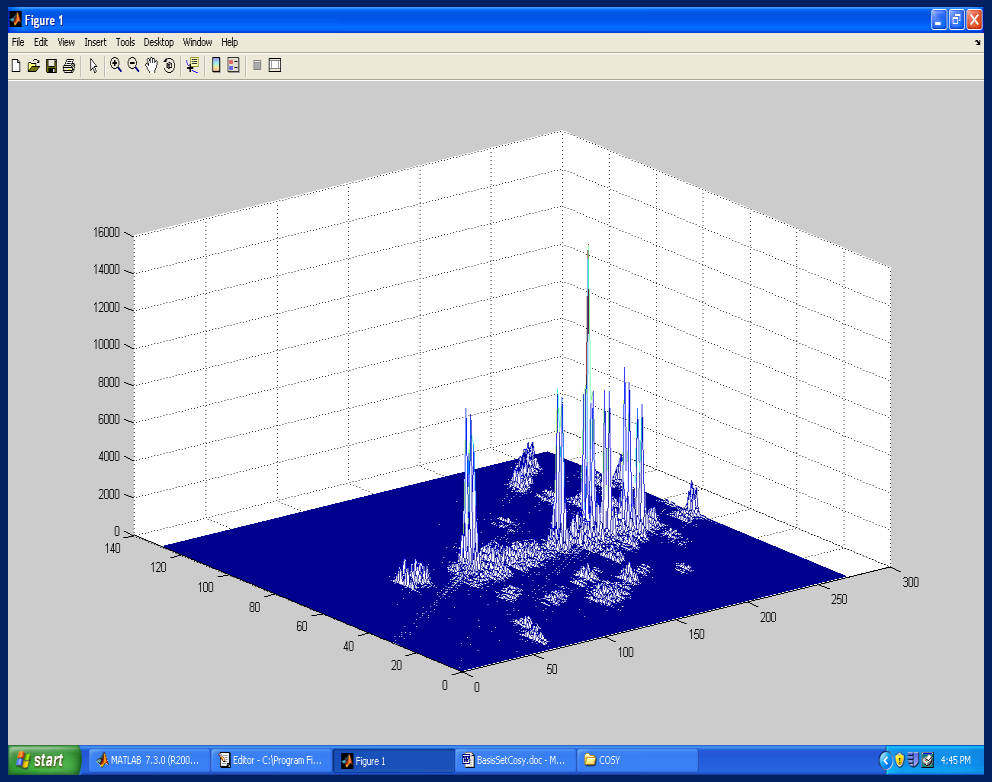
- ProFit (Prior-Knowledge Fitting) is used for 2D quantitation
- Based on a linear combination of the prior knowledge spectra:
  - Part of the fitting is done in time domain and part in frequency domain
  - Part of the fitting is done using a linear approach and part using a non-linear approach.
  - Divided in three parts: (1) basis set generation (or prior knowledge generation), (2) reconstruction, which is applied both to the basis set and to the data being fitted and (3) fitting of the data using the prior knowledge.



Schulte et al. (2006)/ Frias-Martinez et al. (2008)

Prior Knowledge Generation

- GAMMA library in combination with the chemical shift and J-coupling values reported in the literature
  - One set for 3T another for 1.5T (100 Δt1, 2000 Hz)
  - 15 metabolites Phantom
  - 20 metabolites (in vivo):creatine (Cr), N-acetylaspartate (NAA), glycerylphosphocholine (GPC), phosphorylcholine (PCh), alanine (Ala), aspartate (Asp), γ-aminobutyric acid (GABA), glucose (Glc), glutamine (Gln), glutamate (Glu), glycine (Gly), glutathione (GSH), lactate (Lac), myo-inositol (mI), N-acetylaspartylglutamate (NAAG), phosphoethanolamine (PE), taurine (Tau), scyllo-inositol (Scy) and ascorbate (Asc).



TOSHIBA
Leading Innovation >>>

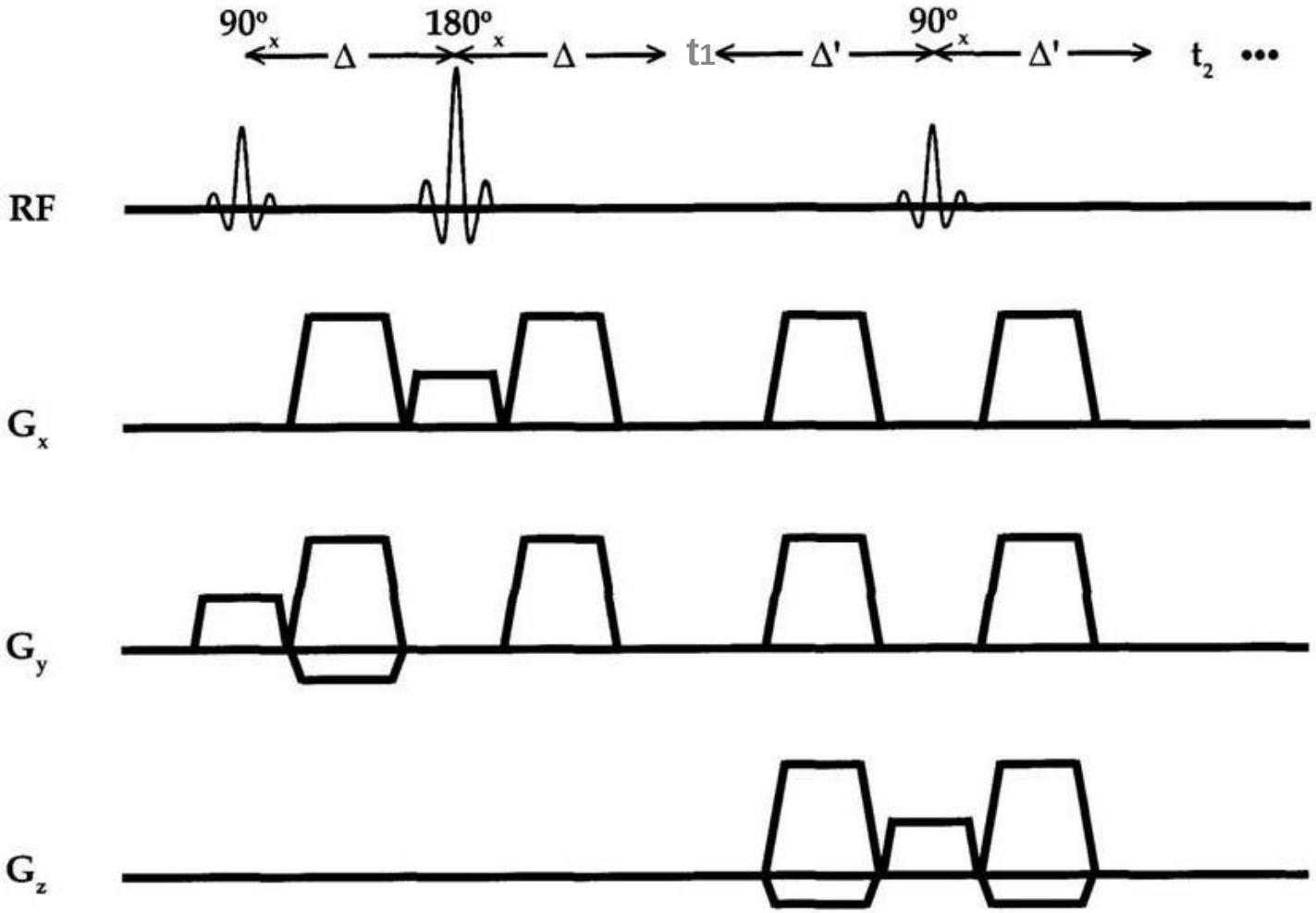
3T Human Brain COSY data processed using ProFit

