MRI with hyperpolarized contrast agents

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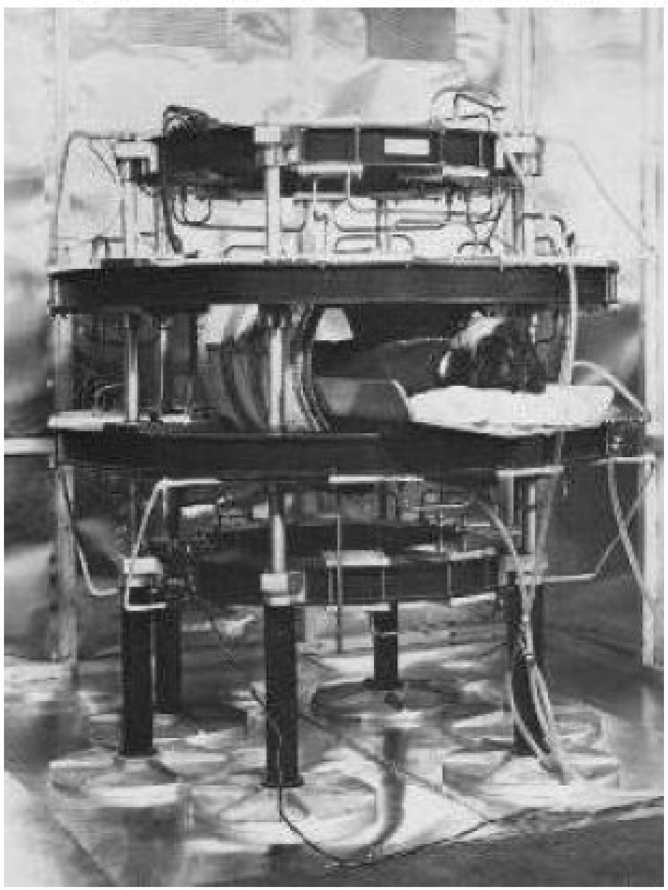
- Magnet Resonance Imaging
- Contrast media
- Pyruvic acid
- EPR and DNP measurements
- Summary

Magnet Resonance Imaging I




Magnet Resonance Imaging II

- radio frequency region
  - no ionizing radiation

- MR – images consist of many information,
  - grey tone of voxel (signal intensity) depends on:
    - spin density (PD: ^{1}H, ^{13}C, ^{19}F, ^{23}Na, ^{31}P in biological tissue)
    - spin-lattice-relaxation time T_1
    - spin-spin-relaxation time T_2
    - molecular motion (flow, diffusion, perfusion)
    - susceptibility
    - chemical shift

Magnet Resonance Imaging III

frequency [Hz]	wavelength [m]	energy [eV]	radiation type		impact
10^{26}	10^{-18}	10^{12}			
10^{24}	10^{-16}	10^{10}			
10^{22}	10^{-14}	10^{8}	X – ray		break of
10^{20}	10^{-12}	10^{6}	γ - ray		molecules
10^{18}	10^{-10}	10^{4}			
10^{16}	10^{-8}	10^{2}	UV		e^- excitation
10^{14}	10^{-6}	10^{0}	light		vibration
10^{12}	10^{-4}	10^{-2}	infra red		rotation
10^{10}	10^{-2}	10^{-4}			
10^{8}	10^{0}	10^{-6}	FM	MRI	??
10^{6}	10^{2}	10^{-8}	SW		
10^{4}	10^{4}	10^{-10}	MW		
10^{2}	10^{6}	10^{-12}	LW		
10^{0}	10^{8}	10^{-14}			

Magnet Resonance Imaging IV

Gyro magnetic ratio of some nuclei

Nucleus	^{1}H	^{31}P	^{19}F	^{13}C
γ*[MHz/T]	42.6	17.2	40.0	10.8

Larmor frequency of protons

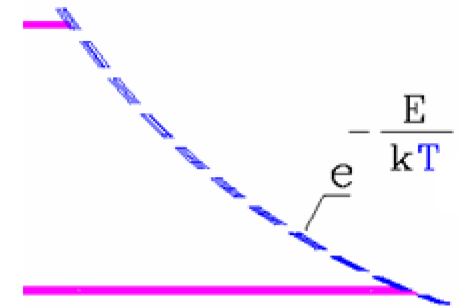
$$f_0 = \gamma * \left[\frac{MHz}{T}\right] \cdot B[T] \qquad \omega_0 = 2\pi f_0$$

B	50 μT	0,5 T	1 T	4 T
f_0	2.13 kHz	21.3 MHz	42.6 MHz	170.4 MHz

Magnet Resonance Imaging V

Isotope	Spin	Gyro magnetic ratio [108 rad/s/T]	Natural abundance [%]	sensitvity S/S_{1H} (B=const) [%]
^{1}H	1/2	2,675	99,98	100,00
^{31}P	1/2	1,084	100,00	6,65
^{23}Na	3/2	0,708	100,00	9,27
^{13}C	1/2	0,673	1,11	$1,75 \times 10^{-2}$
^{14}N	1	0,193	99,63	$1,0 \times 10^{-1}$
^{17}O	5/2	-0,363	0,038	$1,11 \times 10^{-3}$
^{19}F	1/2	2,518	100,00	83,4
^{35}Cl	3/2	0,262	75,77	$3,58 \times 10^{-1}$
^{39}K	3/2	0,125	93,26	$4,76 \times 10^{-2}$

Magnet Resonance Imaging VI



- Boltzmann statistic:

$$P = \frac{N^- - N^+}{N^- + N^+} = \tanh^{-\gamma \cdot \hbar \cdot B_0 / kT}$$

- Example: protons at B=1T and T= 37°C (310K):

$$P = 0.00032\,\% \qquad \frac{N^-}{N^+} = 1.0000066 \quad : \quad 6.6\ ppm$$

- Polarized target conditions: B = 2.5T, T = 1K:

$P = 0.26\,\%$ enhancement of E=790

- Dynamically polarized:

$P = 80\,\%$ enhancement of E=24000

Contrast medium in MRI I

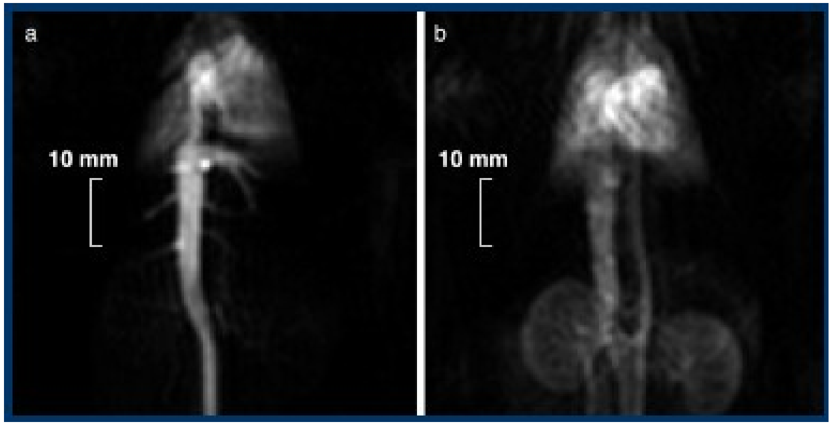
- MRI shows local strength of transversal magnetization $M_T'(x,y)$
- Contrast: $K = \frac{I_1 - I_2}{I_1 + I_2}$ $I_{1,2}$ = signals of tissue 1 and 2
- K depends on noise in $I_{1,2}$
- the larger the voxel the higher the signal and lower the noise
- but reduction of spatial resolution

