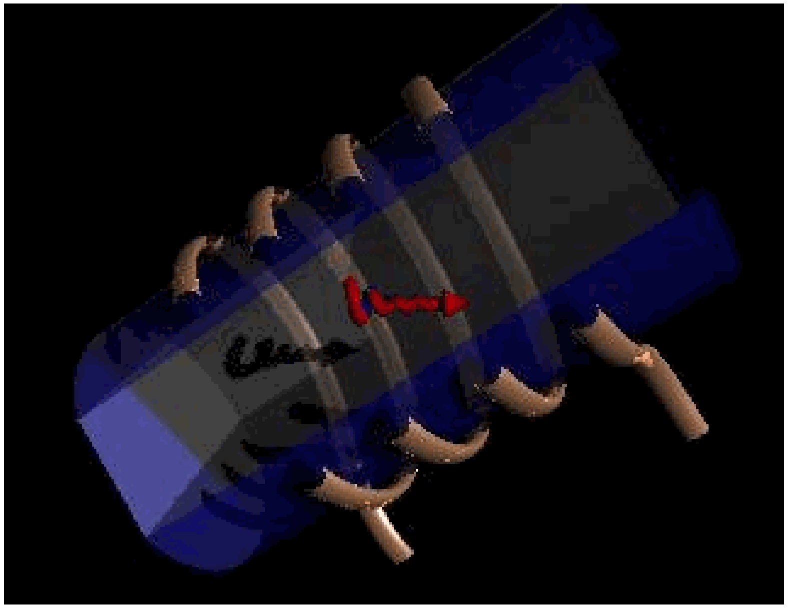
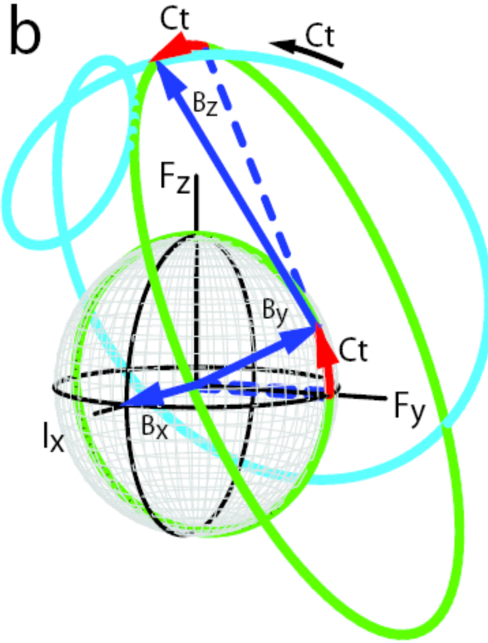
Quantum Control in Magic-Angle-Spinning Solid-State NMR:

Tailoring the Hamiltonian Through Modulation and Demodulation





Kavli Institute for Theoretical Physics, UCSB, Santa Barbara, June 18, 2009

AARHUS UNIVERSITET

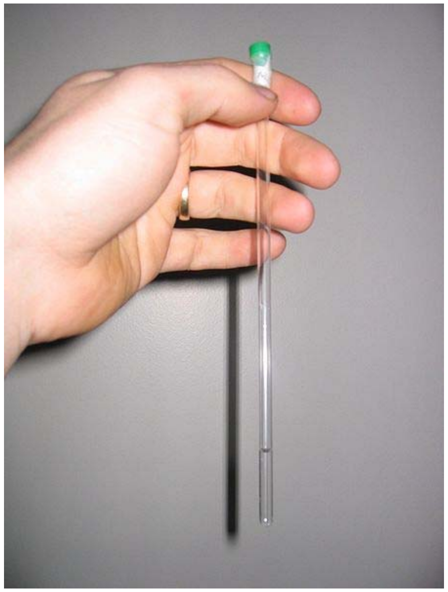
Center for Insoluble Protein Structures

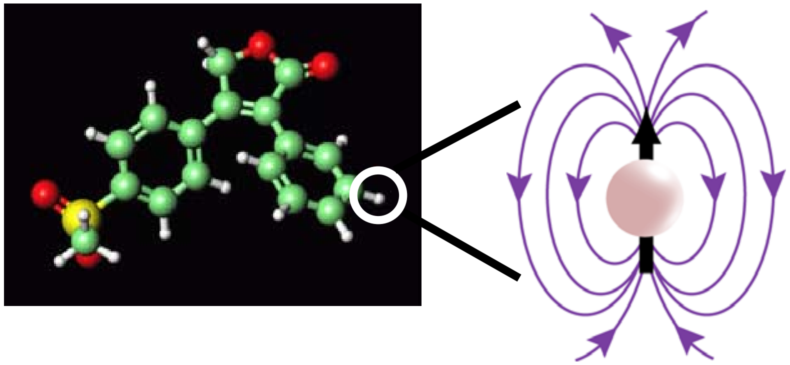
Niels Chr. Nielsen

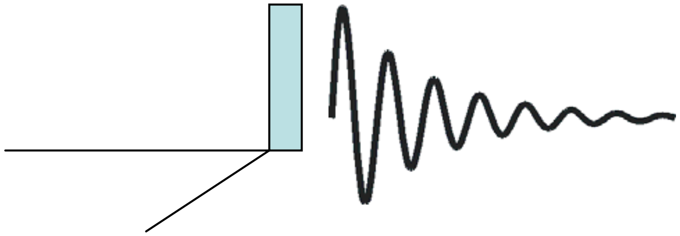
Outline

- Introduction to NMR and motivation for going into solids
- The challenges of solid-state NMR – leading to our control problem
- Ways to tailor our nuclear spin Hamiltonian to provide information
- Dipolar recoupling in solid-state NMR
- Optimal control solutions to the problem

Background

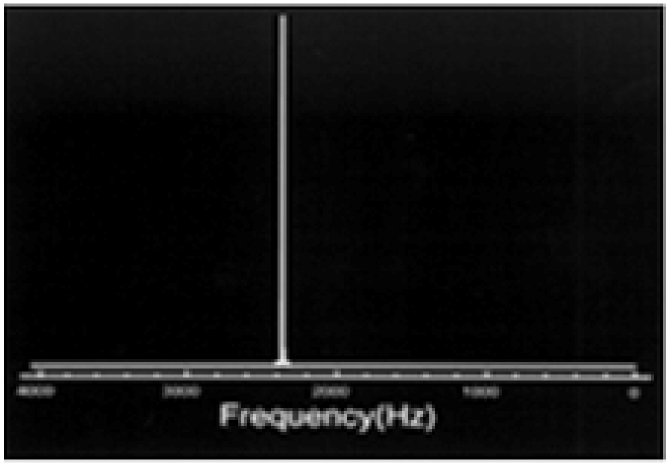




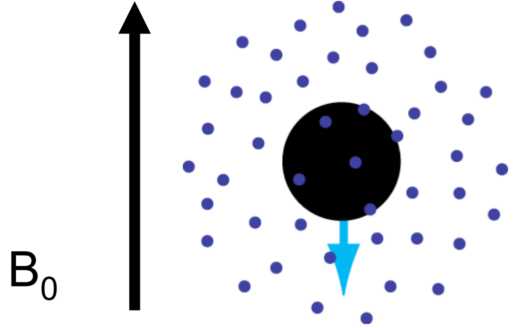


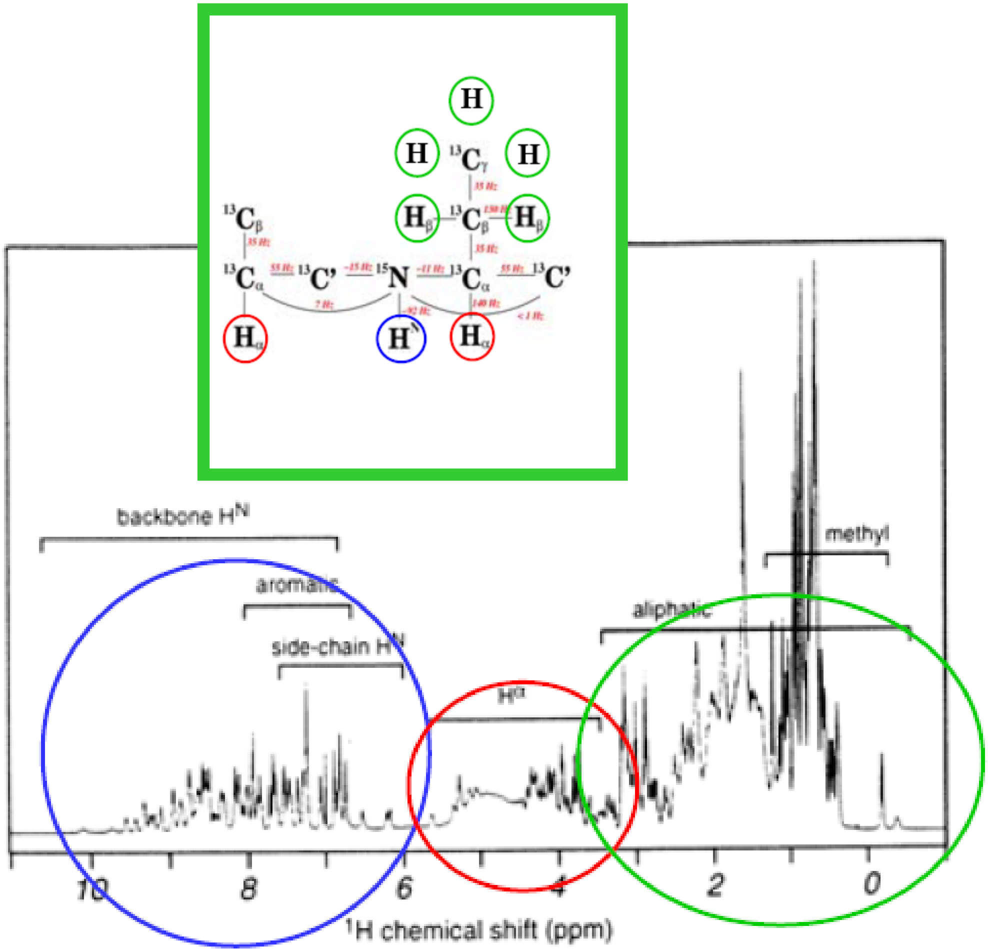
RF Pulse

Fourier
Transform



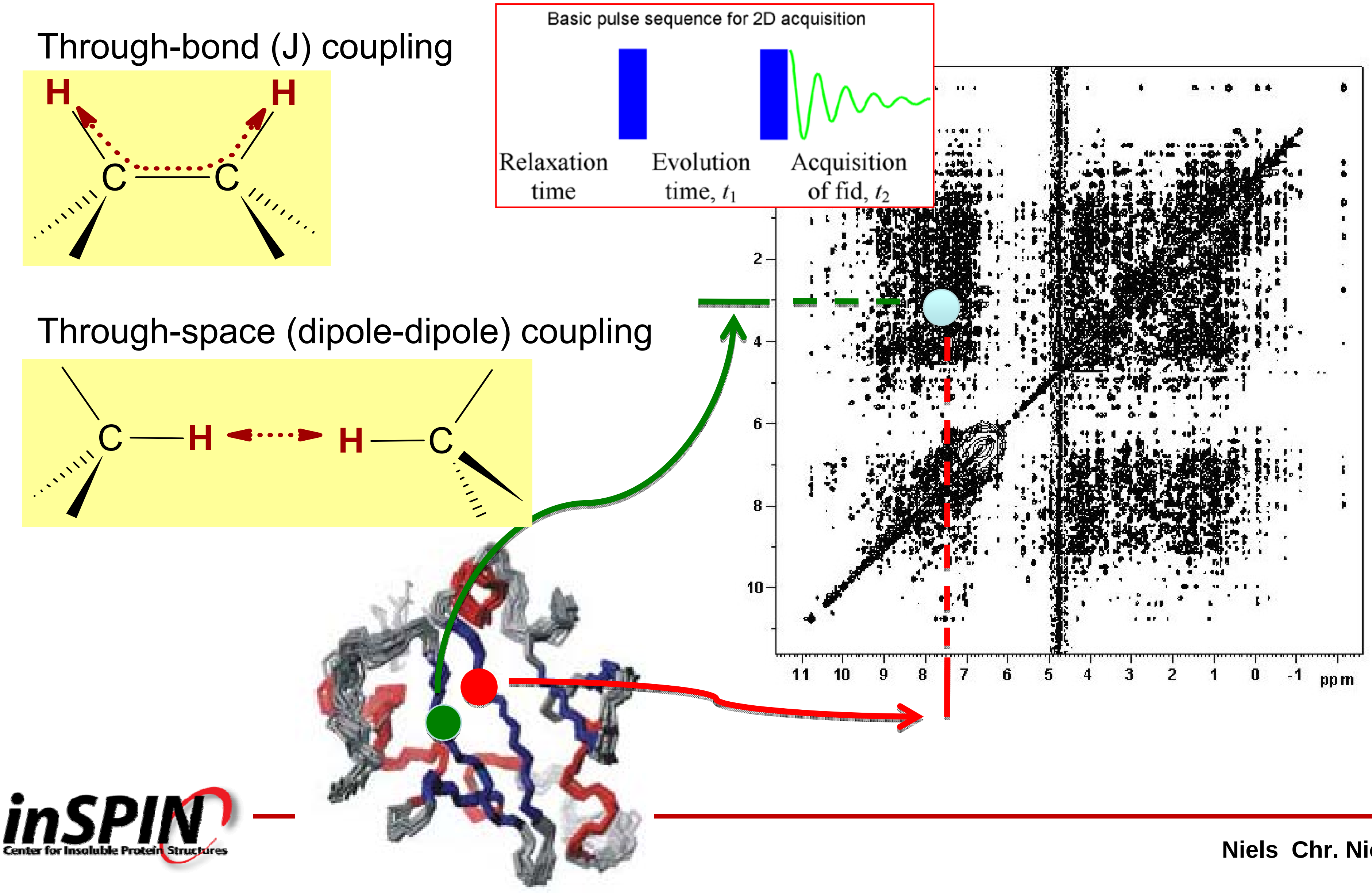
Chemical Shift – the resonance frequency depends on the electronic surrounding





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

Basic pulse sequence for 2D acquisition

Relaxation time

Evolution time, t_1

Acquisition of fid, t_2

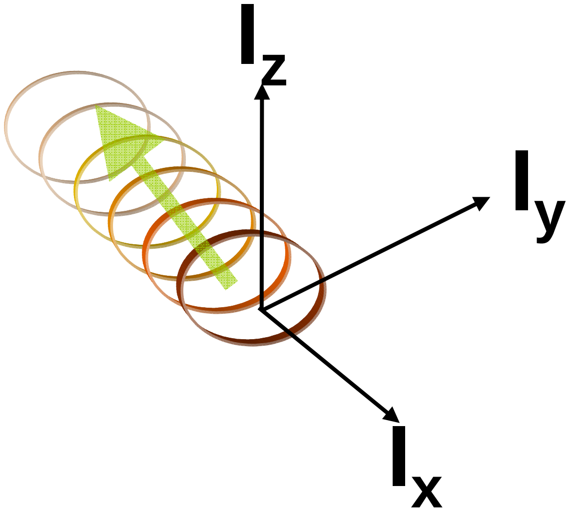
Controls in liquid-state NMR spectroscopy

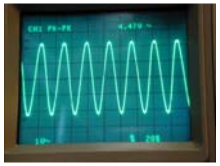
STATIC FIELD
CHEMICAL SHIFT B_o

$H = \omega_o I_z$

$H_\sigma = \omega_\sigma I_z$

RF FIELD

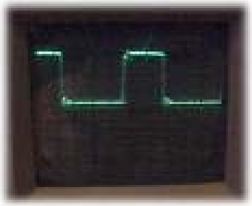




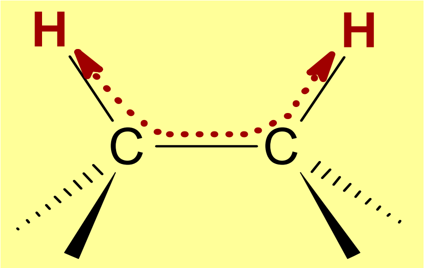
$H = 2\omega_{rf}\cos(\omega_c t)\, I_x$

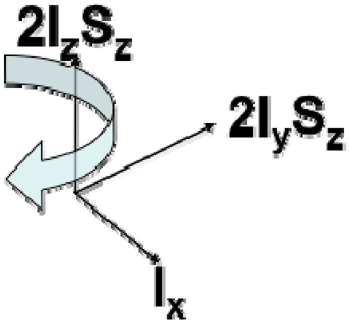
Rotating frame:

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

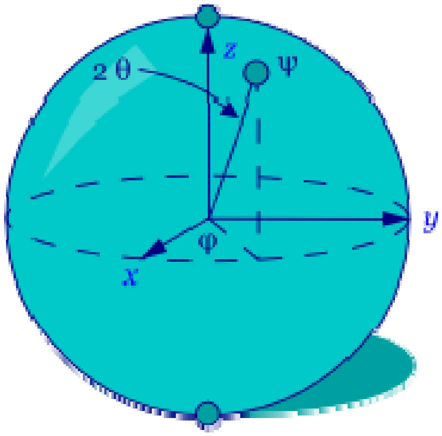


J COUPLING





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



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

Product operator calculations in liquid-state NMR

Rf pulse:

$$I_z \xrightarrow{\theta I_x} c_\theta I_z - s_\theta I_y$$

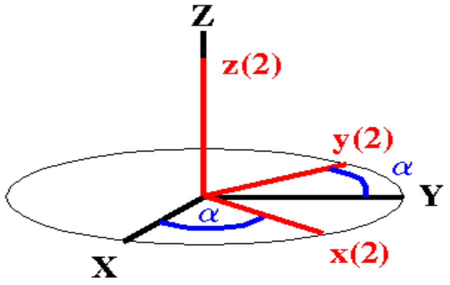
The evolution angle:
$\Theta,\phi = \omega t$

Evolution under isotropic shielding:

$$I_x \xrightarrow{\Phi I_z} c_\Phi I_x + s_\Phi I_y$$

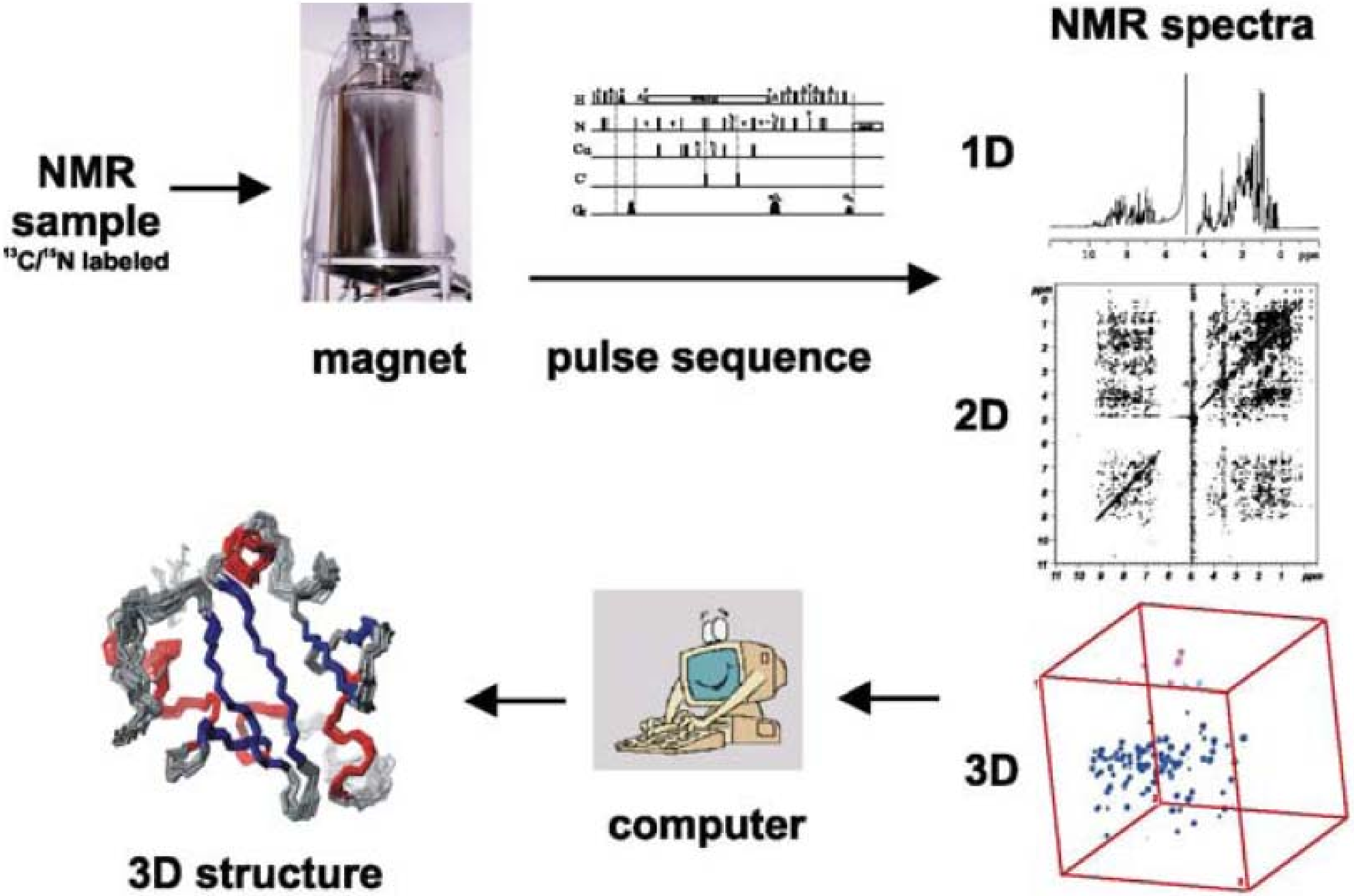
Evolution under J coupling:

$$I_x \xrightarrow{\Phi\, 2I_zS_z} c_\Phi I_x + s_\Phi 2I_yS_z$$

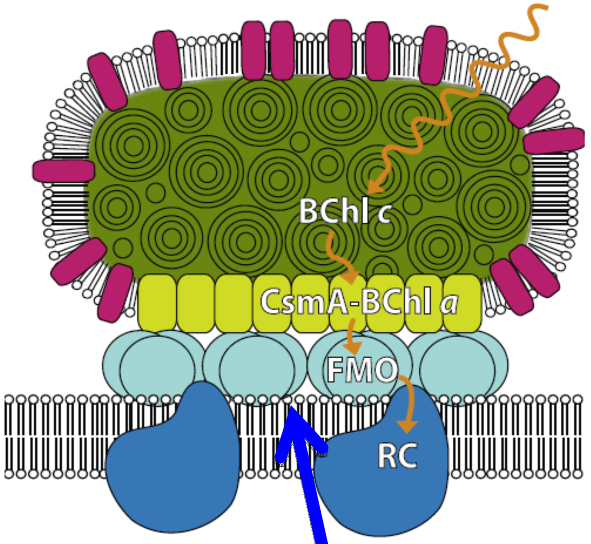


$\{I_x, I_y, I_z\}$
$\{I_x, 2I_yS_z, 2I_zS_z\}$
$\{2I_zS_x, S_y, 2I_zS_z\}$

Protein NMR spectroscopy

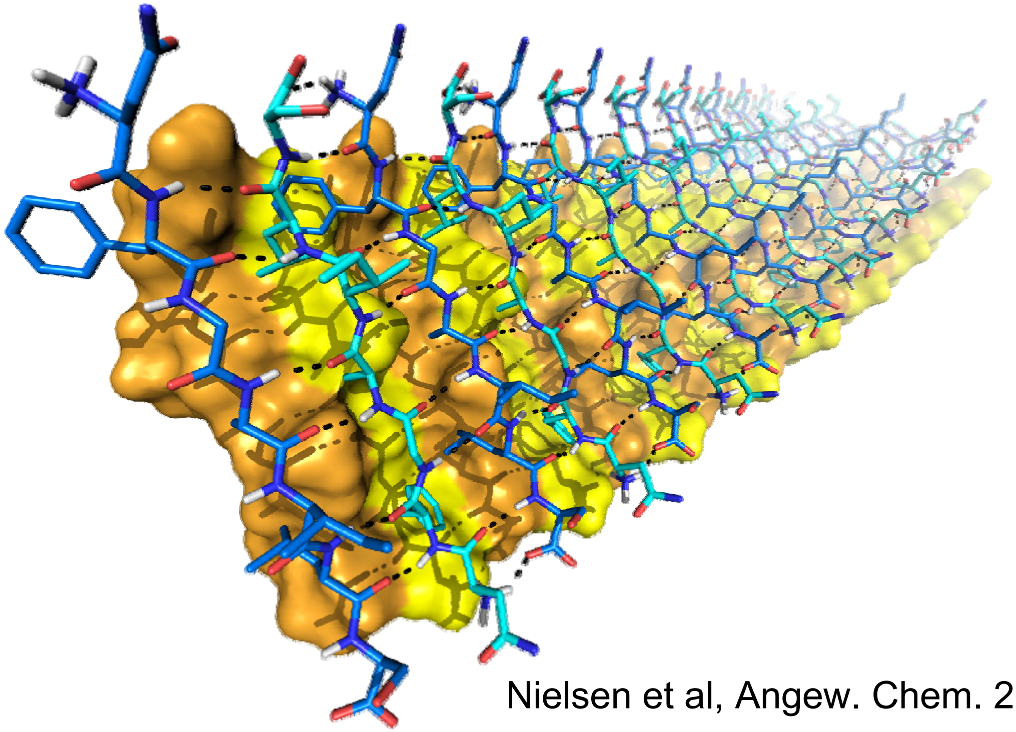


Motivation – we want to design experiments for the same purpose for solids

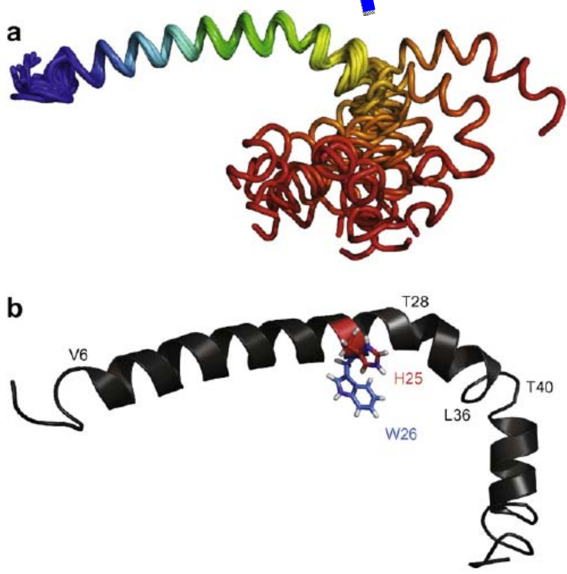


GREEN SULFUR BACTERIA

Amyloid fibril structures



Nielsen et al, Angew. Chem. 2009

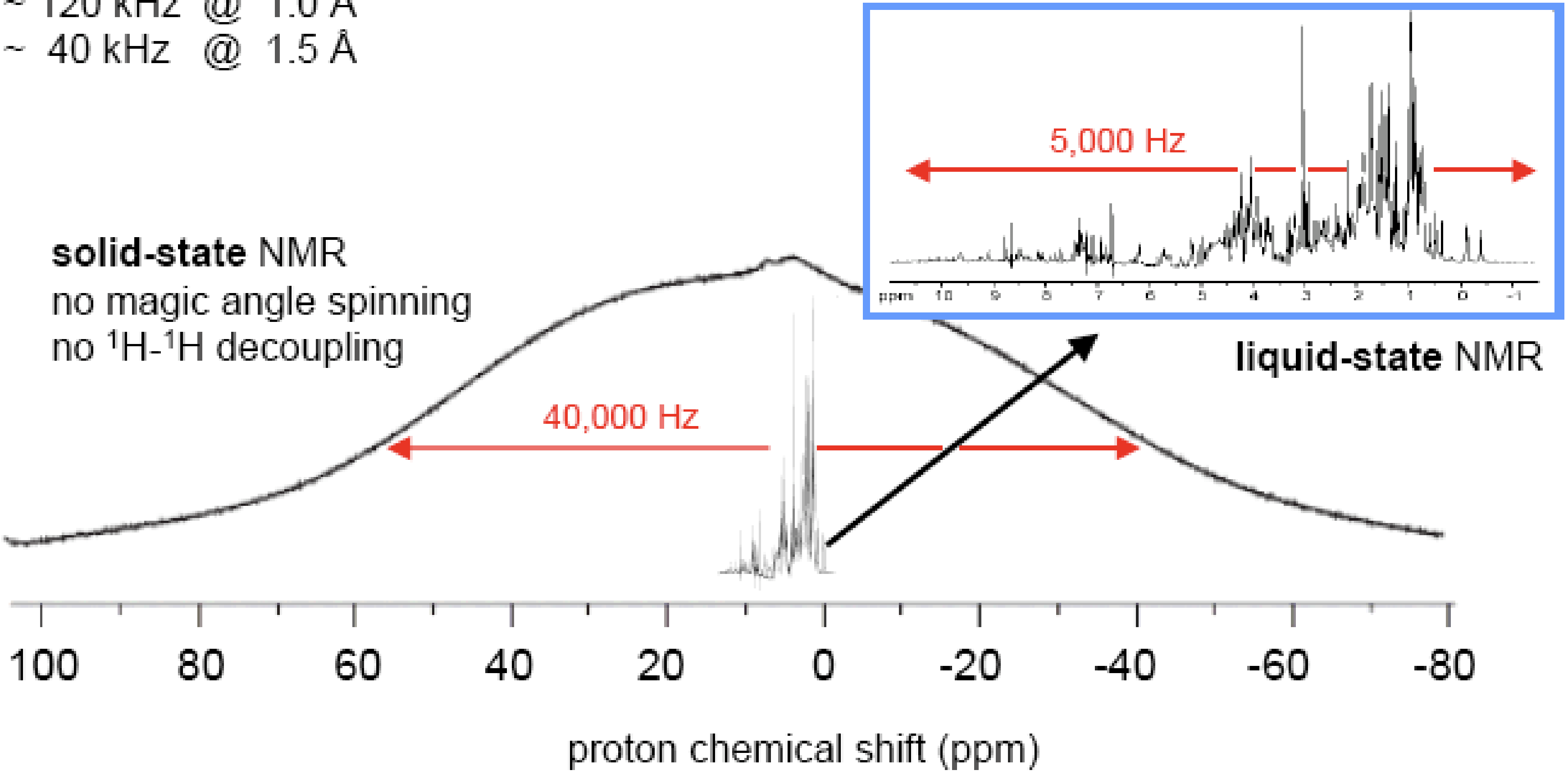


Pedersen, Dittmer, Miller, and Nielsen,
FEBS Lett., 2008

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

dipolar coupling between protons:

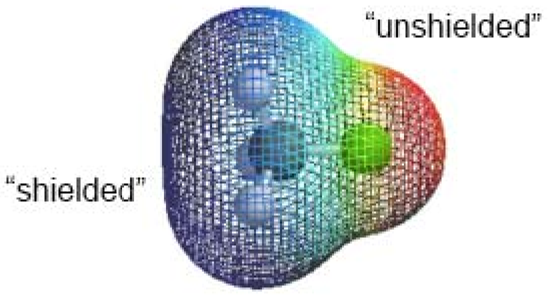
~ 120 kHz @ 1.0 Å
~ 40 kHz @ 1.5 Å



solid-state NMR
no magic angle spinning
no ^{1}H-^{1}H decoupling

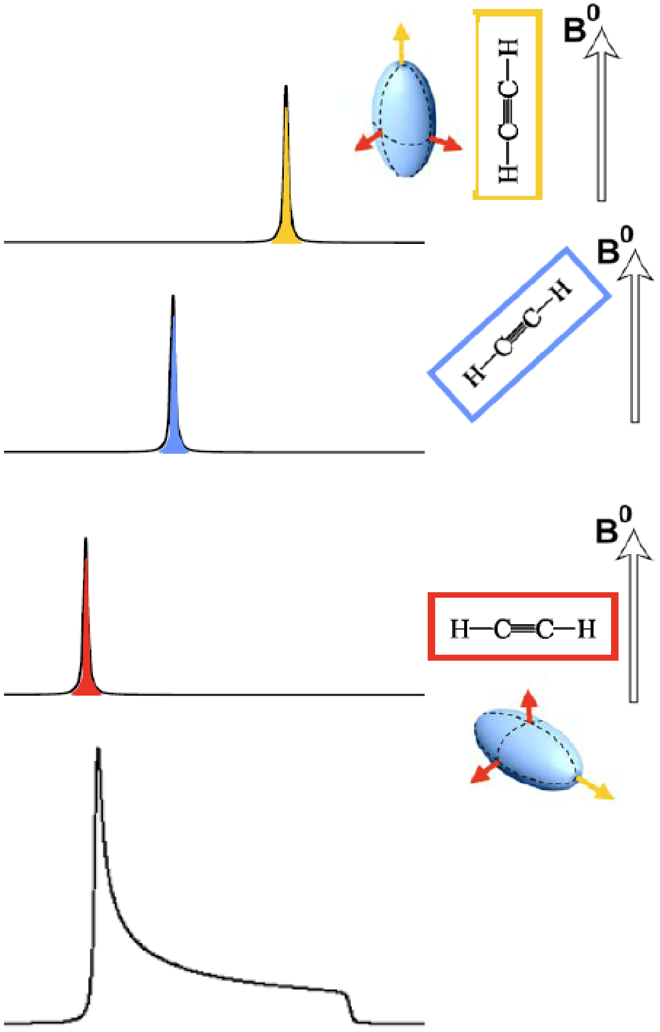
liquid-state NMR

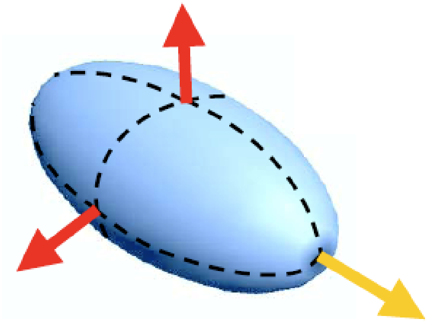
Origin to broadening: Chemical shielding anisotropy

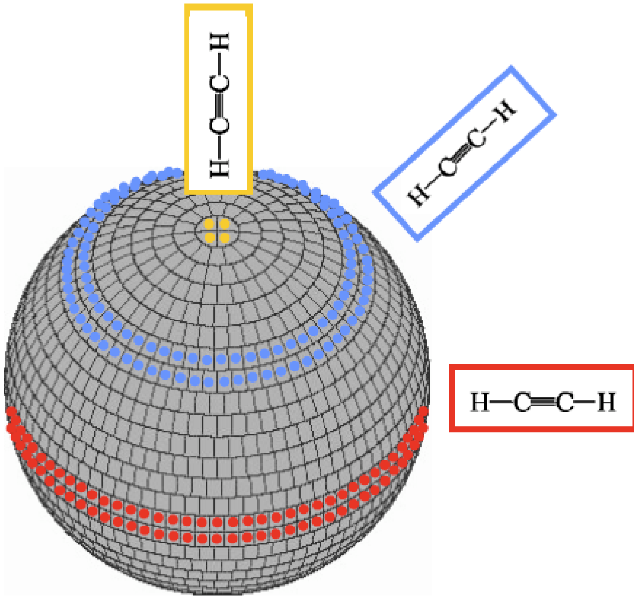


The electrons shields the magnetic field – an orientation dependent manner

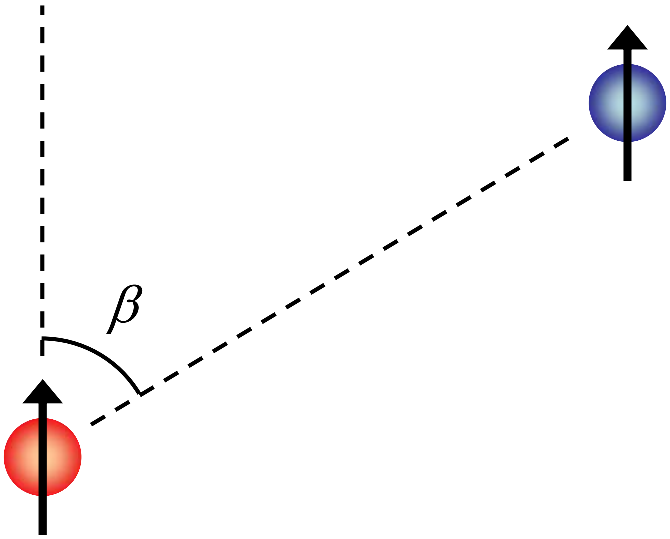
– in liquids the molecules "tumbles" fast averaging this effect

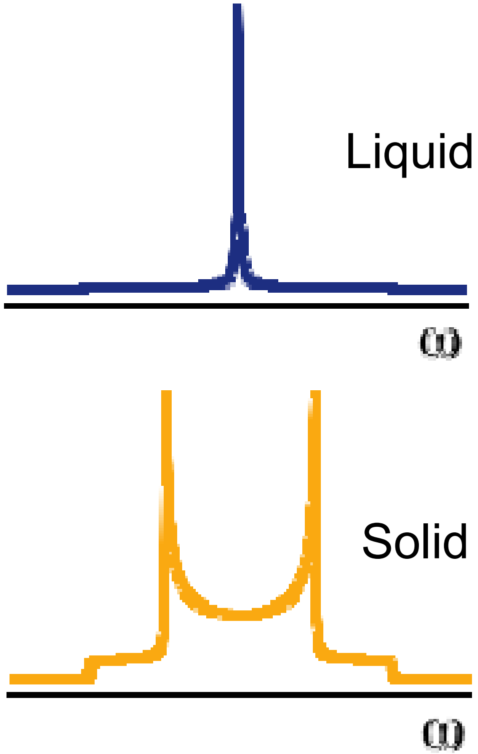






Another origin to broadening: Dipole-dipole coupling



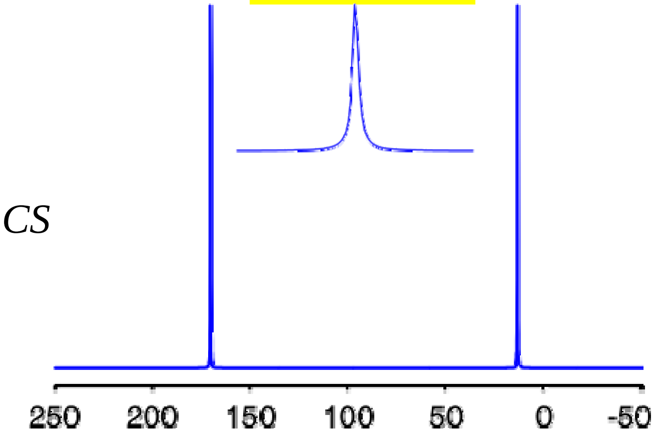


{ = 0 in isotropic liquids
≠0 in solids or oriented media

Typically several interactions …

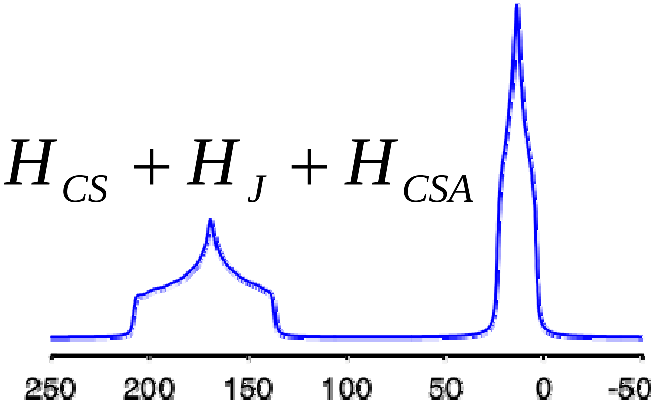
Isotropic

$$H = H_{CS}$$

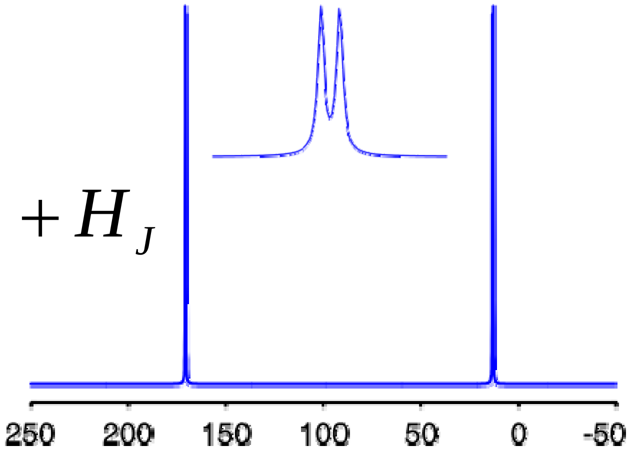


Anisotropic

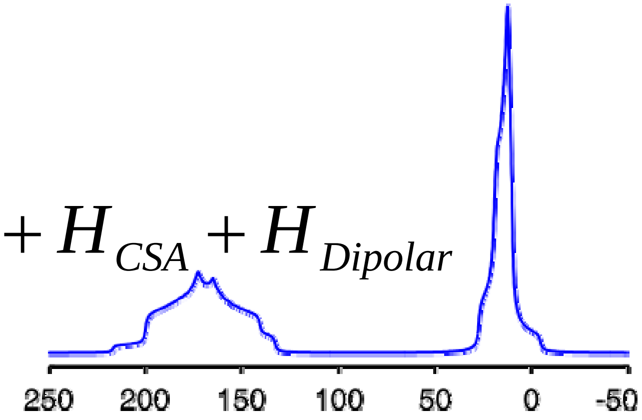
$$H = H_{CS} + H_J + H_{CSA}$$



$$H = H_{CS} + H_J$$

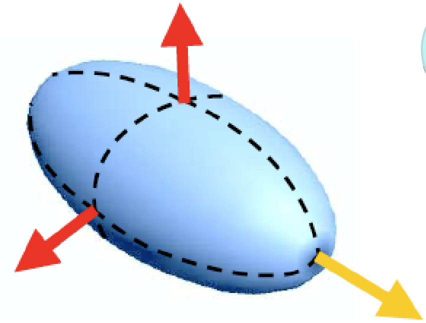


$$H = H_{CS} + H_J + H_{CSA} + H_{Dipolar}$$



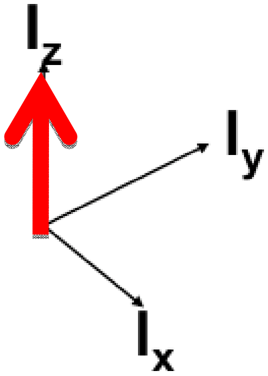
$$H = H_{CS} + H_J + H_{CSA} + H_{Dipolar} + H_Q$$

Spin and Spatial parts of the Internal Hamiltonian



Spatial part

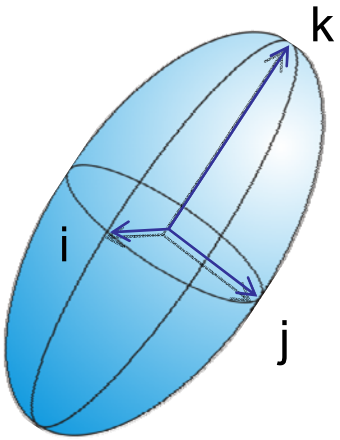
Spin part



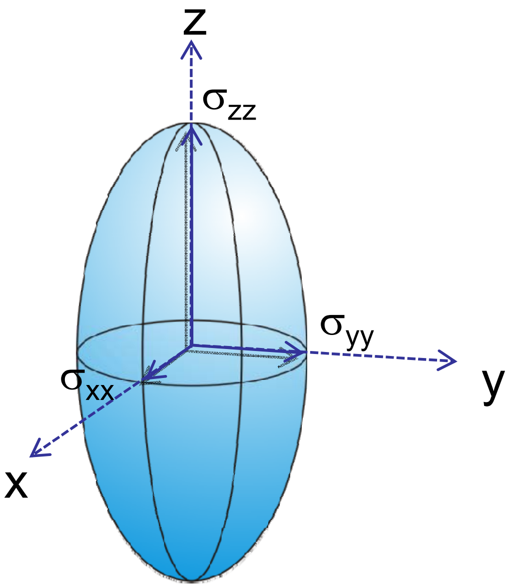
Chemical shift

Dipole-dipole coupling

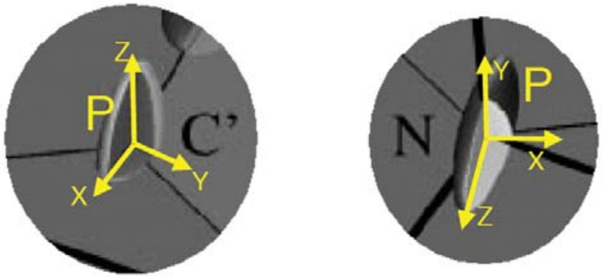
Spatial tensor: Principal Axis Frame



$$\begin{array}{cc} & \text{ijk} \\ \sigma = & \begin{pmatrix} \sigma_{xx} & \sigma_{xy} & \sigma_{xz} \\ \sigma_{yx} & \sigma_{yy} & \sigma_{yz} \\ \sigma_{zx} & \sigma_{zy} & \sigma_{zz} \end{pmatrix} \end{array}$$



$$\sigma_{PAS} = \begin{pmatrix} \sigma_{xx} & 0 & 0 \\ 0 & \sigma_{yy} & 0 \\ 0 & 0 & \sigma_{zz} \end{pmatrix}$$



Different principal axis Frame for different Interactions

Irreducible tensors

$$H_\lambda = C^\lambda \sum_{j=0}^{2} \sum_{m=-j}^{j} (-1)^m (R^\lambda_{j,-m})^L T^\lambda_{j,-m}$$

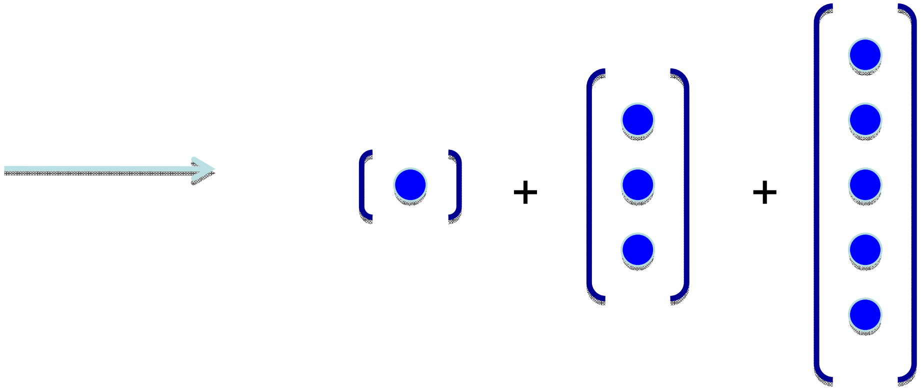
Cartesian Tensor

$$\sigma = \begin{pmatrix} \sigma_{xx} & \sigma_{xy} & \sigma_{xz} \\ \sigma_{yx} & \sigma_{yy} & \sigma_{yz} \\ \sigma_{zx} & \sigma_{zy} & \sigma_{zz} \end{pmatrix}$$

=

R

Irreducible Tensors



$R_{0,0}$ $R_{1,m}$ $R_{2,m}$

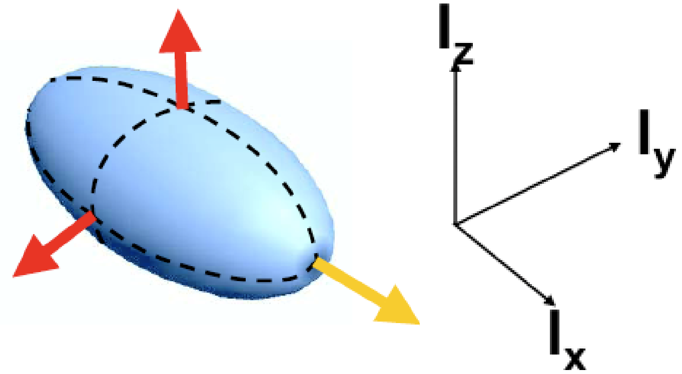
Hamiltonians containing isotropic and anisotropic components

Fundamental constant

Spatial part

Spin part

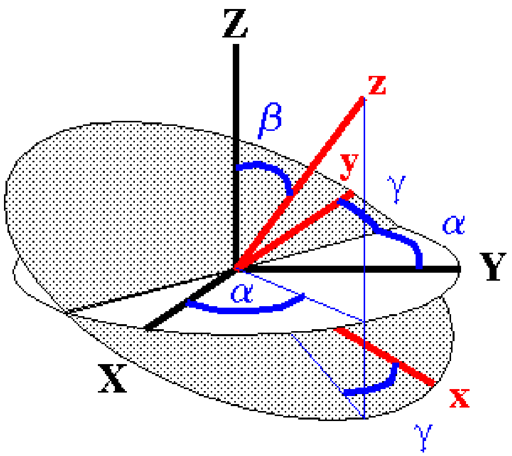
$$H_\lambda = C^\lambda \sum_{j=0}^{2} \sum_{m=-j}^{j} (-1)^m (R^\lambda_{j,-m})^L T^\lambda_{j,-m}$$



Rotations in spin and spatialspace:

$$\boxed{T^{F2}_{j,m} = \sum_{m'=-j}^{j} T^{F1}_{j,m'} D^{(j)}_{m',m}(\Omega)}$$

Euler angles $\Omega = \{\alpha, \beta, \gamma\}$



$$D^{(j)}_{m',m}(\Omega) = e^{-im'\alpha} d^{(j)}_{m',m}(\beta) e^{-im\gamma}$$

Wigner Matrix

Reduced Wigner matrix elements $d^{(j)}_{m',m}(\beta)$ for $j = 1$ and 2.[a]

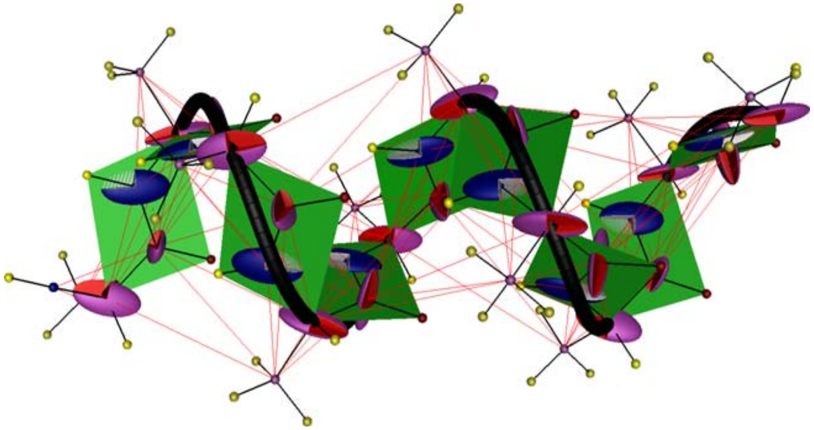
j	$m' \backslash m$	-2	-1	0	1	2
1	-1		$\frac{1}{2}(1+c_\beta)$	$\frac{1}{\sqrt{2}}s_\beta$	$\frac{1}{2}(1-c_\beta)$	
	0		$-\frac{1}{\sqrt{2}}s_\beta$	c_β	$\frac{1}{\sqrt{2}}s_\beta$	
	1		$\frac{1}{2}(1-c_\beta)$	$-\frac{1}{\sqrt{2}}s_\beta$	$\frac{1}{2}(1+c_\beta)$	
2	-2	$\frac{1}{4}(1+c_\beta)^2$	$\frac{1}{2}(1+c_\beta)s_\beta$	$\sqrt{\frac{3}{8}}s_\beta^2$	$\frac{1}{2}(1-c_\beta)s_\beta$	$\frac{1}{4}(1-c_\beta)^2$
	-1	$-\frac{1}{2}(1+c_\beta)s_\beta$	$c_\beta^2 - \frac{1}{2}(1-c_\beta)$	$\sqrt{\frac{3}{8}}s_{2\beta}$	$\frac{1}{2}(1+c_\beta) - c_\beta^2$	$\frac{1}{2}(1-c_\beta)s_\beta$
	0	$\sqrt{\frac{3}{8}}s_\beta^2$	$-\sqrt{\frac{3}{8}}s_{2\beta}$	$\frac{1}{2}(3c_\beta^2-1)$	$\sqrt{\frac{3}{8}}s_{2\beta}$	$\sqrt{\frac{3}{8}}s_\beta^2$
	1	$-\frac{1}{2}(1-c_\beta)s_\beta$	$\frac{1}{2}(1+c_\beta) - c_\beta^2$	$-\sqrt{\frac{3}{8}}s_{2\beta}$	$c_\beta^2 - \frac{1}{2}(1-c_\beta)$	$\frac{1}{2}(1+c_\beta)s_\beta$
	2	$\frac{1}{4}(1-c_\beta)^2$	$-\frac{1}{2}(1-c_\beta)s_\beta$	$\sqrt{\frac{3}{8}}s_\beta^2$	$-\frac{1}{2}(1+c_\beta)s_\beta$	$\frac{1}{4}(1+c_\beta)^2$

[a] Abbreviations: $c_\beta = \cos\beta$, $s_\beta = \sin\beta$.

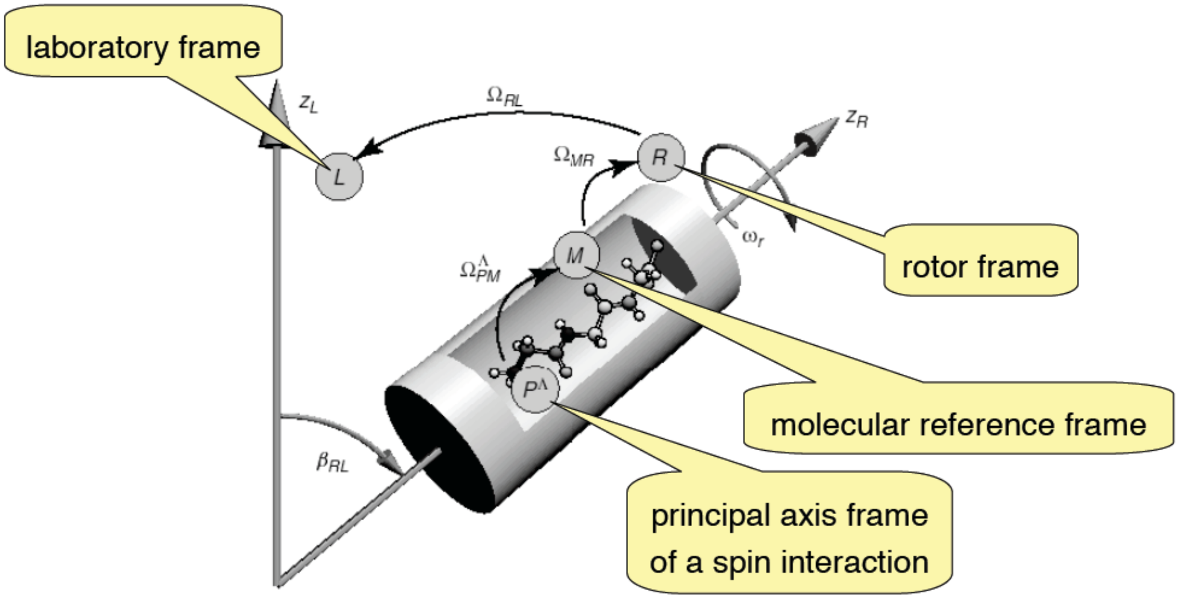
ReducedWigner Matrix

The SpatialTensor

$$H_D^{IS} = \omega_D(t) 2 I_z S_z \qquad \omega_D(t) = \frac{1}{\sqrt{6}} C^D (R_{2,0}^D)^L$$



MEASURED



laboratory frame

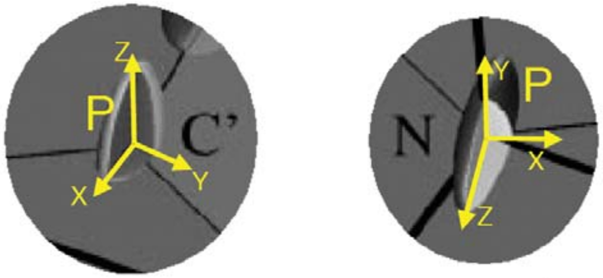
rotor frame

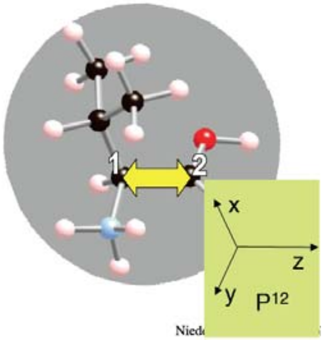
molecular reference frame

principal axis frame of a spin interaction

KNOWN

The Principal axis frame (diagonal interaction tensor)





$$\overset{\leftrightarrow}{\delta}^j = \begin{pmatrix} \delta_{xx}^j & \delta_{xy}^j & \delta_{xz}^j \\ \delta_{yx}^j & \delta_{yy}^j & \delta_{yz}^j \\ \delta_{zx}^j & \delta_{zy}^j & \delta_{zz}^j \end{pmatrix}$$

inSPIN Center for Insoluble Protein Structures

Niels Chr. Nielsen

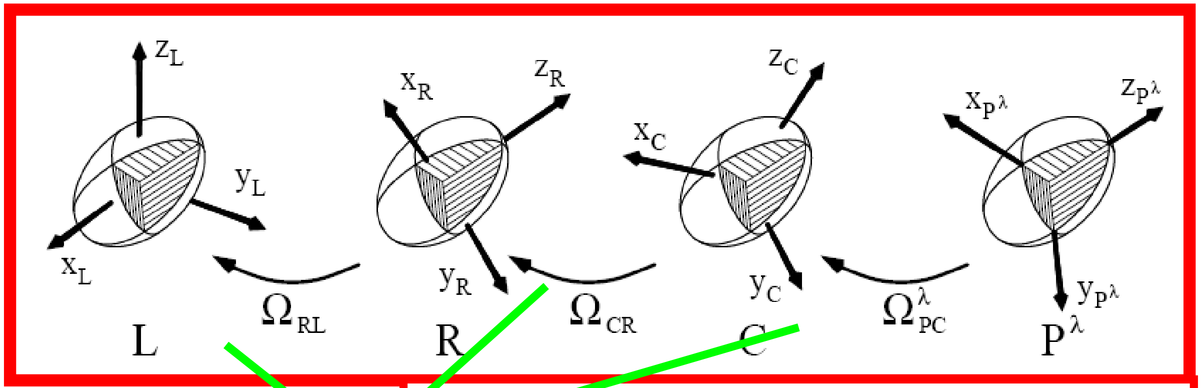
Spatial transformations

$$H_D^{IS} = \omega_D(t)2I_zS_z$$

$$\omega_D(t) = \frac{1}{\sqrt{6}}C^D(R^D_{2,0})^L$$

TO BE MEASURED

KNOWN



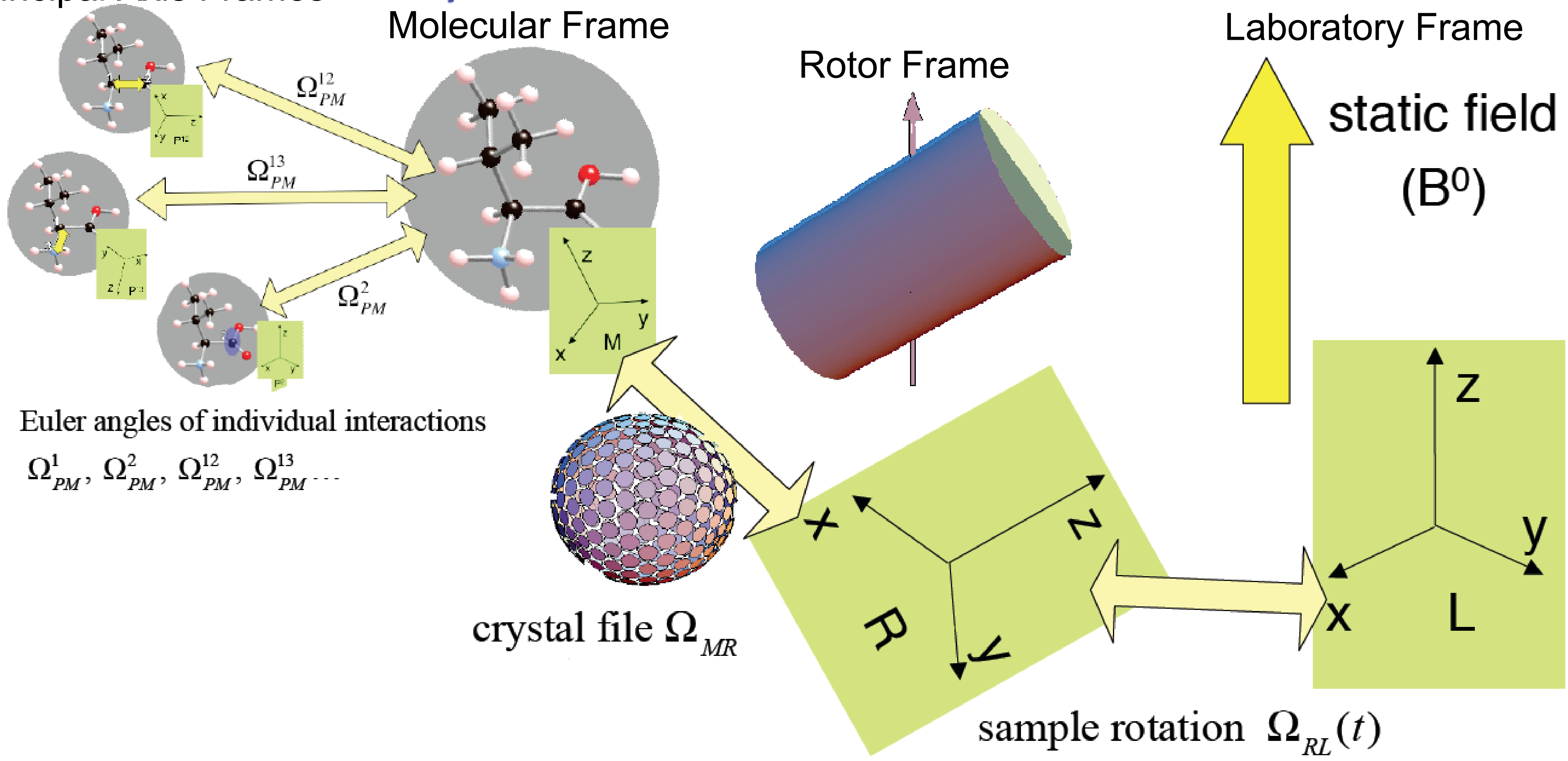
$$D^{(j)}_{m',m}(\Omega) = e^{-im'\alpha}d^{(j)}_{m',m}(\beta)e^{-im\gamma}$$

$$(R^\lambda_{2,m})^L = \sum_{m',m'',m'''}(R^\lambda_{2,m'''})^P D^{(2)}_{m''',m''}(\Omega^\lambda_{PC})D^{(2)}_{m'',m'}(\Omega_{CR})D^{(2)}_{m',m}(\Omega_{RL})$$

$$\boxed{(R^\lambda_{2,0})^L = \sum_{m'}(R^\lambda_{2,m'''})^R d^{(2)}_{m',0}(\beta^\lambda_{RL})e^{-im'\omega_r t}}$$