	3 T 2D COSY ProFit *in-vivo*	
	Ratio/Cr	**CRLB**
Cr303	1±0	0.48±0.26
Cr391	0.87±0.15	0.97±0.59
NAA	1.4±0.32	0.56±0.27
GPC	0.11±0.05	4.8±4.8
PCh	0.11±0.05	4±4.42
Cho	0.1±0.01	2.37±0.77
Ala	0.11±0.03	5.2±3.03
Asp	0.4±0.1	4.7±3.4
GABA	0.34±0.27	7.6±4
Glc	0.28±0.11	4.2±2.9
Gln	0.25±0.16	10±7.1
Glu	1.37±0.35	2.28±1.77
Gly	0.12±0.08	7.38±4
GSH	0.16±0.08	4.02±2.9
Lac	0.17±0.08	4.6±2.06
mI	0.86±0.1	2.02±1.28
NAAG	0.35±0.1	1.71±1.22
PE	0.21±0.11	5±0.28
Tau	0.2±0.07	4.07±1.31
Scy	0.05±0.00	4.6±2.7
Asc	0.28±0.18	3.48±1.2
NAA+NAAG	1.6±0.23	0.27±0.04
GPC+PCh+Cho	0.29±0.04	0.86±0.46
Gln+Glu	1.53±0.34	1.79±0.34

-2D L-COSY/JPRESS enable resolving more peaks than 1D MRS

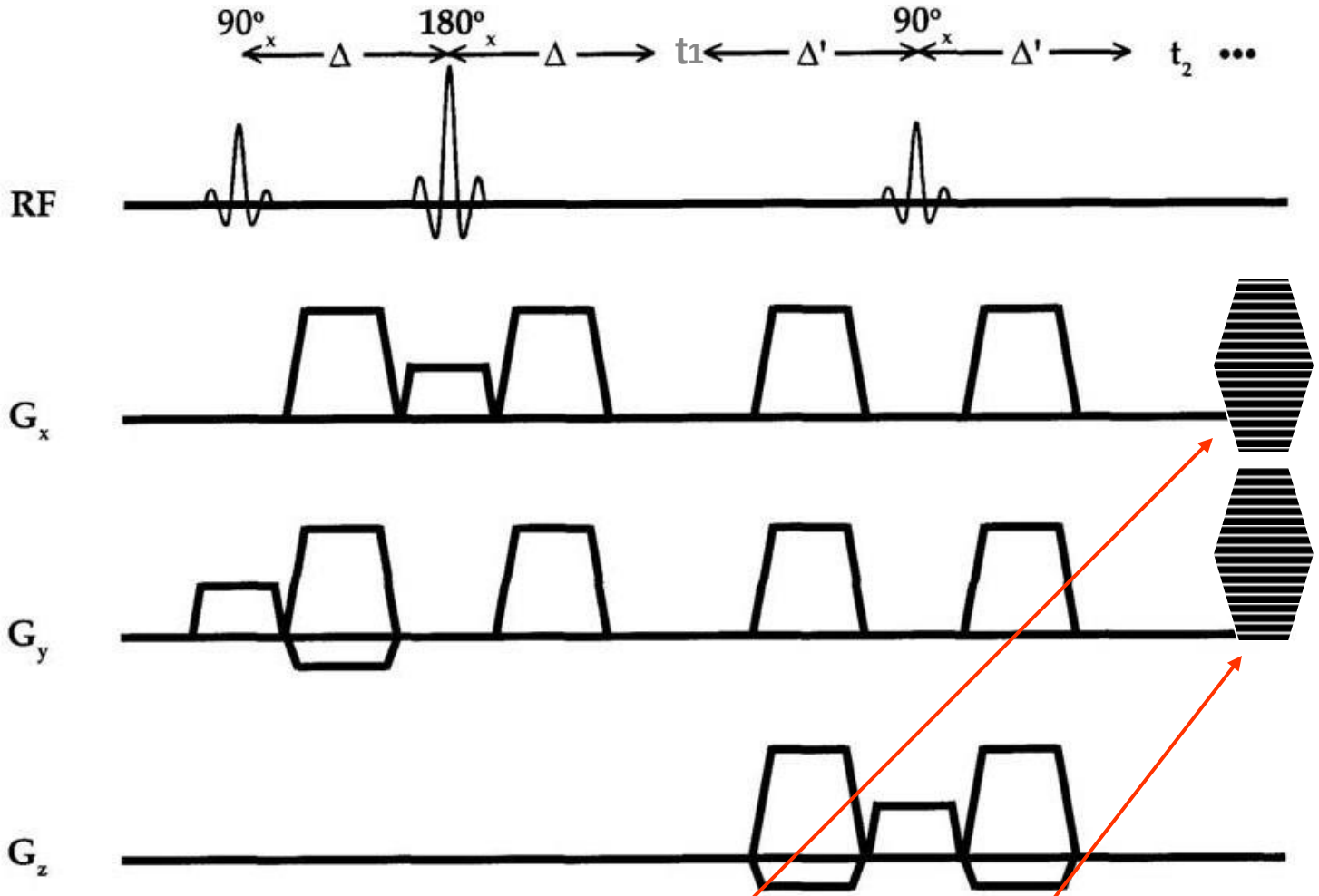
-For applications in cancer and other pathologies, there is a need for multi-voxel based 2D MRS

2D spectral+ 2D Spatial Encoding



Total Scan time = 2s*128*8= 34minutes

TR * N (t1 Encodings) * Averages



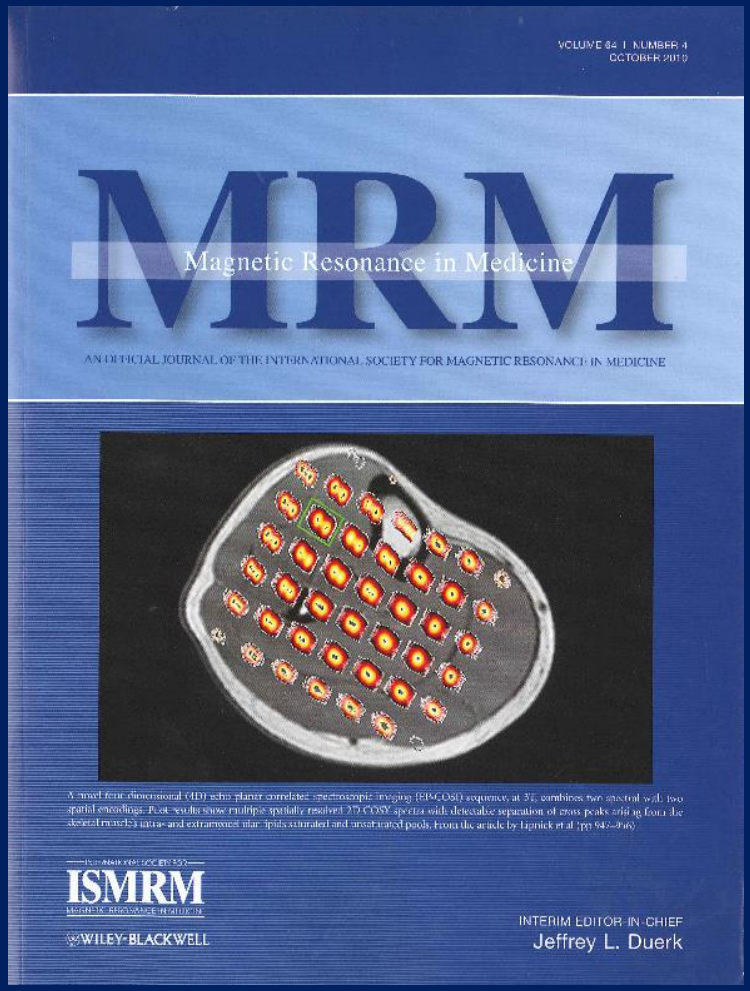
= 2s*128*1*16*16
= 546minutes
Or
=2s*128*1*16
= 18.2 hours