⇒ strong mutual dependency of contrast, noise and resolution

⇒ contrast media, e.g. ^{13}C enrich-ed and dyn. polarized

Contrast medium in MRI II

- ^{13}C-labeled urea polarized under DNP-conditions, then melted and injected during seconds: ^{13}C-sensitive MRI shows a picture of the blood vessels of a rat
- possible future: polarized, ^{13}C-labeled contrast media:
  - no background noise, high reso-
  - lution by short measuring time (1H)
  - small, labeled molecules as markers for tissue blood flow
  - examining metabolism in „real time"
- further possible contrast medium: Pyruvic acid
- ⇒ **Bochum EPR- and polarization measurements**



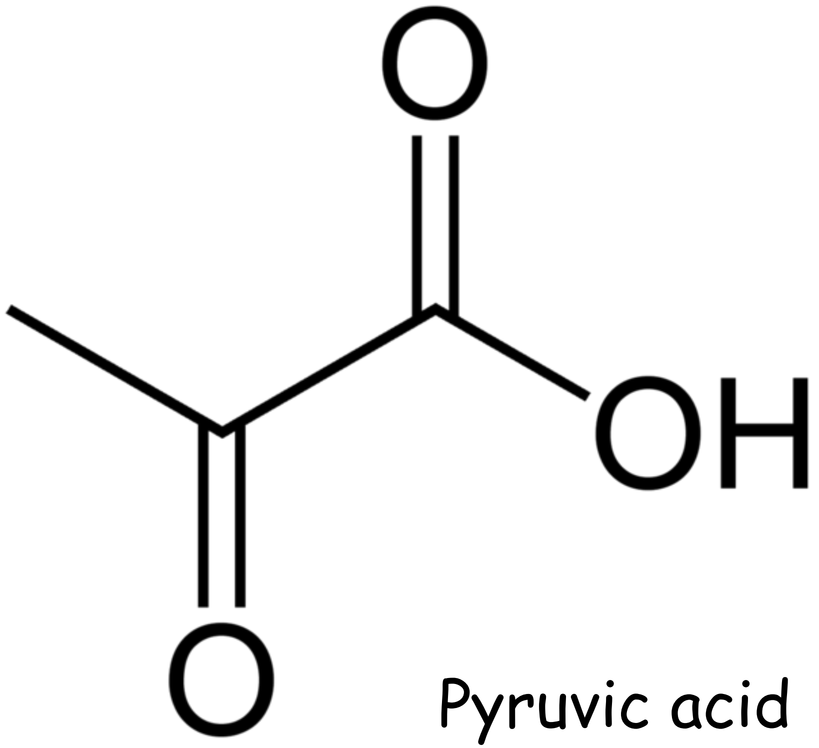
Left: after 1sec ; Right: after 3sec;

Material: Pyruvic acid

Pyruvic acid

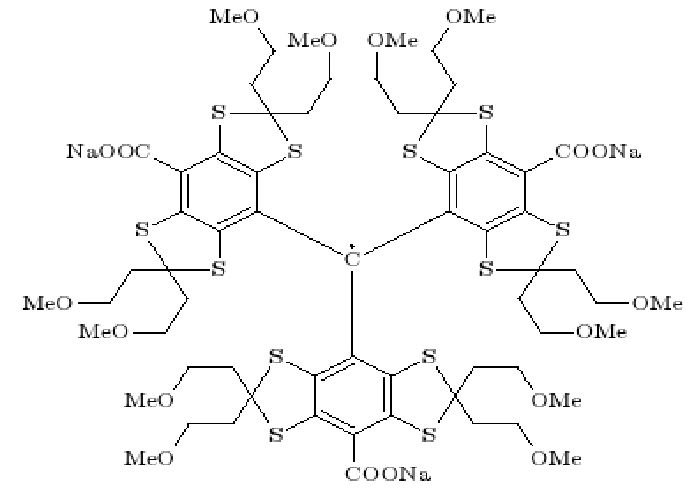
(Brenztraubensäure)

- Pyruvic acid (CH3COCO2H) is an alpha-keto acid
- Pyruvate plays an important role in biochemical processes.
- The carboxylate anion of pyruvic acid is known as pyruvate.



Pyruvic acid

Polarization measurements with pyruvic acid-2-^{13}C-d3

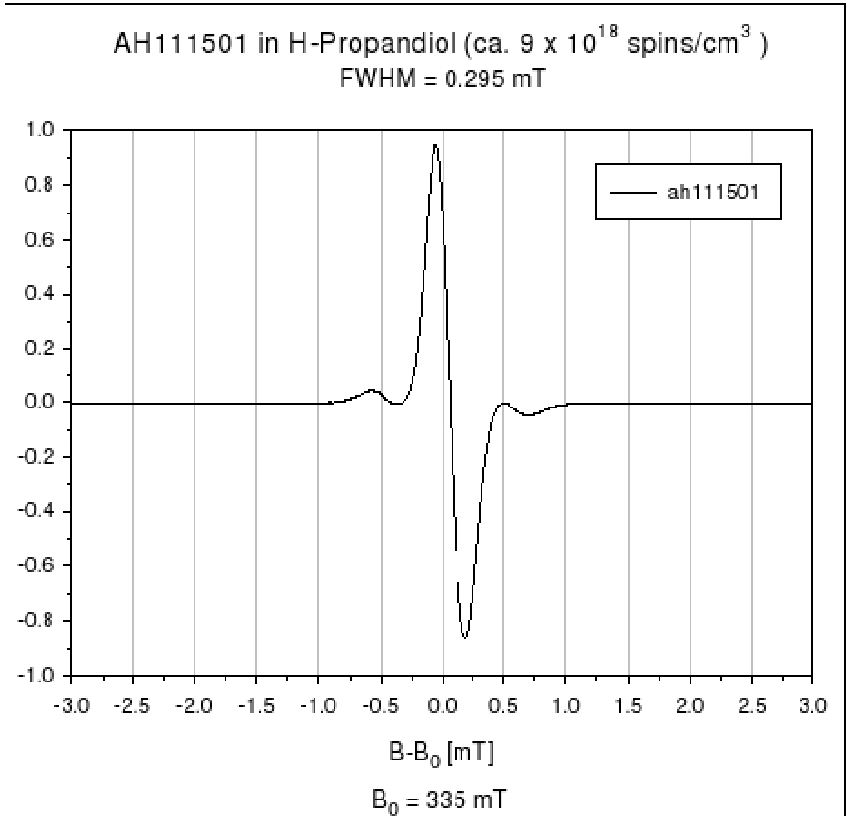


- labelled with ^{13}C and D
- Doped (~10^{19} e-/cm^3) with trityl radical AH111501
  - spin less nucleus shielding the paramagnetic center
  - symmetrical setup
  - ➔ narrow EPR-Line
- Measurement with tree nuclei

