UNIVERSITY OF OXFORD

Radcliffe Department of Medicine
Medical Sciences Division

Exploring advanced functional imaging

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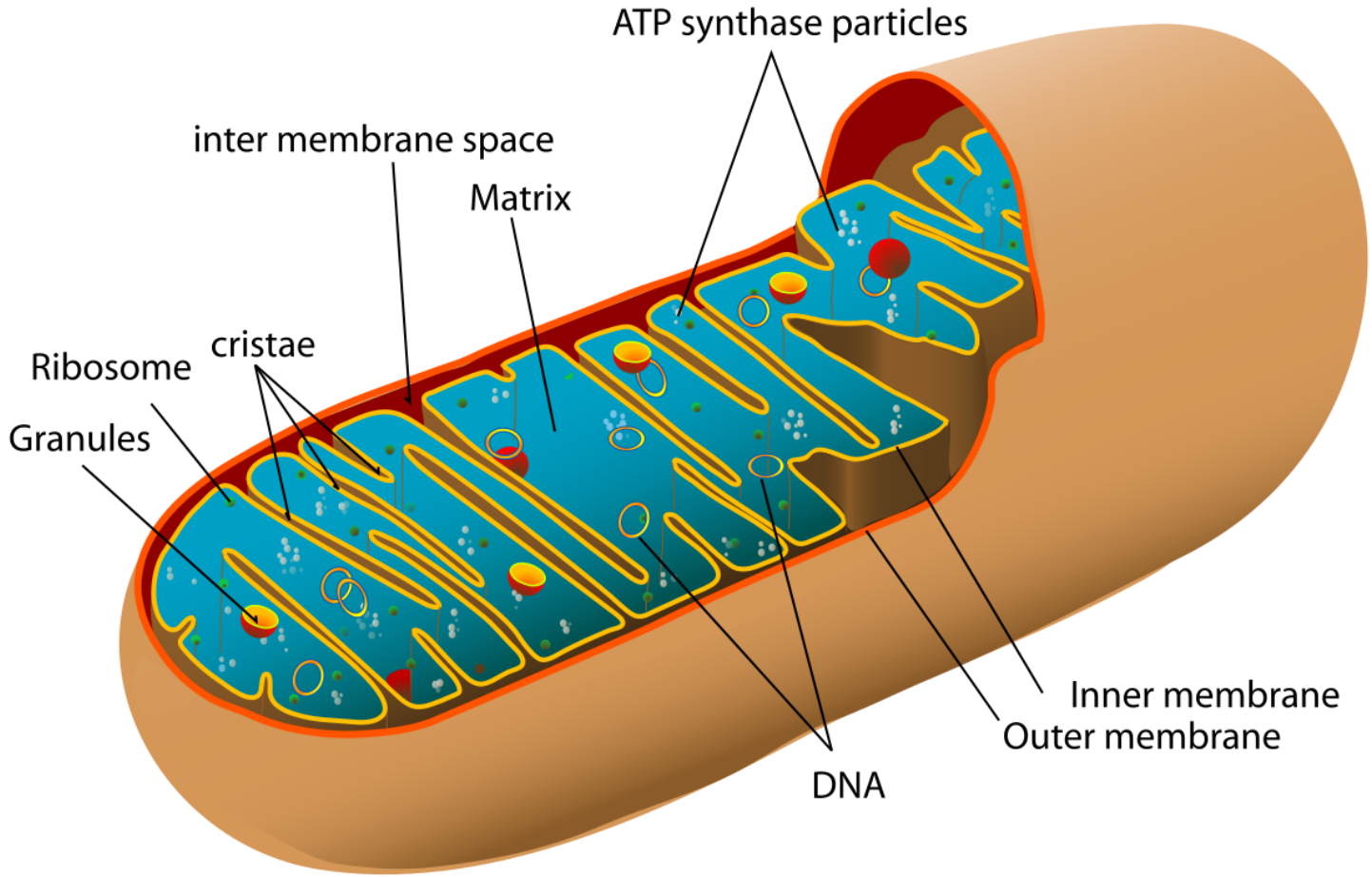
09/07/2025

Learning objectives

- To understand dynamic nuclear polarization and sodium magnetic resonance imaging, and their potential uses

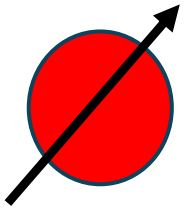
- To appreciate the challenges and opportunities involved in metabolic MRI

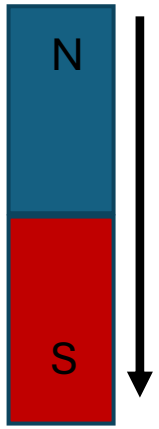

ATP synthase particles
inter membrane space
Matrix
cristae
Ribosome
Granules
Inner membrane
Outer membrane
DNA

MRI signal

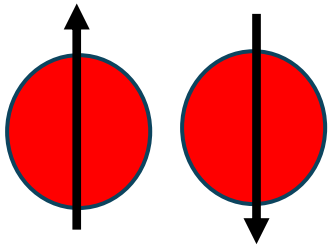
Nuclear Magnetic Resonance (NMR) is a physics ‘phenomenon’.

Proton





Protons

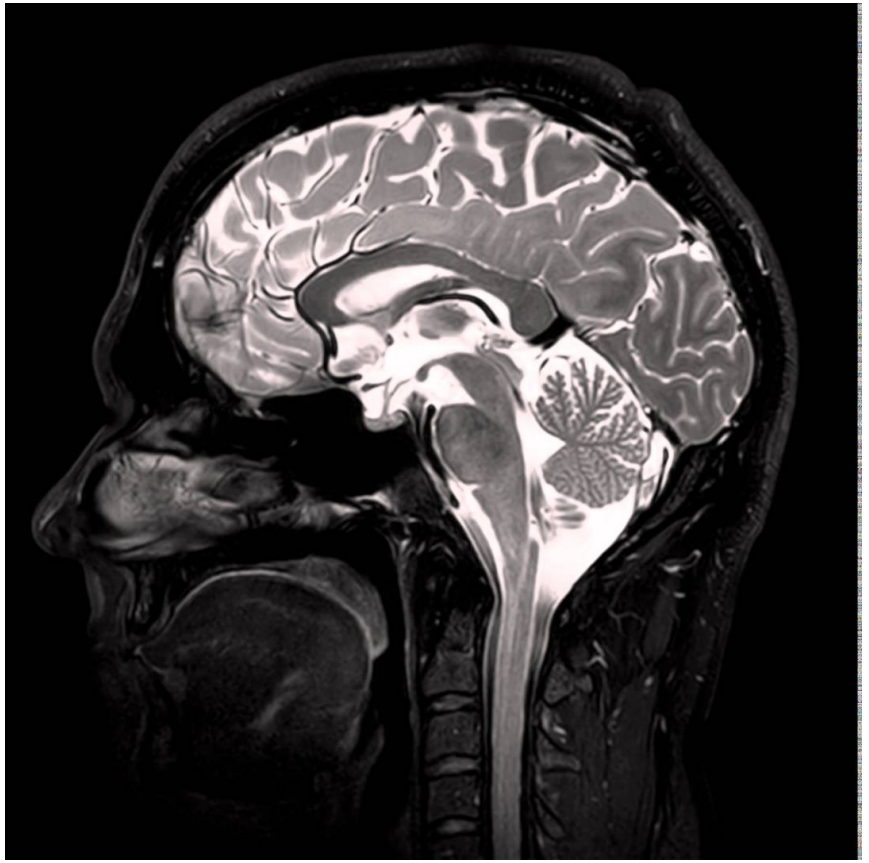


Slightly more pointing with the field (1ppm per Tesla)

