INTRODUCTION TO MAGNETIC RESONANCE SPECTROSCOPY (MRS)

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PHYS-473

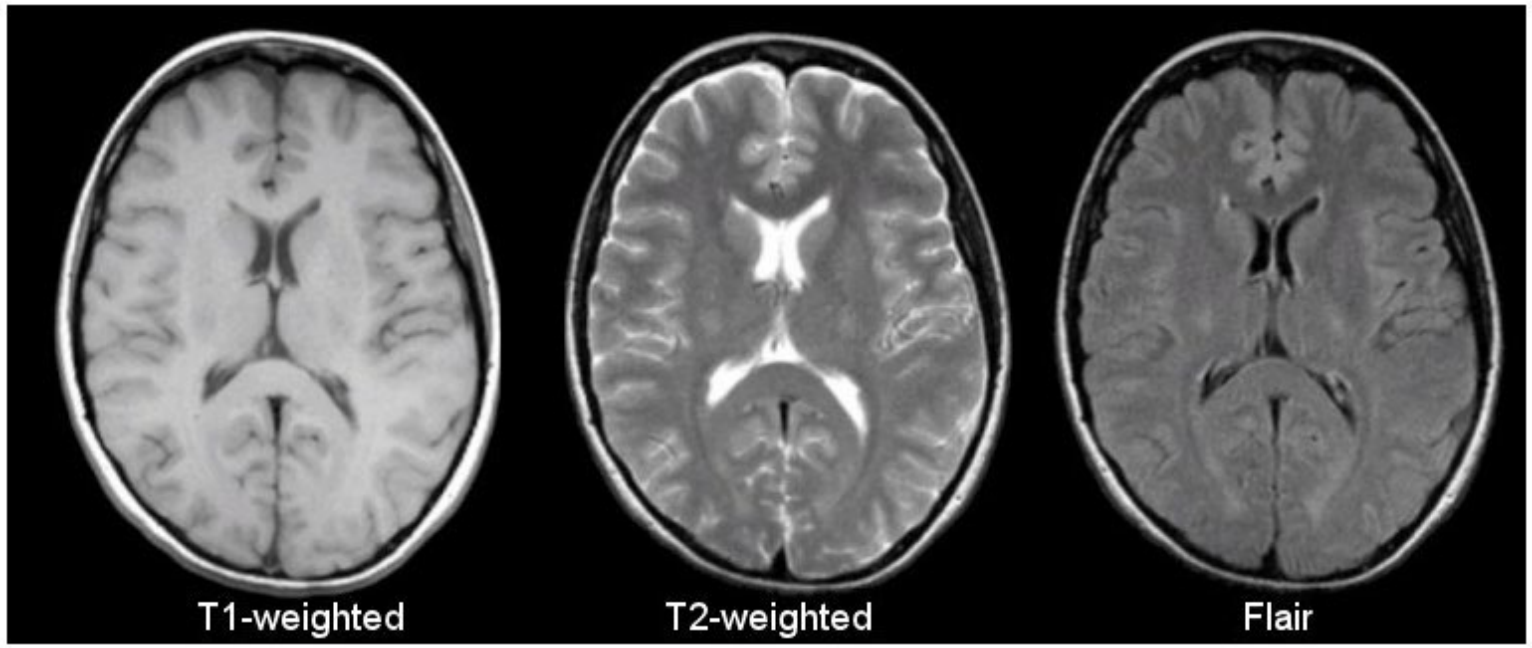
MRI Practicals on CIBM preclinical imaging systems

MAGNETIC RESONANCE IMAGING

https://nationalmaglab.org

MAGNETIC RESONANCE IMAGING

Applications: soft tissue

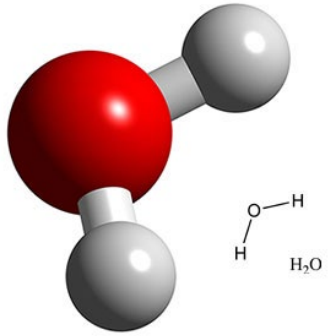


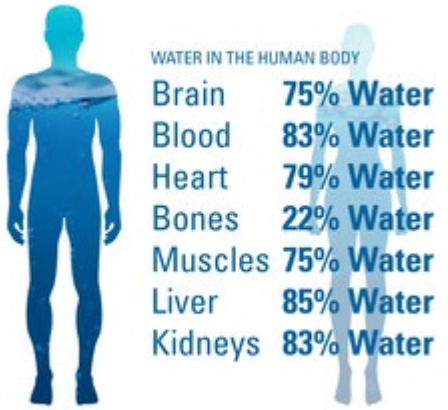
Tissue	T1-Weighted	T2-Weighted	Flair
CSF	Dark	Bright	Dark
White Matter	Light	Dark Gray	Dark Gray
Cortex	Gray	Light Gray	Light Gray
Fat (within bone marrow)	Bright	Light	Light
Inflammation (infection, demyelination)	Dark	Bright	Bright

https://case.edu/med/neurology/NR/MRI%20Basics.htm

MAGNETIC RESONANCE IMAGING -> SPECTROSCOPY

MRI:
Imaging ^{1}H of water

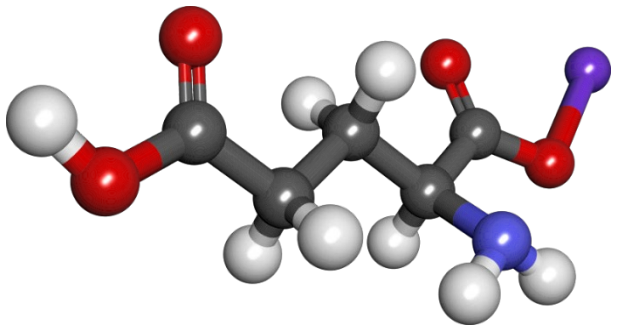




usgs.gov

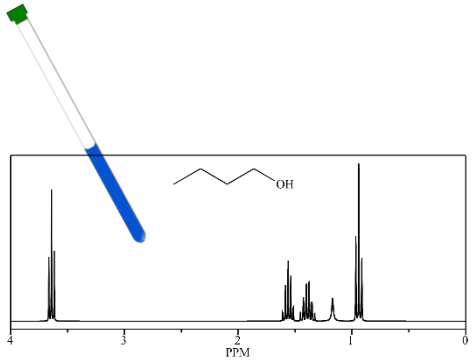
~ 55 M

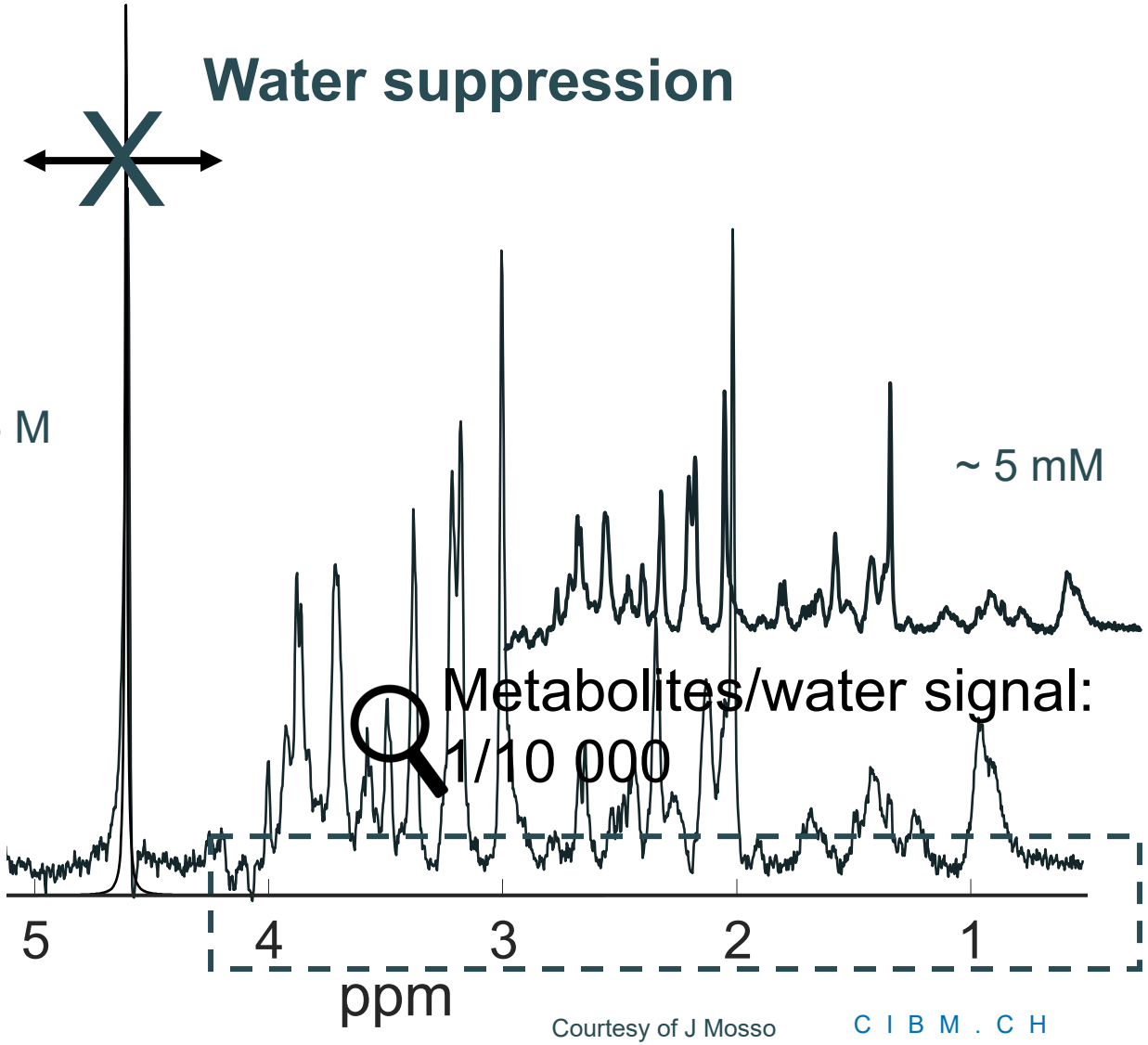
MRS:
Measuring ^{1}H of biomolecules



glutamate

As chemical NMR…
but *in vivo*



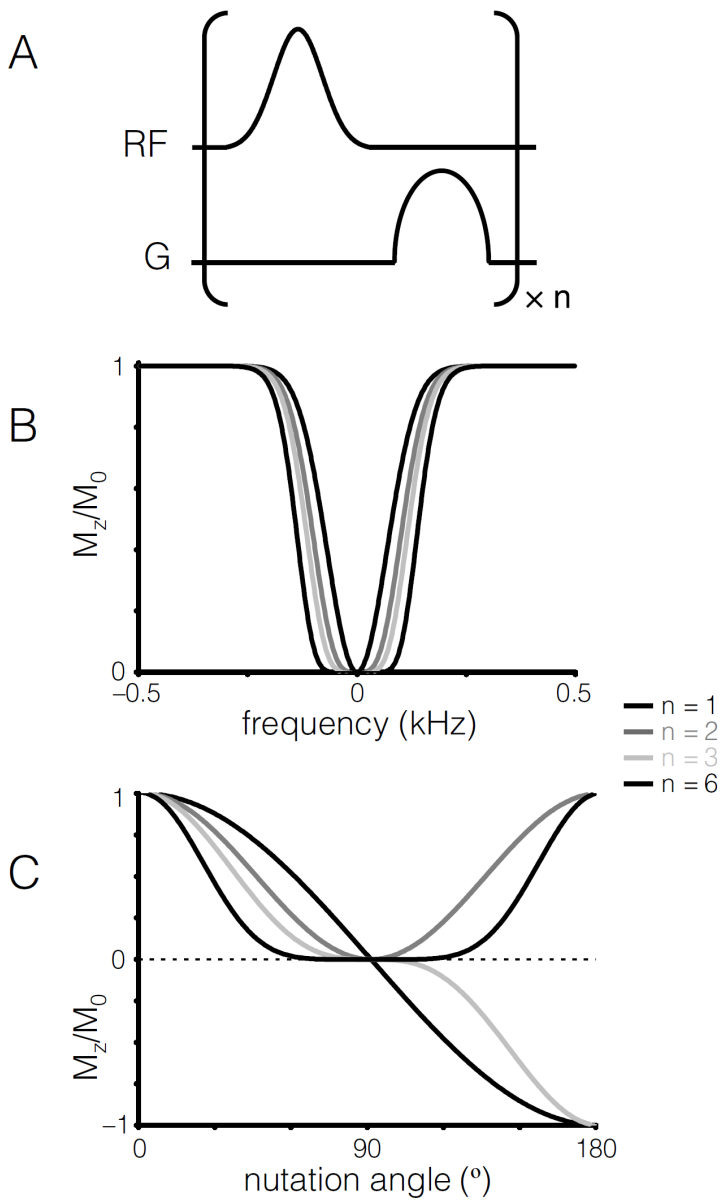


Courtesy of J Mosso

WATER SUPPRESSION MODULE

CHESS (chemical shift selective)

