Nuclear Magnetic Resonance and hyperpolarization

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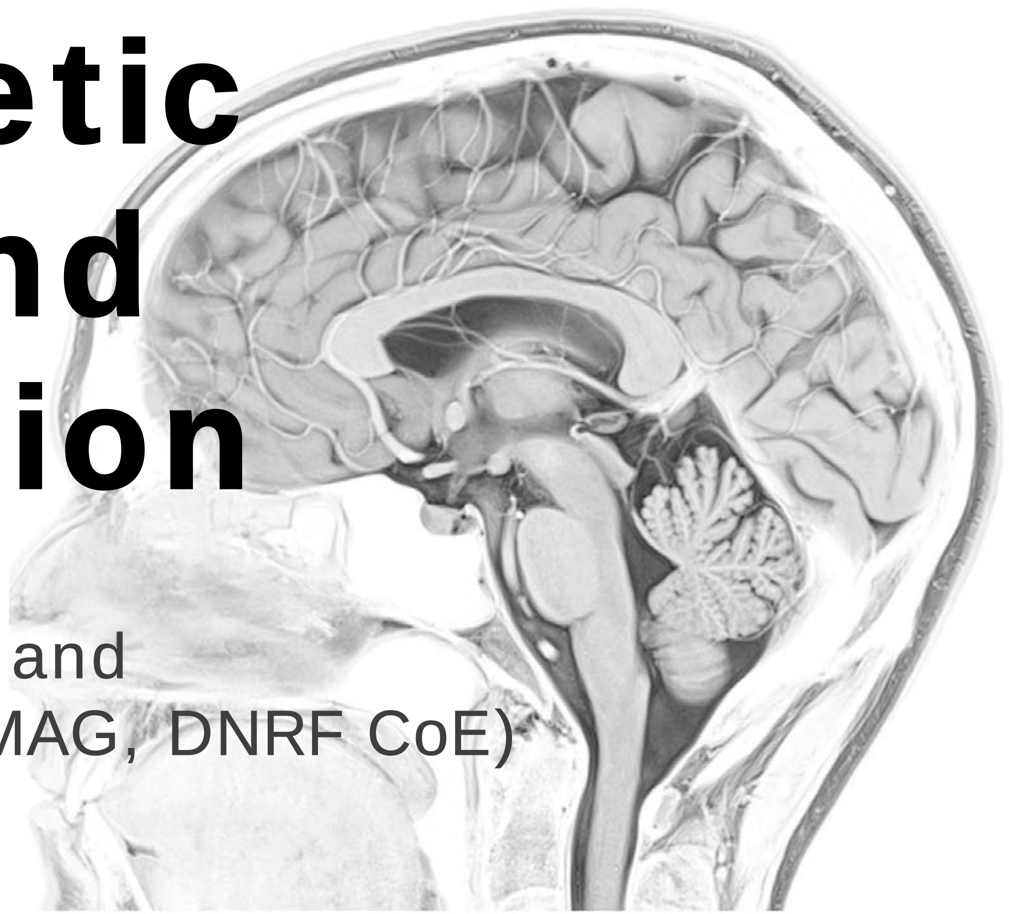

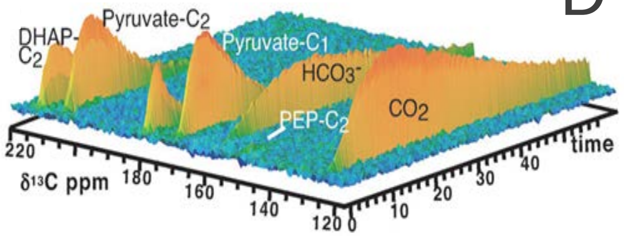

Also affiliated with the DRCMR at
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Center for Magnetic Resonance
DTU Health Tech

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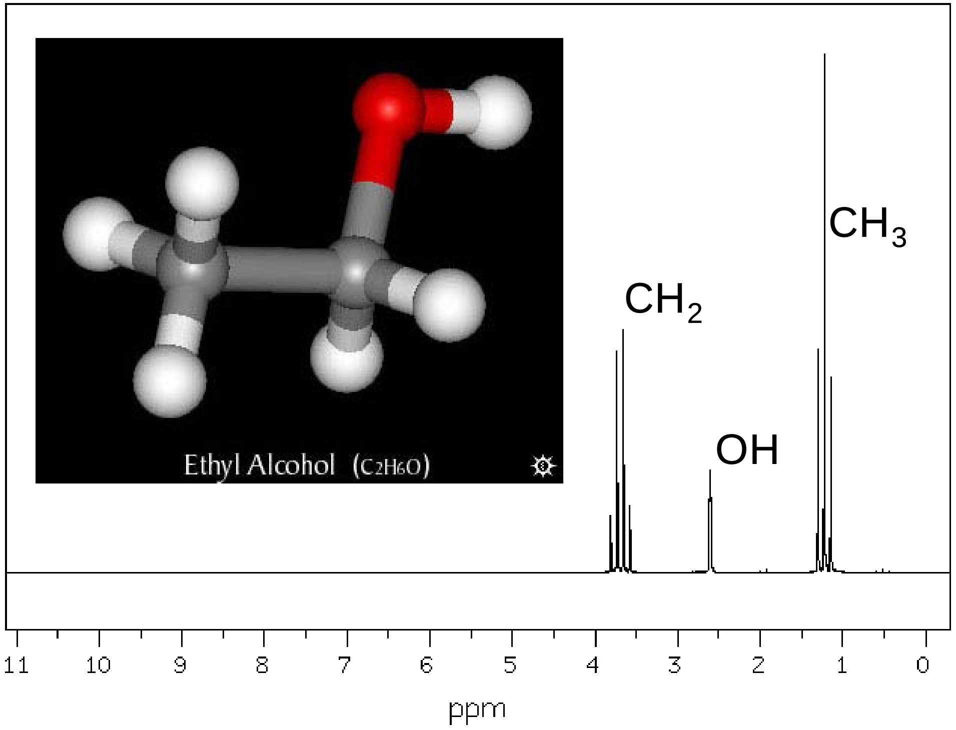
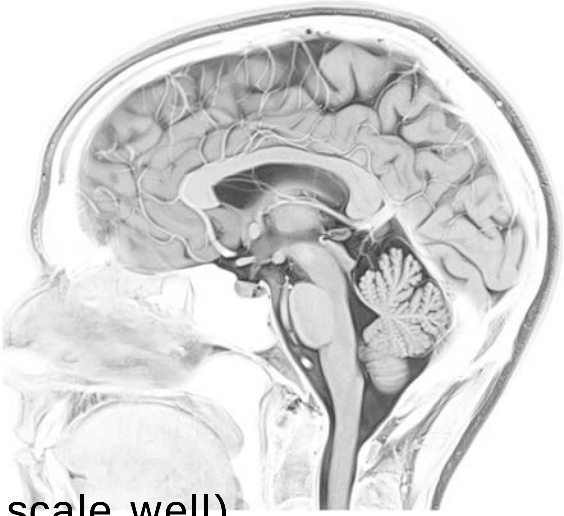
HYPERMAG

Introduction

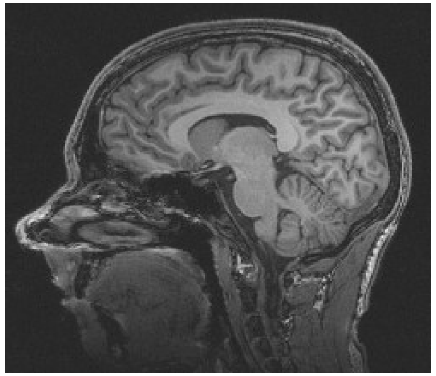
- Widely applied techniques with elements of QM:
  - NMR: Nuclear Magnetic Resonance
    - Widely used for chemical analysis and structure determination.
  - MRI: Magnetic Resonance Imaging
    - Extremely flexible diagnostic technique used at all major hospitals.
  - Hyperpolarized MR:
    - Enhancing the NMR and MRI signals by factor ~100.000 compared to normal NMR in some situations.
- Motivation for inclusion in a QM summer school:
  - Prototypical QM systems, e.g. 2-level dynamics explains all MRI.
  - Classical description fares amazingly well and gives insight.
  - Cross-over techniques, e.g. spin-echo sequences and formalism.
  - Accessible QM manipulation, e.g. for quantum computing (doesn't scale well).

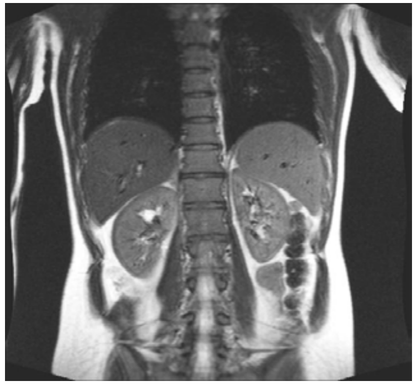




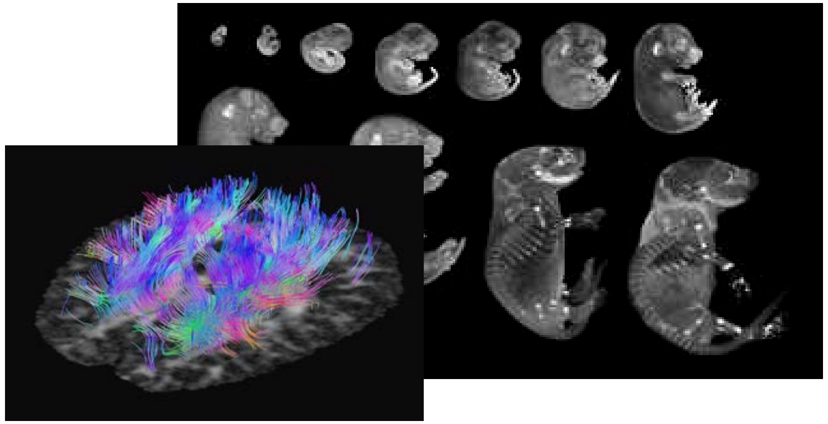
Magnetic Resonance Imaging and Spectroscopy (MRI, NMR)

Macrostructure:

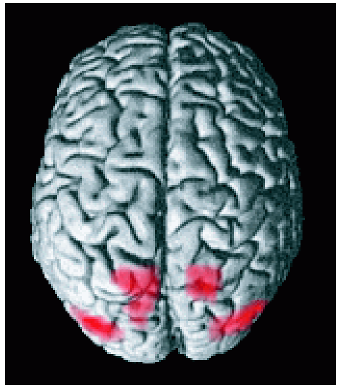




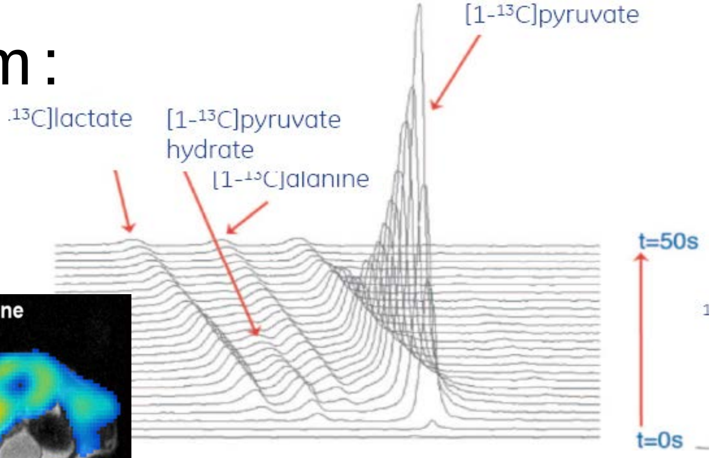
Microstructure:

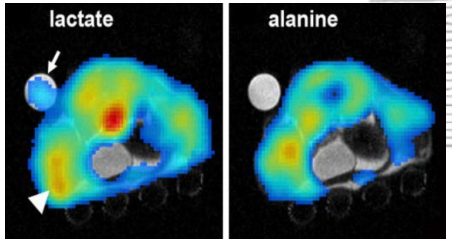


Function:



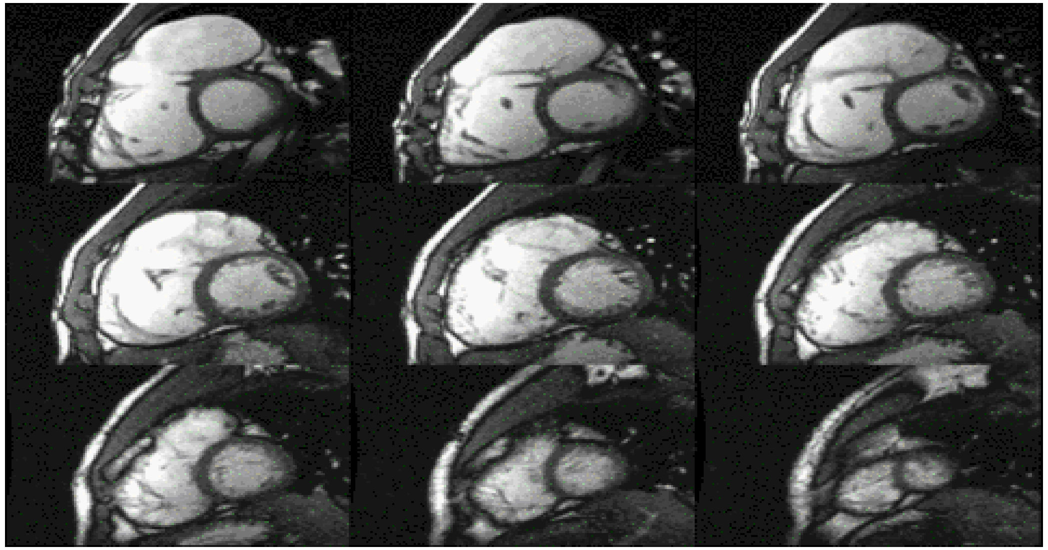
Metabolism:



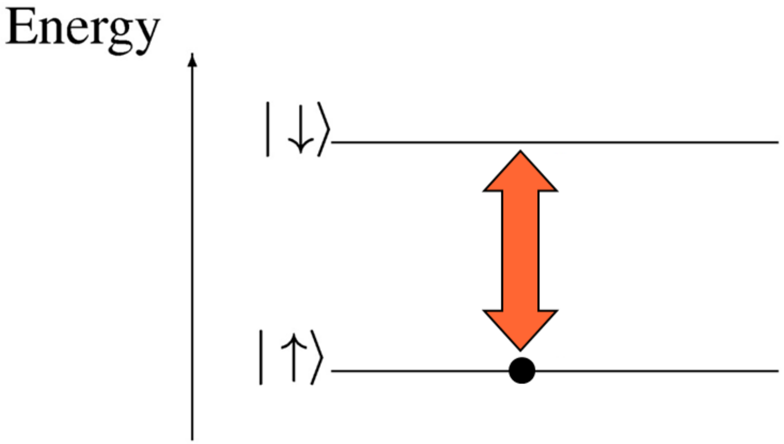


MRI characteristics

- Extremely flexible:
  - all body parts
  - all orientations
  - Many contrast mechanisms:
    - Structure/anatomy, flow, diffusion, metabolism, pH, thinking,...
- Safe, non-invasive: No radiation or side effects
- Limitations:
  - Field inhomogeneity and motion can be problematic.
  - Expensive, demanding, ~mM detection limit
  - Imaging speeds: Milliseconds to minutes.



Cardiac MRI



The flexibility arises from measuring spin systems with extremely long coherence times, typically around 100ms !