$$\frac{N_+}{N_-} = \exp(-\frac{\hbar\gamma B_0}{kT})$$

The excess pointing with the field give us our signal in MRI

Conventional MRI

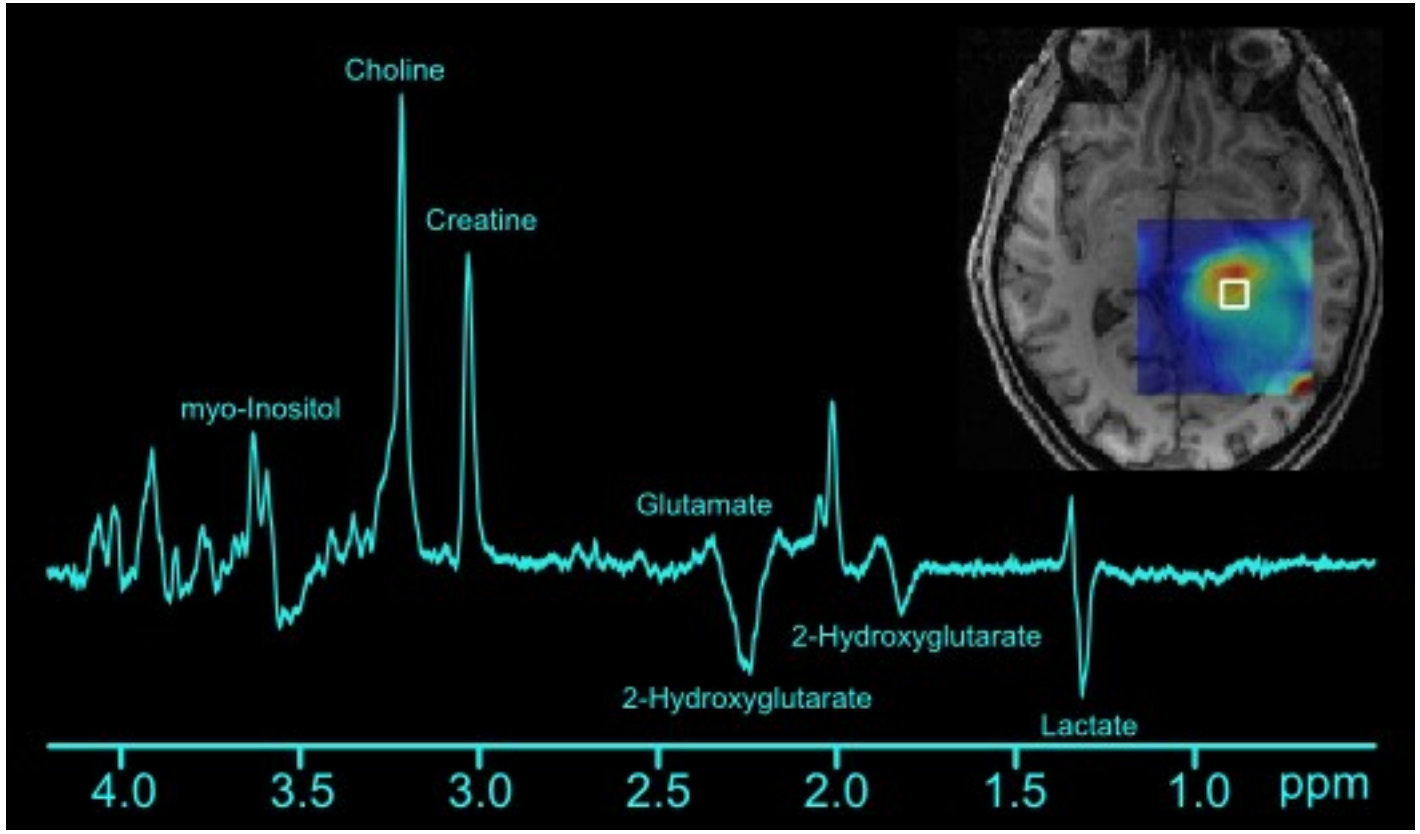


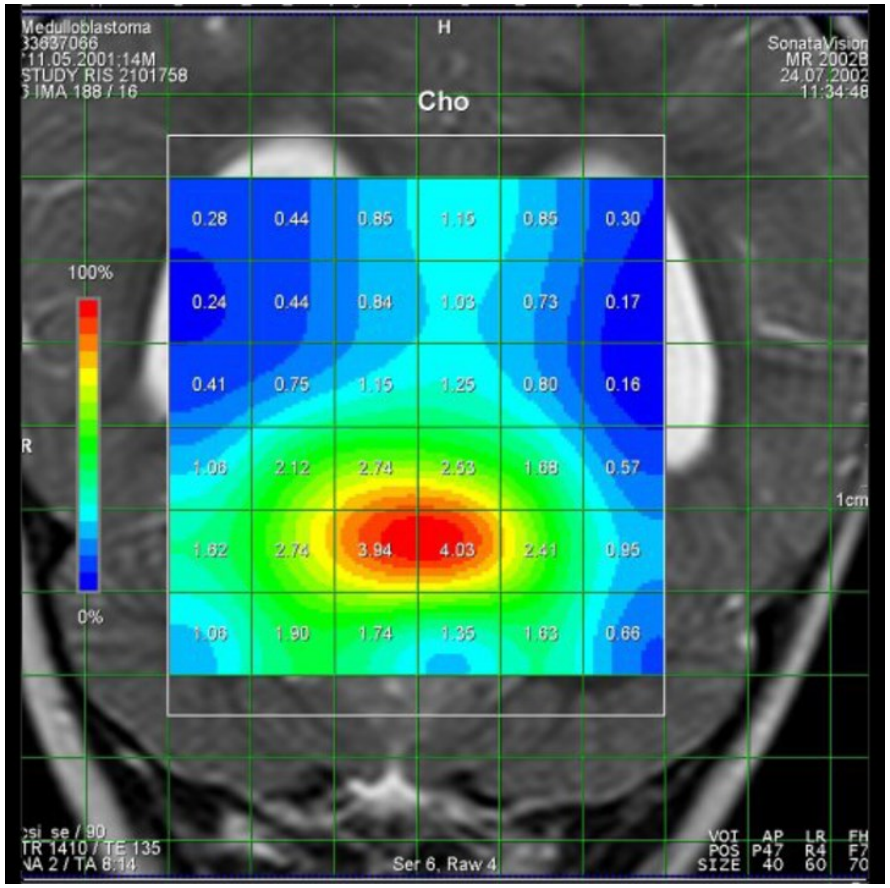
High resolution MRI (11.7T)

Metabolic MRI

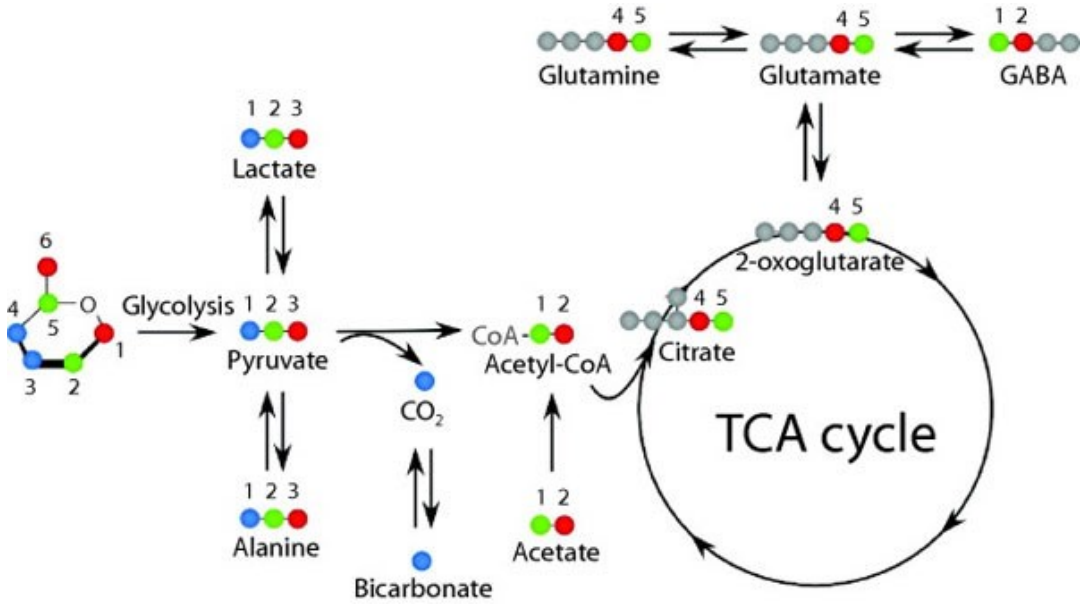
- ^{1}H Magnetic Resonance Spectroscopy
- Signal is based on static pools of ^{1}H labelled metabolites
- Signal <<< less than water
- Requirements to suppress background signals from fat/water

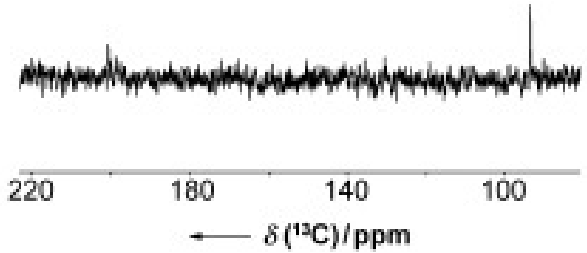
^{1}H MRS


Choline
Creatine
myo-Inositol
Glutamate
2-Hydroxyglutarate
2-Hydroxyglutarate
Lactate
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm


Medulloblastoma
H
Cho
SonataVision
MR 2002B
0.28 0.44 0.85 1.15 0.85 0.30
0.24 0.44 0.84 1.03 0.73 0.17
0.41 0.75 1.15 1.25 0.80 0.16
1.08 2.12 2.74 2.53 1.68 0.57
1.62 2.74 3.94 4.03 2.41 0.95
1.08 1.90 1.74 1.35 1.63 0.66
100%
0%
1cm
Ser 6, Raw 4