Isolatedinfluence from MAS

Summary of rotations



Principal Axis Frames

Molecular Frame

Rotor Frame

Laboratory Frame

static field

(B^0)

Ω_{PM}^{12}

Ω_{PM}^{13}

Ω_{PM}^{2}

Euler angles of individual interactions

$\Omega_{PM}^{1}, \Omega_{PM}^{2}, \Omega_{PM}^{12}, \Omega_{PM}^{13} \ldots$

crystal file Ω_{MR}

sample rotation $\Omega_{RL}(t)$

From Levitt

InternalHamiltonian – all in oneTable

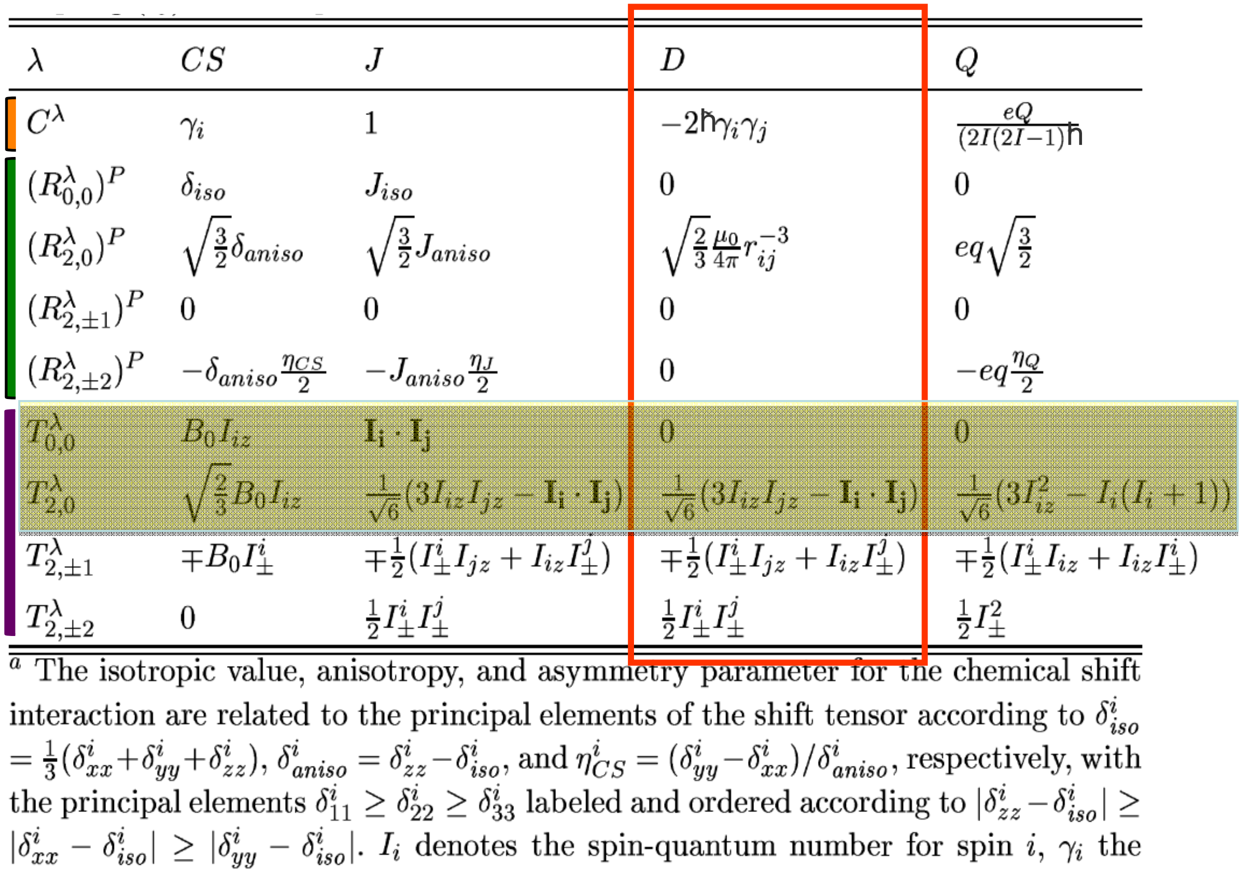
$$H_\lambda = C^\lambda \sum_{j=0}^{2} \sum_{m=-j}^{j} (-1)^m (R^\lambda_{j,-m})^L T^\lambda_{j,-m}$$

Interaction

Fundamental constants

Spatial part

Spin part



λ	CS	J	D	Q
C^λ	γ_i	1	$-2\hbar\gamma_i\gamma_j$	$\frac{eQ}{(2I(2I-1)\hbar}$
$(R^\lambda_{0,0})^P$	δ_{iso}	J_{iso}	0	0
$(R^\lambda_{2,0})^P$	$\sqrt{\frac{3}{2}}\delta_{aniso}$	$\sqrt{\frac{3}{2}}J_{aniso}$	$\sqrt{\frac{2}{3}}\frac{\mu_0}{4\pi}r_{ij}^{-3}$	$eq\sqrt{\frac{3}{2}}$
$(R^\lambda_{2,\pm1})^P$	0	0	0	0
$(R^\lambda_{2,\pm2})^P$	$-\delta_{aniso}\frac{\eta_{CS}}{2}$	$-J_{aniso}\frac{\eta_J}{2}$	0	$-eq\frac{\eta_Q}{2}$
$T^\lambda_{0,0}$	$B_0 I_{iz}$	$\mathbf{I_i}\cdot\mathbf{I_j}$	0	0
$T^\lambda_{2,0}$	$\sqrt{\frac{2}{3}}B_0 I_{iz}$	$\frac{1}{\sqrt{6}}(3I_{iz}I_{jz} - \mathbf{I_i}\cdot\mathbf{I_j})$	$\frac{1}{\sqrt{6}}(3I_{iz}I_{jz} - \mathbf{I_i}\cdot\mathbf{I_j})$	$\frac{1}{\sqrt{6}}(3I_{iz}^2 - I_i(I_i+1))$
$T^\lambda_{2,\pm1}$	$\mp B_0 I^i_\pm$	$\mp\frac{1}{2}(I^i_\pm I_{jz} + I_{iz}I^j_\pm)$	$\mp\frac{1}{2}(I^i_\pm I_{jz} + I_{iz}I^j_\pm)$	$\mp\frac{1}{2}(I^i_\pm I_{iz} + I_{iz}I^i_\pm)$
$T^\lambda_{2,\pm2}$	0	$\frac{1}{2}I^i_\pm I^j_\pm$	$\frac{1}{2}I^i_\pm I^j_\pm$	$\frac{1}{2}I^2_\pm$

[a] The isotropic value, anisotropy, and asymmetry parameter for the chemical shift interaction are related to the principal elements of the shift tensor according to $\delta^i_{iso} = \frac{1}{3}(\delta^i_{xx}+\delta^i_{yy}+\delta^i_{zz})$, $\delta^i_{aniso} = \delta^i_{zz}-\delta^i_{iso}$, and $\eta^i_{CS} = (\delta^i_{yy}-\delta^i_{xx})/\delta^i_{aniso}$, respectively, with the principal elements $\delta^i_{11} \geq \delta^i_{22} \geq \delta^i_{33}$ labeled and ordered according to $|\delta^i_{zz}-\delta^i_{iso}| \geq |\delta^i_{xx} - \delta^i_{iso}| \geq |\delta^i_{yy} - \delta^i_{iso}|$. I_i denotes the spin-quantum number for spin i, γ_i the

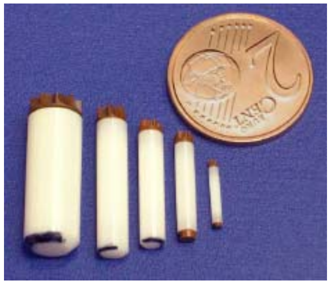
High-field approximation:

$$H_D = C^D (R^D_{2,0})^L T^D_{2,0} = \sqrt{6}\omega_D T^D_{2,0}$$

$$= \omega_D(2I_zS_z - I_xS_x - I_yS_y)$$

- rank j=1 not relevant
- shiftspintensor is rank 1

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*)...

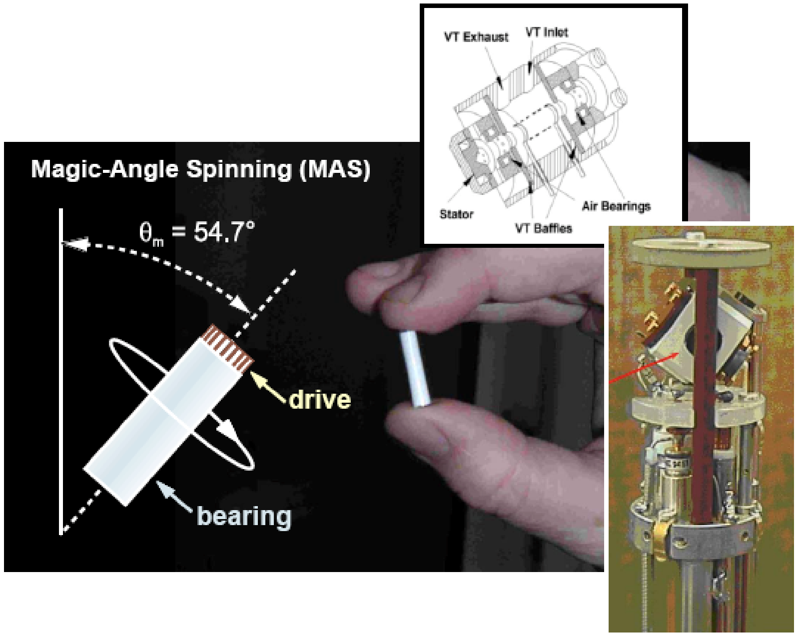
a 3.2 mm rotor spinning at 24 kHz...

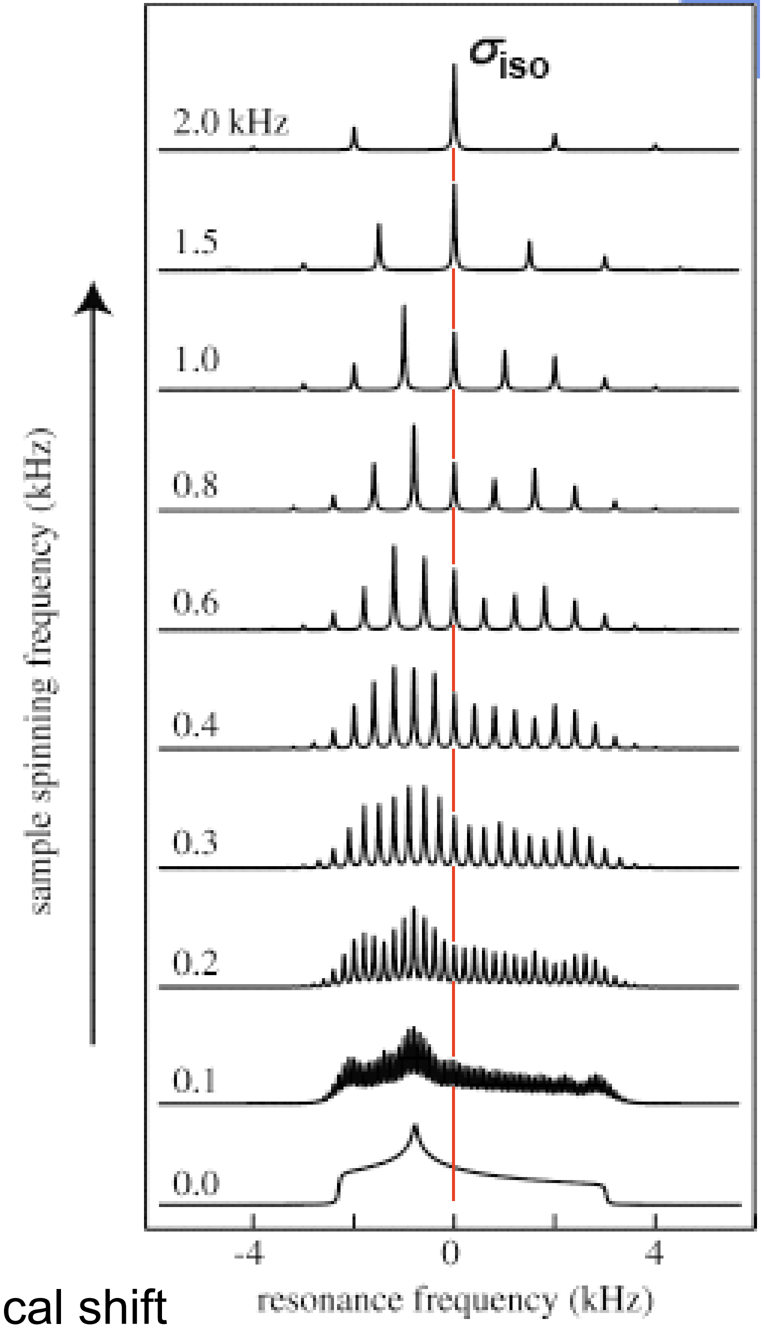
... has a speed of 240 m/s when it would roll on the floor ...

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

From van Rossum

Regain of resolution:
Magic-angle spinning





Isotropic chemical shift

Averaging of anisotropic interactions by MAS

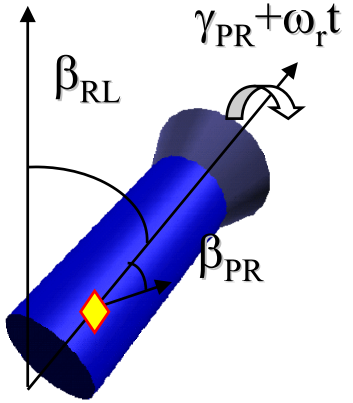
$$\rho(t) = e^{-i\phi 2I_zS_z}\rho(0)e^{i\phi 2I_zS_z} \qquad \phi = \int_0^t \omega_D(t)dt$$

The evolution angle

Rotor synchronized sampling: t = 0, τ_r, $2\tau_r$, ...

$$\phi = \sum_{m=-2}^{2}\int_0^{n\tau_r}\omega_D^{(m)}e^{im\omega_r t}dt = \omega_D^{(0)} = -b_{IS}d_{0,0}^{(2)}(\beta_{PR}^D)d_{0,0}^{(2)}(\beta_{RL}^D)$$

$$= -b_{IS}\frac{1}{2}(3c^2_{\beta_{PR}}-1)\underline{\frac{1}{2}(3c^2_{\beta_{RL}}-1) = 0}$$



$$\beta_{RL} = tan^{-1}\sqrt{2}$$

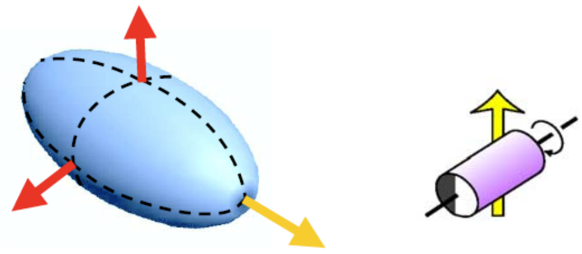
Fast MAS

$$\overline{\tilde{H}}_D^{(1)}(t) = \frac{\omega_r}{2\pi}\int_0^{2\pi/\omega_r}\tilde{H}_D(t)dt = \omega_D^{(0)} = 0$$

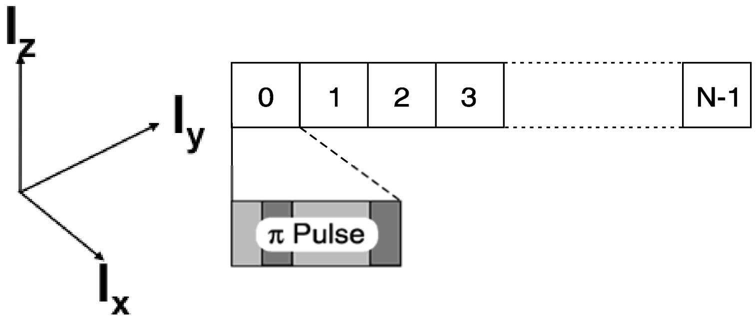
Individual Manipulation of Spin and Spatial parts

Spatial part

Spin part



SAMPLE ROTATION



RF IRRADIATION

The equation of motion

Liouville-von-Neuman
equation

$$\frac{d}{dt}\rho(t) = -i\left[H(t), \rho(t)\right] \rightarrow \left\{ \begin{array}{l} \rho(t) = U(t)\rho(0)U^{\dagger}(t) \\ \\ U(t) = Te^{-i\int_0^t H(t)dt} \end{array} \right.$$

Hamiltonian

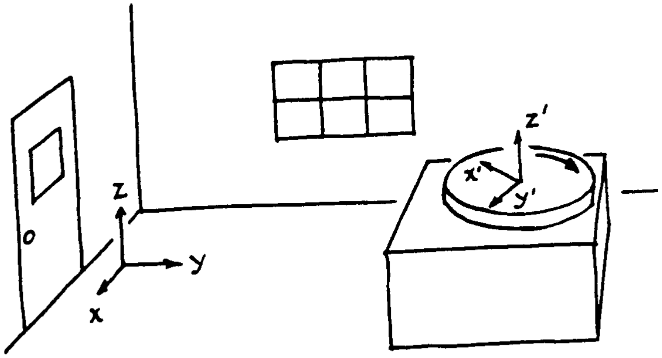
Density
operator

Propagator

Our handle to information and manipulation

Rotating Frames & Effective Hamiltonians

The rotating frame



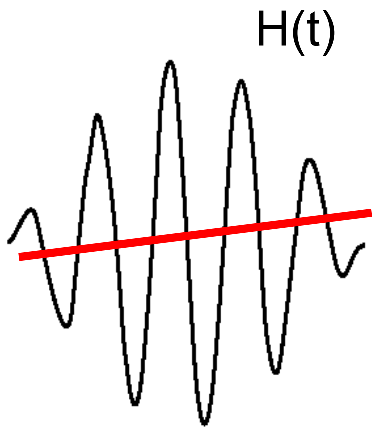
From: RE. Fukushima & S.B.W. Roeder (1981) Experimental pulse NMR

$$H(t) = H_{big}(t) + H_{small}(t)$$

$$\tilde{\rho}(t) = U_{big}^{\dagger}\rho(t)U_{big}$$

$$\boxed{\tilde{H}(t) = U_{big}^{\dagger}H(t)U_{big} - iU_{big}^{\dagger}\frac{d}{dt}U_{big}(t) = \tilde{H}_{small}(t)}$$

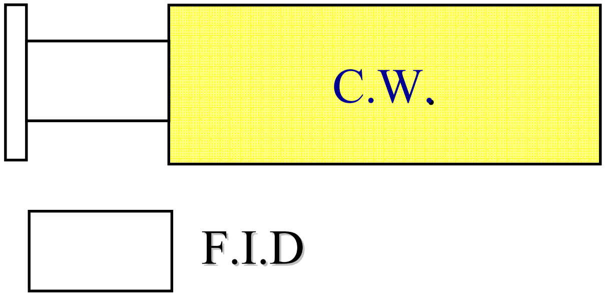
$$\frac{d}{dt}\tilde{\rho}(t) = -i\left[\tilde{H}(t), \tilde{\rho}(t)\right]$$



$$H_{eff} = H^{(1)} + H^{(2)} + H^{(3)} + \ldots$$

$$\begin{aligned} H^{(1)} &= \frac{1}{\tau_c}\int_{t_0}^{t} dt_1 H(t_1), \\ H^{(2)} &= \frac{1}{2i\tau_c}\int_{t_0}^{t} dt_1 \int_{0}^{t_1} dt_2 [H(t_1), H(t_2)], \end{aligned}$$

Modulating the spin part: HeteronuclearDipolarDecoupling



$$H(t) = \omega_S(t)S_z + \omega_{IS}(t)2I_zS_z + \omega_{rf}(I_x)$$

1. Interaction frame of rf

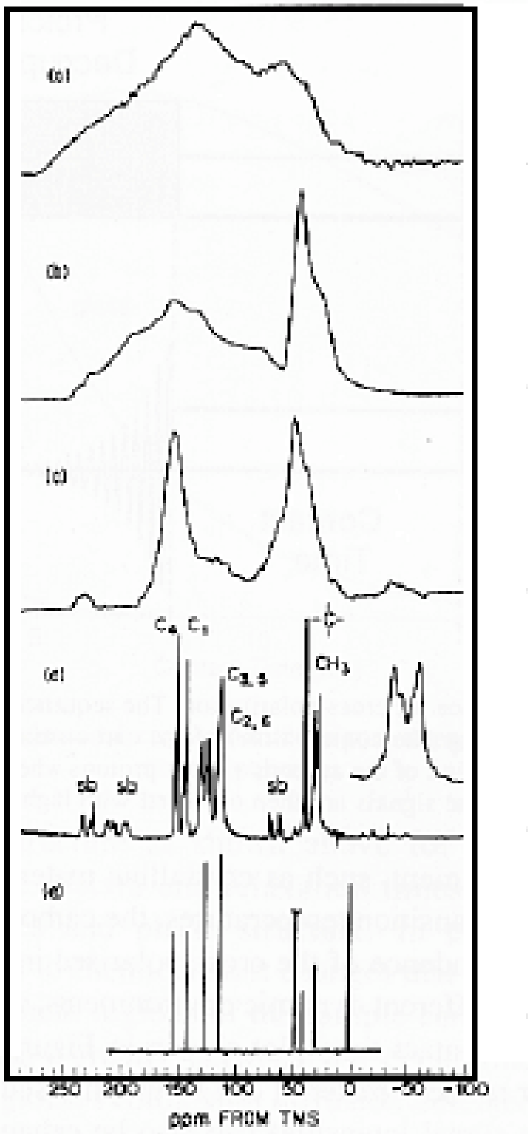
$$\tilde{H}_{IS}(t) = \omega_{IS}(t)e^{i\omega_{rf}tI_x}2I_zS_ze^{-i\omega_{rf}tI_x}$$

$$= \omega_{IS}(t)[c_{\omega_{rf}t}2I_zS_z + s_{\omega_{rf}t}2I_yS_z]$$

2. Average Hamiltonian

$$\boxed{\overline{\tilde{H}}^{(1)}_{IS} = \omega_{IS}(t)\frac{\omega_{rf}}{2\pi}\int_{0}^{2\pi/\omega_{rf}}[c_{\omega_{rf}t}2I_zS_z + s_{\omega_{rf}t}2I_yS_z]dt = 0}$$