Total Scan time

TR* N (t1 Encodings) *N (y-Phase Encodings) N (X-Phase Encodings) * N (t1 Encodings) * Averages

4D Spectroscopic Imaging

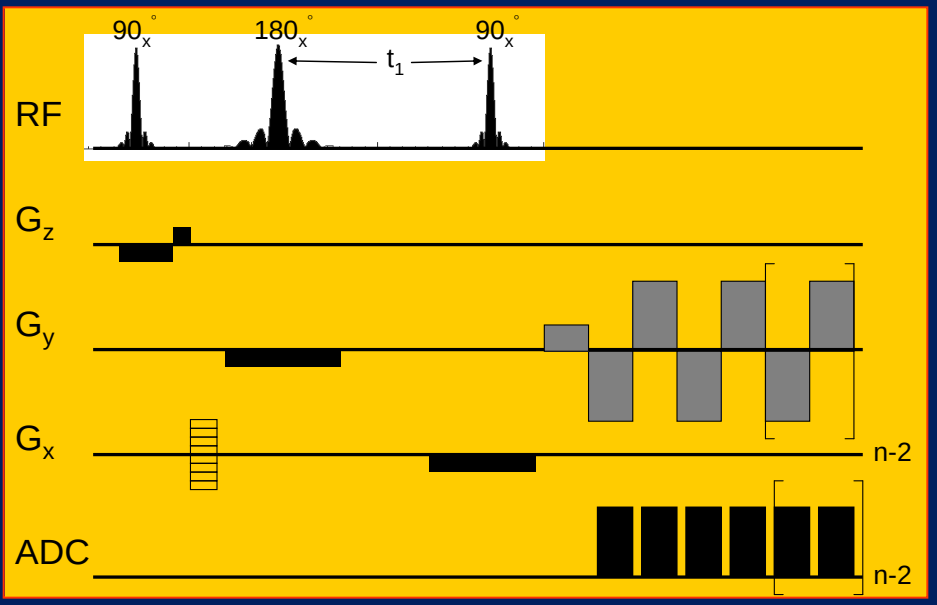
- For greater spatial coverage, 2D spectroscopy can be combined with a 2D spectroscopic imaging sequence to yield enhanced spatially localized metabolic information (2D spatial + 2D spectral)
- EPCOSI published in 2010 combining EPSI and L-COSY

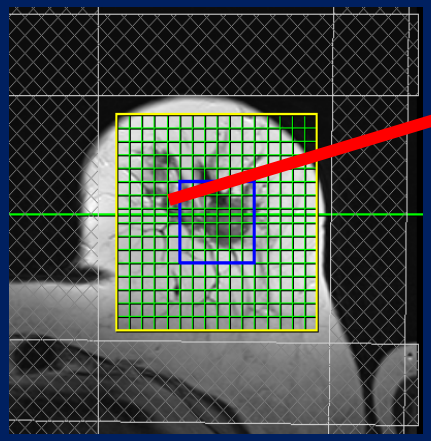


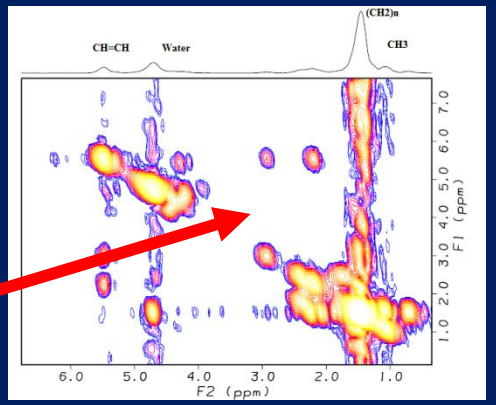
Lipnick *et al.* Magn. Reson. Med. **64**, 947-956 (2010)

4D EP-COSI

Multi-voxel Based Echo-Planar Correlated Spectroscopic Imaging (EP-COSI)







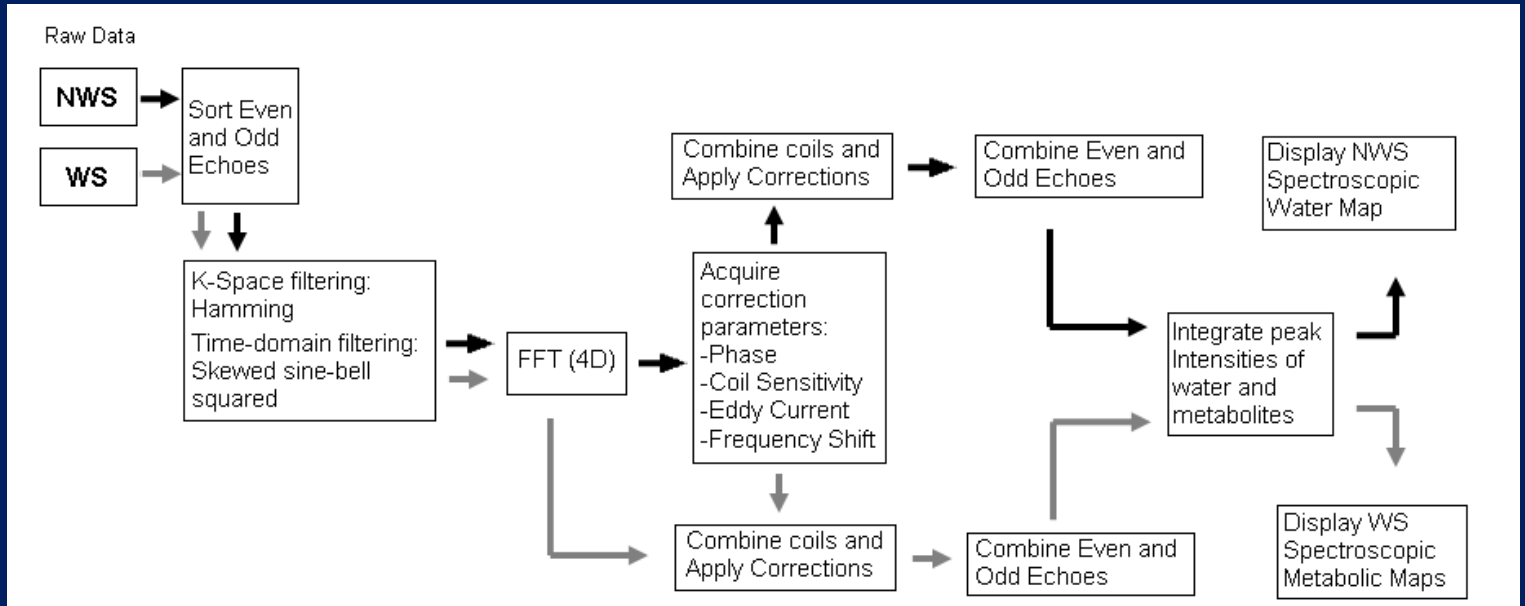
Scan time = N (X-Phase Encodings) * N (t1 Encodings) * TR

= 1.5s*50*1*16 = 20minutes

Lipnick et al, MRM 2010

4D EP-COSI Post-Processing

- Result of EP-COSI is a 4 dimensional data set
  - $s(k_x, k_y, t_2, t_1)$ [for a 8-channel Parallel acq.]
    512(2*2*2*4)x100x16x16x8 > 3GBytes
- Data is reorganized into a 4D matrix (t_2, t_1, x, y)
- Must separate signal acquired during positive and negative gradient acquisitions (signals co-added at the end to increase S/N)



Lipnick et al.
MRM 2010

Single-slice based multi-voxel 2D MRS

Total duration for a 4D EP-JRESI/EP-COSI scan

for 16kx*16ky, TR = 1s, 64t1 increments and 1 average, the scan time is 17 minutes

How can we accelerate 4D EP-JRESI and EP-COSI more to be clinically feasible?