MR imaging and spectroscopy

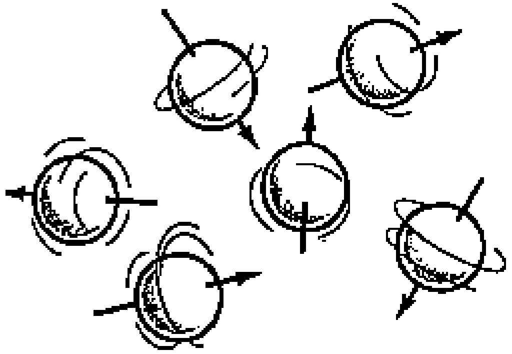
- Ingredients:
  - Strong magnetic field, e.g. 3T *in vivo*
  - radio waves, e.g. 120 MHz
  - sample with magnetic nuclei
    - preferably spin ½

Spectrometers at DTU Chemistry

MR scanner at Hvidovre Hospital

Spin basics

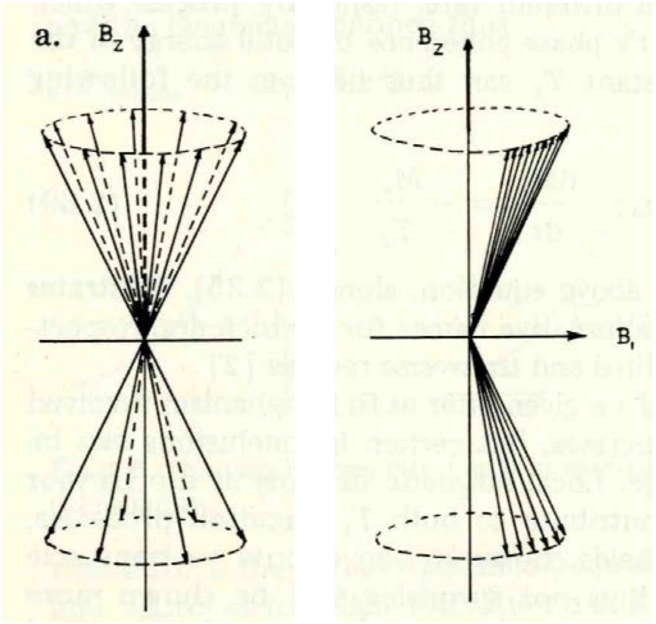
- Hydrogen nuclei (protons) have spin that makes them magnetic. In absense of field, directional distribution is uniform.

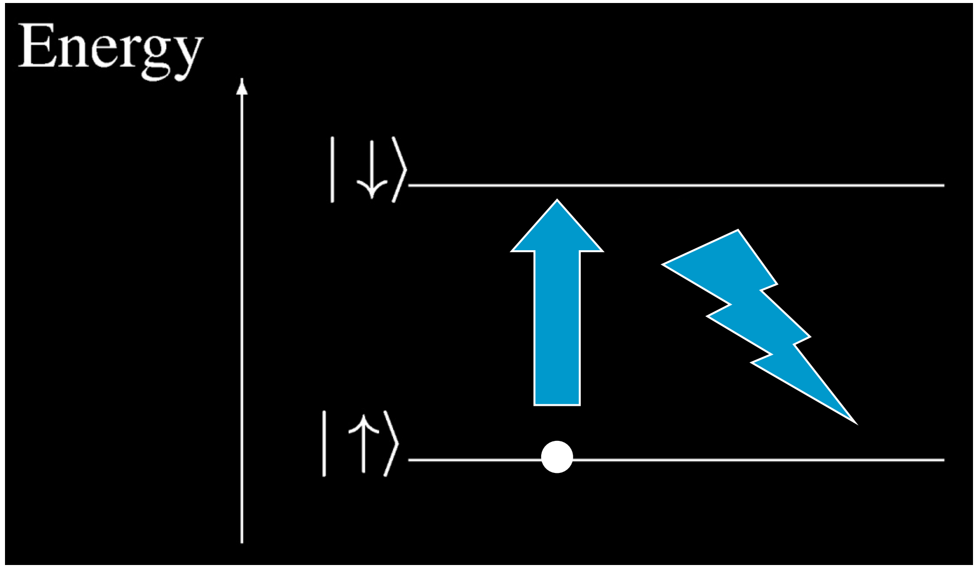


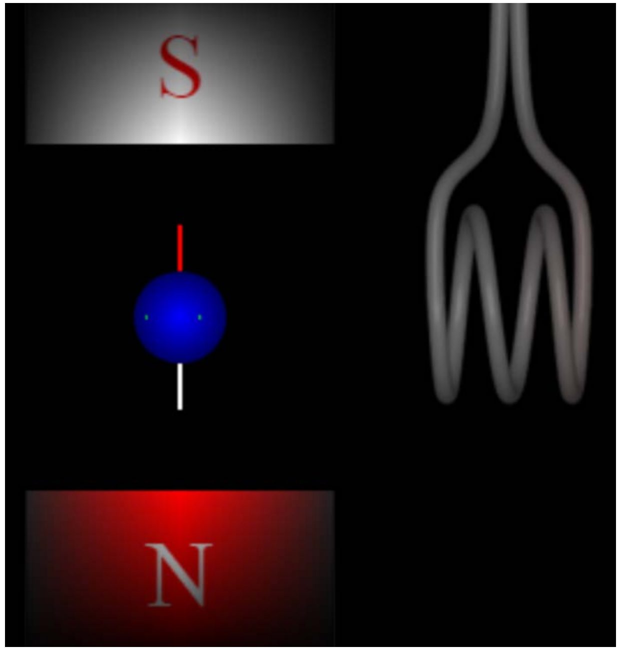
- This picture has severe flaws that are not important for NMR. I'll go with it.
- It gives you predictive power despite being wrong.
- Spin ½ nuclei largely behave like charged rotating balls.

Magnetic resonance - a typical explanation

- In absense of field, the directional distribution is uniform.
- When a magnetic field **B_0** is applied, QM tells us that nuclei will align parallel or anti-parallel with the field.

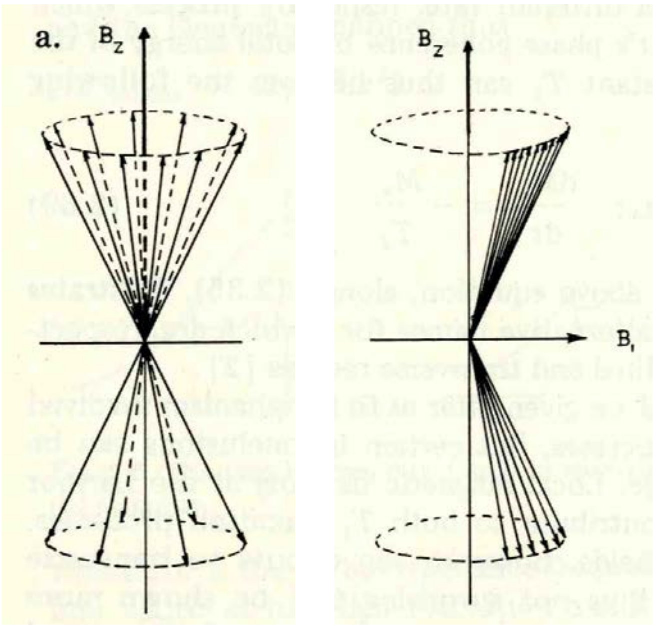


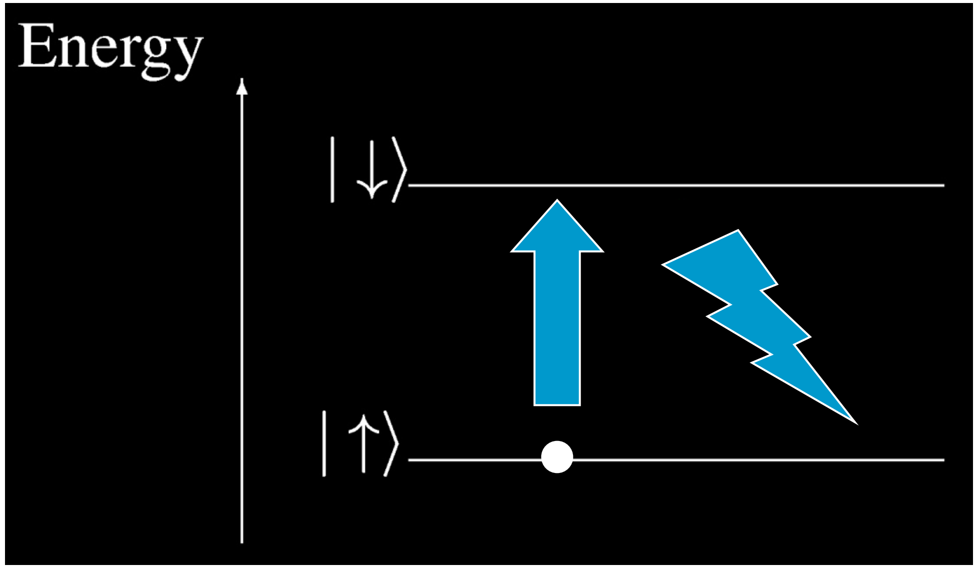




- Nice and simple,... and largely **wrong** (unsuported by QM). It opens more questions than it answers.

Problems?





Exam questions from hell:

- Why would almost half the nuclei align *anti-parallel* to the field?
  - The least expected orientation classically.
- Are nuclei forced into ”cone states” instantly? Field strength needed?
- How can radio waves limit the angular spread?
- Can radio waves change the magnetization size? It seems so.
- Why don’t spin flips just equalize populations?
- Why doesn’t inversion maximize the signal?

This model needs fixing!

Origins of common misconception

Well-known aspects of QM:

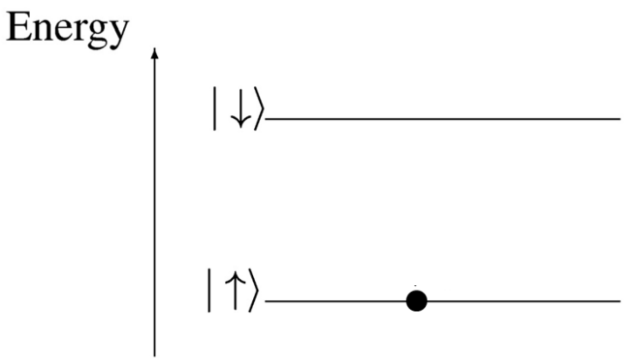
–Microscopic systems such as atoms can only exist in discrete states with specific energies.

–Transitions between these states happen in sudden “quantum jumps” and involve exchange of energy.

–The timings of the jumps are truly unpredictable.

Sorry, this is highschool QM. So 1913. Go modern!

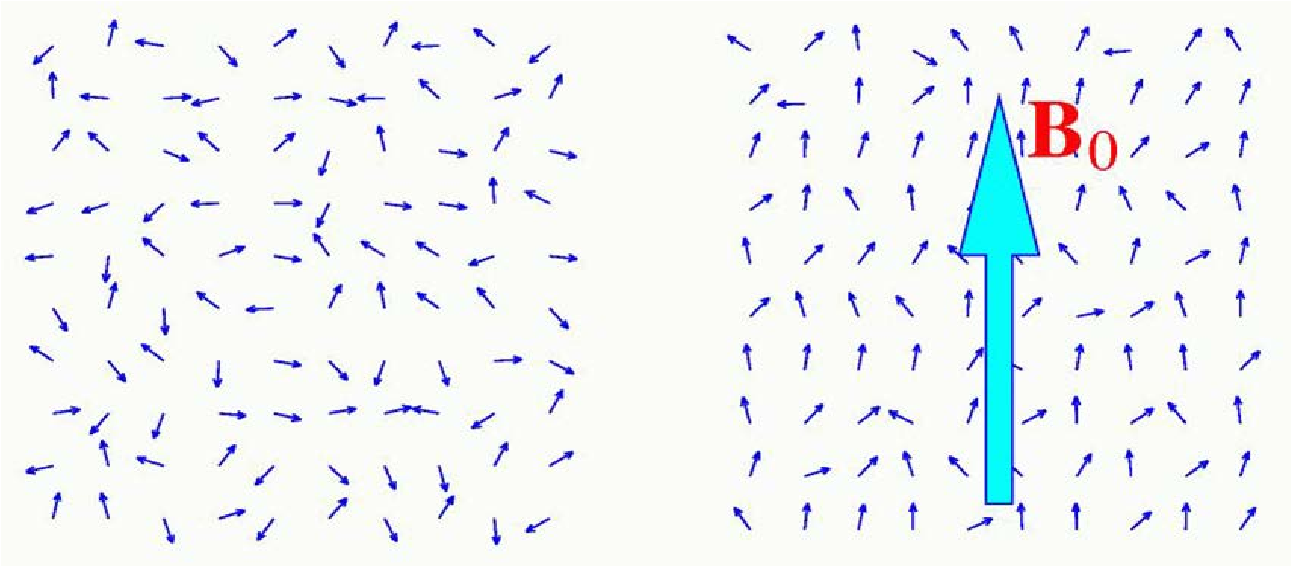
Take 2: Polarization – QM and classical



- Boltzmann:

$$P_\uparrow = \frac{\exp(-E_\uparrow/kT)}{\exp(-E_\uparrow/kT) + \exp(-E_\downarrow/kT)} = \frac{\exp(\hbar\gamma B_0/2kT)}{\exp(\hbar\gamma B_0/2kT) + \exp(-\hbar\gamma B_0/2kT)}$$

$$\langle \mu_z \rangle = \frac{\hbar\gamma}{2}(P_\uparrow - P_\downarrow) \simeq \frac{\hbar^2\gamma^2 B_0}{4kT}$$



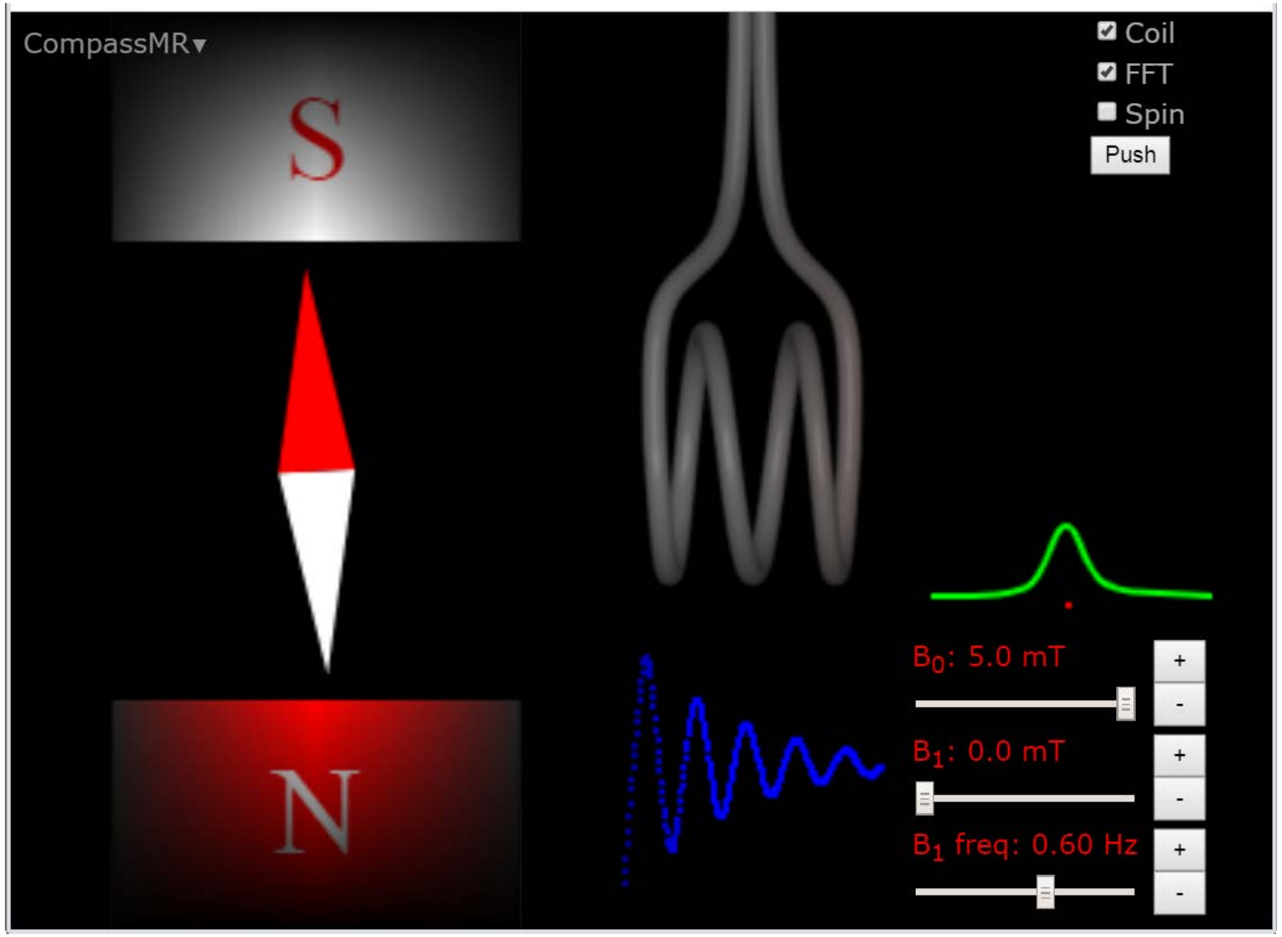
Classical derivation:
- Spin is taken for granted: $\mu = \sqrt{3/4}\hbar\gamma$
- Boltzmann:

$$P(\theta) = \frac{\exp\left(-E(\theta)/kT\right)}{\int_0^\pi \exp\left(-E(\theta)/kT\right)\sin\theta \, d\theta}$$

$$\begin{aligned}\langle \mu_z \rangle &= \int_0^\pi P(\theta)(\mu\cos\theta)\sin\theta\, d\theta \\ &= \mu\frac{\int_{-1}^{1}\exp(\mu B_0 u/kT)u\, du}{\int_{-1}^{1}\exp(\mu B_0 u/kT)\, du} \simeq \frac{\hbar^2\gamma^2 B_0}{4kT}\end{aligned}$$