Effect of MAS and decoupling



← no MAS, no decoupling

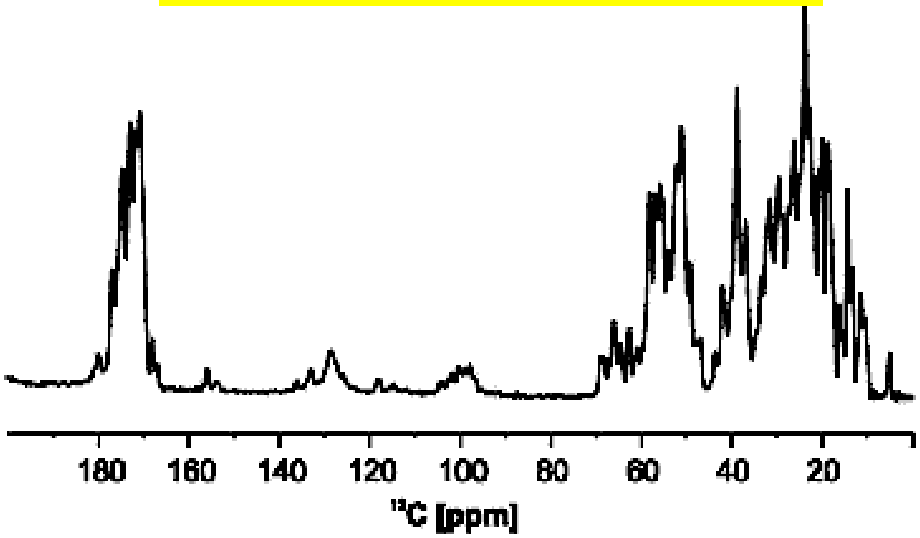
← no MAS, decoupling

← MAS, no decoupling

← MAS, decoupling

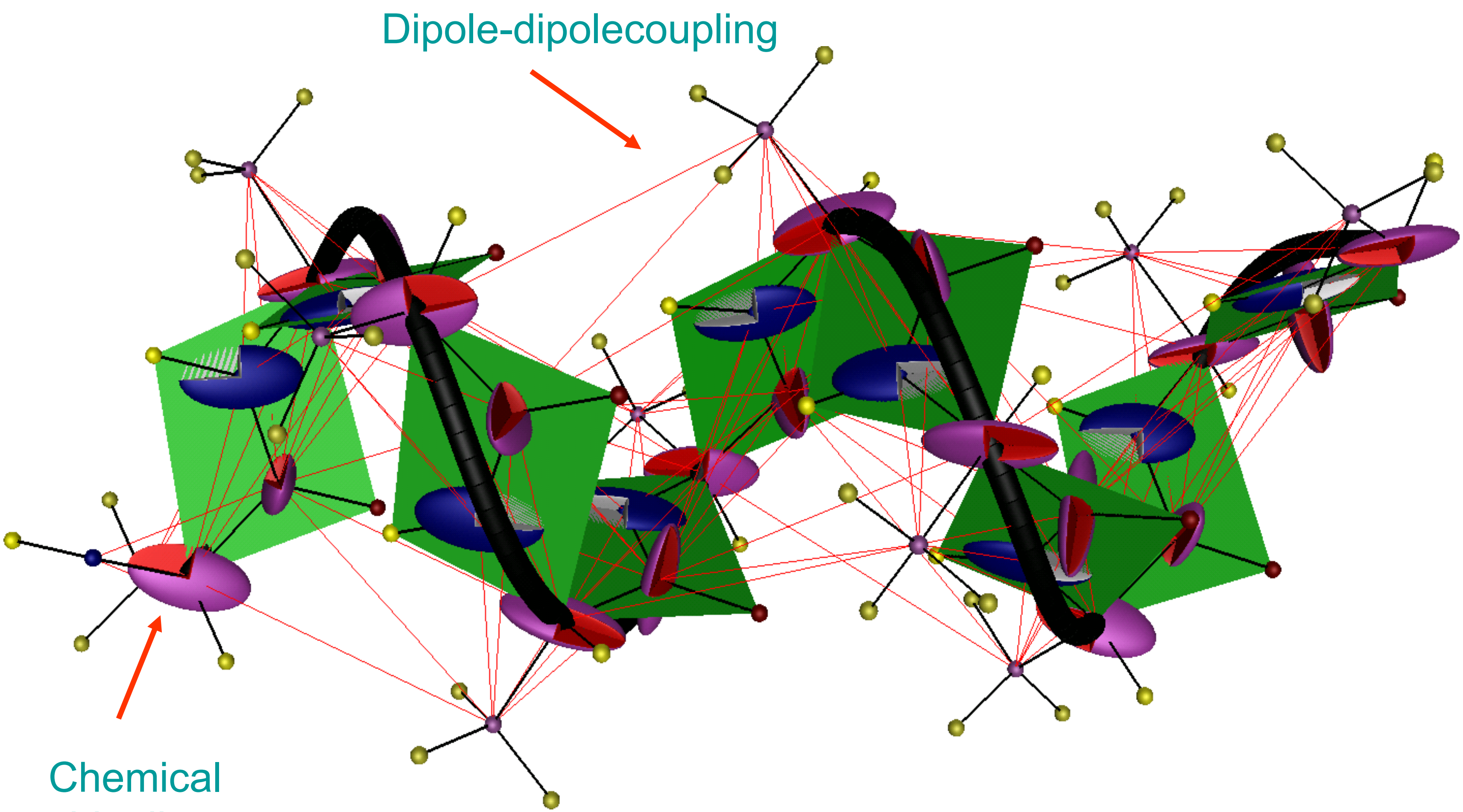
← solution NMR

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
- regain of control


Dipole-dipolecoupling

Chemical shieldingtensor

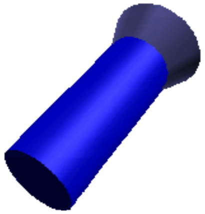
MODULATION & CONTROLLED DEMODULATION

inSPIN Center for Insoluble Protein Structures

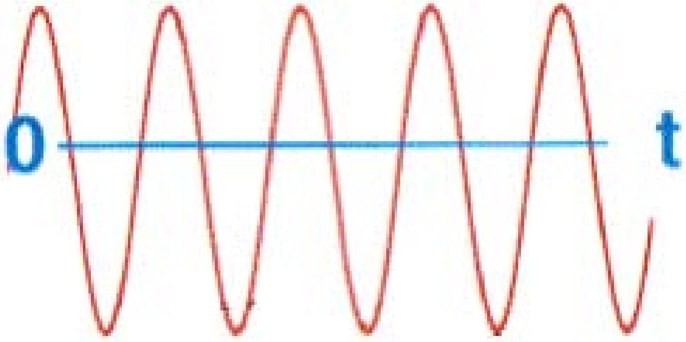
Niels Chr. Nielsen

Tailoring of the Hamiltonian:
Recoupling of dipolar coupling interactions

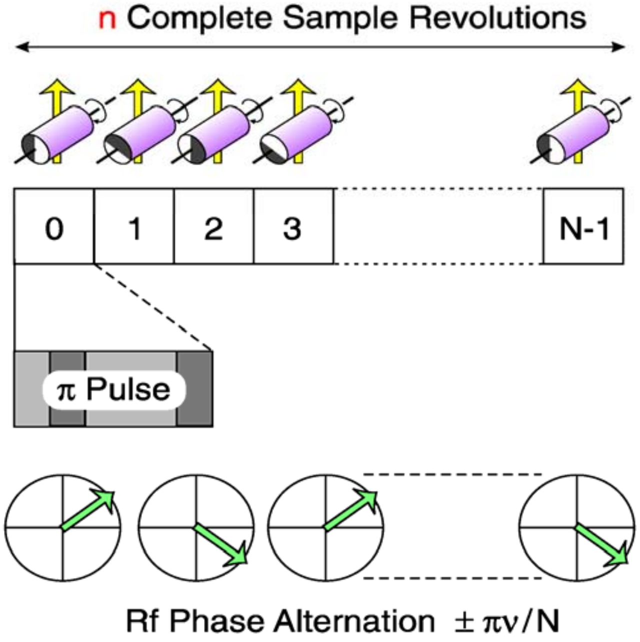
MODULATION



Sample rotation destroys
exploitation of dipolar couplings



+



DEMODULATION

x

for p=-m

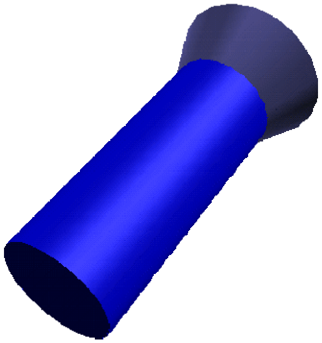
AARHUS UNIVERSITET

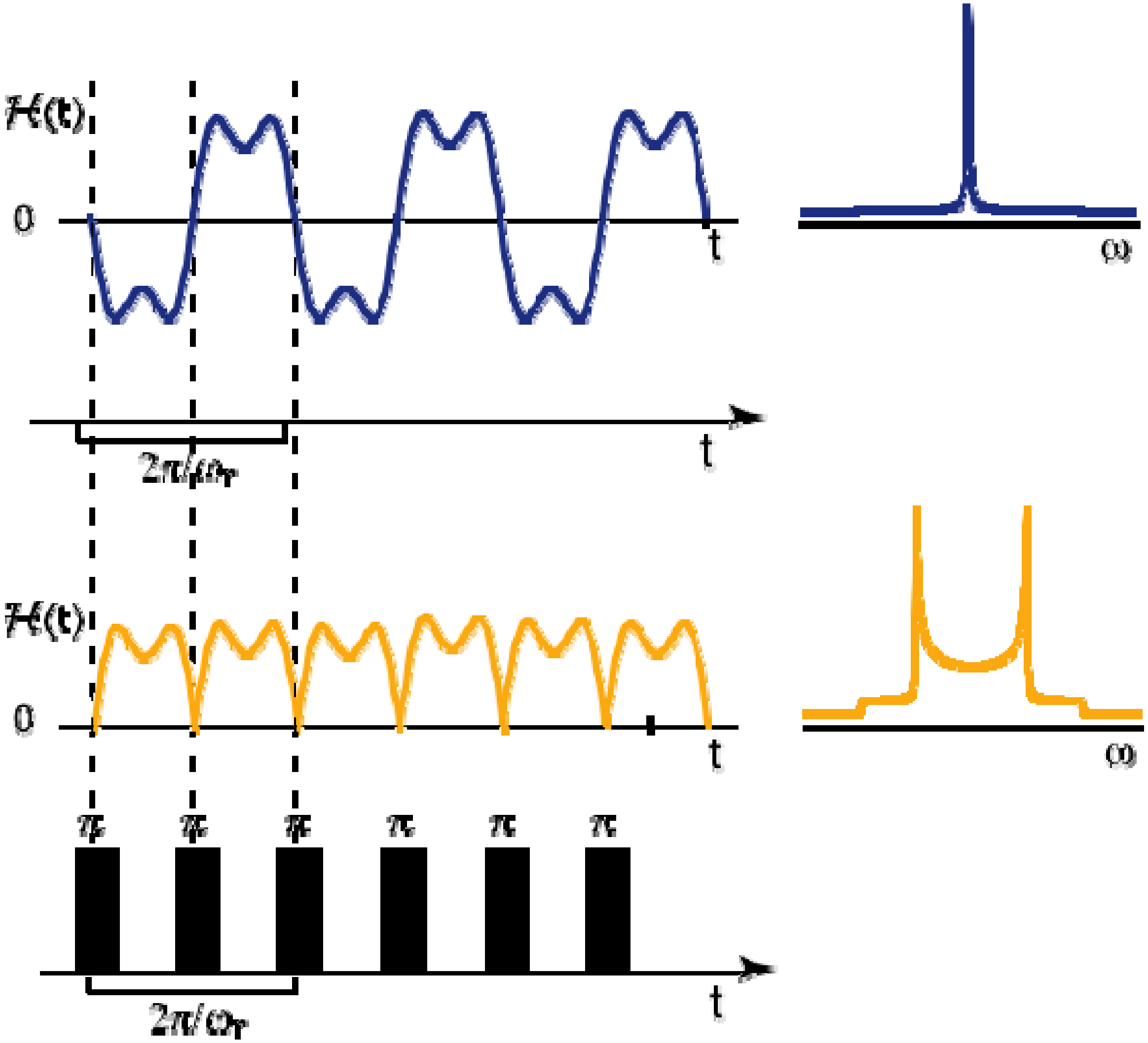
Center for Insoluble Protein Structures

Niels Chr. Nielsen

Disrupting averaging of dipolar couplings – using rf pulses in synchrony with sample revolution

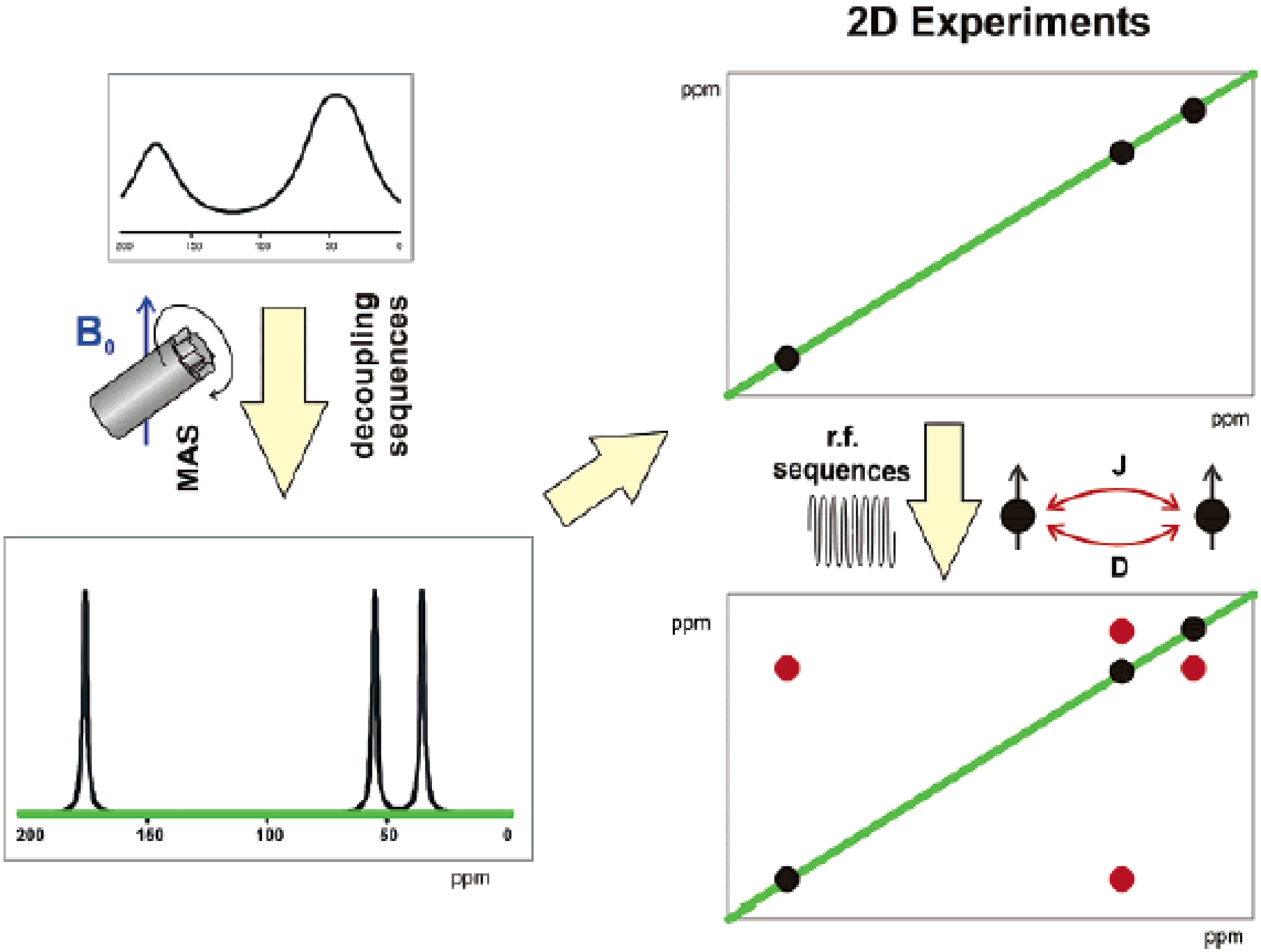
Sample rotation destroys exploitation of dipolar couplings





Simultaneous rf irradiation brings it back again

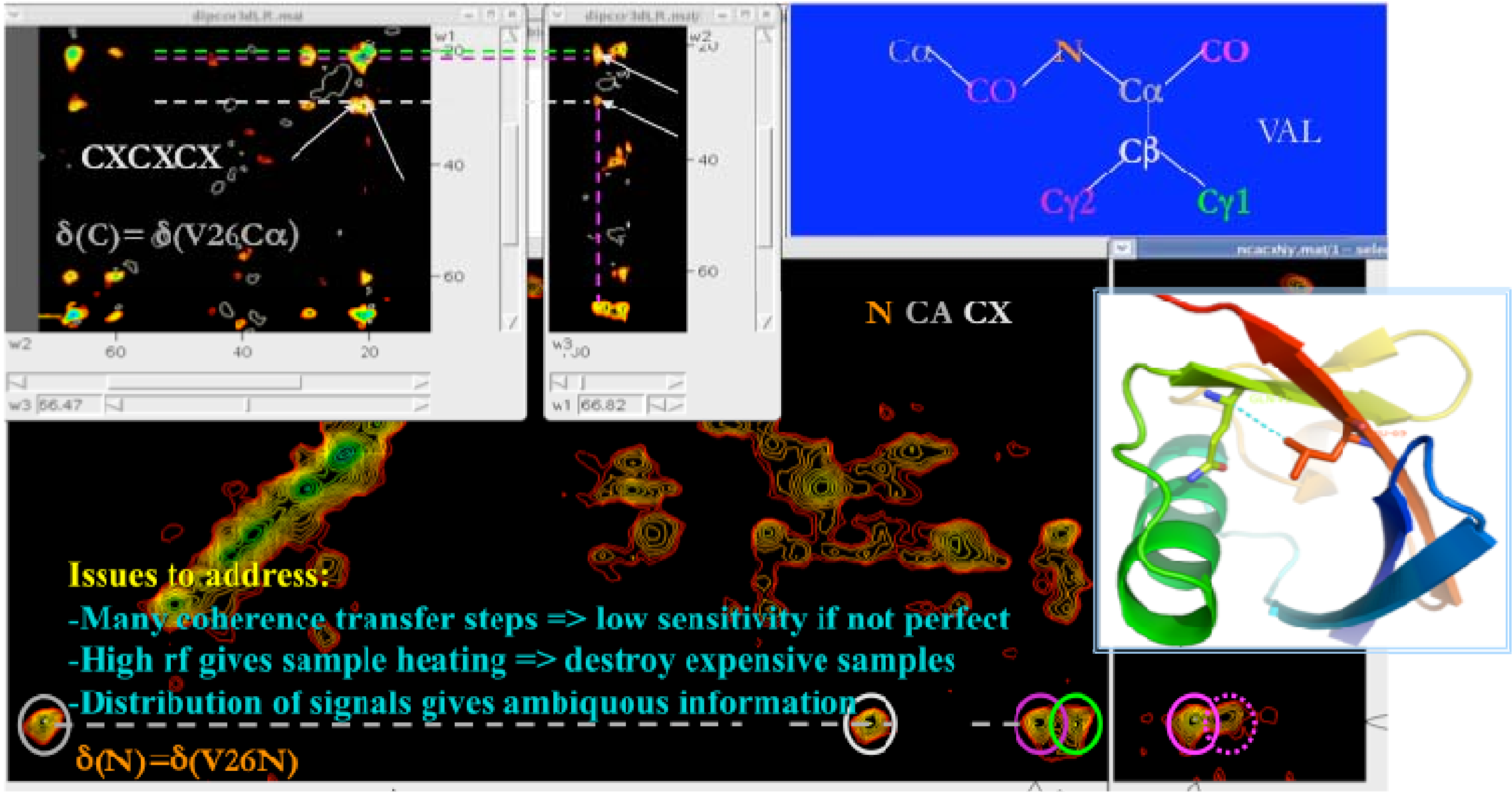
Tailoring of the Hamiltonian => assignment



Magic Angle Spinning NMR of Proteins

A major aim is to develop methods providing
- high sensitivity
- high specificity
- high-precision structures

Structural information regained using dipolar recoupling



Issues to address:
-Many coherence transfer steps => low sensitivity if not perfect
-High rf gives sample heating => destroy expensive samples
-Distribution of signals gives ambiquous information

DipolarRecoupling:

How do weget the anisotropy back – selectively?

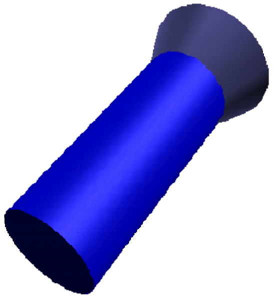
$$H(t) = \omega_I(t)I_z + \omega_S(t)S_z + \omega_{IS}(t)2I_zS_z \qquad + \omega_{rf}^{I} I_x + \omega_{rf}^{S} S_x$$

Sample rotation averages this one!!

$\omega_{rf}^{I} = q\omega_r$

$\omega_{rf}^{S} = p\omega_r$

Add in some rfirrad.



$$\underbrace{\sum_{m=-2}^{2} \omega_{IS}^{(m)} e^{im\omega_r t} \longrightarrow 0 \qquad\qquad e^{-im\omega_r t}}_{\omega_{IS}^{(m)}}$$

RECOUPLING

HeteronuclearDipolarRecoupling:

$$H(t) = \omega_I(t)I_z + \omega_S(t)S_z + \underline{\omega_{IS}(t)2I_zS_z} \quad + \omega_{rf}^I I_x + \omega_{rf}^S S_x$$

→ Rfinteractionframe

$$U_{rf}(t) = e^{-i\omega_{rf}^S t S_x} e^{-i\omega_{rf}^I t I_x}$$

$$\tilde{H}_\lambda(t) = U_{rf}^\dagger(t) H_\lambda(t) U_{rf}(t)$$

$\omega_{rf}^S = p\omega_r$

$\omega_{rf}^I = q\omega_r$

$$\tilde{H}_{IS}(t) = \sum_{m=-2}^{2} \omega_{IS}^{(m)} e^{im\omega_r t} \, (c_{p\omega_r t} c_{q\omega_r t} 2I_zS_z + c_{p\omega_r t} s_{q\omega_r t} 2I_zS_y$$

$$+ s_{p\omega_r t} c_{q\omega_r t} 2I_yS_z + s_{p\omega_r t} s_{q\omega_r t} 2I_yS_y)$$

OK, we have now modulations – but to appreciate recoupling we recast in terms of exponentials

$$\begin{aligned} e^{ix} &= c_x + is_x \\ e^{-ix} &= c_x - is_x \end{aligned}$$

Heteronuclear Dipolar Recoupling:

Recoupling conditions

$$\tilde{H}_{IS}(t) = \frac{1}{4}\sum_{m=-2}^{2}\omega_{IS}^{(m)}\Big\{ \left(e^{i(p+q+m)\omega_r t} + e^{-i(p+q-m)\omega_r t}\right)(2I_zS_z - 2I_yS_y)$$
$$+ \left(e^{i(p-q+m)\omega_r t} + e^{-i(p-q-m)\omega_r t}\right)(2I_zS_z + 2I_yS_y)$$
$$- i\left(e^{i(p+q+m)\omega_r t} - e^{-i(p+q-m)\omega_r t}\right)(2I_zS_y + 2I_yS_z)$$
$$+ i\left(e^{i(p-q+m)\omega_r t} - e^{-i(p-q-m)\omega_r t}\right)(2I_zS_y - 2I_yS_z)\Big\}$$

→Average Hamiltonian over rotor period

$$\overline{\tilde{H}}_{IS}^{(1)} = \frac{\omega_r}{2\pi}\int_0^{2\pi/\omega_r}\tilde{H}_{IS}(t)dt$$
$$= \frac{1}{4}\{(\omega_{IS}^{-(p+q)} + \omega_{IS}^{(p+q)})(2I_zS_z - 2I_yS_y) + (\omega_{IS}^{-(p-q)} + \omega_{IS}^{(p-q)})(2I_zS_z + 2I_yS_y)$$
$$- i(\omega_{IS}^{-(p+q)} - \omega_{IS}^{(p+q)})(2I_zS_y + 2I_yS_z) + i(\omega_{IS}^{-(p-q)} - \omega_{IS}^{(p-q)})(2I_zS_y - 2I_yS_z)\}$$

Four experiments that provide recoupling

$$\boxed{\begin{array}{lll} A: & p+q=-n, & p-q=r \quad , \\ B: & p+q=n, & p-q=r \quad , \\ C: & p-q=-n, & p+q=r \quad , \\ D: & p-q=n, & p+q=r \quad , \end{array}}$$

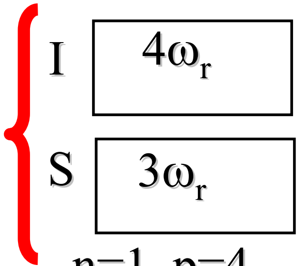
n = 1, 2

r > |2|

Heteronuclear Dipolar Recoupling:

One of the Four Experiments:

$$\overline{\tilde{H}}_{IS}^{D} = \frac{\kappa_n}{2}\{c_\gamma(2I_zS_z + 2I_yS_y) + s_\gamma(2I_zS_y - 2I_yS_z)\}$$



n=1, p=4

Which n? -- the scaling factor equals the dipolar Fourier component => n=1 largest scaling

$$\kappa_{\pm 1} = \frac{1}{2\sqrt{2}} b_{IS} s_{2\beta}$$

$$\kappa_{\pm 2} = -\frac{1}{4} b_{IS} s_\beta^2$$

The DCP experiment

Note: only the difference in the rf field strengths matters – but try to avoid other resonances!

HeteronuclearDipolarRecoupling:

The DCP experiment

Experiment D:

$$\overline{\tilde{H}}^{D}_{IS} = \frac{\kappa_n}{2}\{c_\gamma\underbrace{(2\underset{\downarrow\,-x}{I_z}S_z + 2\underset{\downarrow\,-x}{I_y}S_y)}_{ZQ_x} + s_\gamma\underbrace{(2\underset{\downarrow\,-x}{I_z}S_y - 2\underset{\downarrow\,-x}{I_y}S_z)}_{ZQ_y}\}$$

→ Tiltedframe
-π/2 around y

Fictitious spin-1/2

$$I_x^{23} = I_xS_x + I_yS_y$$

$$I_y^{23} = I_yS_x - I_xS_y$$

$$I_z^{23} = \tfrac{1}{2}(I_z - S_z)$$

$$I_z^{14} = \tfrac{1}{2}(I_z + S_z)$$

$$(\overline{\tilde{H}}^{D}_{IS})^T = e^{i\frac{\pi}{2}(I_y+S_y)}\overline{\tilde{H}}^{D}_{IS}e^{-i\frac{\pi}{2}(I_y+S_y)} = \kappa_n e^{-i\gamma I_z^{23}} I_x^{23} e^{i\gamma I_z^{23}}$$

$$U^T(t) = \exp\{-i(\overline{\tilde{H}}^{D}_{IS})^T t\} = e^{-i\gamma I_z^{23}} e^{-i\kappa_n t I_x^{23}} e^{i\gamma I_z^{23}}$$

$$\rho^T(0) = I_z = I_z^{14} + I_z^{23}$$

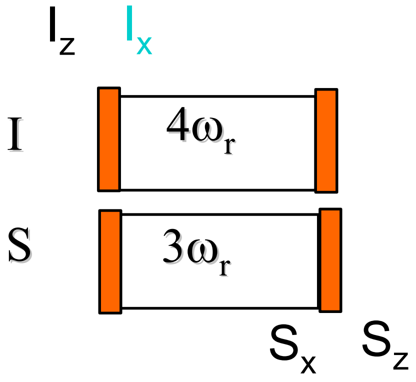
$$\boxed{\rho^T_{DCP}(t) = U^T(t)\rho^T(0)(U^T)^\dagger(t) = I_z^{14} + c_{\kappa_n t} I_z^{23} - s_{\kappa_n t}[c_\gamma I_y^{23} + s_\gamma I_x^{23}]}$$

Full transfer of I_z to S_z for $\kappa_n t = \pi$

$$\kappa = (1/2\sqrt{2})\, b_{IS} \sin(2\beta)$$

HeteronuclearDipolarRecoupling

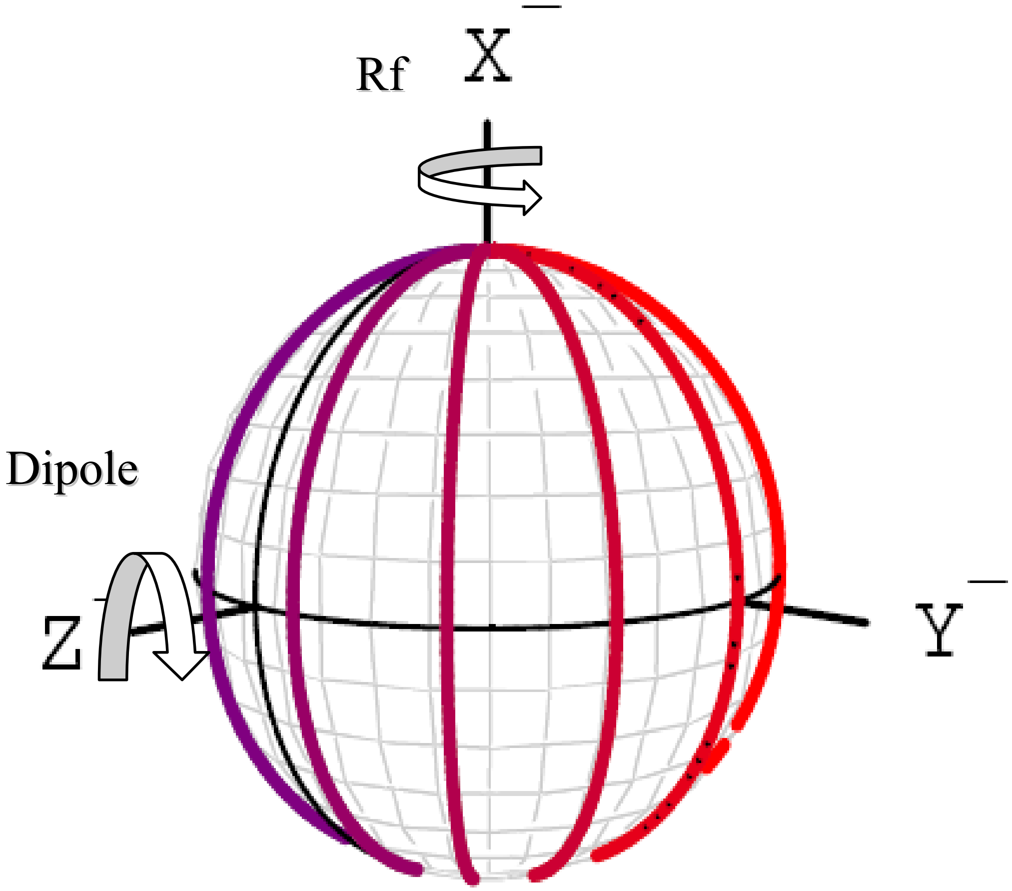
DCP is just an inversion



$$Z^{\pm} = I_z S_z \mp I_y S_y$$

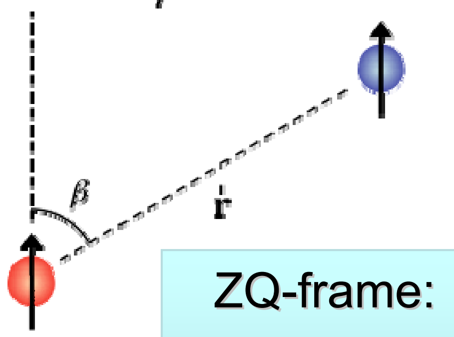
$$X^{\pm} = \frac{1}{2}(I_x \pm S_x)$$

$$Y^{\pm} = I_y S_z \pm I_z S_y$$



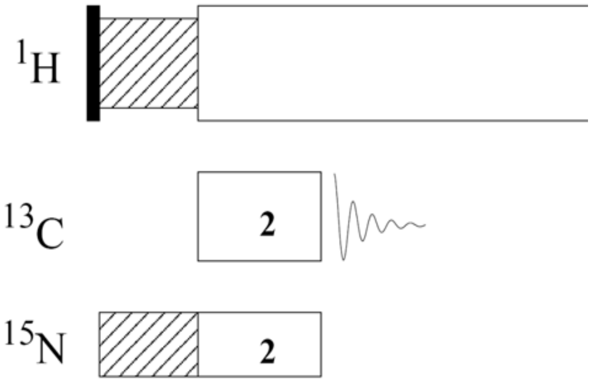
CompositeDipolarRecoupling

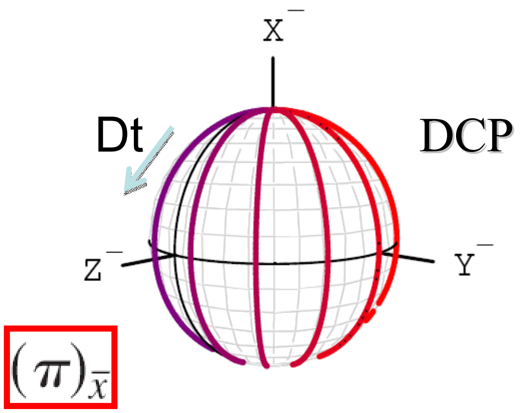
$$D \propto \frac{1}{r^3}\left(3\cos^2\beta - 1\right)$$



