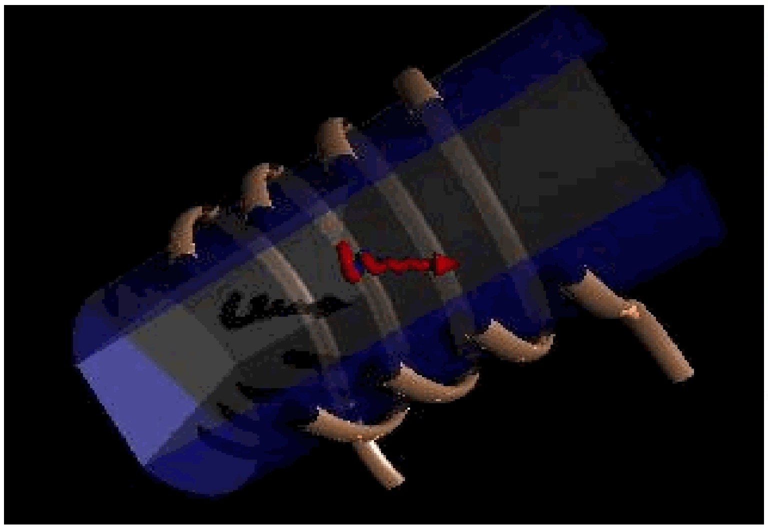
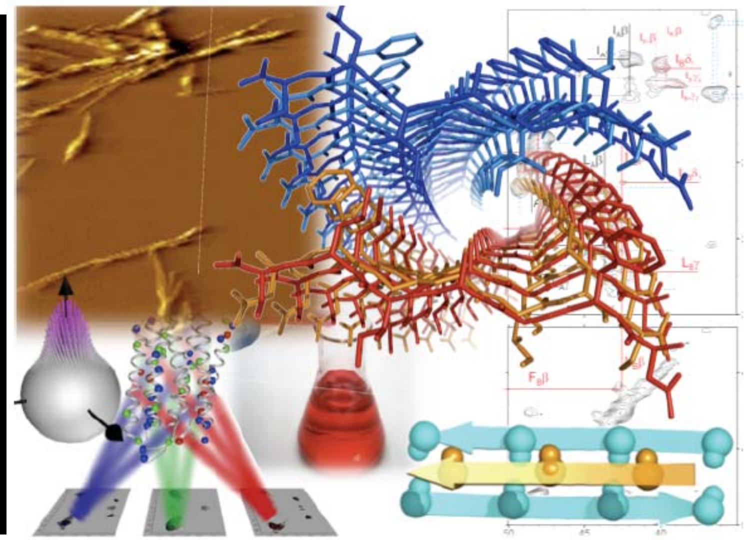
Optimal Control in Solid-State NMR



Control



Quantum System

Kavli Institute for Theoretical Physics, UCSB, Santa Barbara, May 21, 2009

AARHUS UNIVERSITET

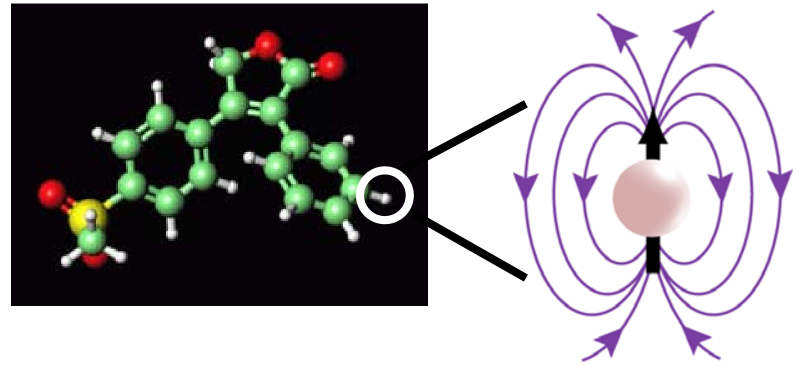
Center for Insoluble Protein Structures

Niels Chr. Nielsen

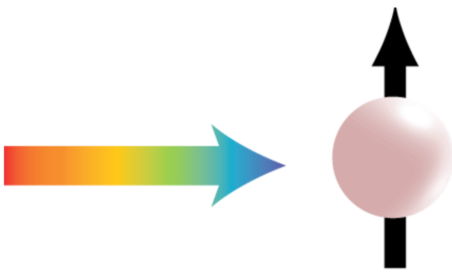
Outline:

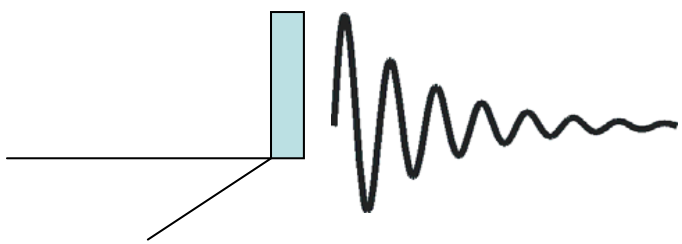
- Brief introduction to the solid-state NMR spectroscopy
- Optimal control in solid-state NMR
- New solid-state NMR experiments, low-field NMR, DNP, and MRI

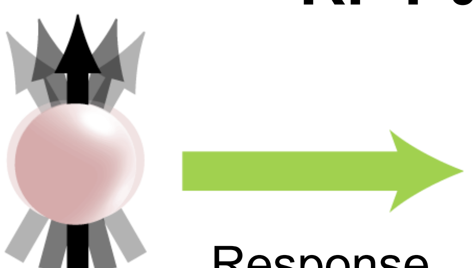
NMR spectroscopy: Uses magnetic fields and rf irradiation to manipulate nuclear spins

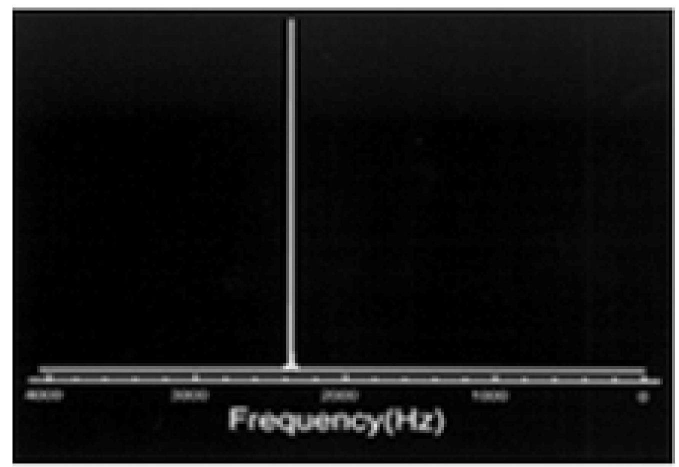


Polarization by B0
Rf irradiation









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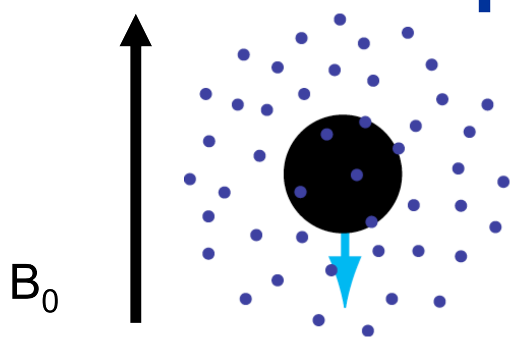
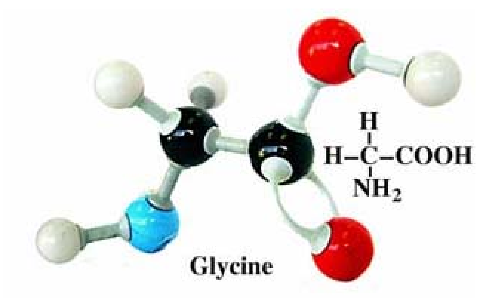
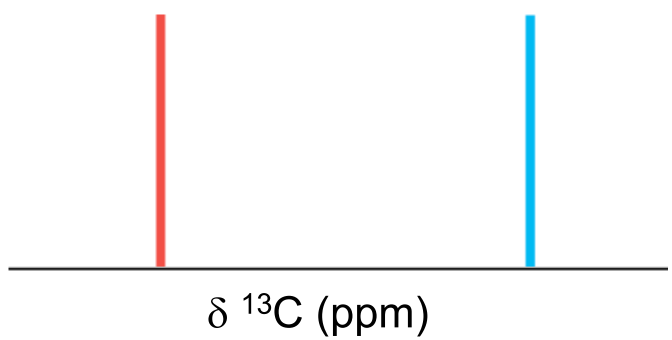
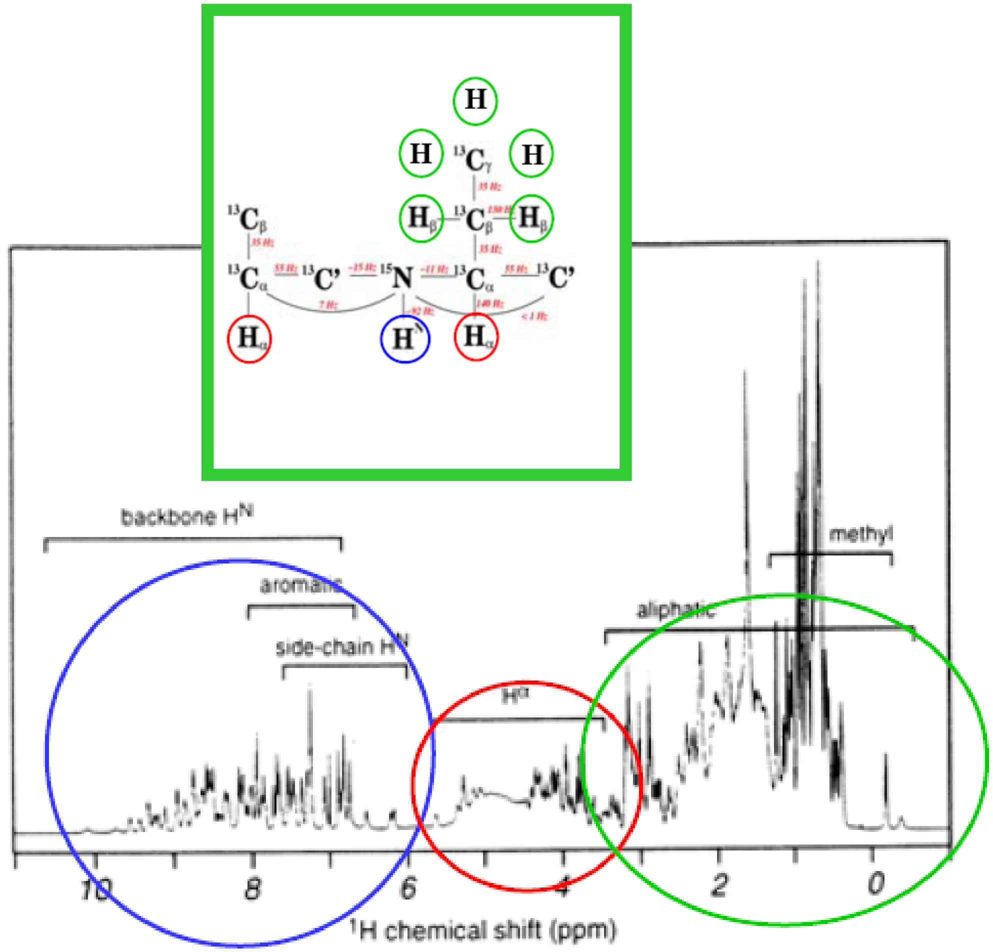
Chemical Shift – the resonance frequency depends on the electronic surrounding





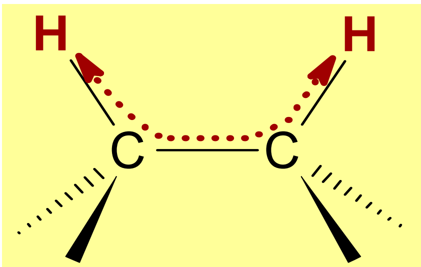




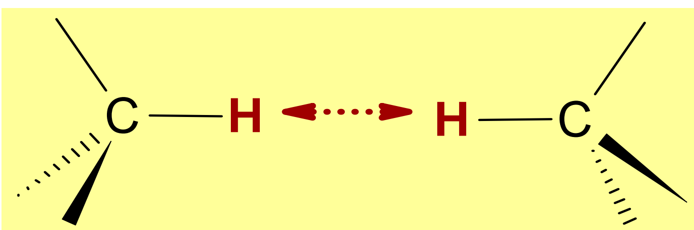
Very crowded for big molecules

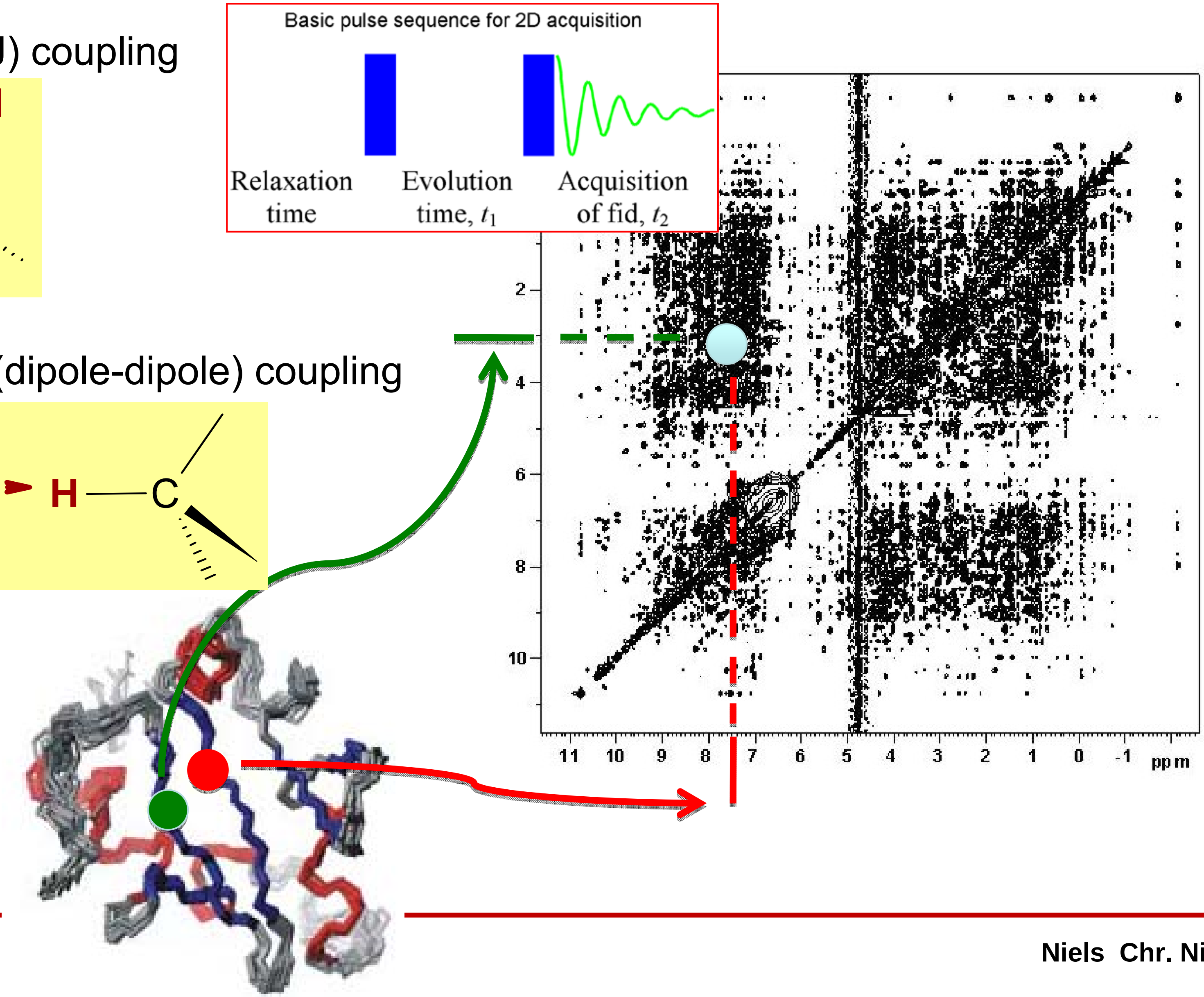
Scalar couplings and dipolar cross-relaxation allows for communication between spins: 2D NMR

