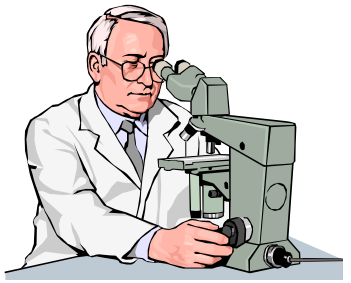


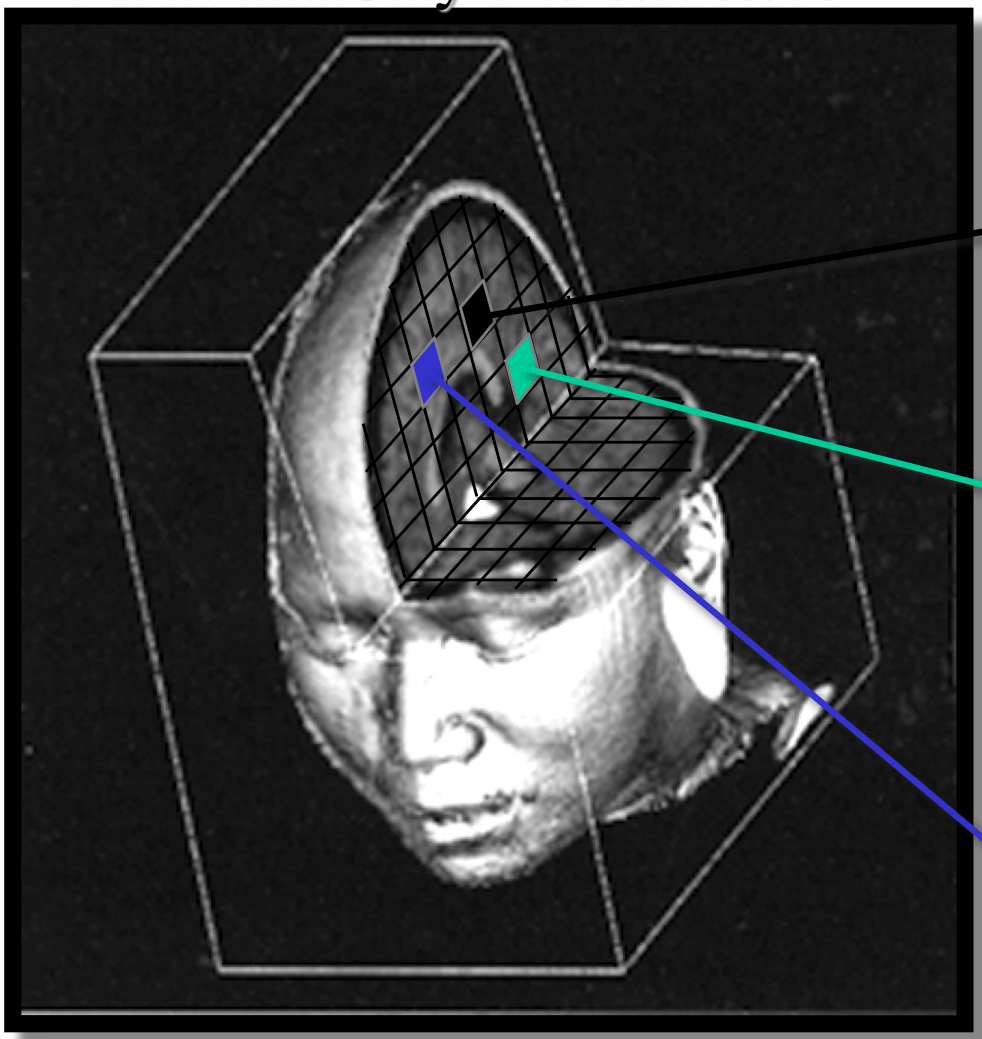
# Lecture #14
# In Vivo MRS-detectable Metabolites

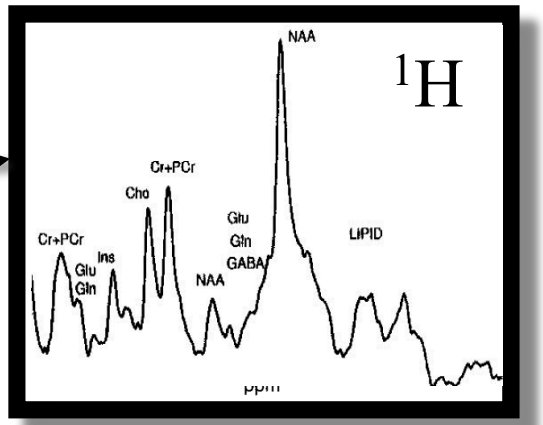
- Topics
  - $^{1}$H-MRS
  - $^{31}$P-MRS
  - $^{13}$C-MRS
  - Other nuclei
- Handouts and Reading assignments
  - de Graaf, Chapter 2.
  - de Graaf, Chapter 3, 158-171.