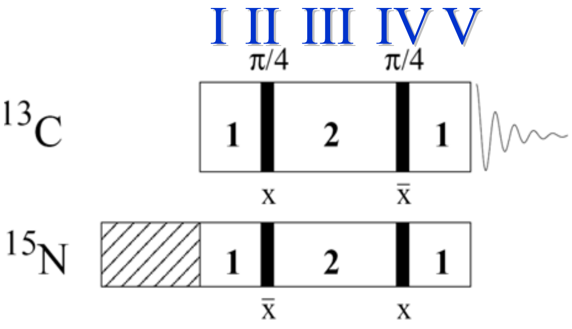
ZQ-frame:

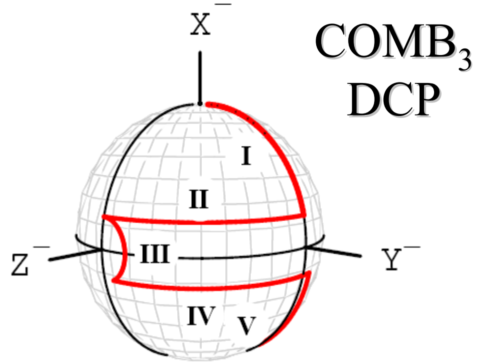
$I_x \xrightarrow{\pi} S_x$



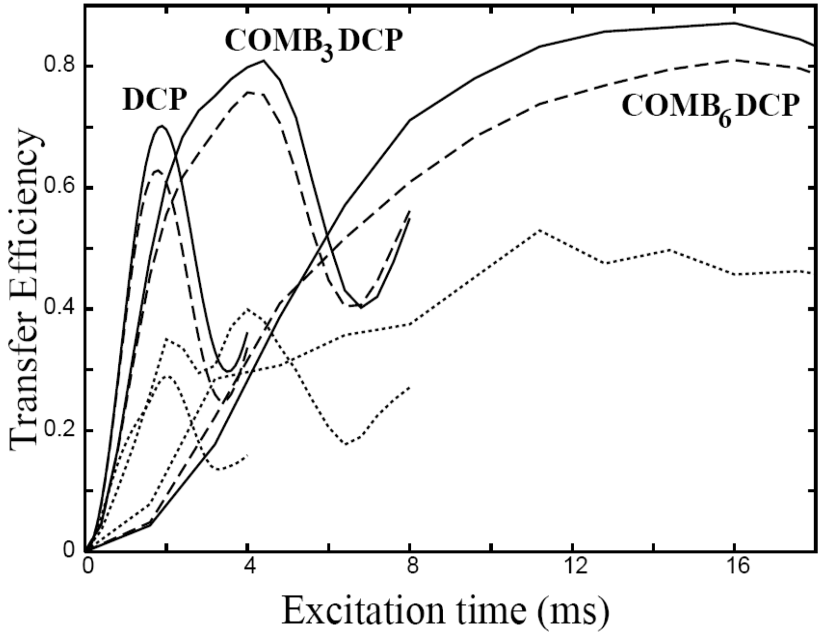


$(\pi)_{\bar{x}}$



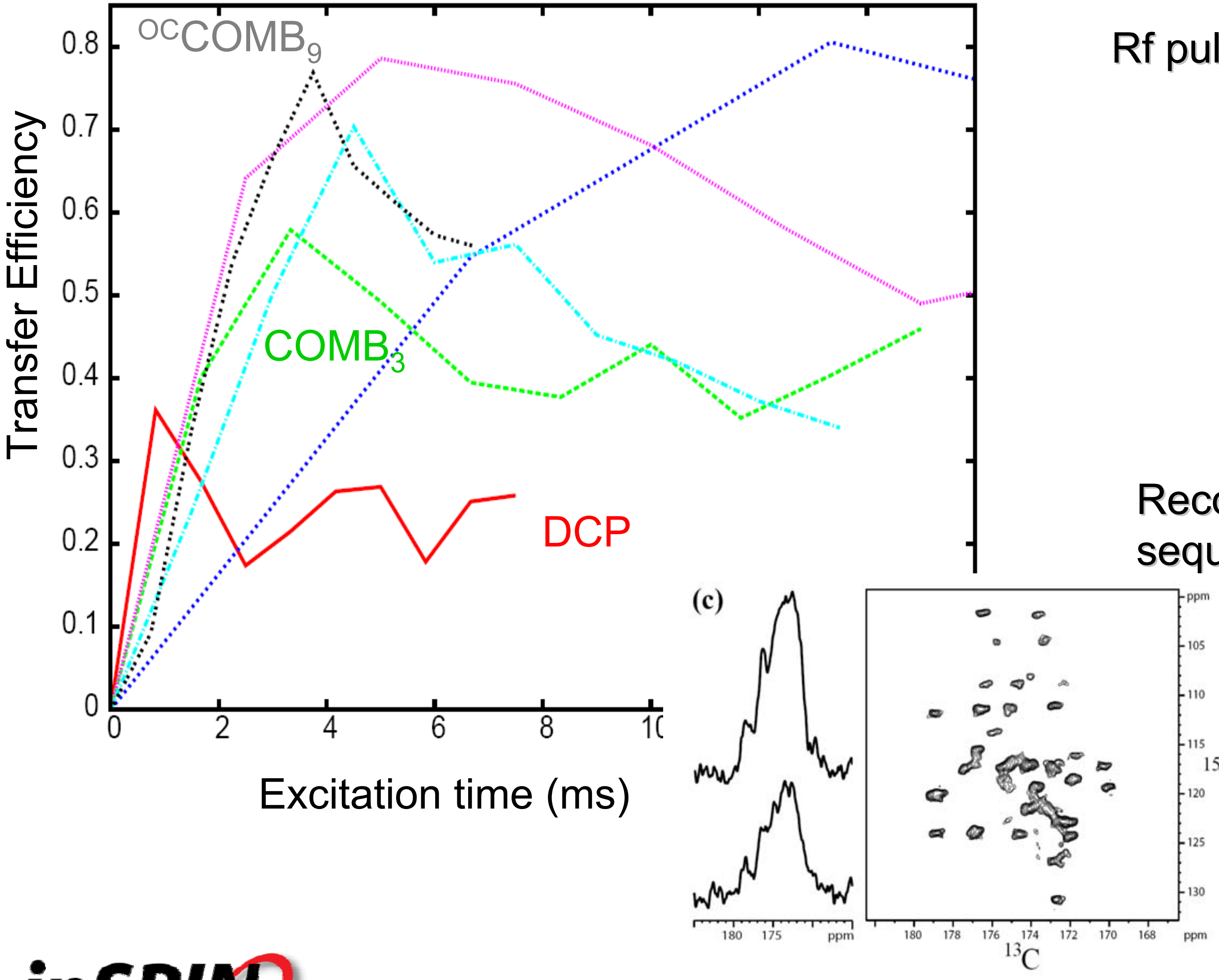


$(\pi/2)_y(\pi)_{\bar{x}}(\pi/2)_y$

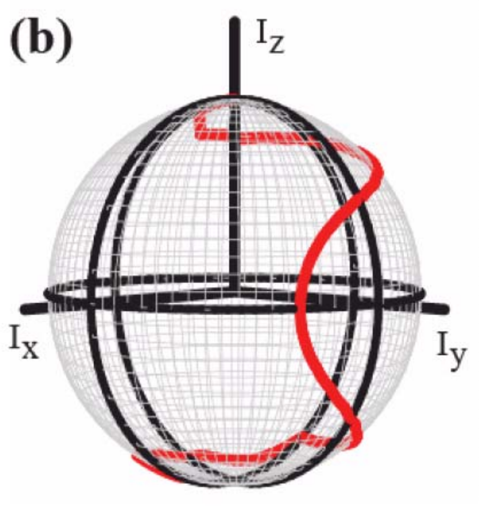


Better compensation towards orientation (β) variation of dipolar coupling

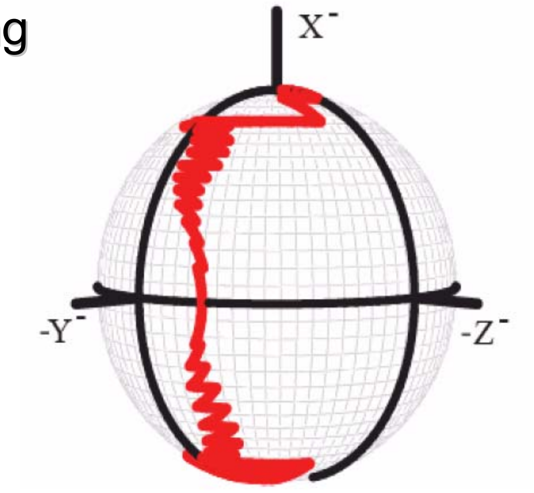
Optimal Control version withReduced Dimensionality



Rf pulses



Recoupling sequence

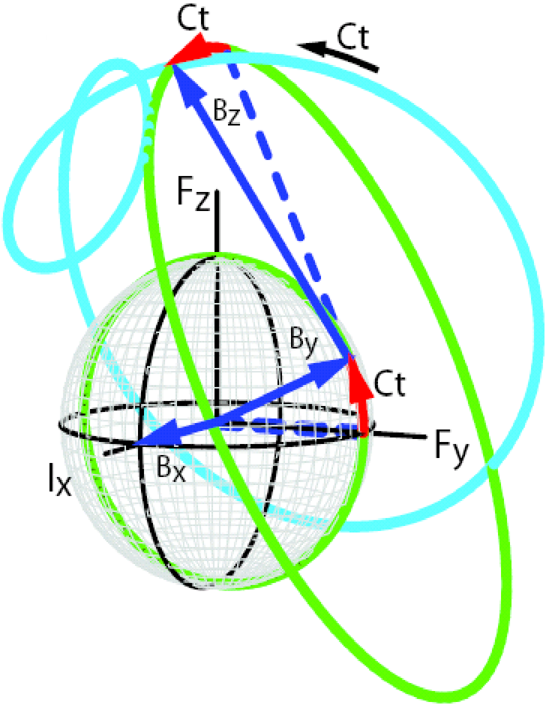


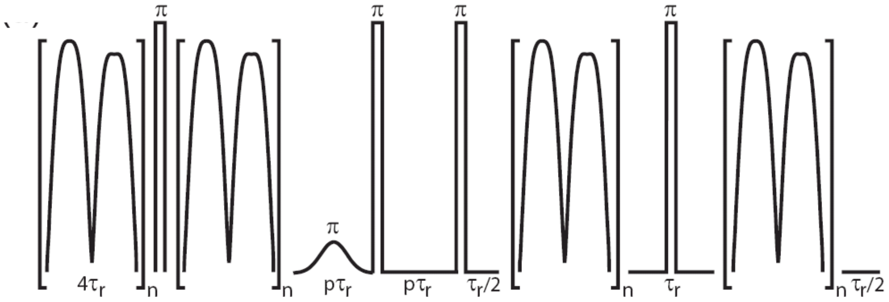
inSPIN Center for Insoluble Protein Structures

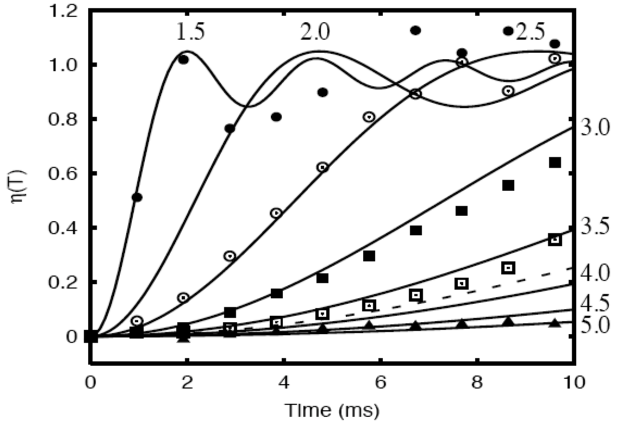
Hansen, Kehlet, Vosegaard, Glaser,Khaneja, Nielsen,
Chem. Phys. Lett. 447, 154 (2007)

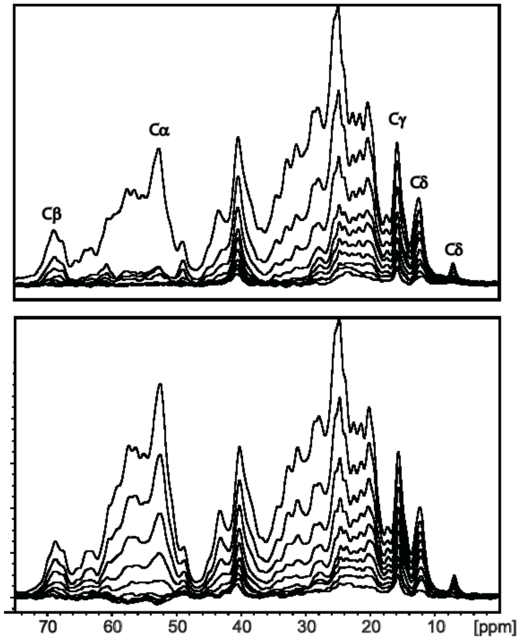
Niels Chr. Nielsen

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





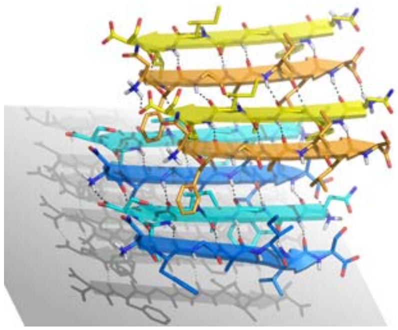




Triple-Oscillating-Field-techniqUe
TOFU

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

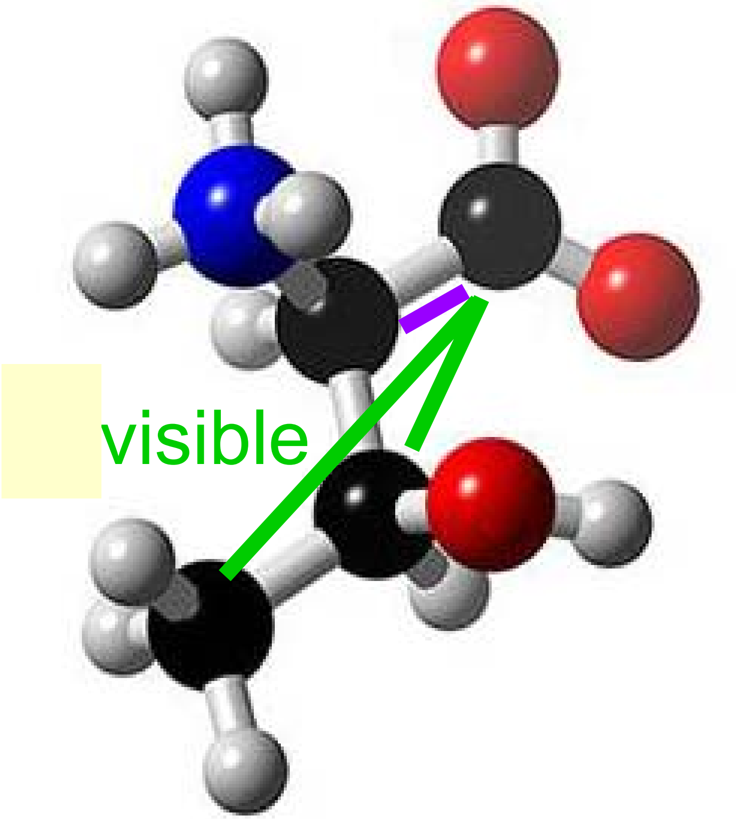
^{13}C-^{13}C distances up to 5 Å with 0.1-0.2 Å accuracy



The Dipolar Truncation Problem

$$2I_zS_z-I_xS_x-I_yS_y \xrightarrow{\text{recoupling}} 2I_xS_x\pm 2I_yS_y \text{ (planar)}$$

$$[2I_xS_x-2I_yS_y,\ 2R_xS_x-2R_yS_y] \neq 0$$

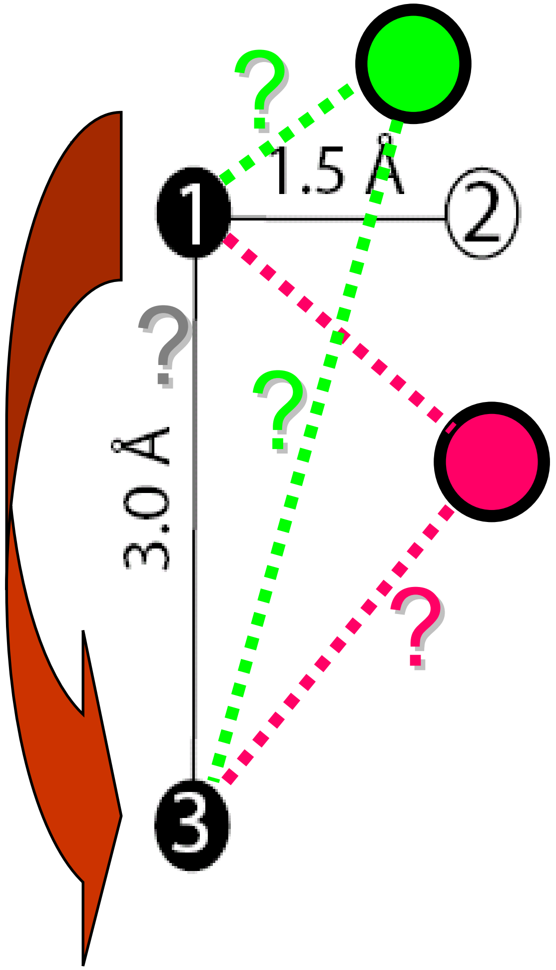


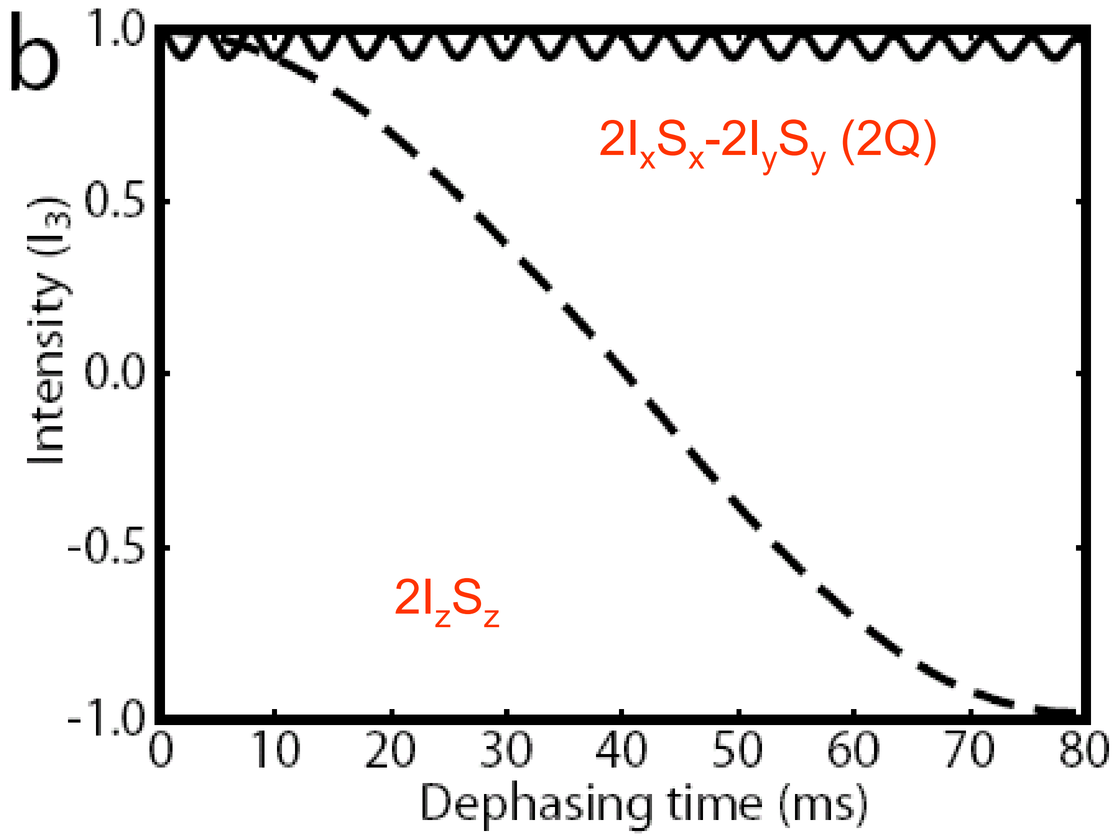
Solution!

$$2I_zS_z-I_xS_x-I_yS_y \xrightarrow{\text{recoupling}} 2I_zS_z \text{ (Ising)}$$

$$[2I_zS_z,\ 2R_zS_z] = 0$$

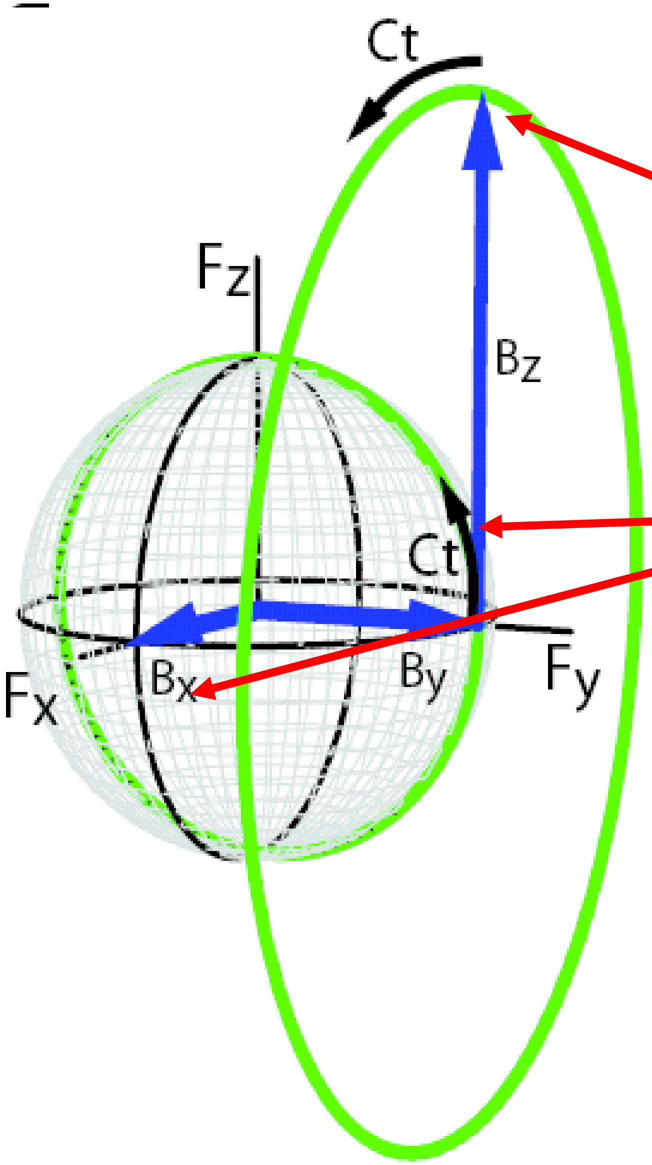
Planar vs Ising Dephasing





OBS: Dipolartrunction is not solved by introducing a thirdspin
– and sequential transfers

TripleOscillatingFieldtechniqUe (TOFU)



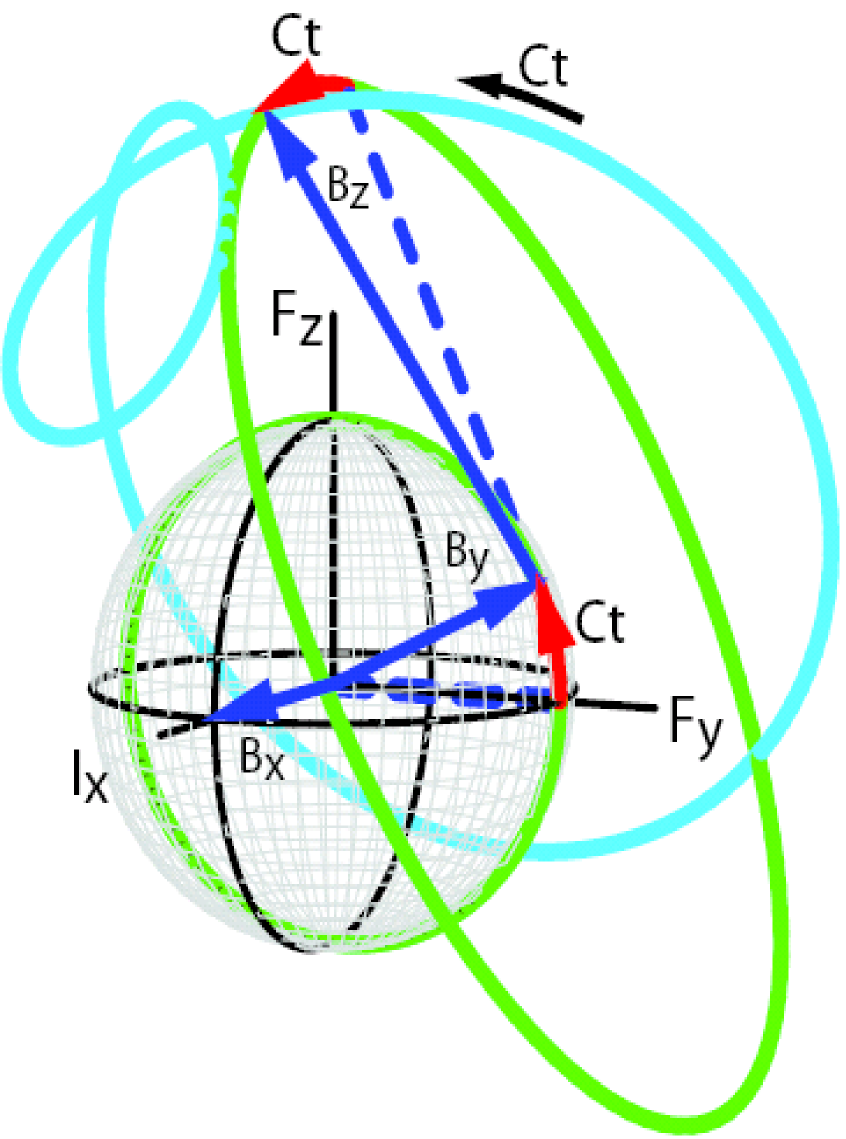
$2I_zS_z - I_xS_x - I_yS_y$ (Dipolar)

$$H_{rf}(t) = CF_x + C\exp(-iCtF_x)\,F_y\,\exp(iCtF_x)$$
$$+\; B\exp(-iCtF_x)\exp(-iCtF_y)\,F_z\,\exp(iCtF_y)\exp(iCtF_x)$$

+ isotropic shift

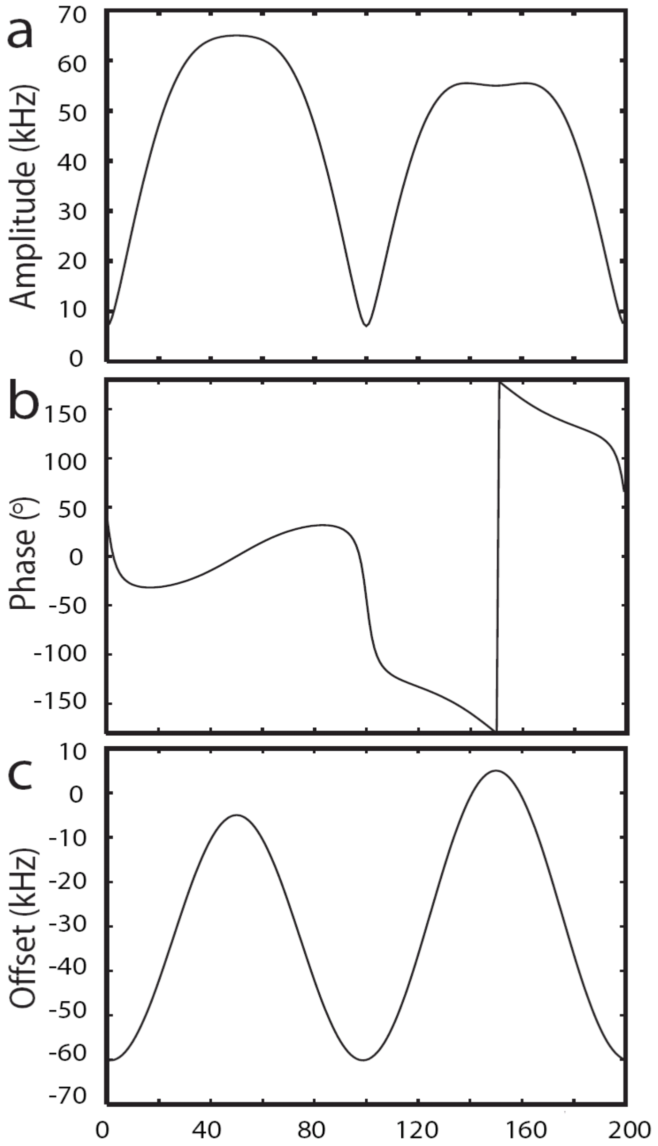
$2I_zS_z$ (Ising)

TripleOscillatingFieldtechniqUe(TOFU)