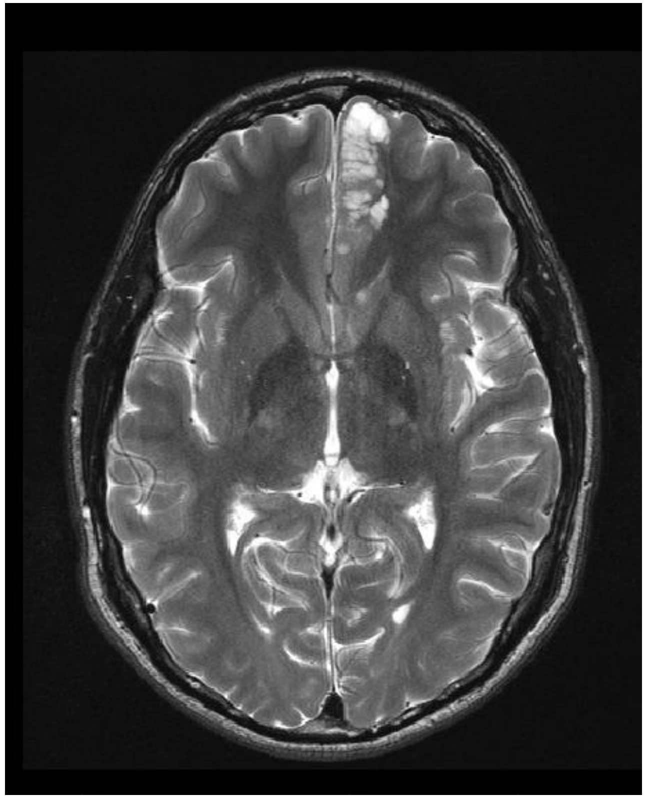
Even for fields of several tesla, the eq. polarization is ppm!

Next step: Compass Magnetic Resonance



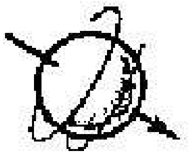
http://drcmr.dk/CompassMR or similar Android app

Compass MR: Very simple, yet powerful

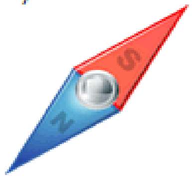


- Interpreting MRI intensities:
  - High intensity: The corresponding ”compass needle” vibrated much when the signal was measured.
  - This was done some time after excitation (TE)….
    - …during which, the motion was damped more or less.
      - more attenuation in brain tissues, less in fluid.
  - Only one relaxation time for a compass.
  - Signal is from more nuclei, so two for samples.
    - T1: Time constant for return to equilibrium.
    - T2: Time constant for dephasing caused by field variation.
- But atomic nuclei move differently from compass needles due to angular momentum.

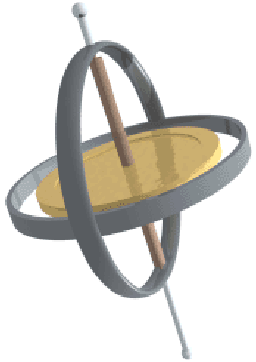
Classical equation of motion for nuclear spin

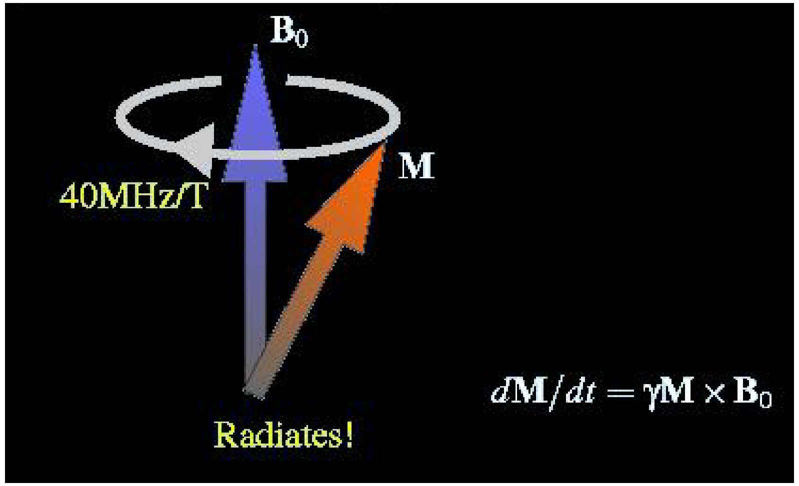


- The magnetic moment is proportional to the spin angular momentum: $\boldsymbol{\mu} = \gamma \mathbf{J}$
- The angular momentum changes when a torque is applied: $d\mathbf{J}/dt = \boldsymbol{\tau}$
- The magnetic field exerts a torque on the nuclei: $\dfrac{d\mathbf{J}}{dt} = \boldsymbol{\mu} \times \mathbf{B}$



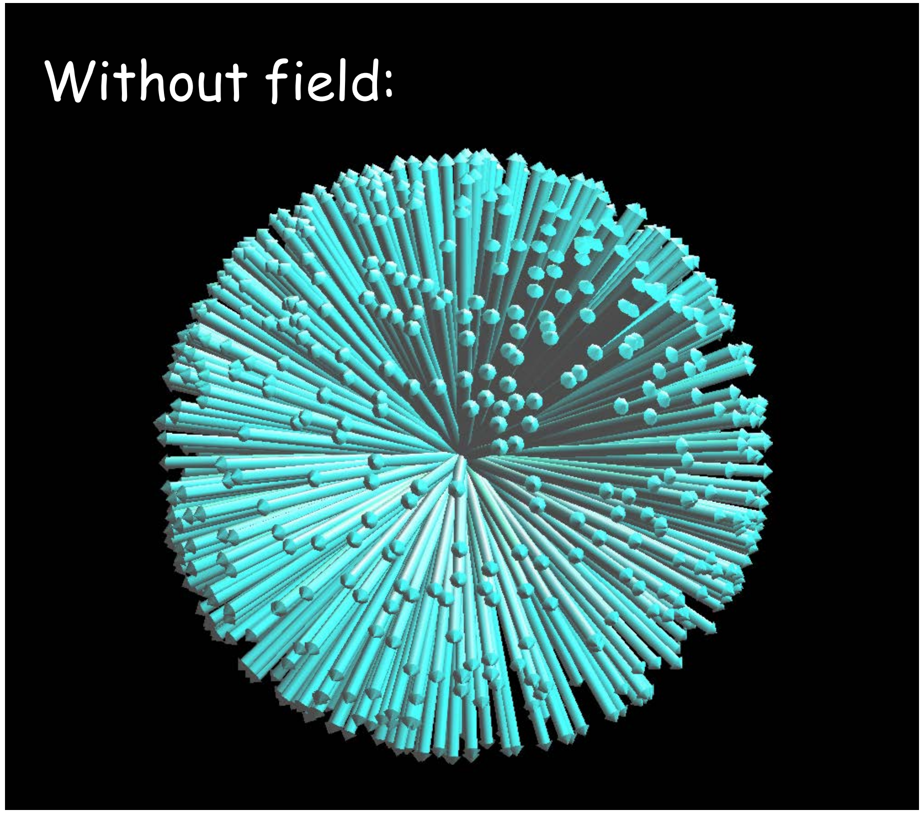
- The resulting equation of motion for a nuclear magnetic moment: $\dfrac{d\boldsymbol{\mu}}{dt} = \gamma \boldsymbol{\mu} \times \mathbf{B}$
- This describes precession of the magnetic moment around the magnetic field:

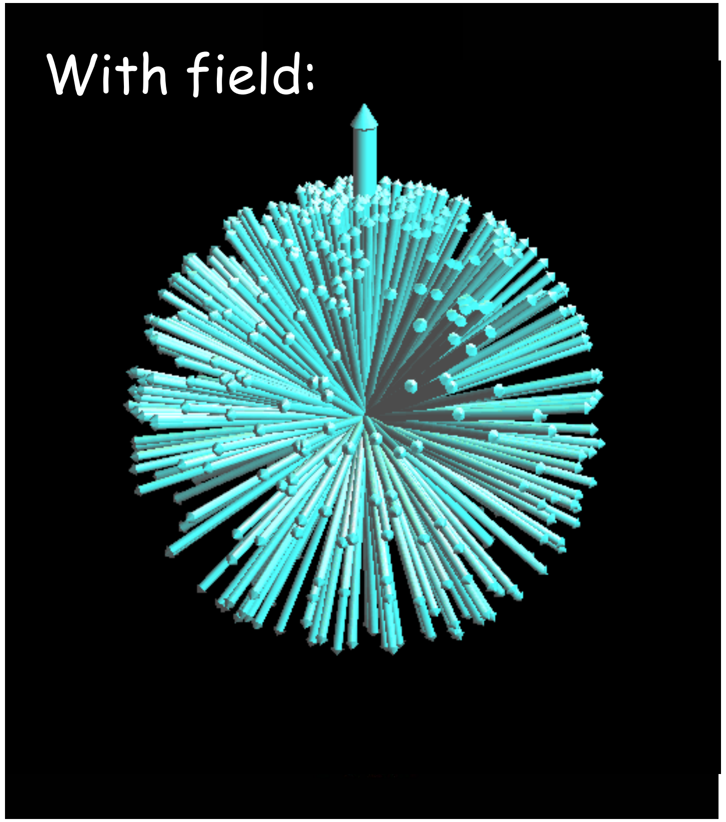




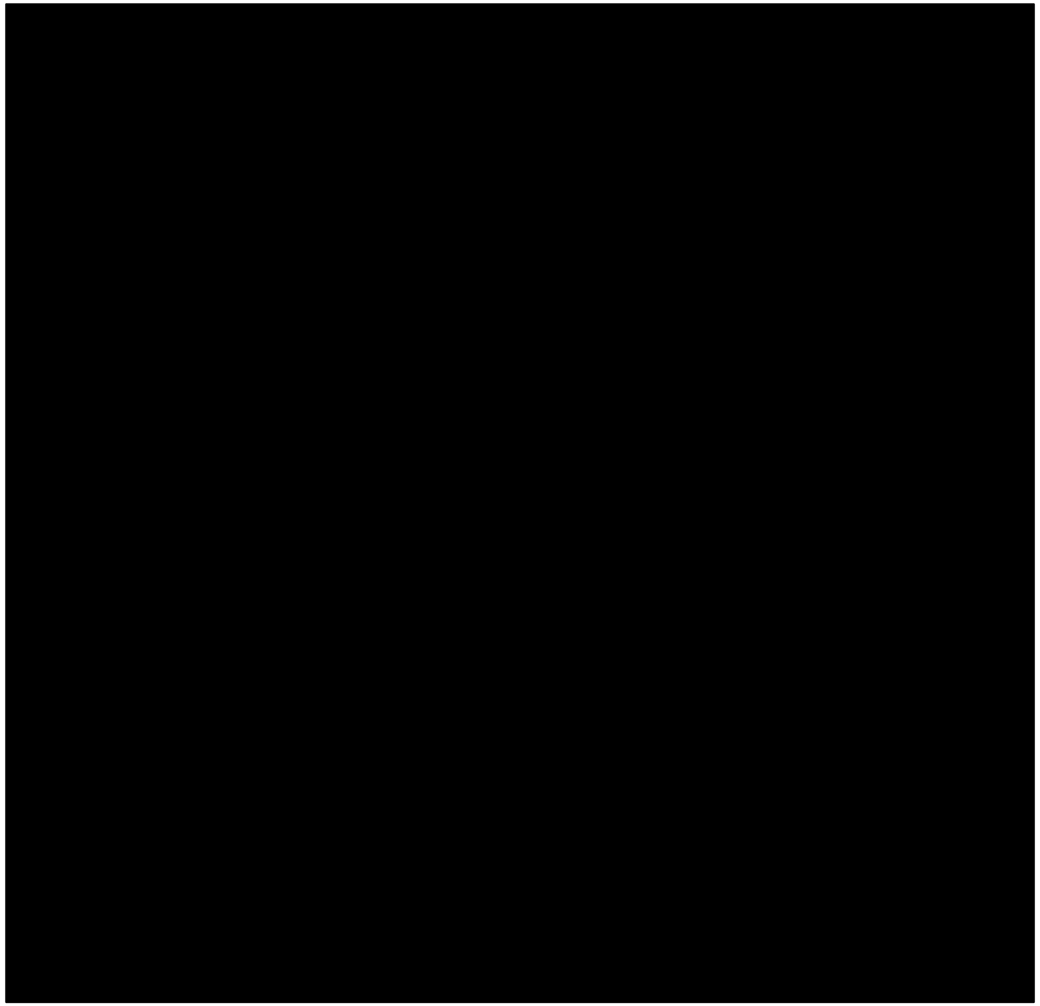
Classical polarization

- Spin distribution is uniform in absence of field:
- Spin distribution is skewed in presence of field:



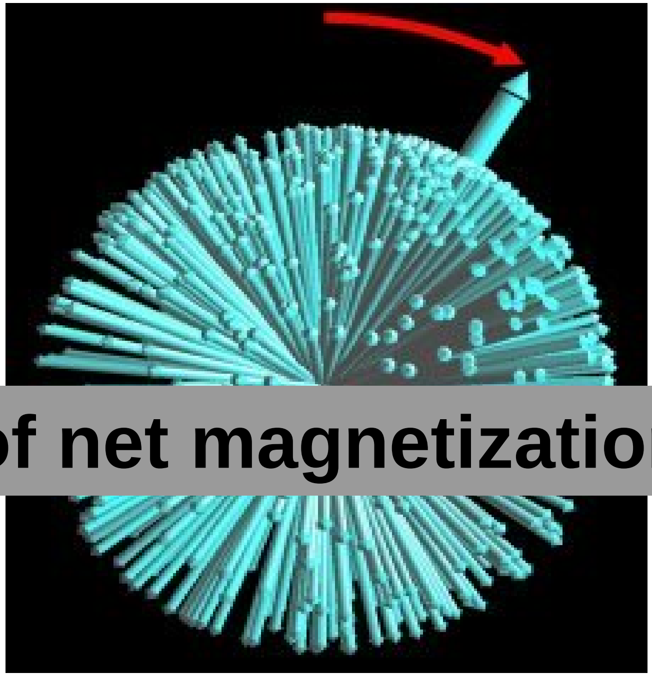


The field causes alignment, while nuclear interactions randomize orientations.