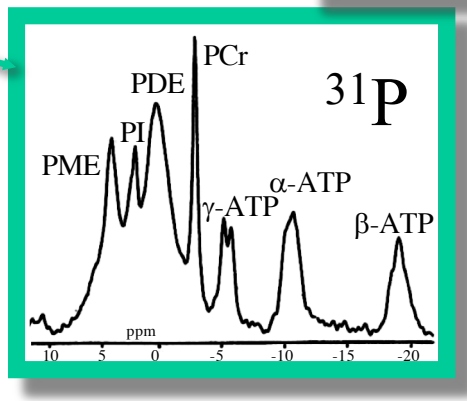
# Introduction

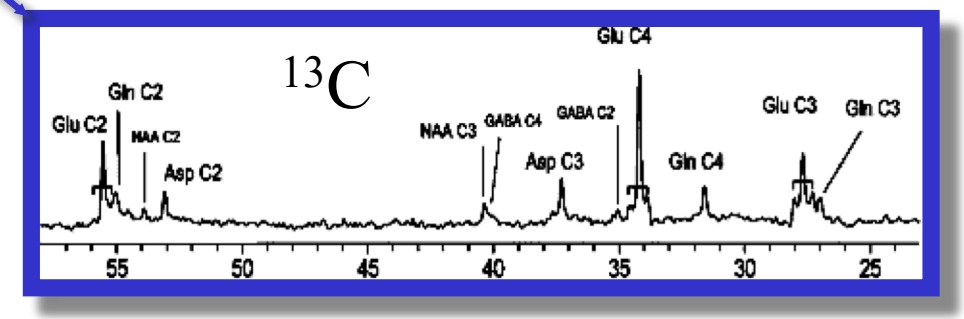
MRI: anatomy and structure

MRS: metabolism and function

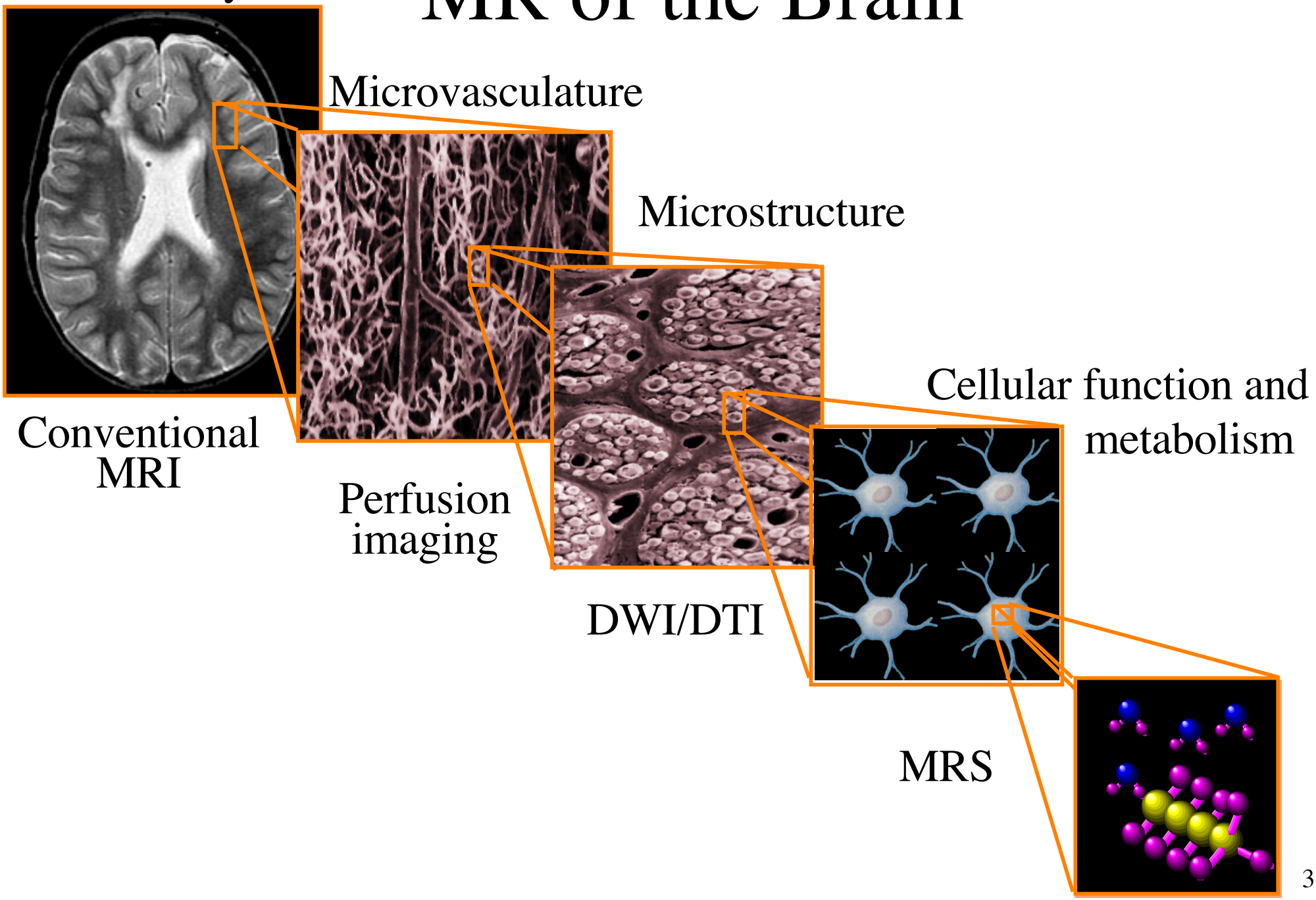




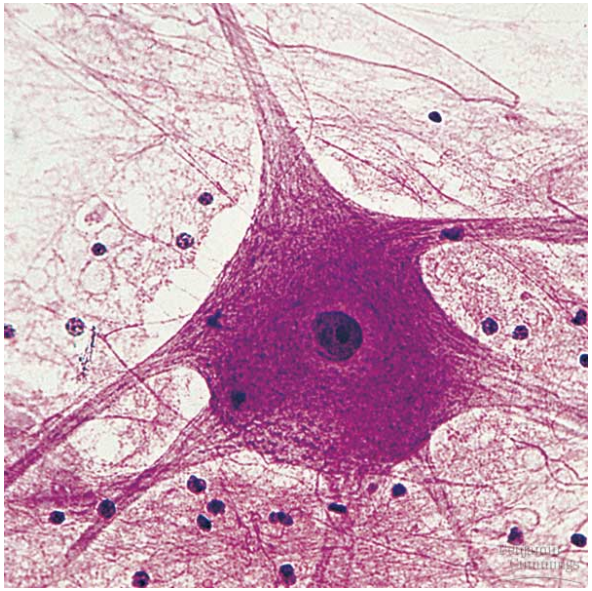



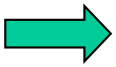
# MR of the Brain

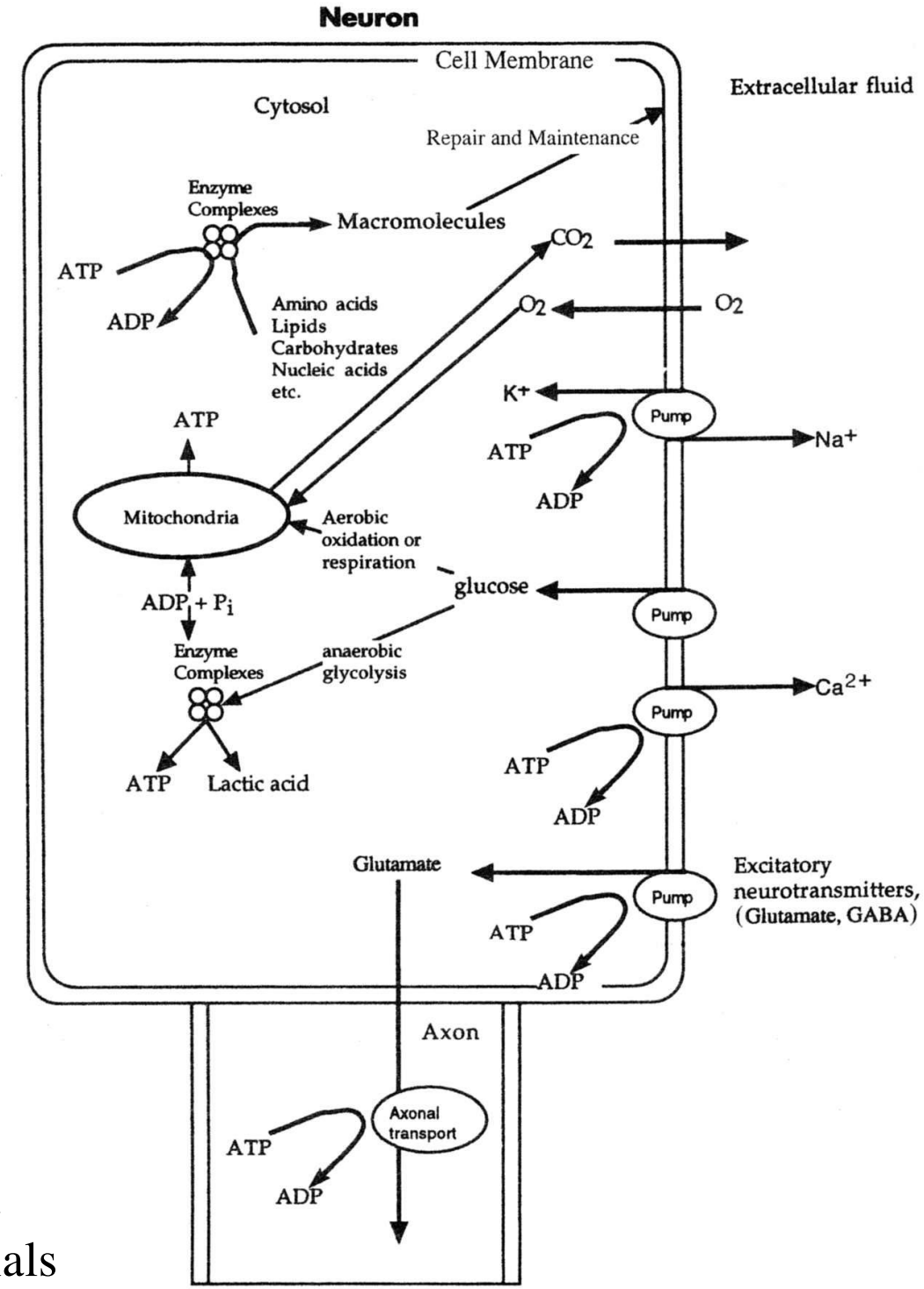


# Cells

Neuron



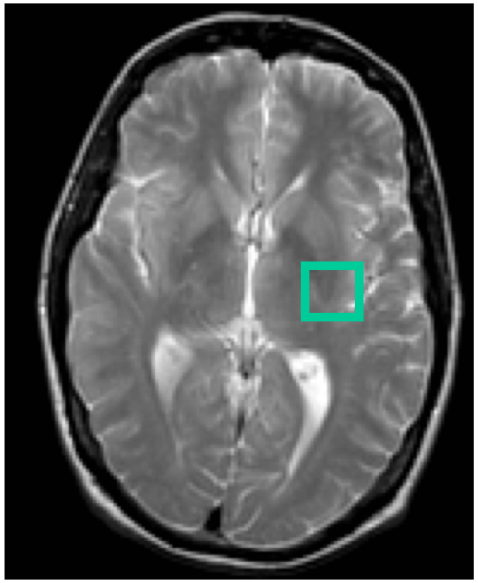


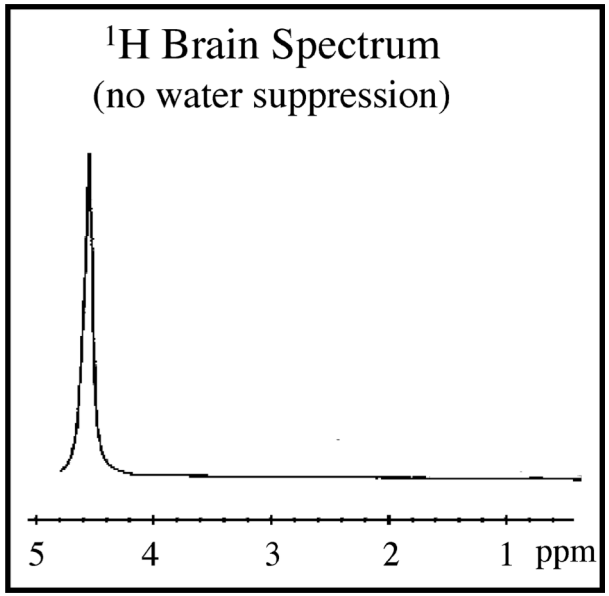


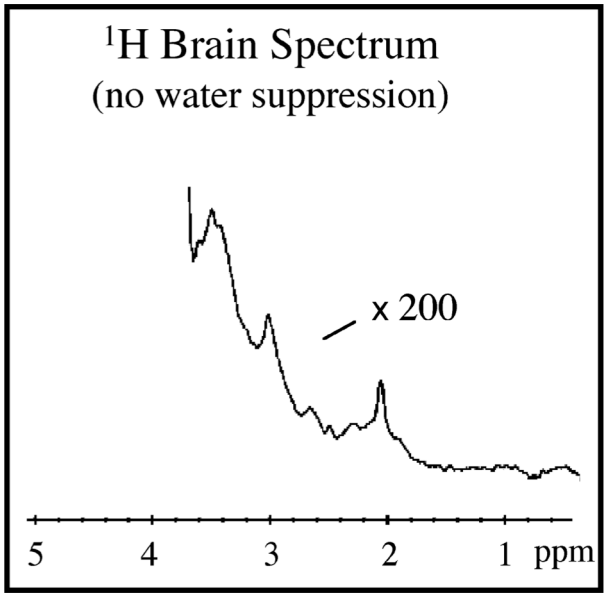

## General cellular functions

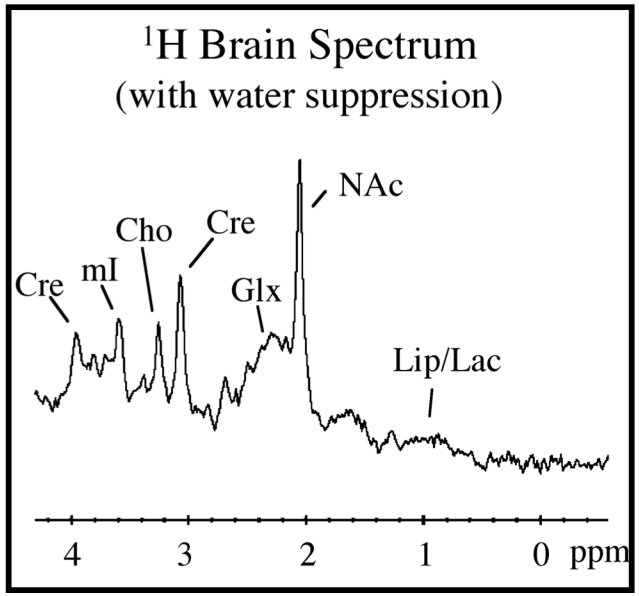
- Turn glucose into energy
- Maintain cellular integrity
  - Ionic balance
  - Osmotic balance
  - Membrane structure
- Perform cell specific functions, e.g. neurons send/receive electrical signals

# $^1$H Brain Spectroscopy





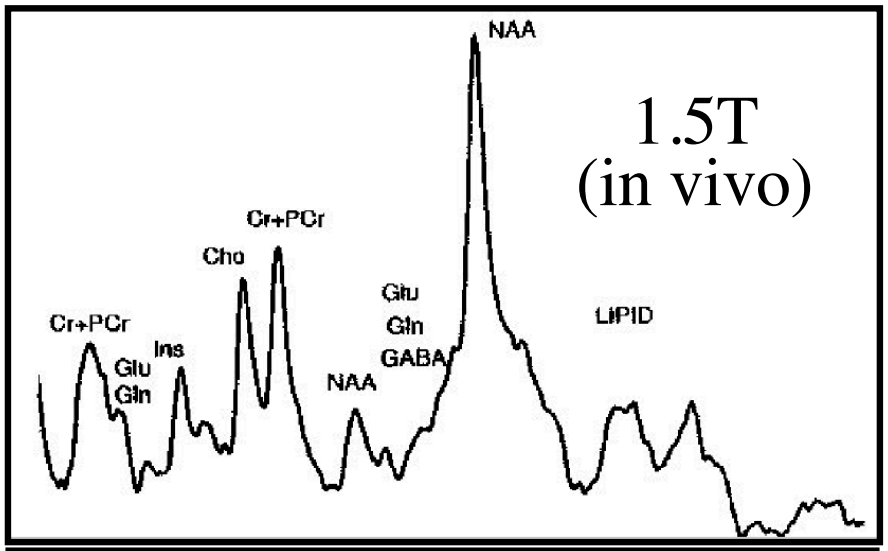



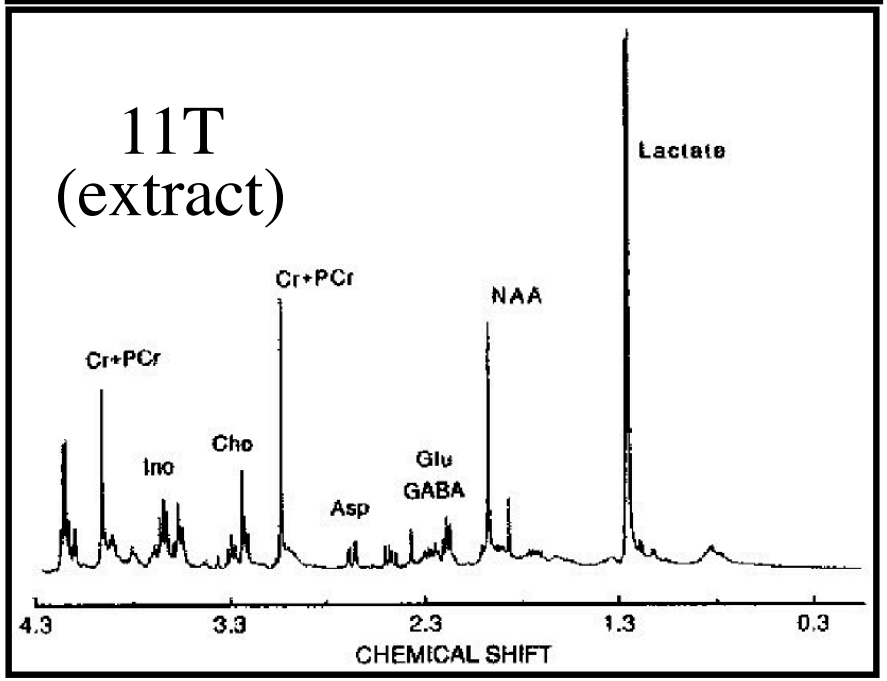



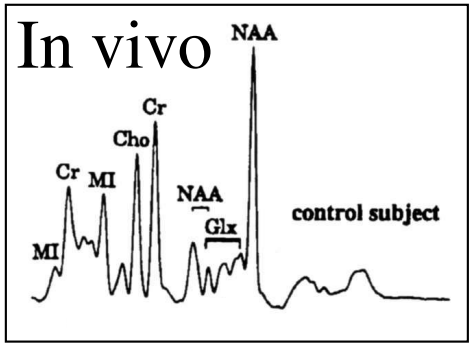

## Some general rules of thumb

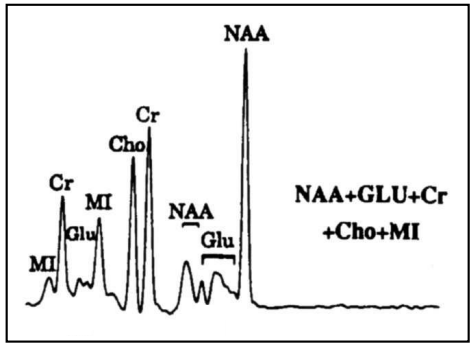
- In vivo MRS does not see everything! Maudsley paper is rather optimistic.
- Concentration limit (of protons) around 1 mM for NMR-detection
- Macromolecules are non-detectable ($T_2$s too short)