➔ Spin temperature theory

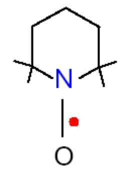
➔ Sold-State-Effect

➔ …

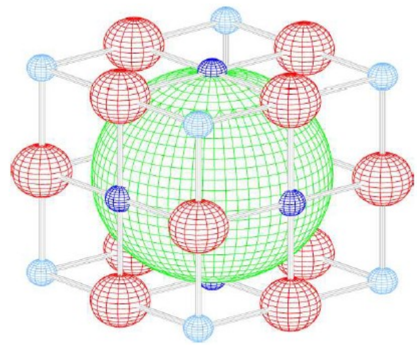


EPR lines of different radicals

TEMPO



^{6}LiD

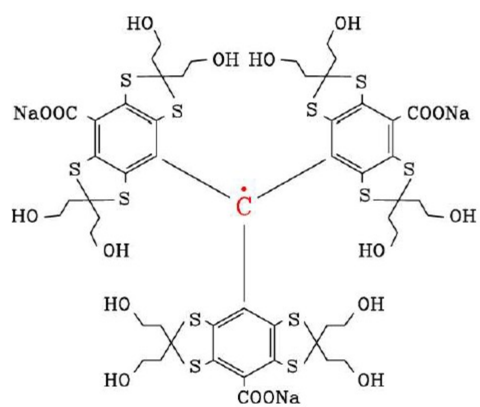


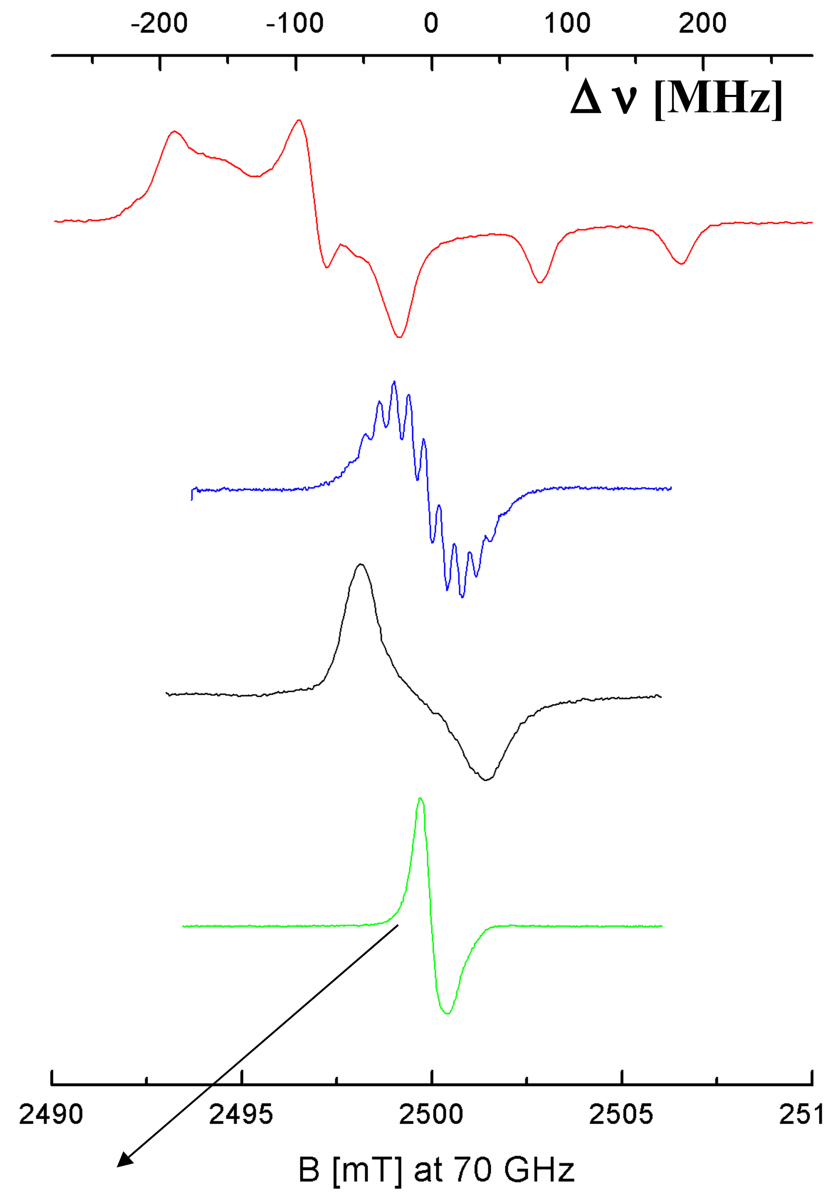
or

butanol

$(C_4D_8)OD$

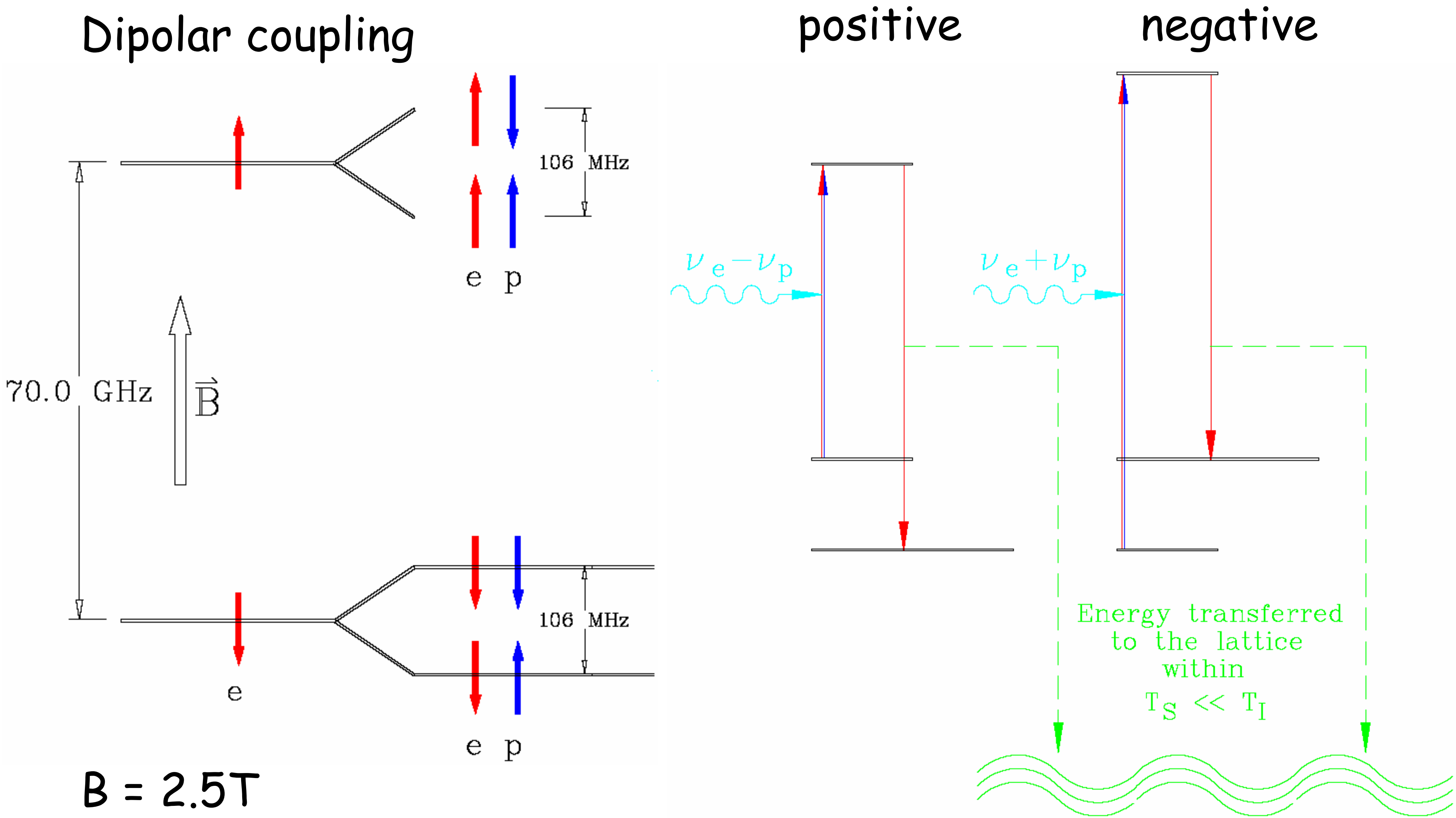
trityl radical





Width ≈ 0.7 mT ≙ 19 MHz ⇒ $\Delta g/g \approx 1.8 \cdot 10^{-4}$