Is further acceleration feasible in MRSI?:

- EPSI/Spiral based MRSI
- Non-uniformly undersampled (NUS) acquisition (2X, 4X, 8X and more)
- Non-linear reconstruction for post-processing
- Can 2D MRS+2D/3D MRSI be acquired in < 20 minutes?

- *Lustig et al. Magn Reson Med 2007*
- *Furuyama et al. Magn Reson Med 2012*
- *Thomas et al. NMR Biomed 2014*
- *Sarma et al. AJNR 2014 (in press)*
- *Burns et al. NMR Biomed 2014 (in press)*

Sparse Reconstruction of 3D MRSI data

Can missing MRSI samples be reconstructed in post-processing?

3 Compressed Sensing Tenets

- ***Sparse*** representation in some transform domain (e.g. wavelet, finite difference)
- ***Incoherent*** artifacts due to undersampling
- ***Nonlinear*** reconstruction enforcing both sparsity and consistency with acquired data

Aliasing

- Shannon-Nyquist theorem says…

Sampling frequency must be at least 2x the highest frequency signal

- If not, *aliasing* will occur
- Aliasing can be *coherent* or *incoherent* depending on undersampling pattern

Aliasing

- Incoherent aliasing looks like noise
- However, “noise” is not random and can be accounted for → exact recovery of under sampled signals (Candes,Tao '04)
- Lustig *et al.* outline an intuitive (and surprisingly effective) way to accomplish this based on iterative thresholding

Split Bregman Algorithm

- *Very fast* for CS type problems (L1 min)
- Easy to code/implement
- Can handle variety of or multiple regularization terms

→ IST based algorithms can only handle minimization of basic L1 term or term with invertible operator (does not work for TV)

Compressed Sensing

- Exploits data redundancy to reconstruct missing samples
- Minimize l_1-norm of a spectrum in some transform domain constrained by data fidelity:

$$\begin{aligned} &\min \ \|\psi f\|_1 \\ &s.t. \ \|RFf - d\|_2 \leq \sigma \end{aligned}$$

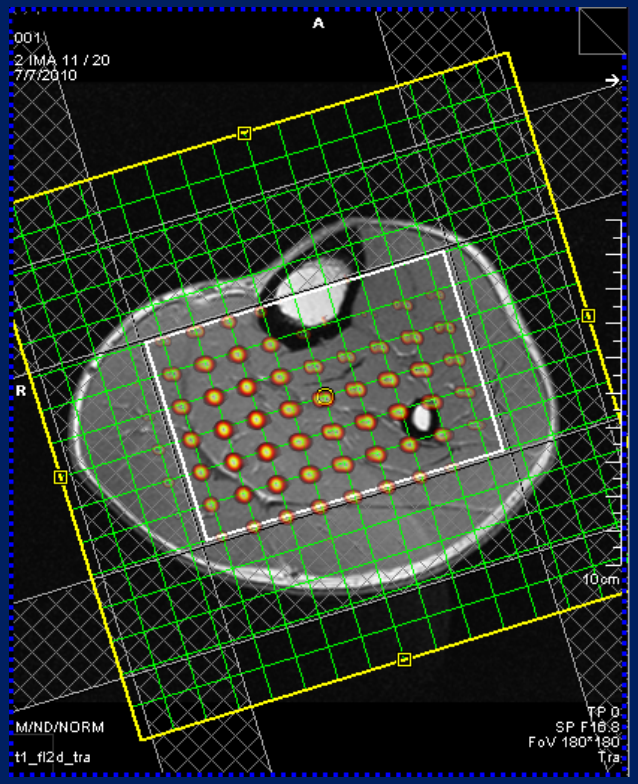
  - d = under-sampled time domain data
  - f = reconstructed frequency domain data
  - F = Fourier transform
  - R = under-sampling mask
  - ψ = sparsifying transform
  - σ = noise standard deviation

- Minimum l_1-norm of an underdetermined system of equations is the *sparsest* solution
  - Relaxation of the l_0-norm sparsity measure

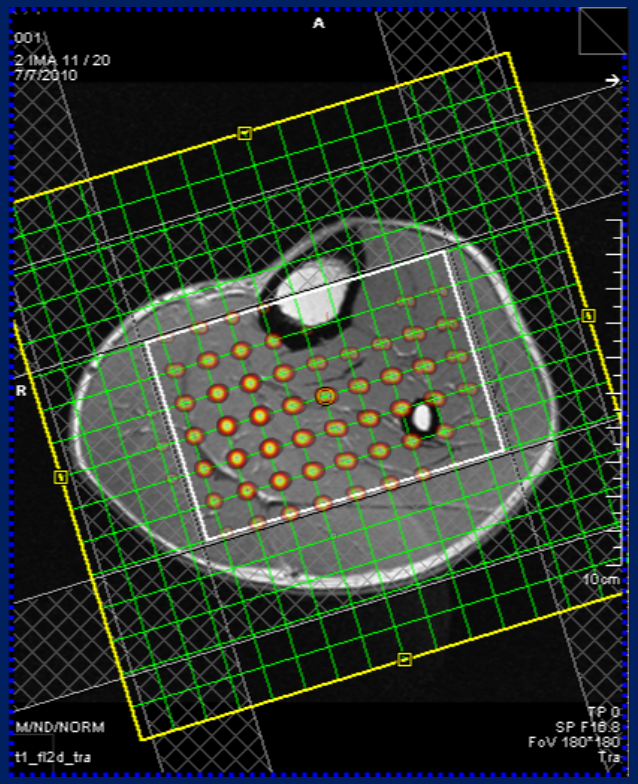
Donoho, IEEE Trans. Info. Theory, *2004*
Candés et al, IEEE Trans. Info. Theory, *2004*