- Uses a frequency-selective pulse on water

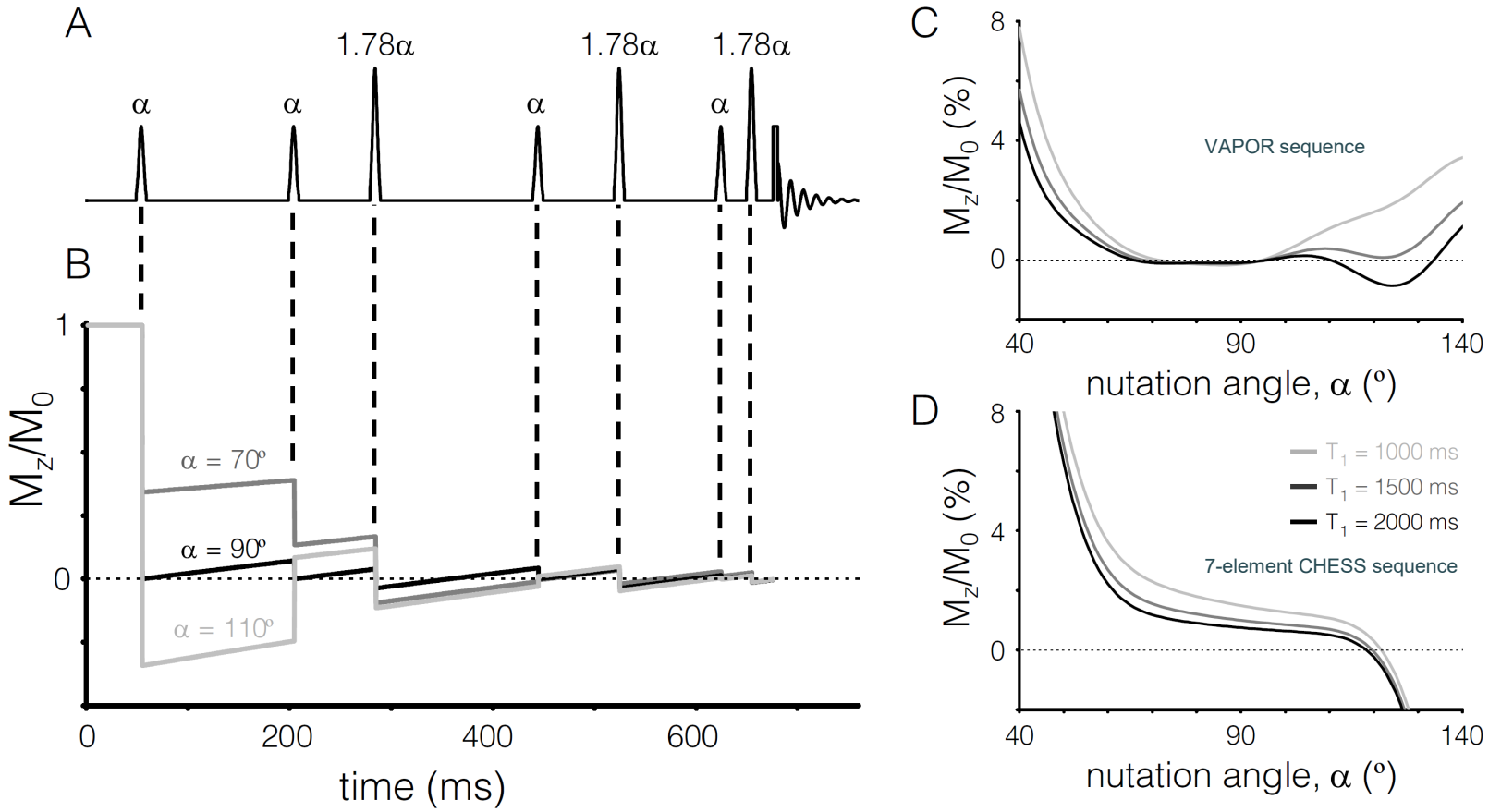


A Haase et al 1985 Phys. Med. Biol. 30 341

WATER SUPPRESSION MODULE

VAPOR (Variable pulse powers and optimized relaxation delays)

- Uses a frequency-selective pulse on water and optimized T1-based suppression

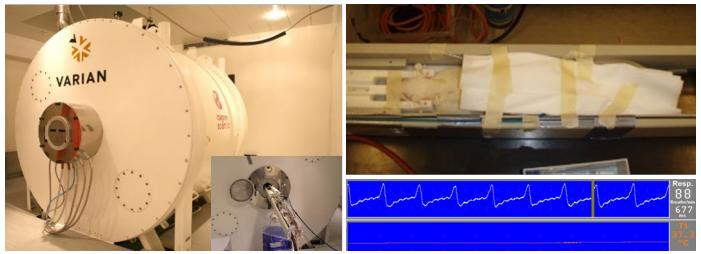


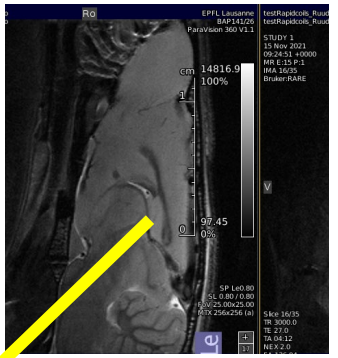
Tkac et al., Magn Reson Med 1999

IN VIVO ^{1}H MR SPECTROSCOPY @ 9.4T

WHAT DO WE MEASURE?

- ***in vivo***
- **non invasive**





Neurochemical Profile

>18 Markers of :

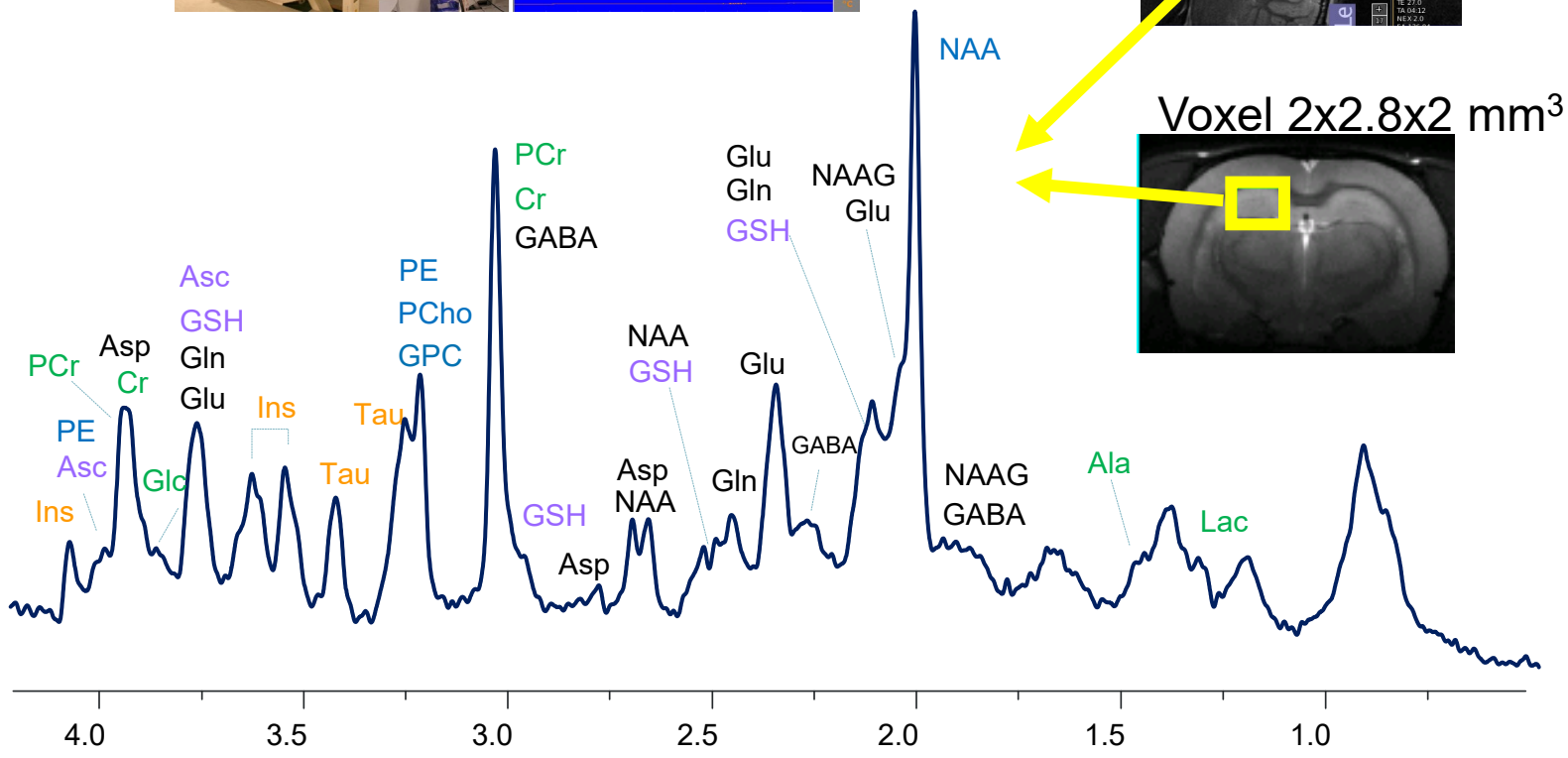
Myelination/Cell proliferation

Energy metabolism

Osmoregulation

Neurotransmitter metabolism

Antioxidants



Voxel 2x2.8x2 mm^3

cristina.cudalbu@epfl.ch

CD Rae et al, Anal Biochem. 2017; CD Rae .Neurochem Res. 2014; V Račkayová et al 2017; Lanz et al, 2017

ROLE OF MAJOR BRAIN METABOLITES

^{1}H MRS	
Single metabolites	
Lactate (Lac)	End product of anaerobic glycolysis Marker of inflammation in the subacute phase
Creatine (Cr), phosphocreatine (PCr)	Energy metabolism, PCr is a reserve of high-energy phosphates
N-acetylaspartate (NAA)	No complete understanding of its function, but reduced levels with brain injury Possibly a marker of neuronal viability, density, and mitochondrial function Also present in oligodendroglia progenitors Precursor of *N*-acetylaspartylglutamate
Myoinositol	Osmolyte, marker of glial cell proliferation
Choline (Cho)	Marker of cell membrane synthesis and breakdown, precursor for acetylcholine
Lipids	Marker of membrane degradation
Glutamate	Excitatory neurotransmitter, high concentrations in neurons
Glutamine	Derivative of glutamate, de novo synthesis exclusively in astrocytes
GABA	Neurotransmitter with excitatory properties in the immature brain (inhibitory in the adult brain)
Aspartate	Excitatory neurotransmitter
Taurine	Osmolyte, antioxidative properties, inhibitory neurotransmitter
Glutathione	Antioxidant

Berger et al., Dev neurosci,(2017)

ADVANTAGES IN VIVO MRS

POWERFUL AND UNIQUE

- Measure simultaneously a high number of metabolites in vivo non-invasively ---------- longitudinal studies
- Metabolite concentrations and different biochemical processes (e.g., metabolite fluxes)
- Metabolism --------- brain, liver, heart,.. ----- humans and rodents
- Concentrations ~0.5 mM – ascorbate, glycine, GSH[1,2,3,4]
- Changes during development[5,6]
- Region-specific[1-9]
  - Cortex, striatum, hypothalamus, substantia nigra, medulla oblongata, corpus callosum, cerebellum …
- Changes during pathology: cancer, dementia, Huntington, Alzheimer, Parkinson, ischemia, hepatic encephalopathy, ….

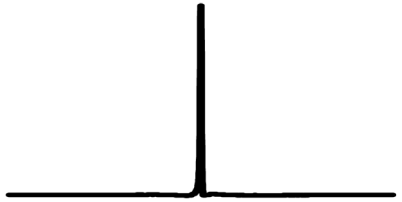
[1]Terpstra M et al, 2010, 2006; [2]Xin L et al, 2010 ; [3]Gambarota G et al, 2009; [4]CD Rae 2017; [5]Račkayová V, et al 2022; [6]Tkac et al, 2003; [7]Kuklak et al, 2010, [8] Lei et al, 2010; [9]Craveiro M et al, 2014

RESONANCE FREQUENCY(IES)

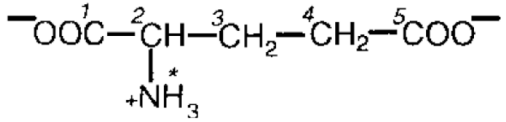
Larmor Frequency and spectral pattern

Larmor frequency: $\omega_0 = \gamma B_0$

600 MHz at 14.1T for ^1H



Glutamate



The Dependence of a Nuclear Magnetic Resonance Frequency upon Chemical Compound*

W. G. Proctor and F. C. Yu
Department of Physics, Stanford University, Stanford, California
January 18, 1950

«Until it is clearly understood, the accuracy of magnetic moments determined under certain chemical conditions remains somewhat in doubt.»

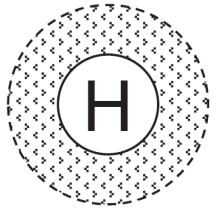
CHEMICAL SHIFT

Electronic shielding

Nominal Larmor frequency:
(«naked» nucleus)

Proton: nucleus of ^{1}H

Real resonance frequency:

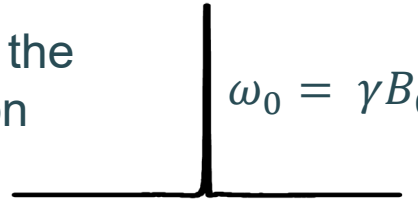


Proton + e cloud: ^{1}H atom

δ is called the chemical shift

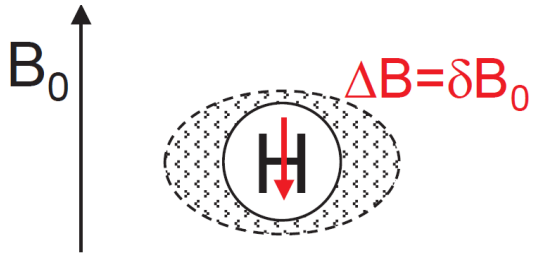
Resonance frequency of the «pure» proton

600 MHz at 14.1T for ^{1}H



$$\omega_0 = \gamma B_0$$

Magnetic shielding effect:



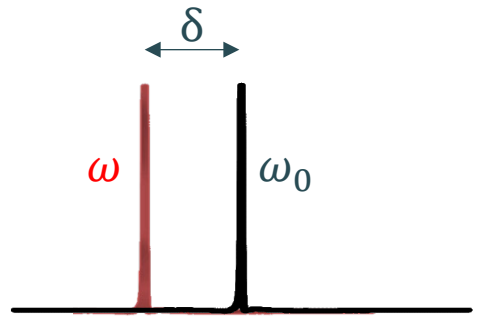
$$\frac{d\vec{M}}{dt} = \gamma\vec{M} \times \overrightarrow{B_{TOT}}$$

$$= \gamma\vec{M} \times \left(\overrightarrow{B_0} - \delta\overrightarrow{B_0}\right)$$

$$= \gamma(1-\delta)\vec{M} \times \overrightarrow{B_0}$$

New resonance frequency:

$$\omega = \gamma(1-\delta)B_0 = \omega_0\,(1-\delta)$$

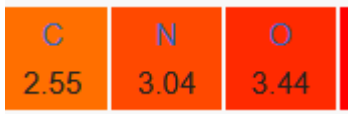


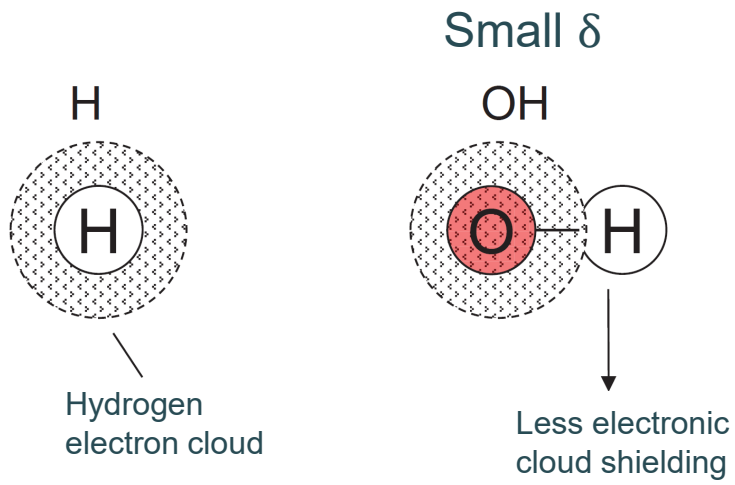
CHEMICAL SHIFT

Electronic shielding from neighbouring atoms

The electron cloud is affected by bonded atoms (valence electrons):

→ Electronegativity effect





→ Resonance frequency is higher in OH than CH

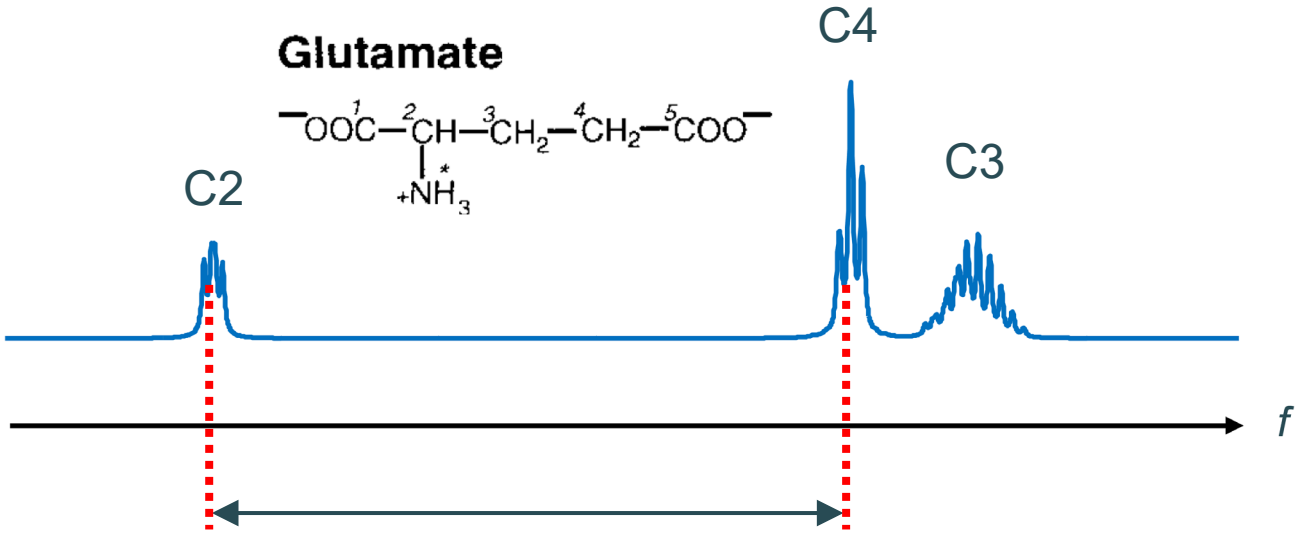
The resonance frequency of a nucleus depends on its chemical environment

$$\omega = \omega_0 (1 - \delta)$$

CHEMICAL SHIFT

Frequency range and units

$$\omega = \gamma B_0 \, (1 - \delta)$$



1280 Hz for B_0 = 14.1 T

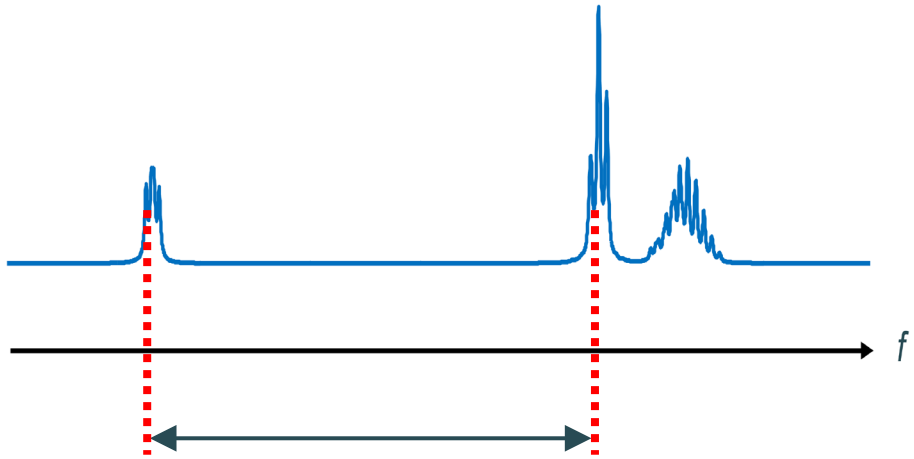
Expressed in Hz:

- The chemical shift is proportional to B_0
- It is small compared to the Larmor frequency

Chemical shift is typically expressed in *parts per million (ppm)* (magnetic field independent)

$$\delta = \frac{\omega - \omega_{ref}}{\omega_{ref}} \times 10^6$$

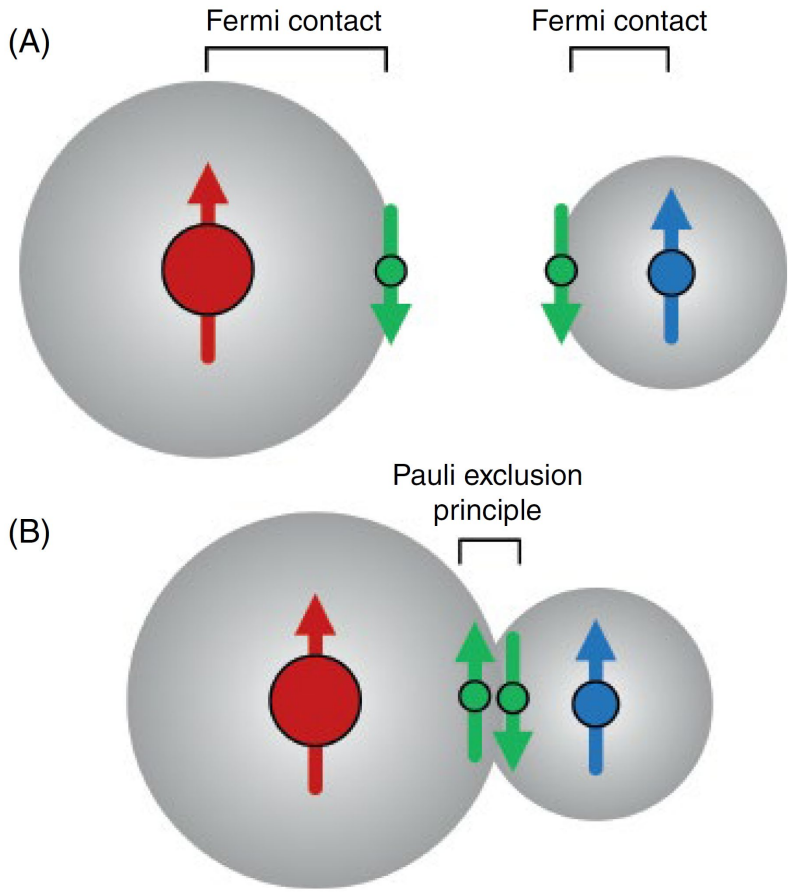
0 ppm is defined by ω_{ref} a reference compound (e.g. tetramethylsilane (TMS) for ^{1}H)



850 Hz for B_0 = 9.4 T

J COUPLING

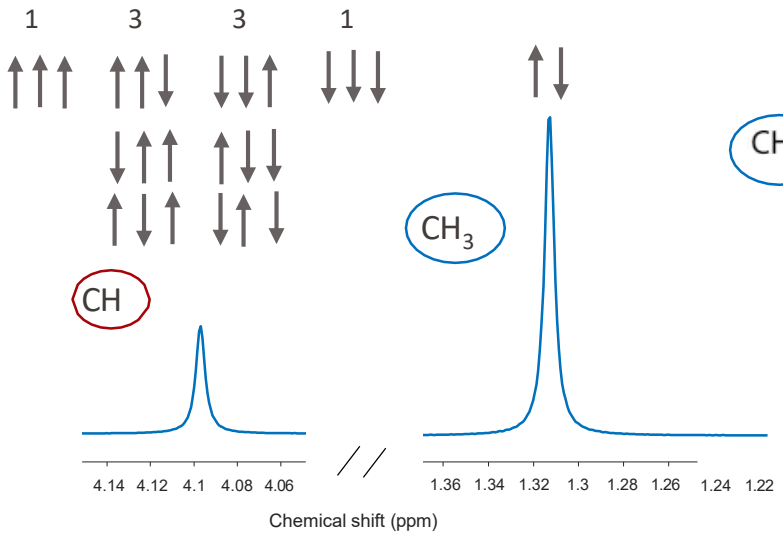
Scalar effect of neighbouring nuclear spins, through the electron bonds

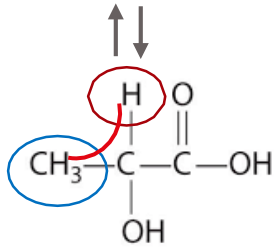


J COUPLING

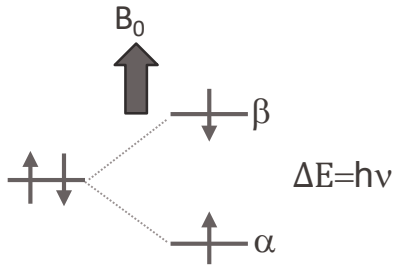
J-coupling (spin-spin coupling, scalar coupling)

Interactions between neighboring nuclear spins





Lactate



Number of splitting peaks: n+1

n: the number of neighboring identical nuclei

J: coupling constant in Hz

n	Pascal's triangle
0	1
1	1 1
2	1 2 1
3	1 3 3 1
4	1 4 6 4 1
5	1 5 10 10 5 1
6	1 6 15 20 15 6 1
7	1 7 21 35 35 21 7 1
8	1 8 28 56 70 56 28 8 1

J COUPLING

J-coupling (spin-spin coupling, scalar coupling)

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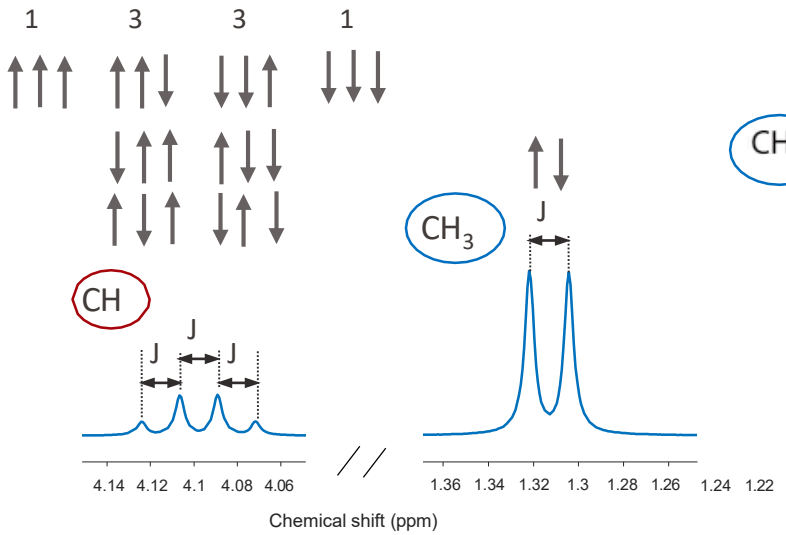
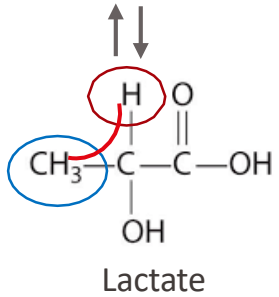
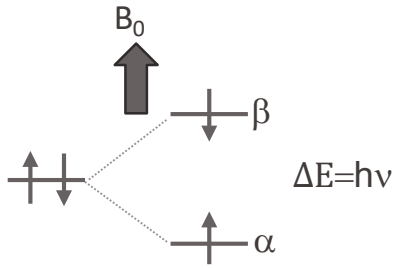