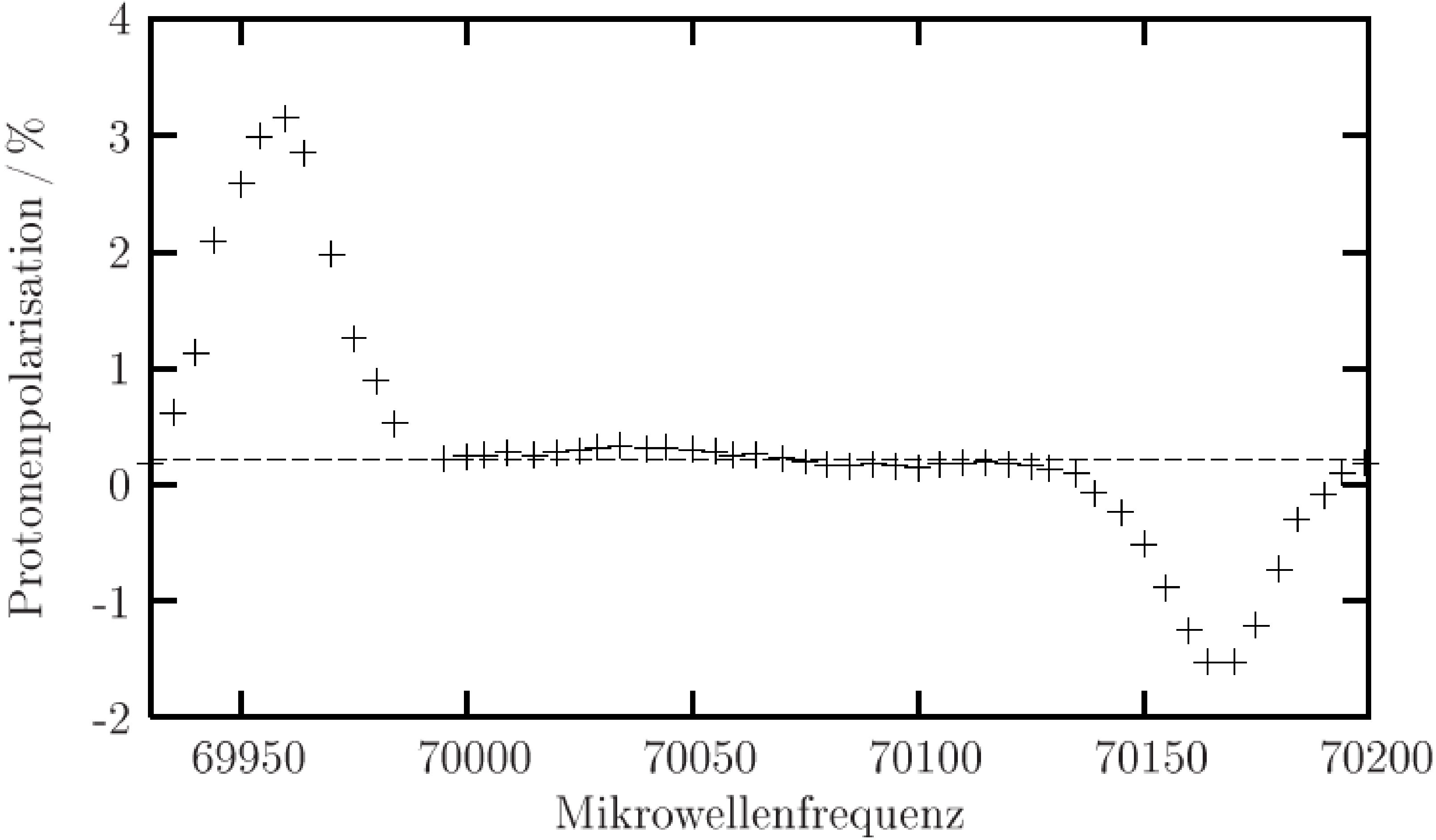
Radical for DNP Solid State Effect



B = 2.5T

Radical for DNP

μ - frequency scan for protons in trityl doped propandiol



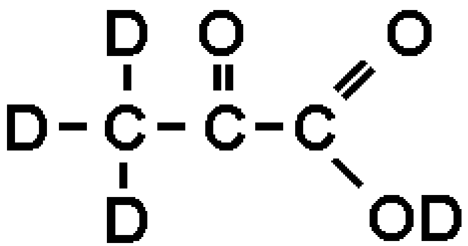
- Solid state effect

Deuterated Pyruvic Acid I

The lineshape covers two signals from the two bonds

- splitting up because of electric field-gradient along the bond

But:

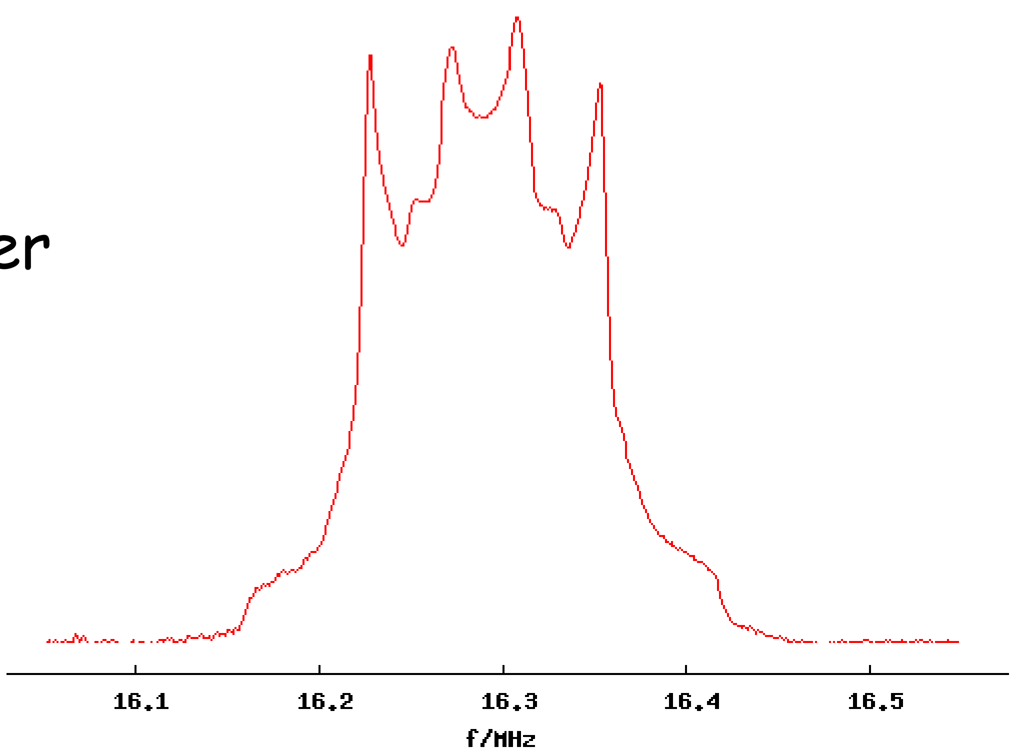


- Inner signal: D-O Bond? Splitting: ~ 40 kHz
- Outer signal: D-C Bond Splitting: ~ 110 kHz
- Area ratio:

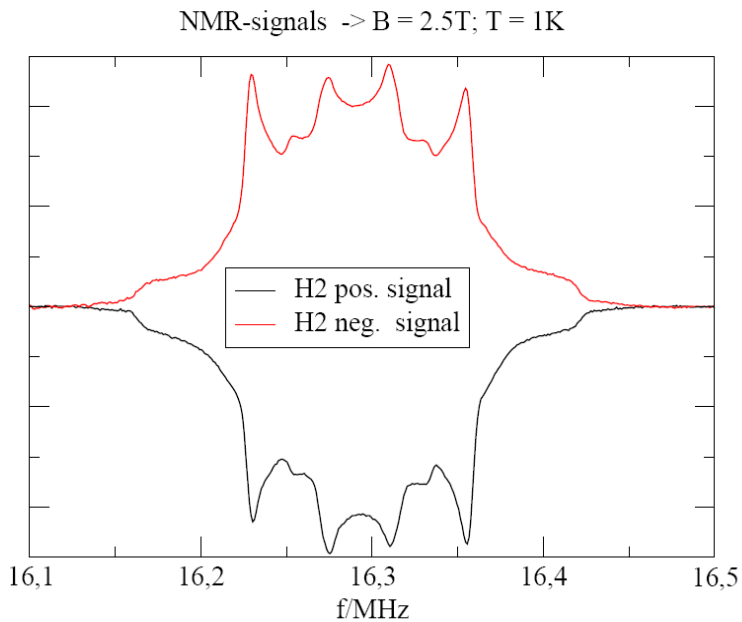
  4,46 : 1 ≠ 3 : 1

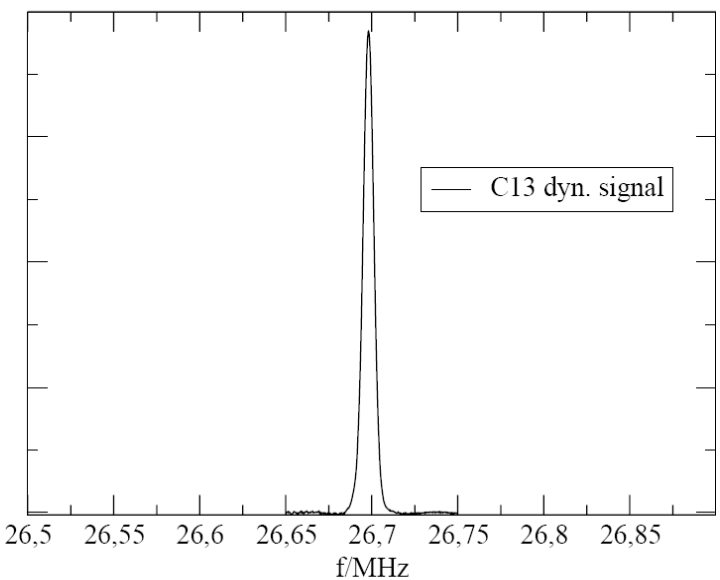
- peak ratio of the inner and outer signals is inverted