Exogeneous tracer MRI

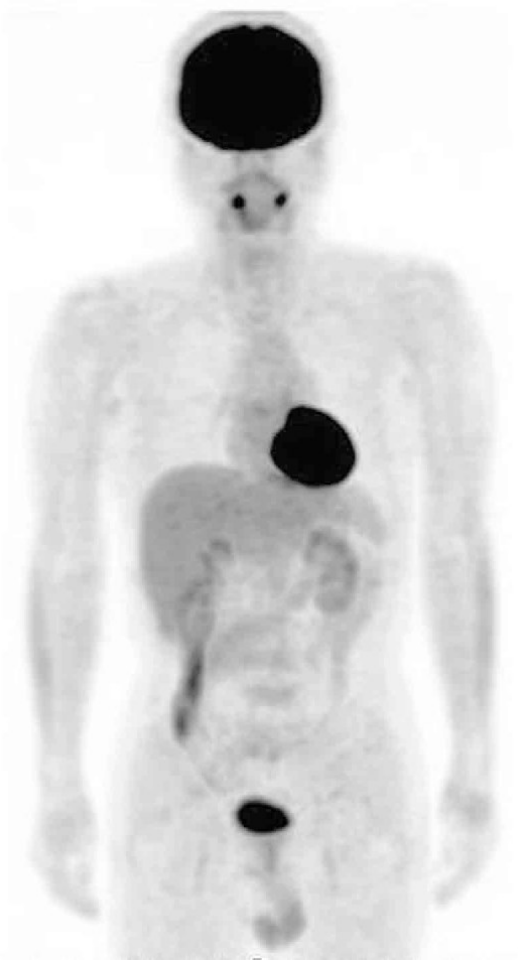


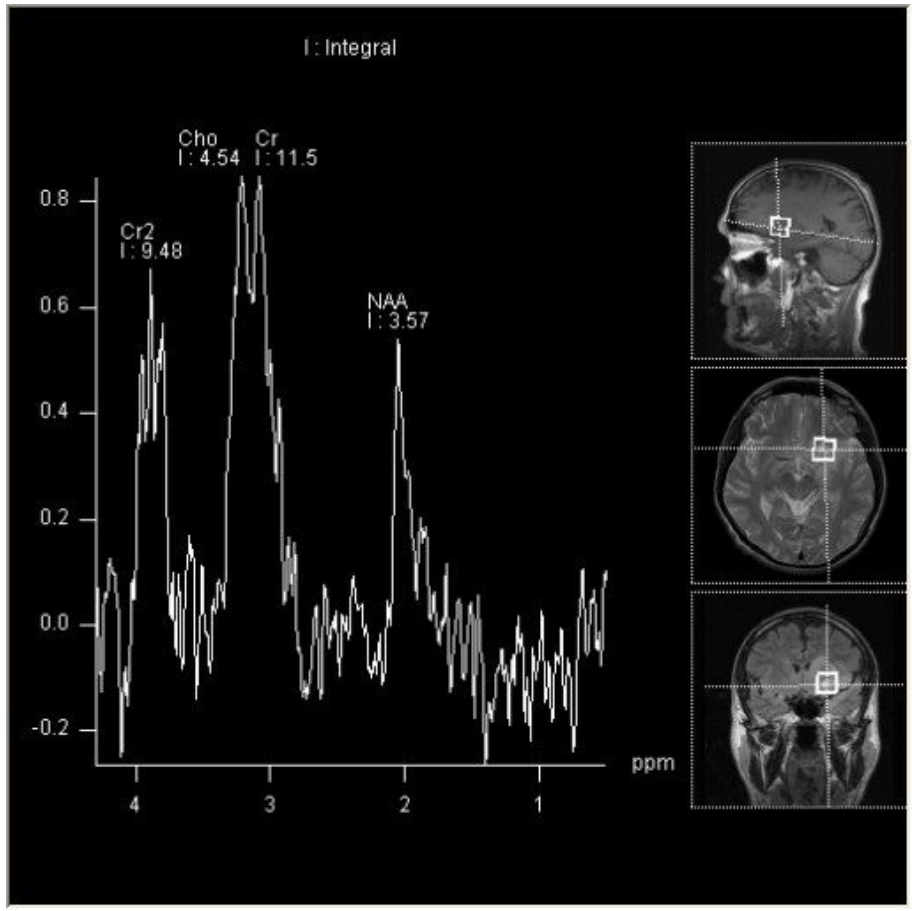


Downsides

Low SNR
Expensive
Time consuming
Low spatial resolution

Imaging cerebral metabolism





Low contrast + metabolic information

Low SNR + spatial coverage

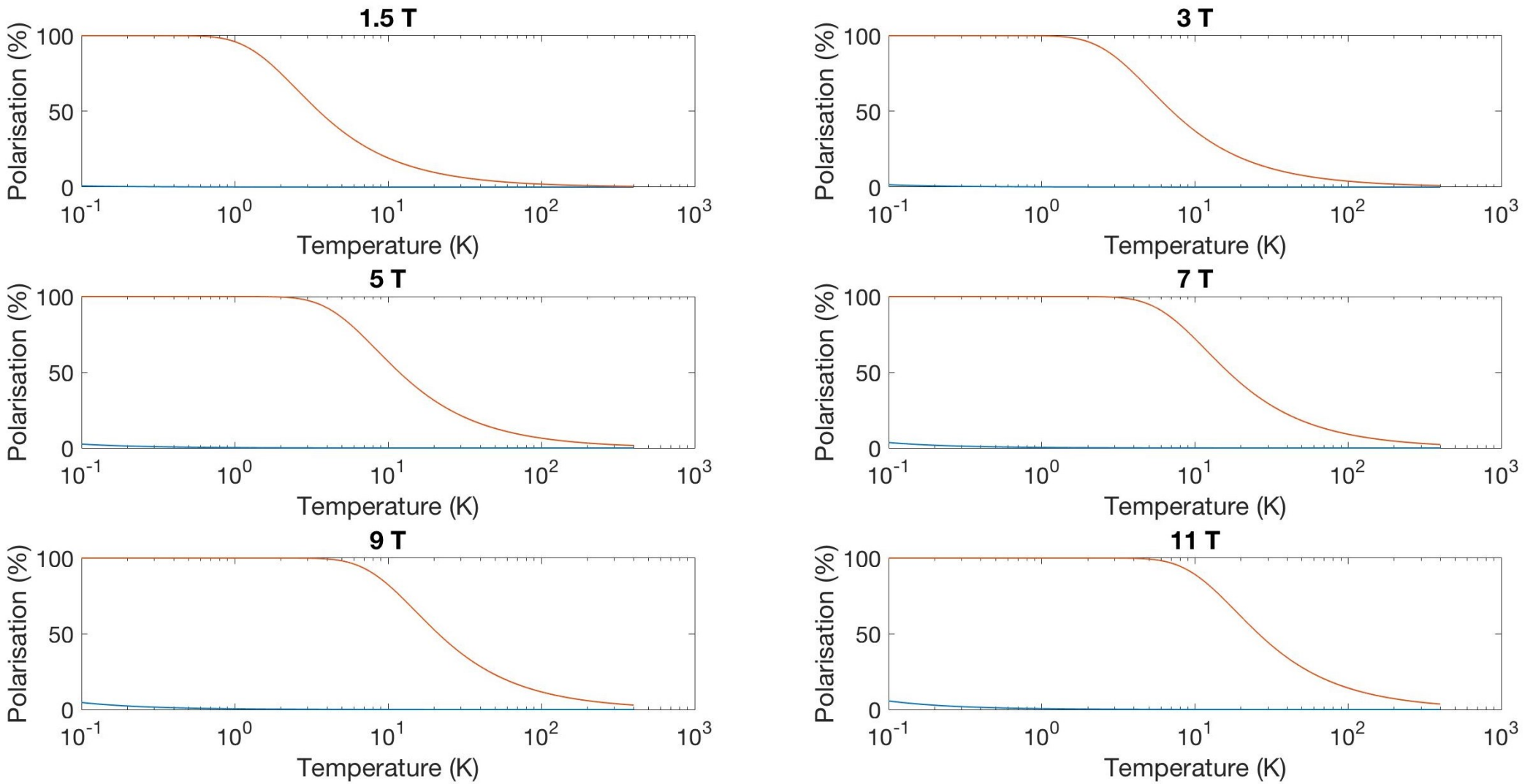
Hyperpolarisation

Remember.... Signal in MRI is proportional to:

Concentration of NMR active nucleus, gyromagnetic ratio, field strength, sample temperature

$$\frac{N_+}{N_-} = \exp(-\frac{\hbar\gamma B_0}{kT})$$

Carbon-13 is 1% natural abundance, so it is very difficult to detect!

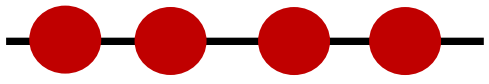

1.5 T
3 T
5 T
7 T
9 T
11 T
Polarisation (%)
Temperature (K)
^{13}C
Electron

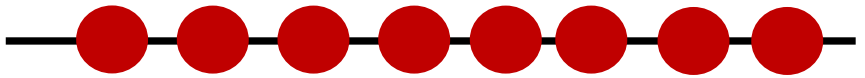
Hyperpolarisation by DNP

$$\frac{N_+}{N_-} = \exp(-\frac{\hbar\gamma B_0}{kT})$$

How can we beat Boltzmann?

Electrons + microwaves

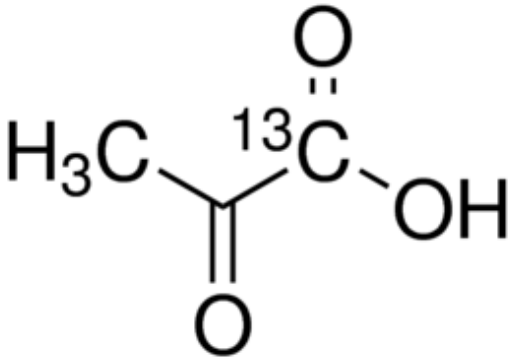




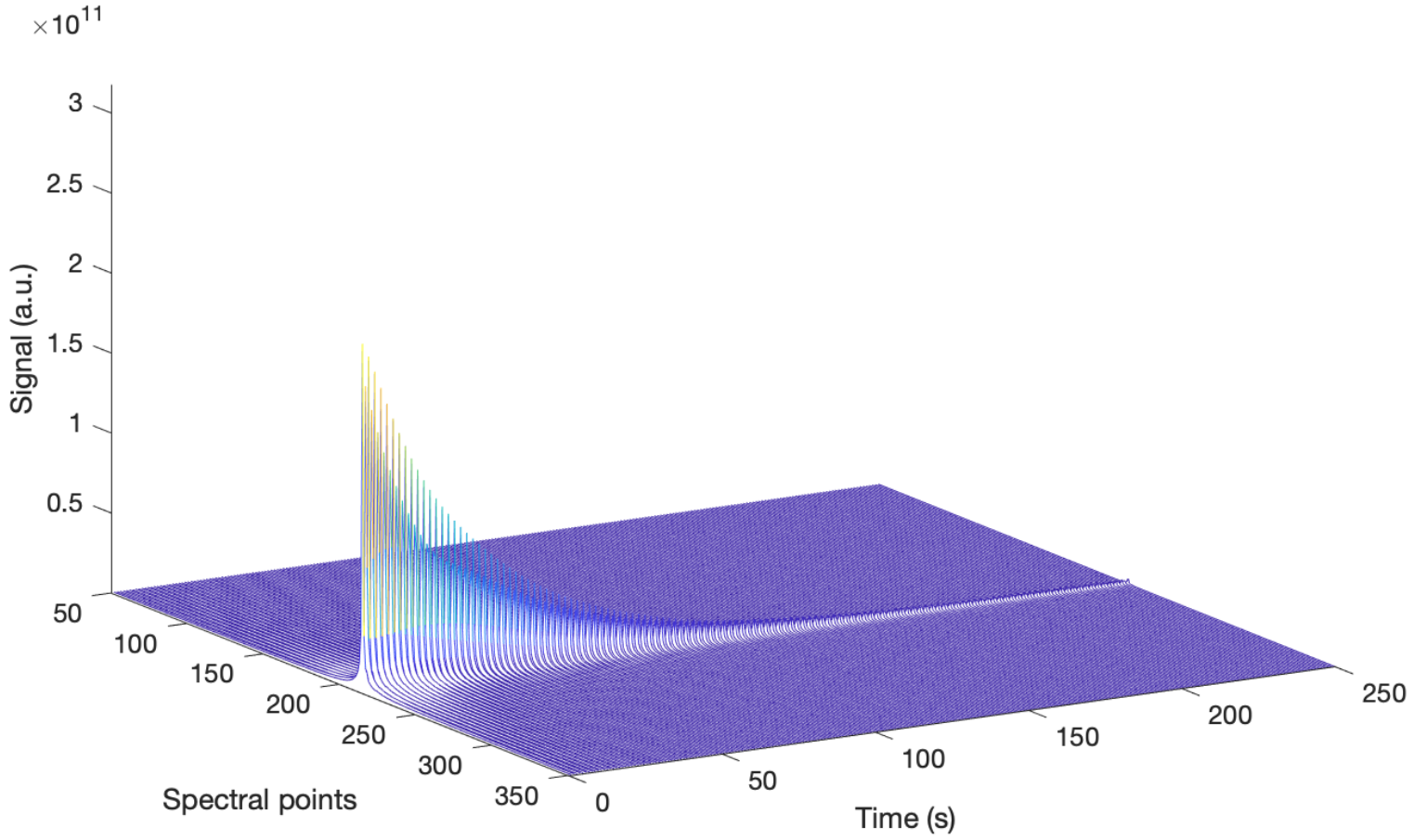
Huge, transient, increase in signal – decays with flip angle and T_1