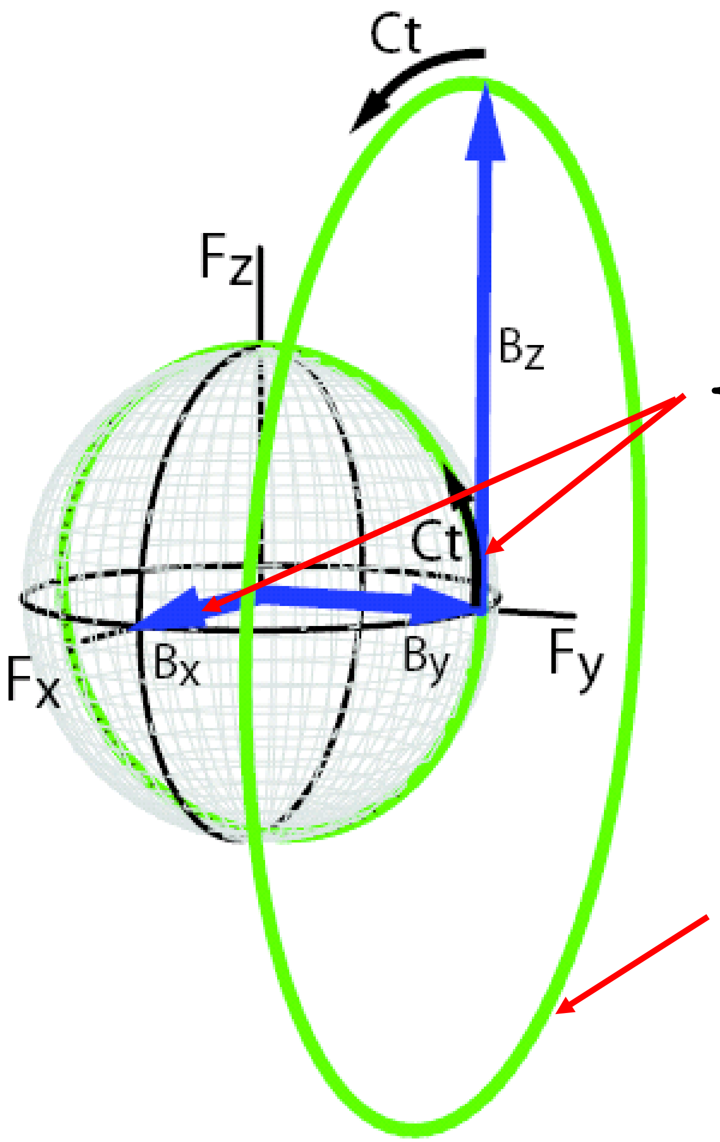
$C = \omega_r/4$

$B = 3\omega_r$



Niels Chr. Nielsen

TOFU: Some Hamiltonian stuff …



$$H_0(t) = \omega_I(t)I_z + \omega_S(t)S_z + \omega_{IS}(t)(3I_zS_z - \overline{I}\cdot\overline{S})$$

$$\tilde{H}_\sigma(t) = \omega_I(t)(\cos^2(Ct)I_z + \sin(Ct)I_y - \frac{1}{2}\sin(2Ct)I_x)$$

$$+\omega_S(t)(\cos^2(Ct)S_z + \sin(Ct)S_y - \frac{1}{2}\sin(2Ct)S_x)$$

$$\begin{aligned}\tilde{H}_{IS}(t) &= \frac{3}{2}\omega_{IS}(t)\{\cos^4(Ct)2I_zS_z + \sin^2(Ct)\cos^2(Ct)2I_xS_x + \sin^2(Ct)2I_yS_y \\ &+ \frac{1}{2}\sin(2Ct)[\cos(Ct)(2I_zS_y + 2I_yS_z) - \sin(Ct)(2I_xS_y + 2I_yS_x) \\ &- \cos^2(Ct)(2I_zS_x + 2I_xS_z)]\} \quad ,\end{aligned}$$

$$\begin{aligned}H_A(t) &= \omega_I(t)\cos^2(Ct)I_z + \omega_S(t)\cos^2(Ct)S_z \\ &+ \frac{3}{2}\omega_{IS}(t)\{\cos^4(Ct)(3I_zS_z - \overline{I}\cdot\overline{S}) + (I_xS_x + I_yS_y)\}\end{aligned}$$

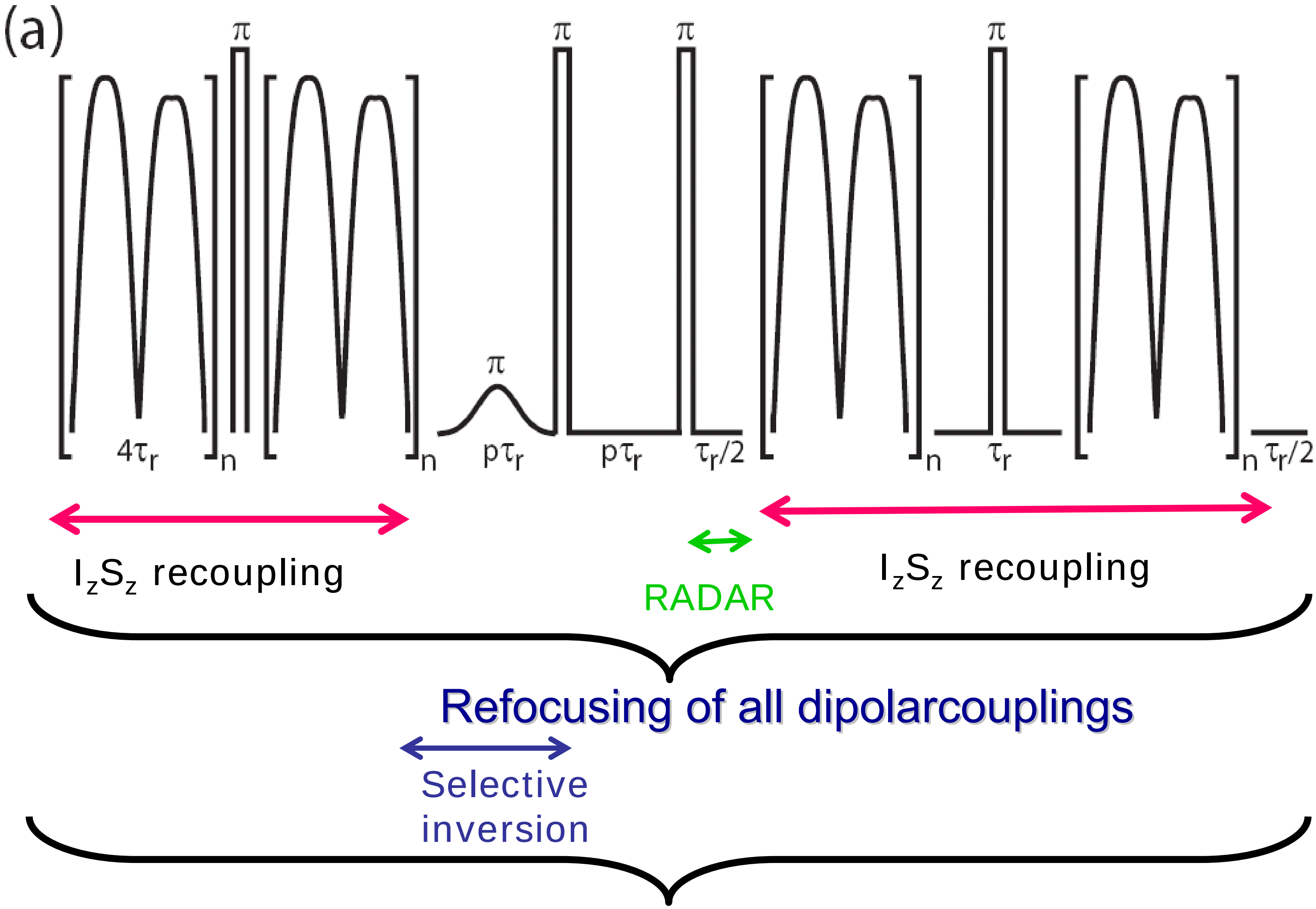
$$\overline{H_A} = \frac{1}{2}\omega_I^{(0)}I_z + \frac{1}{2}\omega_S^{(0)}S_z + \frac{3}{16}c_{IS}^{(1)}\cos\gamma\{2I_zS_z - I_xS_x - I_yS_y\}$$

$$\cos^2(Ct) = \tfrac{1}{2} + \tfrac{1}{4}\exp(i2Ct) + \tfrac{1}{4}\exp(-i2Ct)$$

$$\cos^4(Ct) = \tfrac{3}{8} + \tfrac{1}{4}\exp(i2Ct) + \tfrac{1}{4}\exp(-i2Ct) + \tfrac{1}{16}\exp(i4Ct) + \tfrac{1}{16}\exp(-i4Ct)$$

$$\overline{H_A} = \frac{3}{16}c_{IS}^{(1)}\cos\gamma\; 2I_zS_z$$

Triple Oscillating Field techniqUe +
Rotor assisted dipolar recoupling (RADAR)



I_zS_z recoupling

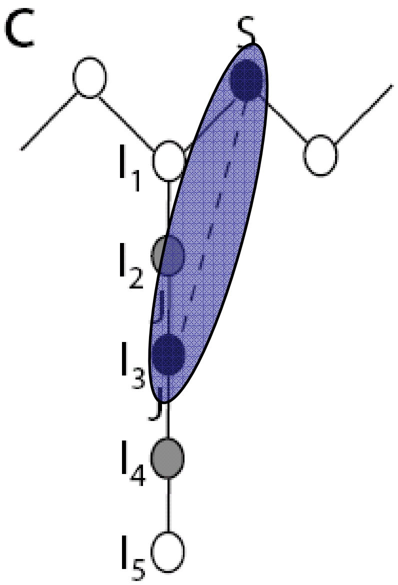
RADAR

I_zS_z recoupling

Refocusing of all dipolarcouplings

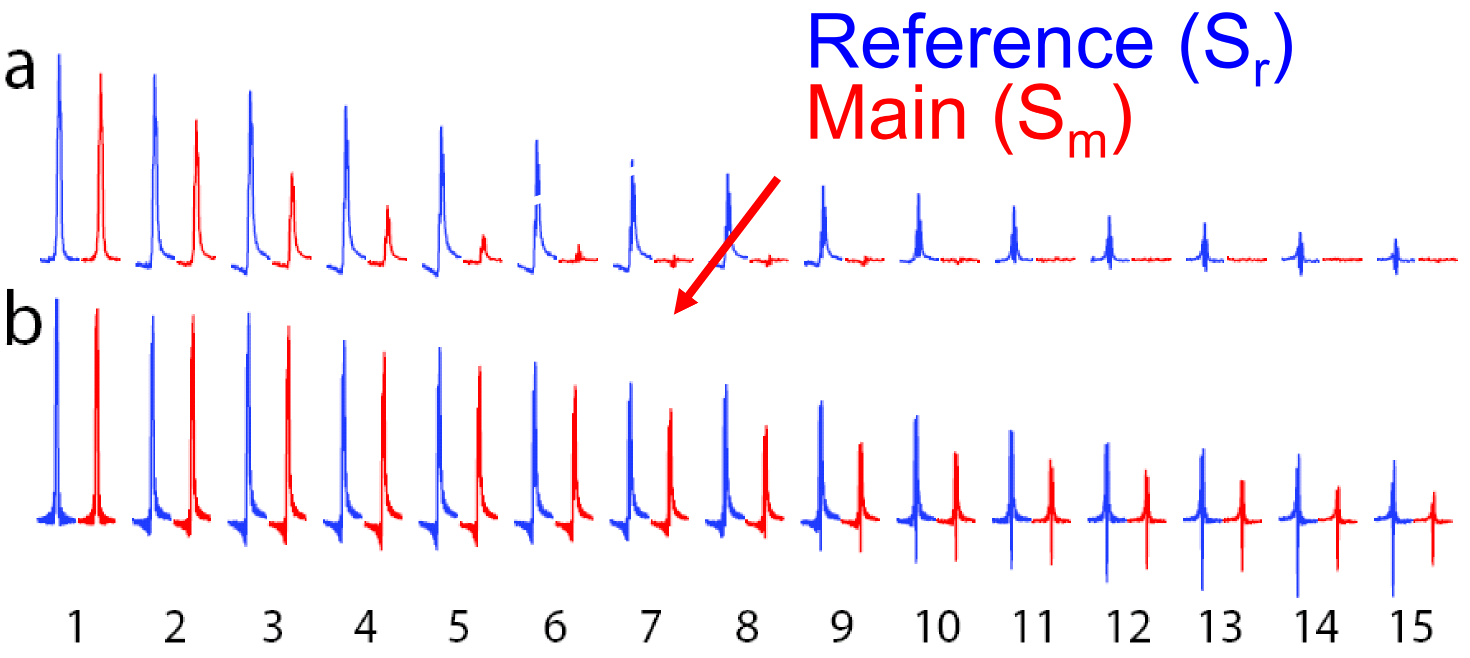
Selective
inversion

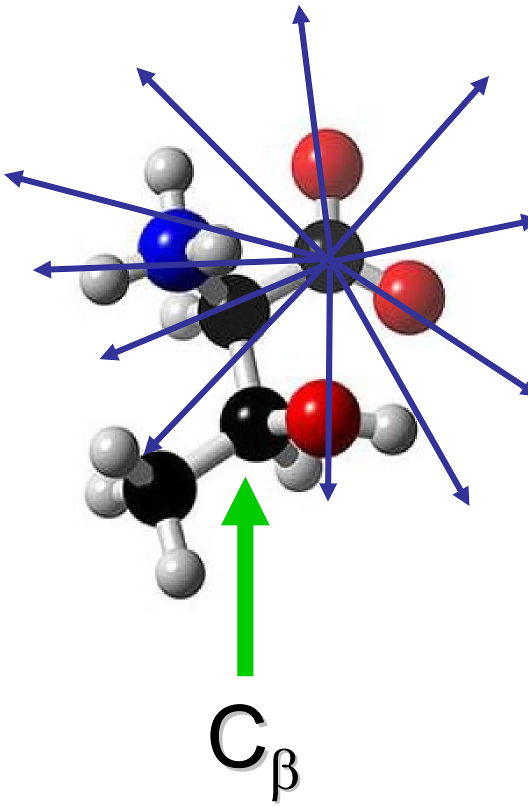
Dipolar couplings to C' active + surrounding J's active



Khaneja & Nielsen,
J. Chem. Phys. 128,
015103 (2008).

TOFU + RADAR: U-^{13}C,^{15}N-*L*-threonine





FRESNEL

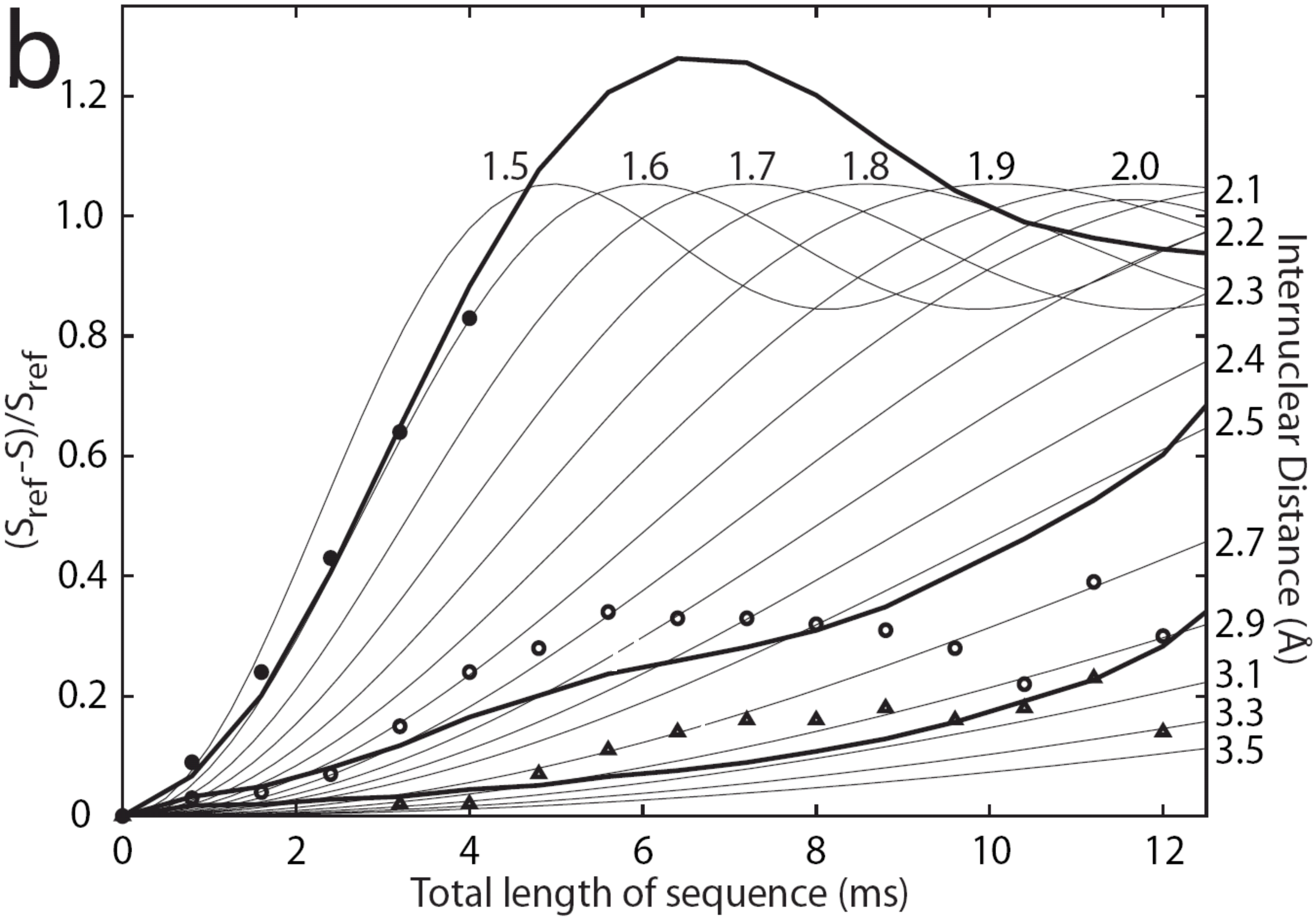
$$\eta(T) = \frac{S_r(t) - S_m(t)}{S_r(t)} = 1 - \int \cos(\omega_k^{DD} T)$$

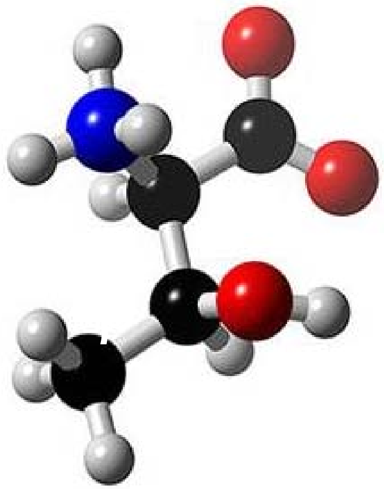
Easyread-out

Khaneja & Nielsen,
J. Chem. Phys. 128
015103 (2008).

Accurate distances by ssNMR:

U-^{13}C,^{15}N-*L*-Threonine



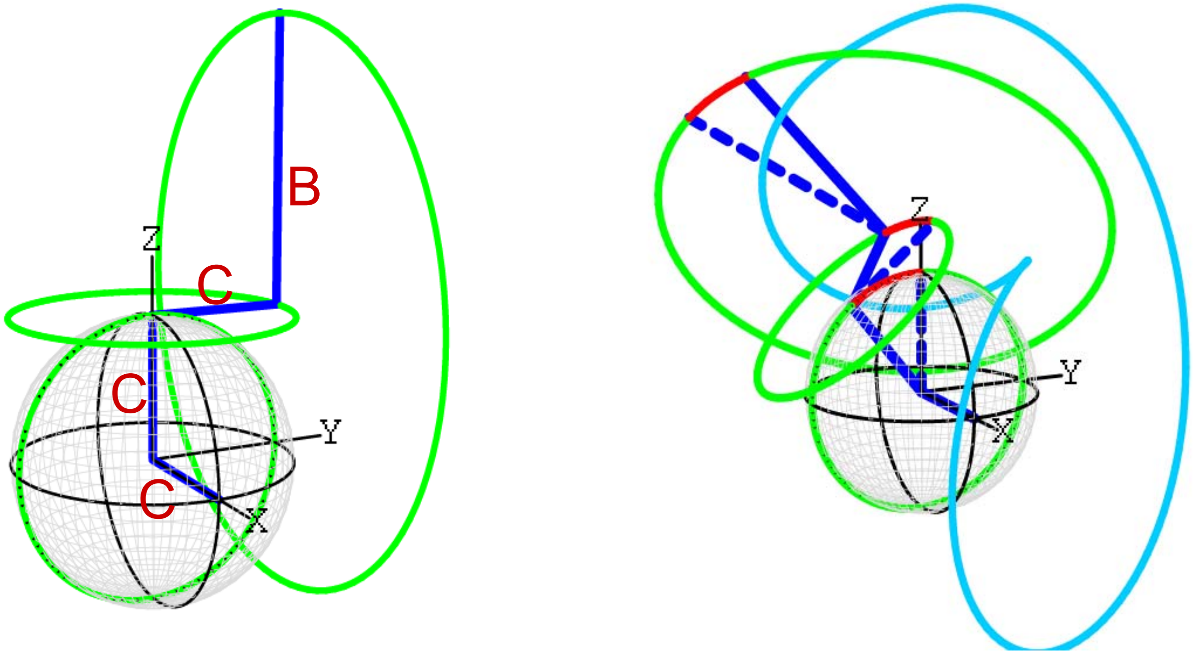


Khaneja & Nielsen,
J. Chem. Phys. 128,
015103 (2008).

Larger dipolar scaling –
Multiple Oscillating Field Techniques

TOFU is a good step aheadtowardsaccurate distance meausrements!
But the dipolarscaling is toolow to measurelong-rangeconstraints

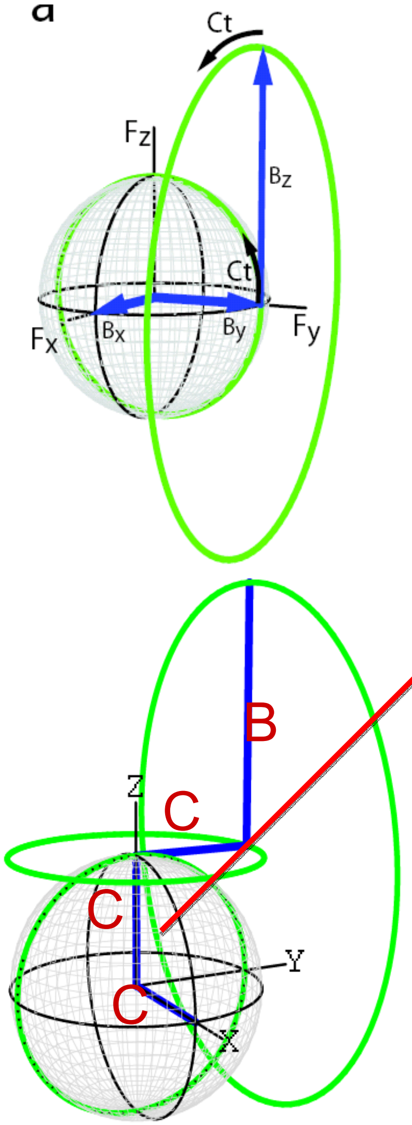
$$\tilde{H}_{IS}(t) = 2.5\mathrm{x}\,\boxed{\frac{3}{16}}\,c_{IS}^{(1)} \cos\gamma\; 2I_zS_z \qquad c_{IS}^{(1)} = (1/2\sqrt{2})\,b_{IS}\sin(2\beta)$$



B=3.75 ω_r
C=0.25 ω_r

Straasøe, Bjerring, Khaneja, Nielsen, J. Chem. Phys., in Press (2009)

Larger dipolar scaling –
Multiple Oscillating Field Techniques



$$I_zS_z \xrightarrow{-\mathrm{Ct}F_x} c_{Ct}^2 I_zS_z + s_{Ct}^2 I_yS_y + s_{Ct}c_{Ct}(I_zS_y + I_yS_z)$$

$$\xrightarrow{-\mathrm{Ct}F_z} c_{Ct}^2 I_zS_z + s_{Ct}^4 I_xS_x + c_{Ct}^2 s_{Ct}^2 I_yS_y + s_{Ct}c_{Ct}^2(I_zS_y + I_yS_z) + s_{Ct}^2 c_{Ct}(I_zS_x + I_xS_z) + c_{Ct}s_{Ct}^3(I_xS_y + I_yS_x)$$

$$\xrightarrow{-\mathrm{Ct}F_y} c_{Ct}^4 I_zS_z + s_{Ct}^6 I_zS_z + 2s_{Ct}^3 c_{Ct}^2 I_zS_z + s_{Ct}^2 c_{Ct}(c_{Ct} + s_{Ct}^2 c_{Ct} - s_{2Ct}) I_xS_x + s_{Ct}^2 c_{Ct}^2 I_yS_y + \dots$$

$$c_{Ct}^4 = \frac{3}{8} + \frac{1}{2}c_{2Ct} + \boxed{\frac{1}{8}c_{4Ct}}$$

$$c_{Ct}^4 + s_{Ct}^6 + 2s_{Ct}^3 c_{Ct}^2 = \frac{1}{32}(22 + c_{2Ct} + \boxed{10c_{4Ct}} - c_{6Ct} + 8s_{Ct} + 4s_{3Ct} - 4s_{5Ct}). \qquad ($$

Straasøe, Bjerring, Khaneja, Nielsen, J. Chem. Phys., in Press (2009)

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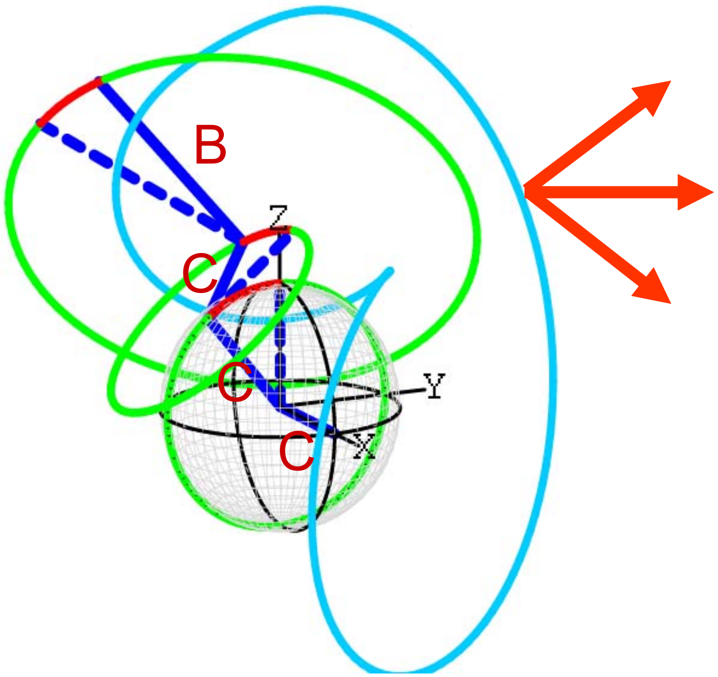
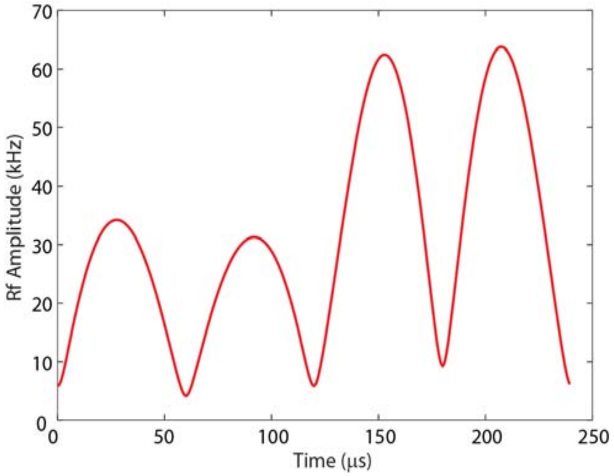
Niels Chr. Nielsen