4D SI with Compressed Sensing

- Retrospective study of healthy calf muscle



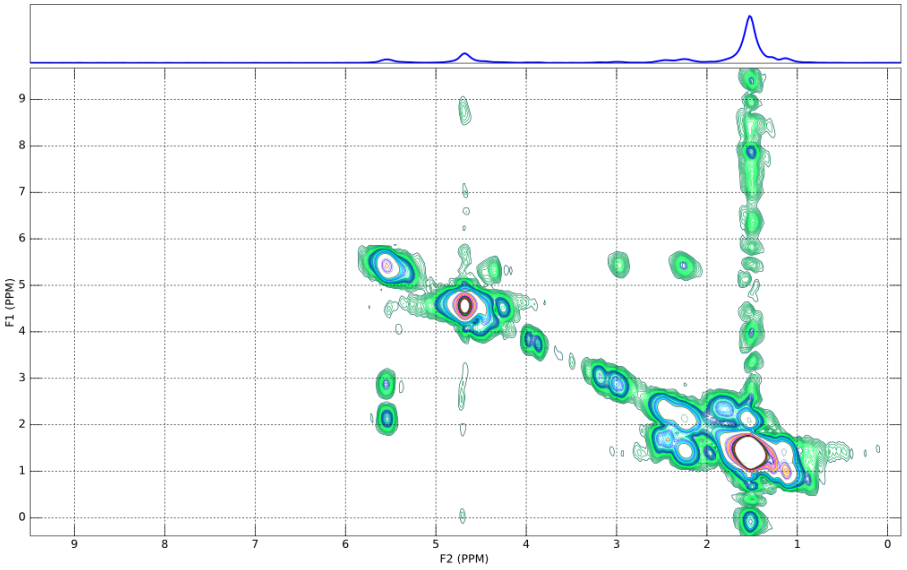
fully sampled



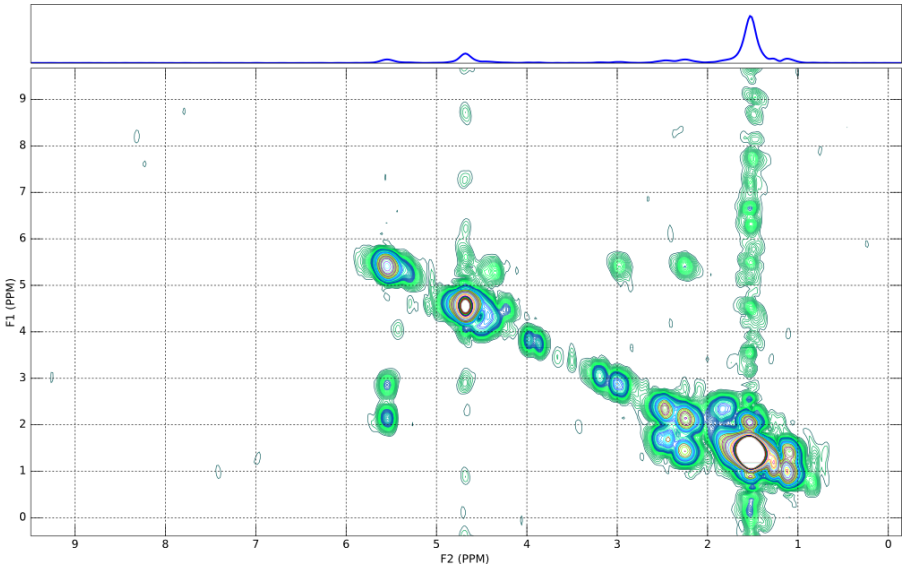
33% of original data

4D SI with Compressed Sensing

- Retrospective study of healthy calf muscle



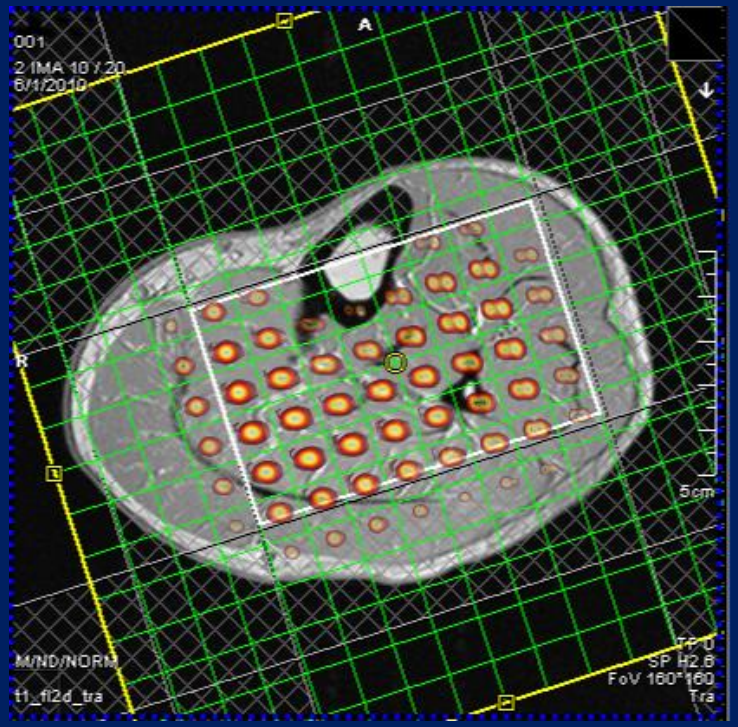
fully sampled tibialis anterior



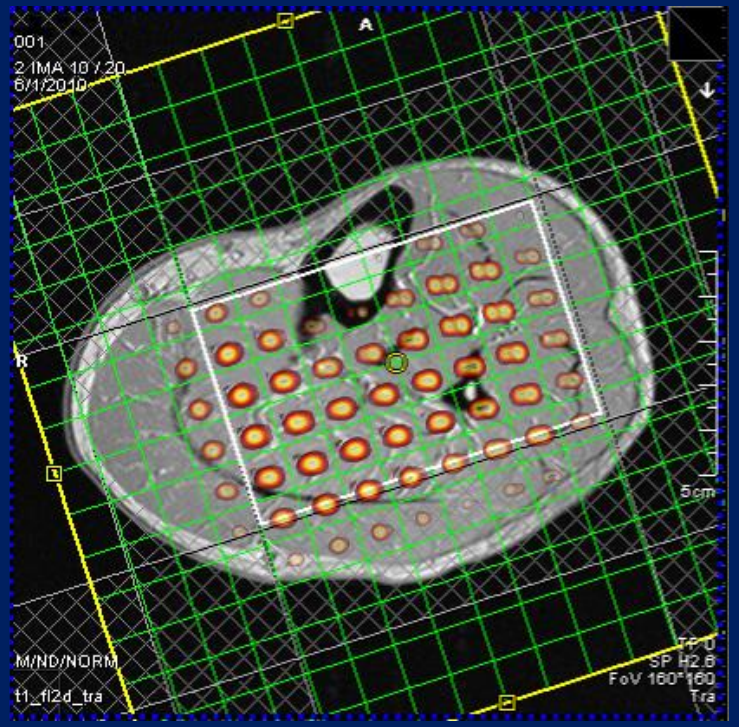
33% of original data

4D SI with Compressed Sensing

- Retrospective study of diabetic calf muscle



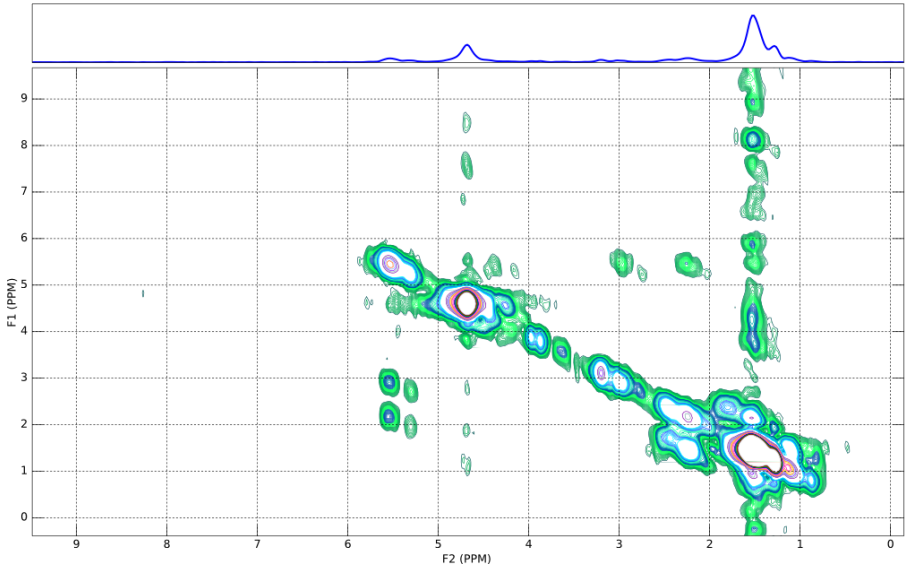
fully sampled



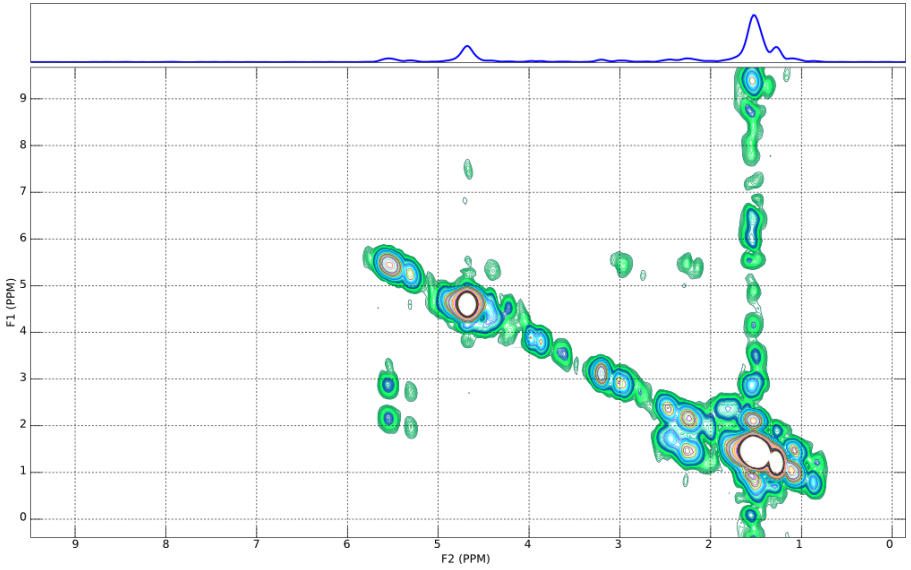
33% of original data