The classical expectation

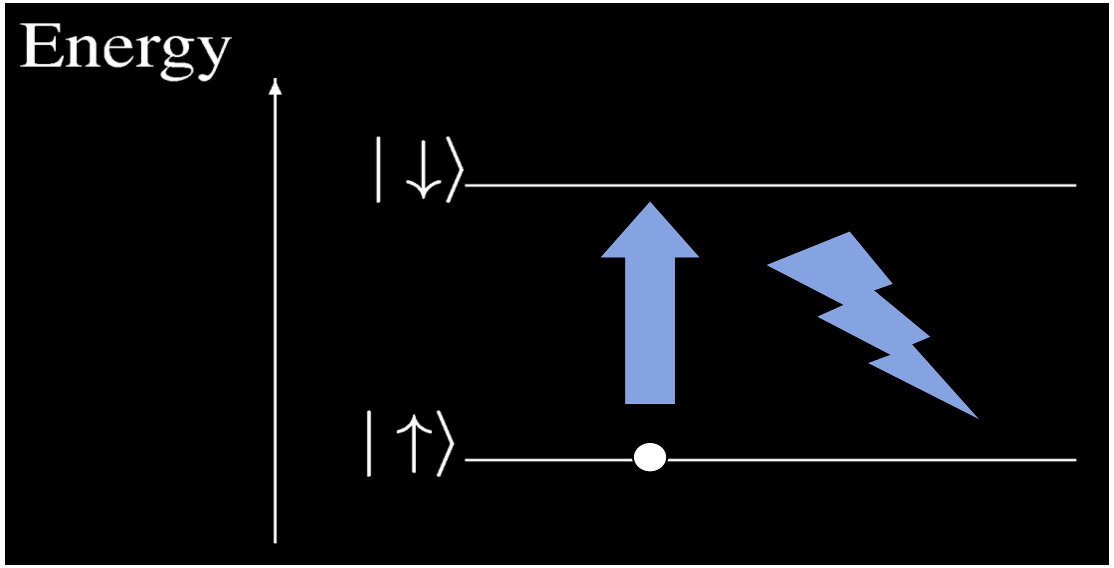
- Precession around the instantaneous field. Hence relative spin orientations are preserved by homogeneous fields.
- On resonance example:
  - No precession around $\mathbf{B_0}$ in the rotating frame of reference.
  - Precession happens around stationary B1.



Sufficient to keep track of net magnetization!

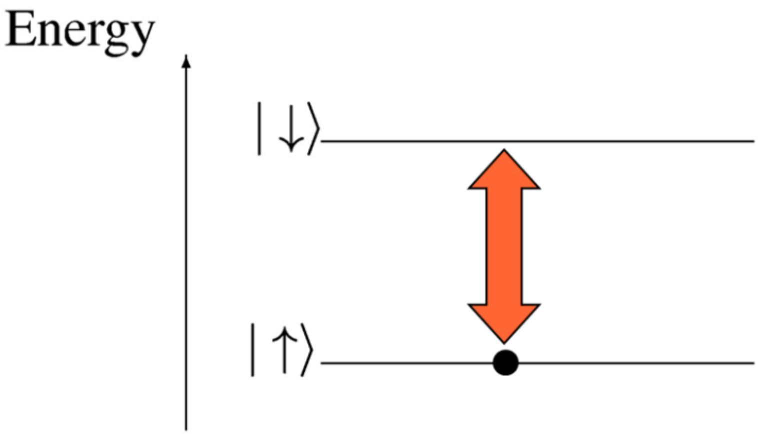
Reconciliation?

- The relation between the descriptions?



  - For simple NMR, the two descriptions can be made very similar. Both are valid after introducing coherent interaction!

QM description of MR



Meaningful, if you realize that this picture describes vector dynamics.

General state is a superposition:

$$|\psi\rangle = a|S_z = ½\rangle + b|S_z = -½\rangle$$

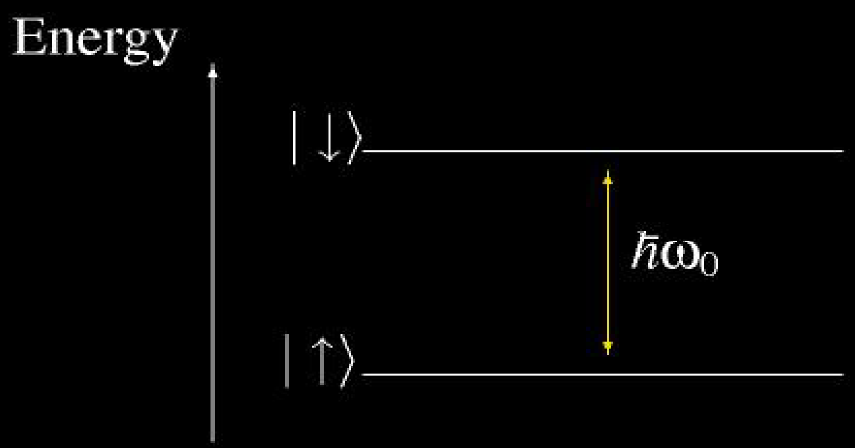
Any basis wil do. Same degrees of freedom as classical dipole.

The density operator formalism

The density operator for a pure state:

$$\rho \equiv |\psi\rangle\langle\psi|$$

- A useful alternative to the wave vector.
- Diagonal elements express populations.
- Off-diagonal express coherence.



Density operator for an ensemble

$$\rho \equiv \sum_n (|\psi\rangle\langle\psi|)_n$$

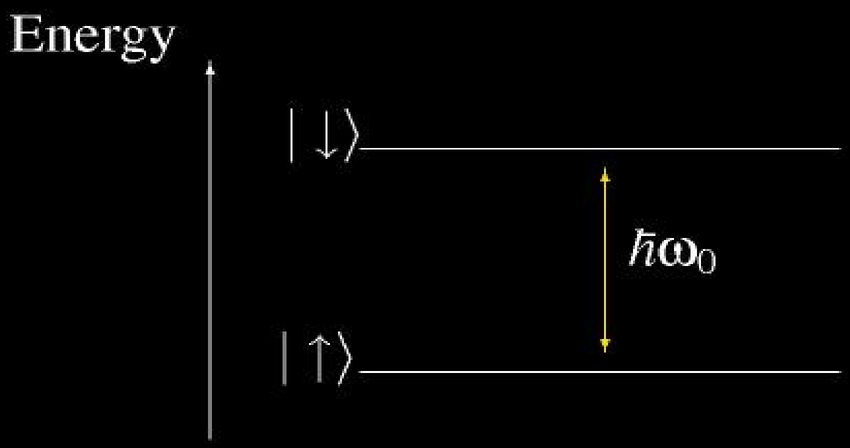
Expectation value of an operator

$$\langle \mathbf{A} \rangle = \mathrm{Trace}(\mathbf{A}\rho)$$

Evolution described by the Liouville equation:

$$i\hbar\frac{\partial\rho}{\partial t} = [H, \rho]$$

A two-level system



Density operator:

$$\rho = \begin{pmatrix} \rho_{\uparrow\uparrow} & \rho_{\uparrow\downarrow} \\ \rho_{\downarrow\uparrow} & \rho_{\downarrow\downarrow} \end{pmatrix}$$

Populations change on timescale T1:

$$\rho_{\uparrow\uparrow} = \langle\uparrow|\psi\rangle\langle\psi|\uparrow\rangle = P_{\uparrow}, \qquad \rho_{\downarrow\downarrow} = P_{\downarrow}, \qquad P_{\uparrow} + P_{\downarrow} = 1$$

Coherences decay on timescale T2:

$$\rho_{\uparrow\downarrow} = \langle\uparrow|\psi\rangle\langle\psi|\downarrow\rangle \qquad \rho_{\downarrow\uparrow} = \rho^*_{\uparrow\downarrow}$$

Operators

Raising, lowering and magnetic moment operators:

$$S_+ = S_x + iS_y, \qquad S_- = S_x - iS_y$$

$$\mu_x = \frac{\hbar\gamma}{2}(S_+ + S_-) = \frac{\hbar\gamma}{2}\begin{pmatrix} 0 & 1 \\ 1 & 0 \end{pmatrix}$$

$$\mu_y = \frac{\hbar\gamma}{2i}(S_+ - S_-) = \frac{\hbar\gamma}{2i}\begin{pmatrix} 0 & 1 \\ -1 & 0 \end{pmatrix}$$

$$\mu_z = \frac{\hbar\gamma}{2}S_z = \frac{\hbar\gamma}{2}\begin{pmatrix} 1 & 0 \\ 0 & -1 \end{pmatrix}$$

$$\langle \mu_x \rangle = \mathrm{Trace}(\mu_x \rho) = \frac{\hbar\gamma}{2}(\rho_{\downarrow\uparrow} + \rho_{\uparrow\downarrow})$$

Time evolution

Time evolution of the magnetization:

$$\frac{\partial\langle\mu_x\rangle}{\partial t} = \frac{\partial(\mathrm{Tr}(\mu_x\rho))}{\partial t} = \frac{\hbar\gamma}{2i}\left(i\frac{\partial\rho_{\downarrow\uparrow}}{\partial t} + i\frac{\partial\rho_{\uparrow\downarrow}}{\partial t}\right) = \frac{\gamma}{2i}\left([H,\rho]_{\downarrow\uparrow} + [H,\rho]_{\uparrow\downarrow}\right)$$

$$= \frac{\gamma}{2i}\left((H_{\downarrow\uparrow} - H_{\uparrow\downarrow})(\rho_{\downarrow\downarrow} - \rho_{\uparrow\uparrow}) + (\rho_{\downarrow\uparrow} - \rho_{\uparrow\downarrow})(H_{\downarrow\downarrow} - H_{\uparrow\uparrow})\right)$$

Consequently, for $H = -(\mu_x B_x + \mu_y B_y + \mu_z B_z)$:

$$\frac{\partial\langle\mu_x\rangle}{\partial t} = \hbar\gamma^2\left(\frac{-B_y\left(\rho_{\uparrow\uparrow} - \rho_{\downarrow\downarrow}\right)}{2} + \frac{B_z\left(\rho_{\downarrow\uparrow} - \rho_{\uparrow\downarrow}\right)}{2i}\right) = -\gamma B_y\langle\mu_z\rangle + \gamma B_z\langle\mu_y\rangle$$

Cyclic permutation:

$$\frac{\partial\langle\mu\rangle}{\partial t} = \gamma\langle\mu\rangle \times \mathbf{B}$$

Valid even for single nuclei. Measuments on ensembles cause insignificant collapse.

The Bloch vector

- The Bloch vector:
  - Introduced by Feynman, Vernon & Hellwarth, 1957.
  - Showed that QM two-level dynamics can generally be understood in terms of classical MR.
  - The Bloch vector is a QM property inspired by classical MR.
  - A vector in an abstract space that moves as the magnetization vector in real space.
  - Points up for the up state, down for the down state, and can point in any other direction.

- Bottom line: Basic ”classical MR” <u>is</u> quantum mechanics,
  - but not for spin > ½, J-coupling, entanglement,…

The Bloch vector

- Rewrite any superposition as follows:

$$|\psi\rangle = \cos(\theta/2)\,|S_z = ½\rangle + \sin(\theta/2)\exp(i\varphi)\,|S_z = -½\rangle$$

  – The arbitrary overall phase was here fixed.

- Any superposition can be represented by a unit vector with polar angles (θ,φ).

- This is the Bloch vector.
  – It evolves like a classical magnetic dipole.

- Eigenstate for $S_{\theta,\varphi}$:

$$|\theta,\phi\rangle = \cos(\theta/2)\,|S_z = ½\rangle + \sin(\theta/2)\exp(i\varphi)\,|S_z = -½\rangle$$

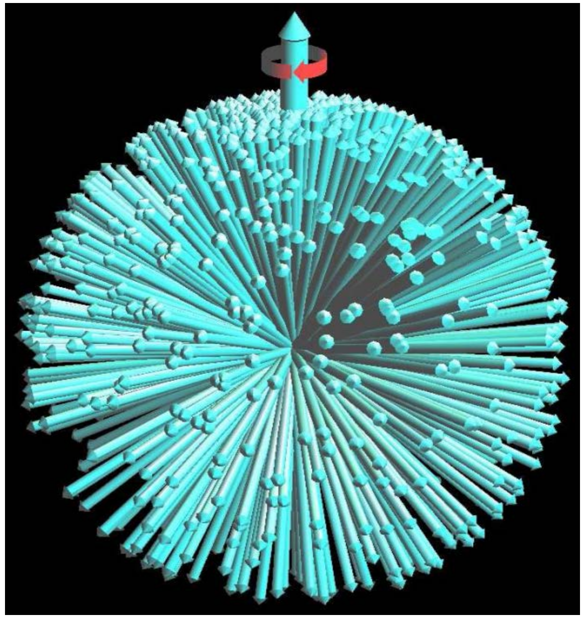
Magnetic Resonance

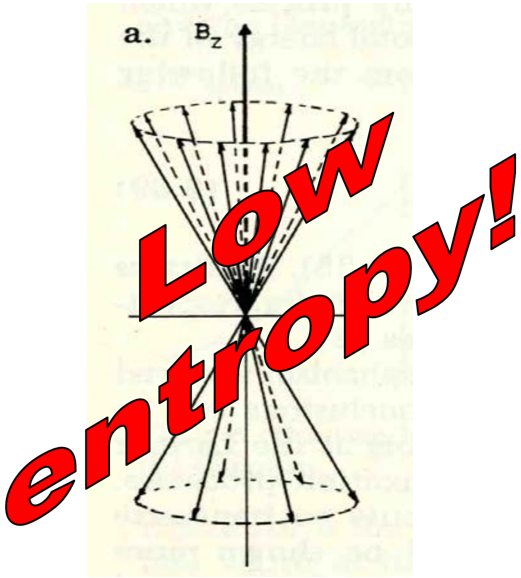
- Spins precess around B_0 and around…
  - …a weak field B_1-field that rotates around B_0.

But wait a minute…

Why is the spherical distribution more correct than the cone picture ???