Through-bond (J) coupling



Through-space (dipole-dipole) coupling





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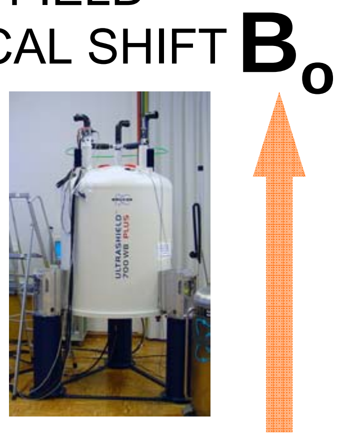
Controls in liquid-state NMR spectroscopy

STATIC FIELD

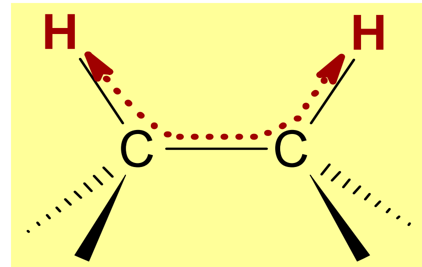
CHEMICAL SHIFT

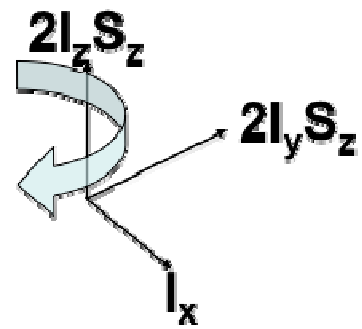


$H = \omega_o I_z$

$H_\sigma = \omega_\sigma I_z$

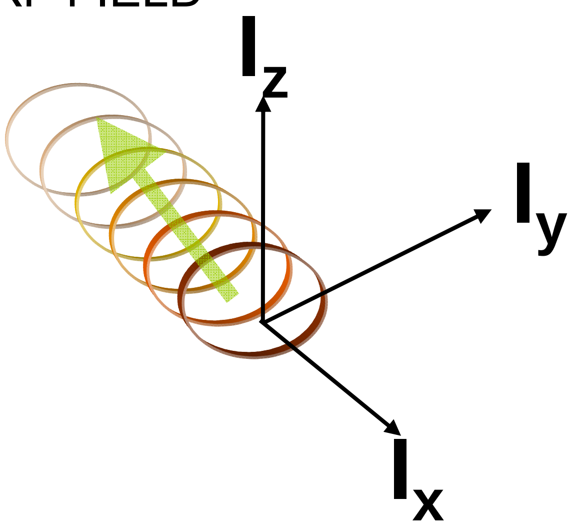
J COUPLING

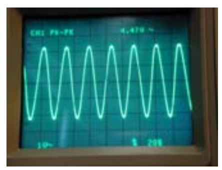




Generates two-spin operators, which may be used to drive coherence/polarization transfer between coupled spins

RF FIELD

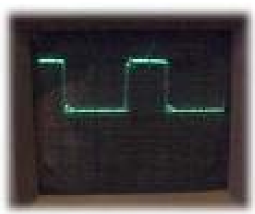


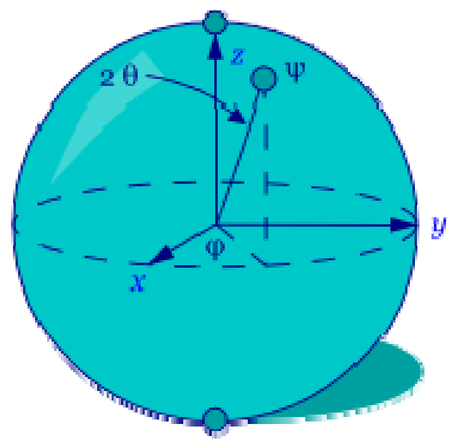


$H = 2\omega_{rf}\cos(\omega_c t)\, I_x$

Rotating frame:

$H = \omega_{rf}\, I_x$

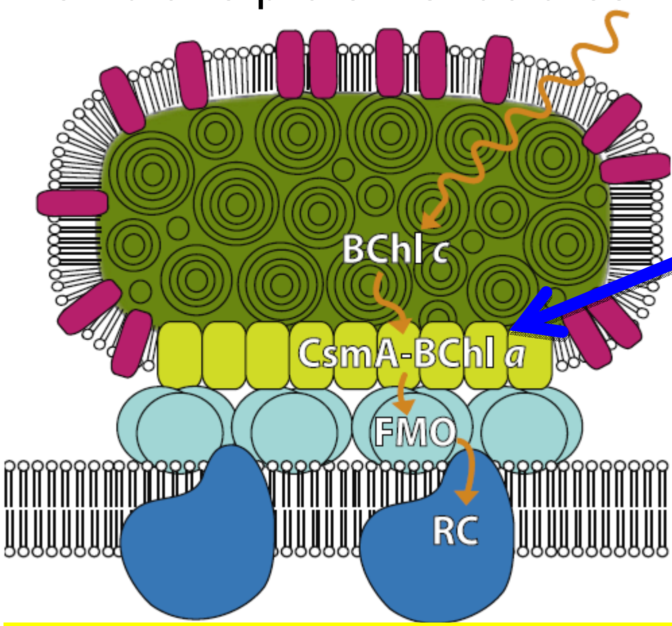


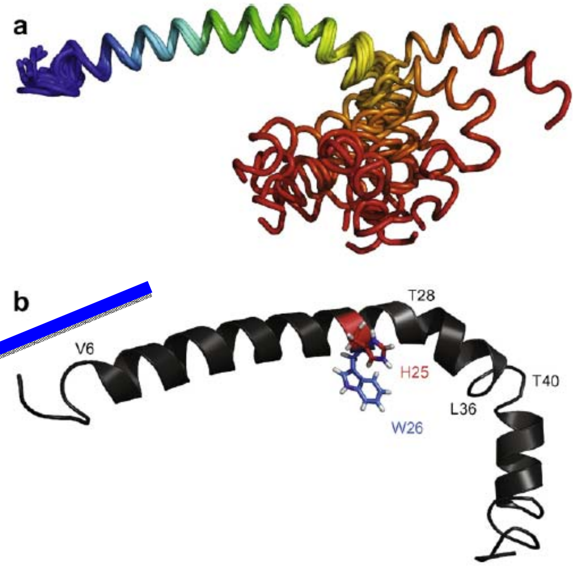


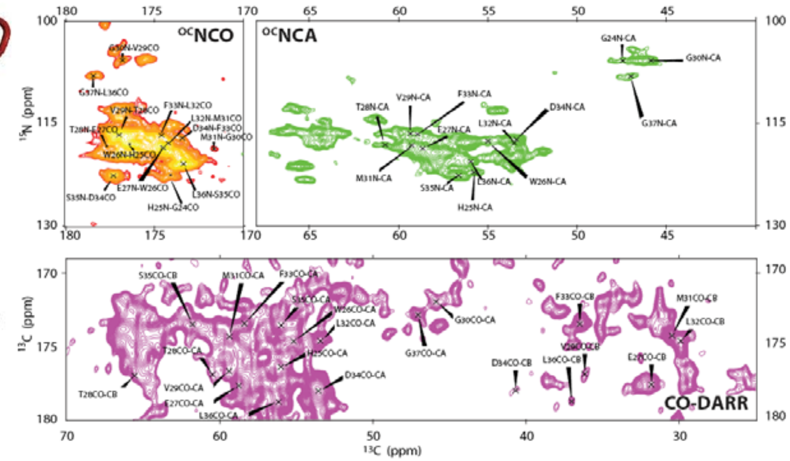
Rotations in 3D (I_x, I_y, I_z) or $(I_x, 2I_yS_z, 2I_zS_z)$ operator spaces

Structure of proteins in immobile environments

Membrane protein structures



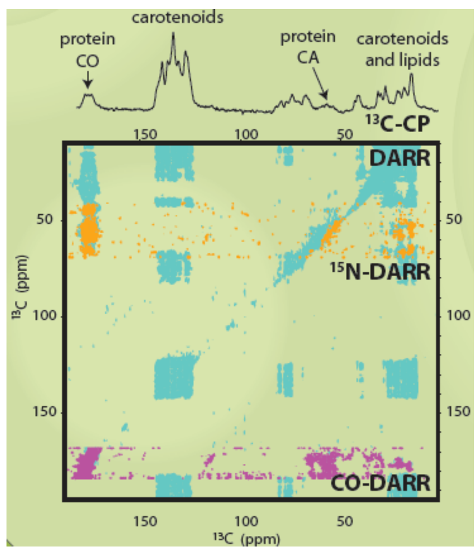




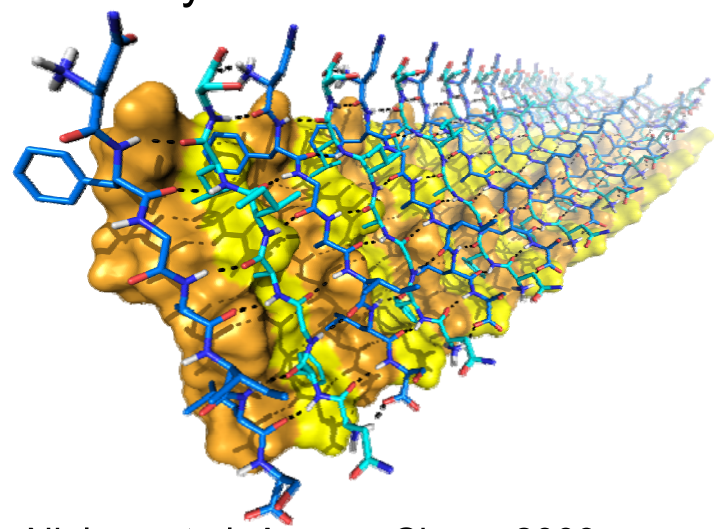
GREEN SULFUR BACTERIA

Chlorobidumtepidum

Pedersen, Dittmer, Miller, and Nielsen, *FEBS Lett., 2008*



Amyloid fibril structures

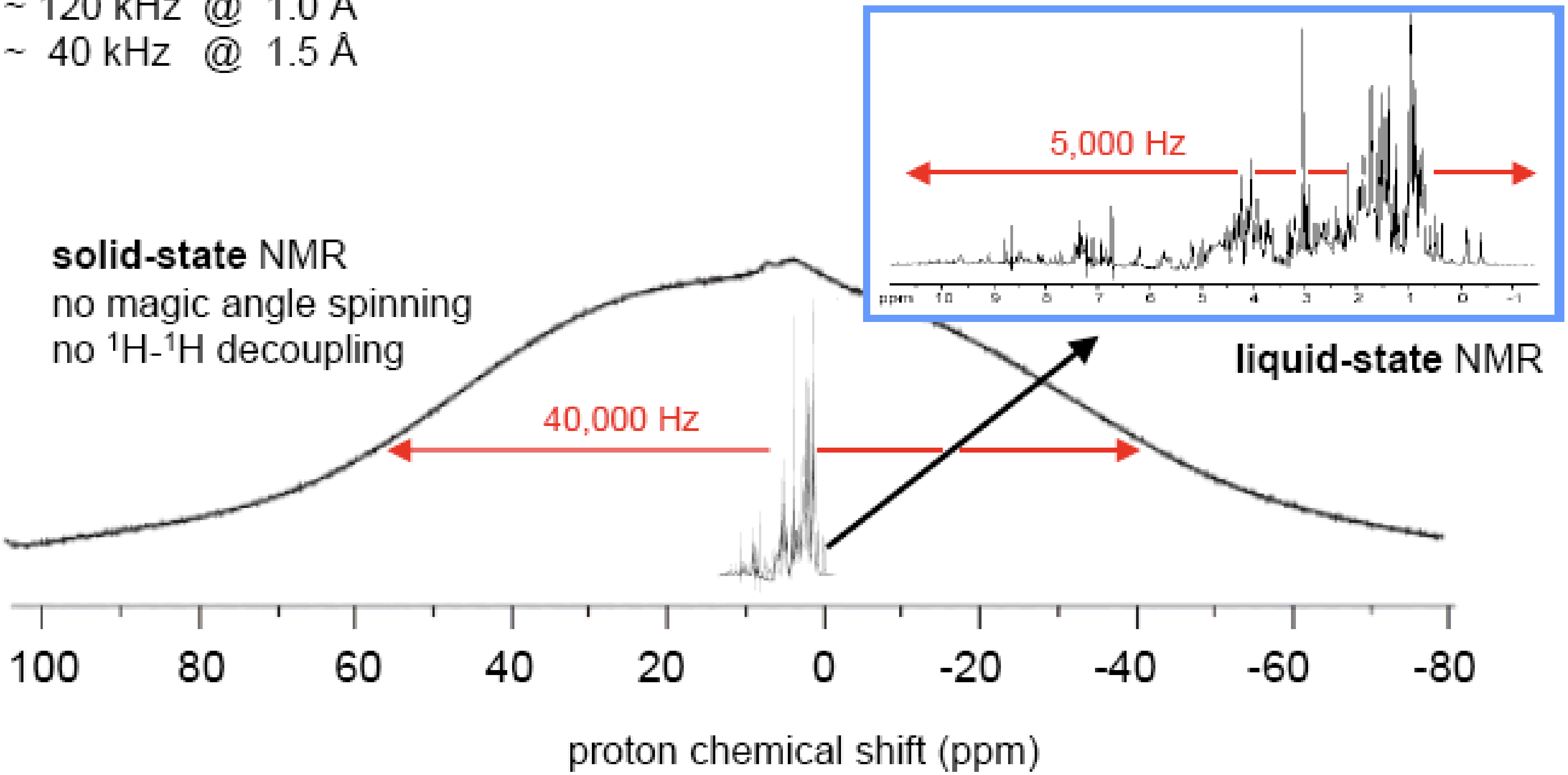


Nielsen et al, Angew. Chem. 2009

For solids, anisotropic interactions destroy the resolution and the sensitivity is low

dipolar coupling between protons:

~ 120 kHz @ 1.0 Å
~ 40 kHz @ 1.5 Å



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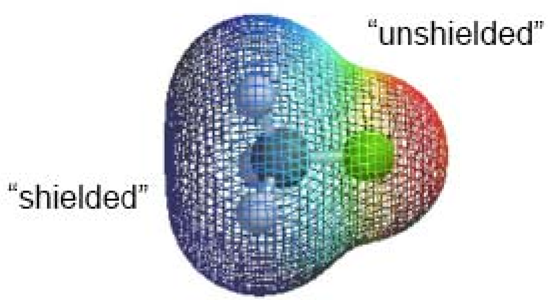
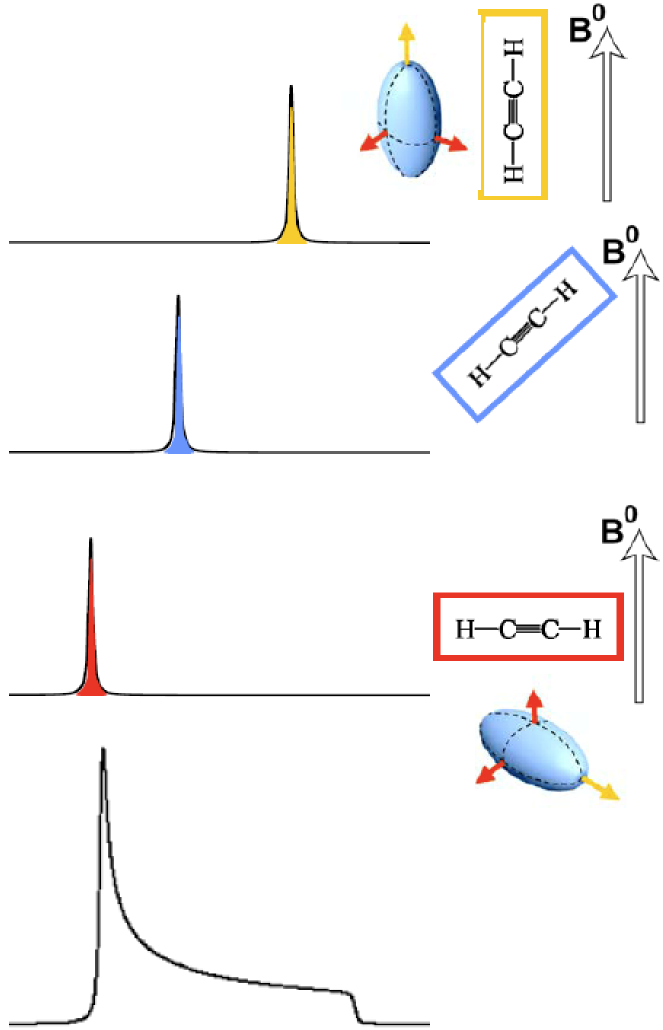
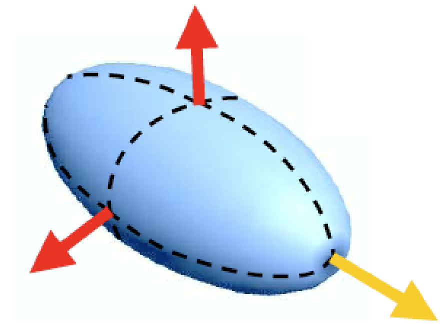
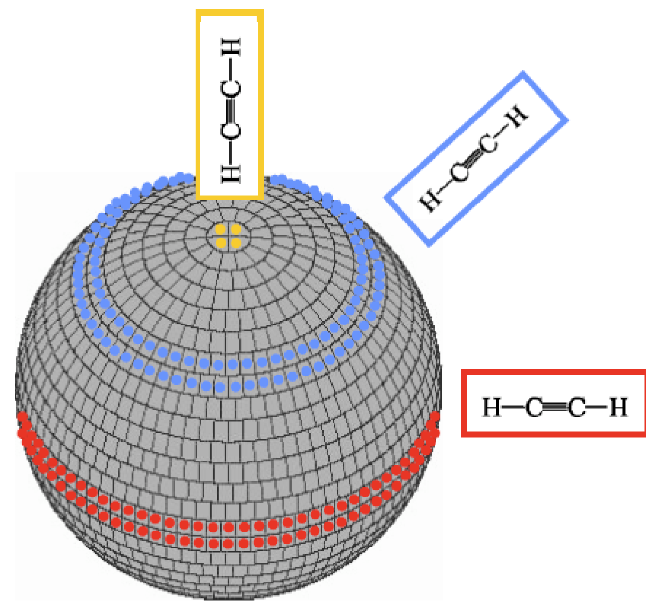
Origin to broadening: Chemical shielding anisotropy



The electrons shields the magnetic field – an orientation dependent manner







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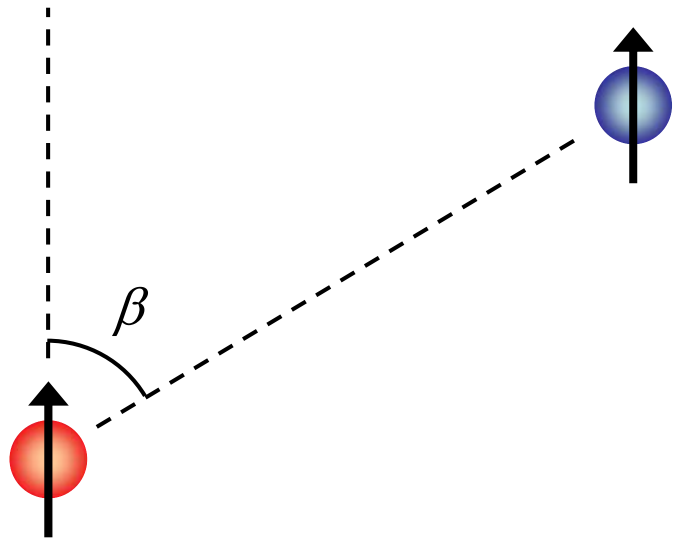
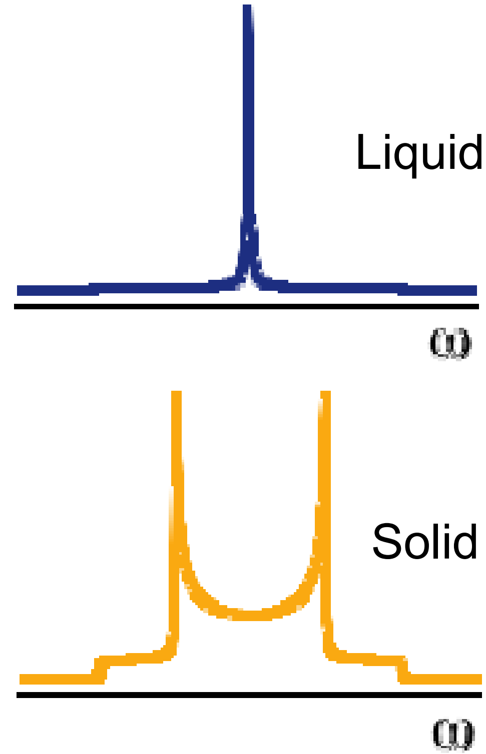
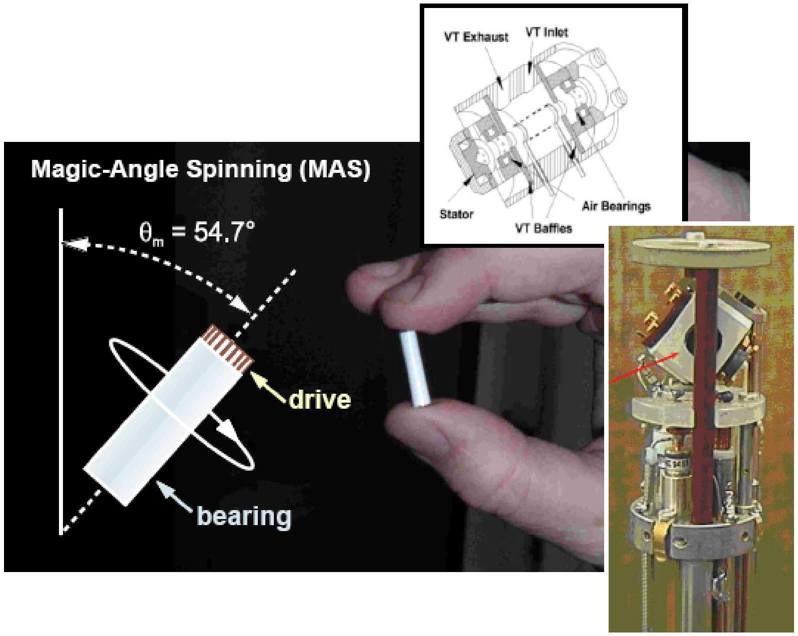
Origin to broadening: Dipole-dipole couplings

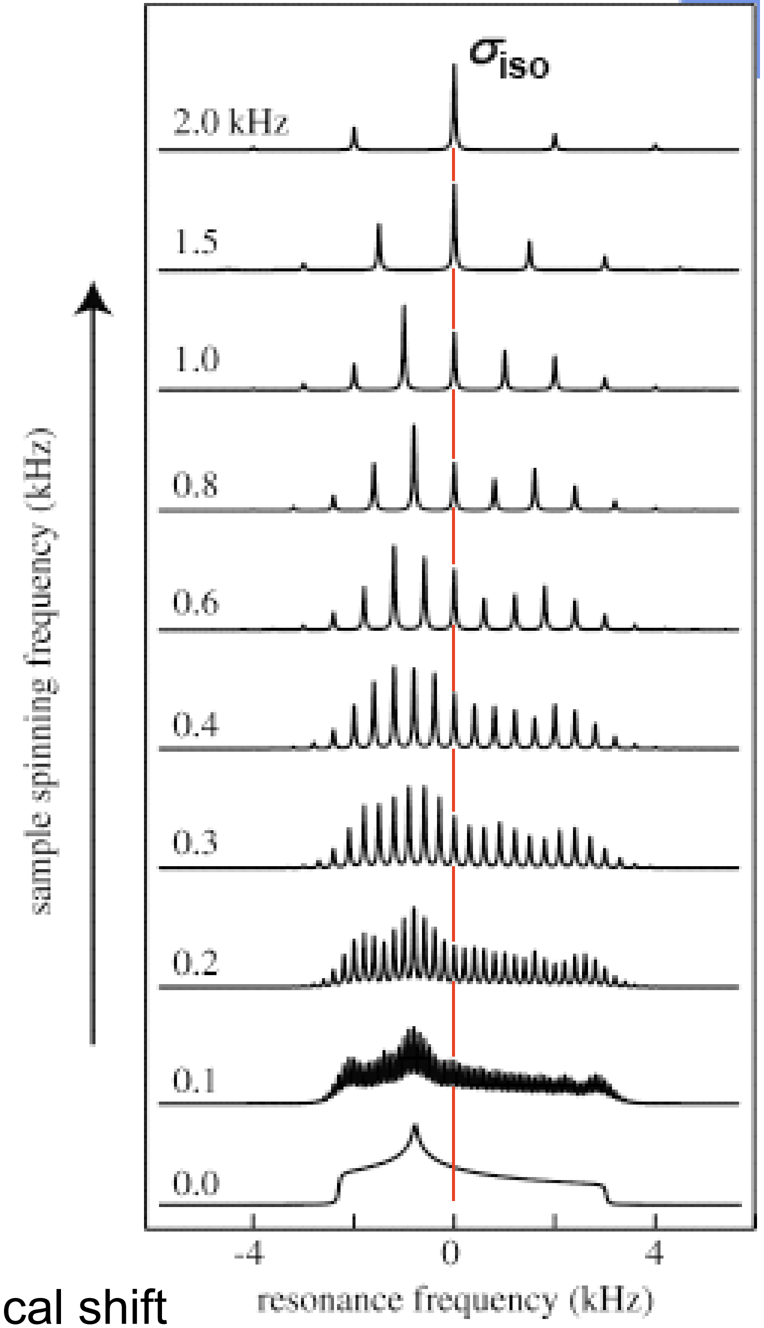




{ = 0 in isotropic liquids
≠0 in solids or oriented media

Regain of resolution:
Magic-angle spinning





Isotropic chemical shift

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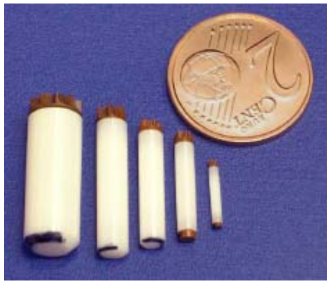
To mimic molecular motion we have to spin fast



4.0 mm	→	15 kHz	(1,400,000 x *g*)
3.2 mm	→	25 kHz	(2,700,000 x *g*)
2.5 mm	→	35 kHz	(3,500,000 x *g*)

(50,000 x *g*)…

a 3.2 mm rotor spinning at 24 kHz…

… has a speed of 240 m/s when it would roll on the floor …

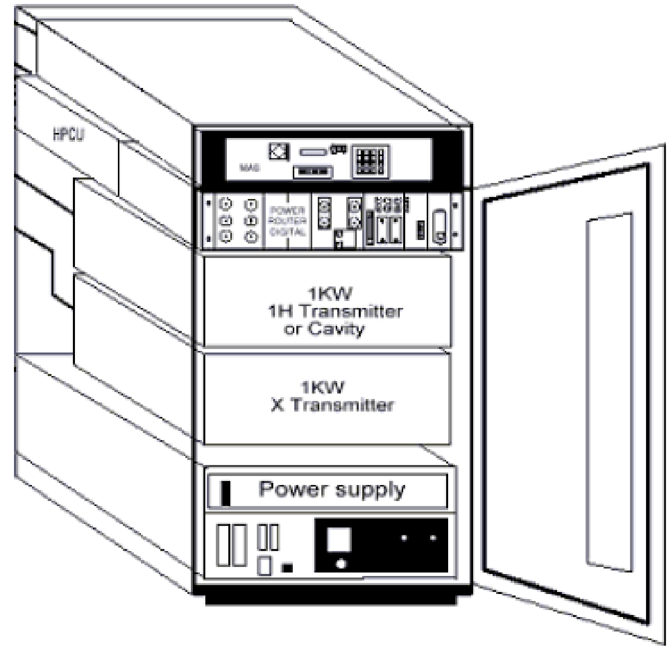
… and needs only 46 hours to roll around the earth…

From van Rossum

Strong rf irradiation:
to remove dipolar coupling

720,844 mm^3
(1 mW / mm^3)

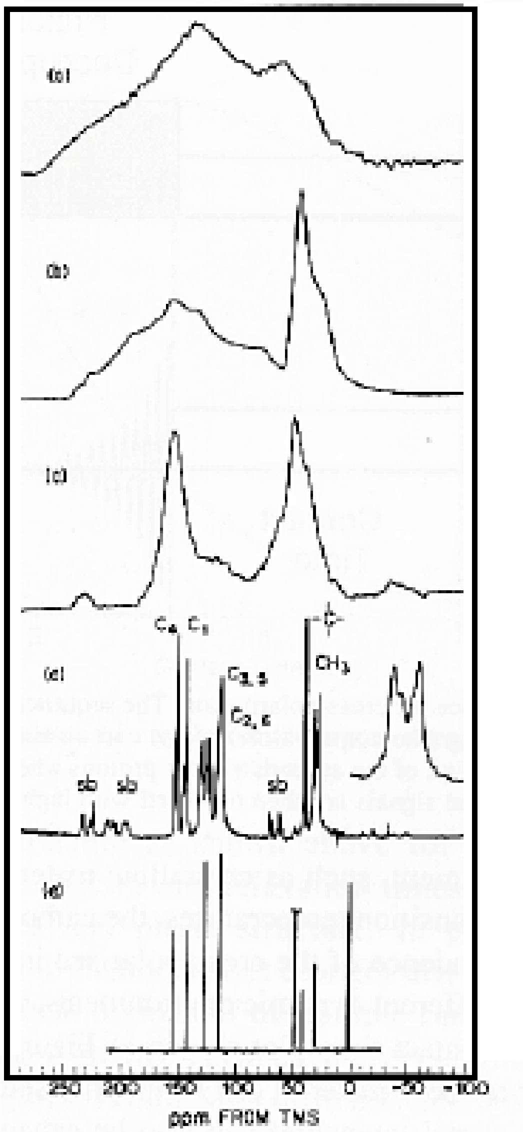
67 mm^3
(15 W / mm^3)



15 mm^3
(70 W / mm^3)