# $^{1}$H Brain Spectroscopy

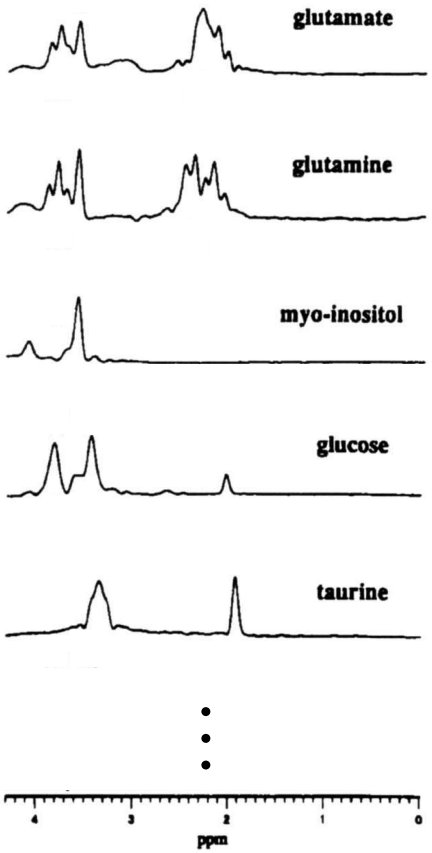


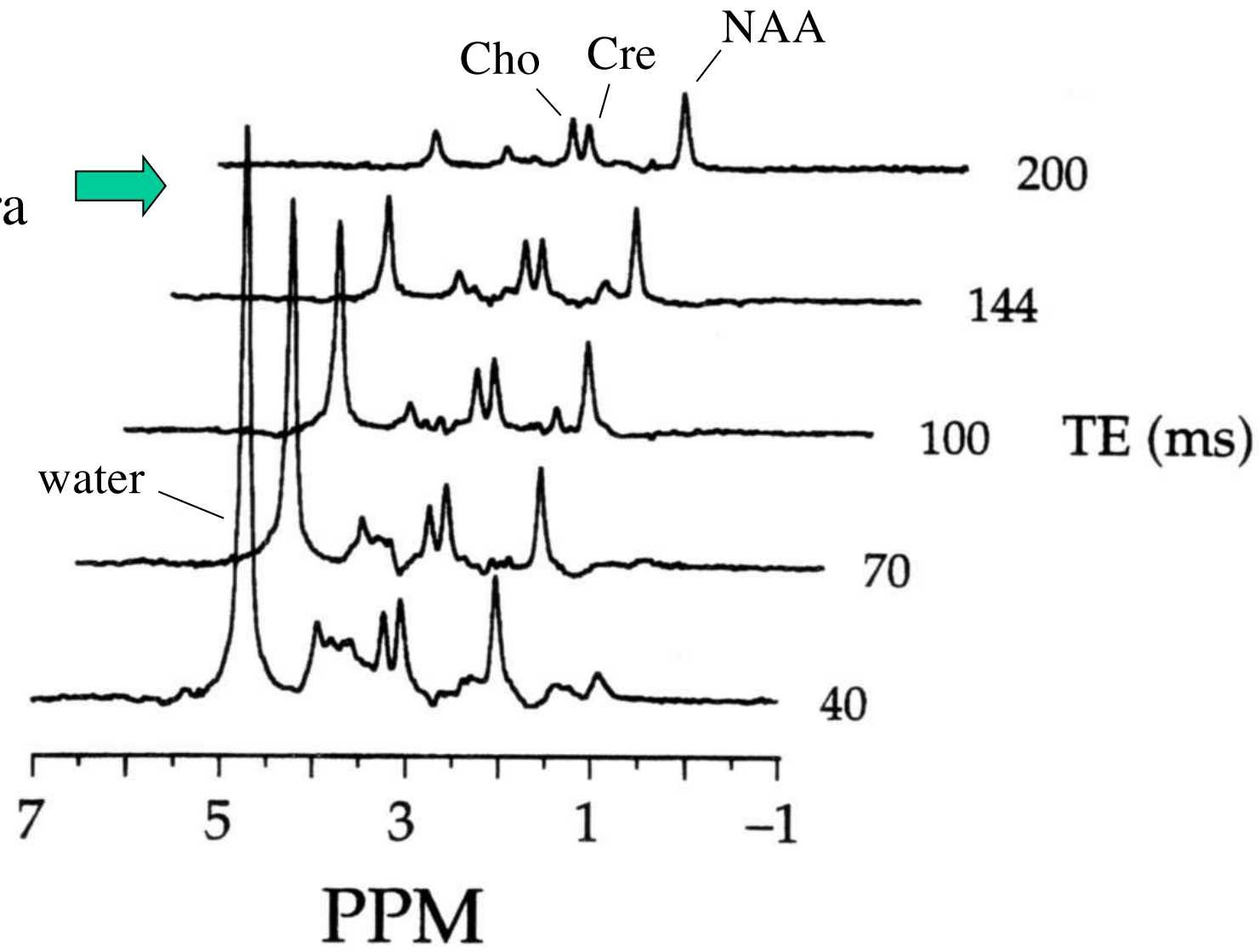

GE MRS phantom



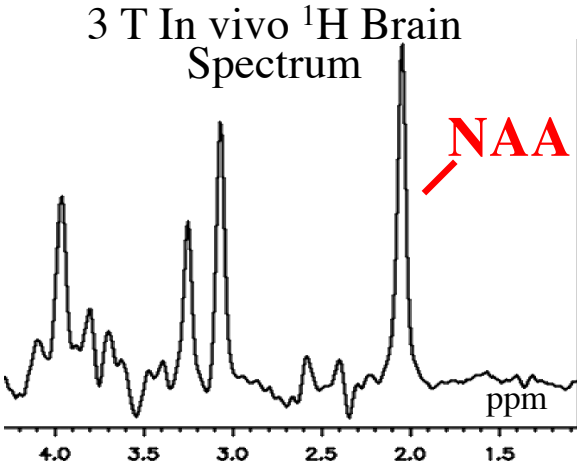

In vitro solutions

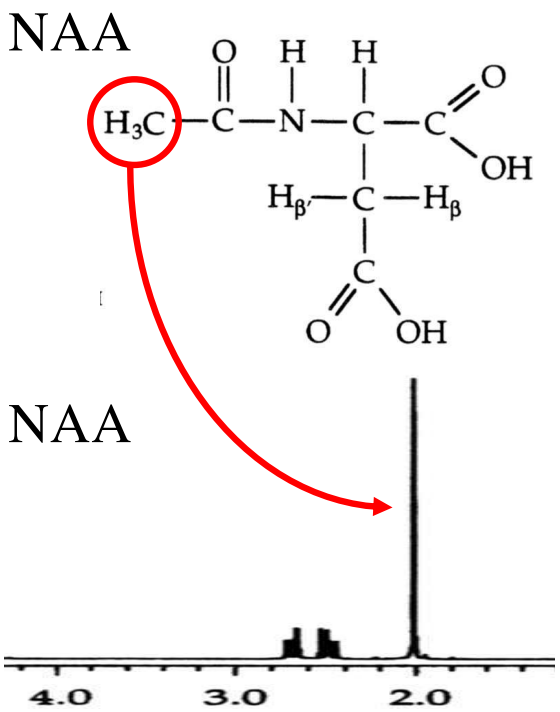
# $^{1}$H Brain Spectra

We'll start with "late" echo spectra

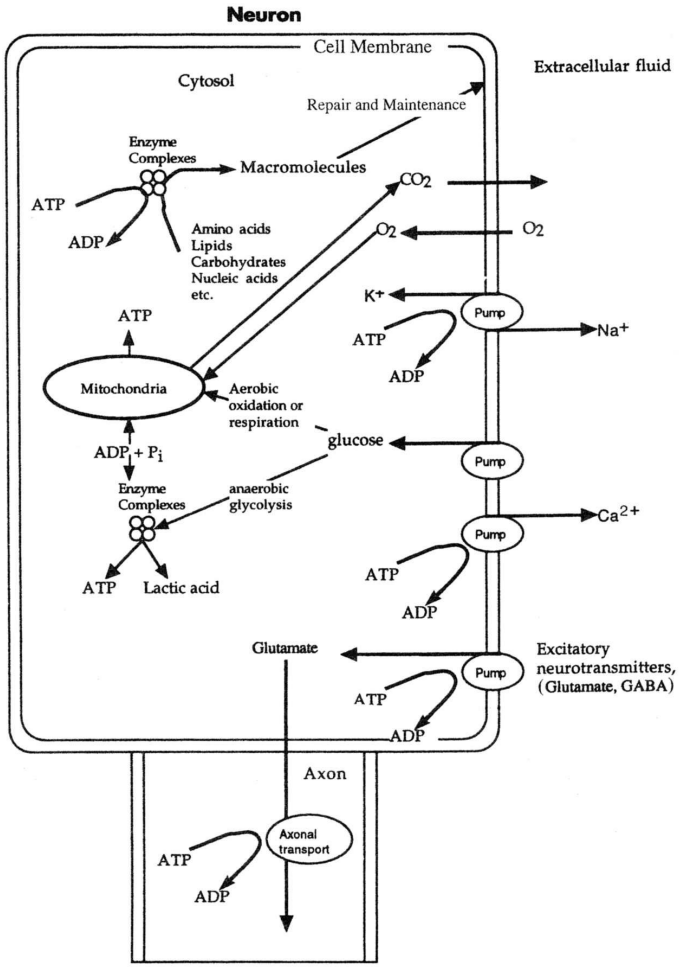


# N-acetyl Aspartate (NAA)



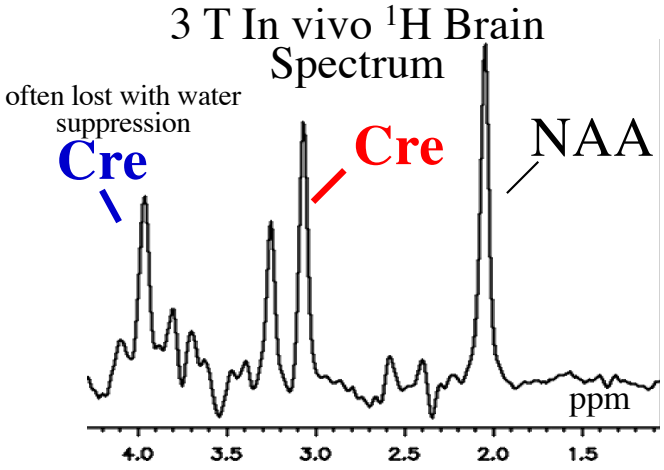

## Biochemical role?




## NAA

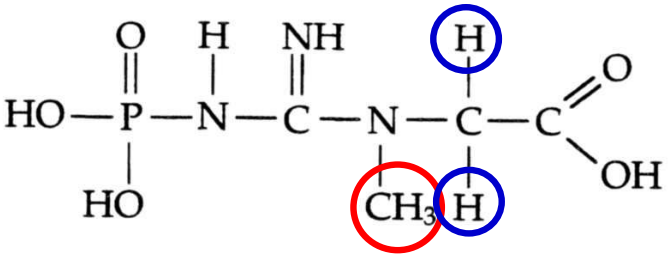
- Largest peak in a $^1$H-MRS brain spectrum
- Neuronal marker
- 2.0 ppm
- Approx 10 mM

# Creatine (Cre)

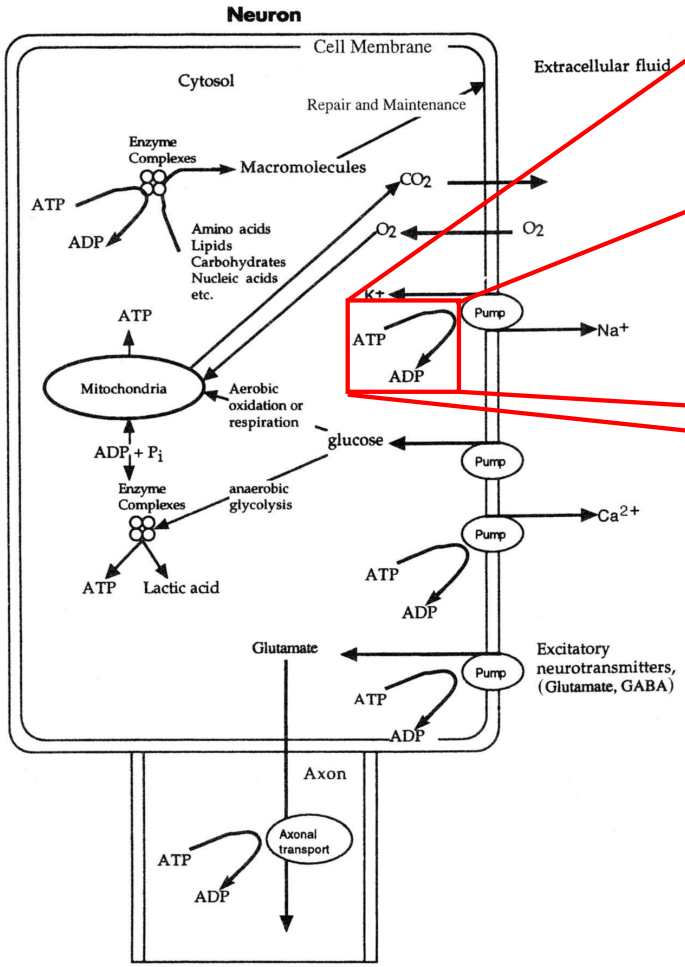



"Cre" peak from both creatine and phosphocreatine (often called referred to as total creatine peak)