– Two distributions with the same density matrix:

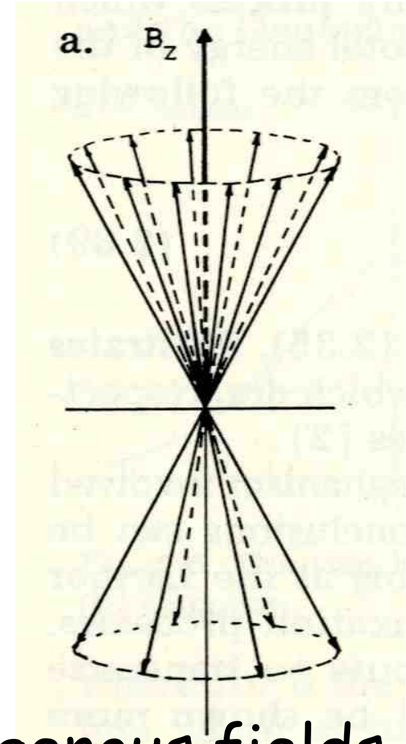


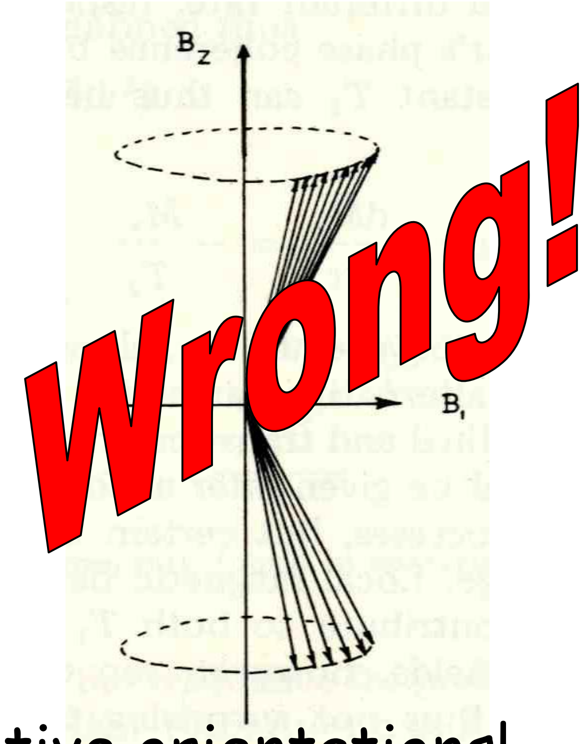


– Observations depend only on the density matrix, so aren't the descriptions equally good?

Magnetic resonance made complicated

- If you accept cone states as describing thermal equilibrium,...
- ...you also have to accept rotated versions after excitation:

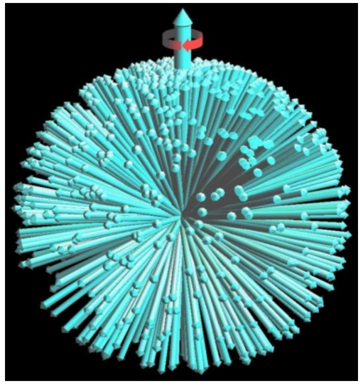




Homogenous fields cannot change relative orientations!

Dirt under the carpet…

- Ignored so far:
  - The overall spin state is not a product state. Entanglement/decoherence would soon occur.
    - Bloch vectors can then no longer be assigned.
  - The sample is not in a pure states.
    - Thermal equilibrium is a mix of classical uncertainty and quantum indeterminism.
- Bottom line:
  - Individual spins in thermal equilibrium do not have a direction, not even an unknown direction!
- But we can experimentally assign them one, consistent with the density operator….
  - and show that it evolves exactly as expected classically.



QM and classical descriptions

- QM is <u>not</u> classical mechanics. Differences:
  - Interference (e.g., cancellation of possibilities)
  - Entanglement (non-factorizable states)
  - QM is probabilistic at the most fundamental level.
  - ...
- However, QM and classical formulations need not be very different.
  - Mathematical differences can be deceptive.
  - Similar superpositions, eigenstates, correlations, spectral structures for simplest proton NMR.

Limits of classical MR

- Spin itself is a quantum phenomenon.

- Nuclear interactions:
  - J-coupling:
    - Nuclear interaction mediated by electrons (intramolecular effect)
    - Causes spectral splitting which is not unexpected classically.
    - Not surprising that nuclei couple through electronic cloud, but only QM gets it right.
      - ”Exchange interaction” is an important contribution that does not exist classically.

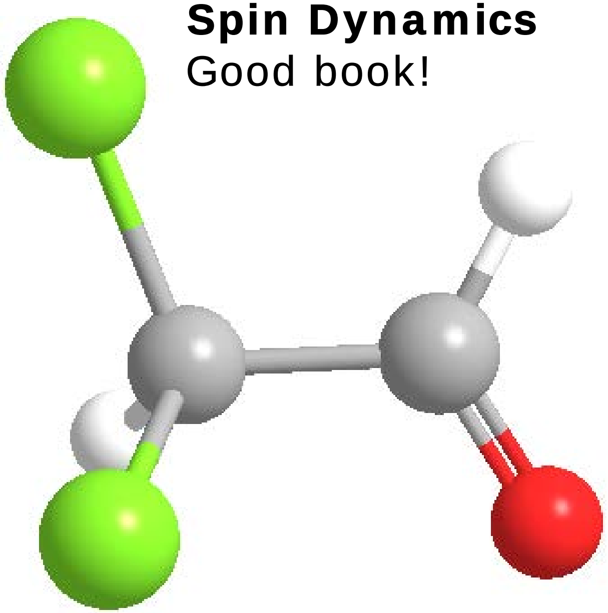
  - Relaxation mediated by dipolar interaction is expected clasically,
    - but QM is needed for a quantitative description.
    - The general behaviour is consistent with classical mechanics.

- For spectroscopy, a quantum description is highly recommended.
  - The operator formalism is really convenient.

DTU

Example molecule: 2 weakly coupled protons

Dichloroacetaldehyde
Example from
Malcolm H. Levitt's
Spin Dynamics
Good book!



Protons experiencing

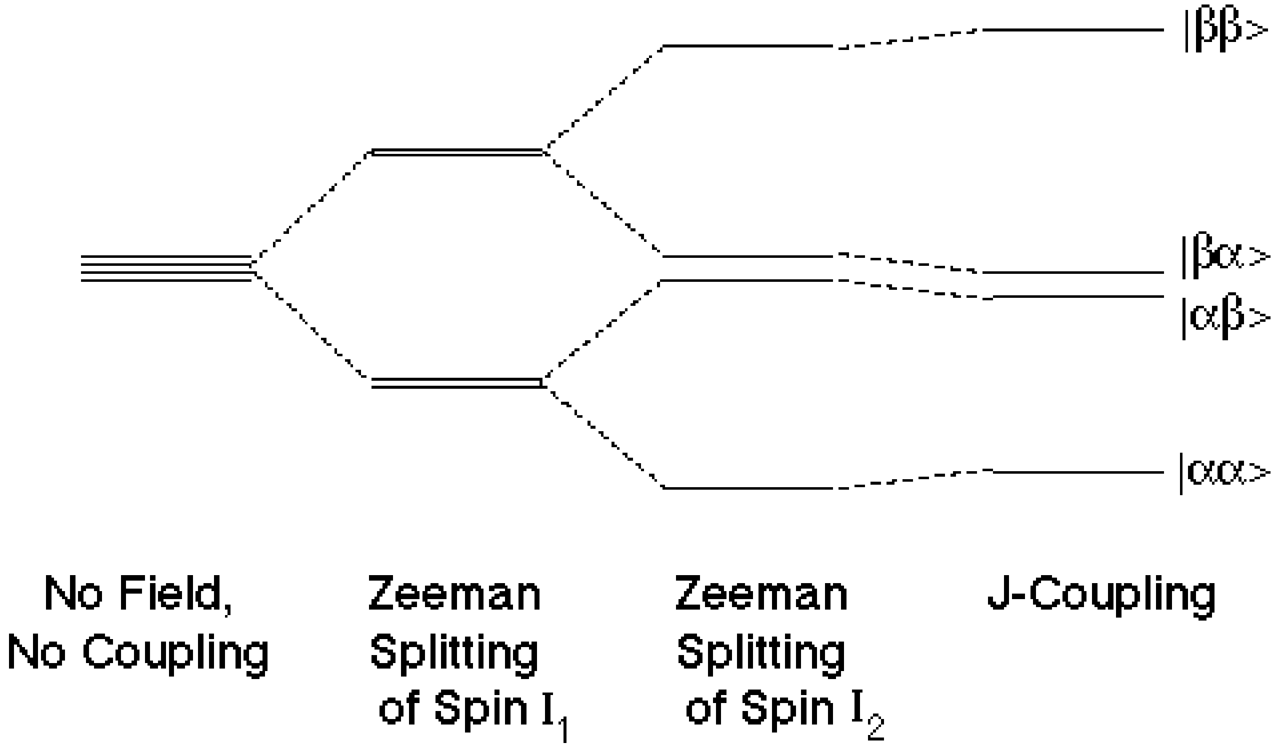
- different magnetic field due to electronic screening (chemical shift)
- indirect magnetic coupling via electronic cloud (weak J-coupling or scalar coupling)
- Direct magnetic interaction with other magnetic nuclei in the solution (causes relaxation)

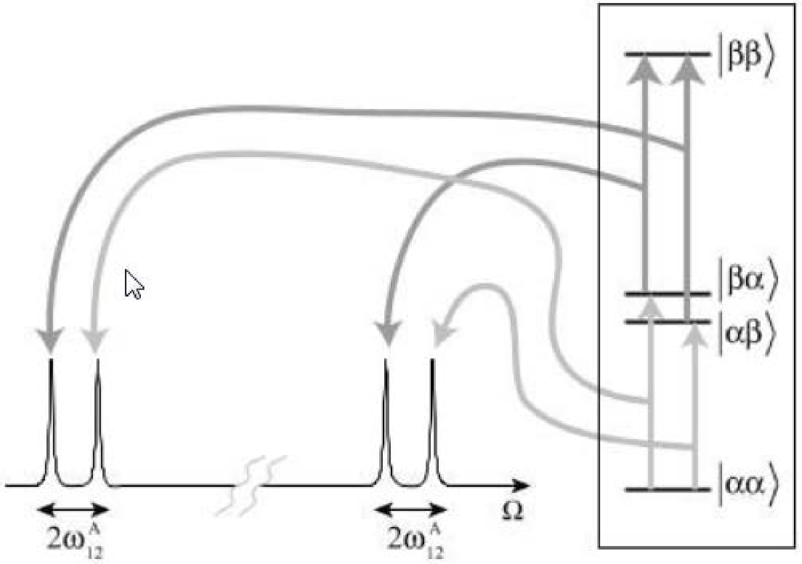
- Approximate Hamiltonian (strong field & tumbling):

$$\widehat{\mathcal{H}}_{\mathrm{A}}^{0} = \omega_1^0 \hat{I}_{1z} + \omega_2^0 \hat{I}_{2z} + \omega_{12}^{\mathrm{A}} 2\hat{I}_{1z}\hat{I}_{2z} \quad \text{with} \quad 2\omega_{12}^{\mathrm{A}} = 2\pi J_{12} + 2d_{12}$$

J_{12} is scalar coupling strength and dipolar coupling d_{12} vanishes in isotropic liquids.

Energy levels and spectra





Peak splitting by J-coupling:

$$2\omega_{12}^{A} = 2\pi J_{12}$$

We normally don't do frequency sweeps, but pulsed NMR.
Need for calculating evolutions.
Smooth transitions, no jumps.

The spin operator formalism

Towards the spin operator formalism:

- Sørensen, Eich, Levitt, Bodenhausen, Ernst
  - Prog NMR Spectroscopy 16, 163-192 (1983).

Ingredients:

- The density operator formalism
  - Exemplified by deriving the Bloch equations.
- The time evolution operator.
- A convenient basis for nuclear interactions.
- A good example: The homo-nuclear spin-echo experiment

Aim: Calculation of spectral structure for coupled nuclei.

The spin operator formalism(2)

The time evolution operator:

$$|\psi(t)\rangle = U(t)\,|\psi_{t=0}\rangle$$

$U(t) = \exp(-iHt/\hbar)$ for constant Hamiltonian H.

$$\begin{aligned}\rho(t) &= |\psi(t)\rangle\langle\psi(t)| \\ &= U(t)\,|\psi_{t=0}\rangle\langle\psi_{t=0}|\,U^{-1}(t) \\ &= U(t)\,\rho(t=0)\,U^{-1}(t)\end{aligned}$$

Piece-wise constant Hamiltonian H:

$$\rho\left(t = \sum_{i=1}^{N} \delta t_i\right) = \left(\prod_{i=N}^{1} U_i\right)\rho(t=0)\left(\prod_{i=1}^{N} U_i^{-1}\right)$$

The spin operator formalism(3)

A two-spin basis: $\rho = \sum_{(a,b,c,d=\uparrow,\downarrow)} C_{abcd} |ab\rangle\langle cd|$.

A better choice: The density operator is written as superposition of...

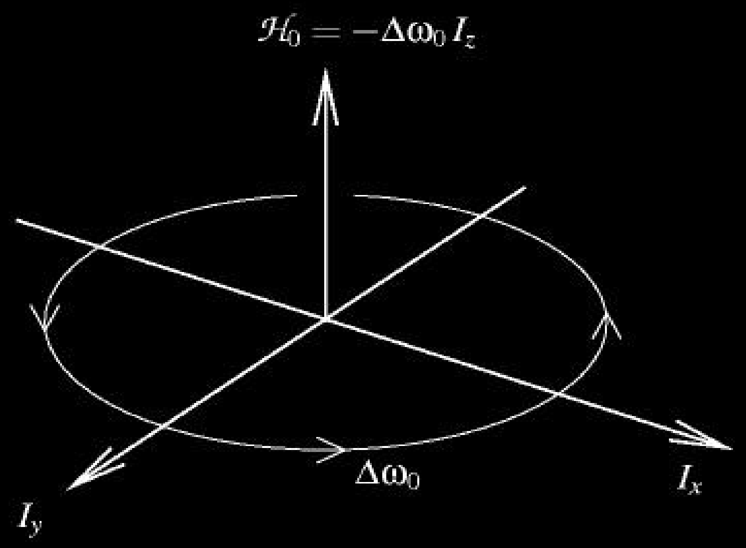
- Observable magnetization and polarization:
  - $I_{1x}, I_{1y}, I_{1z}, I_{2x}, I_{2y}, I_{2z}$
    Implicit two-spin operators: $I_{1x} = I_{1x} \otimes 1_2$
- Anti-phase magnetization:
  - $2I_{1x}I_{2z}, 2I_{1y}I_{2z}, 2I_{1z}I_{2x}, 2I_{1z}I_{2y}$
- Zero and multi-quantum coherences:
  - $2I_{1x}I_{2x}, 2I_{1x}I_{2y}, 2I_{1y}I_{2x}, 2I_{1y}I_{2y}$
- Isotropic magnetization: 1 (invariant, implicit).

The spin operator formalism(4)

DTU

The nuclear interactions cause rotations in state space.

- Rotation caused by Zeeman interaction (main field precession, CS).