From van Rossum

Effect of MAS and strong rf irradiation



← no MAS, no decoupling

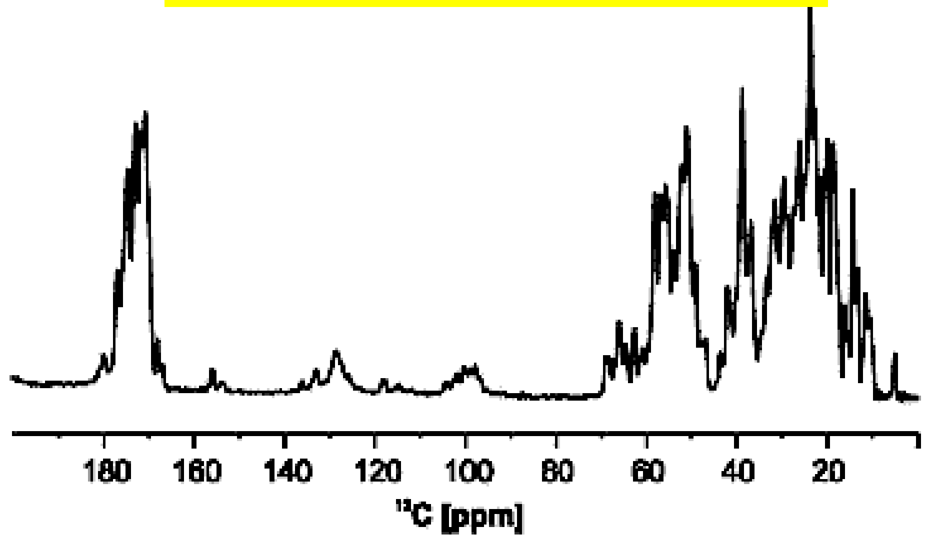
← no MAS, decoupling

← MAS, no decoupling

← MAS, decoupling

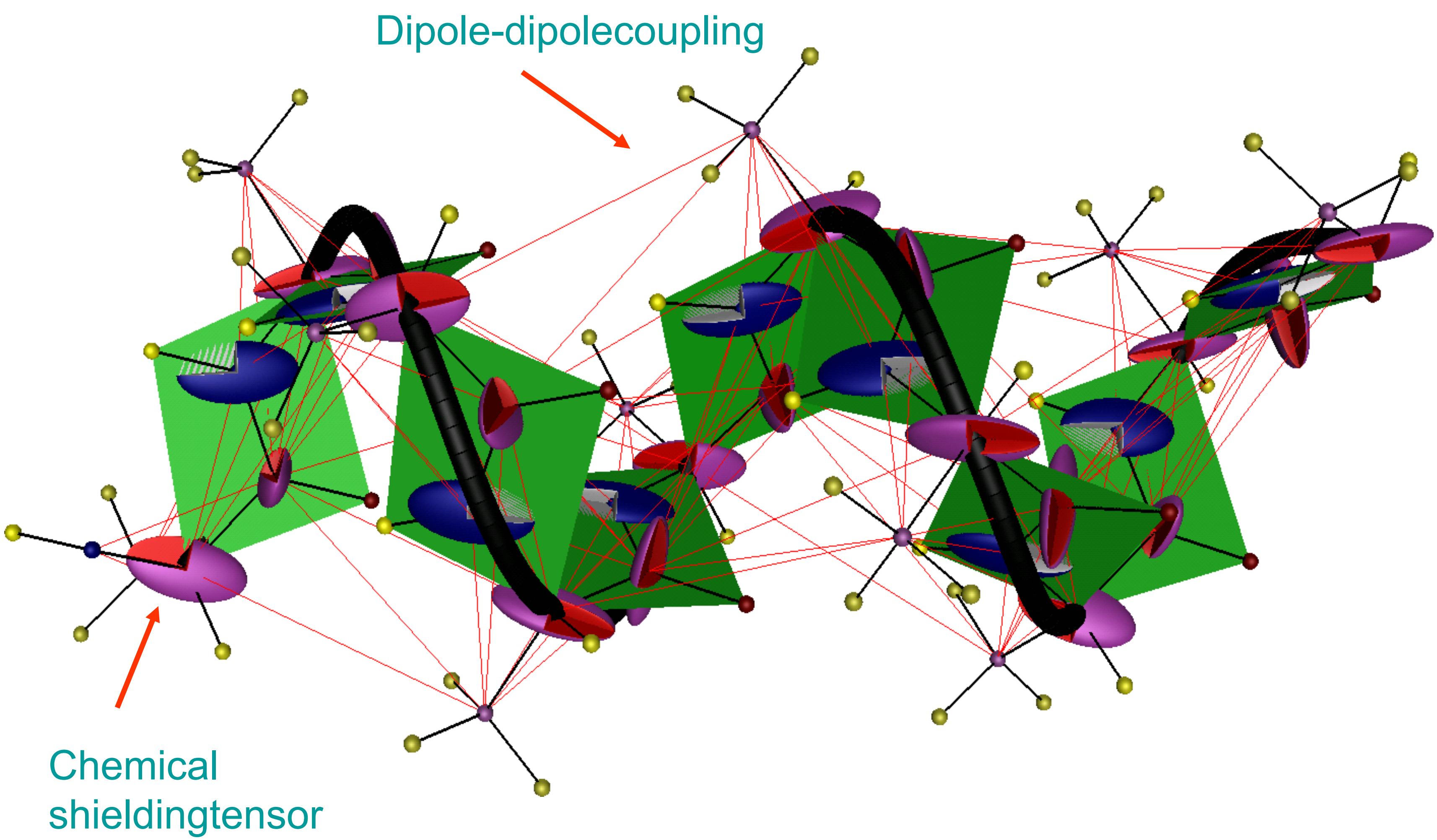
← solution NMR

A solid protein: Nanocrystals



A good high-resolution solid-state NMR spectrum brings us at the level where liquid-state NMR started

Detailed structure information
- do we regain control with too much power



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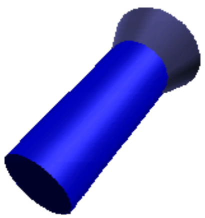
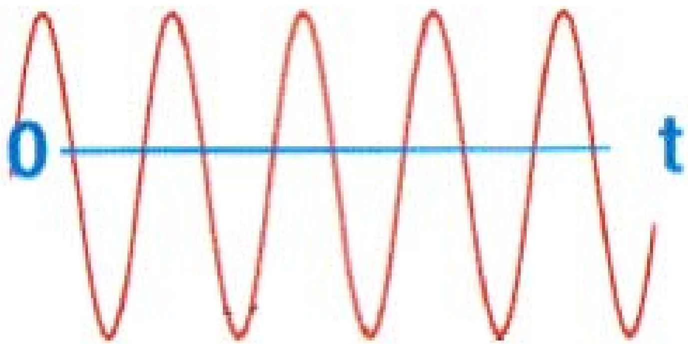
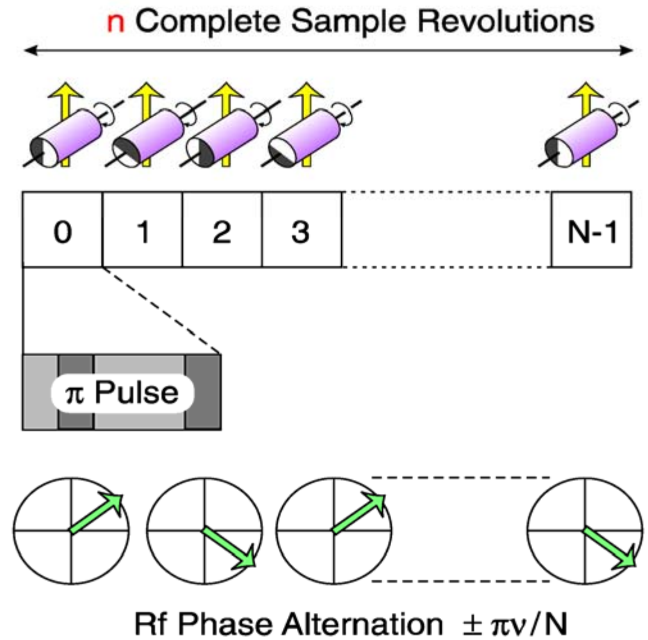
Tayloring of the Hamiltonian:
Recoupling of dipolar coupling interactions



Sample rotation destroys
exploitation of dipolar couplings



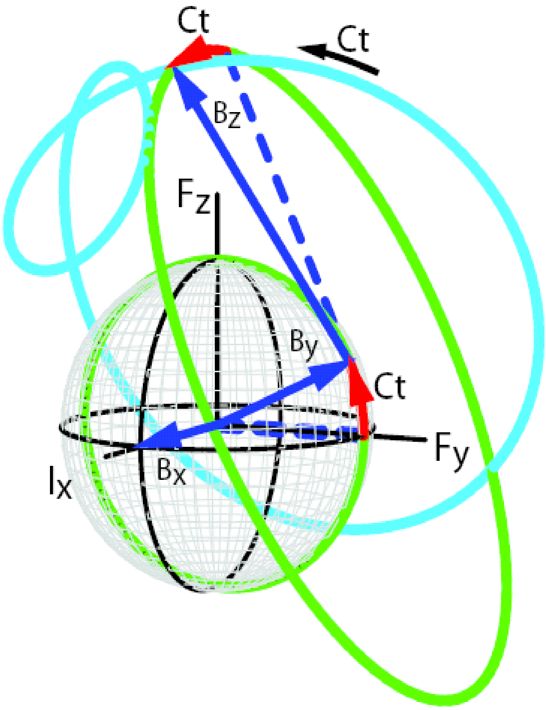
+

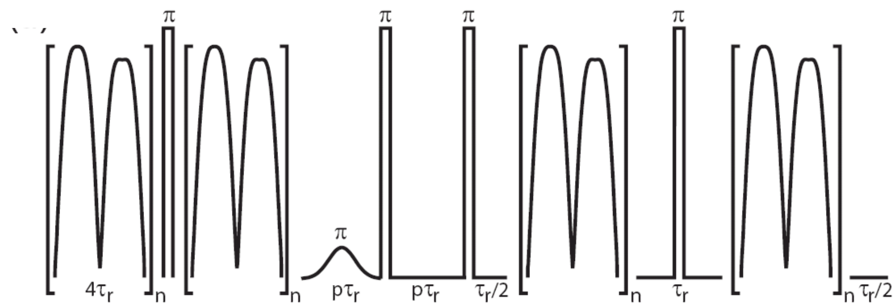


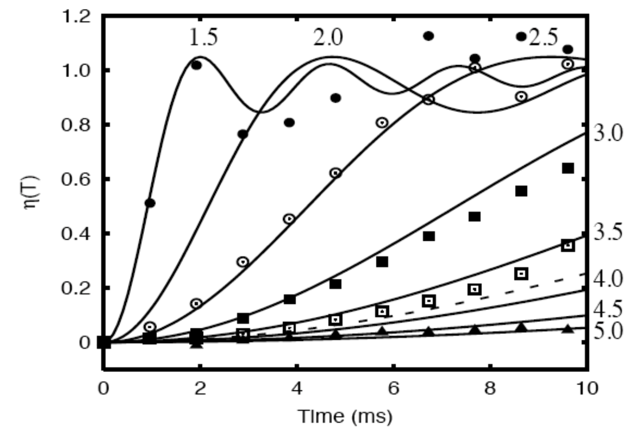
x

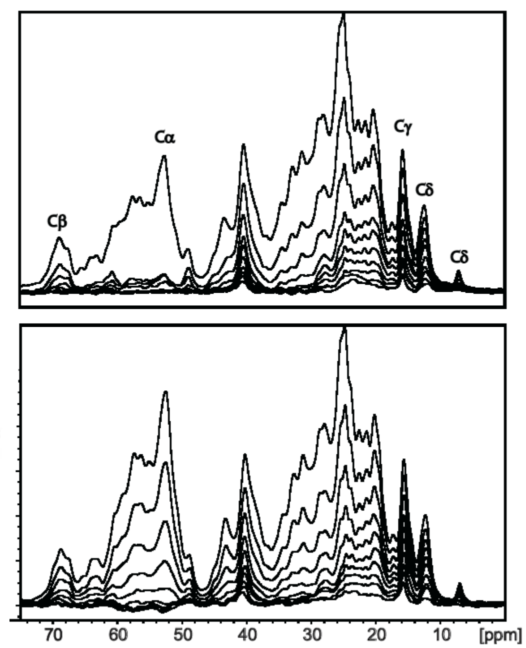
for p=-m

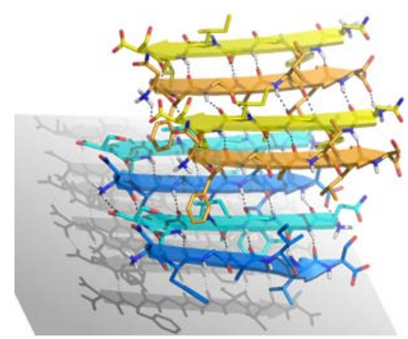
Accurate distance in MAS solid-state NMR: Recoupling without dipolar truncation – NMR robotics











Triple-Oscillating-Field-techniqUe
TOFU

Khaneja and Nielsen,
J. Chem. Phys., 2009
Straasø et al,
J. Chem. Phys., 2009

^{13}C-^{13}C distances up to 5 Å with 0.1-0.2 Å accuracy

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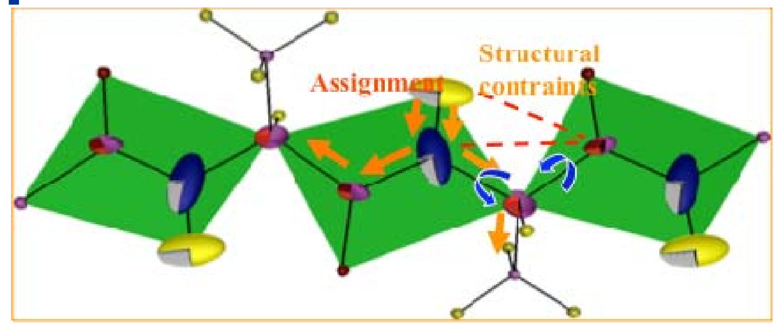
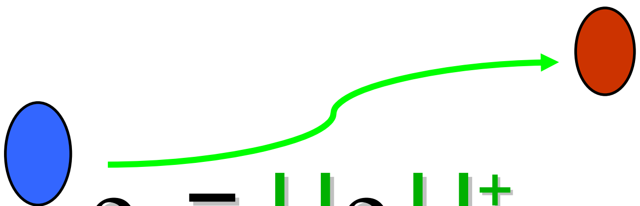
Optimal control design of NMR experiments

- improved sensitivity
- band selective operation
- less rf power consumption

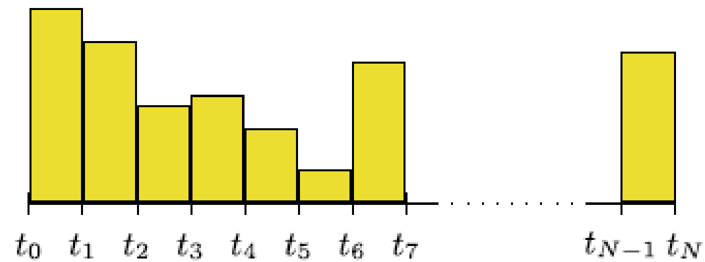
Kehlet et al, *JACS, 2004*
Maximov et al, *J. Chem. Phys., 2008*
Tosner et al, *J. Magn. Reson. 2009*