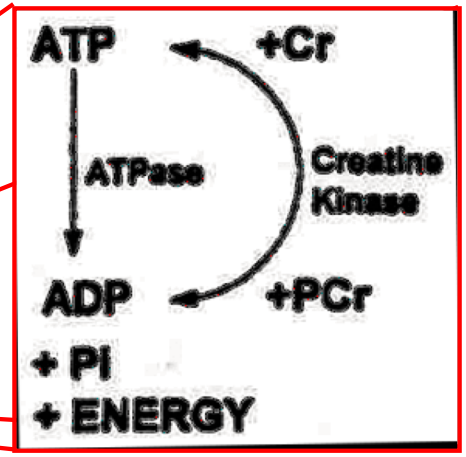
PCr




## Biochemical role



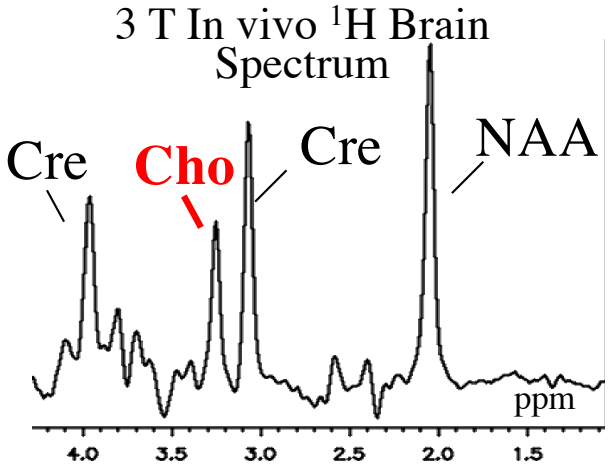

Fast reaction to buffer energy levels while glucose is metabolized



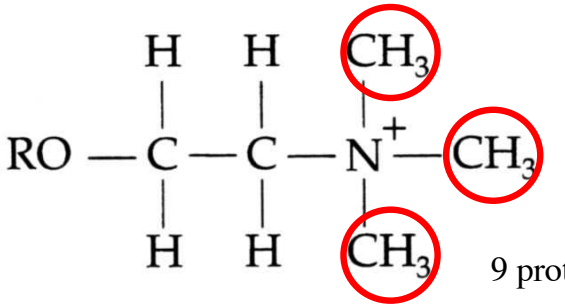

## Cre

- Reflects cellular energetics
- 3.0 ppm
- Cre+PCr="tCr"
- Approx 5-10 mM

# Choline (Cho)

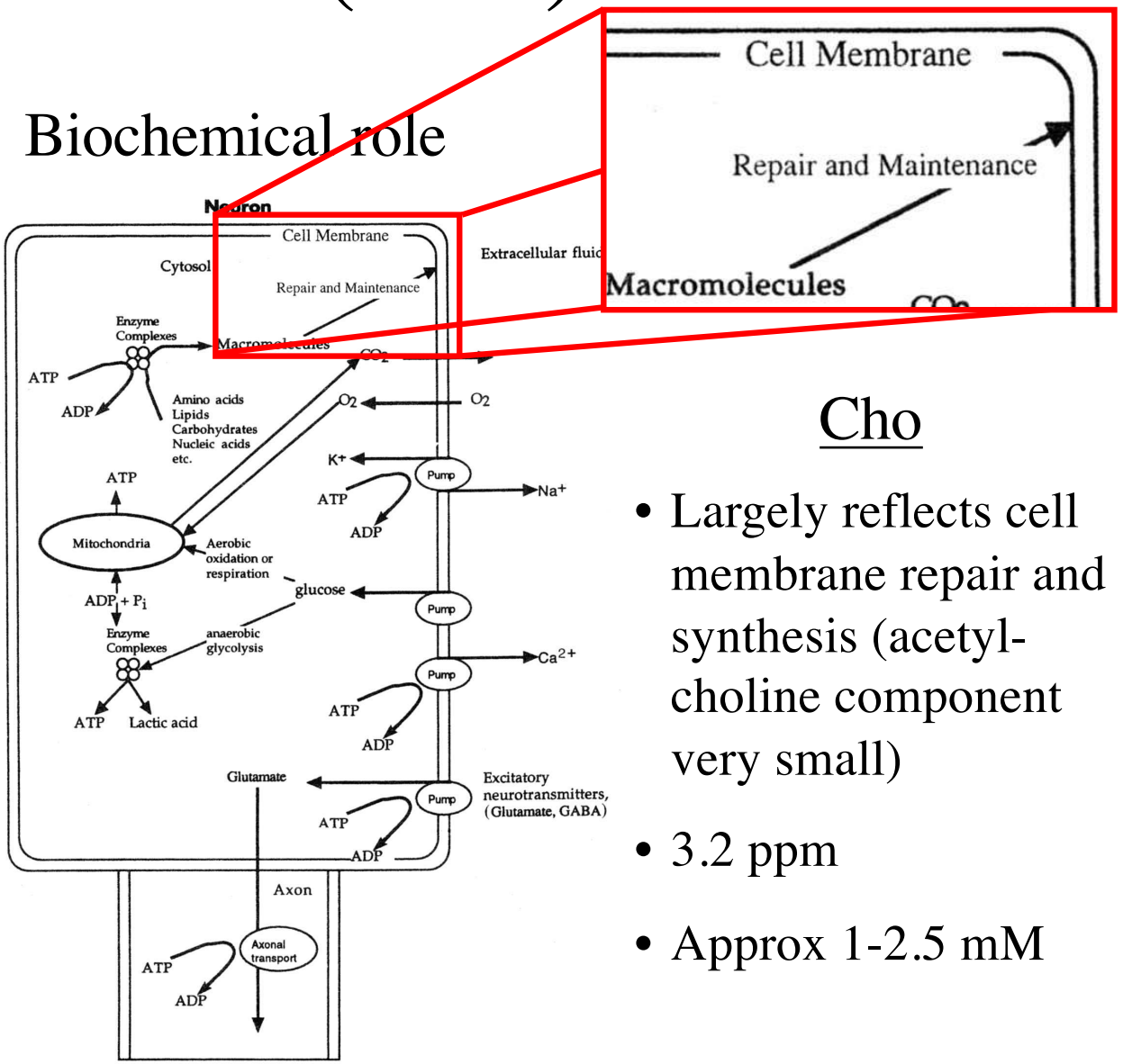



"Cho" peak from several choline containing compounds: phosphocholine, glycerphophocholine, etc.




9 protons!

## Biochemical role

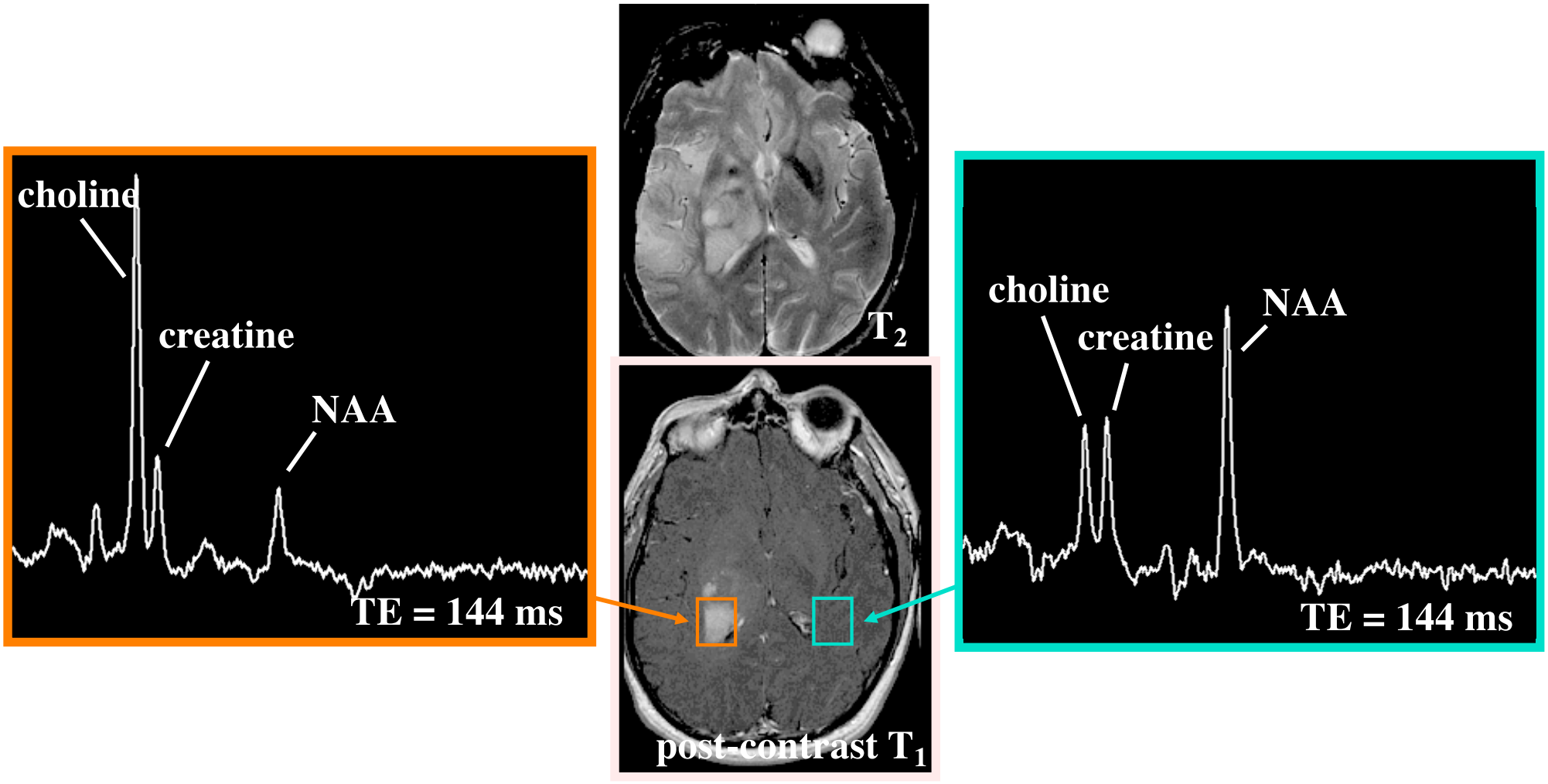



## Cho

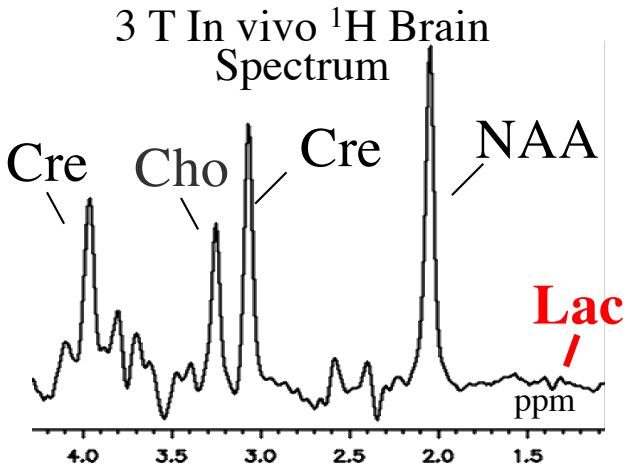
- Largely reflects cell membrane repair and synthesis (acetyl-choline component very small)
- 3.2 ppm
- Approx 1-2.5 mM

# Example: Brain Tumor

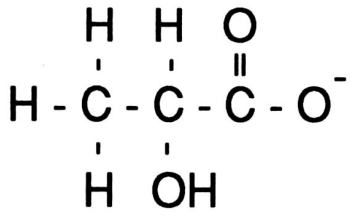
52 y.o male:  MRI #1 - rule out stroke, MRI # - tumor?