Lactate



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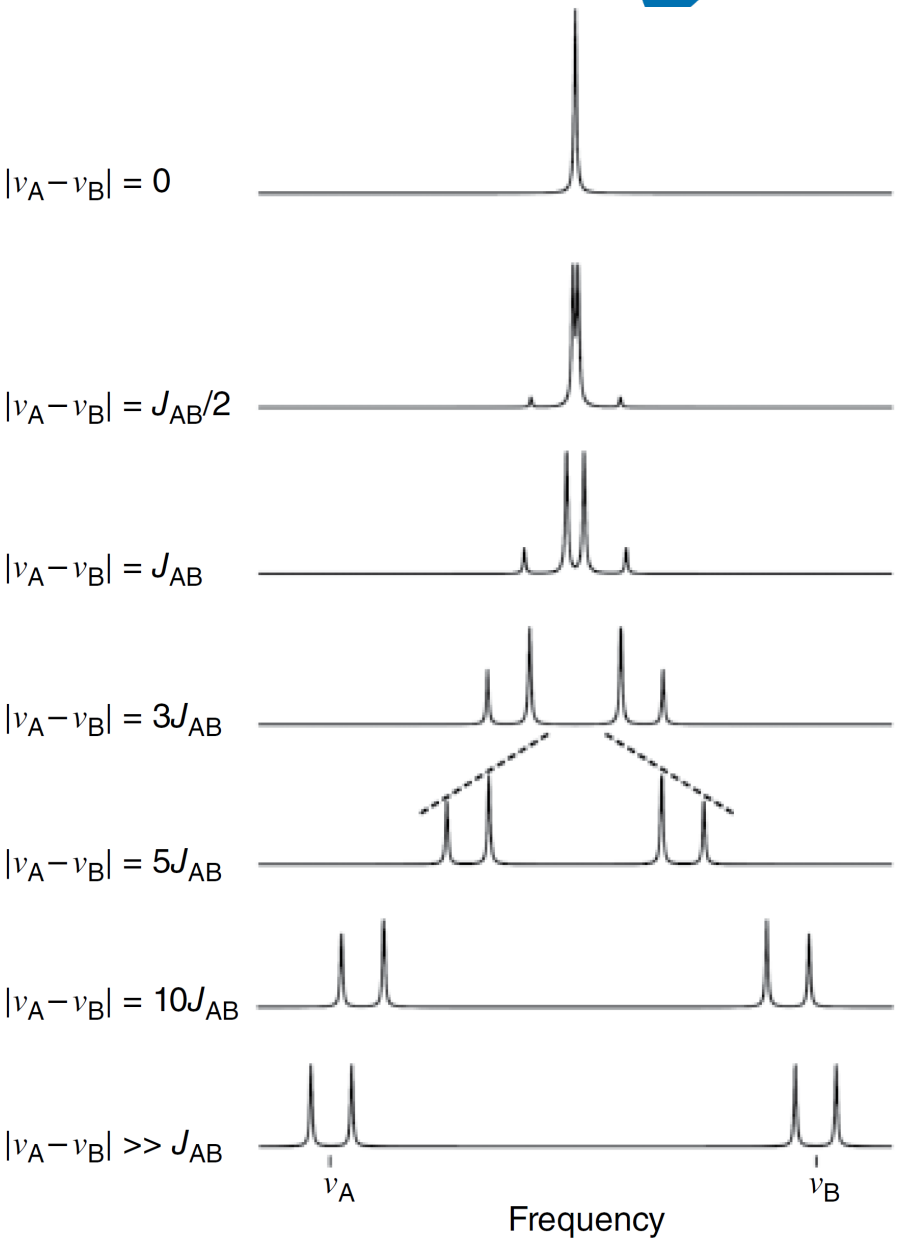
J COUPLING

Properties

- J is independent of the magnetic field
- The pattern might depend on its strength
  - Weakly coupled systems ($(f_2 - f_1 \gg J_{12})$) follows standard splitting (case for heteronuclear coupling, like ^{13}C-^{1}H)
  - Strongly coupled systems, show complex patterns (roof effect)

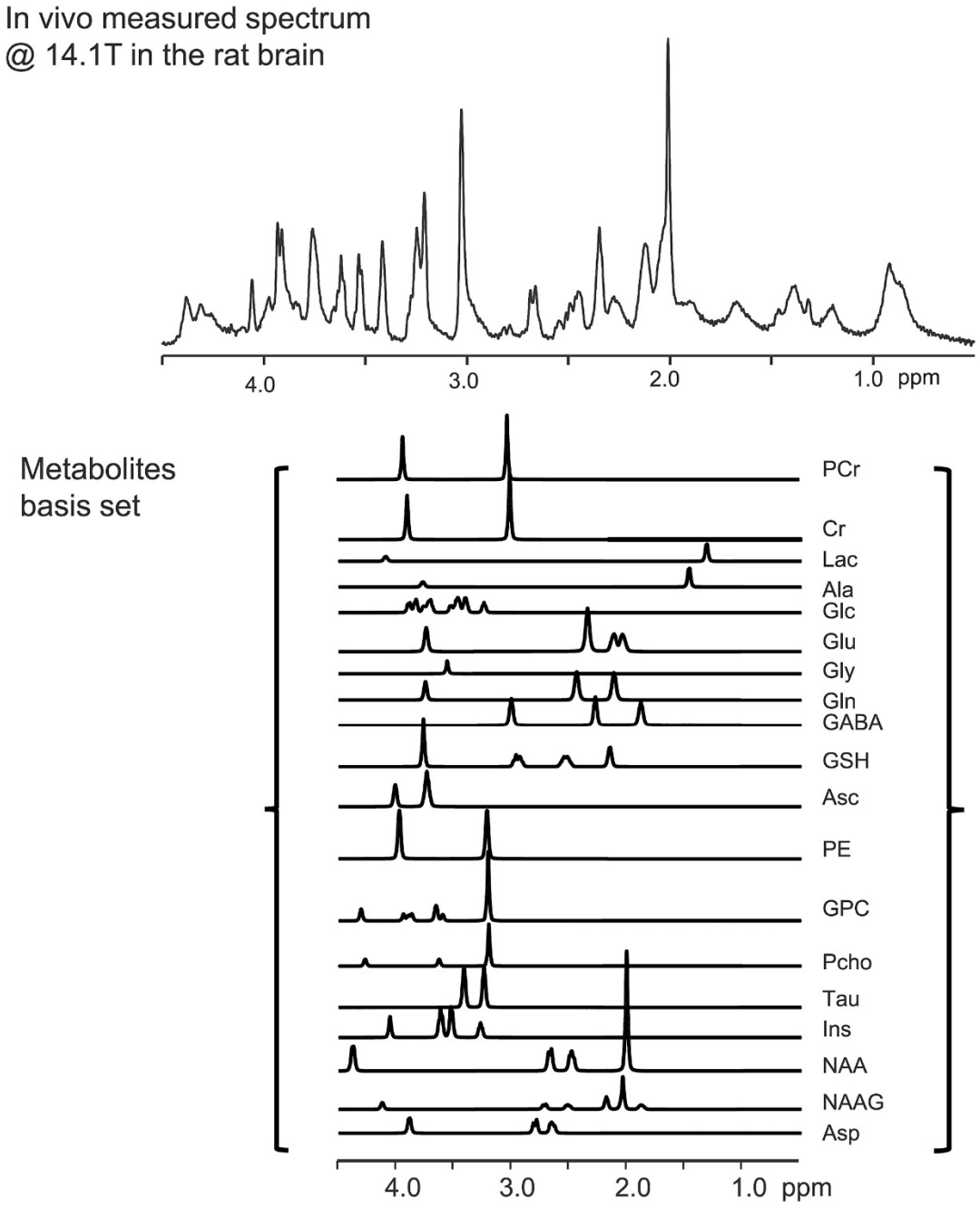


MOLECULAR SIGNATURE IN TOTAL SPECTRUM

Each molecule is recognisable by a specific spectral pattern.

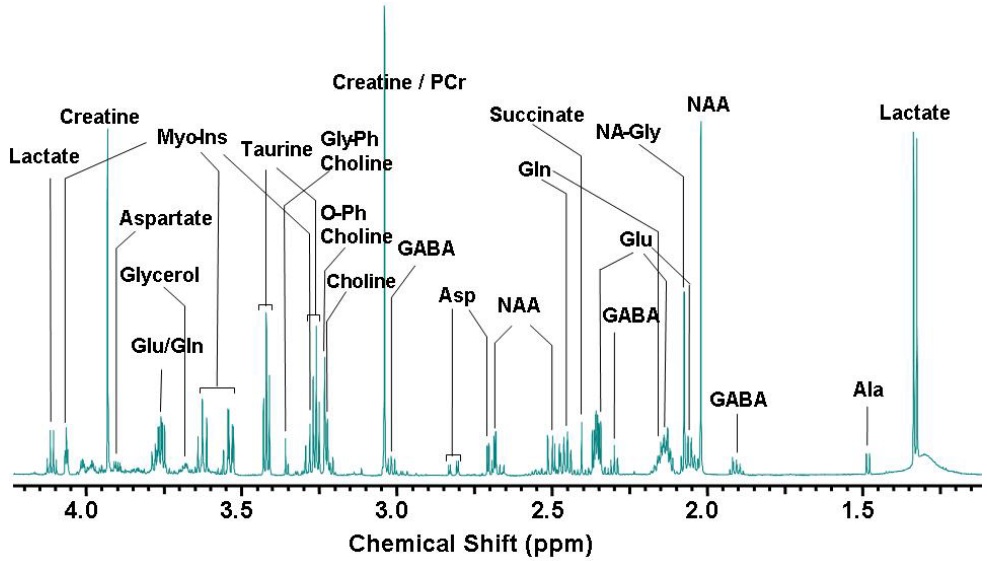
The combination of all spectral patterns gives the total measured spectrum.

The reverse decomposition process is called spectral quantification.



MAGNETIC RESONANCE SPECTROSCOPY

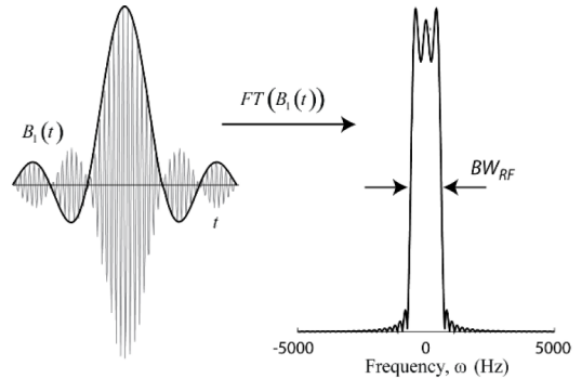
- NMR Spectroscopy



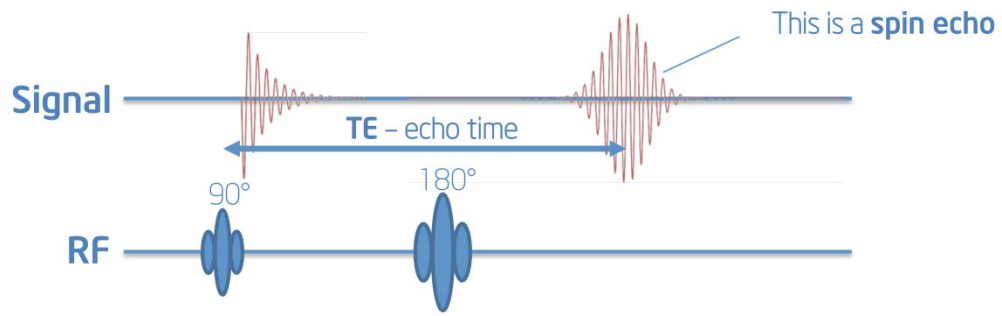
IN VIVO LOCALISED SPECTROSCOPY

RF PULSES ARE NEEDED FOR ALL MRI / MRS ACQUISITIONS

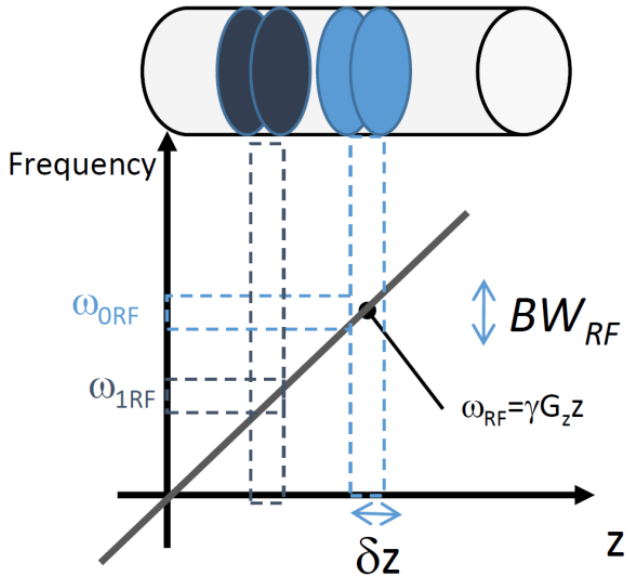
For slice selection, a gradient is applied during an RF-pulse, which is characterized by its excitation bandwidth (BW_{RF})



A simple pulse sequence – Spin Echo



A 'spin echo' will still use gradients – but it is the refocusing via the RF pulse which makes the distinction