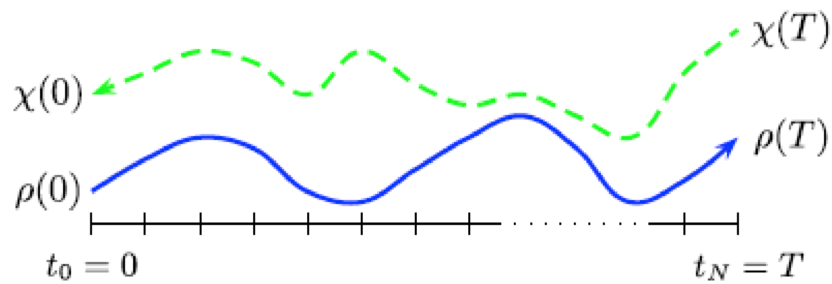
$\rho_f = U \rho_i U^+$

Optimal control => Design of $\bar{U}$

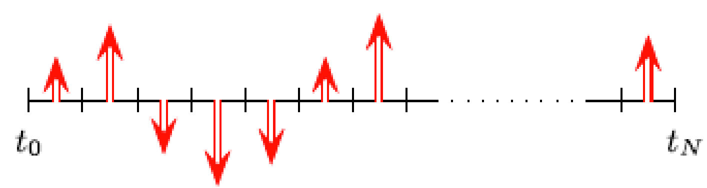


$$J_i = \phi_i - \lambda \int_0^T \sum_k u_k^2(t) \mathrm{d}t$$

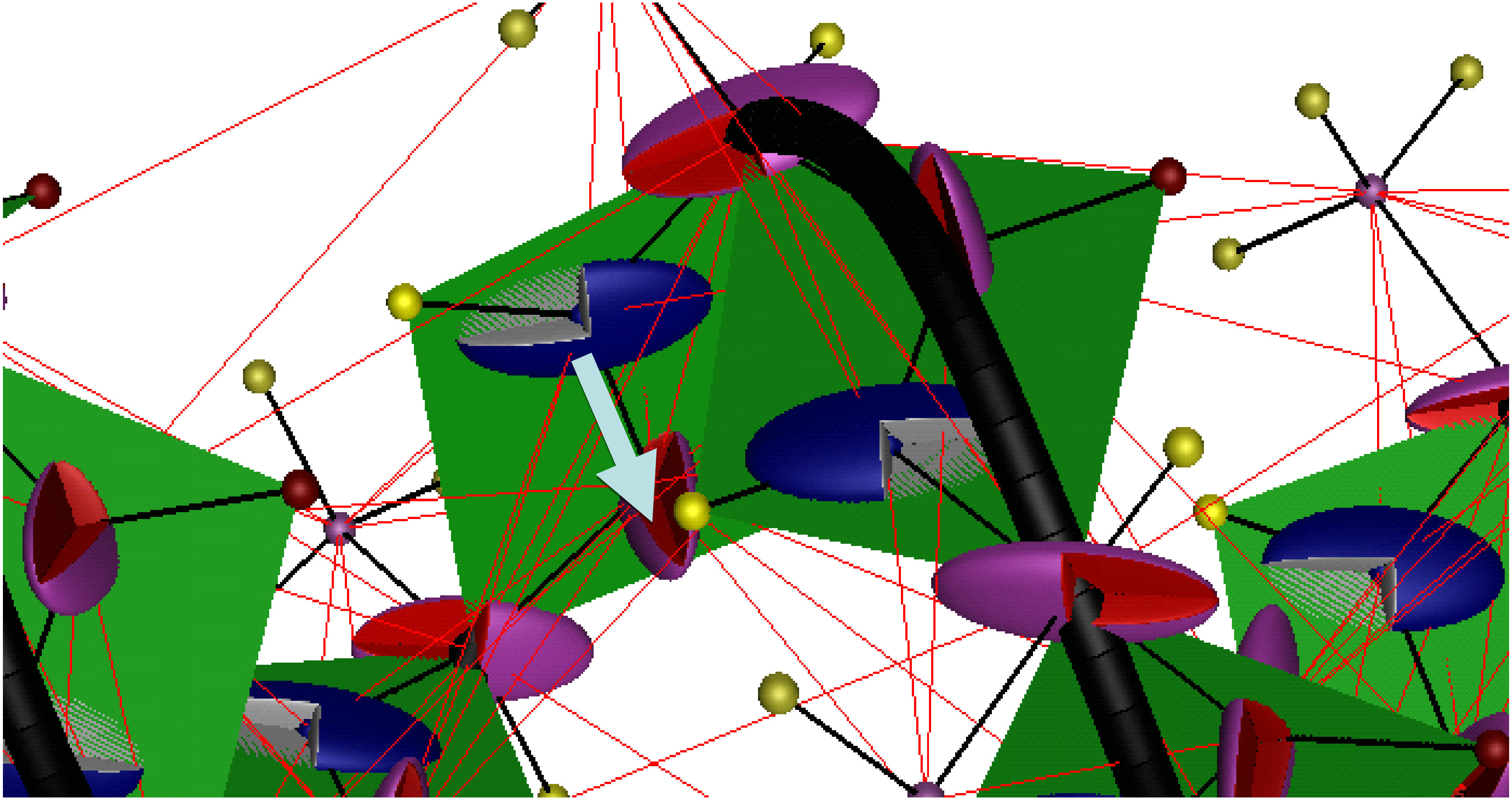
Final cost   Runningcost



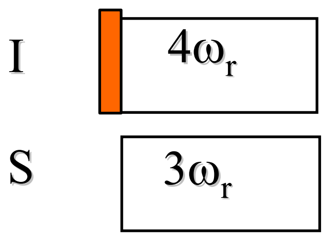
Final cost $\phi_1 = \mathrm{Tr}\left\{C^\dagger \rho(T)\right\}$

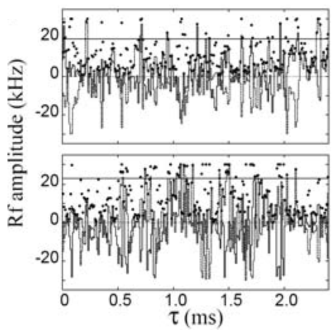


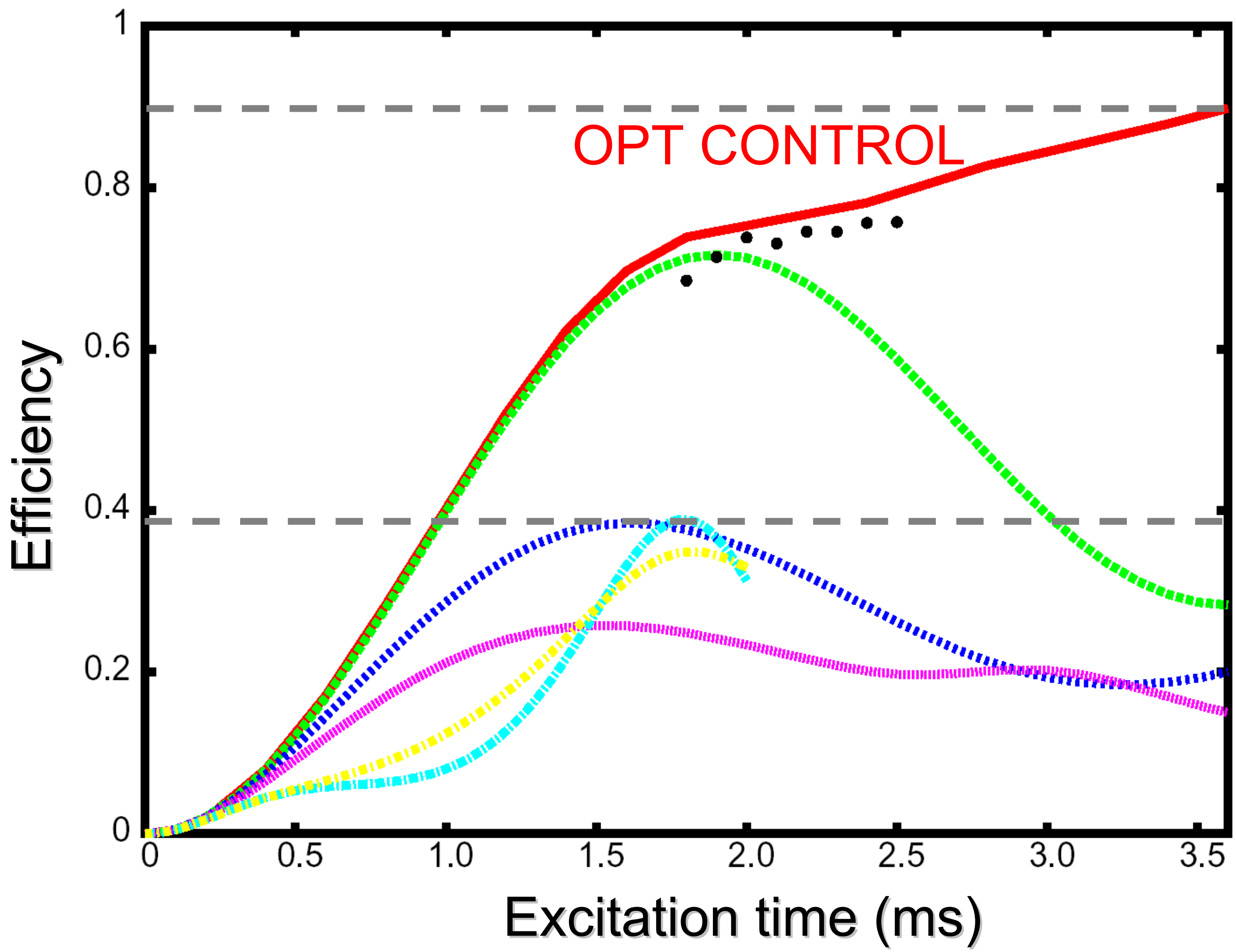
A specific case – many exists



Traditional recoupling vs. optimal control

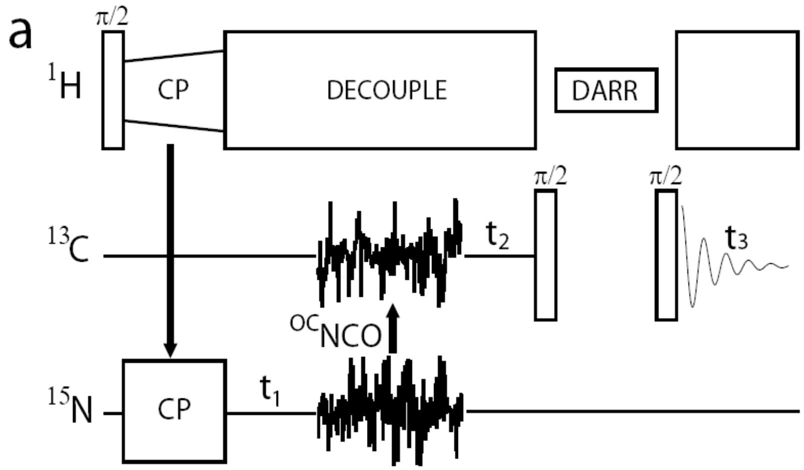




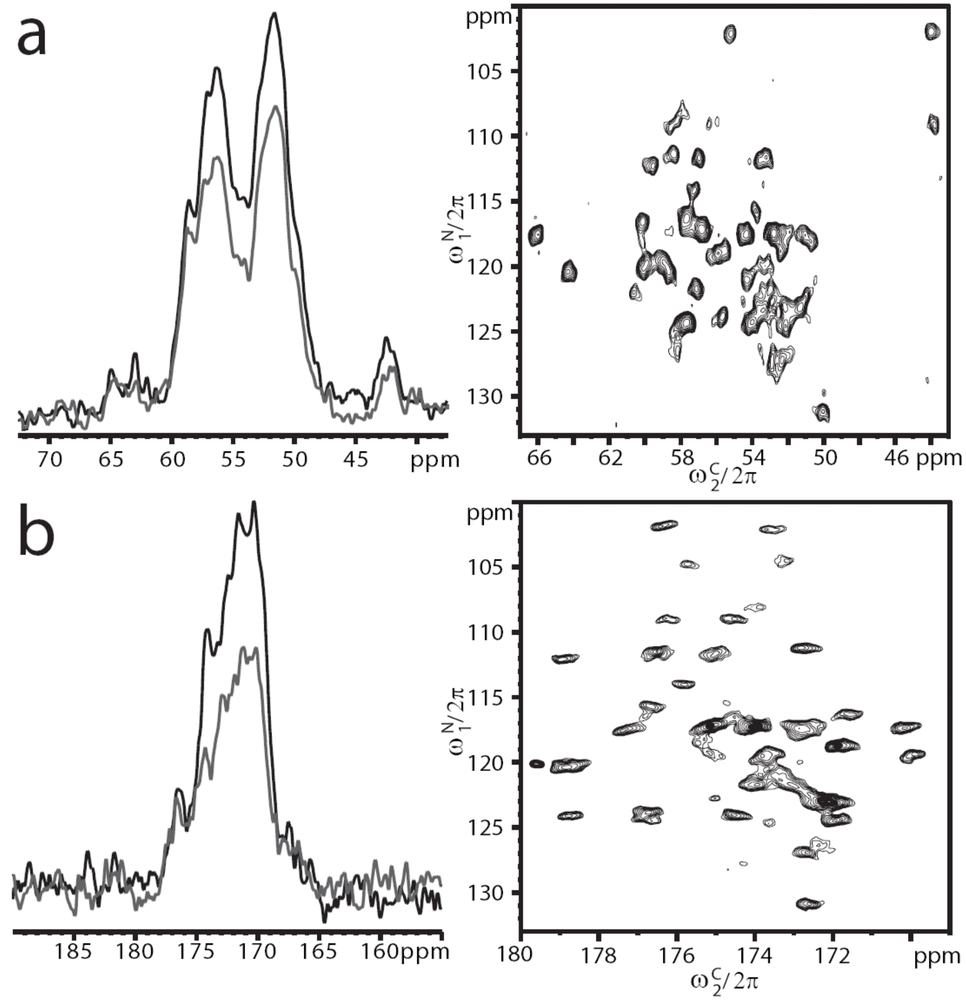


Gain: ~100%

3D NCOCX: U-^{13}C,^{15}N-ubiquitin



Optimal Control



50-100%
Higher sensitivity
(less sample/less time)

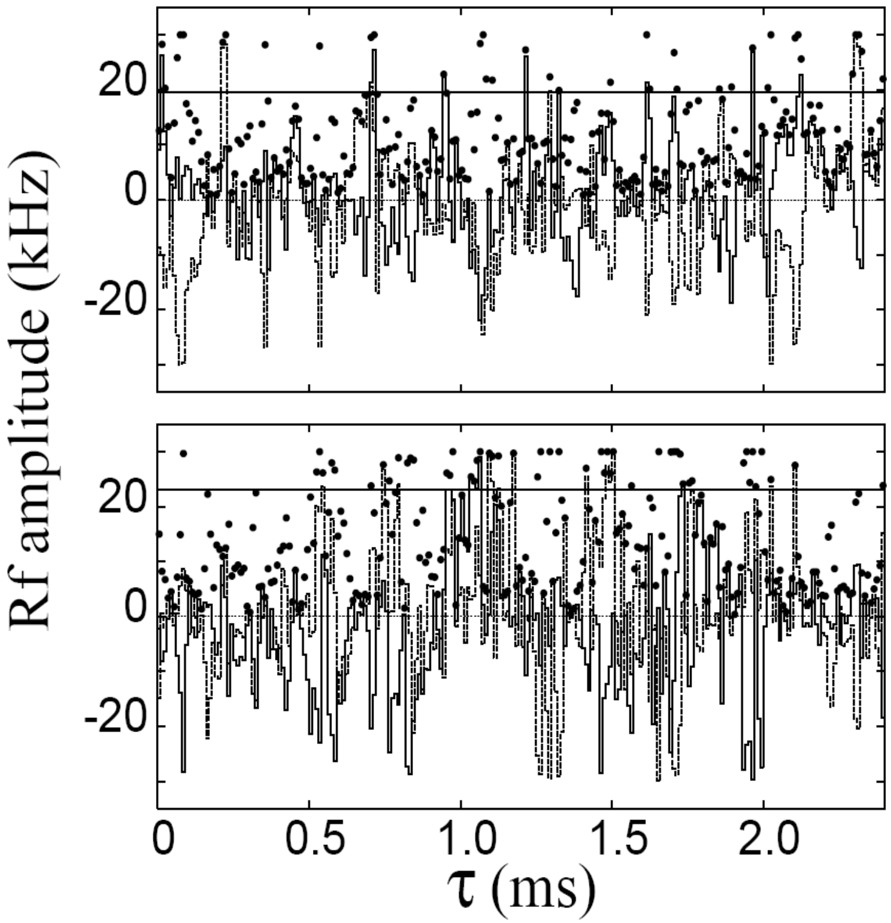
Less sample heating
(in the order of
1/10 – 1/4 power

Kehlet, Bjerring, Sivertsen, Glaser, Khaneja, Nielsen, J. Magn. Reson 188, 216 (2007)

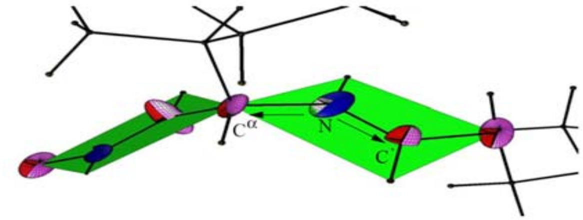
$^{15}N \rightarrow ^{13}C$ in NCO and NCA at highfield– sequence&robustness