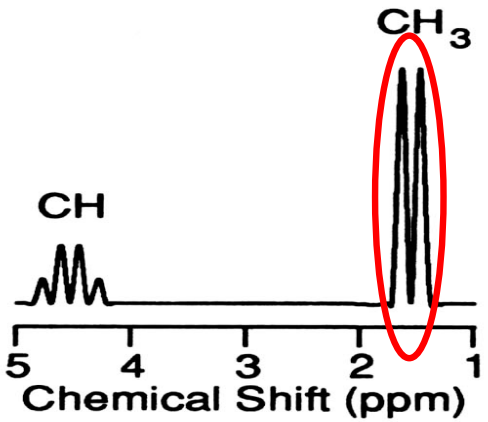


# Lactate (Lac)

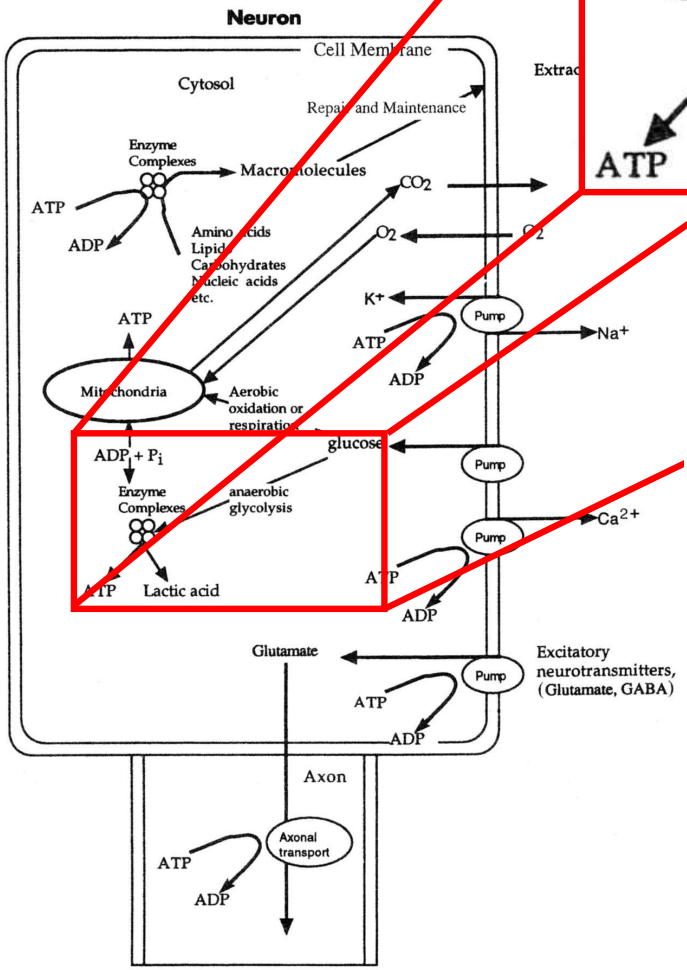


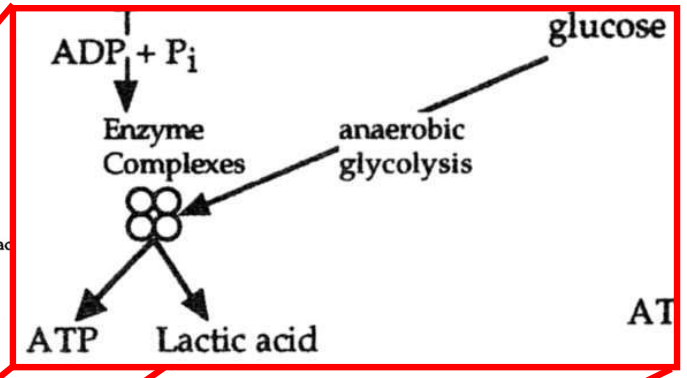

Lac




## Biochemical role

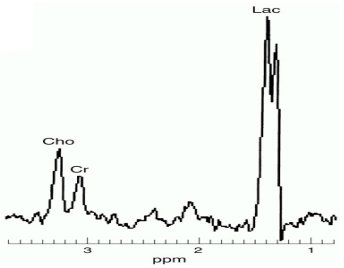



## Lac

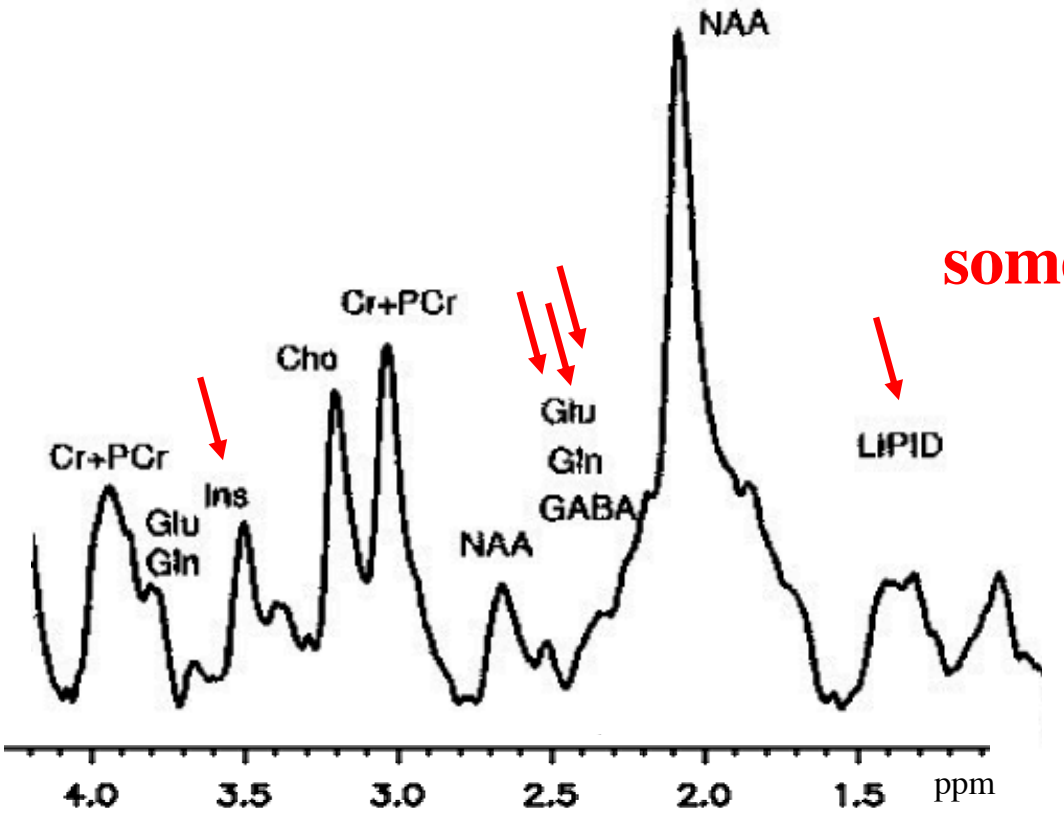
- Indicator of anaerobic metabolism
- Doublet at 1.3 ppm
- Approx 0.4 mM (normal brain tissue)

Cerebral infarct
Non-selective SE, TE=288 ms (2/J)




Kamada, et al, *J. N Psych*, **70**:675, 2001.

# Short TE $^{1}$H-MRS Brain Spectra

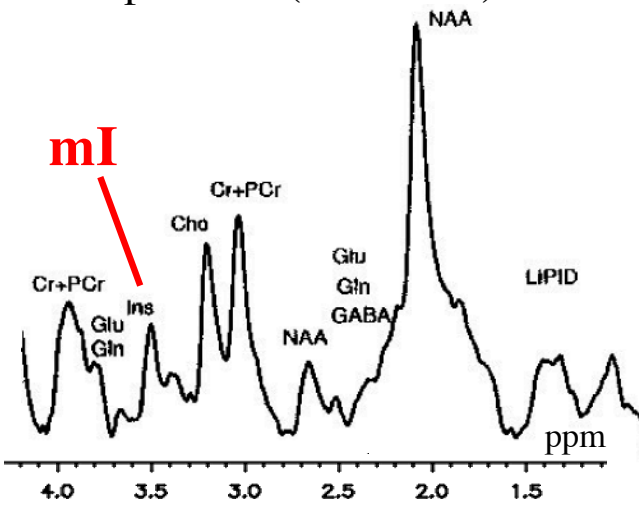



**some new peaks**

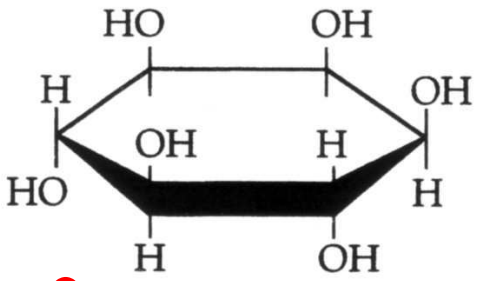
1.5T $^{1}$H-MRS In Vivo Brain Spectrum
TE = 35 ms

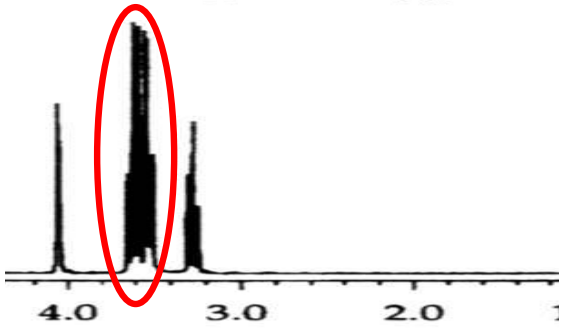
# myo-Inositol (mI)

1.5 T In vivo $^{1}$H Brain Spectrum (TE=35ms)

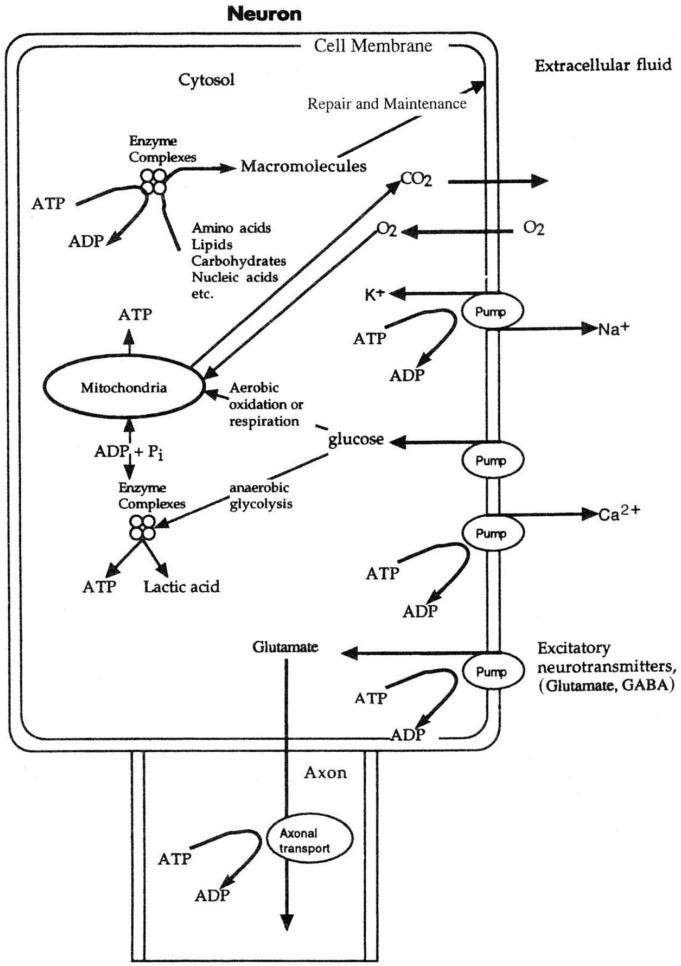



mI



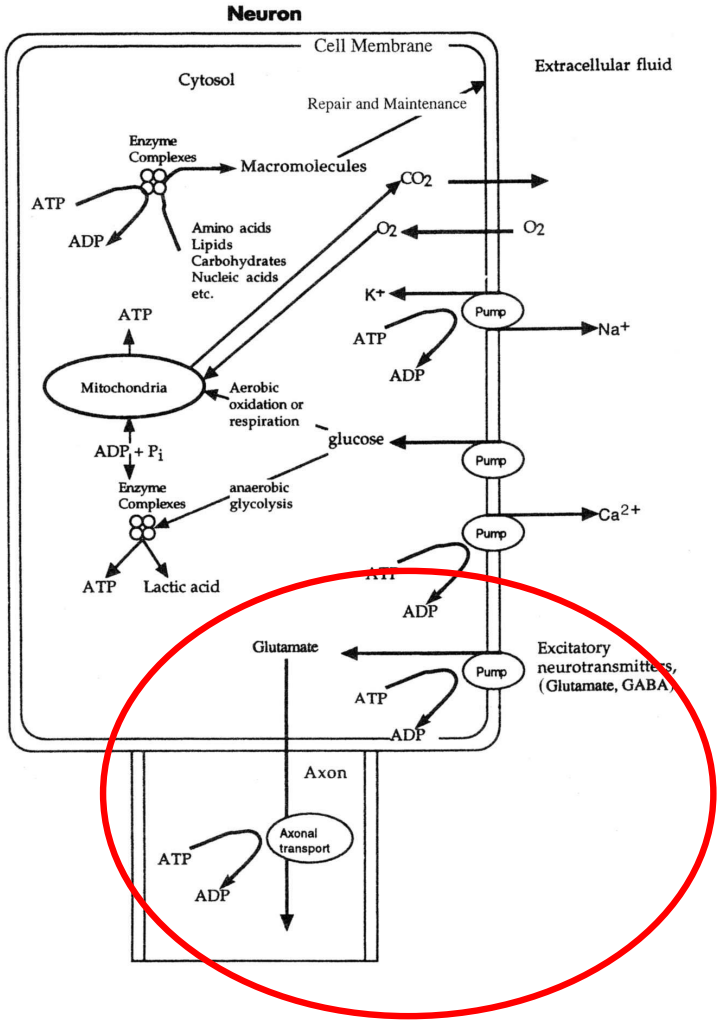

## Biochemical role?

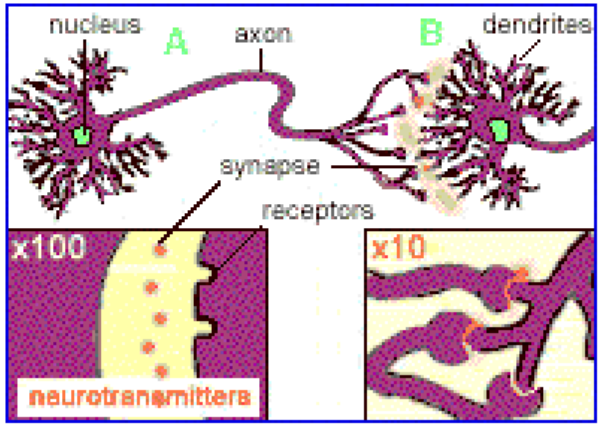



## mI

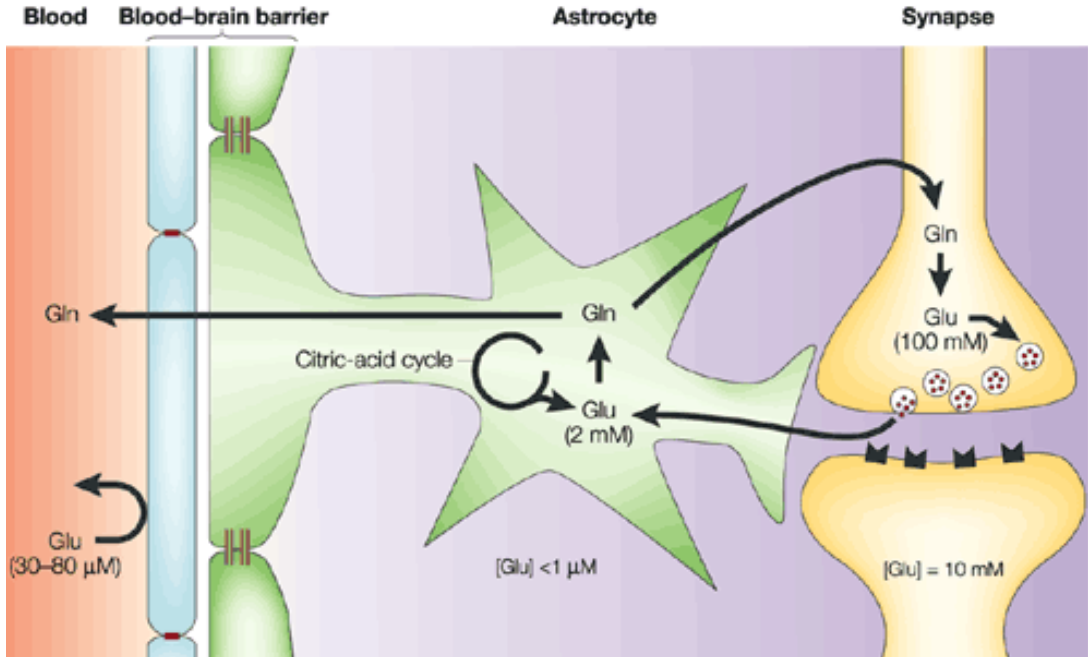
- Suggested as a glial marker.
- Glial cells provide structural support for neurons in addition to involvement in neurotransmitter processes.
- Largest peak at 3.6 ppm
- Approx 4-8 mM