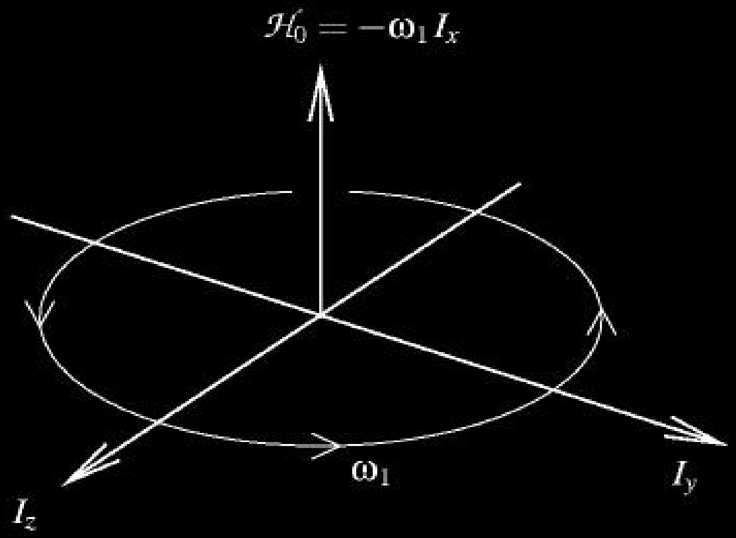
- Rotation matrix:

$$R_z(\phi) = \exp(-\phi I_z) = \begin{pmatrix} \exp(-i\phi/2) & 0 \\ 0 & \exp(i\phi/2) \end{pmatrix}$$

HYPERMAG

The spin operator formalism(5)

- Rotation caused by RF field interaction (precession around B1):

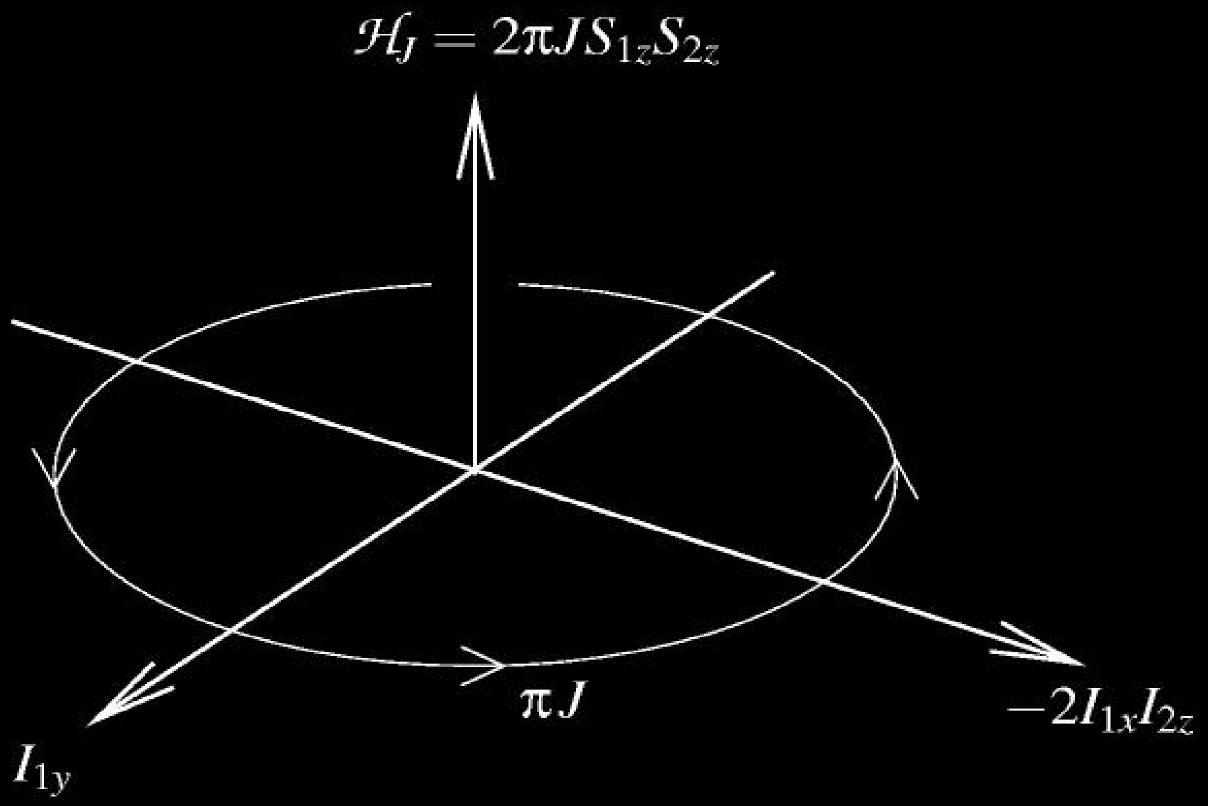


- Rotation matrix:

$$R_x(\phi) = \exp(-\phi I_x) = \begin{pmatrix} \cos(\phi/2) & -i\sin(\phi/2) \\ -i\sin(\phi/2) & \cos(\phi/2) \end{pmatrix}$$

The spin operator formalism(6)

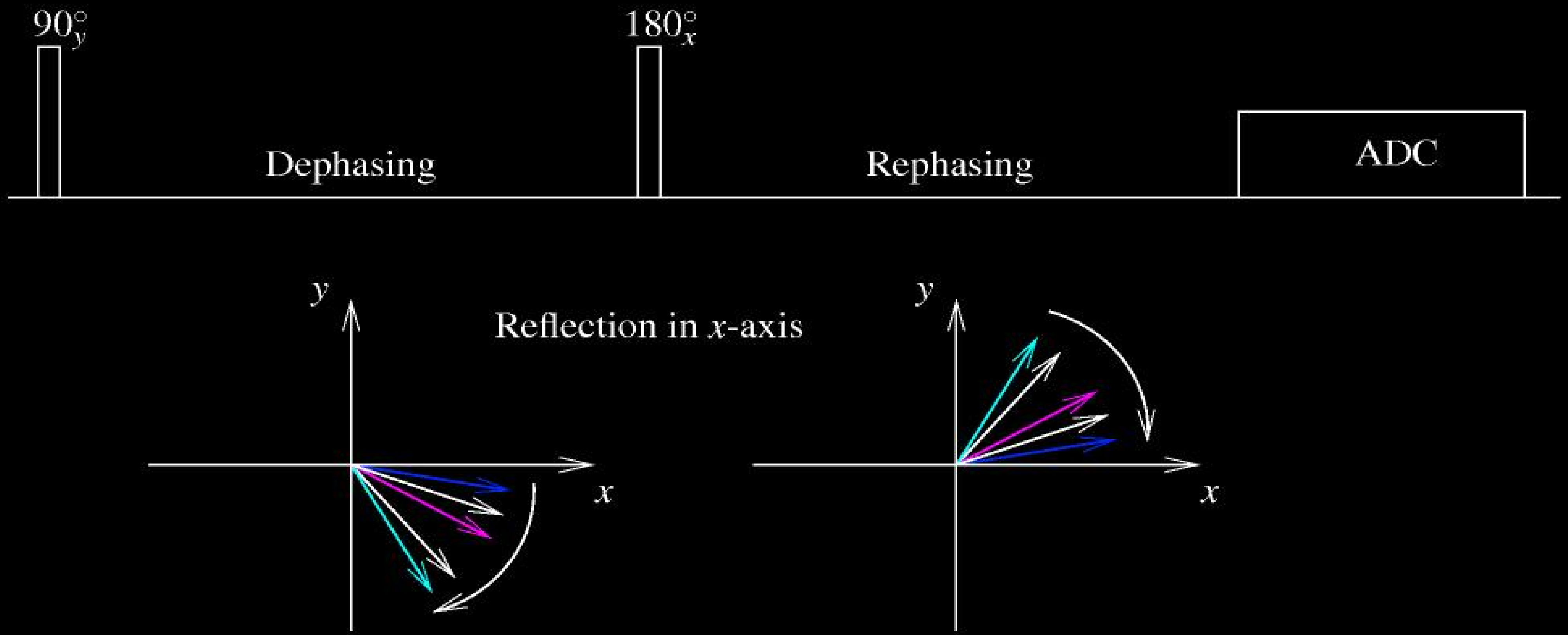
- Rotation caused by scalar coupling:



Effect on the FID:

- Modulation of signal oscillating at Larmor frequency, i.e. splitting.

The homo-nuclear spin-echo



Zeeman and scalar interaction for two interacting nuclei:

The homo-nuclear spin-echo(2)

Ingredients:

- U1: 90 degree flip
- U2: TE/2 Scalar coupling.
- U3: TE/2 Zeeman evolution.
- U4: 180 degree flip
- U5: TE/2 Zeeman evolution.
- U6: TE/2 Scalar coupling.

$$\rho_0 \xrightarrow[U_1]{\frac{\pi}{2}(S_{1x}+S_{2x})} \rho_1 \xrightarrow[U_2]{\theta S_{1z}S_{2z}} \rho_2 \xrightarrow[U_3]{\phi_1 S_{1z}+\phi_2 S_{2z}} \rho_3$$

$$\xrightarrow[U_4]{\pi(S_{1y}+S_{2y})} \rho_4 \xrightarrow[U_5]{\phi_1 S_{1z}+\phi_2 S_{2z}} \rho_5 \xrightarrow[U_6]{\theta S_{1z}S_{2z}} \rho_6$$

The homo-nuclear spin-echo(3)

Move operators around to simplify matters, e.g. get rid of Zeeman.

Permutation: $U_3U_4 = U_4U_4^{-1}U_3U_4 = U_4U_3^{-1}$.

Likewise, $U_2U_4 = U_4U_2$.

Finally, $U_1\rho_0U_1^{-1} = -S_{1y} - S_{2y}$.

At time of detection:

$$\begin{aligned}\rho_6 &= \exp(-2i\theta S_{1z}S_{2z})(-S_{1y} - S_{2y})\exp(2i\theta S_{1z}S_{2z}) \\ &= \cos(\theta)(-S_{1y} - S_{2y}) + \sin(\theta)(2S_{1x}S_{2z} + 2S_{2x}S_{1z})\end{aligned}$$

- TE determines whether we get signal or anti-phase coherence at t =TE.
- One evolves into the other during detection.

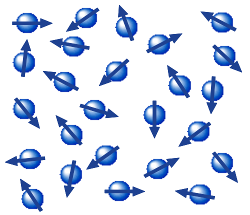
Hyperpolarization by dissolution DNP:
Enhancing the liquid state NMR/MRI signal factor ~100.000

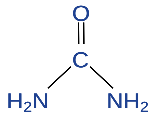
A locally developed technique with much potential

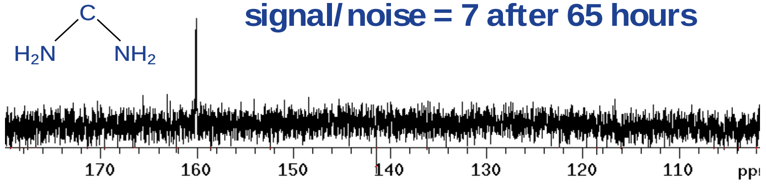
Hyperpolarized MR

Normal MR is fueled by thermal polarization:

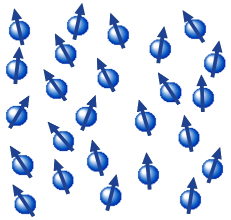
Conventional ^{13}C NMR spectrum of urea (the ^{13}C nuclear spins are only weakly aligned)

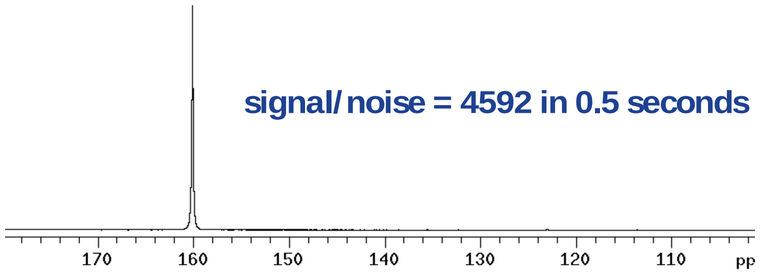






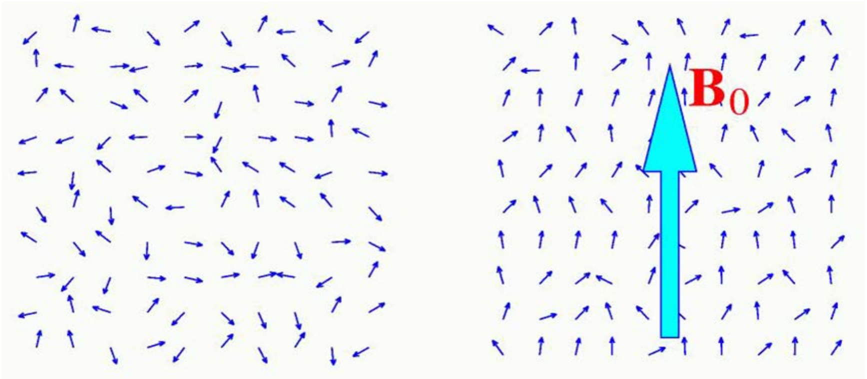
Hyperpolarized spectrum of the same sample (the spins are strongly aligned)





Hyperpolarized MRI:

- Substance is polarized outside scanner and injected.
- Example degree of alignment: 20% instead of ppm



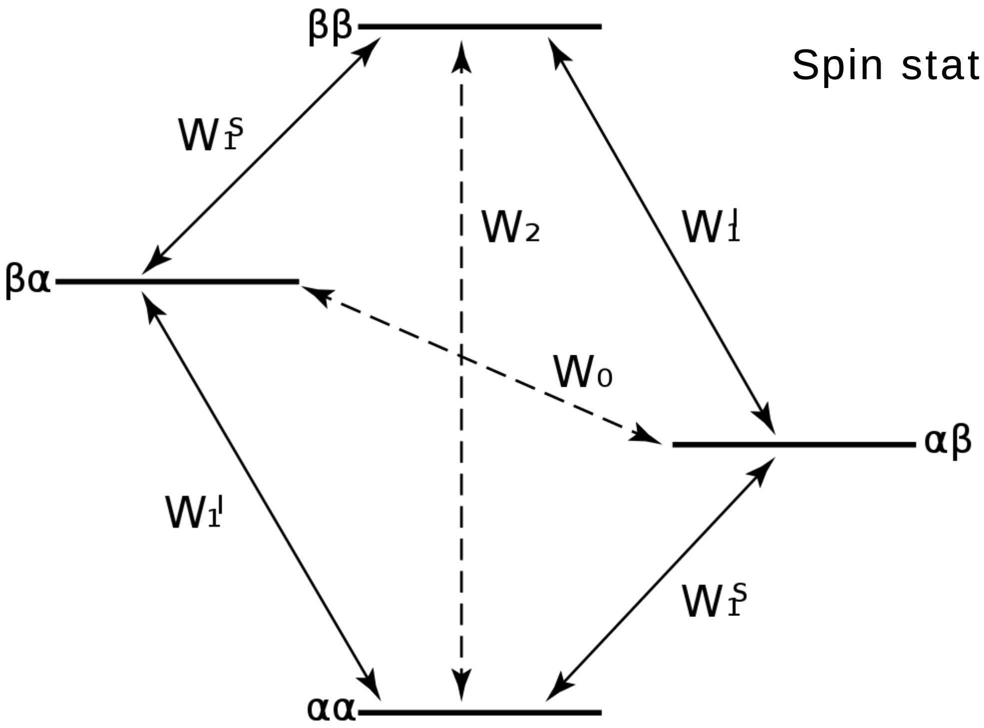
Weak signal for non-abundant, low-gamma nuclei like ^{13}C
(normal carbon is not magnetic)

Dissolution DNP enhances polarization factor 10000:
Ardenkjær-Larsen et al, PNAS, 2003

Related: Overhauser effect for two kinds of nuclei, I and S

When nuclei S are saturated, nuclei I can be polarized. Even in steady state!

- Very non-intuitive: When nuclei S are heated, nuclei I may be cooled.
- Initially Ramsey, Bloch & Rabi were very skeptical.