  ➔ Field gradient with other sign as for the D-O bond



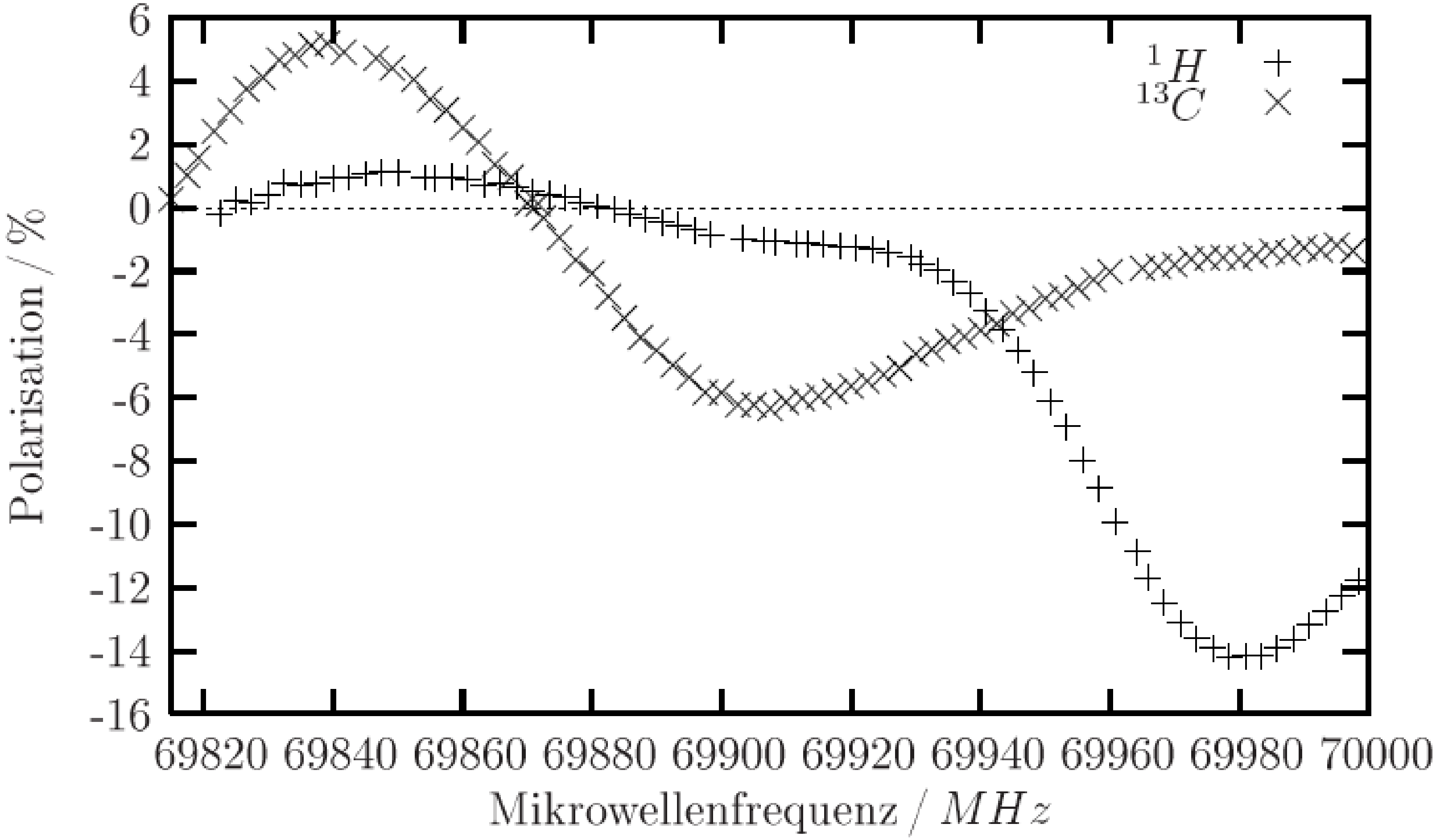
Deuterated Pyruvic Acid II





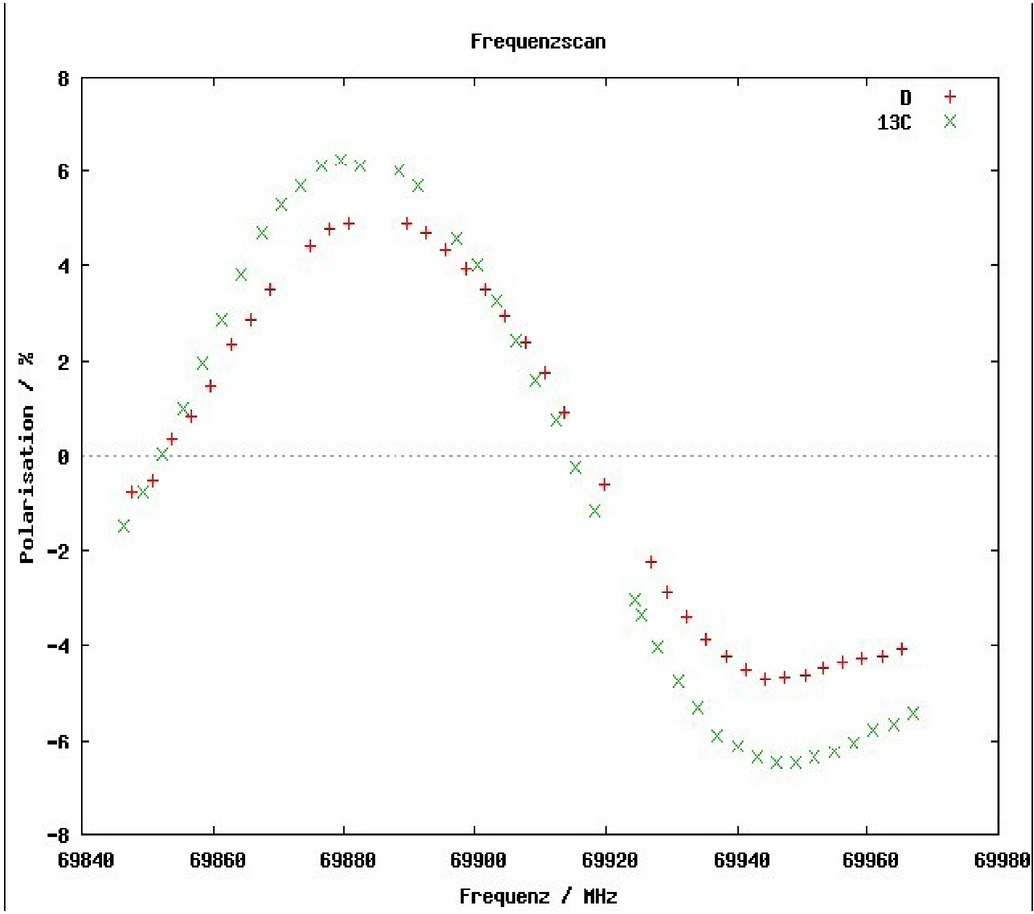
- dynamic signals from D and ^{13}C at T = 1K and B = 2.5 T
- advantage of the ^{13}C: signal is very narrow and therefore relatively high