Hyperpolarised ^{13}C MRI

Pyruvate + ^{13}C atom



But it decays…



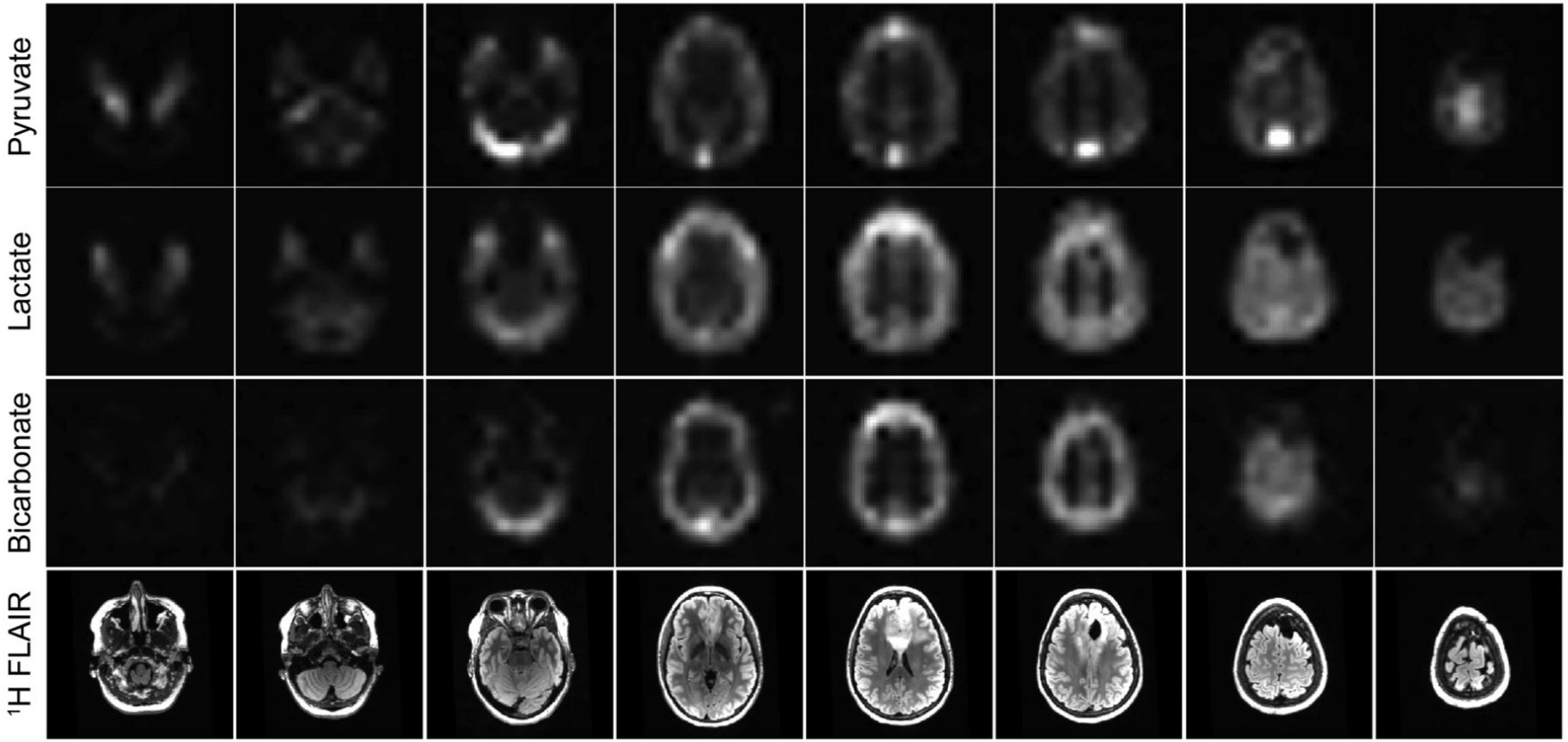
To consider when acquiring signal..

Spectral information **Spatial information** **Temporal information**

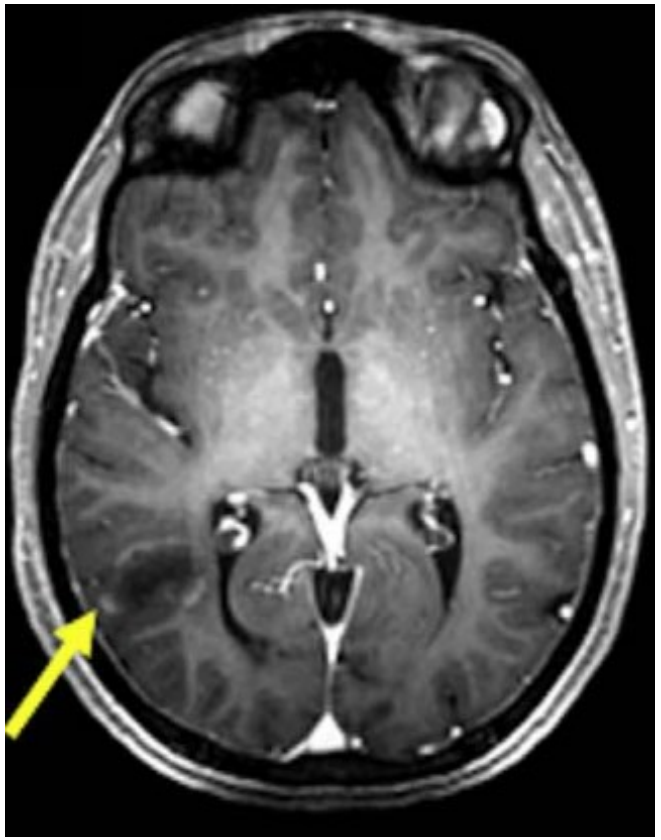
T_1/T_2^* of the isotopic label

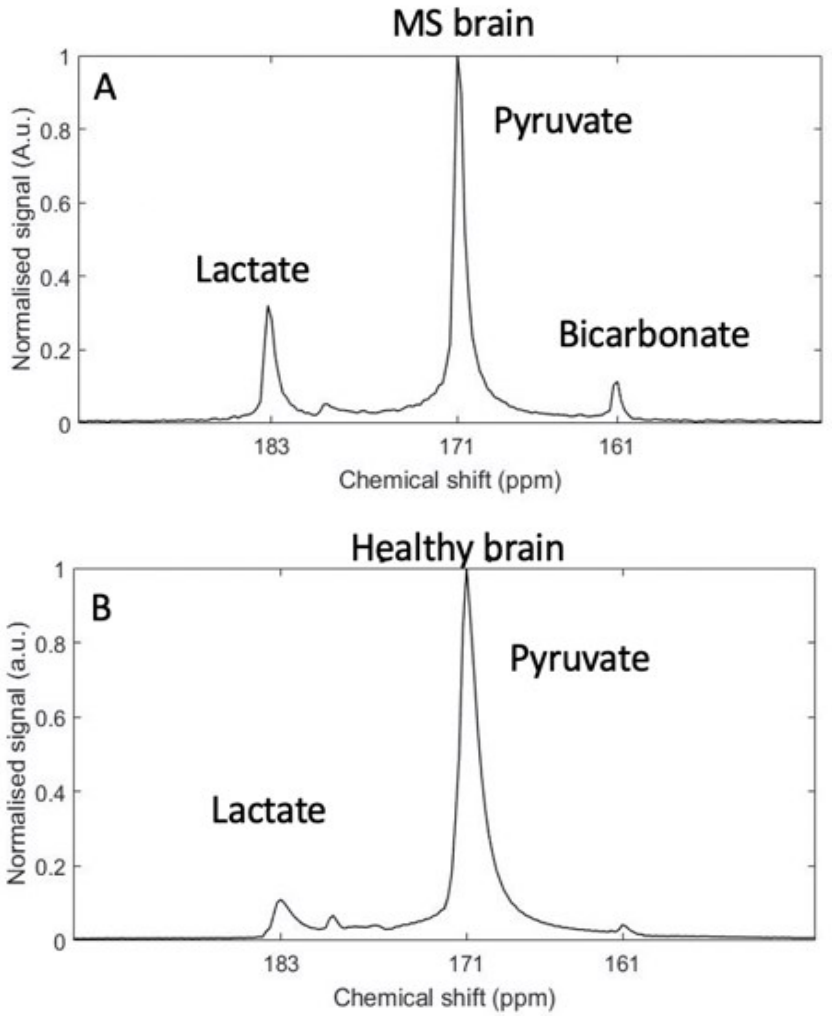
Concentration **Perfusion** **Reaction speed**

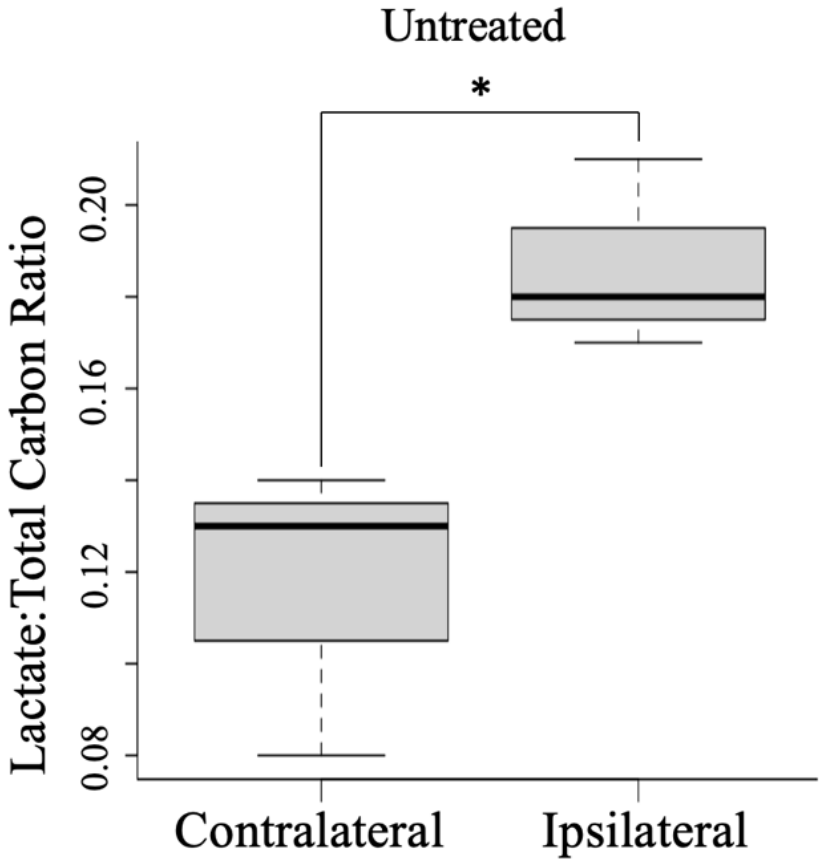
Example brain metabolic imaging



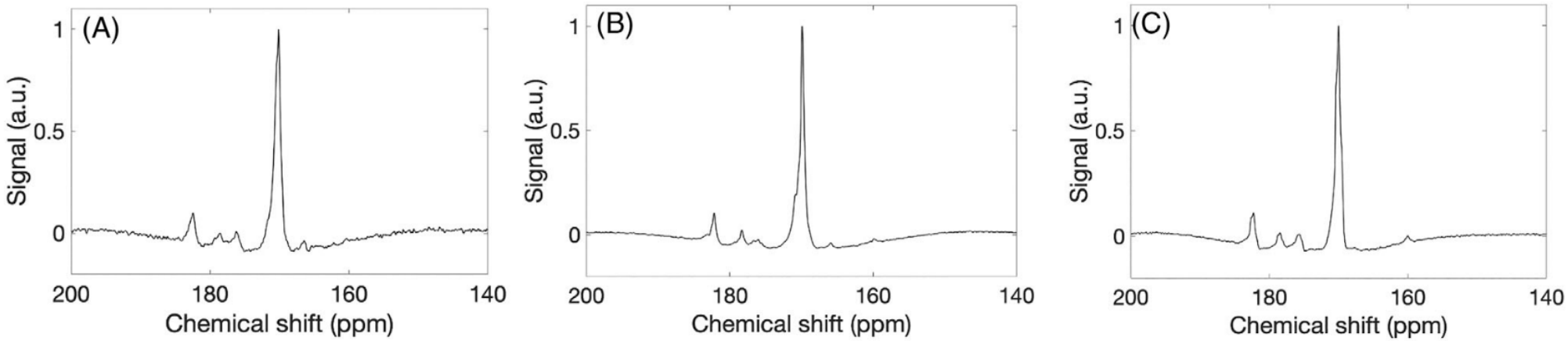
[1] Hyperpolarized 13 C MRI data acquisition and analysis in prostate and brain at University of California San Francisco, NMR in Biomed, 2020