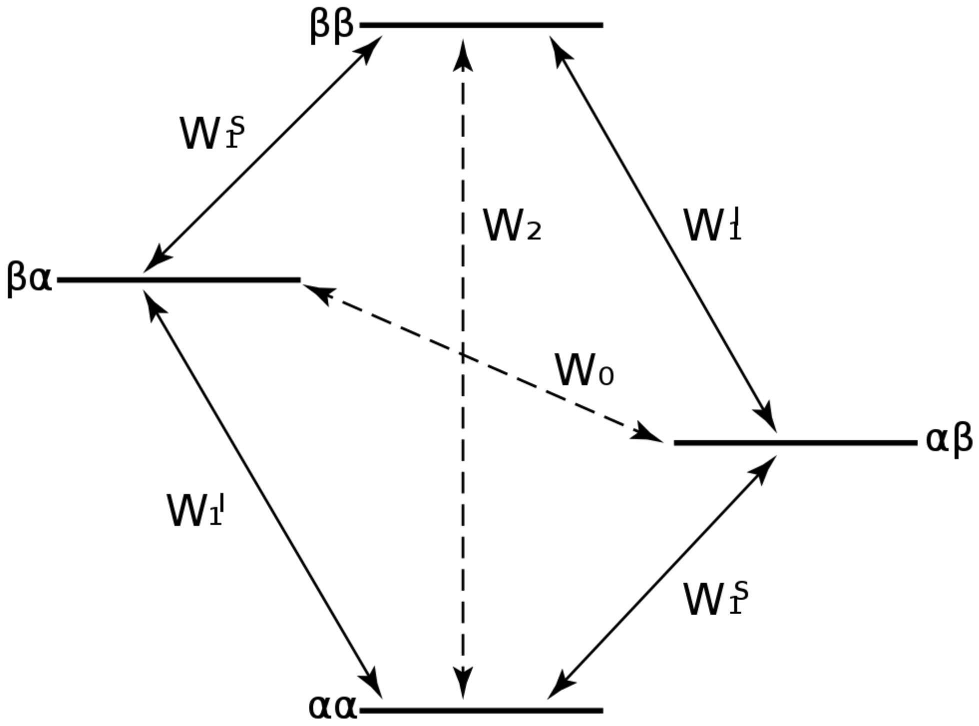
Spin states: $|IS\rangle$

Enhancement of spin I signal by saturating spin S:

$$\eta_I^S = \frac{\gamma_S}{\gamma_I}\left(\frac{W_2 - W_0}{2W_1^I + W_0 + W_2}\right)$$

- W_0 and W_2 involves motional degrees of freedom.

Pseudo explanation



Spin states: $|IS\rangle$

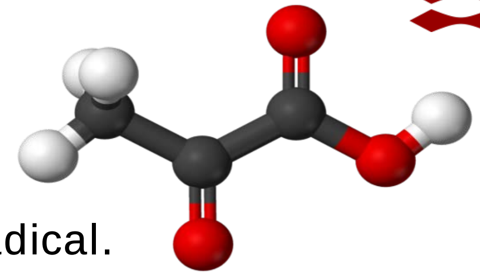
Enhancement follows from SS balancing (see Levitt, for example)

Attempt of short explanation:

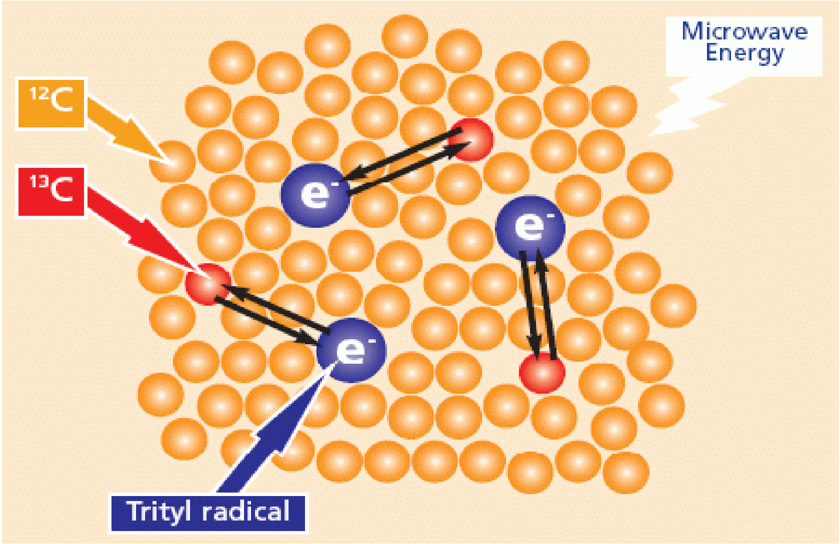
- Saturation makes nucleus S dressed states $|-\rangle$ and $|+\rangle$ relevant.
- Depending on couplings and detunings, the dipolar interaction mixes nucleus I states into the dressed states to various extent.
- The states are non-degenerate, and the low energy state is most populated in driven thermal equilibrium.
- This may result in S polarization in some circumstances.
- Exercise: Check math, and possibly reject argument.

- Works for hyperfine interaction also! (electron/nuclear spin coupling)
- Overhauser variants in solids:
  - Solid effect, cross effect, thermal mixing, spin diffusion…
  - Dynamic nuclear polarization (DNP)

Dissolution DNP in practise

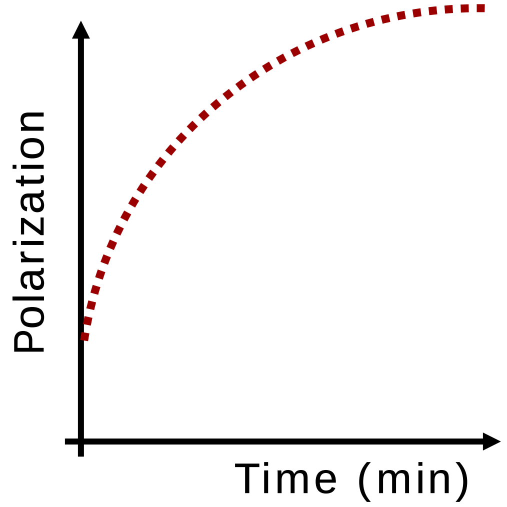


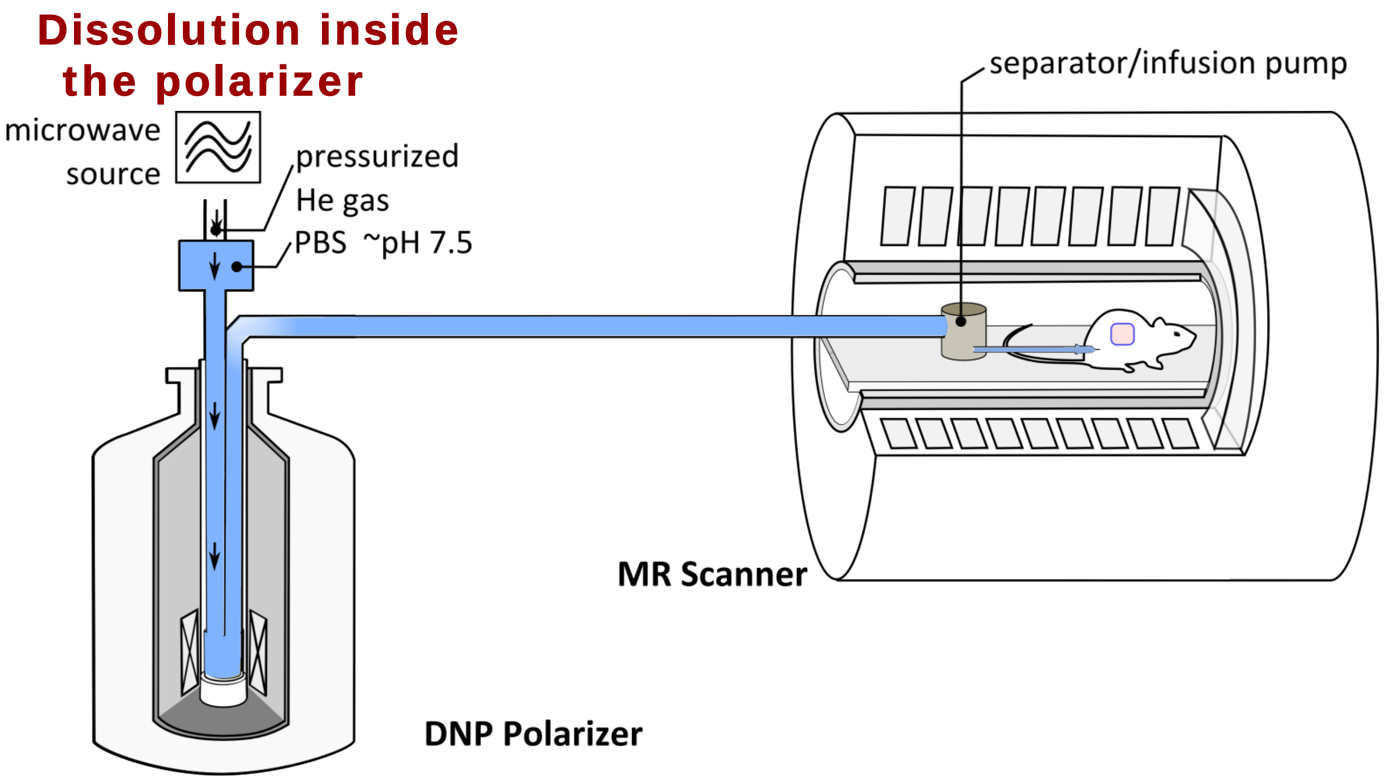
- Dynamic Nuclear Polarization (DNP):
  - Sample: Small molecule with low-γ nucleus, e.g. ^{13}C labelled pyruvate. Add radical.
  - Sample is cooled to ~1K in a strong magnetic field (~3T). Electrons are ~fully polarized.
  - Magnetization is transferred from electrons to nuclei using micro waves.
    - Hyperfine interaction + Overhauser
  - Sample is rapidly dissolved at high field, removed from magnet, and chemically cleaned.
  - Run to scanner/spectrometer! Inject into sample, animal or human.
  - Result: Signal enhancement by ~4-5 orders of magnitude.



Ardenkjær-Larsen et al, PNAS, 2003

Increasing NMR sensitivity in solution: the dissolution-DNP experiment



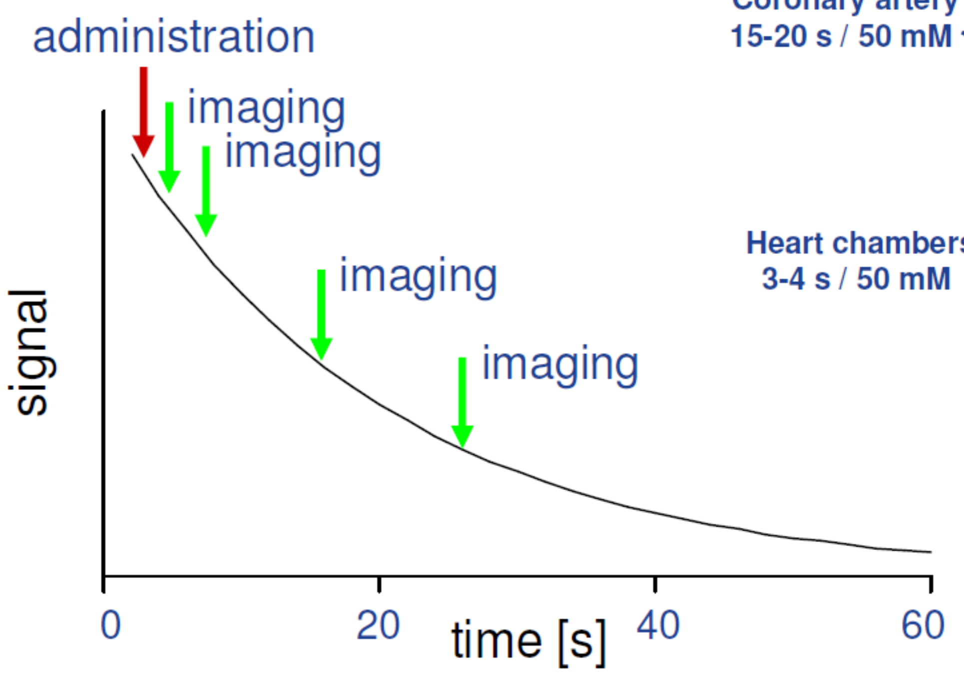


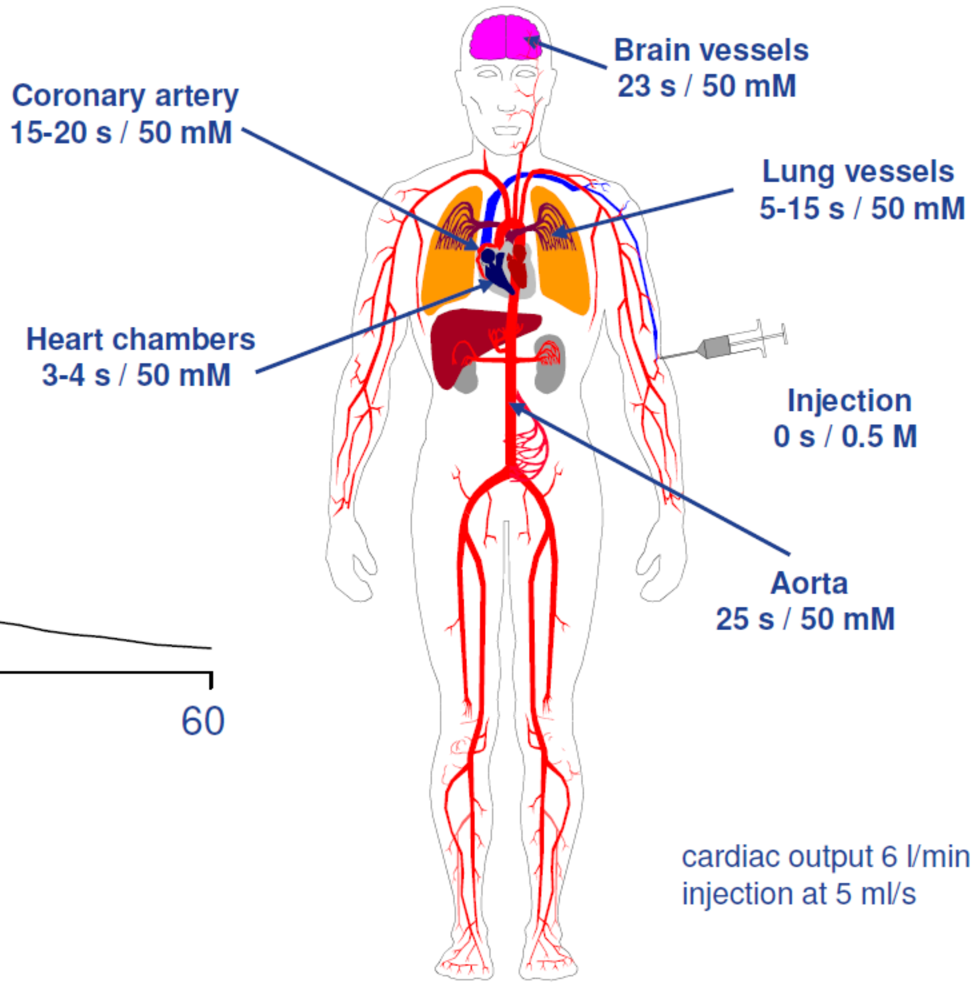
Measuring apparatus as close as possible

polarization (90min) dissolution and transfer (3s) infusion (9s) acquisition (120s)

Graphics: Andrea Capozzi

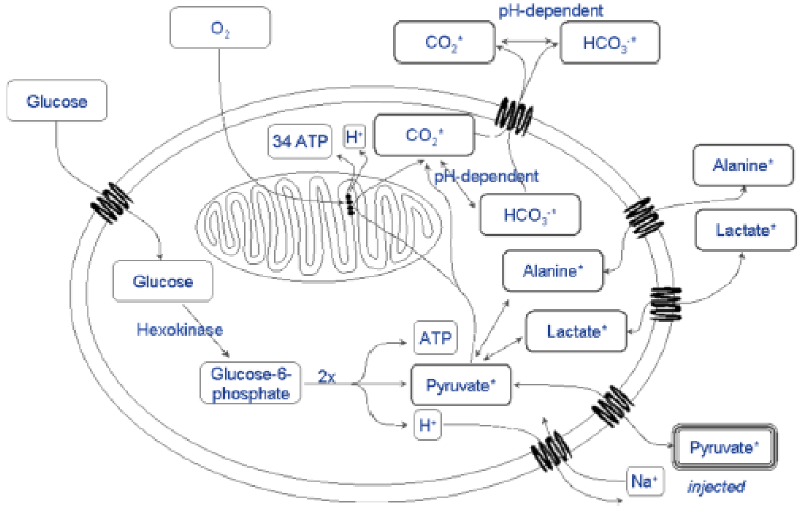
It also works in humans...if you are fast