^{15}N

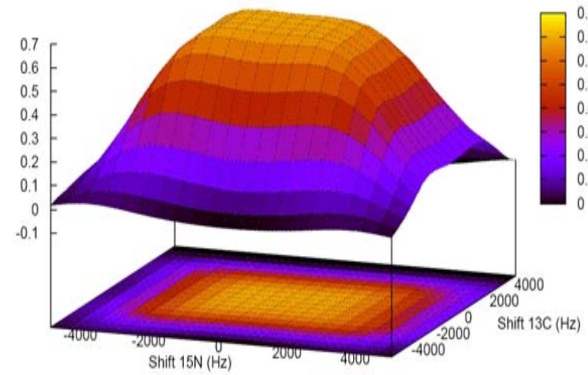
^{13}C



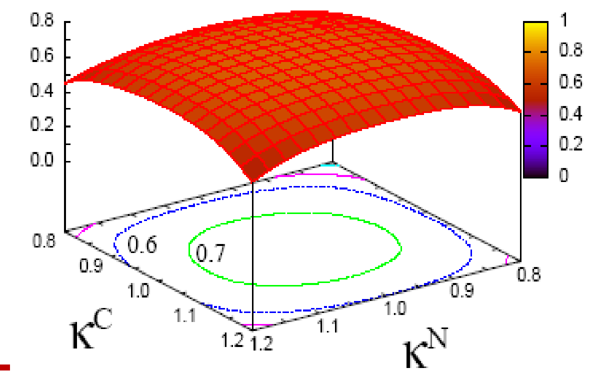
Transfer



Offset
$^{15}N/^{13}C$



Rf inhomogeneity
$^{15}N/^{13}C$



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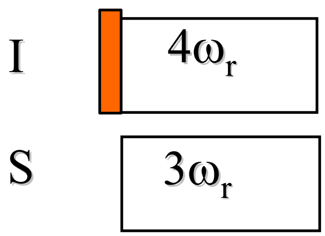
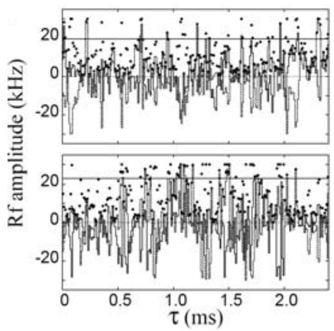
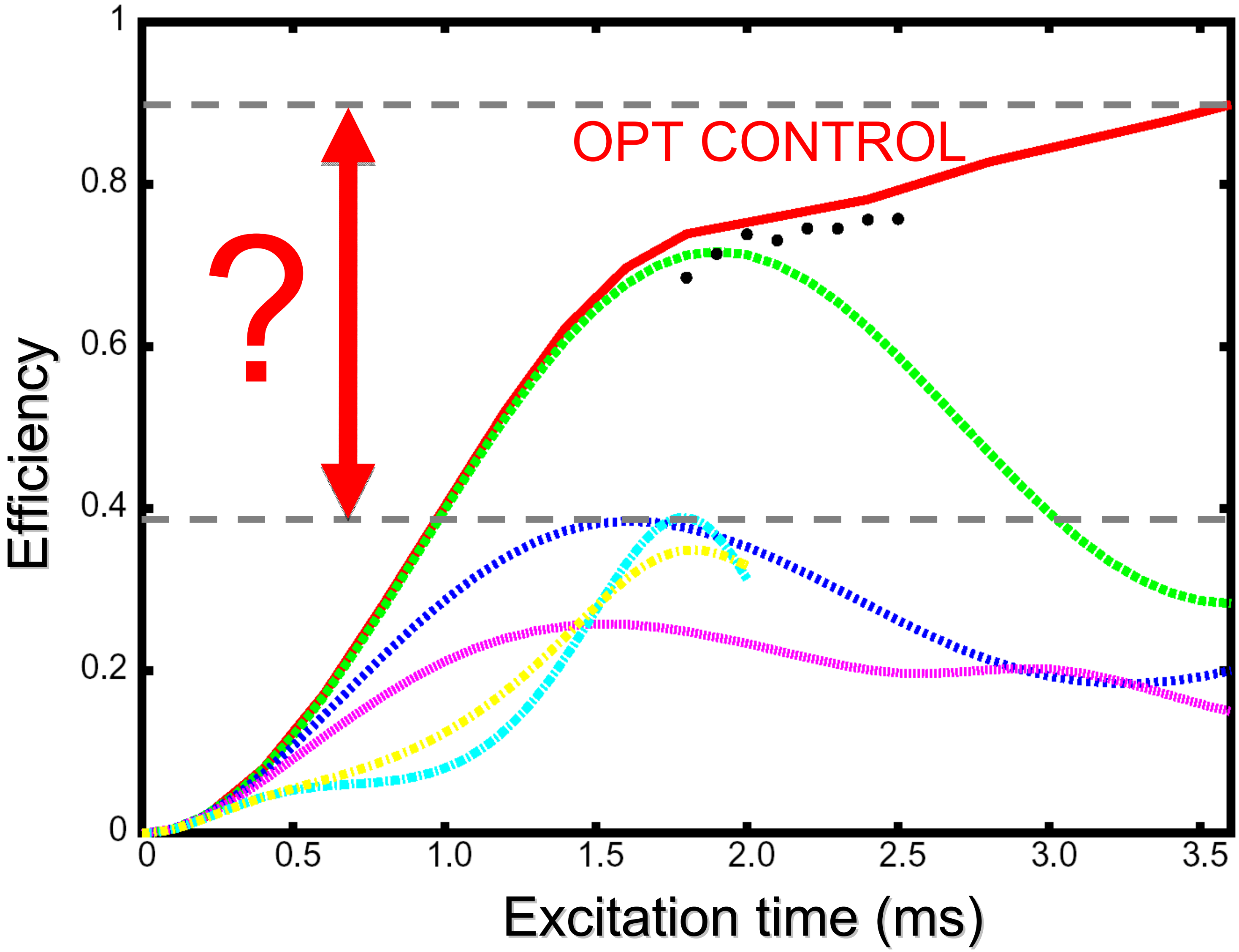
Niels Chr. Nielsen

Traditional recoupling vs. optimal control







Gain: ~100%

CompositeDipolarRecoupling

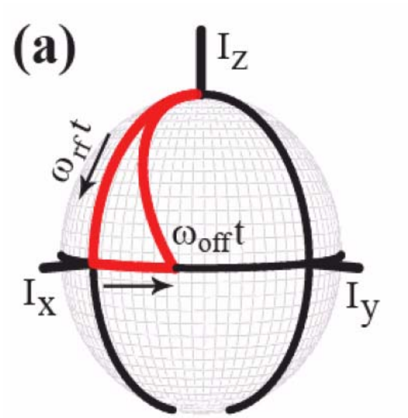
A marriagebetweenAnalytics and Optimal ControlNumerics

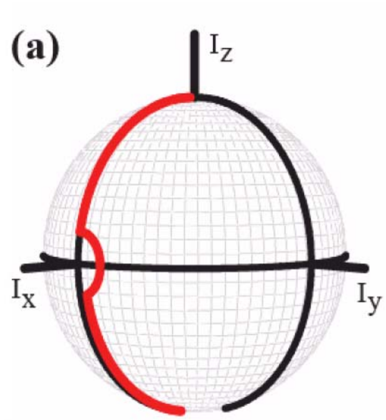
$(\pi/2)_y$

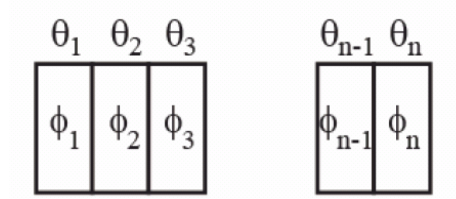
$(\pi/2)_y(\pi)_x(\pi/2)_y$

General translation

Rf pulse:





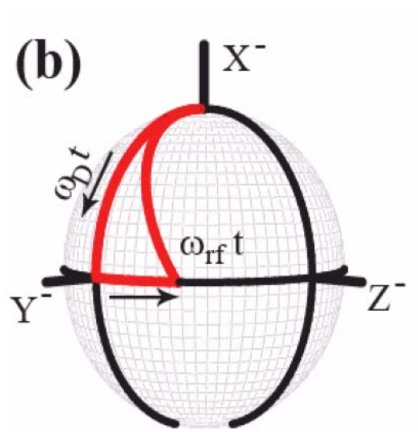


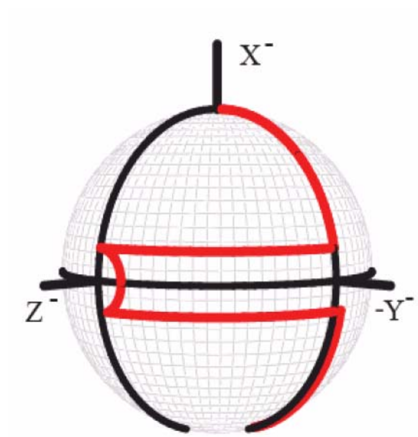
Improved rf inhom compensation

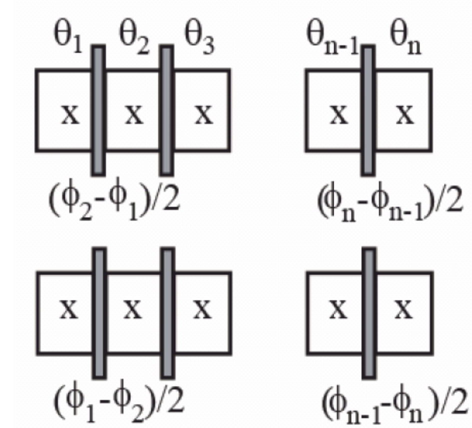
Dipolar recoupling:

ZQ-frame:

$I_x \xrightarrow{\pi} S_x$







Improved β-angle compensation

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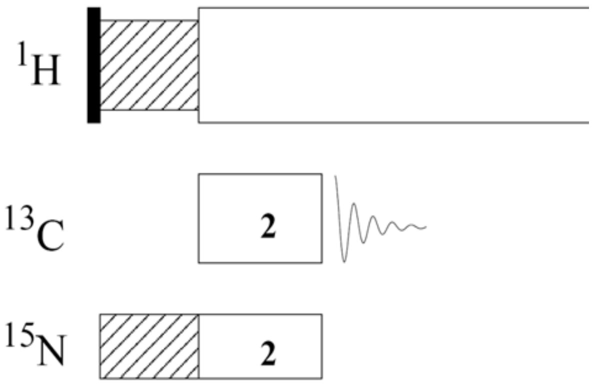
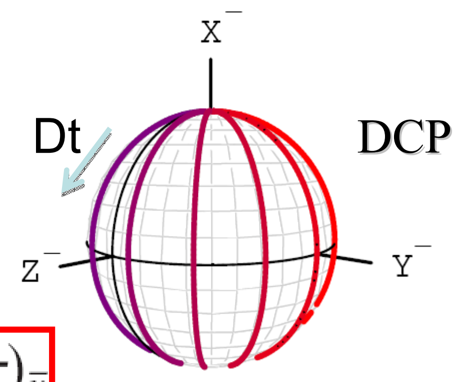
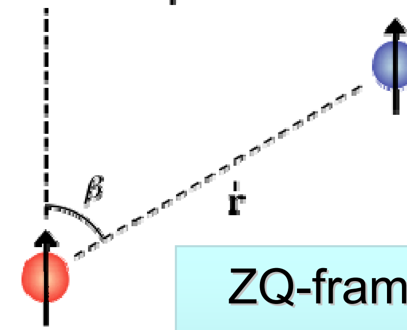
Inspiration from optimal control: CompositeDipolarRecoupling

$$D \propto \frac{1}{r^3}\left(3\cos^2\beta - 1\right)$$



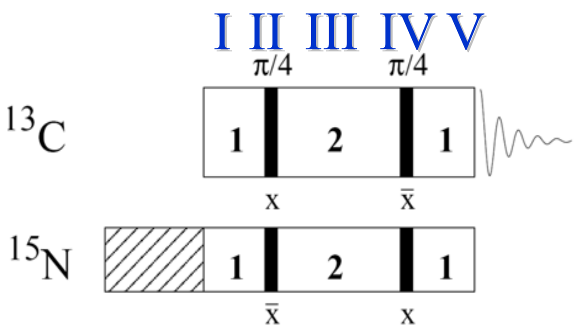


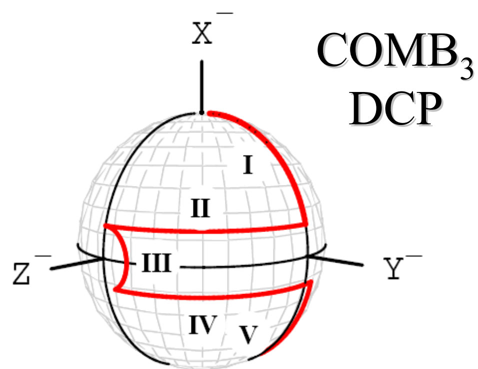
$(\pi)_{\bar{x}}$



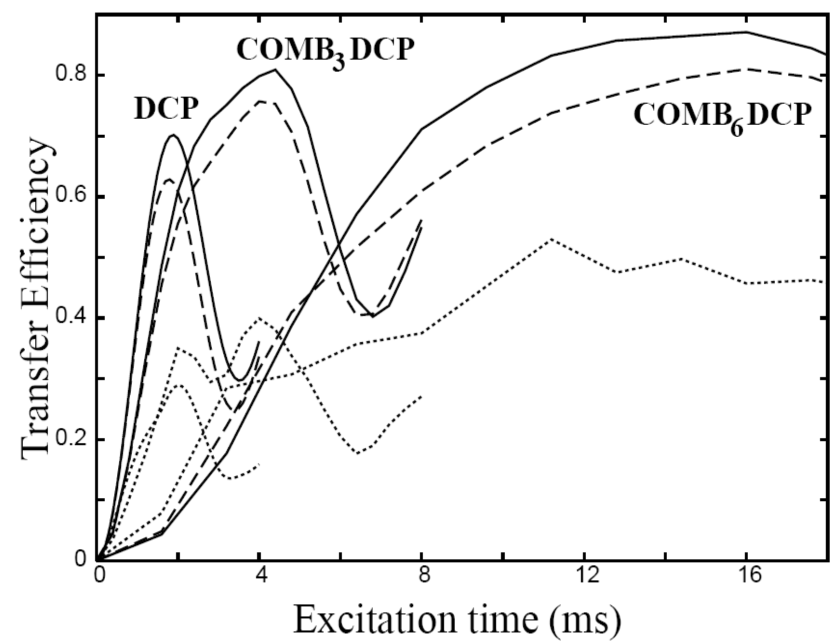
ZQ-frame:

$I_x \xrightarrow{\pi} S_x$





$(\pi/2)_y(\pi)_{\bar{x}}(\pi/2)_y$



Better compensation towards orientation (β) variation of dipolar coupling

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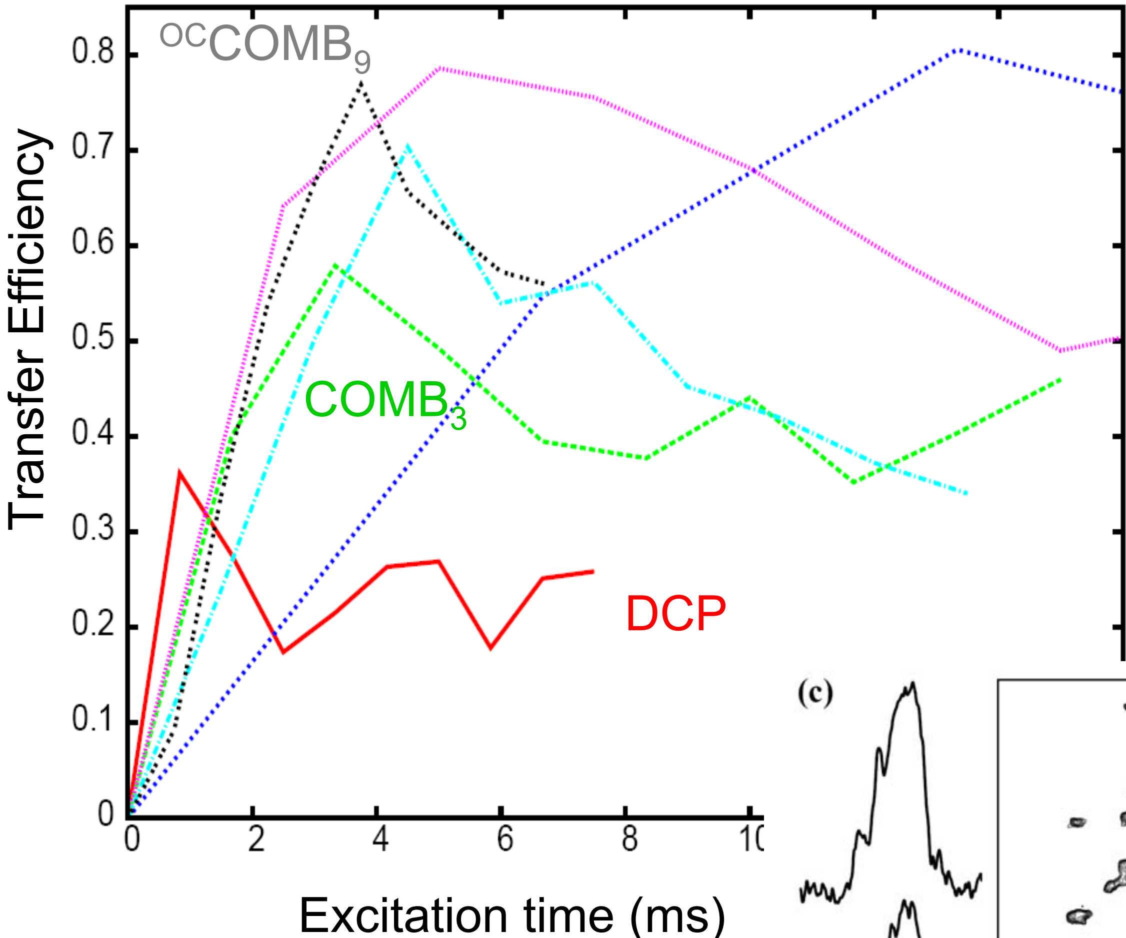
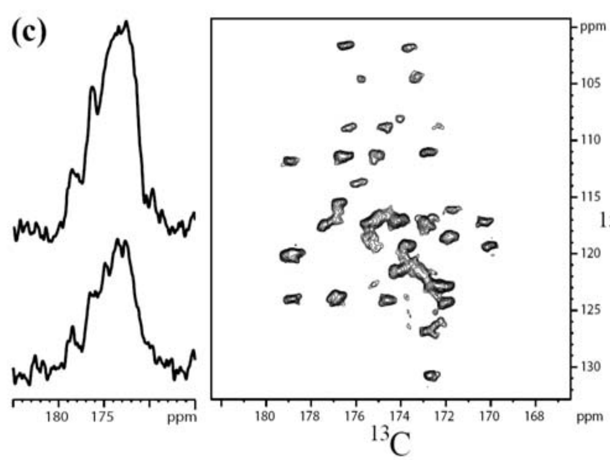
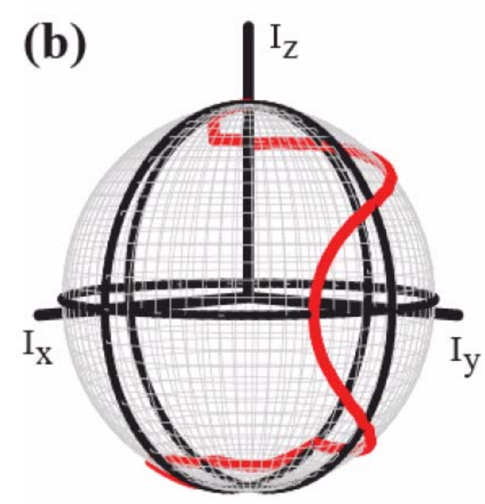
Optimal Control version with Reduced Dimensionality

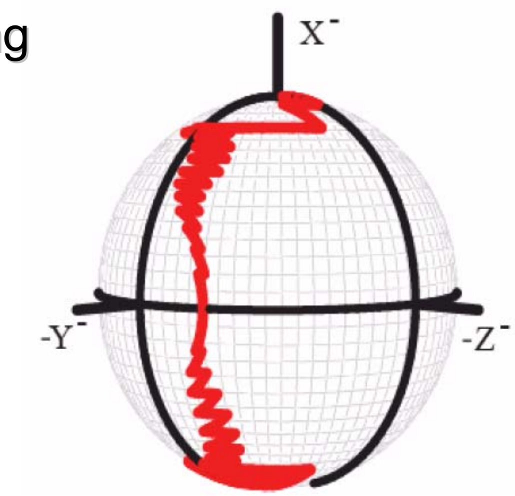




Rf pulses



Recoupling sequence



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Hansen, Kehlet, Vosegaard, Glaser,Khaneja, Nielsen,
Chem. Phys. Lett. 447, 154 (2007)

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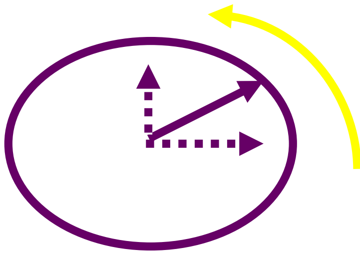
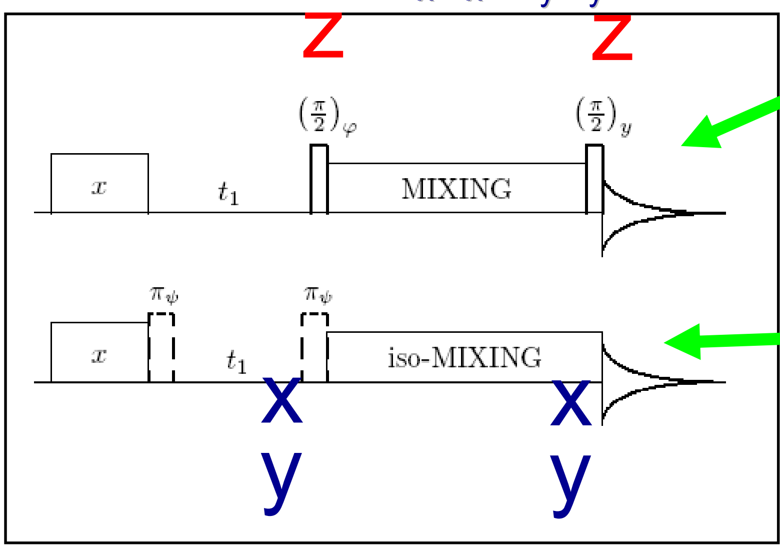
Optimization of *Effective* Hamiltonians
Sensitivity-enhanced 2D solid-state NMR

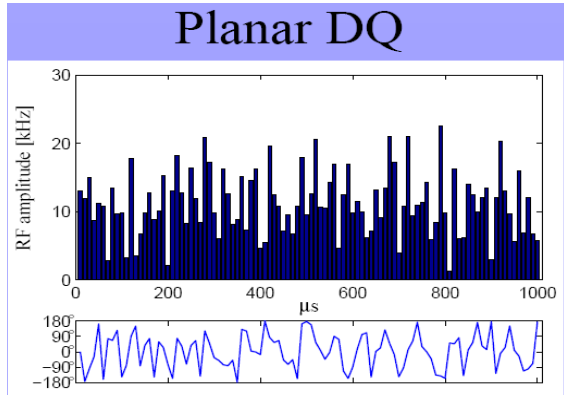


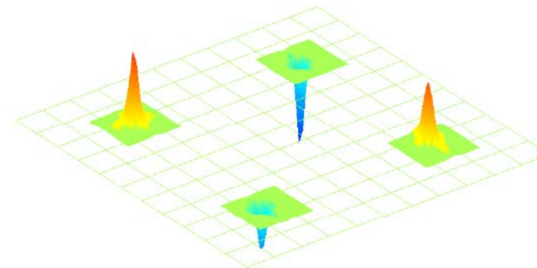
Only transfer of x- or y-component

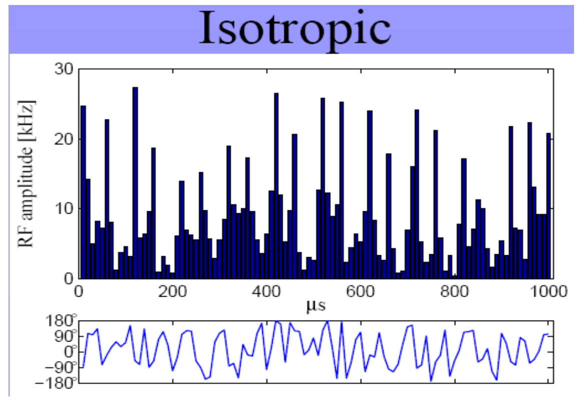
$2I_xS_x-2I_yS_y$

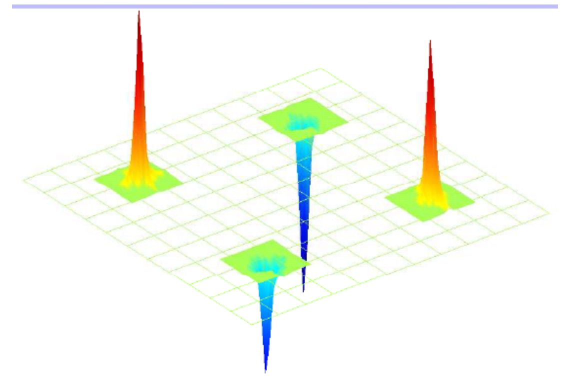


$2I_xS_x+2I_yS_y+2I_zS_z$







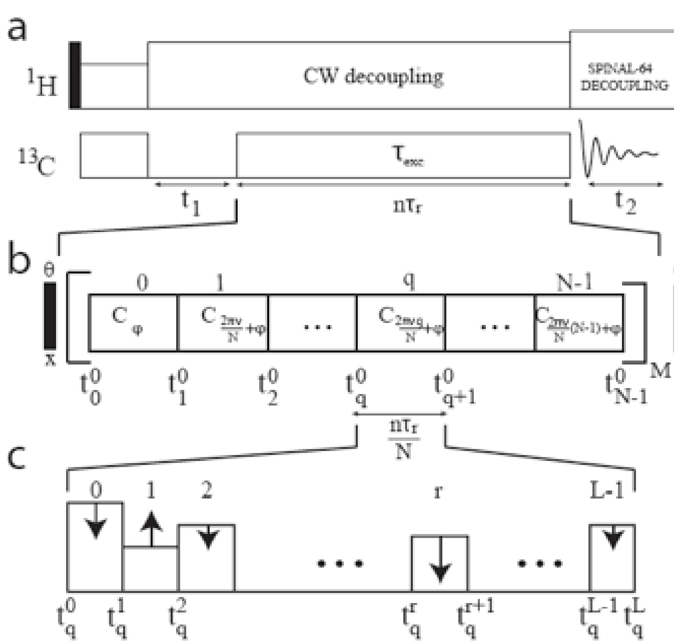


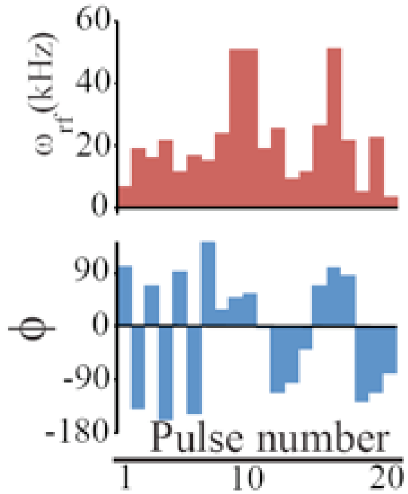
Transfer of bothcomponentsafter t_1 evolution =>√2 sensitivityenhancement

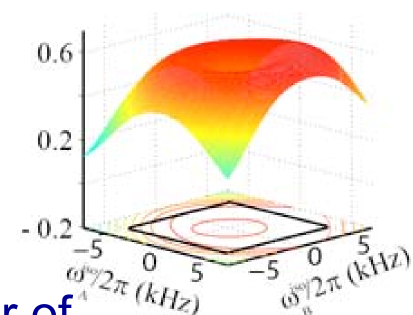
Tosner, Glaser, Khaneja, Nielsen, *J. Chem. Phys.* 125, 184502 (2006)

Symmetry-based optimal control experiments for assignment

^{OC}C7 band-selective mixing for
2D CACB, CACX & 3D NCACB





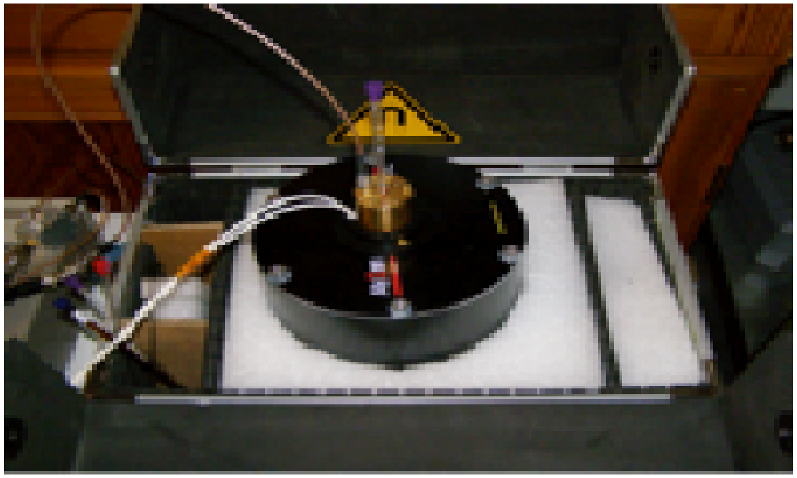


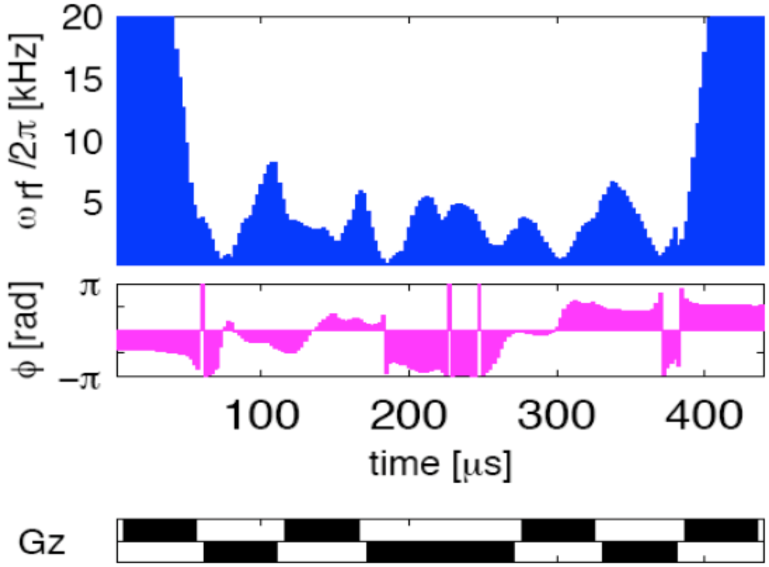
Reducing the RF FIELD's by a factor of
3-4 => only 10-15'th sample heating