# Neurotransmitters



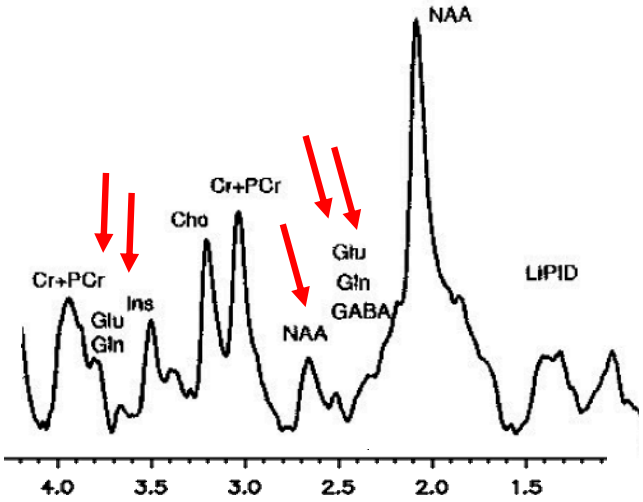




Glutamate is the major excitatory neurotransmitter in the brain

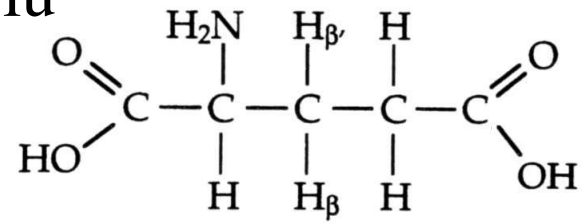


# Glutamate (Glu) and Glutamine (Gln)

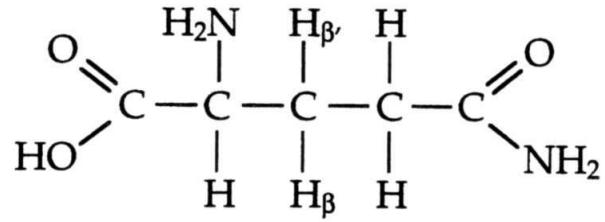
1.5 T In vivo $^{1}H$ Brain Spectrum (TE=35ms)



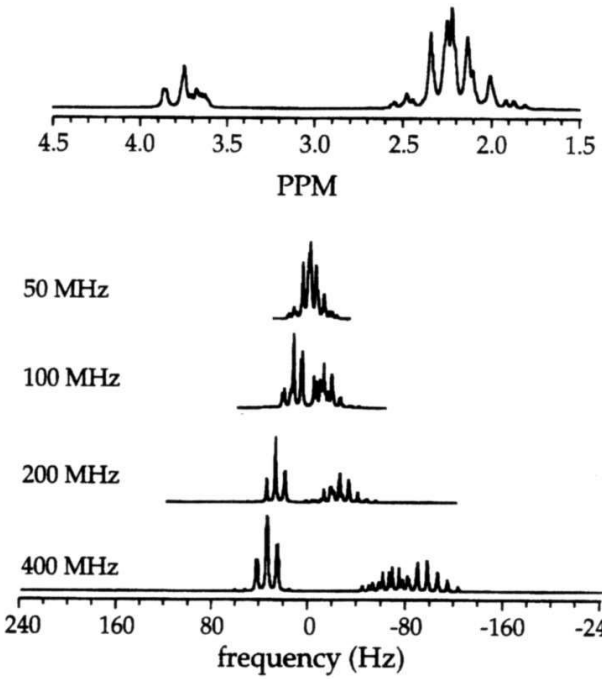

Glu



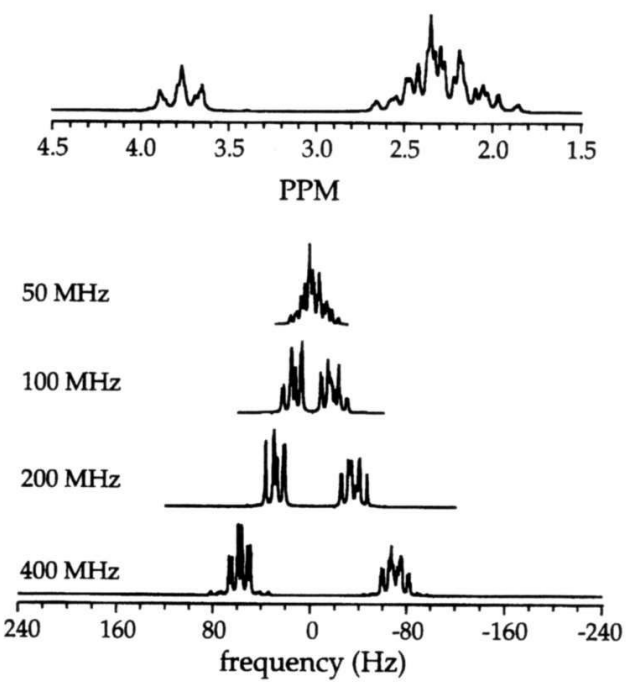

Gln




Glu




Gln

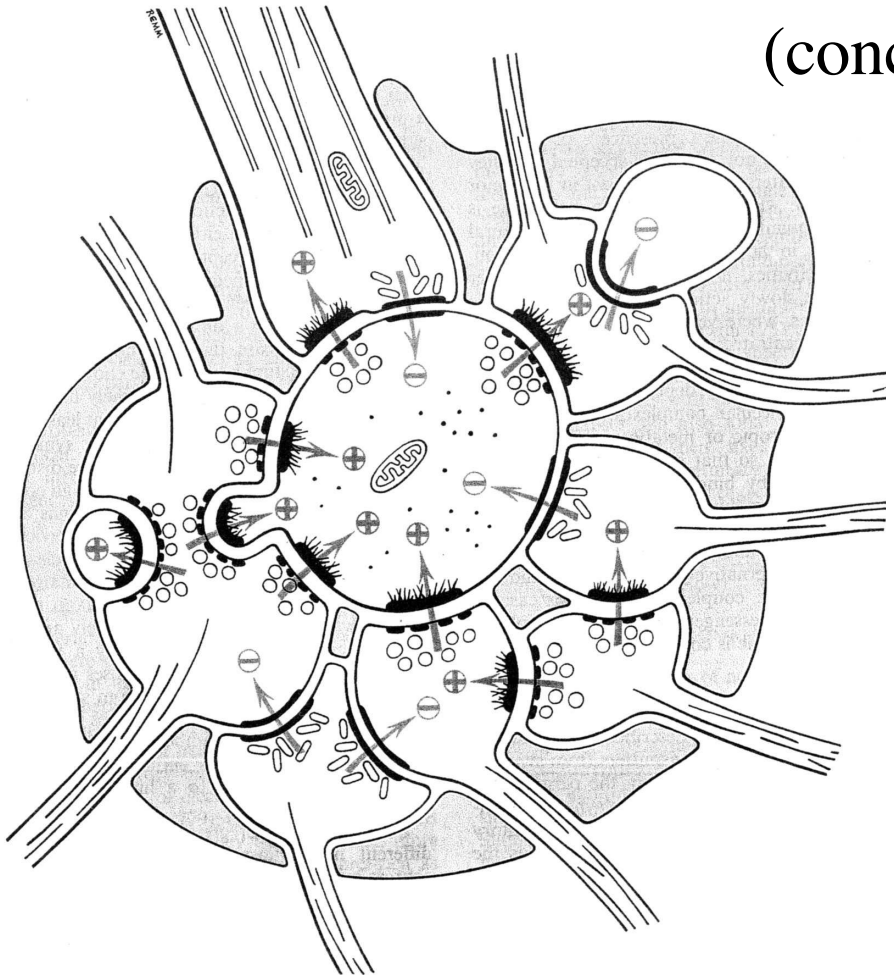



In vivo concentrations

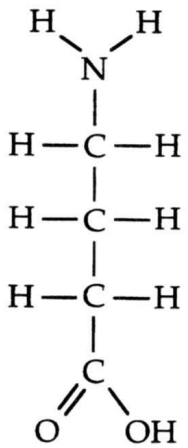
8-10 mM 2-3 mM

# γ-aminobutyric acid (GABA)

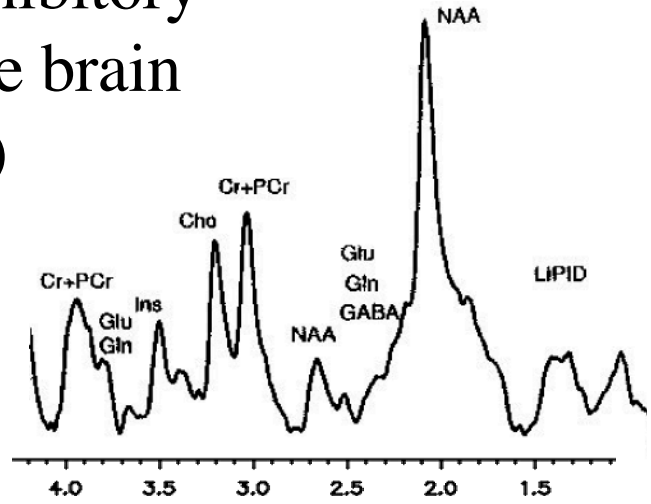
GABA is the major inhibitory neurotransmitter in the brain (conc: 1-2 mM)