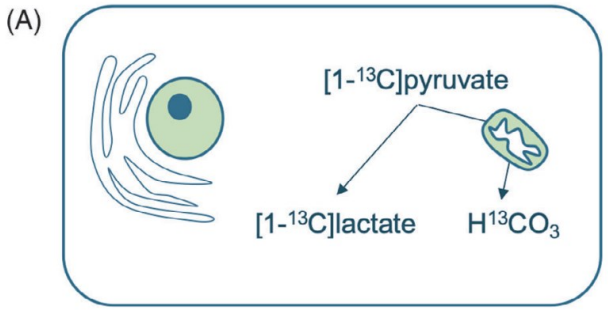


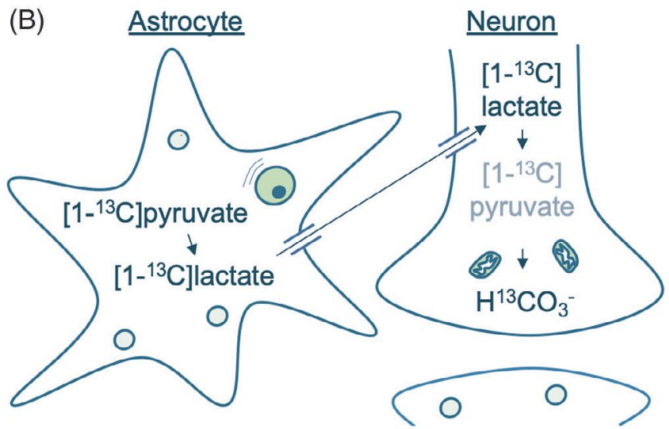

MS brain
A
Pyruvate
Lactate
Bicarbonate
Normalised signal (A.u.)
1
0.8
0.6
0.4
0.2
0
183
171
161
Chemical shift (ppm)
Healthy brain
B
Pyruvate
Lactate
Normalised signal (a.u.)
1
0.8
0.6
0.4
0.2
0
183
171
161
Chemical shift (ppm)

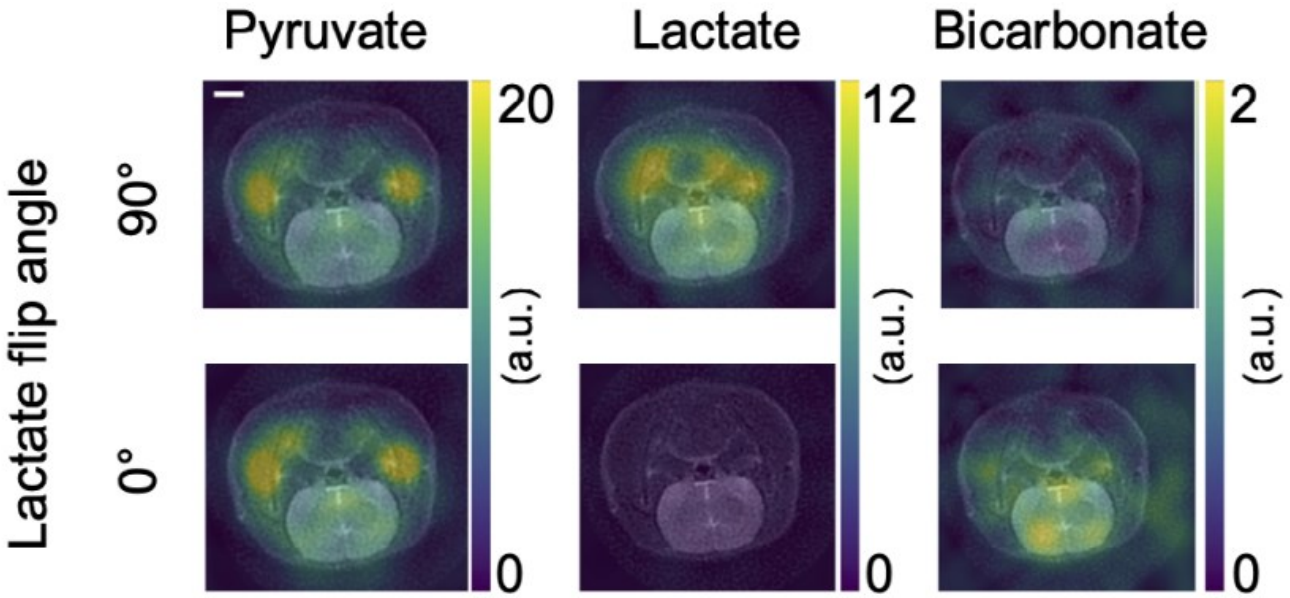

Untreated
*
Lactate:Total Carbon Ratio
0.20
0.16
0.12
0.08
Contralateral
Ipsilateral

There are some confounders...

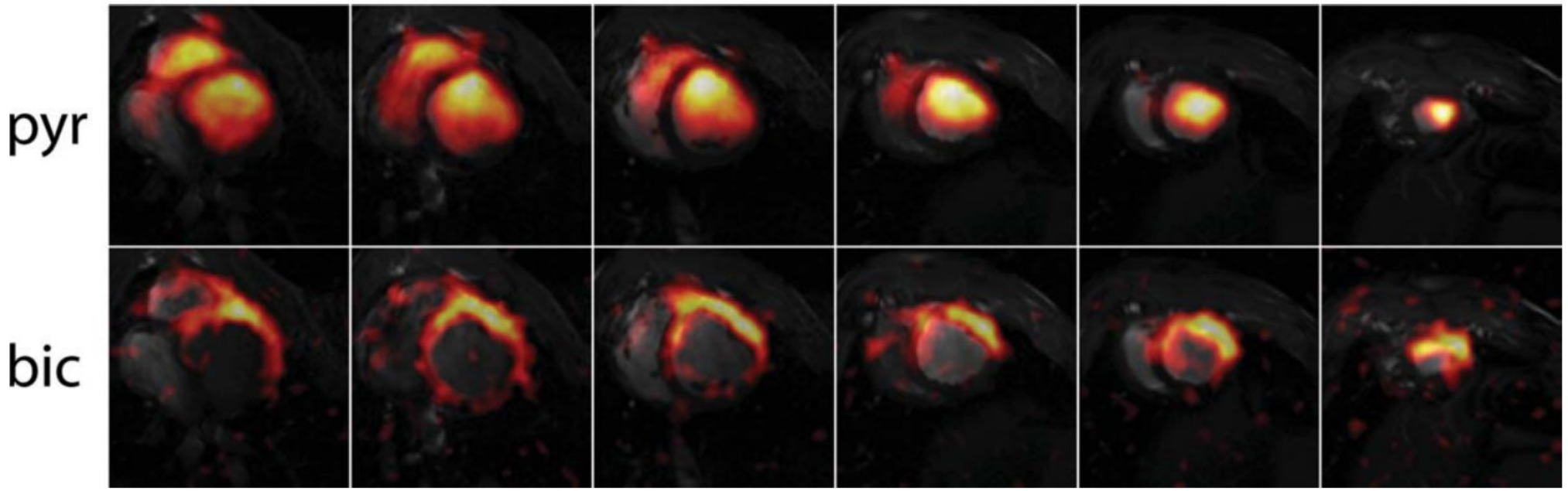








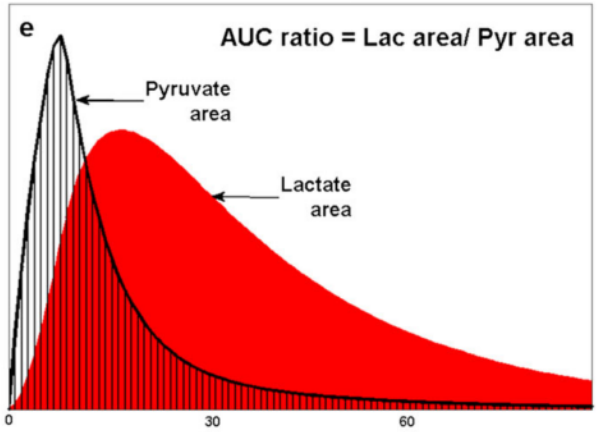
Example heart metabolic imaging



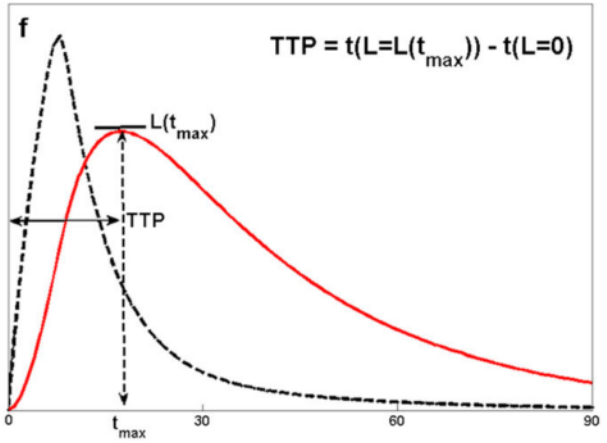
[1] Rapid multislice imaging of hyperpolarized 13C pyruvate and bicarbonate in the heart, MRM, 2010