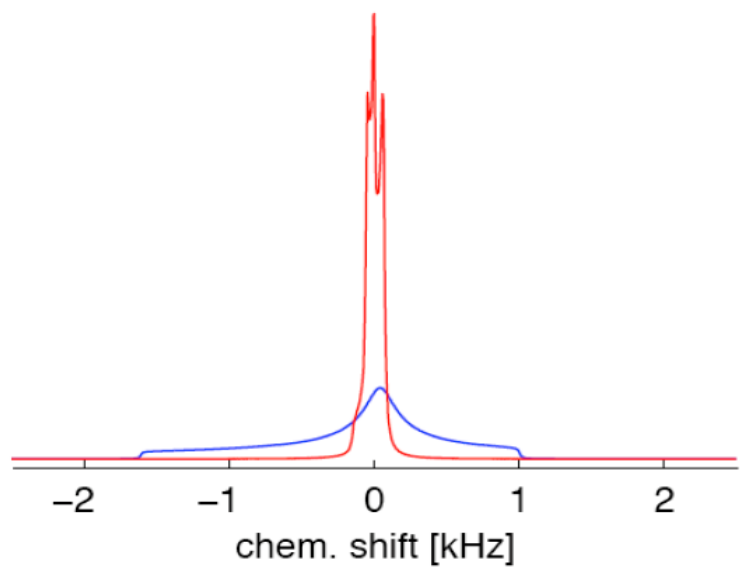
Gain:
X 3-4

Nielsen et al,
J. Chem. Phys.., 2009

Low-field NMR using Optimal Control for Resolution Enhancement







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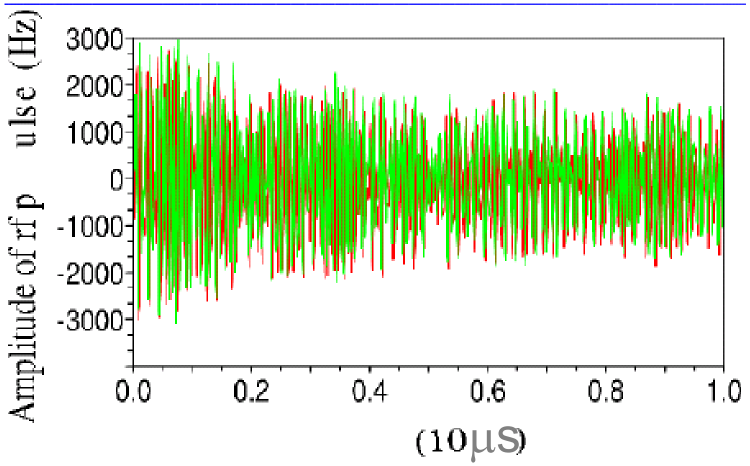
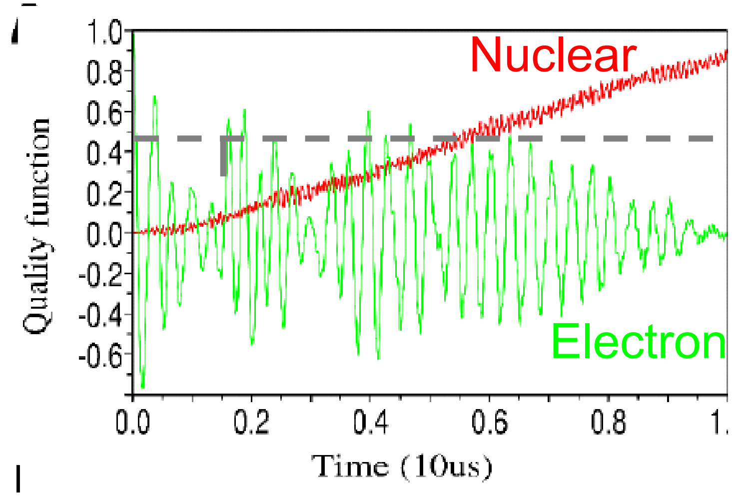
Optimal control and DNP

S(Electron)-I(Nucleus) two-spin system

$$H_0 = \Omega_n I_z + A S_z I_z + B S_z I_x$$

$\Omega_n/2\pi = -14$ MHz [1]H Zeeman
$A/2\pi = 6$ MHz
$B/2\pi = 3$ MHz

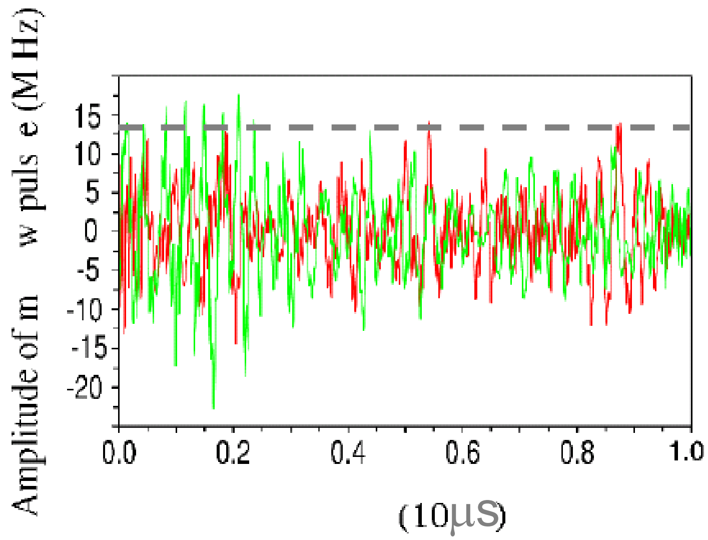




$S_x \rightarrow I_z$

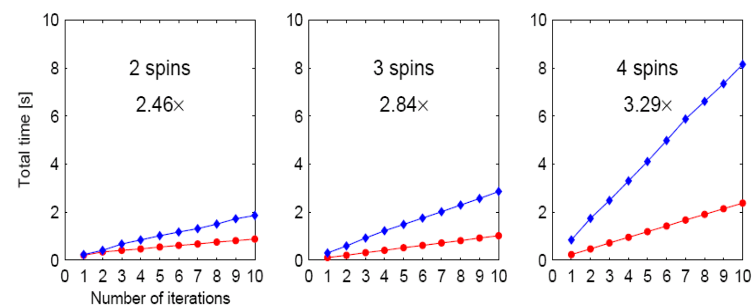
A: secular part of hyperfine interaction

B: Pseudo secular part of hyperfine interaction



Computational time

Krotov: Red
GRAPE: Blue



MW @ 9 GHz (X-band) – ca. 0.3 T (14 MHz) NMR

Jeschke, Schweiger, Mol Phys 1996

Maximov, Tosner, Nielsen, JCP (2008)

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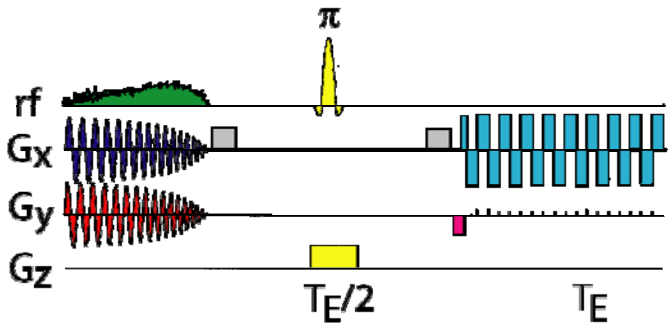
Optimal control in MRI: Excitation of a HALF BRAIN

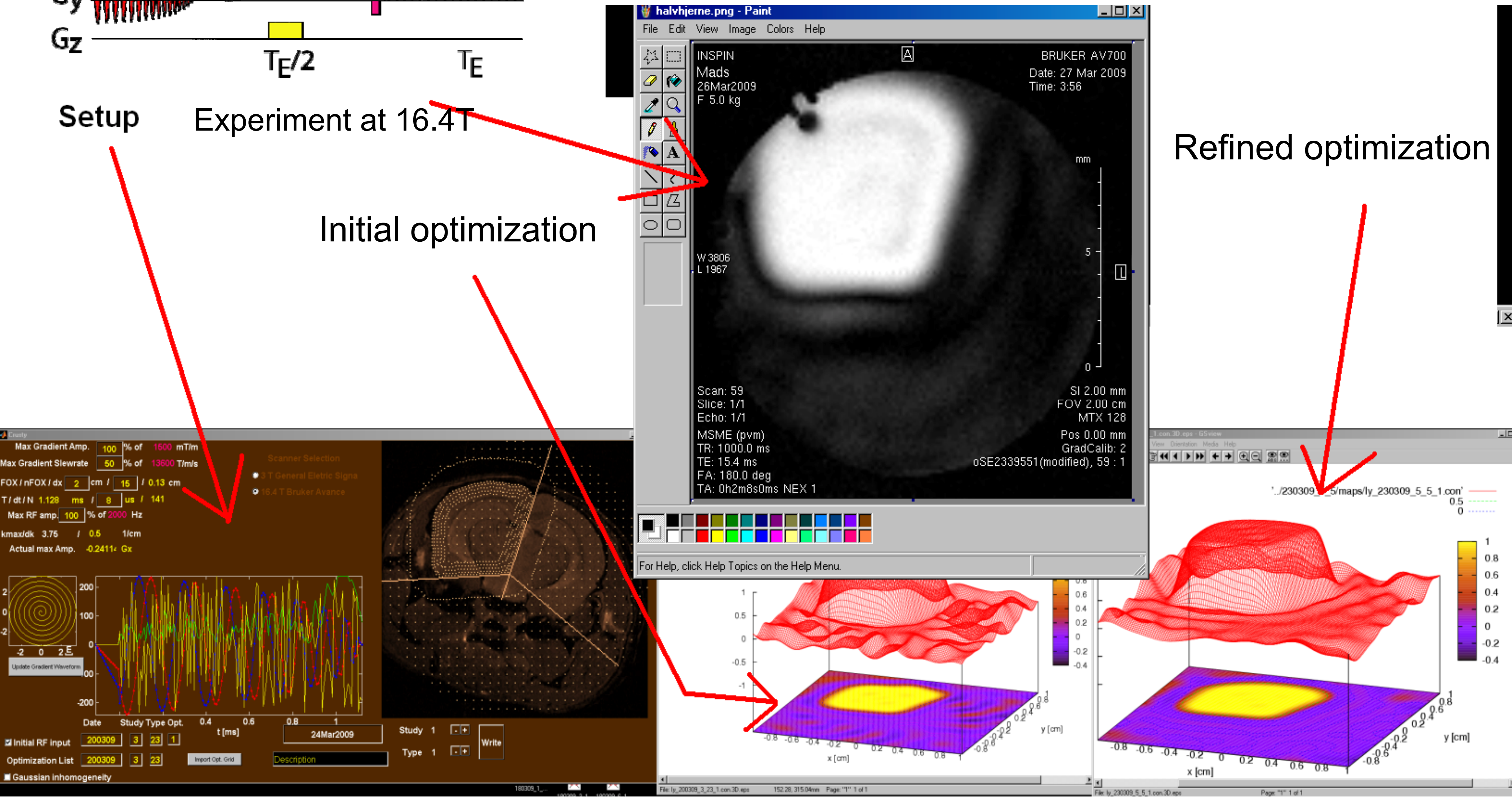


Setup

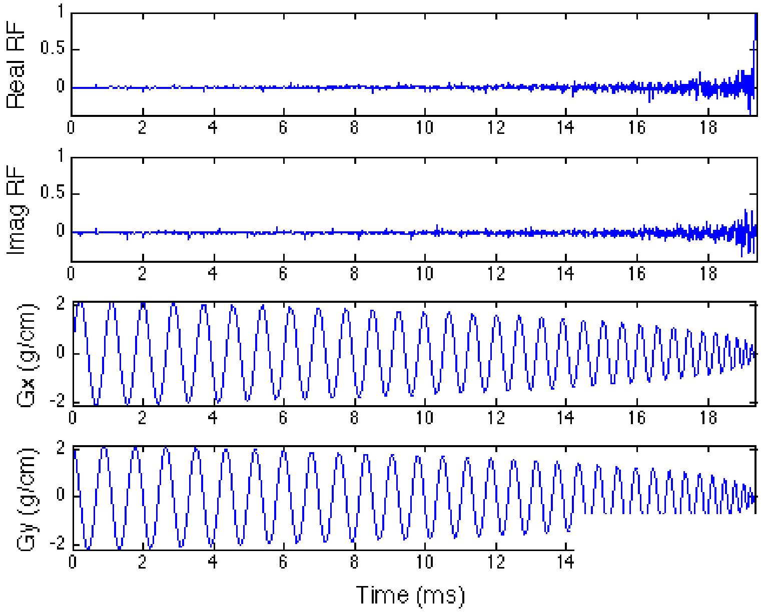
Experiment at 16.4T

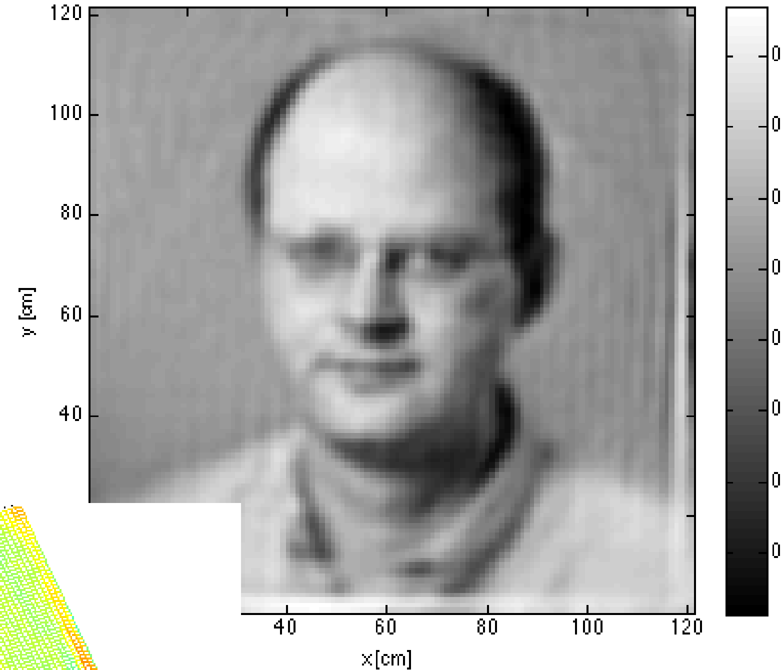
Initial optimization

Refined optimization

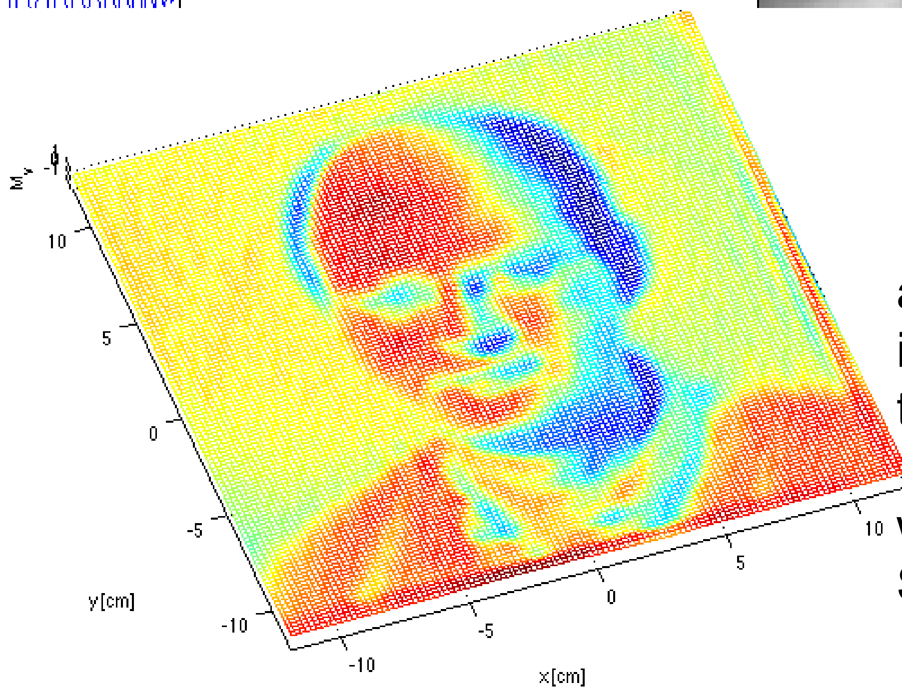


Talkingabouthalfbrains– OC can do amazingthings ..





What do you think this pulse will excite?



and NMR/MRI/DNP is an excellent field to the the capabilities in …

we provided open source Software – you do the rest

Thanks to ….

NavinKhaneja, Harvard
Steffen Glaser, München
ZdenekTosner, Praque

Aarhus:
CindieKehlet
Mads Sloth Vinding
ZdenekTosner
MortenBjerring
Astrid ColdingSivertsen
Ivan Maximov
Thomas Vosegaard
Jonas Ørbæk Hansen
Anders Bodholt Nielsen
Lasse Arnt
Troels Skrydstrup
Daniel Otzen
Jan Enghild
Torsten Kristensen
Sigrid Svane
Jan Mondrup Petersen
Ronnie Pedersen
Kim Hein
Martin Jeppesen

... and YOU for your attention

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Niels Chr. Nielsen