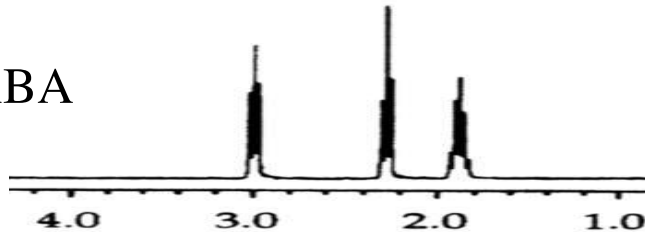


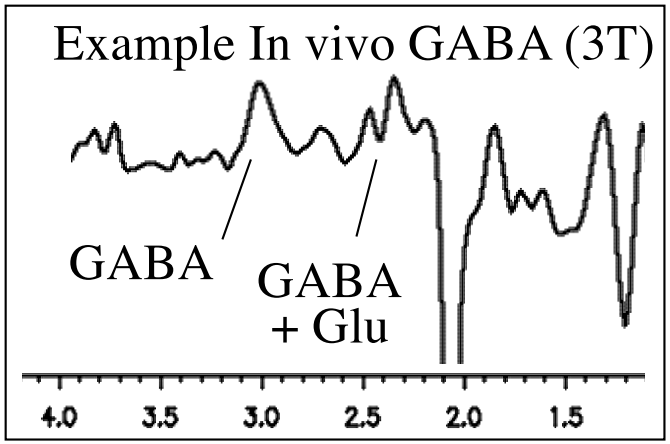
A real neural net



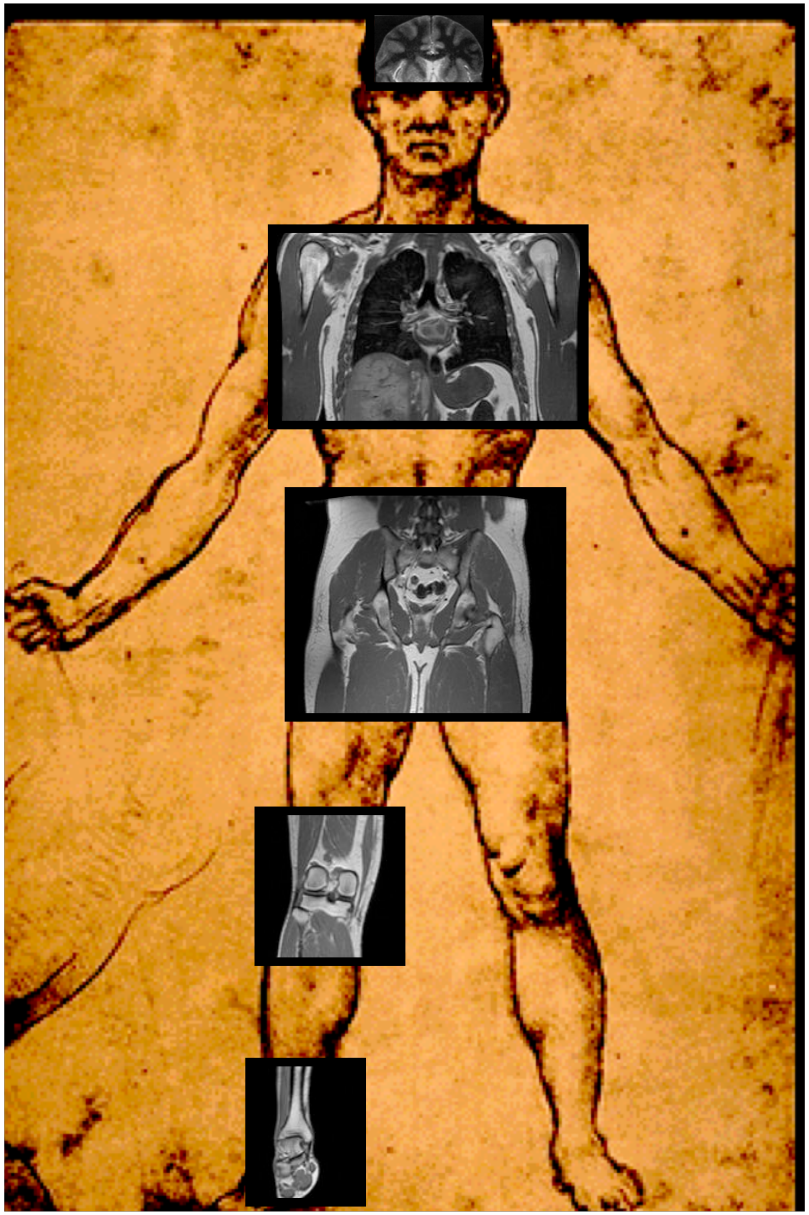

GABA

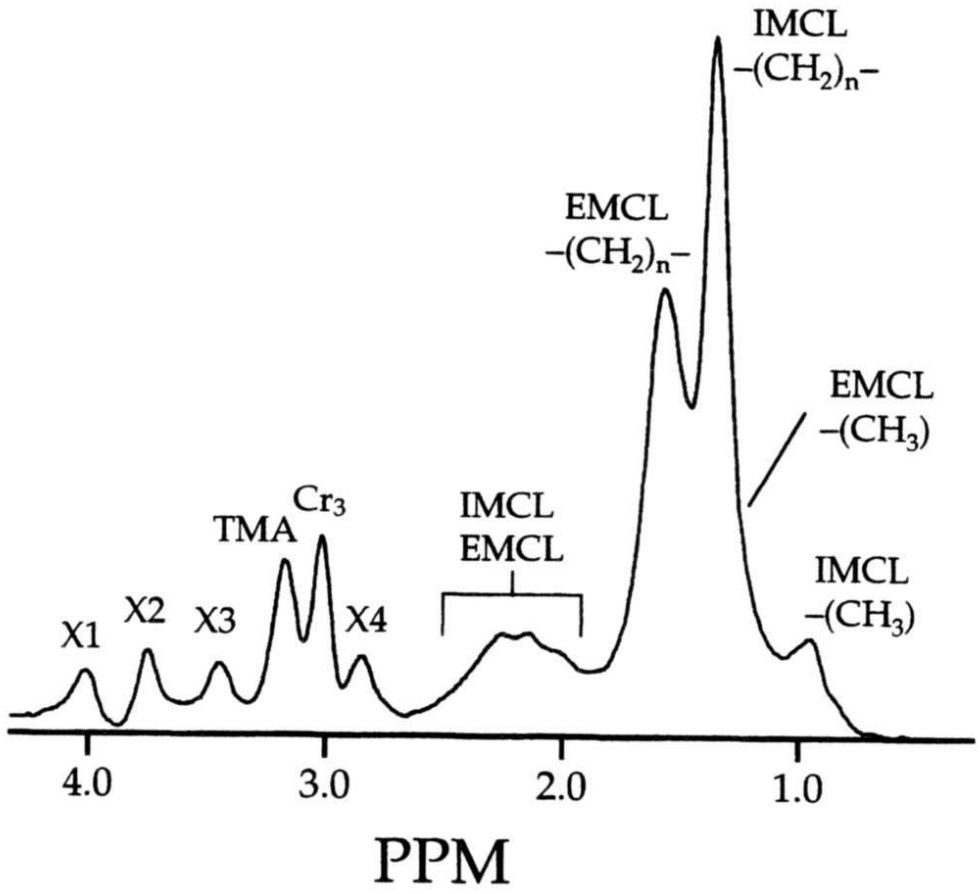


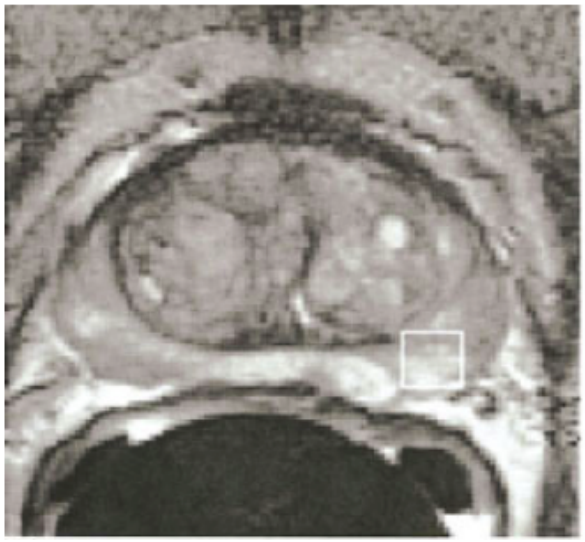



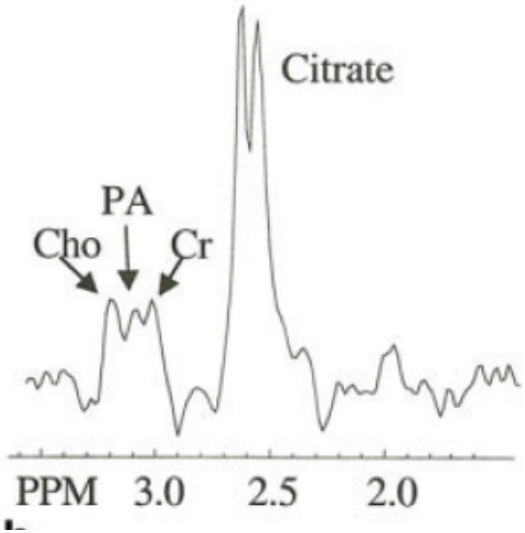
# Muscle and Fat



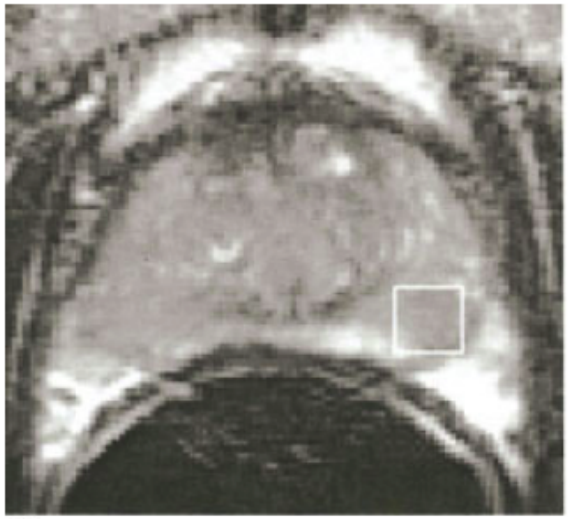


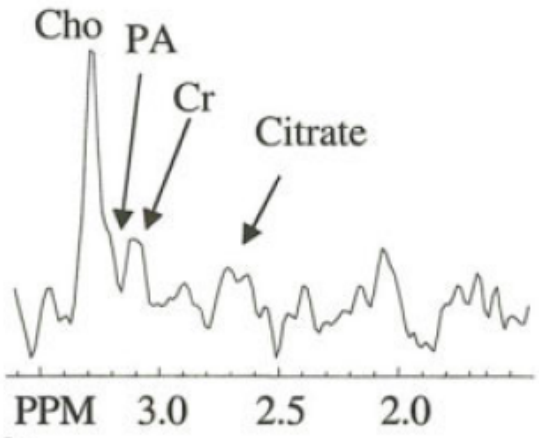
# Prostate






Normal prostate (1.5 T)

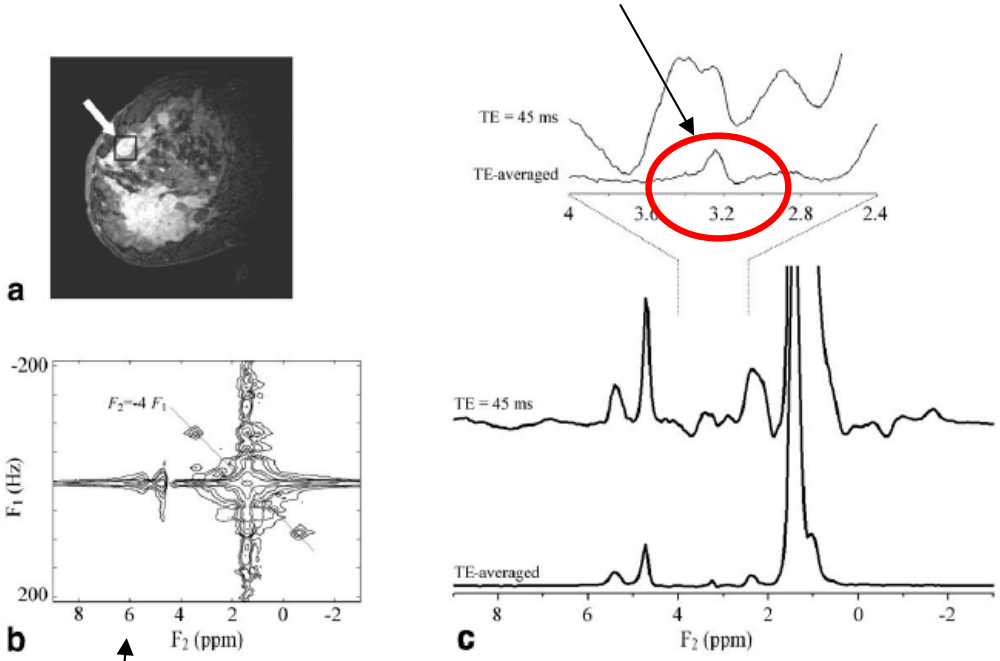




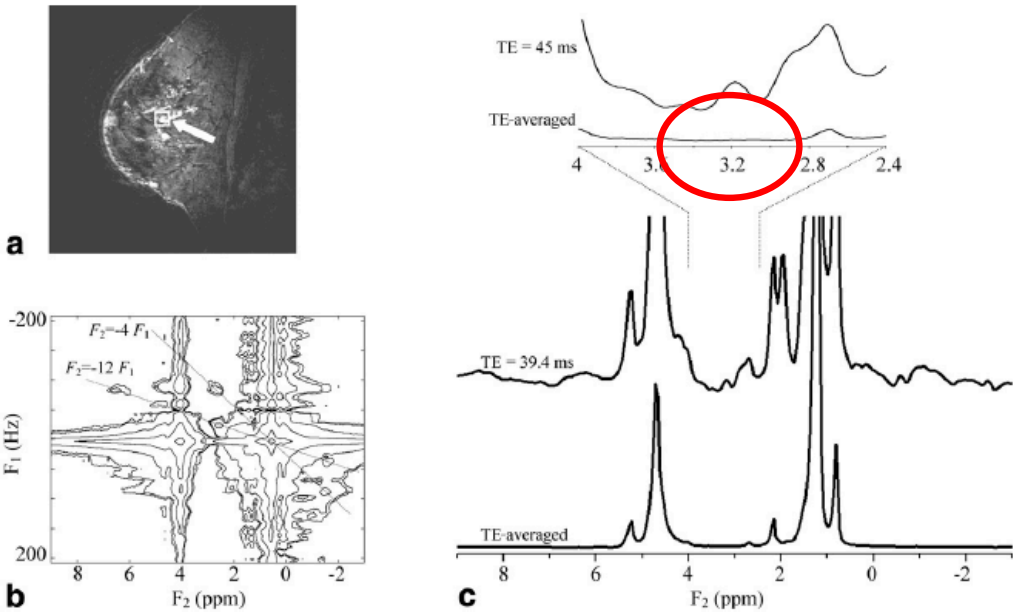

Prostate cancer (1.5 T)

# Breast

Elevated choline




Breast cancer




Noncancerous lesion

2D-J spectrum

# Sensitivity

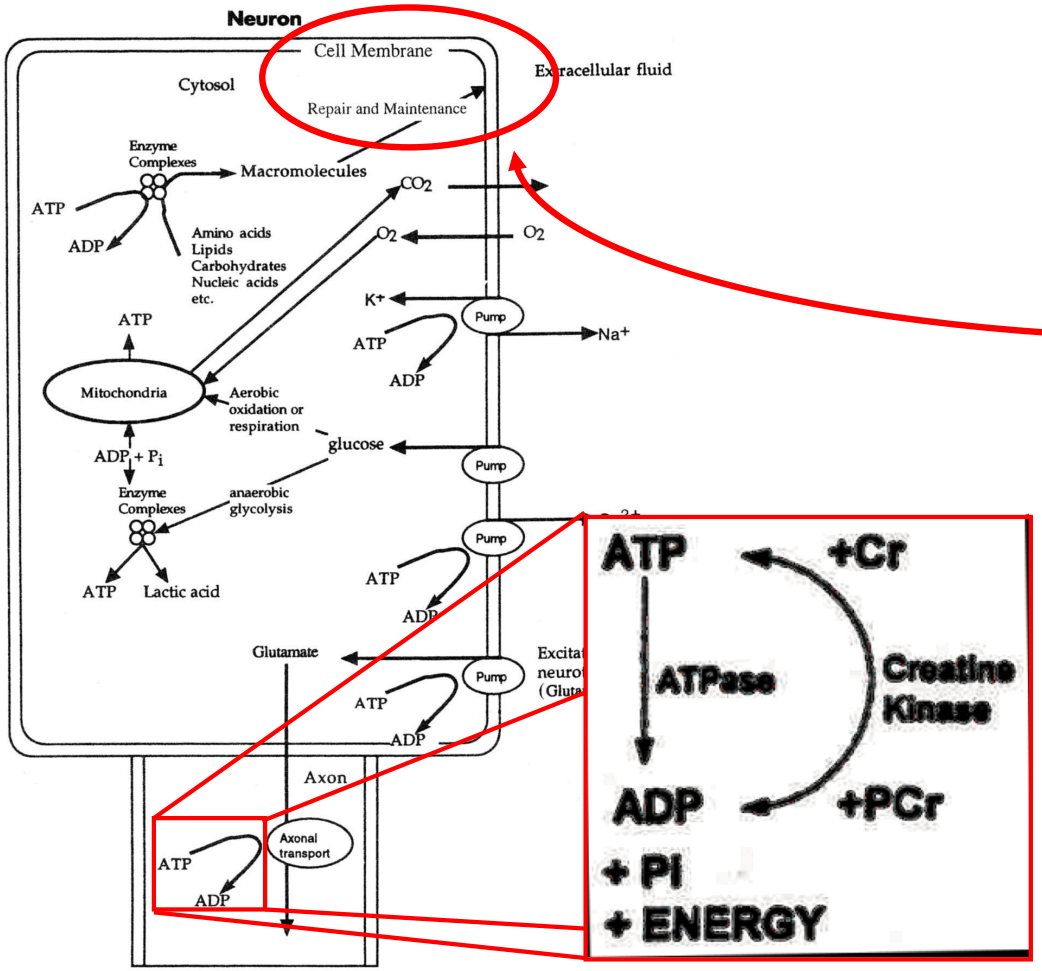
**Table 1.1.** NMR properties of commonly encountered nuclei in *in vivo* NMR