4D SI with Compressed Sensing

- Retrospective study of diabetic calf muscle



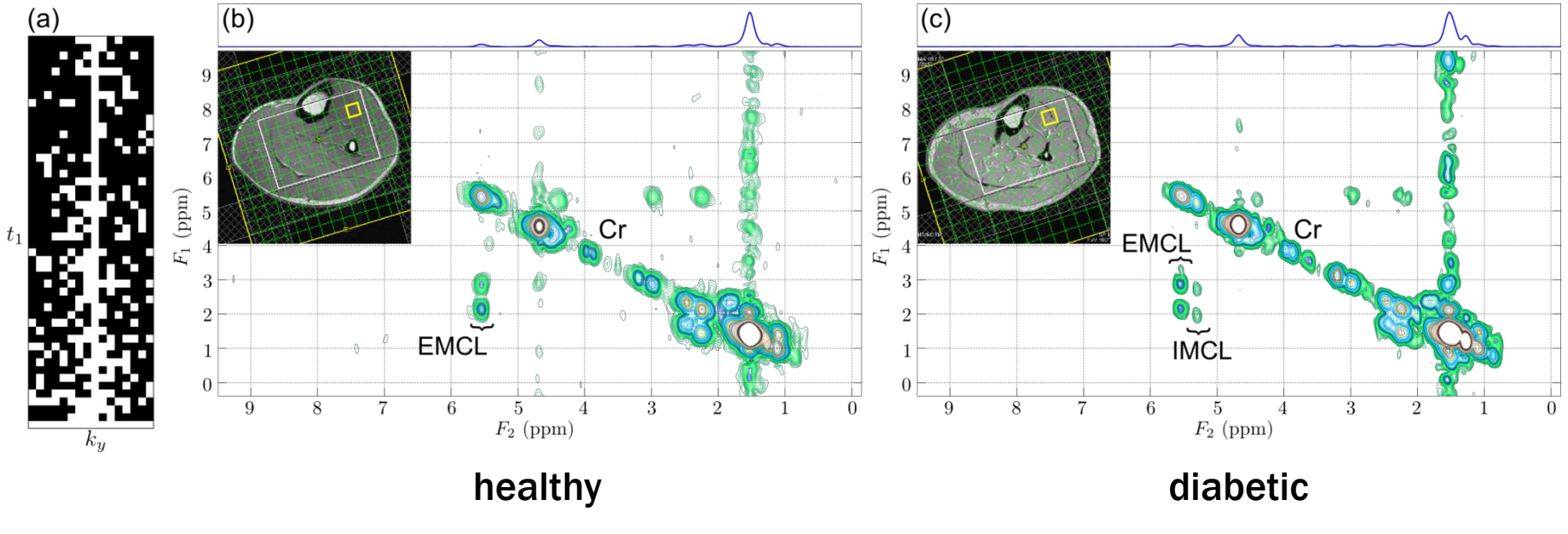
fully sampled tibialis anterior



33% of original data

4D SI with Compressed Sensing

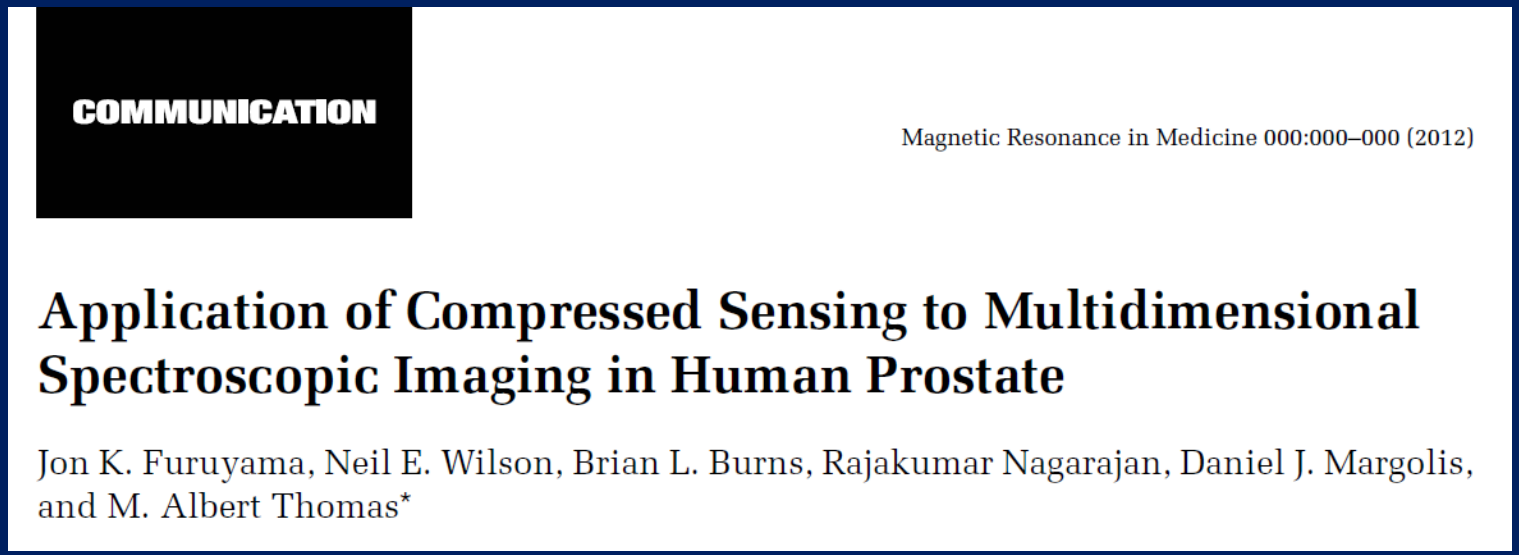
- Retrospective study of human calf muscle reconstructed using only 33% of the fully sampled data



- Disease (diabetes) identification despite reduced data size

4D SI with Compressed Sensing

- Prospective study in human prostate cut scan times from 24 minute scans to 6 minutes



COMMUNICATION

Magnetic Resonance in Medicine 000:000–000 (2012)