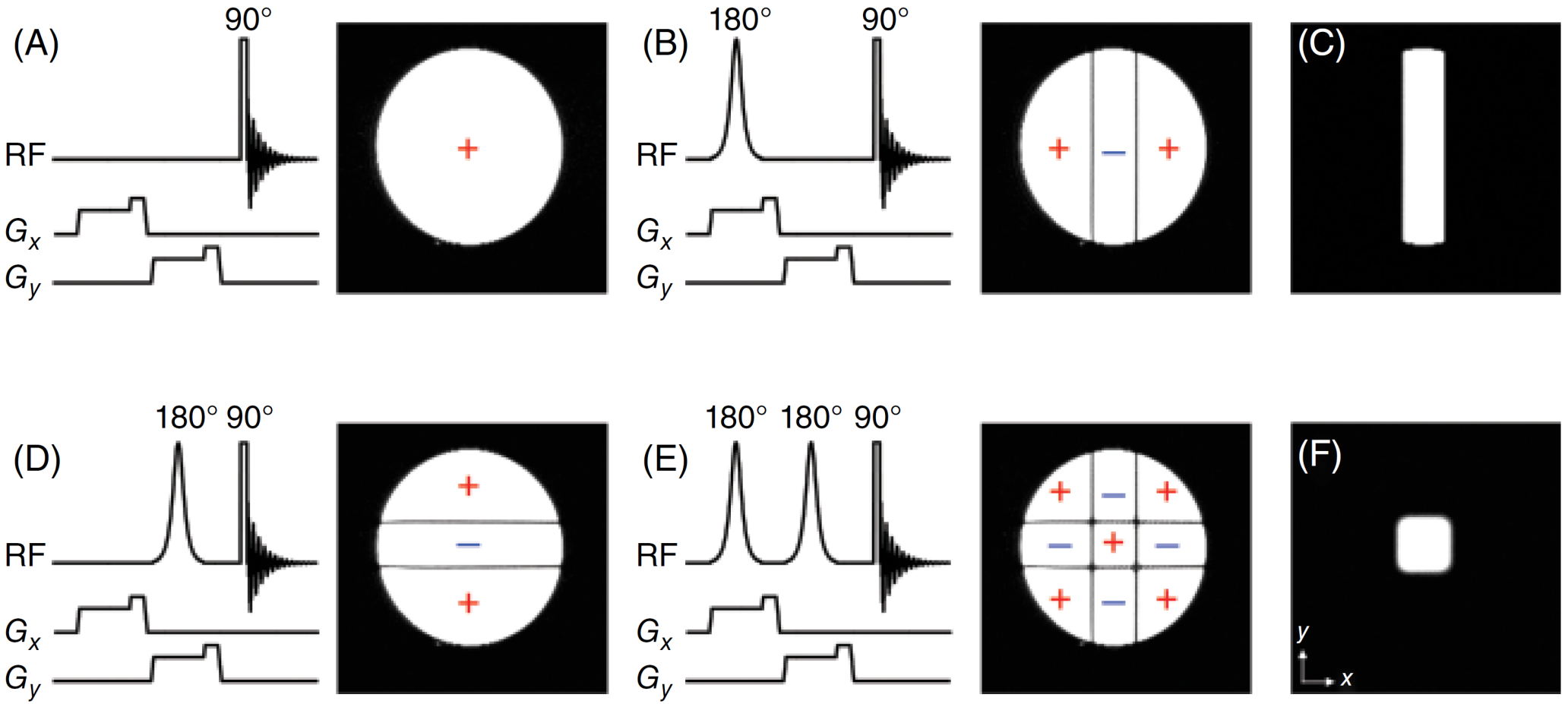


IN VIVO LOCALISED SPECTROSCOPY

- In single voxel spectroscopy (SVS), we can use slice-selection for 1D encoding.
- However, the frequency information carries the chemical indentification
  → Frequency encoding cannot be used for localisation

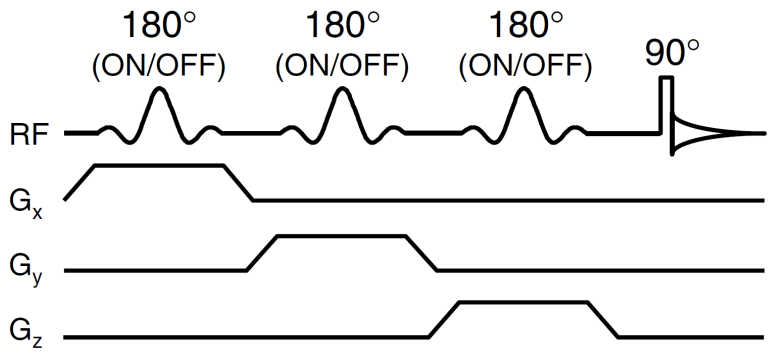
IN VIVO LOCALISED SPECTROSCOPY

ISIS (Image Selected In Vivo Spectroscopy)

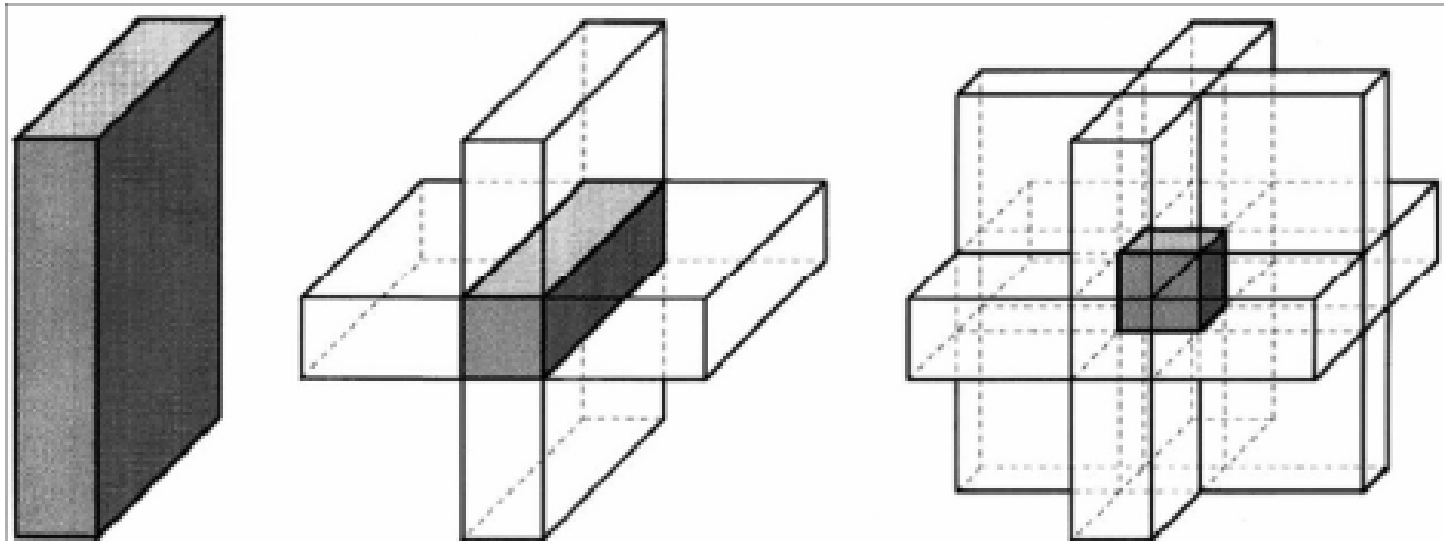


IN VIVO LOCALISED SPECTROSCOPY

ISIS 3D



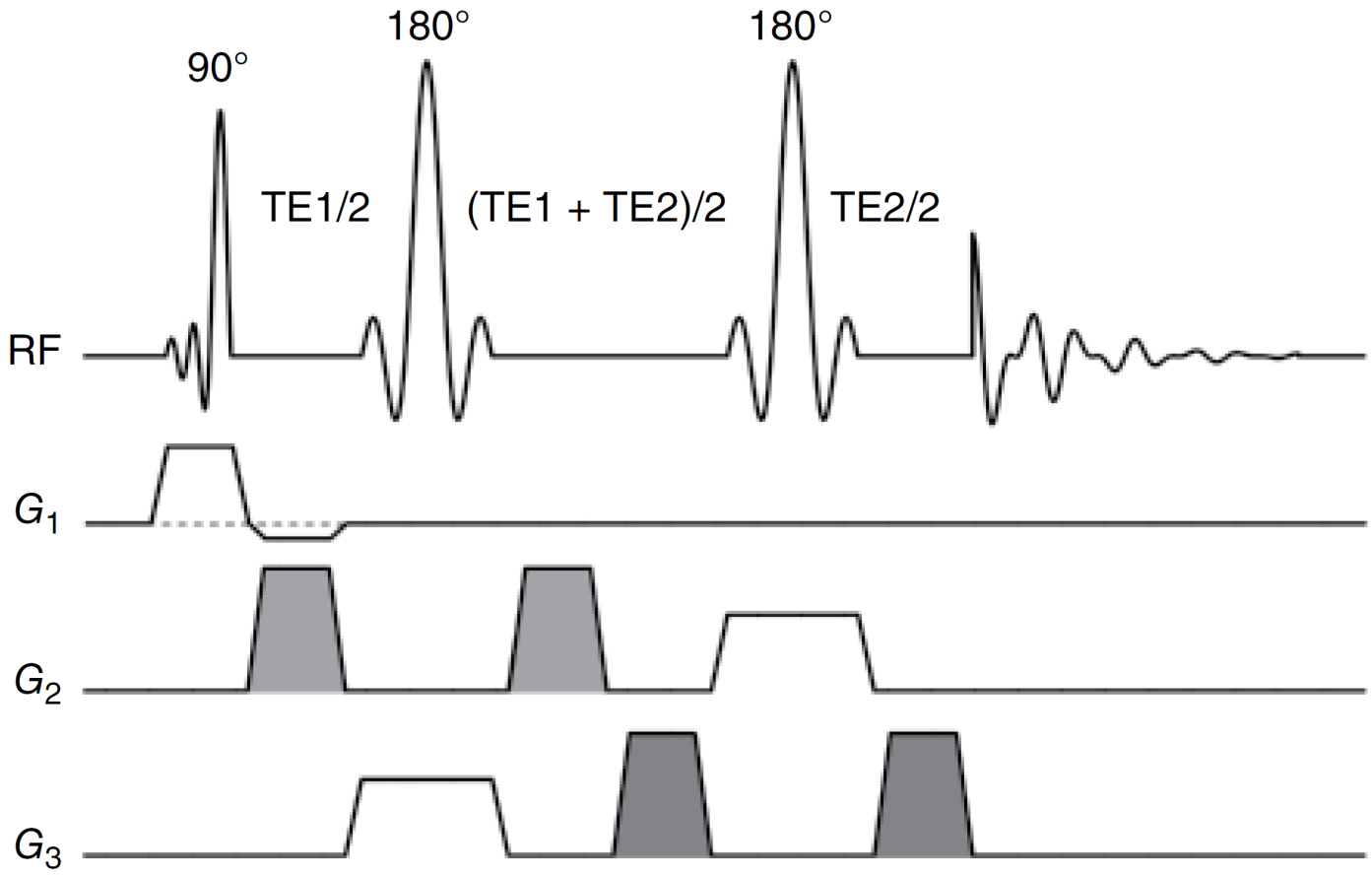
Exp 1	OFF	OFF	OFF	+
Exp 2	OFF	OFF	ON	–
Exp 3	OFF	ON	OFF	–
Exp 4	ON	OFF	OFF	–
Exp 5	OFF	ON	ON	+
Exp 6	ON	OFF	ON	+
Exp 7	ON	ON	OFF	+
Exp 8	ON	ON	ON	–



IN VIVO LOCALISED SPECTROSCOPY

PRESS (Point Resolved Spectroscopy)

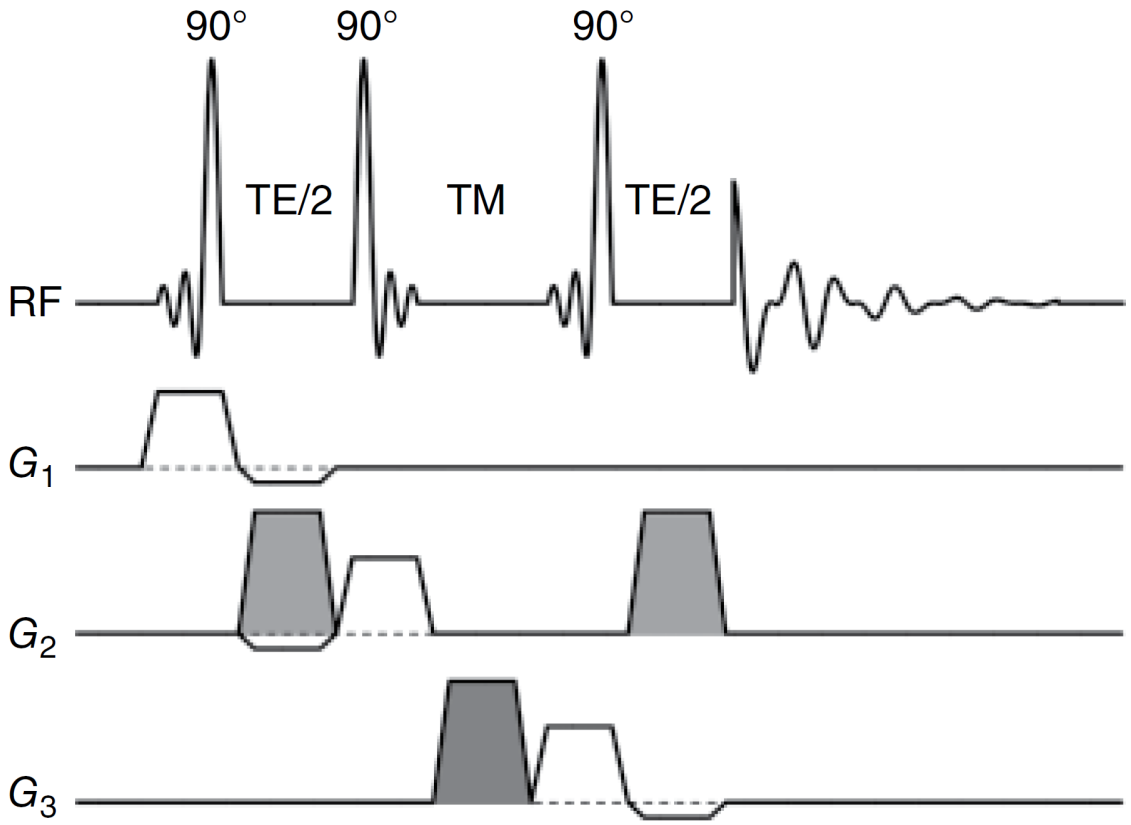
- Strength:
  - full signal intensity detected
  - insensitive to motion
- Weakness:
  - long echo times
  - sufficient B1 peak power necessary for 180° pulses (poor bandwidth)



IN VIVO LOCALISED SPECTROSCOPY

STEAM (STimulated Echo Acquisition Mode)