Kinetic Mapping – Types of Model

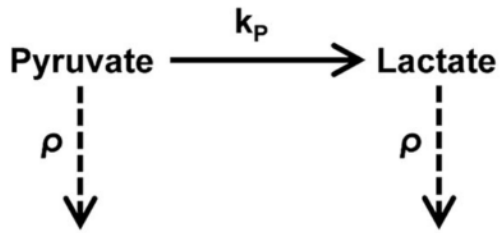
AUC



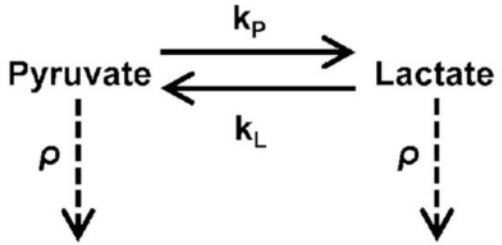
TTP



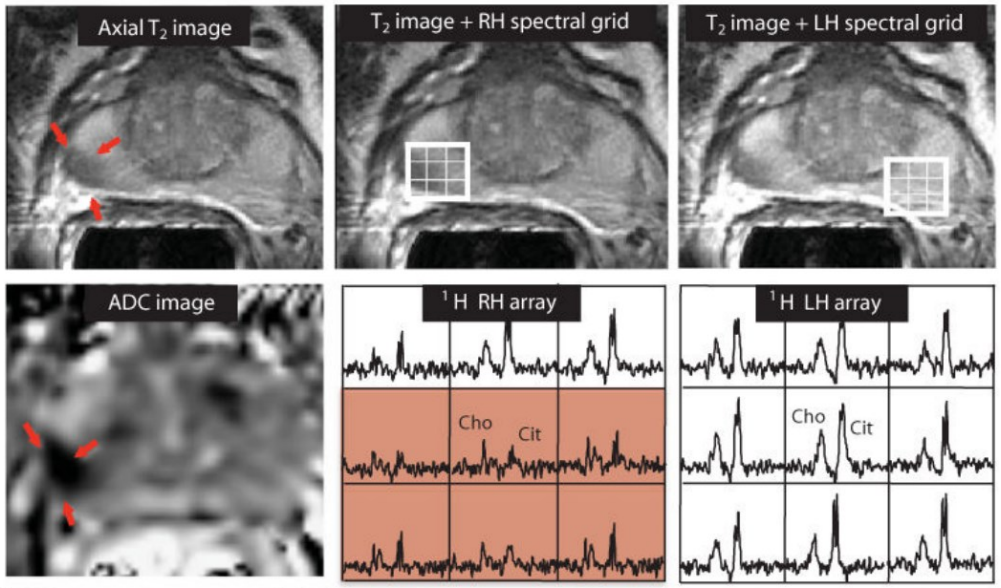
One-way



Two-way



The potential…

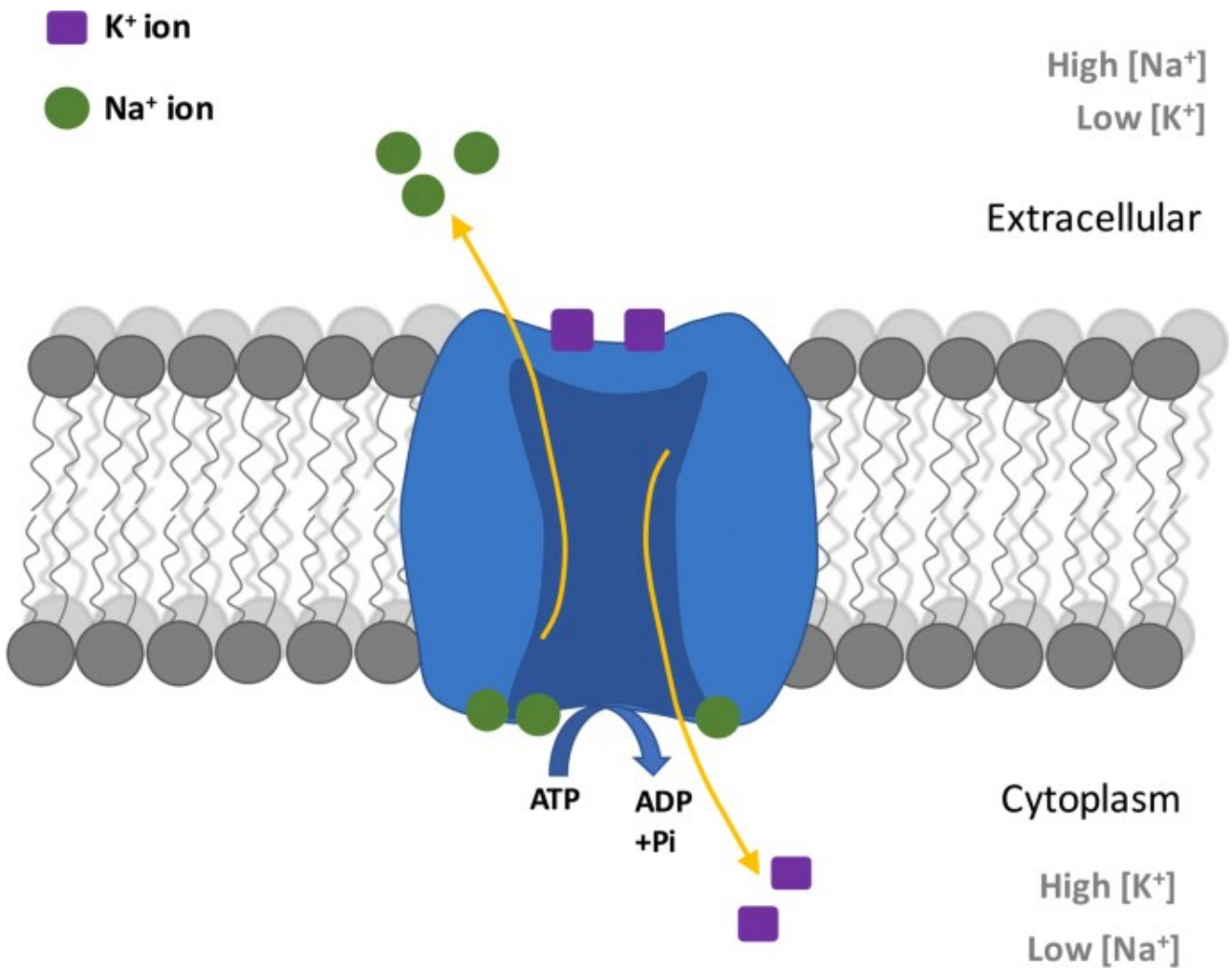


The future…

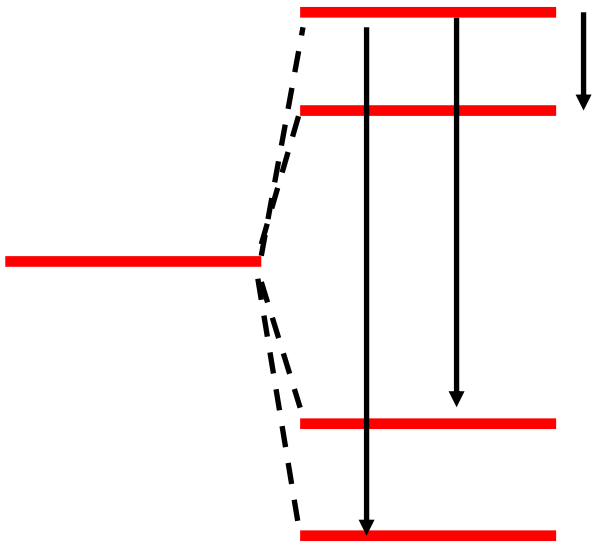
Tracer Name	Potential Use
[1-13C] Pyruvate	LDH/PDH Activity
[2-13C] Pyruvate	TCA Intermediates
[1-13C] lactate	Lactate metabolism
[2,4 – 13C] Fumarate	Cellular Necrosis
[1-13C] Bicarbonate	pH Mapping
[1-13C] Urea	Perfusion

Sodium – why should we be interested?

- Sodium is a key ion in multiple biological processes
- The homeostatic regulation of sodium (intra vs extracellular) is heavily dependent on ATP.
- An alteration in cellular energetics is a common feature of a number of pathologies – from cancer to neurology and beyond.


K+ ion
Na+ ion
High [Na+]
Low [K+]
Extracellular
ATP
ADP
+Pi
Cytoplasm
High [K+]
Low [Na+]

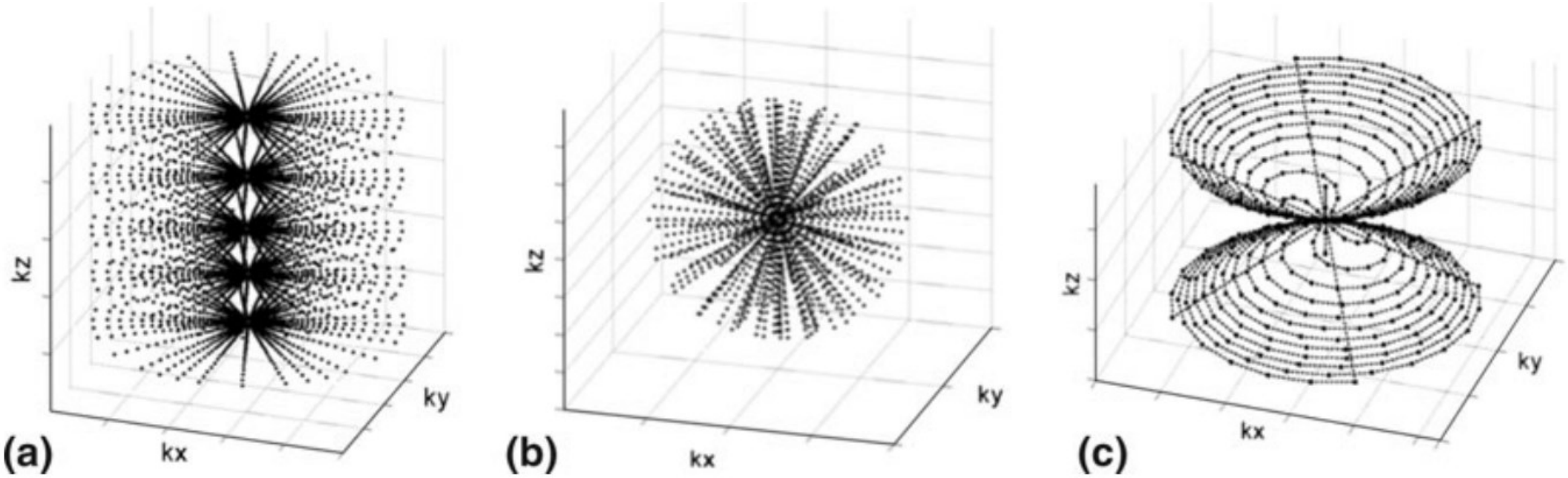
What if we have more than spin ½? The quadrupolar effect for sodium