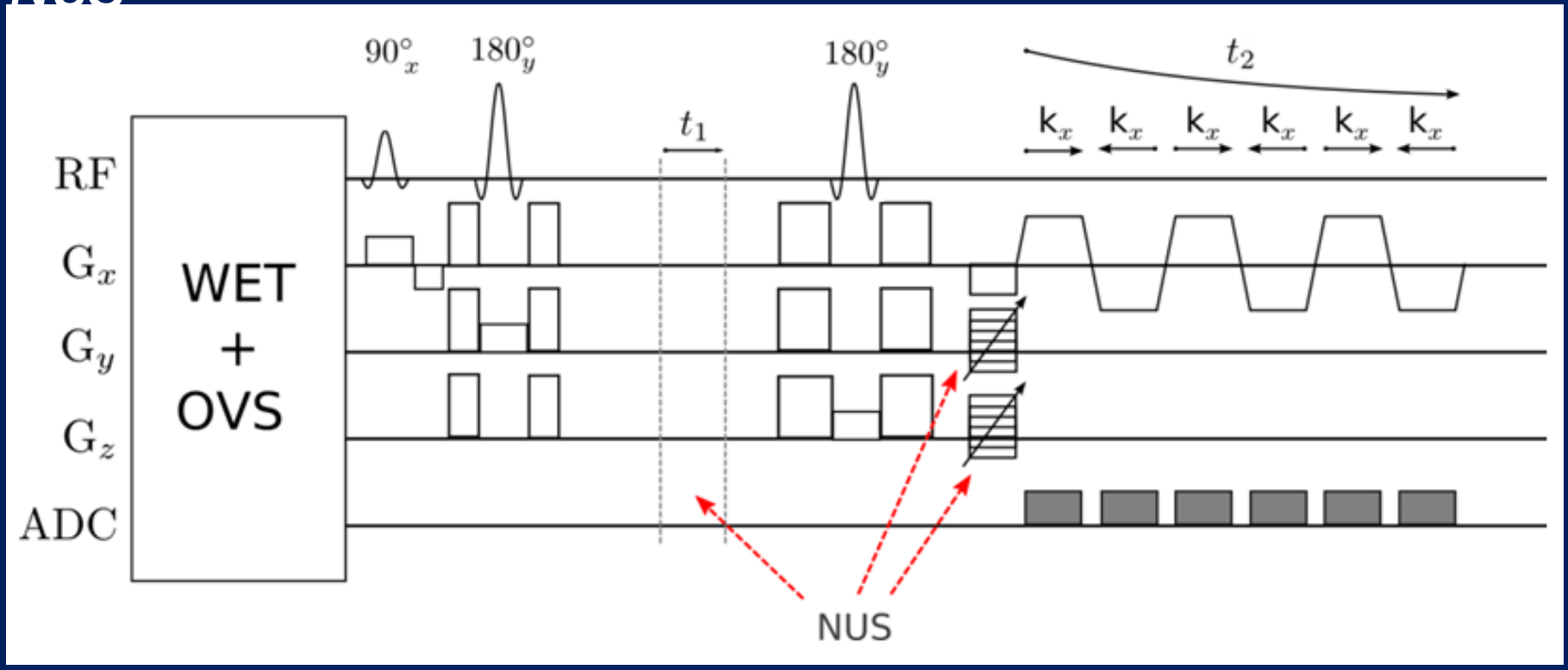
Application of Compressed Sensing to Multidimensional Spectroscopic Imaging in Human Prostate

Jon K. Furuyama, Neil E. Wilson, Brian L. Burns, Rajakumar Nagarajan, Daniel J. Margolis, and M. Albert Thomas*

- The time saved by CS allows for many different modalities with long scans to finally be clinically viable

5D ^{1}H MR Spectroscopic Imaging: 2 Spectral + 3 Spatial Dimensions

5D Echo-Planar J-resolved Spectroscopic Imaging *with NUS*



- 3D CSI/MRSI (32x32x16) -410 minutes
- 3D EPSI (32x16) – 12.8 minutes
- 3D EPSI+2DJRES (32x16x64)- 819 minutes
- 5D EPJRESI (16x8x64) 8X NUS- 21 minutes

Wilson et al, MRM 2015 and 2016

Sampling Mask and Reconstruction

The Sampling Density function used to sample the (k_y, k_z, t_1) volume:

$$\rho(k_y, k_z, t_1) = \exp\left\{-\frac{|k_y|}{n_y} - \frac{|k_z|}{n_z} - \frac{t_1}{n_1}\right\} \quad [1]$$

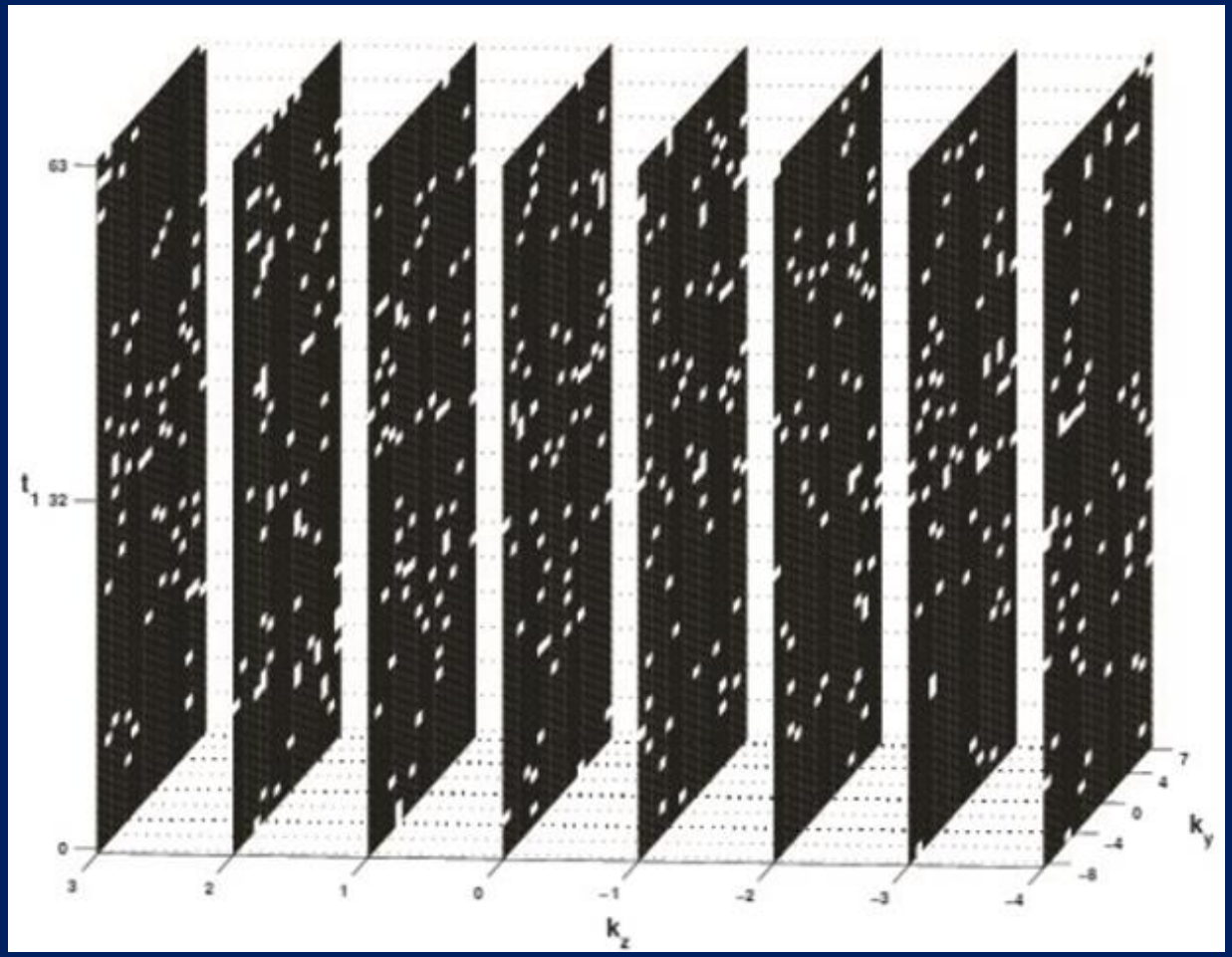
where $\rho(k_y, k_z, t_1)$ is the probability of sampling a point in the (k_y, k_z, t_1) plane. n_y, n_z, and n_1 are the number of points in the k_y, k_z, and t_1 dimensions respecti