Four OscillatingfieLDTechniqUe

FOLD

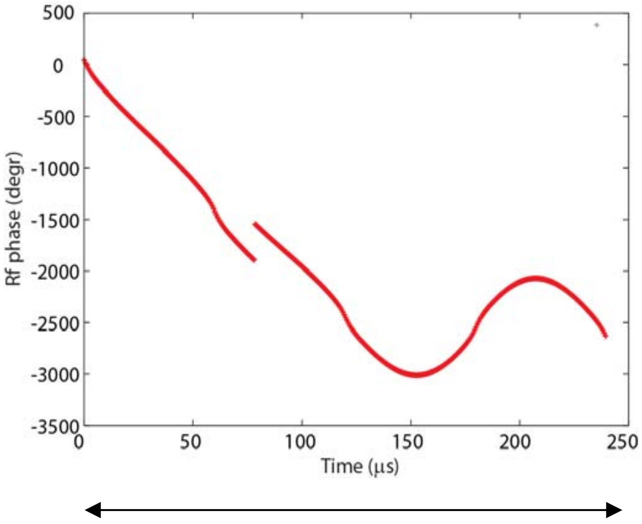


Rf field strength

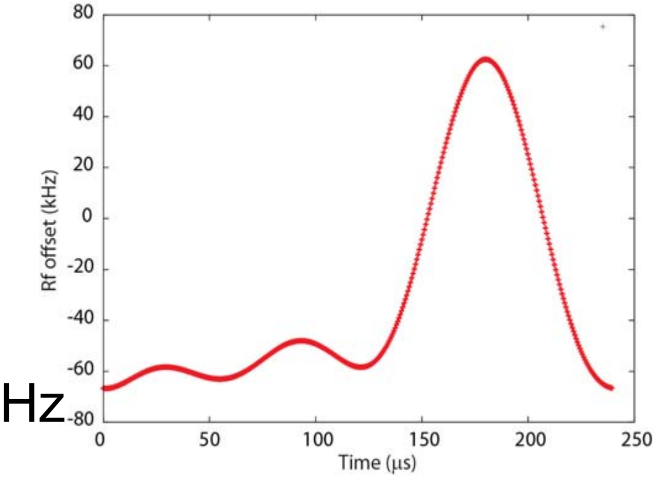


B=3.75 ω_r
C=0.25 ω_r

Rf phase



4 τ_r



$\omega_r/2\pi$ = 16.7 kHz
B=3.75 ω_r
C=0.25 ω_r

Rf offset

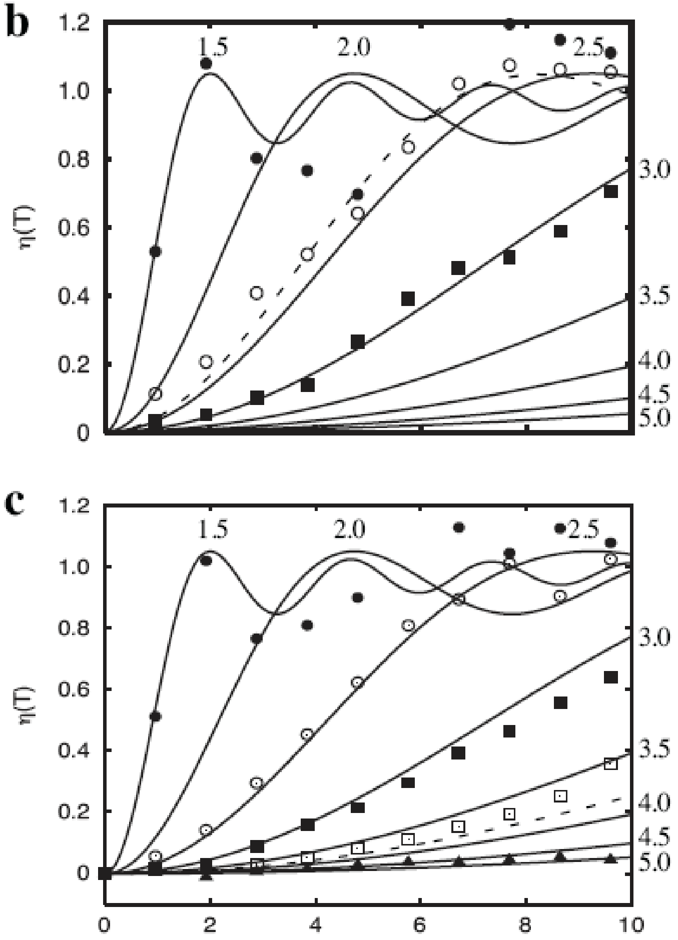
Internuclear distances using FOLD
(16.67 kHz; 700 MHz)

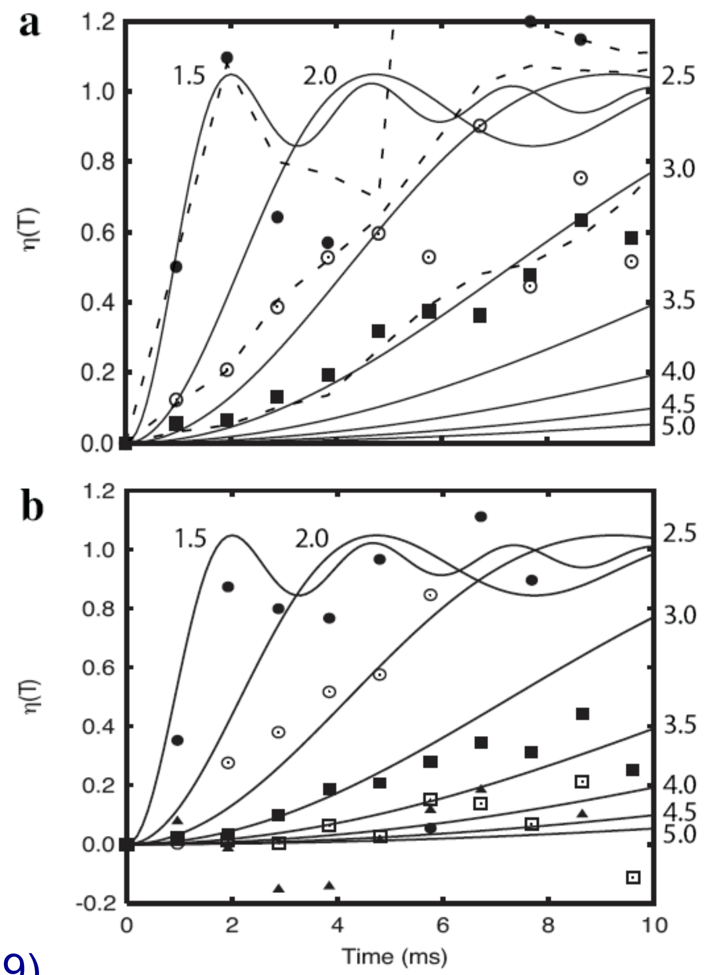
Simulations

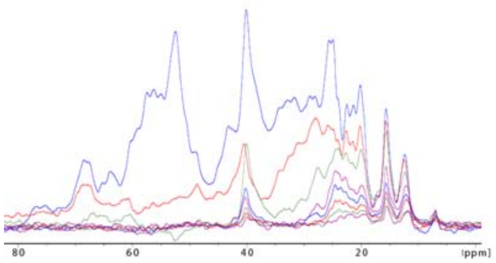
Experiments

L-Threonine

Leucine
(ubiquitin)







Strassøe, Bjerring, Khaneja& Nielsen, J. Chem. Phys., in press (2009)

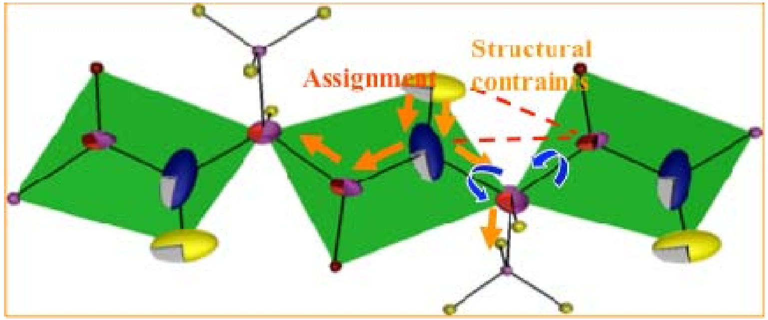
inSPIN Center for Insoluble Protein Structures

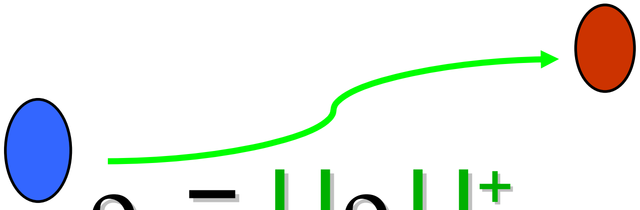
Niels Chr. Nielsen

Optimal control design of NMR experiments

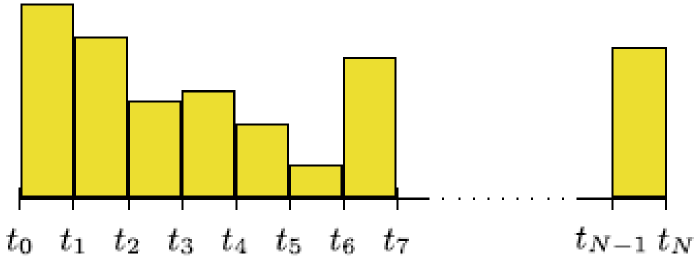
- improved sensitivity
- band selective operation
- less rf power consumption

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





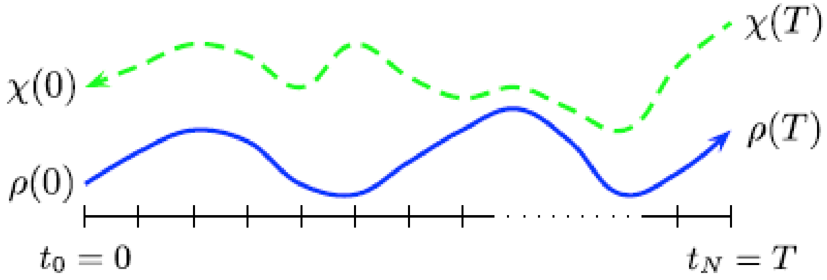
$$\rho_f = U\rho_i U^+$$



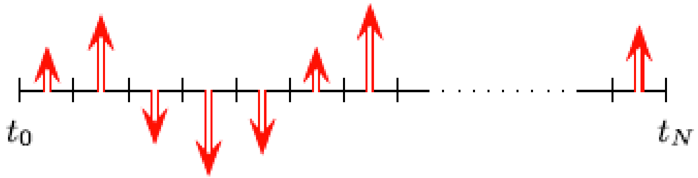
Optimal control => Design of $\bar{U}$

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

Final cost Runningcost



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



inSPIN Center for Insoluble Protein Structures

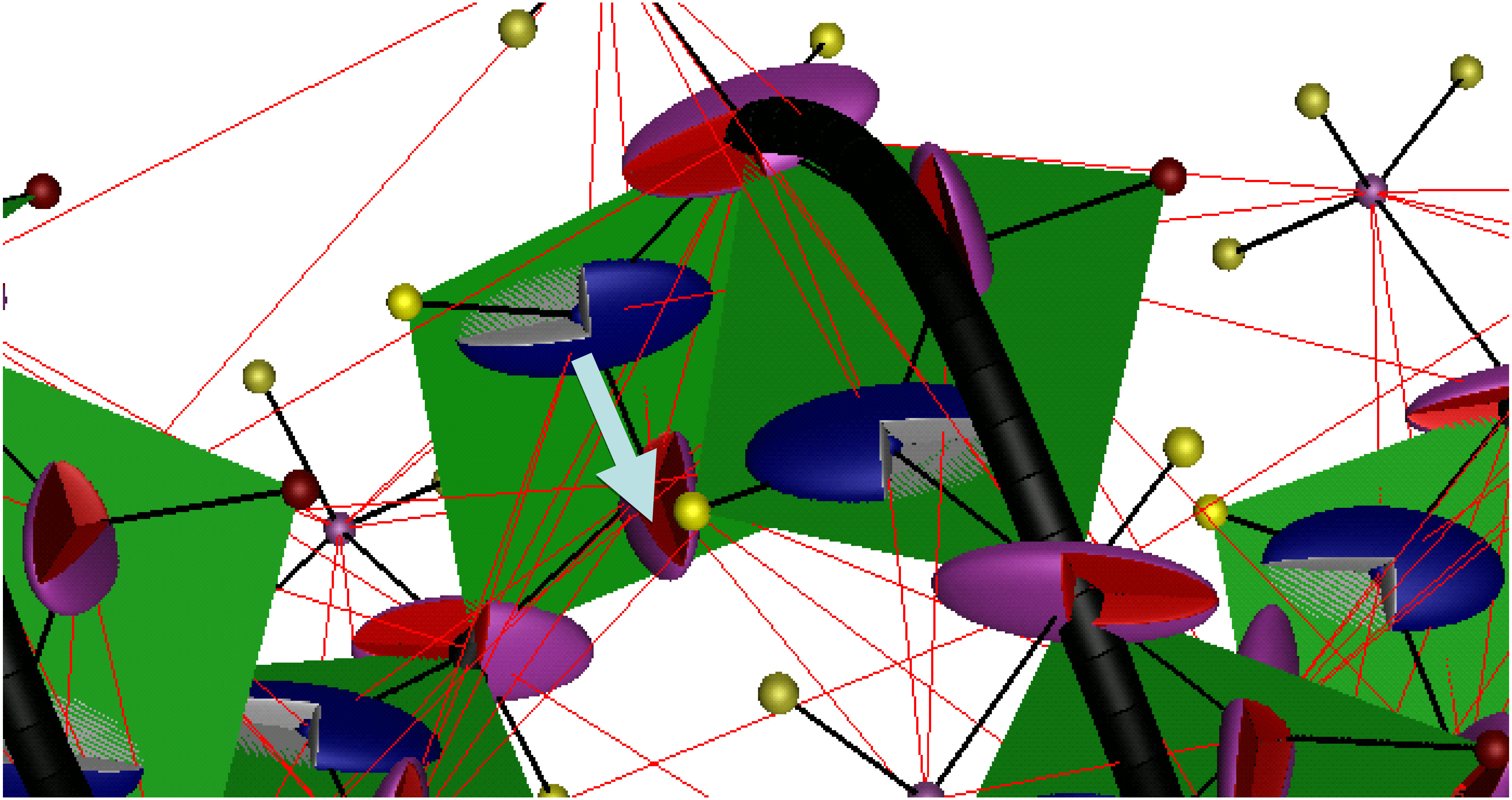
AARHUS UNIVERSITET

Center for Insoluble Protein Structures

Free open source software at
www.bionmr.chem.au.dk

Niels Chr. Nielsen

A specific case – many exists



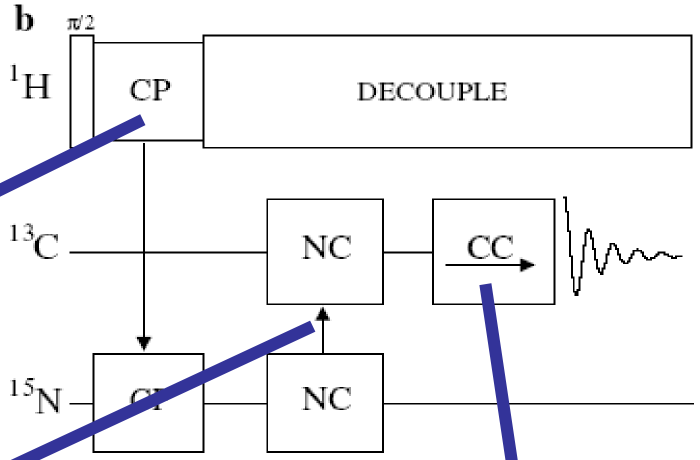
Optimum control in biological solid-state NMR

Optimization of building blocks

- Gain in sensitivity

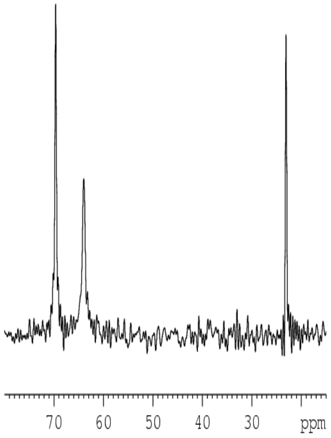
- Reduction of instrumental errors

- Reduced heating problems

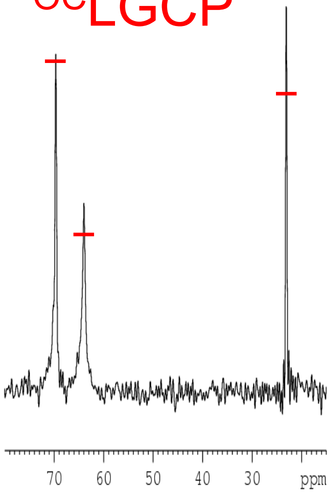


AUTOMATED EXPERIMENT DESIGN

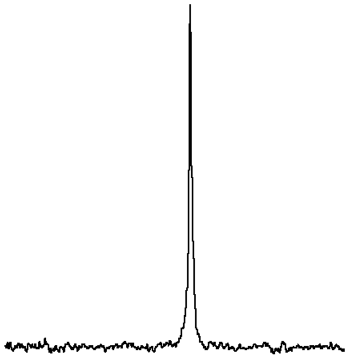
LGCP



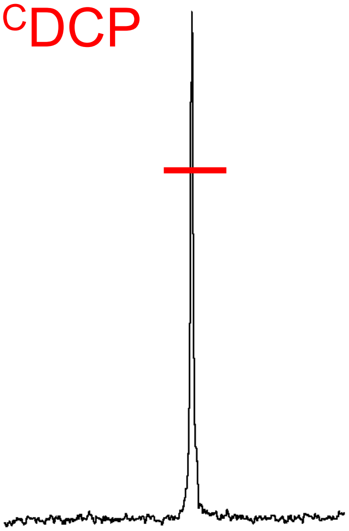
^{OC}LGCP



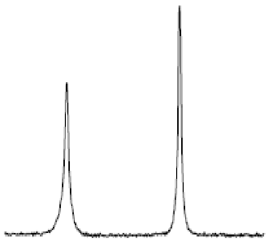
DCP



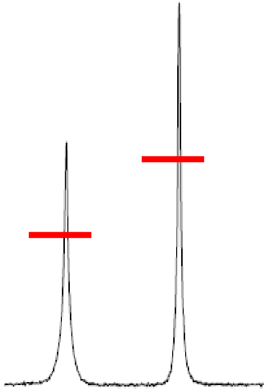
^{OC}DCP



HORROR



^{OC}HORROR



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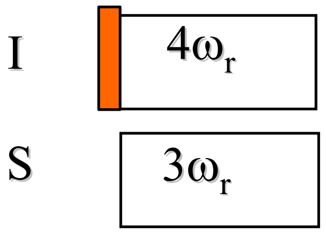
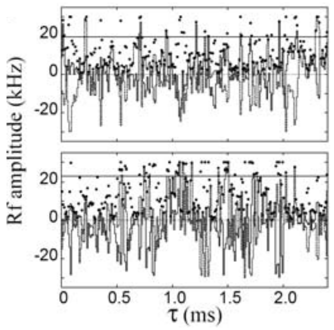
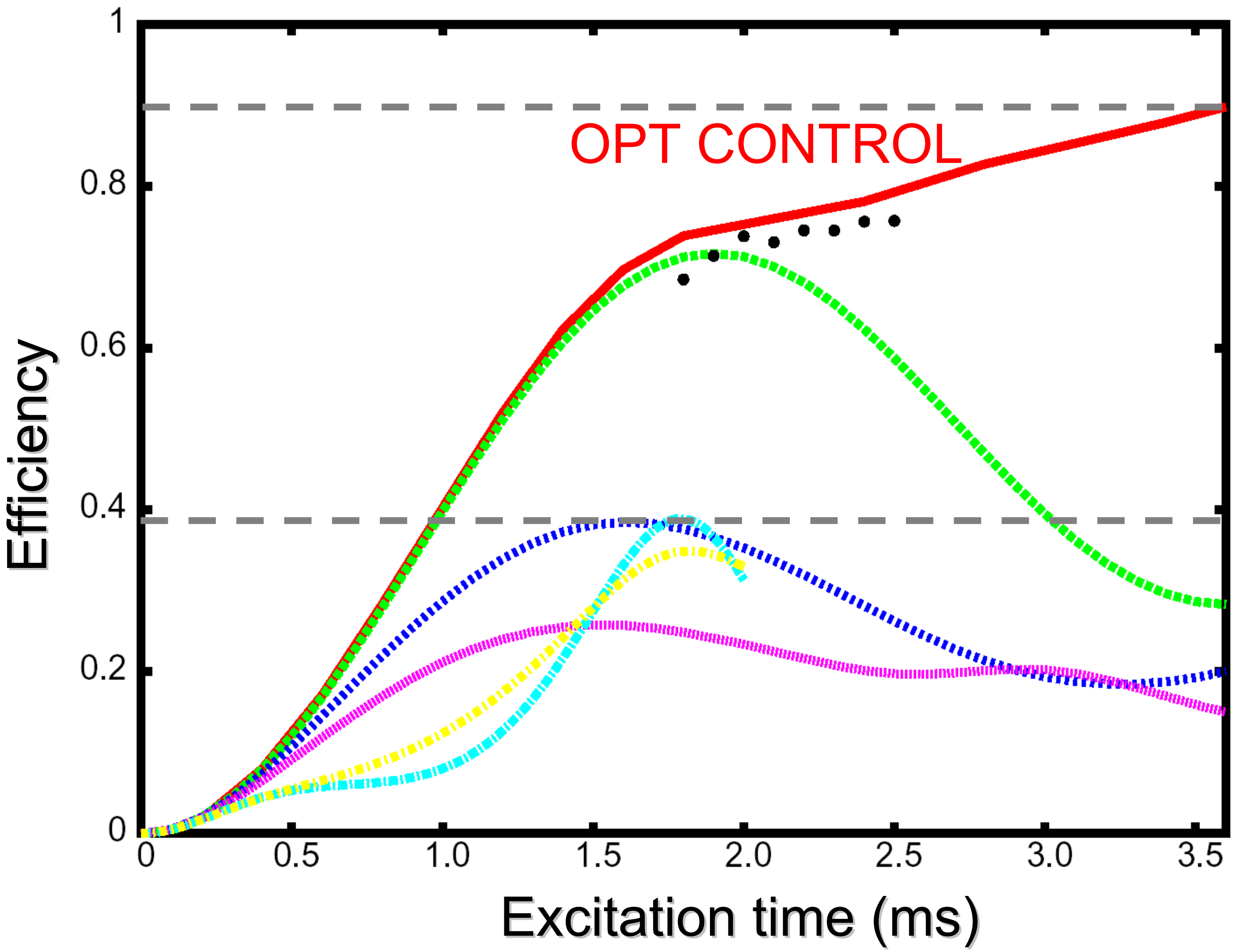
Traditional recoupling vs. optimal control

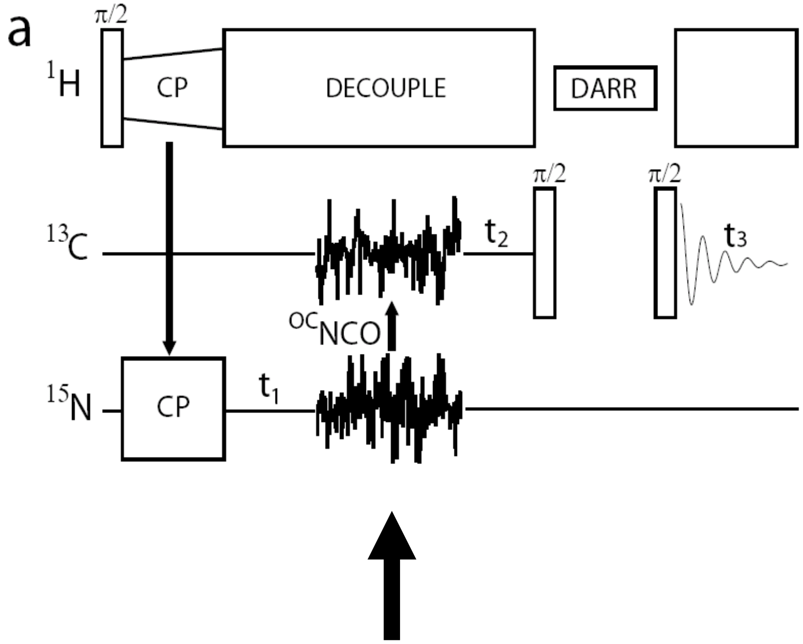




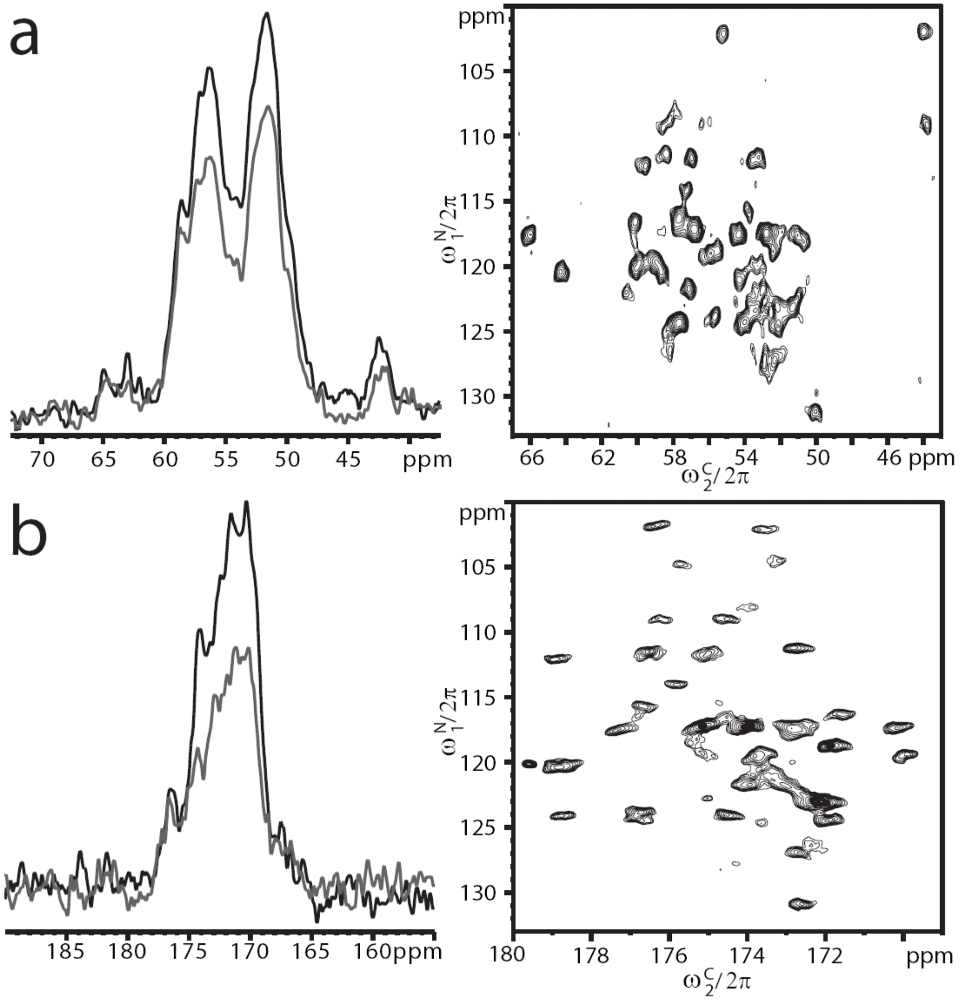


Gain: ~100%

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



Optimal Control

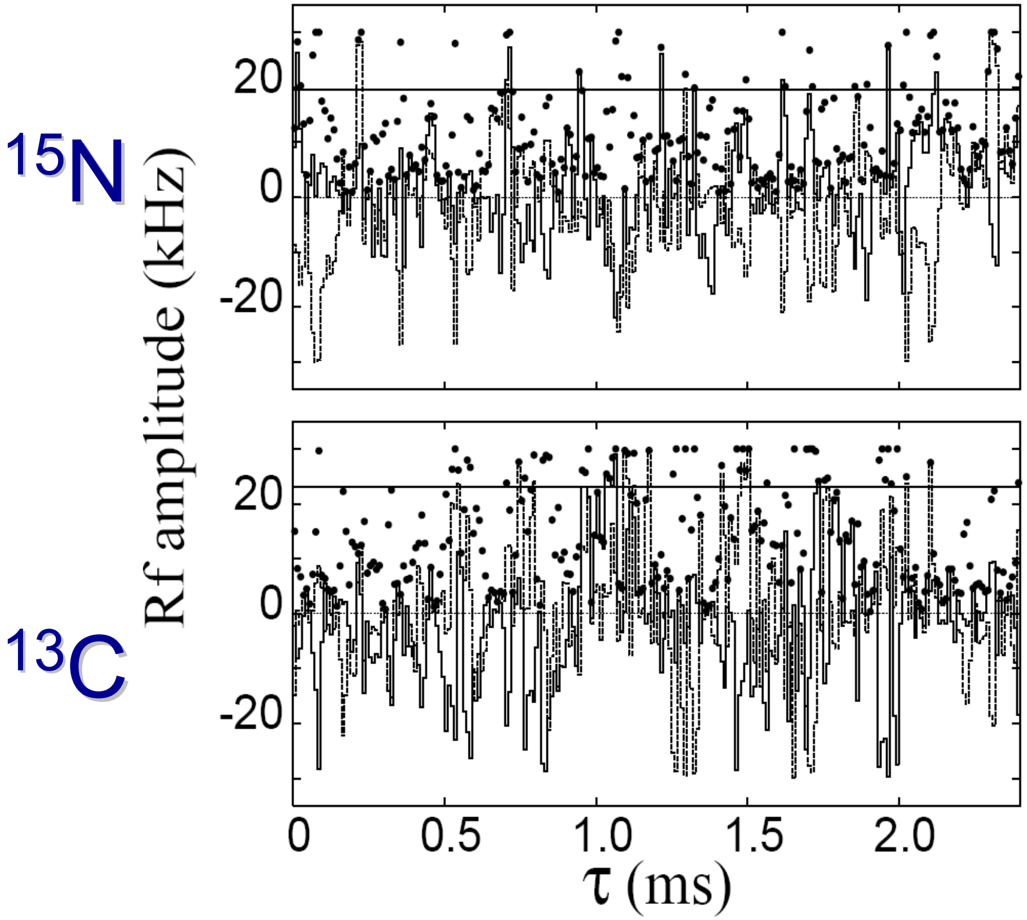


50-100%
Higher sensitivity
(less sample/less time)

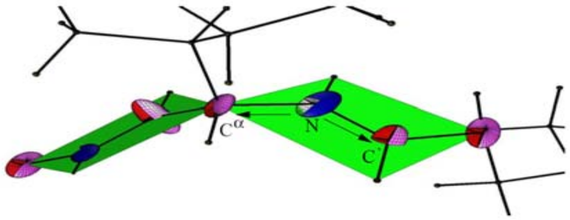
Less sample heating
(in the order of
1/10 – 1/4 power

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

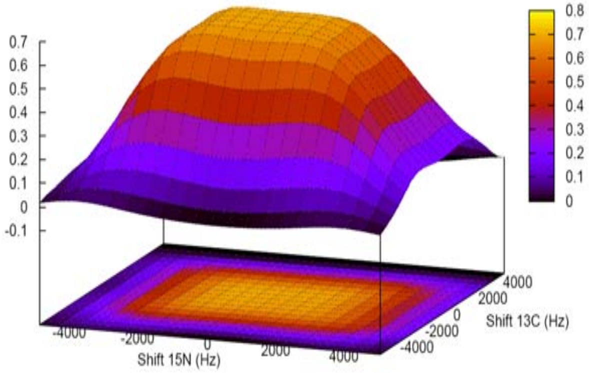
^{15}N→^{13}C in NCO and NCA at highfield–sequence&robustness