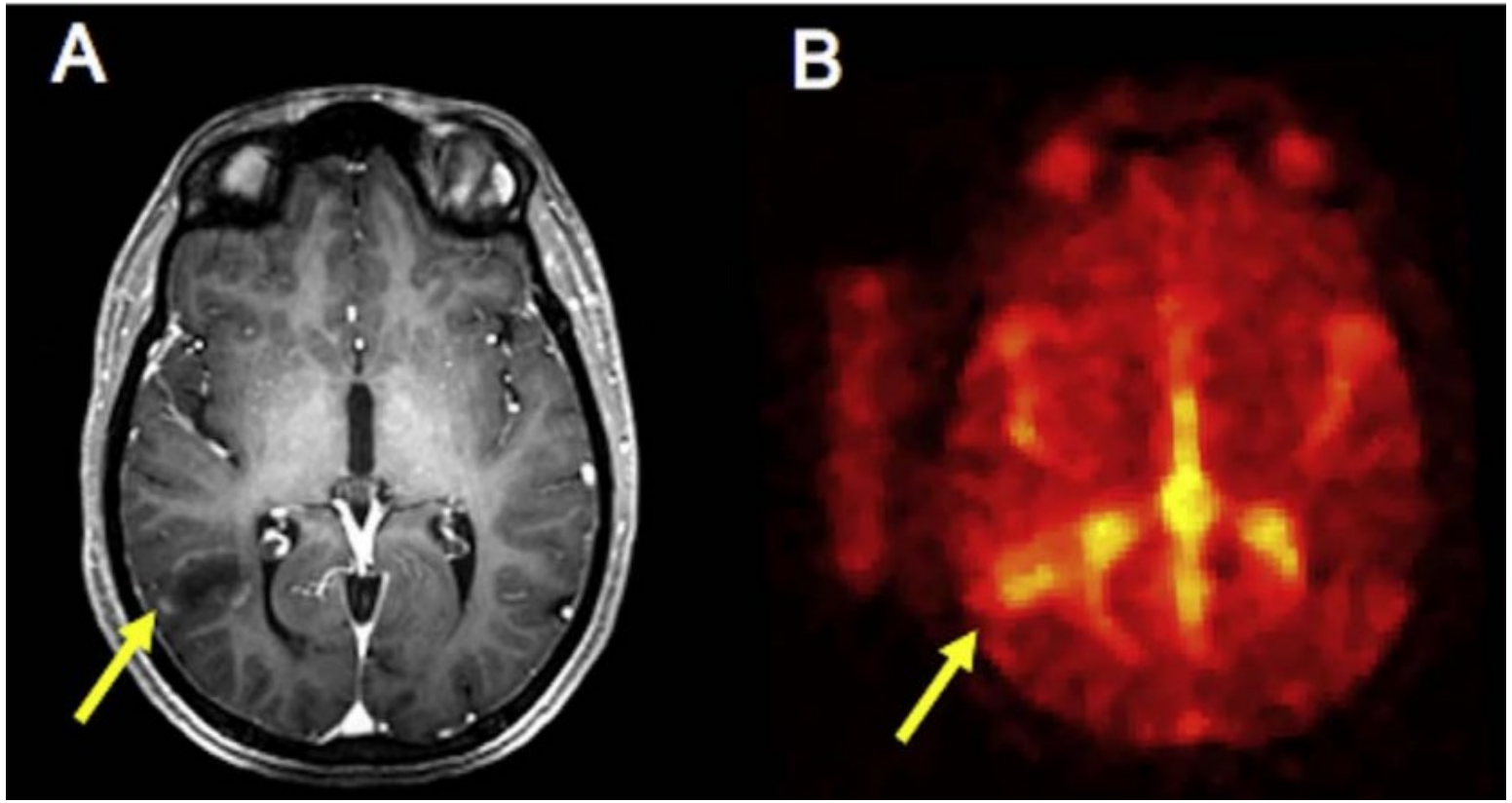
- Increase in energy states leads to a two-component state for T_2*
- One component is fast (~3ms) and the other slow (~20ms)
- This can be readily measured using multi-echo approaches fitting the following equation:

$$Aexp^{(-\frac{TE}{T2*,fast})} + Bexp^{(-\frac{TE}{T2*,slow})}$$

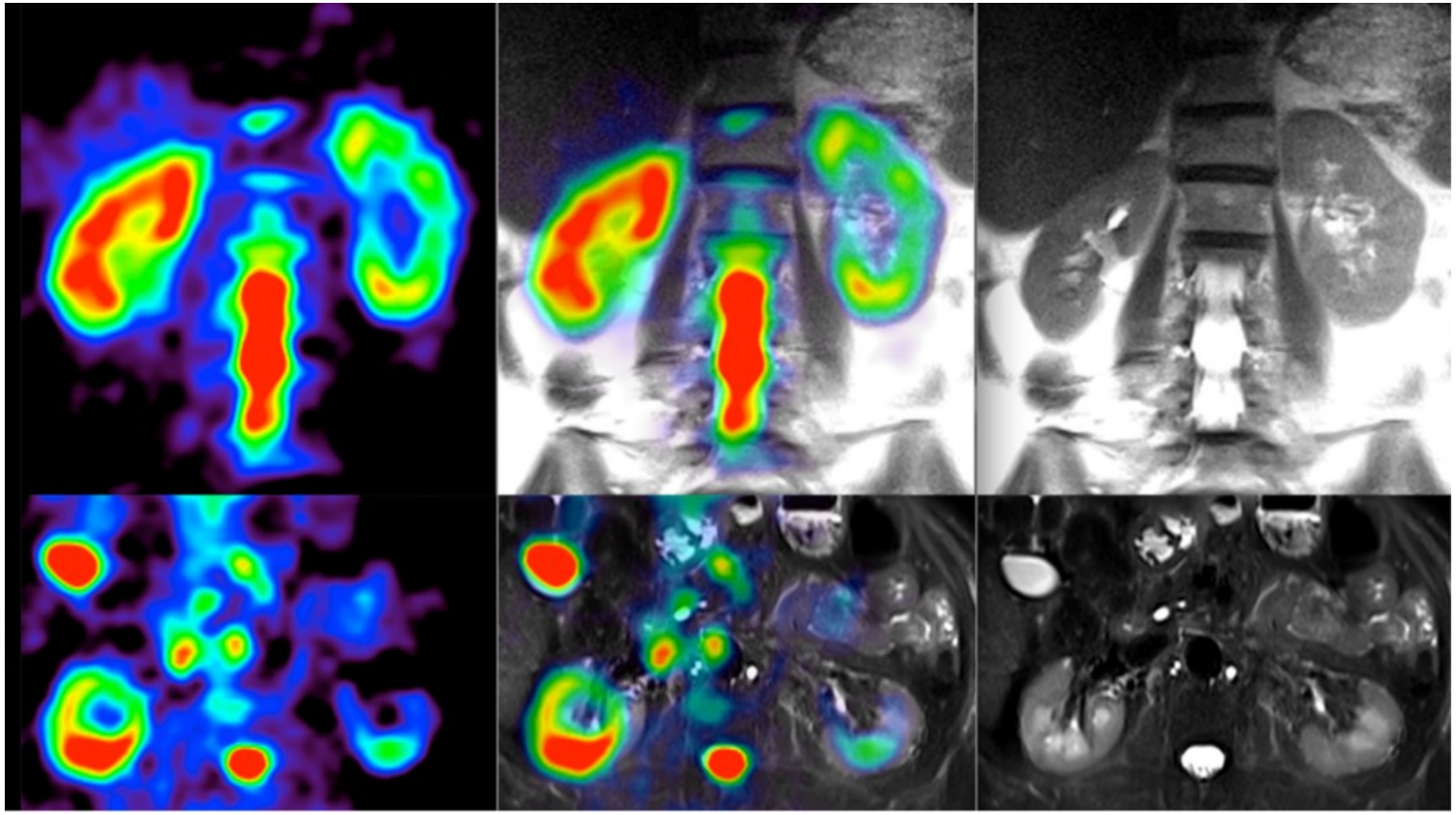
How can we travel faster around k-space?