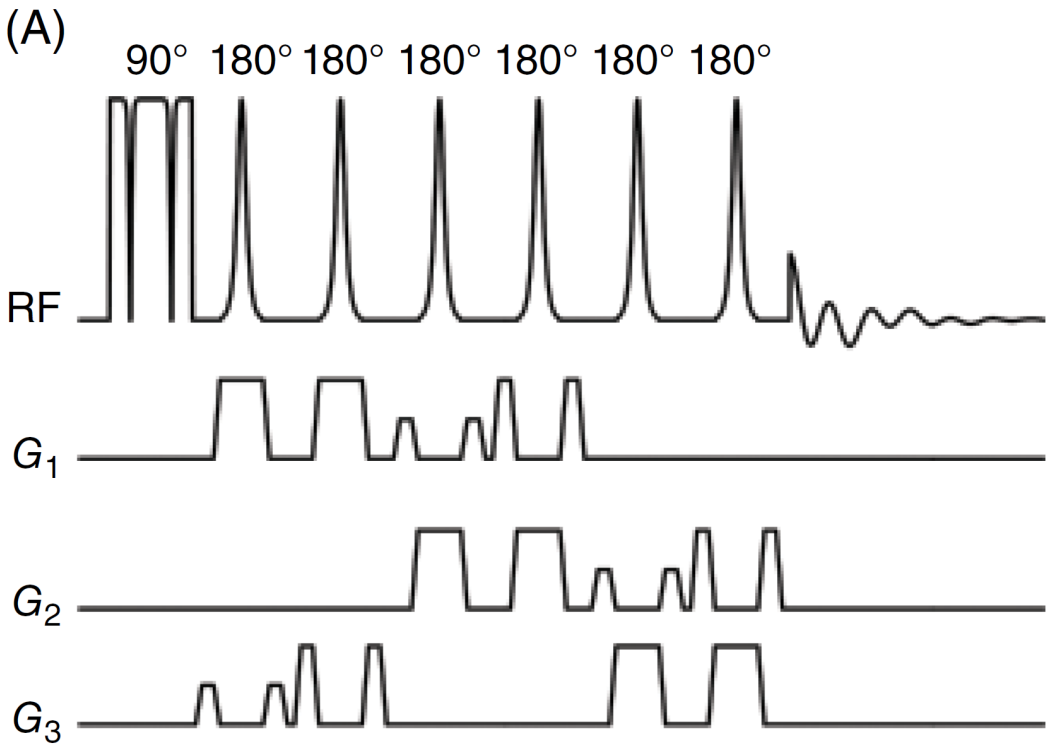
- Strength:
  - short echo time (relative to PRESS)
  - insensitive to motion
  - less sensitive to B1 inhomogeneity than PRESS (90° pulses have better frequency response)
- Weakness:
  - only one half of the magnetization available



IN VIVO LOCALISED SPECTROSCOPY

LASER (Localization by Adiabatic Selective Refocusing)

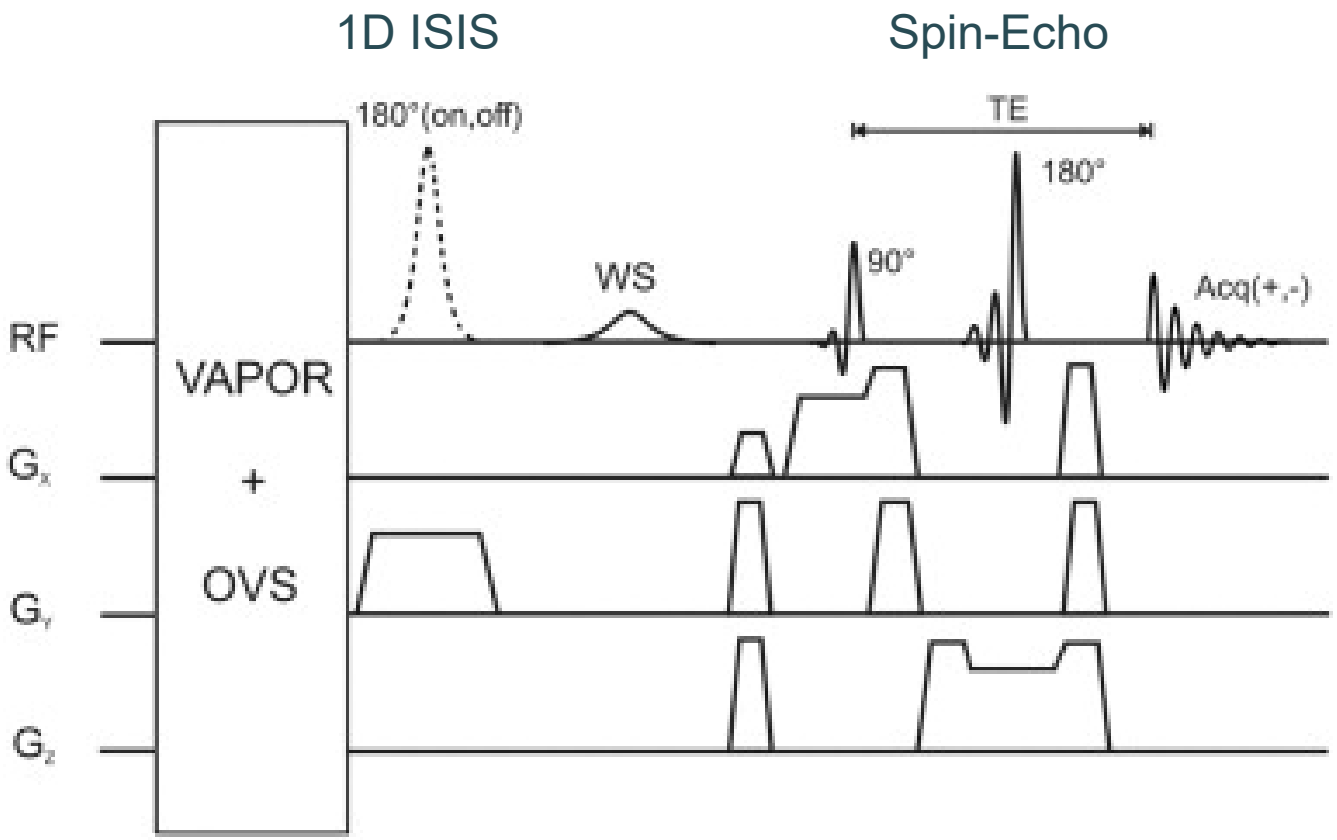
- Strength:
  - full signal intensity detected
  - insensitive to motion
  - insensitive to B1 inhomogeneity
- Weakness:
  - Longer echo time
  - high B1 peak power necessary for adiabatic conditions



IN VIVO LOCALISED SPECTROSCOPY

SPECIAL (SPin ECho Full Intensity Acquired Localized Localized)

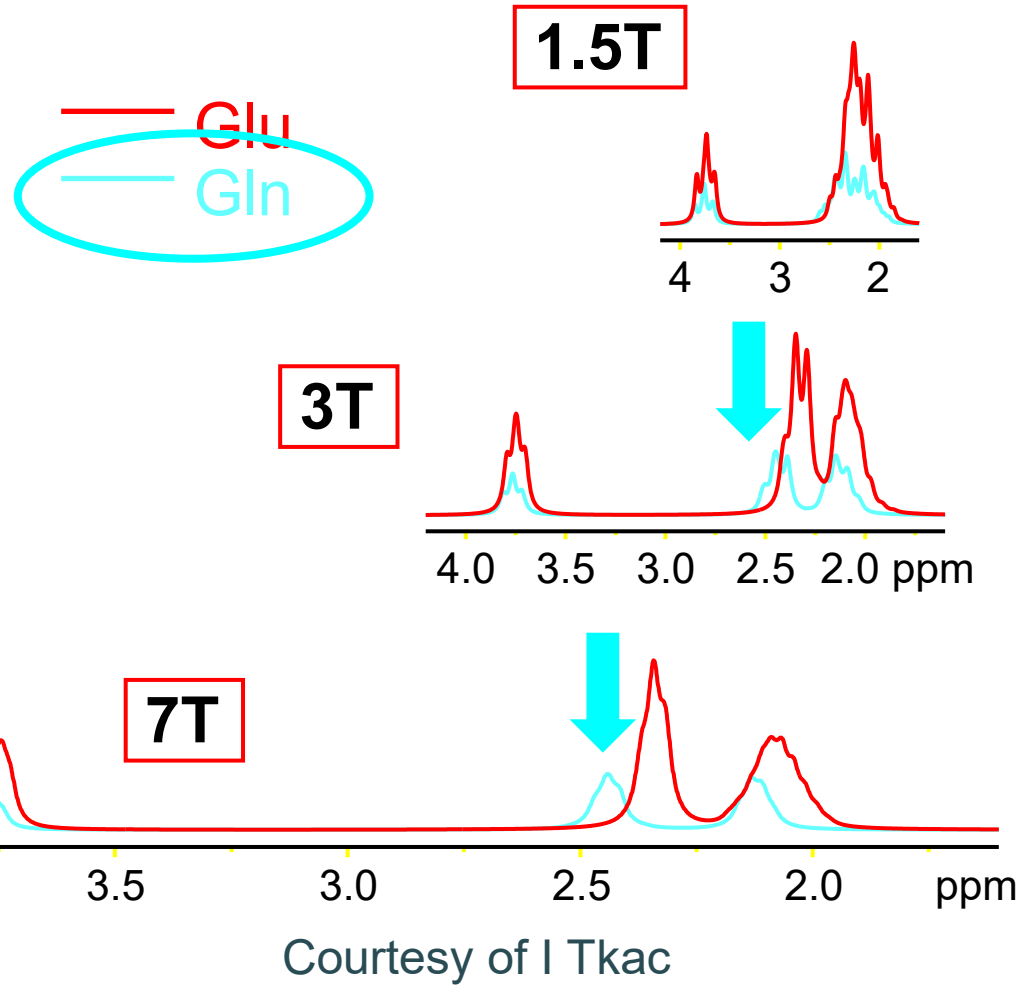
- Strength:
  - full signal intensity detected
  - Short TE
  - insensitive to B1 inhomogeneity
- Weakness:
  - two scans necessary for localization
  - more sensitive to motion than single-shot methods
  - 180° pulse direction suffers more RF bandwidth issues



Mlynárik, MRM 2006

WHY HIGH B_0?

- Enormous progress
  - ↑ SNR
  - ↑ chemical shift dispersion – ↑ resolution
  - decreased strong J-coupling effects
  - Improve quantification precision and accuracy
  - ↓ T_2* - ↑ spectral lw in Hz



Courtesy of I Tkac

Oz G, et al., Clinical proton MR spectroscopy in central nervous system disorders. Radiology. 2014
Wilson M, et al., Methodological consensus on clinical proton MRS of the brain: Review and recommendations. Magn Reson Med. 2019

PRECLINICAL MRS: WHAT?

- MRS applied on animal models for scientific questions that cannot be probed directly with human MRS
- The scope of this presentation will focus on rodent models (rats and mice), and on applications to brain studies.

PRECLINICAL MRS: WHAT?

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SPECIAL ISSUE REVIEW ARTICLE

NMR IN BIOMEDICINE WILEY

Magnetic resonance spectroscopy in the rodent brain: Experts' consensus recommendations

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NMR in Biomedicine Special Issue
Advanced Magnetic Resonance Spectroscopy Experts' Consensus Recommendations

PRECLINICAL MRS: WHY?

- Usefulness of preclinical MRS (rats and mice in most cases)
  - Ethical considerations (ultimately, the goal is not to find ways to cure rodents…)
- Usefulness in terms of biological aspects
  - Animal models
- Usefulness in terms of MR physical aspects
  - New MR acquisition approaches

PRECLINICAL MRS: WHY?

- Usefulness in terms of biological aspects
  - Rats and mice are good biological models of tissue development, function and metabolism
  - Mimicking multiple aspects of the human disease (Transgenic mouse models)
  - *In vivo* state : leaving tissue works as a whole, not as the sum of its components.

Cell cultures can be used for basic cellular/metabolic questions, while *in vivo* studies are key for complex organ functions.

  - Non invasively characterize disease progression, effect of treatments (longitudinal studies)

PRECLINICAL MRS: WHY?

- Usefulness in terms of MR physical aspects
  - The availability of MRI/MRS systems at magnetic field strength of 9.4 T and higher enables studies with high sensitivity and spectral resolution
  - Use of anaesthetics enables long experimental acquisition with minimal motion artefacts and instabilities
  - Opens the way to study deeper biochemical pathways with dynamic MRS (e.g. ^{13}C MRS)
  - Lower restrictions on the gradients and RF limits enable the developments of new MR approaches at lower risk

ANIMAL PHYSIOLOGY AND ANESTHESIA

Effective and standardized rodent MRI/MRS studies require attention to many aspects of the experimental design.