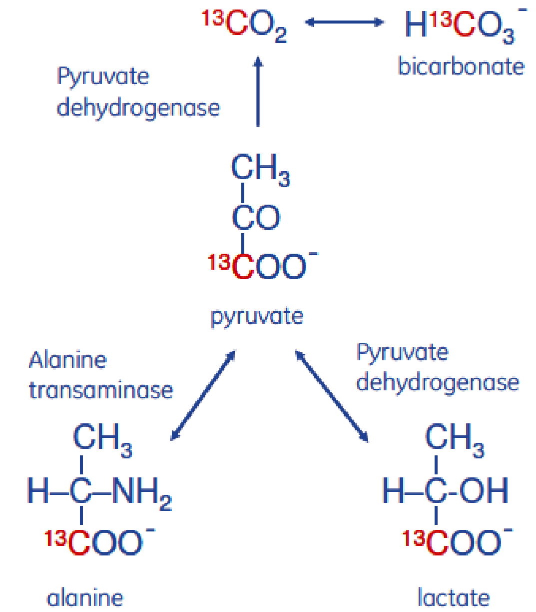


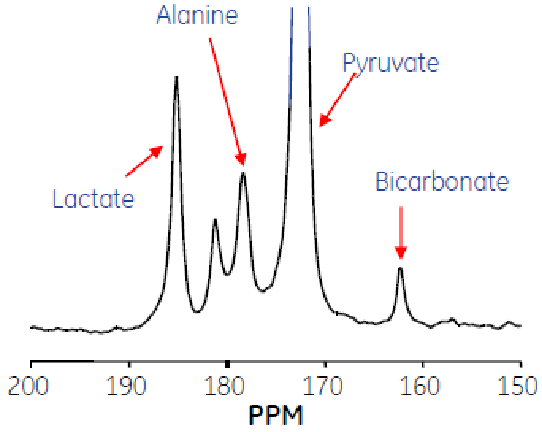


cardiac output 6 l/min
injection at 5 ml/s

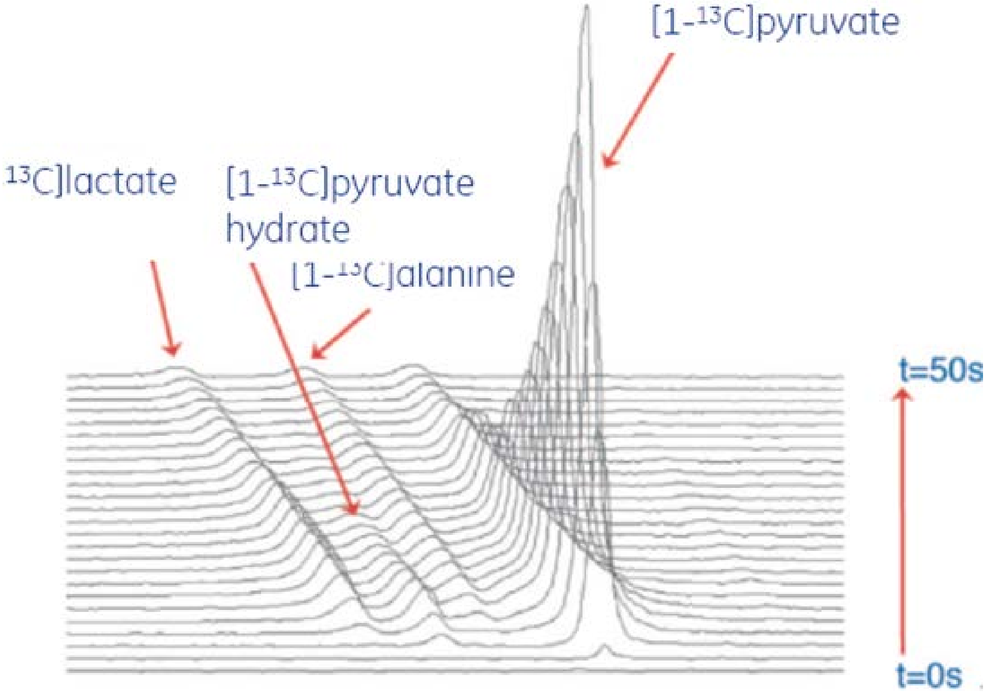
Probing the dynamics of metabolism

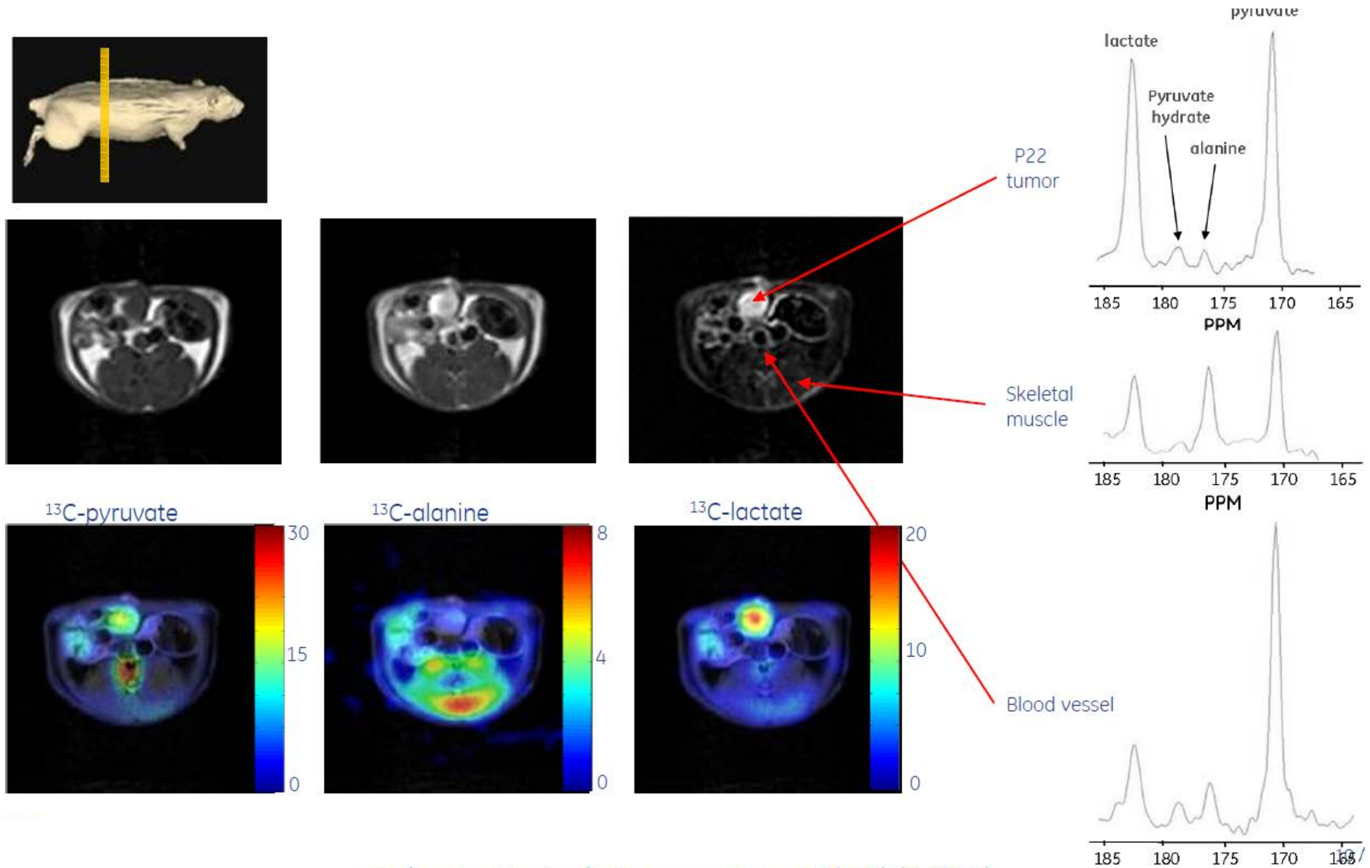






Spectroscopic imaging and metabolic rate determination



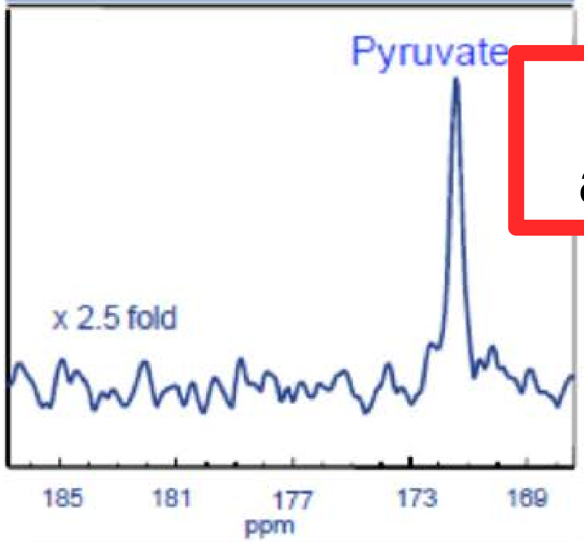


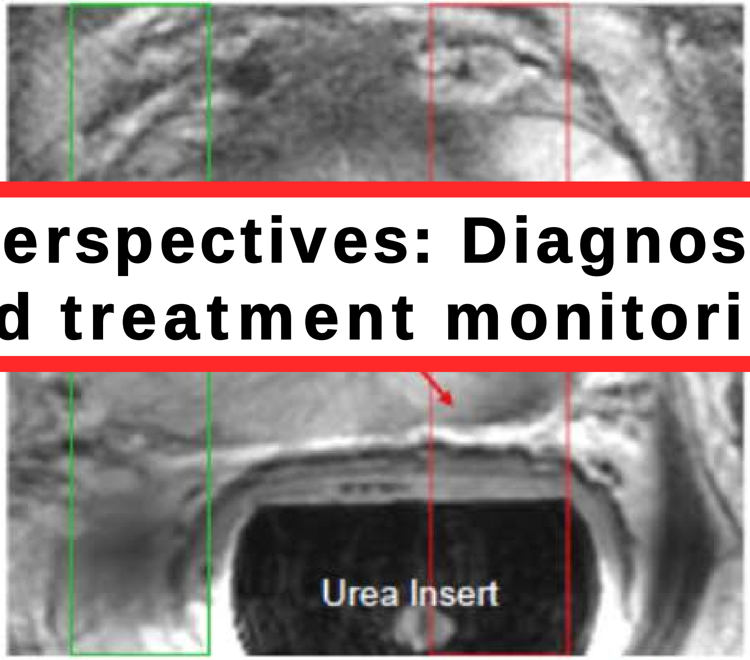
Golman K et al, Cancer Res 66(22) (2006)

Hyperpolarized ^{13}C: First Human Results[1]

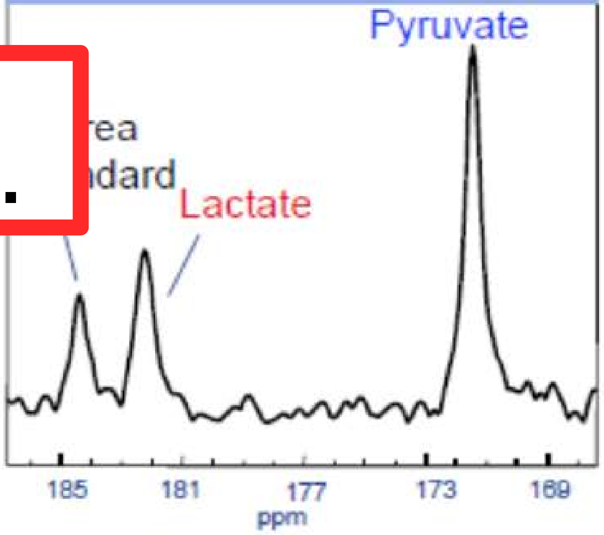
Perspectives: Diagnosis and treatment monitoring.

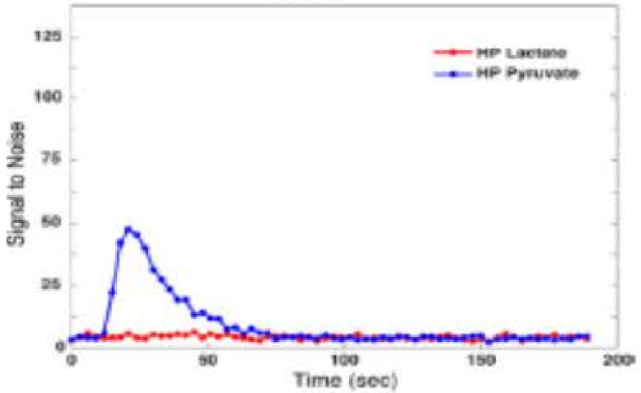
Normal Tissue
36 Seconds After Injection





Malignant
36 Seconds After Injection

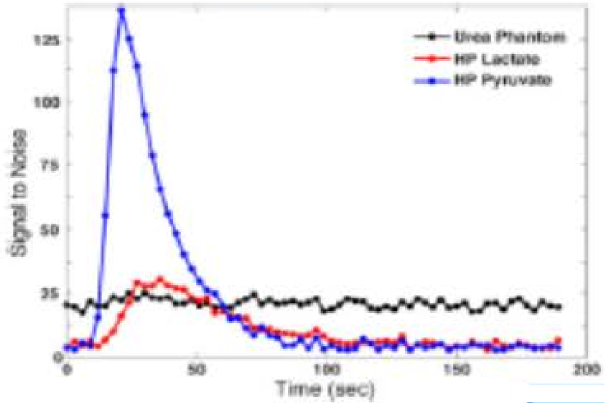


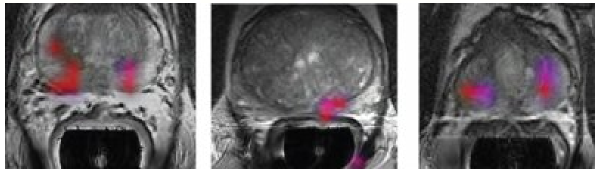


Hyperpolarized Pyruvate (^{13}C)
Injection in Subjects with Prostate Cancer

[1]UCSF received a "May Proceed" letter for hyper-polarized pyruvate (13C) IND on October 8, 2010

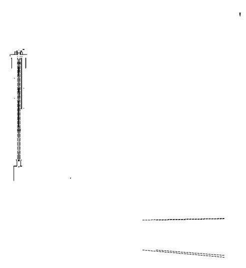
Courtesy of S. Nelson, J. Kurhanewicz and D. Vigneron, Department of Radiology and Biomedical Imaging, UCSF





DNP Polarizer generations

2003



Ardenkjær-Larsen et al, PNAS 2003

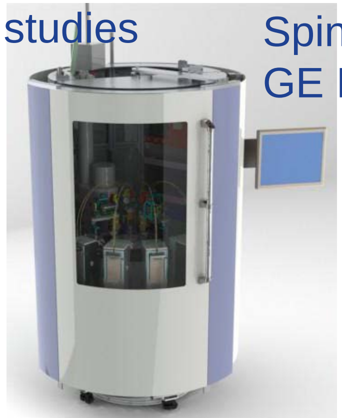
2007

HyperSense™ Oxford Instruments

In vitro only;
In vivo with GE license

UCSF clean room installation for 1st human study

Designed for clinical research, but also useful for animal studies



SpinLab™
GE Healthcare

Ardenkjær-Larsen et al, NMR in Biomedicine 2011

HYPERMAG polarizer
Now commercialized:
http://polarize.dk

Infrastructure

Our hyperpolarization lab is a unique infrastructure (world-class):
Three polarizers covering the widest magnetic field (10 T) and temperature range (1 K)

Thanks for listening - Questions?

Actual group members easily mistaken for professional models