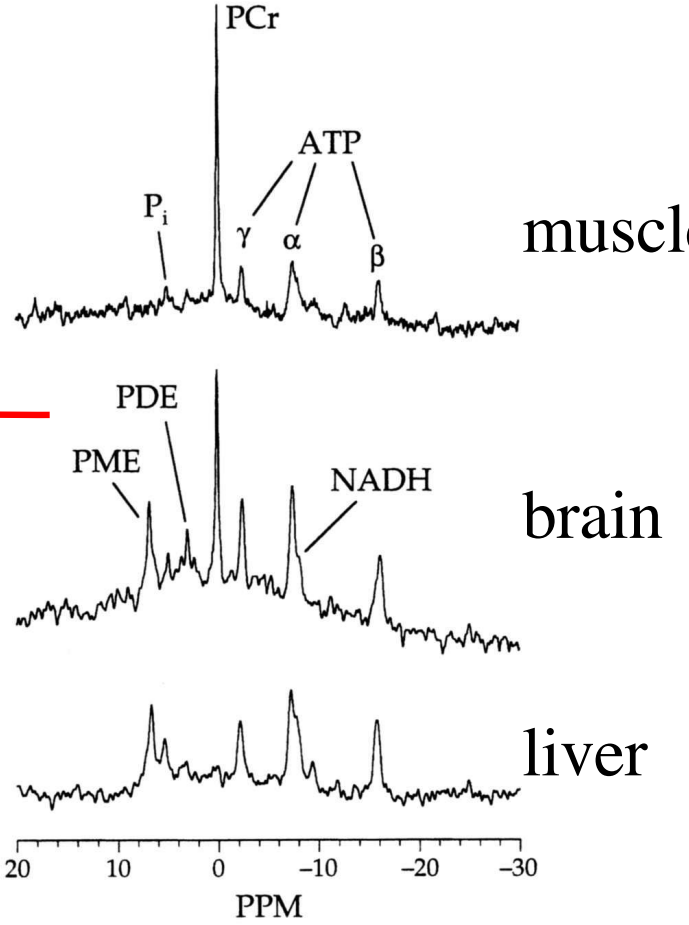
| Isotope | Spin | Gyromagnetic ratio ($10^7$ rads$^{-1}$T$^{-1}$) | NMR frequency at 2.35 T (MHz) | Natural abundance (%) | Relative sensitivity[1] |
|---|---|---|---|---|---|
| $^{1}$H | 1/2 | 26.752 | 100.000 | 99.985 | 1.00 |
| $^{2}$H | 1 | 4.107 | 15.351 | 0.015 | $1.45 \times 10^{-6}$ |
| $^{13}$C | 1/2 | 6.728 | 25.145 | 1.108 | $1.76 \times 10^{-4}$ |
| $^{14}$N | 1 | 1.934 | 7.228 | 99.630 | $1.01 \times 10^{-3}$ |
| $^{15}$N | 1/2 | −2.712 | 10.137 | 0.370 | $3.85 \times 10^{-6}$ |
| $^{19}$F | 1/2 | 25.181 | 94.094 | 100.000 | 0.833 |
| $^{23}$Na | 3/2 | 7.080 | 26.466 | 100.000 | $9.27 \times 10^{-2}$ |
| $^{31}$P | 1/2 | 10.841 | 40.481 | 100.000 | $6.65 \times 10^{-2}$ |
| $^{39}$K | 3/2 | 1.250 | 4.672 | 93.100 | $4.75 \times 10^{-4}$ |

[1]Relative sensitivity is calculated as the product of NMR sensitivity (proportional to $\gamma\ ^{3}\mathrm{I}(\mathrm{I}+1)$) and the natural abundance.

$$\text{in vivo SNR} \propto \rho \frac{\gamma^2 \hbar^2 B_0}{4kT}$$

# $^{31}$P Spectroscopy



# $^{13}C$ Spectroscopy

**Table 2.3.** Chemical shifts of biological relevant $^{13}C$ containing metabolites

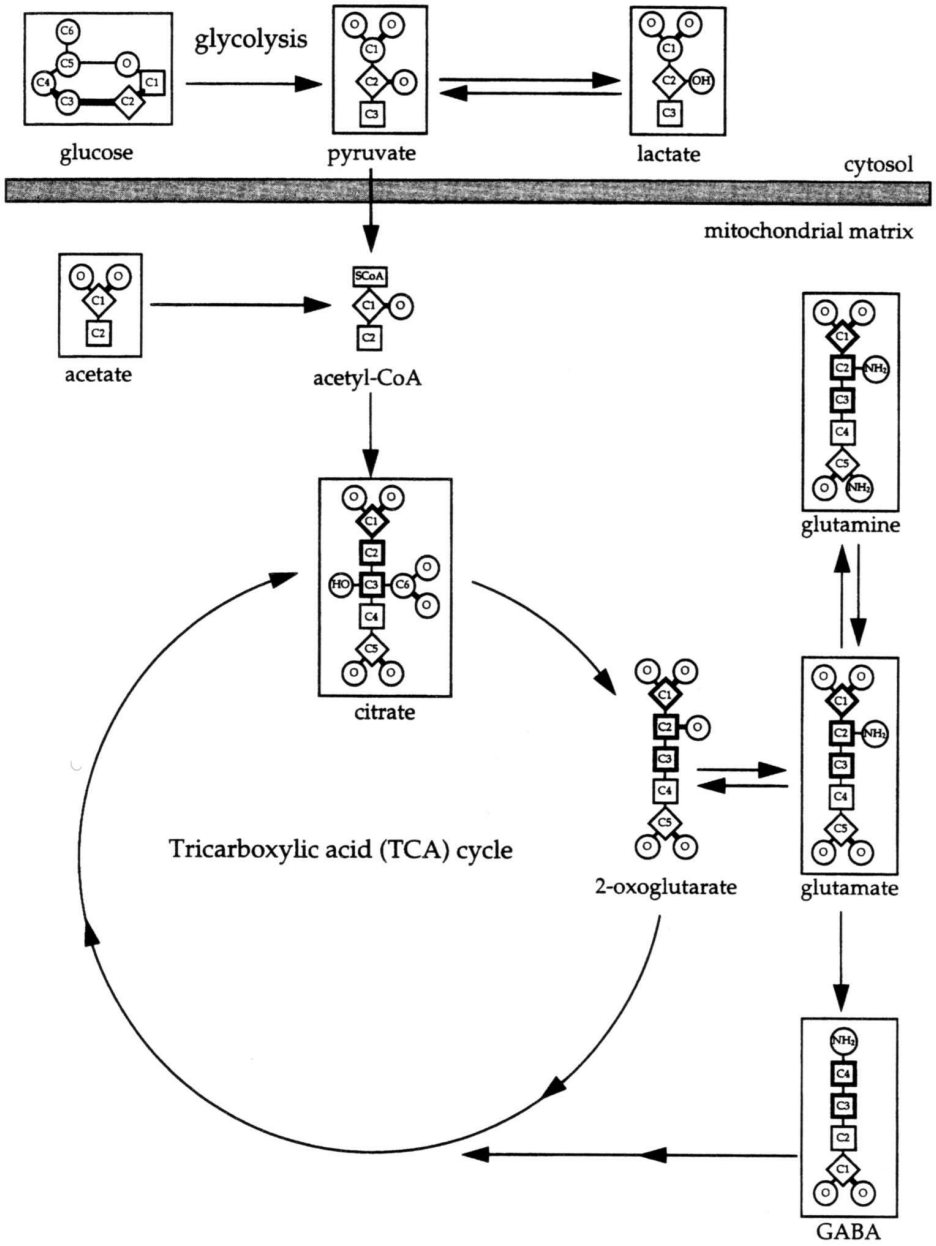
| | Carbon atom | | | | | |
|---|---|---|---|---|---|---|
| Compound | C1 | C2 | C3 | C4 | C5 | C6 |
| Acetate | 182.6 | 24.5 | | | | |
| Alanine | 176.6 | 51.5 | 17.1 | | | |
| Aspartate | 175.1 | 53.0 | 37.4 | 178.4 | | |
| Citrate | 179.7 | 46.8 | 76.0 | 46.8 | 179.7 | 182.3 |
| Creatine | 175.4 | 37.8 | 158.0 | 54.7 | | |
| GABA | 182.3 | 35.2 | 24.6 | 40.2 | | |
| Glycerol | 63.6 | 73.3 | 63.6 | | | |
| β-hydroxy butyrate | 181.2 | 47.6 | 66.8 | 22.9 | | |
| Glucose α | 92.7 | 72.1 | 73.5 | 70.4 | 72.1 | 61.4 |
| β | 96.6 | 79.9 | 76.5 | 70.4 | 76.5 | 61.4 |
| Glutamate | 175.3 | 55.5 | 27.8 | 34.2 | 182.0 | |
| Glutamine | 174.8 | 55.0 | 27.1 | 31.7 | 178.4 | |
| Glycine | 173.3 | 42.5 | | | | |
| Glycogen | 100.5 | — | 74.0 | 78.1 | 72.1 | 61.4 |
| Inositol | 73.3 | 73.1 | 73.3 | 71.9 | 75.1 | 71.9 |
| Lactate | 183.3 | 69.3 | 21.0 | | | |
| Malate | 182.1 | 71.7 | 43.9 | 180.9 | | |
| NAA | 179.7 | 54.0 | 40.3 | 179.7 | 174.3 | 22.8 |
| Succinate | 183.4 | 35.3 | 35.3 | 183.4 | | |
| Taurine | 48.4 | 36.2 | | | | |

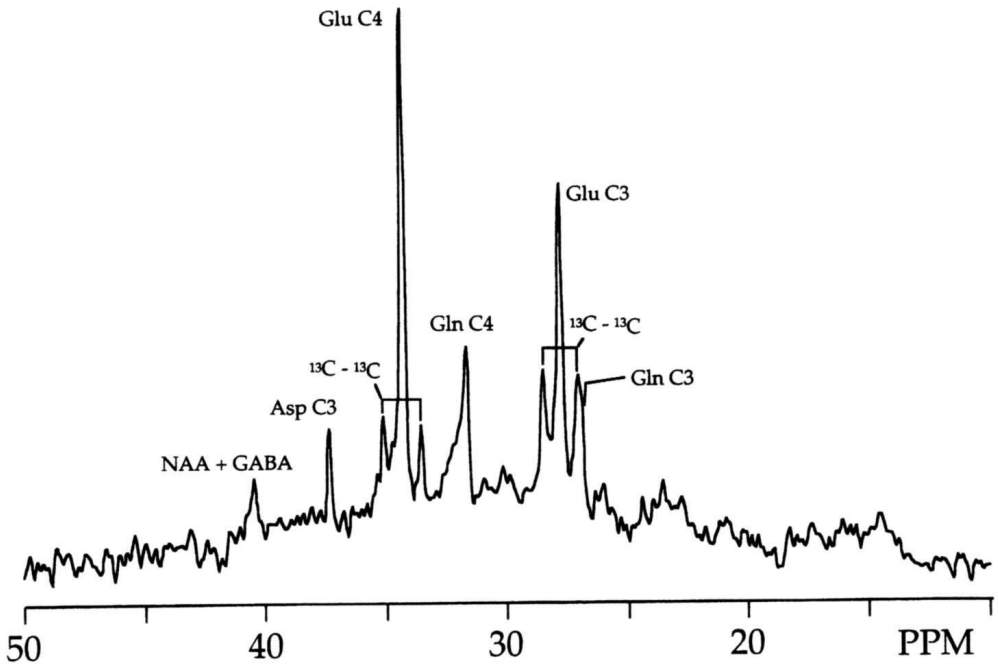
All chemical shifts are referenced relative to 3-(trimethylsilyl)-1-propanesulfonic acid at 0.00 ppm.

Note: very wide chemical shift range

$^{13}C$ natural abundance is low, but $^{13}C$-labeled glucose or acetate infusions can yield important information regarding metabolic fluxes

# Example: $^{13}$C-glucose Infusion

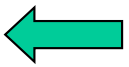


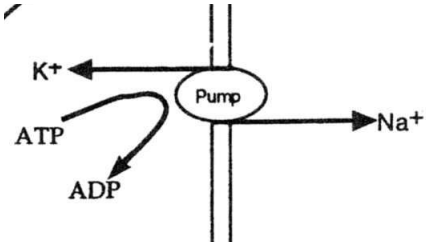

Gruetter, et al., *J. Neurochem.*, 63:1377-1385, 1994.

# Other Nuclei

- Sodium ($^{23}$Na, spin=3/2)
  - Intracellular 10 mM
  - Extracellular 150 mM



Involved in ionic balances, generation of action potentials, regulations of cell volume.




- Fluorine ($^{19}$F)
  - No endogenous $^{19}$F compounds in biological tissue
  - Lots of fluorinated drugs!

# Next Lecture: $^{1}$H MRS Methods