- Anaesthesia is critical for *in vivo* preclinical MRI and MRS
  - ⊕– decreases the stress of the animals, potential pain in case of surgical intervention, biological motions
  - ⊖– decreases respiratory and cardiac activities
- MRS in awake rodents (very few studies)
  - MRS with awake rodents is challenging and requires a relatively long training period[1,2]
  - For awake-rodent MRS studies, monitoring serum cortisone levels and heart rate of the animals is recommended

[1] Xu et al., MRM 2013 [2] Low et al., Pain. 2016

ANIMAL PHYSIOLOGY AND ANESTHESIA

TABLE 2 Characteristics of commonly used anesthetics and their impact on brain metabolites

	Physiological effects	Side effects	Effect on brain metabolites↓↑* statistically significant changes($p < 0.05$)	Type	References
Propofol	Rapid and short-acting anesthesia effect, fast recovery time	Muscle twitching, apnea, hypotension, decreased cardiac output	Lactate ↓, glutamate ↓* (compared with isoflurane)	Injectable	20,21
Halothanes (e.g. isoflurane, sevoflurane)	Rapid and short-acting anesthesia effect, fast recovery time	Respiratory depression, dose dependent hypotension, increased cerebral blood flow, immune suppression	Lactate ↑, GABA ↑, choline-containing compounds ↑, *myo*-inositol ↑, glucose ↓, NAA ↑, total creatine ↑, creatine ↑, glutamate ↑, glutamine ↓, alanine ↑ * (compared with without isoflurane)	Inhaled	22,23
Thiopental	Ultra-short acting	Severe tissue necrosis (if administered via non-i.v. routes), prolonged recovery if the animal has low body fat, myocardial depression, decreased cardiac output, hypotension	Glucose ↑* (compared with light alpha-chloralose)	Injectable	20,24
Pentobarbitone	Poor analgesia characteristics (more reliable for rats than for mice)	Hyperexcitability, significant cardiovascular depression in mice, hypotension in rats	GABA ↓ glucose ↓, taurine ↓, propylene glycol ↑* (compared with isoflurane), glucose ↑ (compared with light alpha-chloralose)	Injectable	20,25–27
Ketamine	Rapid analgesia but less muscle relaxation	Respiratory depression, pain in injection side (due to low pH), increased cardiac output, heart rate, blood pressure	Glutamate ↓* (^{1}H-^{13}C NMR study; 80 mg per kg ketamine treated group compared with saline treated group)	Injectable	18,20,28
Xylazine/ketamine	The synergistic effect causes anesthesia with extended analgesia	Body temperature may decrease, increased urination, defecation, salivation, ocular lesions, hypoglycemia	Alanine ↓, ascorbate (or vitamin C) ↑, aspartate ↑, GABA ↑, glycine ↑, PCr ↑ (compared with isoflurane)	Injectable	27,29
Urethane	Provides long-lasting anesthesia	Mutagenic and carcinogenic in experimental animals	Lactate ↑ (compared with no urethane group)	Injectable	30,31
Alpha-chloralose	Provides long-lasting light anesthesia	Poor analgesic properties, prolonged and poor recovery	Unknown	Injectable	32

PRE-ANESTHETIC CONSIDERATIONS

FOR IN VIVO MRS STUDIES

Stress, strain, sex, circadian cycles, weight and age of the animals affect:
- effectiveness of anaesthesia
- direct impact on MRS measurements of the neurochemical profile

- The correct dosage of the anaesthetic should provide adequate sedation but also adequate analgesia and less variability in physiological parameters during MRI/MRS experiments
- Monitoring and recording the respiration rate and temperature of animals under anaesthesia is essential (if available, pulse oximetry and electrocardiography can provide further control)

SUBJECT FEEDBACK

Major practical difference for the experimentalist

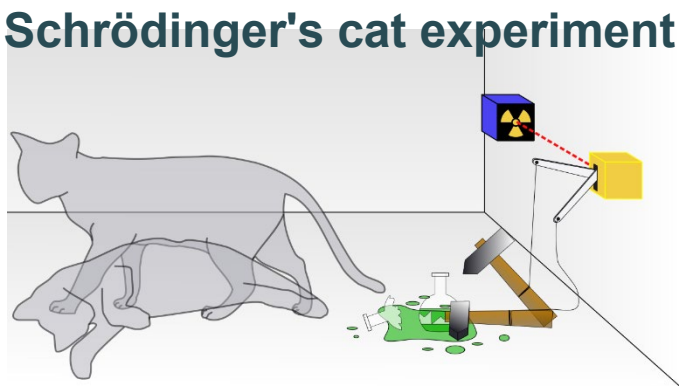
- Human MRS scans are rarely performed over longer periods (>45 minutes) and typically split into 10 minutes scans blocks

  BUT -> You can have a direct feedback from the subject

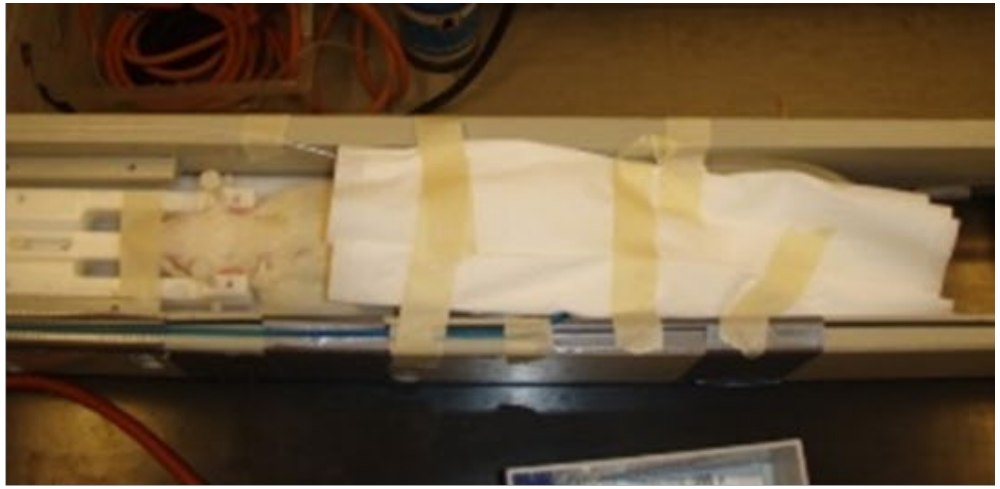
- Rodent MRS scans can be performed over extended periods (> 4 hours) and are less prone to motion

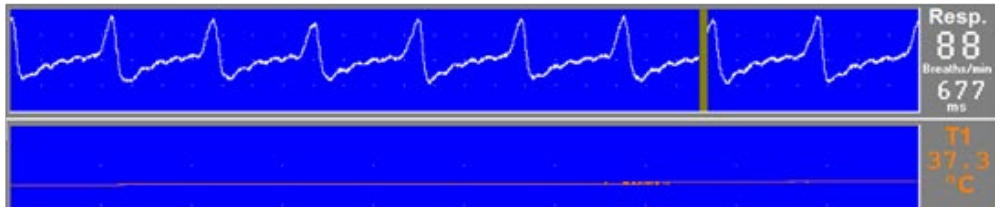
  BUT -> You cannot have a direct feedback from the subject

  -> The animal is invisible in the magnet



ANIMAL PHYSIOLOGY MONITORING AND REGULATION



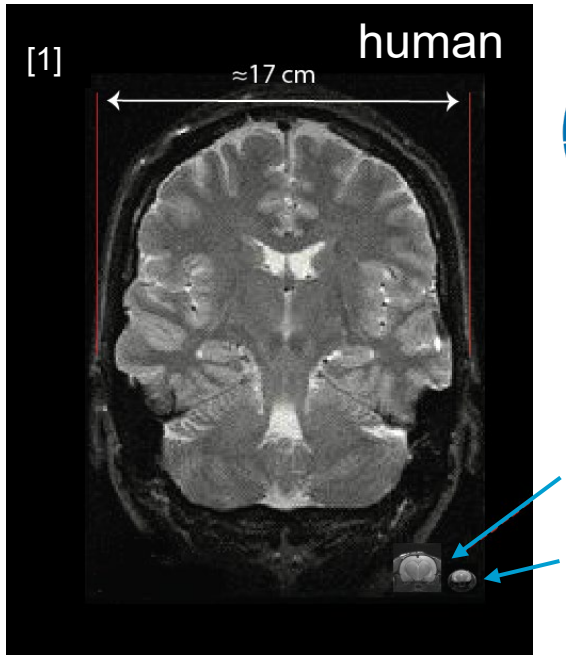


HARDWARE

Main differences with human MRS:

- small brain size

- strong B_0 inhomogeneity induced in the brain by the air/tissue interface

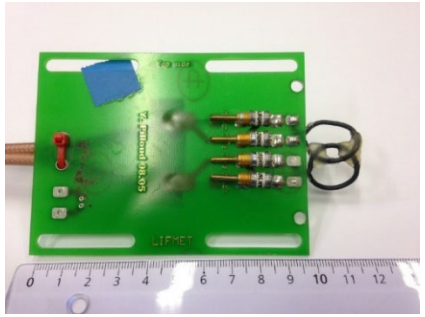


- Small VOIs (rats 50-150 µL, mice 2-15 µL) benefit from ultra-high field (UHF) (≥ 9.4T)
- higher requirements on gradient strength (ideally ≥400 mT/m) compared with that for human systems (typically 70 mT/m for 7 T clinical MR systems)
- Ultra-high field -> increased chemical shift dispersion
  but increased B_0 inhomogeneity requires efficient shimming methods and shim system (FAST (EST)MAP[2,3] or 3D B_0 mapping[4])

[1] in 't Zandt, Proc. Intl. Soc. Mag. Reson. Med. 24 (2016) [2] Gruetter, MRM 1993 [3] Gruetter and Tkac, MRM 2000 [4] Miyasaka et al., MRM 2006

HARDWARE

RF aspects



Surface Tx/Rx

Volume Tx, array Rx

- Lower RF power requirements (much smaller and more efficient coils)
- Surface coils provide much higher SNR from regions close to the RF coil and higher B_1 efficiency than volume coils, but B_1 field is spatially inhomogeneous
- adiabatic RF pulses can mitigate B_1 inhomogeneity
- Contrary to humans, legally unlimited B_1 and strong gradients enable the optimum RF coil choice for optimal SNR and chemical shift displacement error

The problem of tissue heating is still present and should be considered, especially at UHF

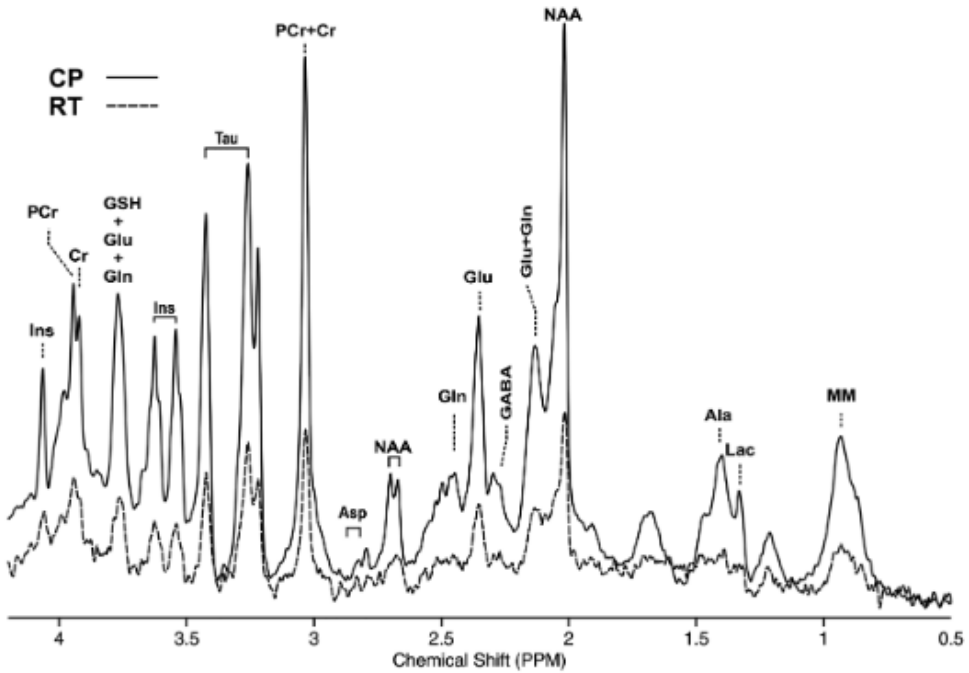
HARDWARE

RF aspects

Cryo-coils

- For small sample volumes, the thermal noise in the coil and the receive pathway is the dominant noise source
- Cryogenically cooled RF coils can be used[1-4]

FIGURE 1 Spectra acquired with the STEAM sequence (TR/TE = 5000/3.5 ms, 384 averages) in a 2.0 × 1.1 × 2.0 mm^3 VOI located in the mouse frontal cortex. A cryogenically cooled ^1H two-element phased-array transmit/receive coil was employed for excitation and signal reception (solid line). As a comparison, a 72 mm diameter birdcage quadrature volume resonator was used for excitation and a ^1H receive-only 2 × 2 surface array coil was used for signal reception (dotted line). A 5.2-fold higher SNR was obtained with the cryoprobe (CP) compared with the room-temperature probe (RT)



C I B M . C H

[1] Kovacs et al., Prog Nucl Magn Reson Spectrosc. 2005 [2] Baltes et al., NMR Biomed. 2009
[3] Mispelter et al., Imperial College Press; 2006 [4] Junge, *eMagRes*. 2012

SEQUENCES AND ACQUISITION PROTOCOLS:

^{1}H MRS

- ultra-short-TE (≤10 ms) spectroscopic localization sequences are usually possible to achieve
- preferentially used because they provide the most accurate quantitative information (minimal J-evolution and T_2 losses)
- TR of 4-5s are typically used (minimizes signal attenuation due to T_1)

SEQUENCES AND ACQUISITION PROTOCOLS:

^{1}H MRS

localization performance of a ^{1}H MRS sequence is very important

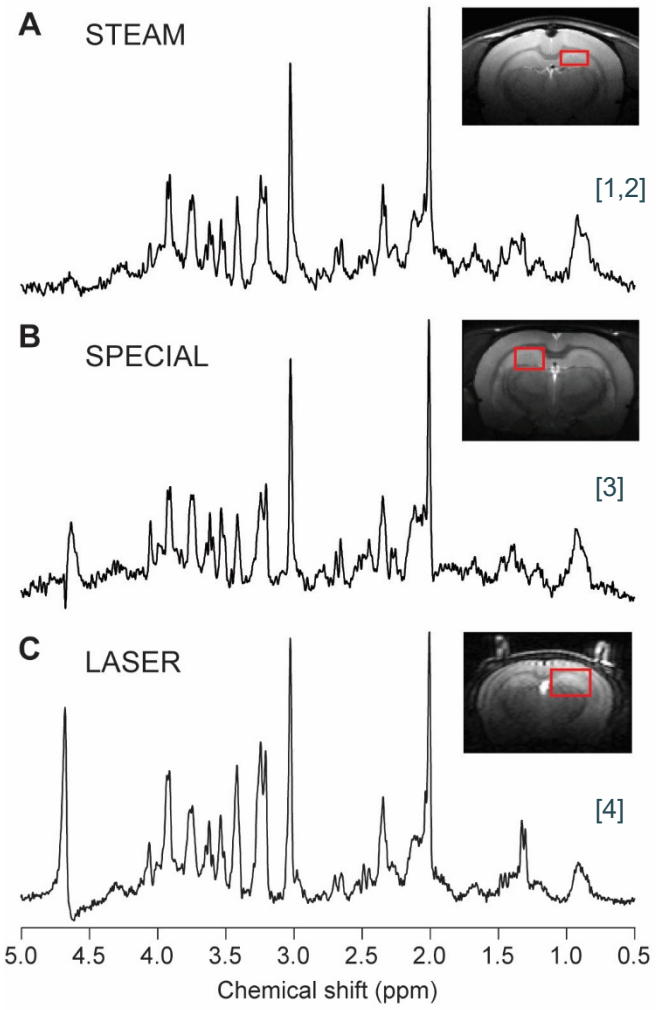
(1) an ability to detect signals originating from the VOI

(2) an ability to suppress signals from outside of the VOI

(3) minimal CSD error related to the bandwidth of the localization pulses

(4) insensitivity to B_1 inhomogeneity, especially when using surface coils

(5) efficient water suppression is important to eliminate the strong water signal



@ 9.4 T
(A) STEAM spectrum: rat brain, 2.3 x 1.3 x 2.5 mm^3 voxel placed in the hippocampus, TR = 5 s, TE = 2 ms, TM = 20 ms, number of averages = 448. Spectrum is shown with Gaussian factor = 0.15.
(B) SPECIAL spectrum: rat brain, 2 x 2.8 x 2 mm^3 voxel placed in the hippocampus, TR = 4, TE = 2.8 ms, number of averages = 160.
(C) LASER spectrum: mouse brain, 1.7 x 2.25 x 2.25 mm^3 voxel placed in hippocampus, TR = 4 s, TE = 27 ms, number of averages = 384.