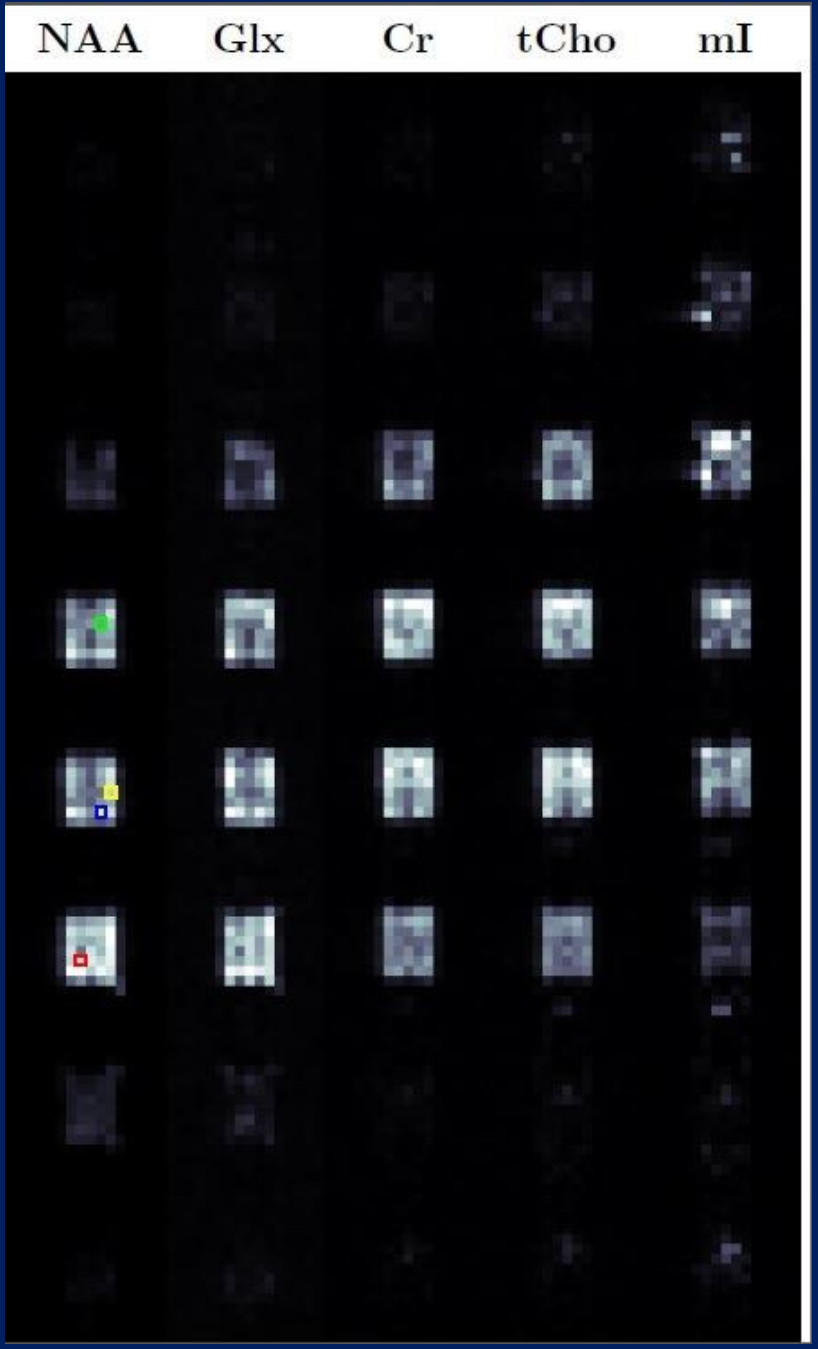
$$\min_u \text{TV}(u) \quad \text{s.t.} \quad ||R\mathcal{F}u - f||_2^2 < \sigma^2 \quad [2]$$

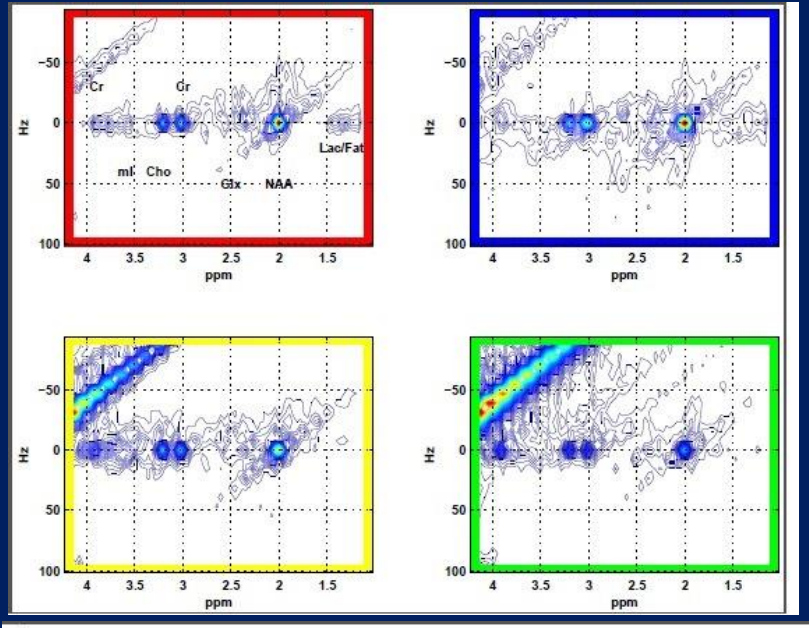
where TV is the total variation, $u = u(x, y, z, F_2, F_1)$ and $f = f(x, k_y, k_z, F_2, t_1)$, R is the sampling operator $\mathcal{F}$ is the Fourier operator acting on the

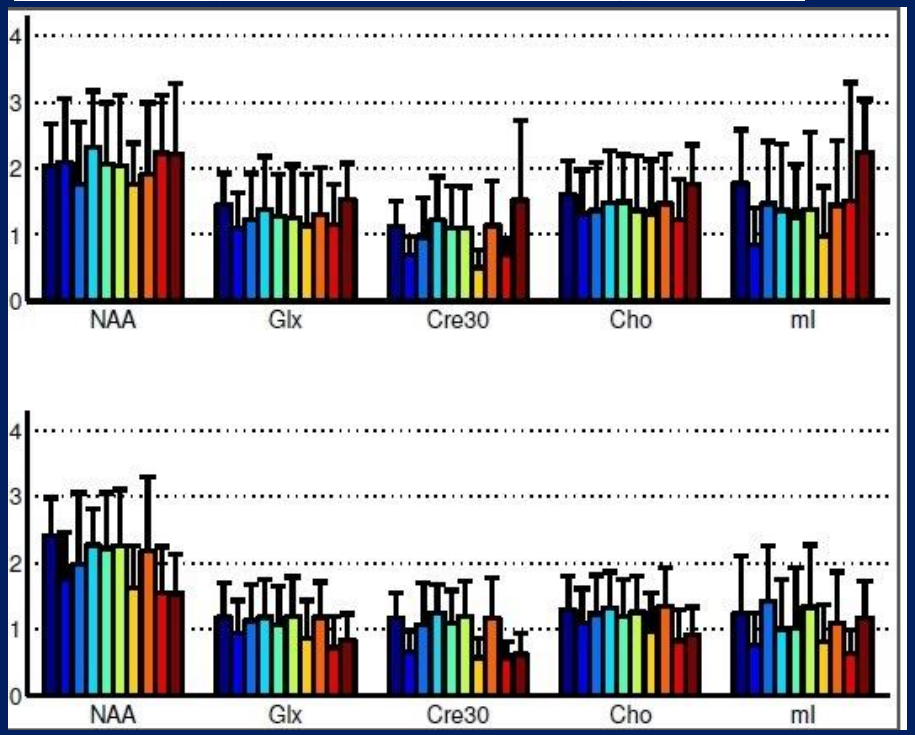
Wilson NE, et al. *MRM* 2016

16x Sampling Mask









5D EP-JRESI 8X NUS-21 min

Wilson et al, MRM 2015 (early view)

How can we record 3D volume based 2D MRS accelerate 4D EP-JRESI and EP-COSI to be included in multiparameteric MRI protocol?

Conclusions

- Spatially resolved 2D MRS has great potential for the biochemical characterization in cancer and other pathologies noninvasively
- Considering the tumor heterogeneity and the VOI size, multi-slice-based multi-voxel 2D MRS techniques need fufther optimization to be included in multiparametric MR protocols

THANK YOU

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UCLA