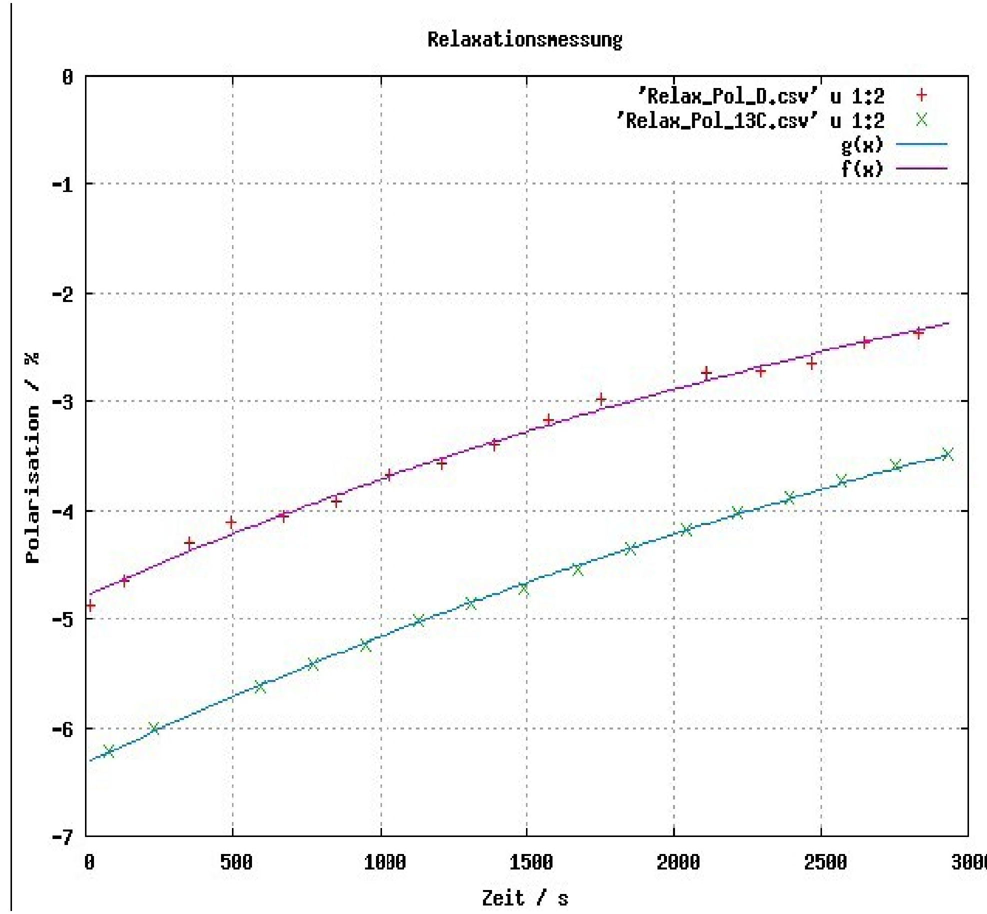
Frequency scan for ^{1}H and ^{13}C



- clear solid state effect for ^{1}H
- thermal mixing for ^{13}C-polarization
- relaxation measurements

Frequency scan for ^{2}H and ^{13}C





Both nuclei polarize with the same μ-wave frequency

- after switching off μ-waves, both nuclei relax independently

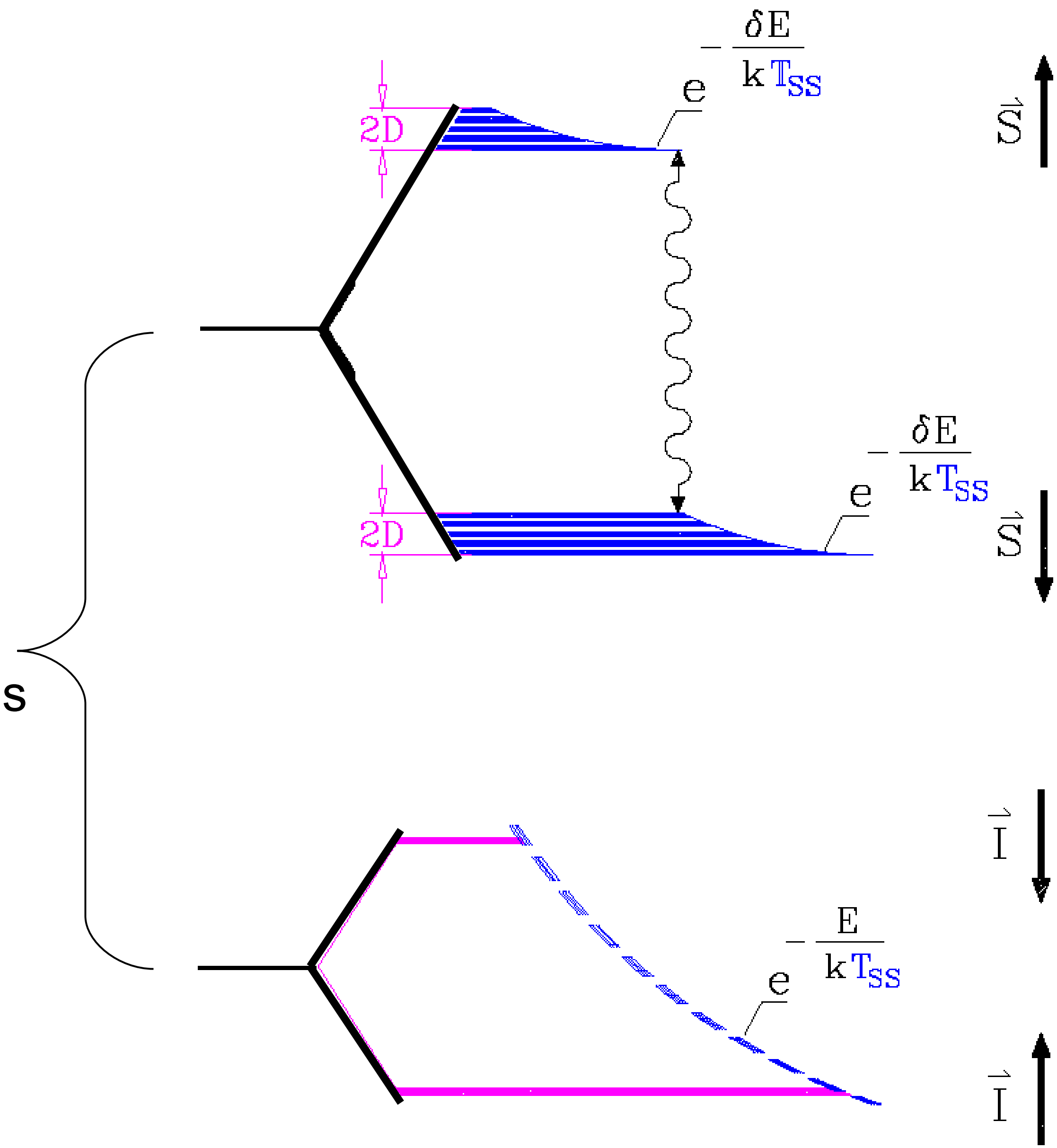
➔ hint on validity of the spin temperature theory