[1] Frahm et al., J Magn Reson. 1987 [2] Tkac et al., MRM 1999 [3] Mlynarik et al., MRM 2006 [4] Garwood and DelaBarre, J Magn Reson. 2001

SEQUENCES AND ACQUISITION PROTOCOLS:

^{1}H MRS

TABLE 3 Comparison of features of ^{1}H MRS localization pulse sequences used in preclinical studies.

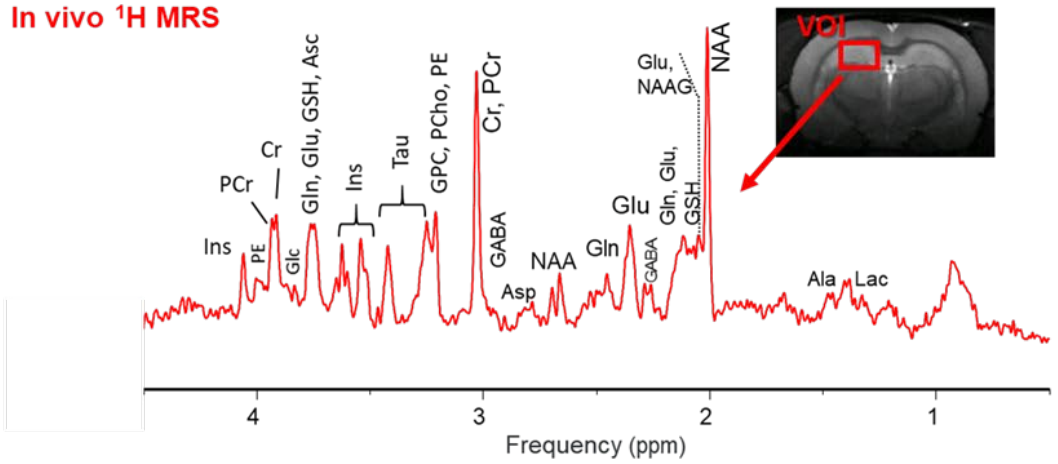
Sequence characteristics	STEAM [1,2]	SPECIAL [3]	LASER [4]
Fraction of available signal (%)	50	100	100
Single-shot method	yes	no	yes
Localization performance	++	++	+++
Sensitivity to B_1 inhomogeneity	−−	−−	−
Sensitivity to motion	−	−−−	−
TE (ms)	2	2.8	15-28
CSDE/ppm in 3 directions at 9.4 T	(9, 9, 9%)[a]	(4, 12, 4%)[b]	(2.4, 2.4, 2.4%)[c]
Flexibility for spectral editing	+++	+++	++
Requirement of T_2 or $T_{1\rho}$ decay knowledge for quantification	no	no	yes

For this table, the original form of SPECIAL is considered rather than semi-adiabatic form of SPECIAL. STEAM refers to the in-house implementation of the typical vendor provided STEAM sequence with improved features, such as shorter TE, better localization and OVS performance.
The evaluation of the localization performance considers the sequences as currently implemented, including OVS modules for STEAM and SPECIAL.
The requirement for $B_{1\ max}$ is not very different between sequences because to achieve such short TE for STEAM and SPECIAL very short localization pulses (which require high B_1) are used.
Large numbers of + signs indicate positive attributes, e.g. enhanced localization performance.
Large numbers of − signs indicate negative attributes, e.g. increased motion sensitivity.
[a]0.5 ms 90° asymmetric sinc pulses for three directions.
[b]0.5 ms 90° and 180° asymmetric sinc pulses for excitation and refocusing; 2 ms AFP for inversion in the 1D ISIS.
[c]4 ms AHP (non-selective) pulse for excitation and six 1.5 ms AFP pulses for refocusing.

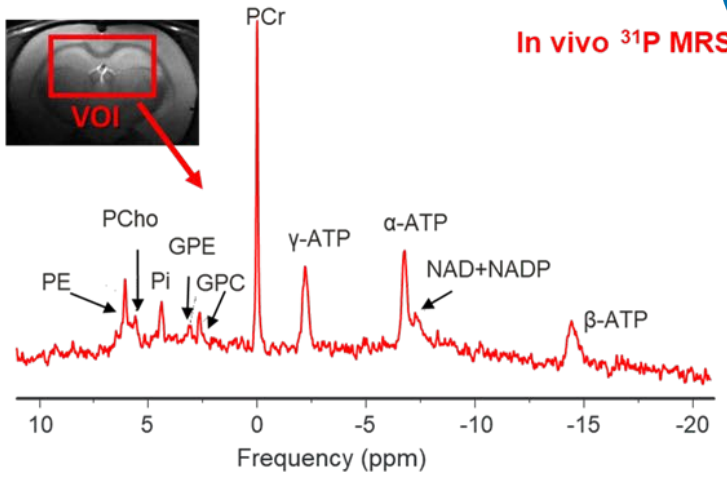
[1] Frahm et al., J Magn Reson. 1987 [2] Tkac et al., MRM 1999 [3] Mlynarik et al., MRM 2006 [4] Garwood and DelaBarre, J Magn Reson. 2001

X NUCLEI MRS – 9.4T

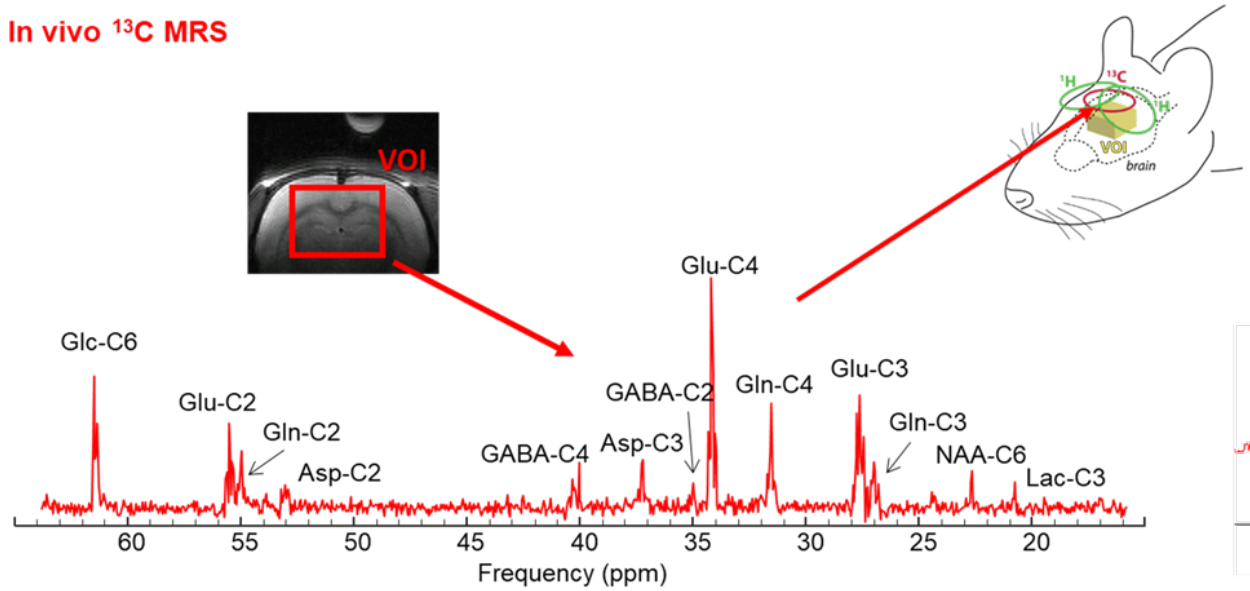
In vivo ^{1}H MRS



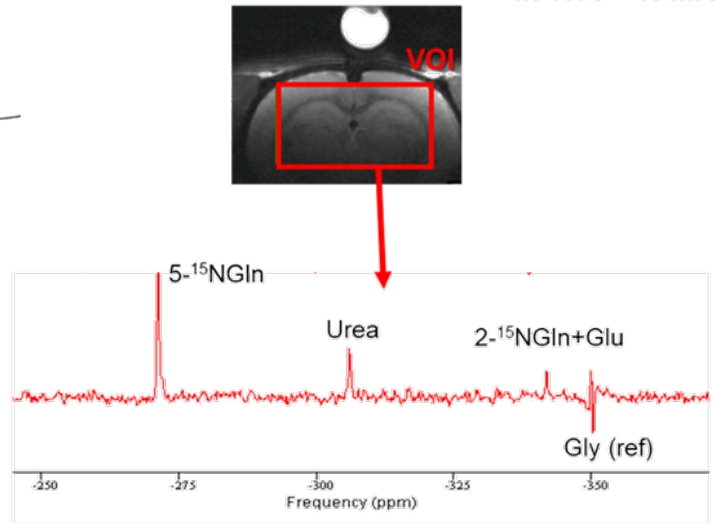
In vivo ^{31}P MRS



In vivo ^{13}C MRS

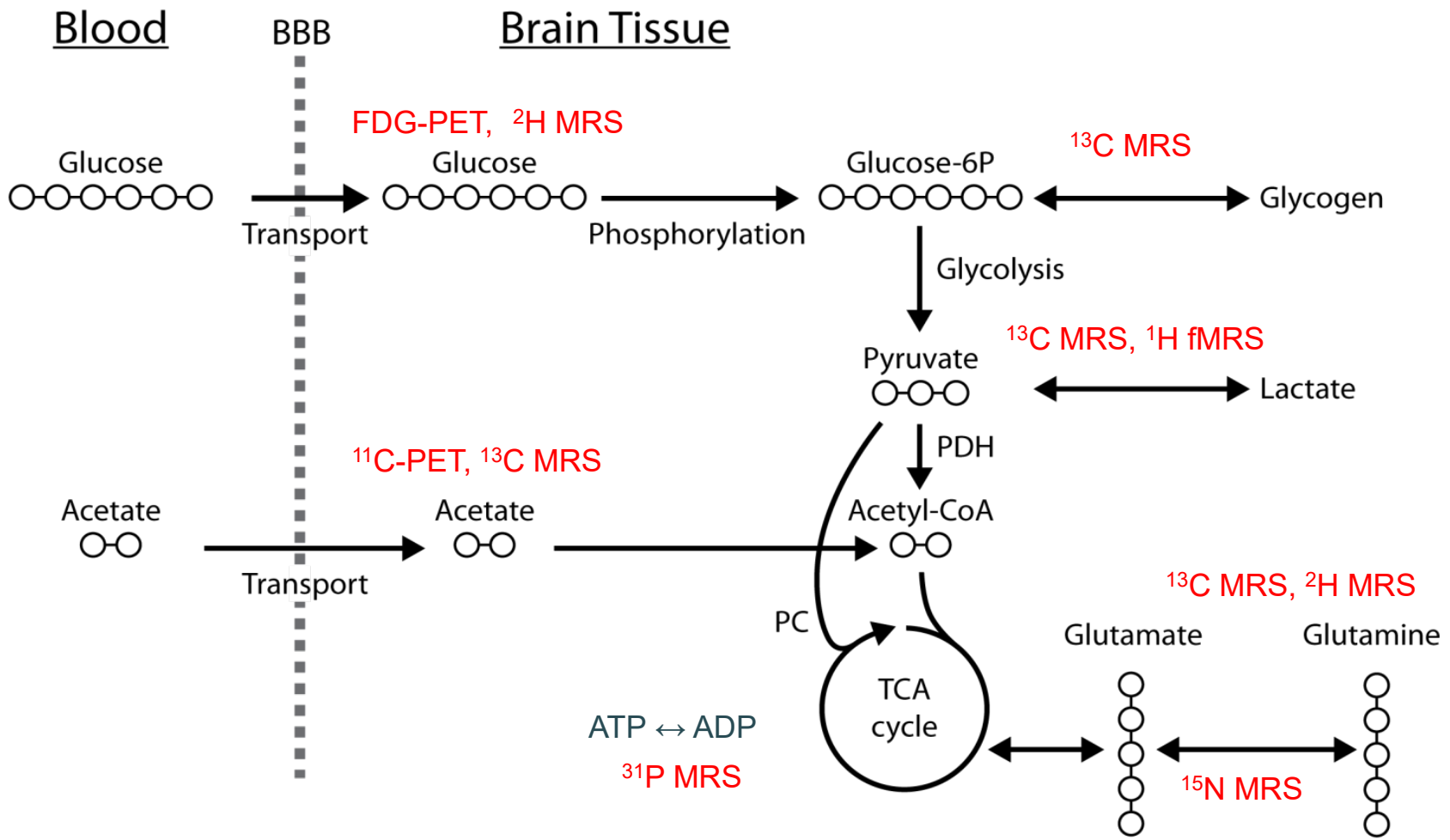


In vivo ^{15}N MRS



Lanz et al, 2017, 2020; Cudalbu et al 2021;

MAIN BIOCHEMICAL PATHWAYS IN BRAIN ENERGY METABOLISM



THANK YOU FOR YOUR ATTENTION

Questions ?

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