Example total sodium imaging

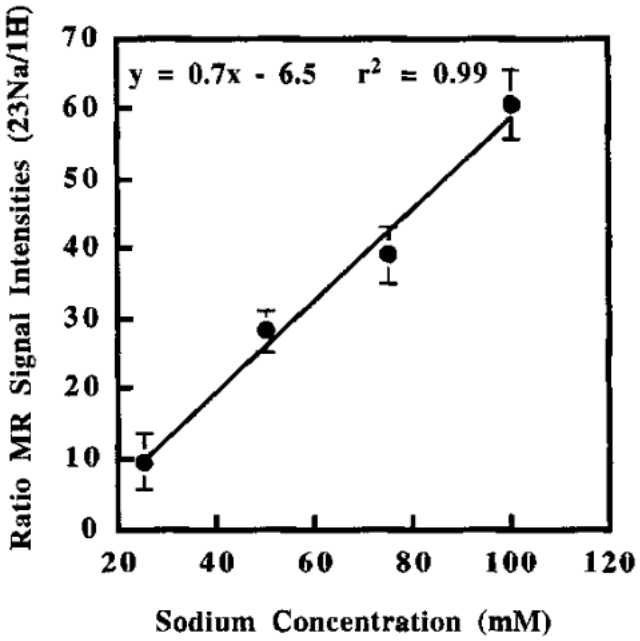


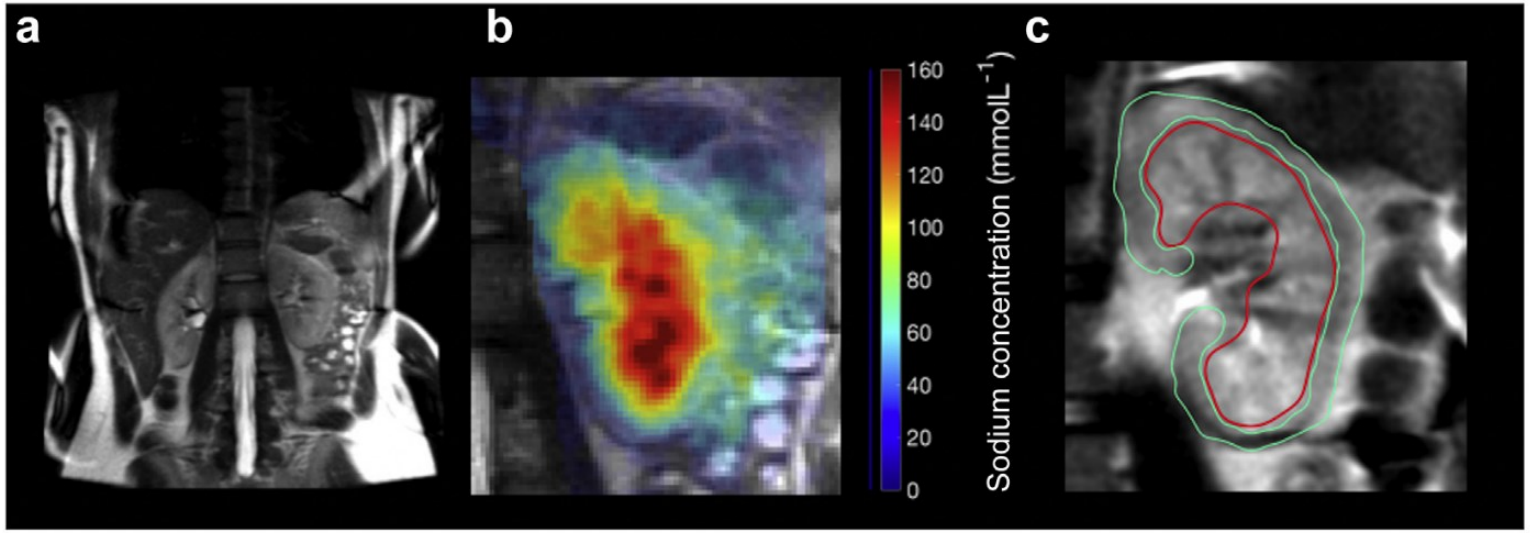
Example total sodium imaging

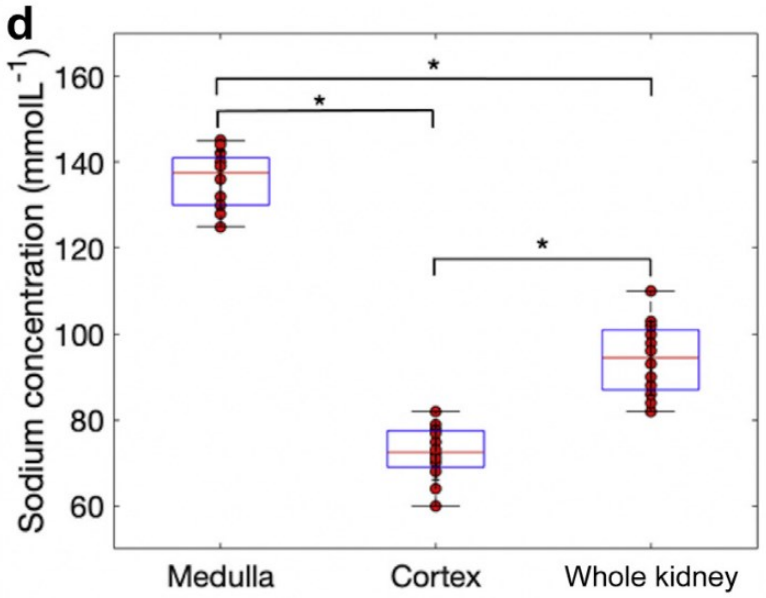


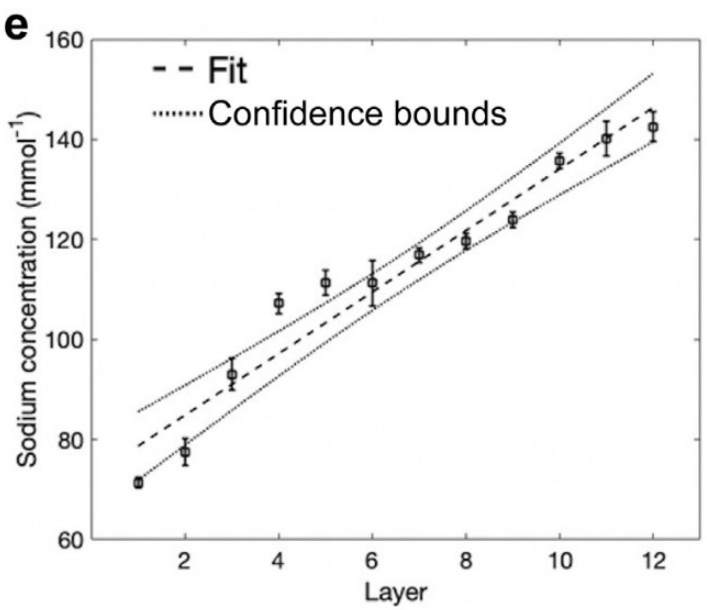
What are those tubes?

- MRI signal is inherently non-quantitative.
- Signal is proportional to T_2*, T_1, M_0, Temperature
- But what if we put calibration standards that have similar relaxation properties to tissue into the field of view?

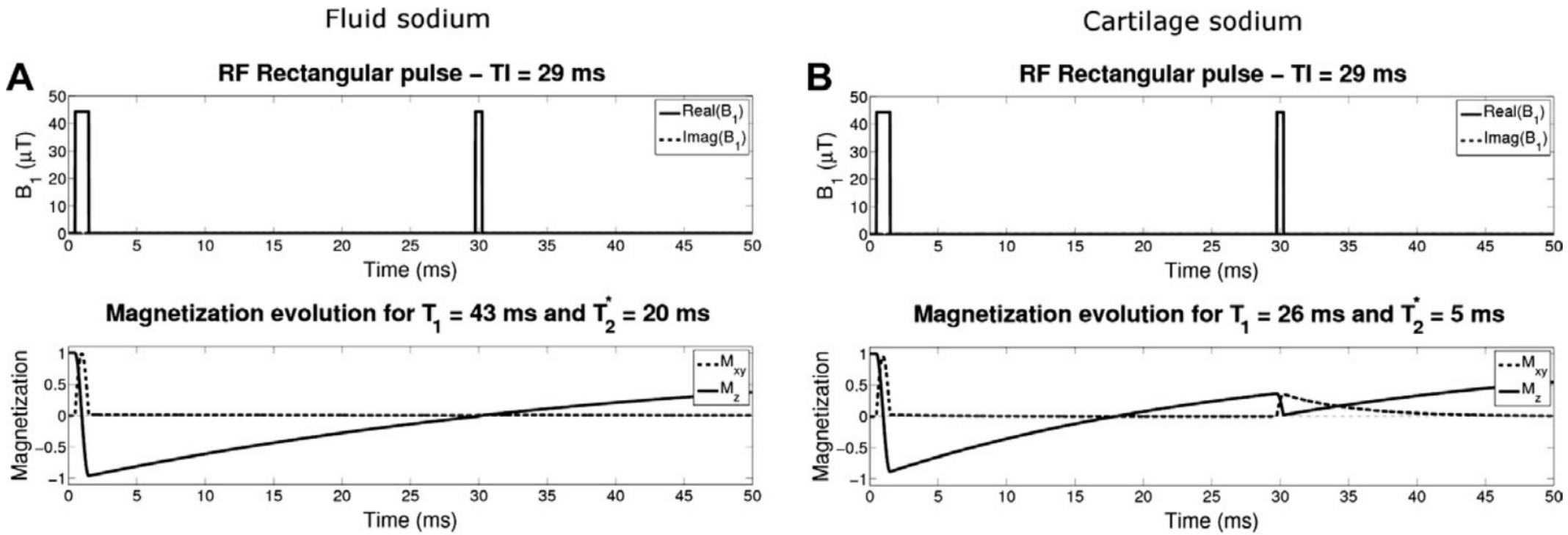


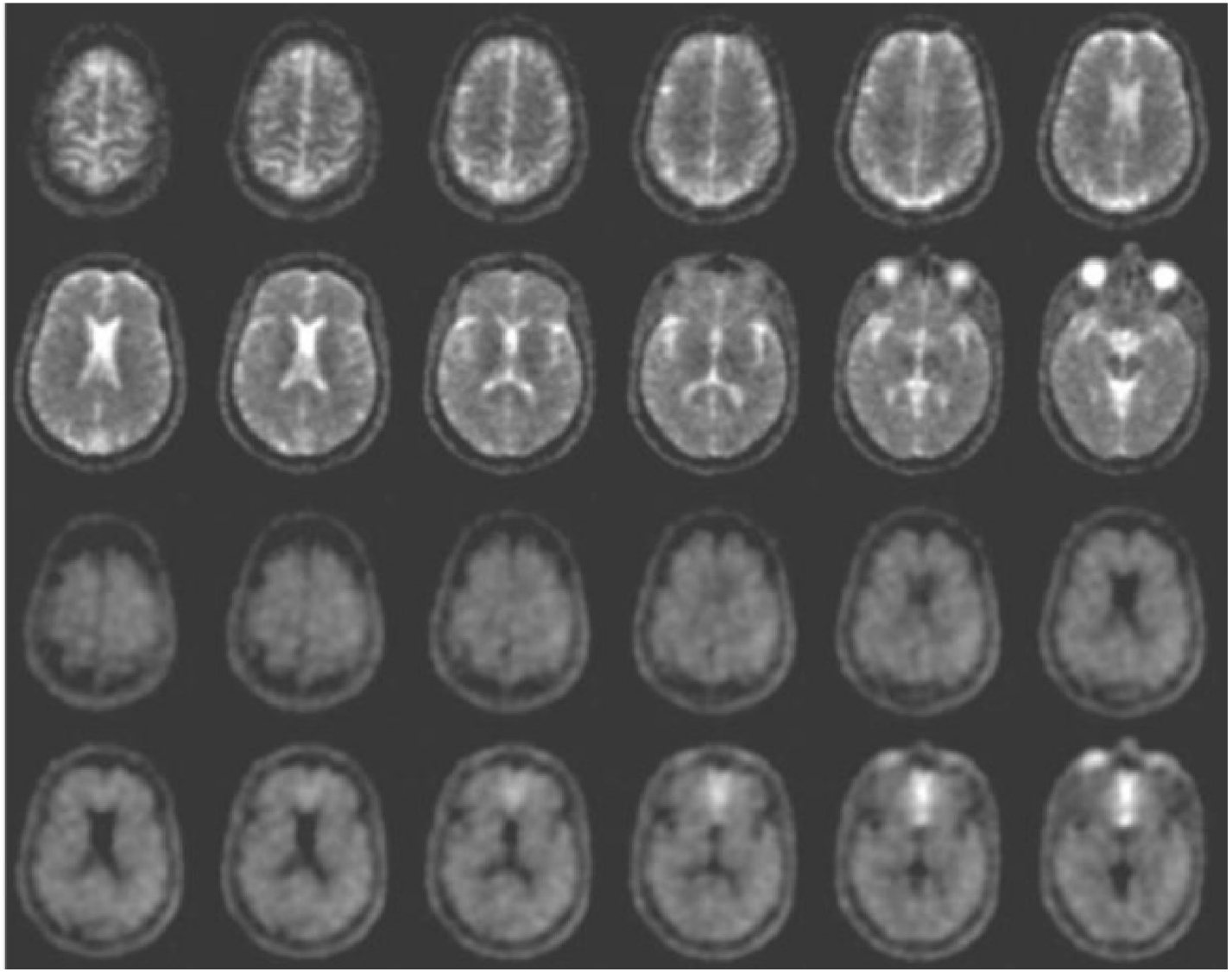

a
b
c
160
140
120
100
80
60
40
20
0
Sodium concentration (mmolL^{-1})


d
Sodium concentration (mmolL^{-1})
160
140
120
100
80
60
*
*
*
Medulla
Cortex
Whole kidney


e
Fit
Confidence bounds
Sodium concentration (mmol^{-1})
160
140
120
100
80
60
2
4
6
8
10
12
Layer

What if we want to estimate intracellular sodium?





Advanced MRI

Paediatric and Adult studies possible

Early therapeutic response

Measuring cellular health

Detecting chronic inflammatory responses

Providing novel imaging information for big data analysis

Summary

- Metabolic MRI is a powerful tool to explore beyond structural imaging
- There are challenges involved in implementation, acquisition, and reconstruction of metabolic data
- A combination of physics, radiology, and clinical expertise is required to ensure studies are well run