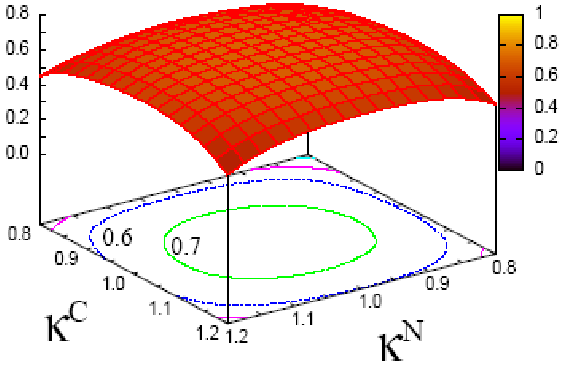
Transfer



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



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



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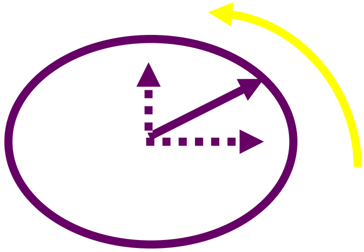
Kehlet, Bjerring, Sivertsen, Glaser, Khaneja, Nielsen, J. Magn. Reson 188, 216 (2007)

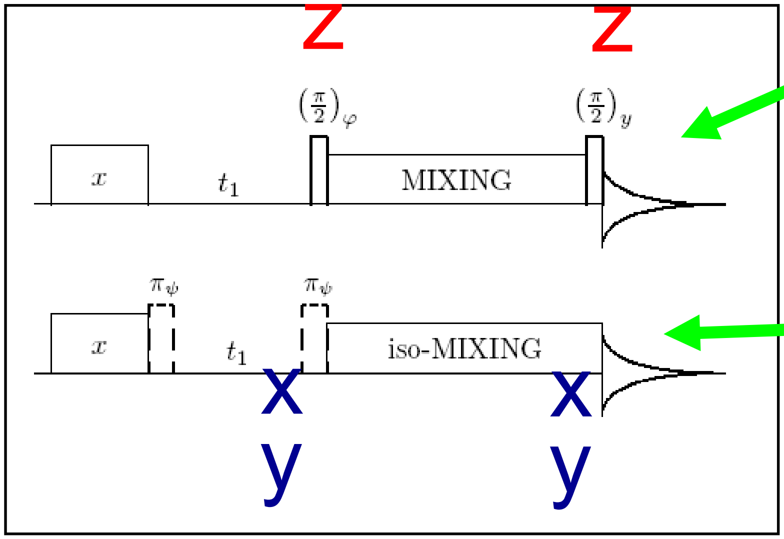
Niels Chr. Nielsen

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

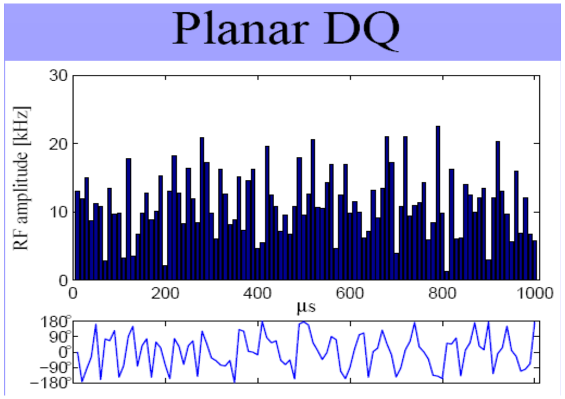


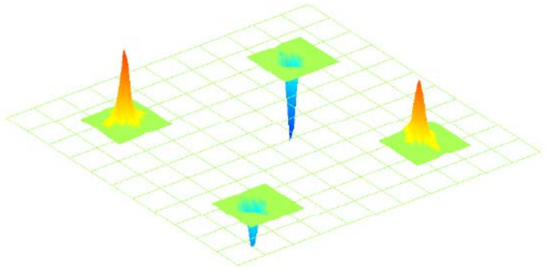
Only transfer of x- or y-component

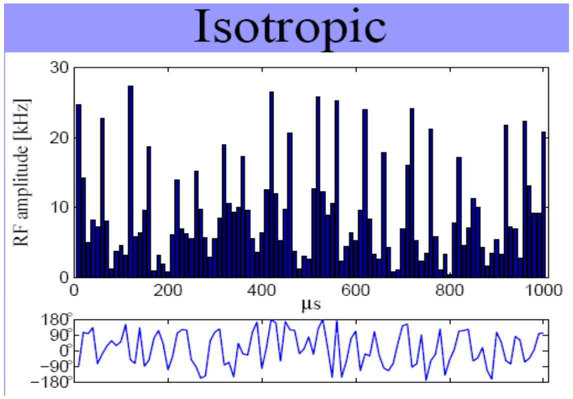
$2I_xS_x-2I_yS_y$

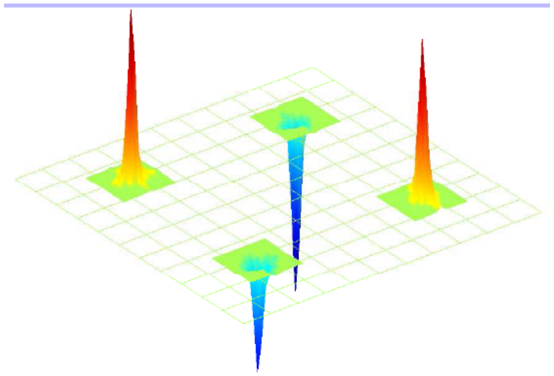


$2I_xS_x+2I_yS_y+2I_zS_z$









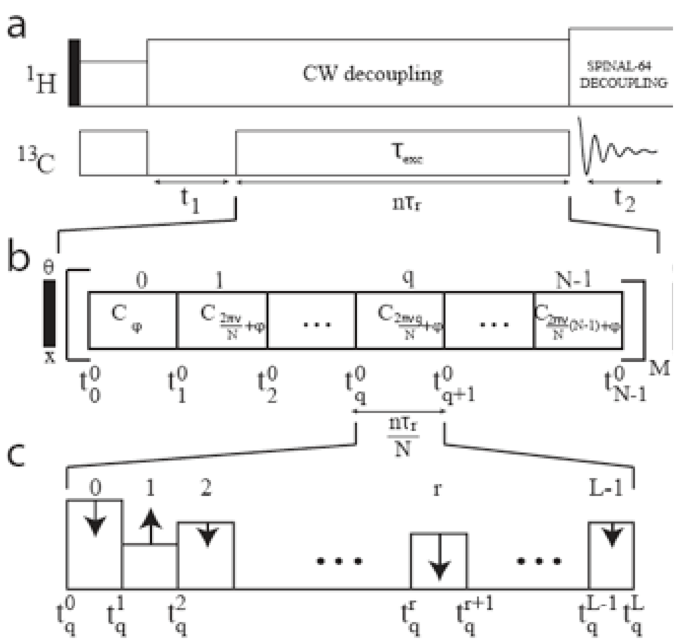
Transfer of both components after t_1 evolution =>√2 sensitivity enhancement

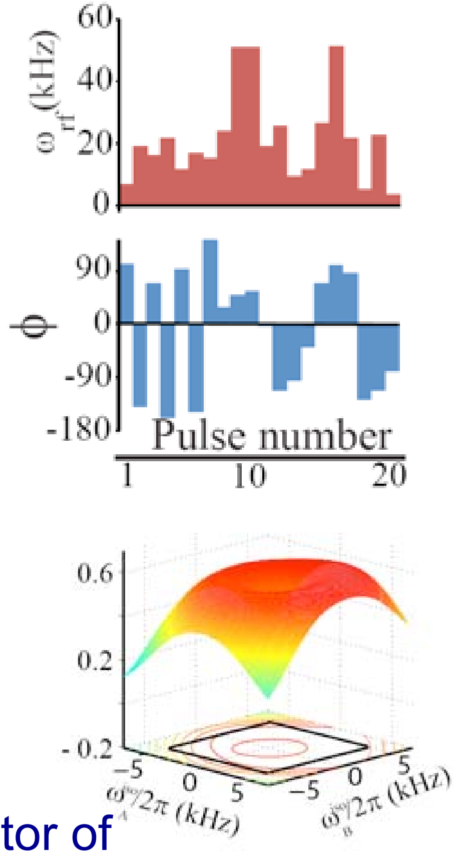
Tosner, Glaser, Khaneja, Nielsen, *J. Chem. Phys.* 125, 184502 (2006)

Niels Chr. Nielsen

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

Optimal control and DNP

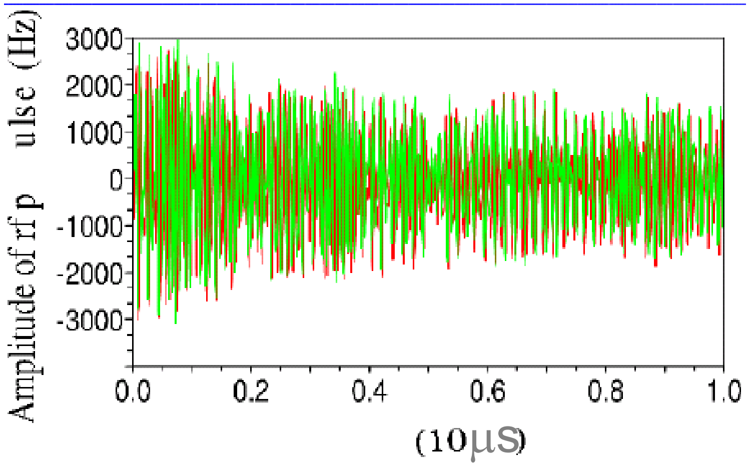
S(Electron)-I(Nucleus) two-spin system

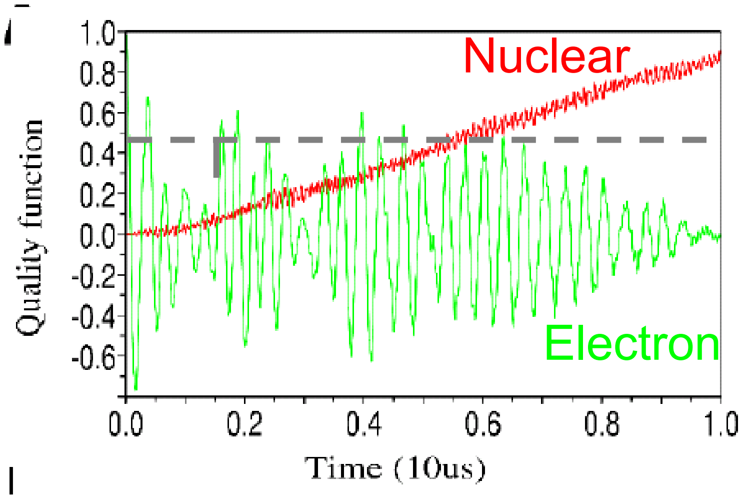
$$H_0 = \Omega_n I_z + A S_z I_z + B S_z I_x$$

$$\Omega_n/2\pi = -14 \text{ MHz}$$ ^{1}H Zeeman

$$A/2\pi = 6 \text{ MHz}$$

$$B/2\pi = 3 \text{ MHz}$$

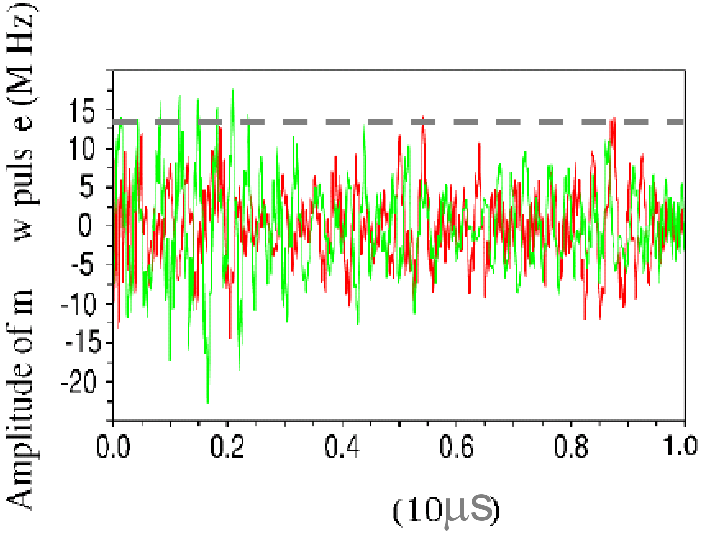




$S_x \rightarrow I_z$

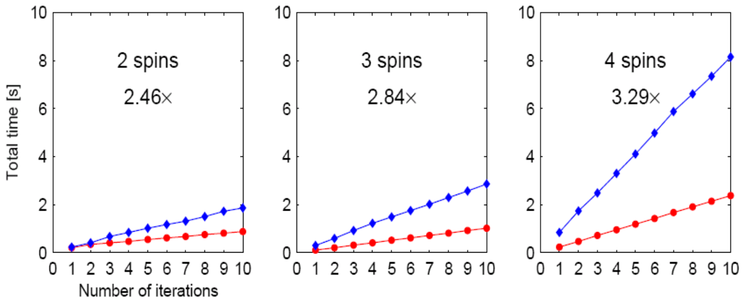
A: secular part of hyperfine interaction

B: Pseudo secular part of hyperfine interaction



Computational time

Krotov: Red
GRAPE: Blue

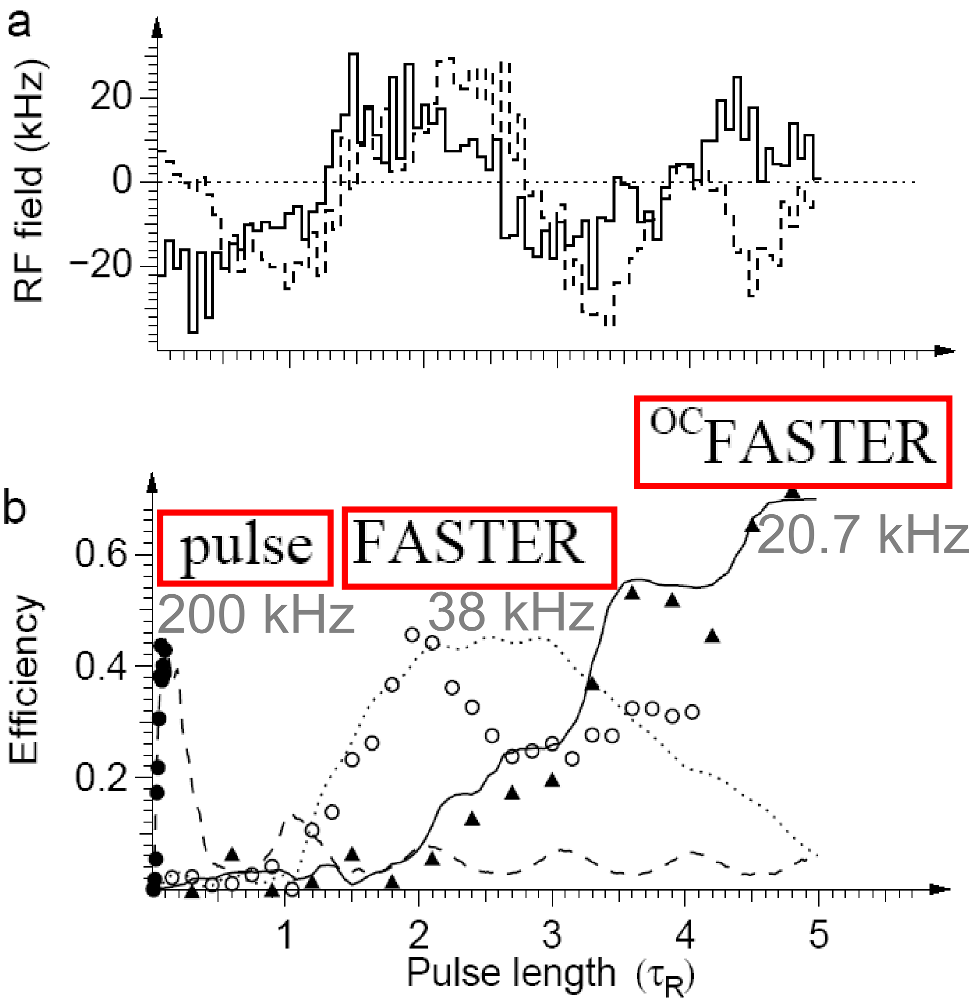


MW @ 9 GHz (X-band) –
ca. 0.3 T (14 MHz) NMR

Jeschke, Schweiger, Mol Phys 1996

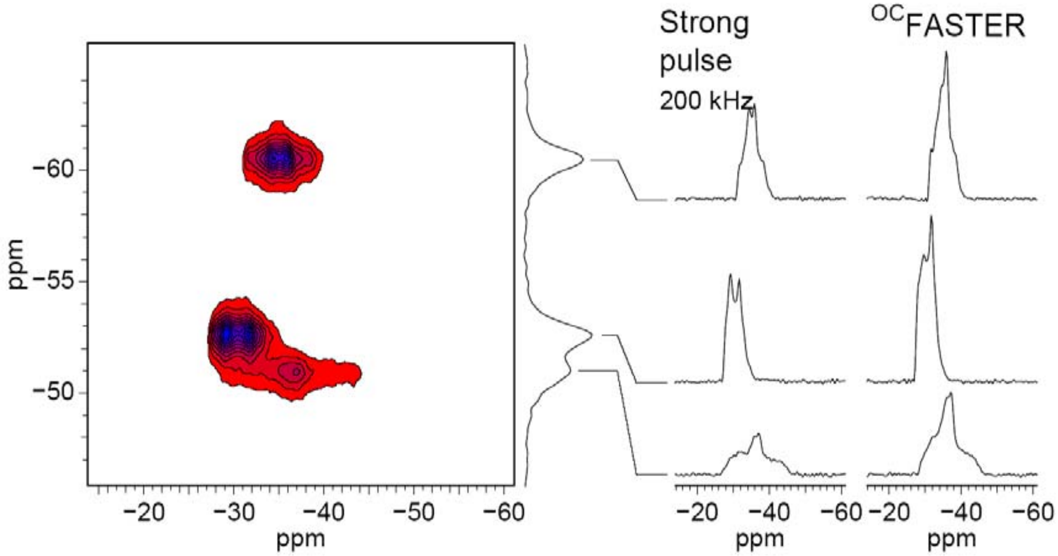
Maximov, Tosner, Nielsen, JCP (2008)

OC is not limited to spin-1/2 cases:
2D MQ-MAS excitation for quadrupolar nuclei



$\nu_R = 30$ kHz $\quad C_Q = 3.3$ MHz

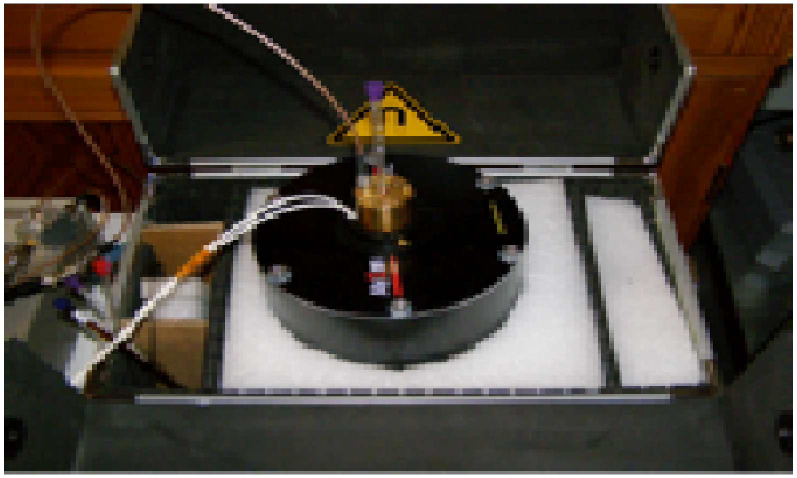
$RbNO_3$ at 9.4 T

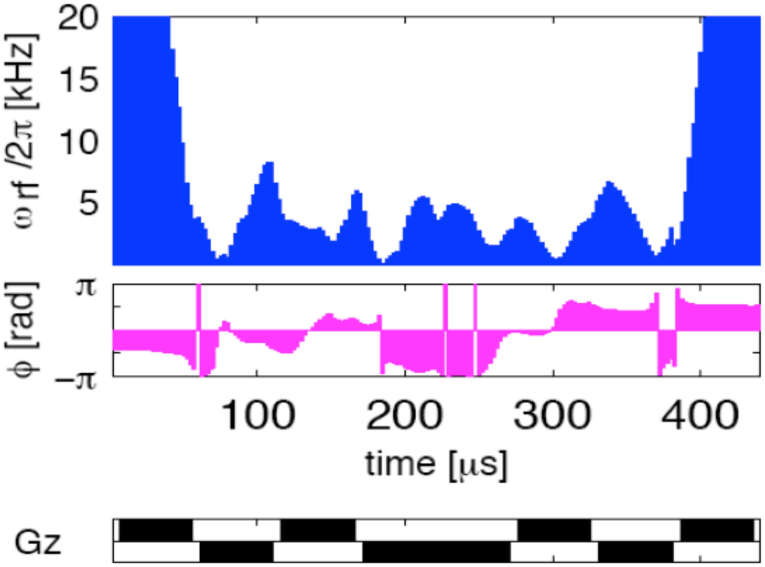


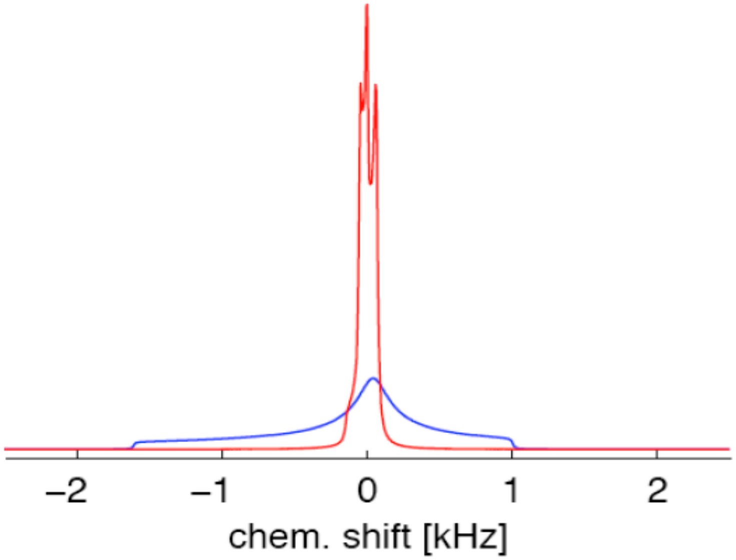
50% gain

Vosegaard, Kehlet, Khaneja, Glaser, and Nielsen, *J. Am. Chem. Soc*, 127, 13768-13769 (2005)

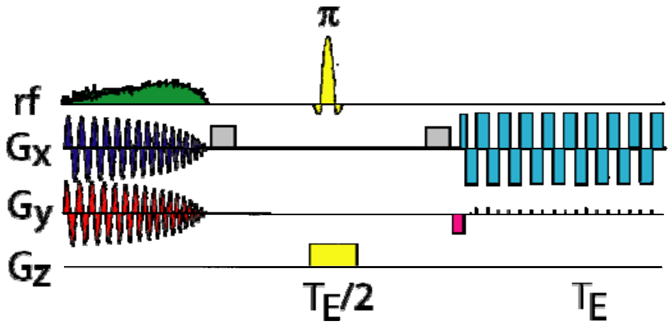
Low-field NMR using Optimal Control for Resolution Enhancement







Optimal control in MRI:Excitation of a HALF BRAIN

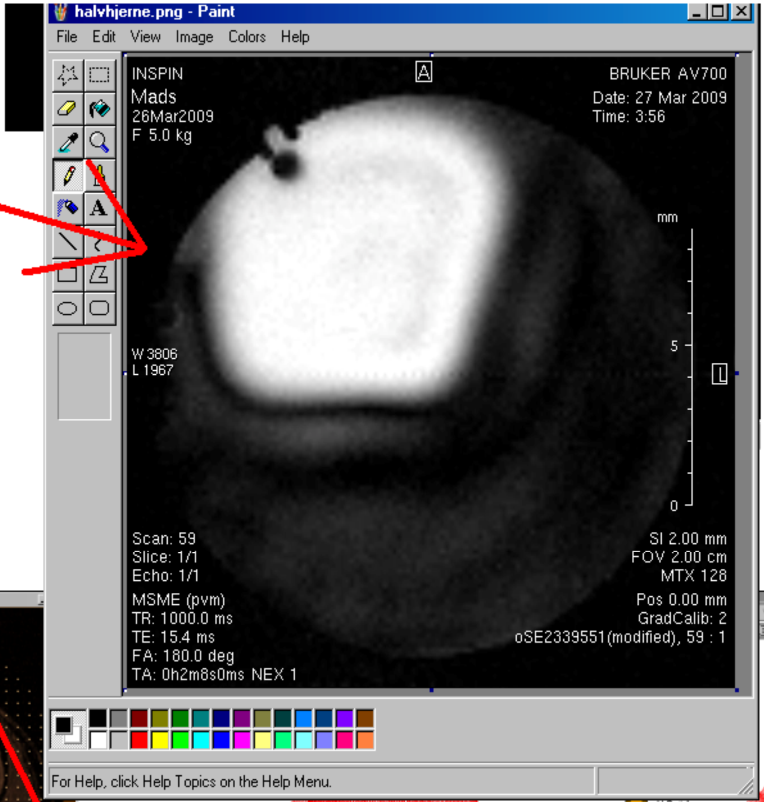


Setup

Experiment at 16.4T

Initial optimization

Refined optimization



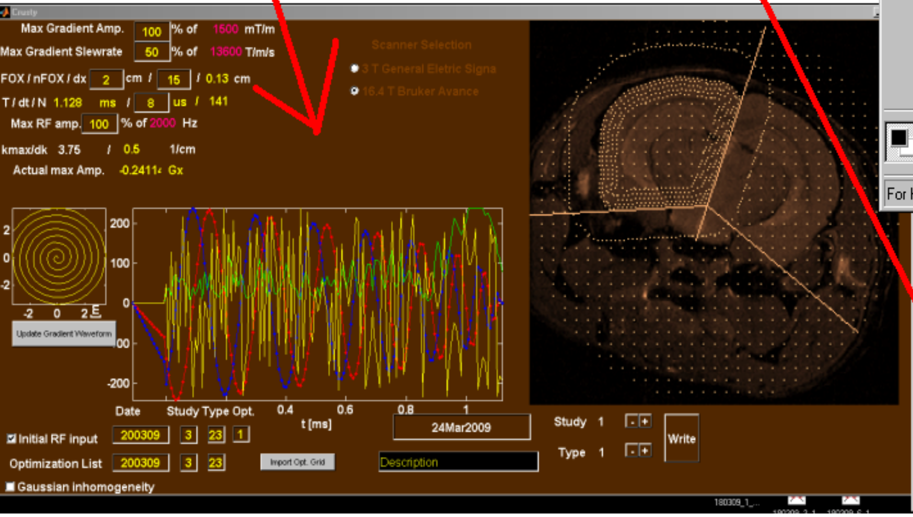
INSPIN
Mads
26Mar2009
F 5.0 kg

BRUKER AV700
Date: 27 Mar 2009
Time: 3:56

W 3806
L 1967

Scan: 59
Slice: 1/1
Echo: 1/1
MSME (pvm)
TR: 1000.0 ms
TE: 15.4 ms
FA: 180.0 deg
TA: 0h2m8s0ms NEX 1

SI 2.00 mm
FOV 2.00 cm
MTX 128
Pos 0.00 mm
GradCalib: 2
oSE2339551(modified), 59 : 1

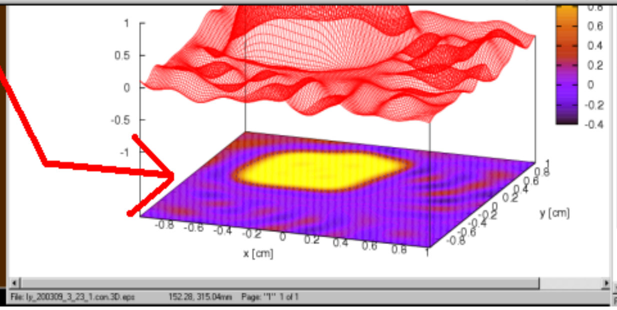


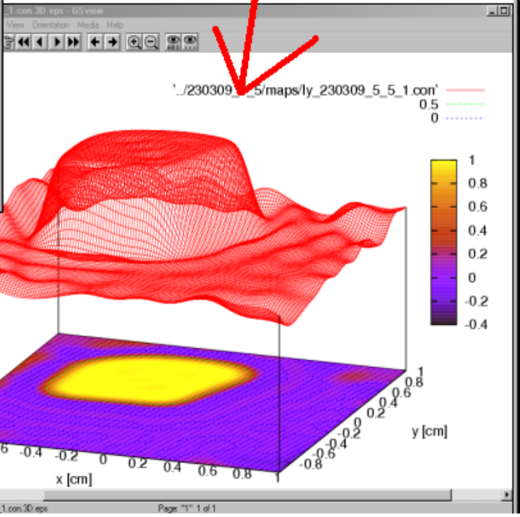
Max Gradient Amp. 100 % of 1600 mT/m
Max Gradient Slewrate 50 % of 13600 T/m/s
FOX / nFOX / dx 2 cm / 15 / 0.13 cm
T / dt / N 1.128 ms / 8 us / 141
Max RF amp. 100 % of 2000 Hz
kmax/dk 3.75 / 0.5 1/cm
Actual max Amp. -0.2411 Gx

○ 3 T General Eletric Signa
● 16.4 T Bruker Avance

Date Study Type Opt.
☑ Initial RF input 200309 3 23 1
Optimization List 200309 3 23
☐ Gaussian inhomogeneity

24Mar2009
Description
Study 1
Type 1





NavinKhaneja, Harvard
Steffen Glaser, München
ZdenekTosner, Praque

Thanks to ....

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