DNP in the Spin Temperature Theory 1

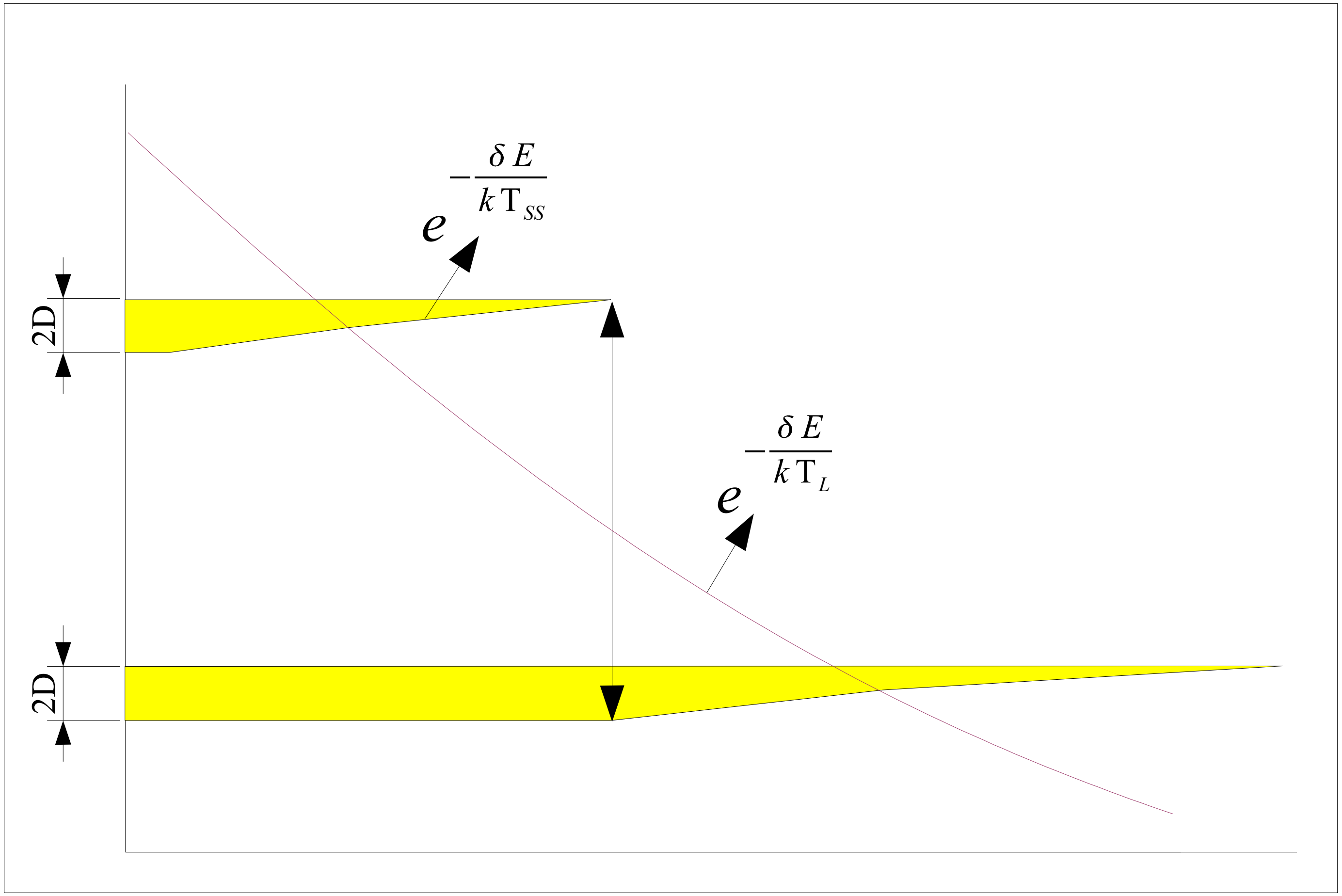
Many electrons
in an external field

$2D \geq h\,\nu_p$
magnetic
electron – nucleus
interaction

Protons
in an external field
$\mu_p = \mu_e/660$



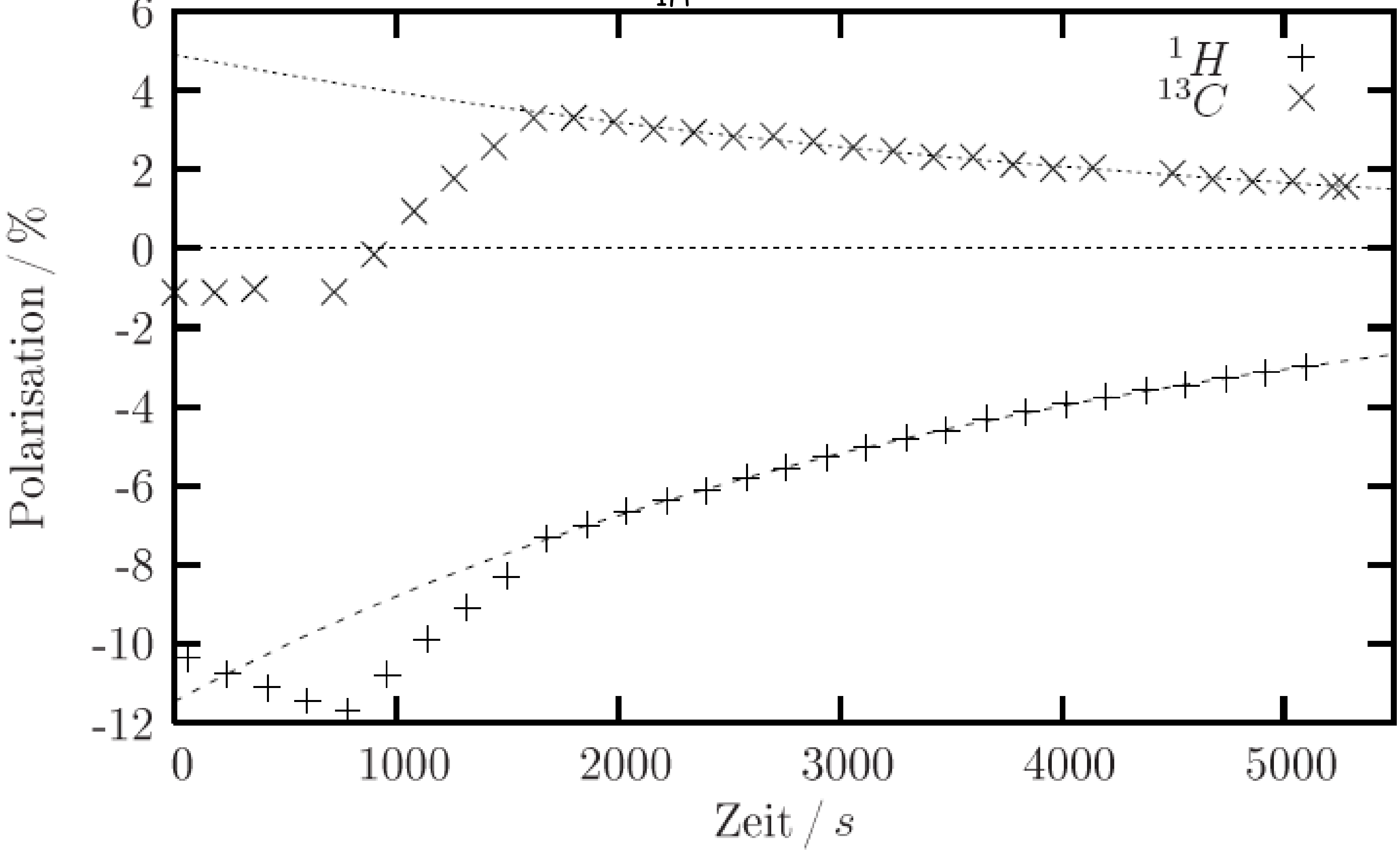
DNP in the Spin Temperature Theory 2



Relaxation times for ^1H and ^{13}C

Relaxation of τ_{13C} = 80 min at T = 1.5 K

Relaxation of τ_{1H} = 63 min at T = 1.5 K



Summary

- Hyperpolarized pyruvic acid with enriched ^{13}C is a very promising contrast medium for MRI

- For DNP optimizations we investigated deuterated pyruvic acid at T=1K and B=2.5T

  - ^{1}H polarization behavior can be described by SSE
  - ^{2}H signal not completely understood
  - ^{13}C and ^{2}H polarization behavior can be described by spin temperature theory