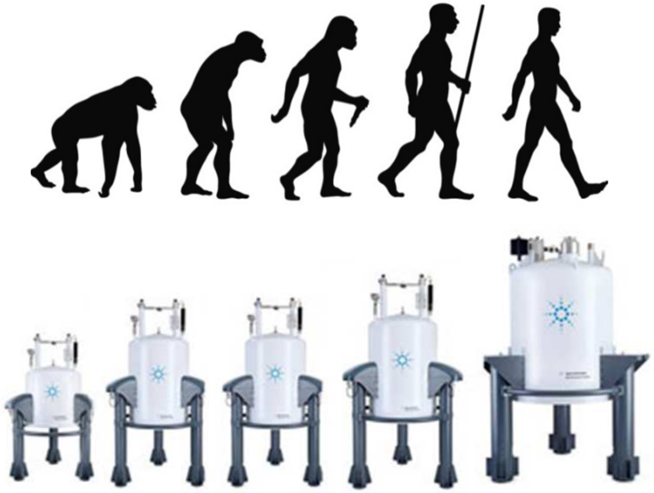
Ecole Thématique :

« Magnétisme et Résonances Magnétiques :
Outils et Applications »

31 mai —> 04 Juin 2015



Principes de base en

Résonance Magnétique Nucléaire (RMN)

Christian Bonhomme

christian.bonhomme@upmc.fr

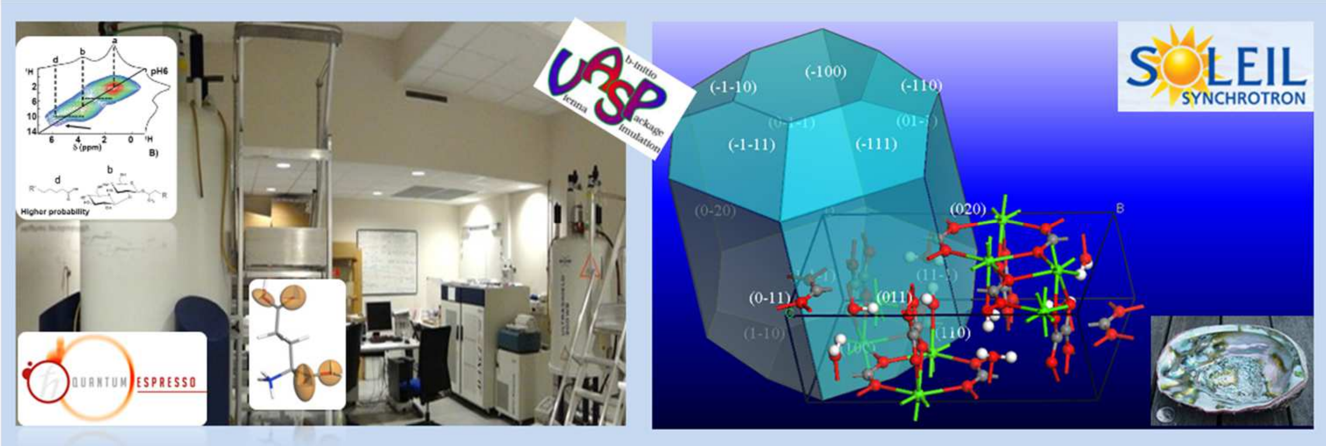
Université P. et M. Curie, Paris 6, Paris, France

SMiLES group

SMiLES

Spectroscopy, **M**odelling, **i**nterfaces for natura**L** **E**nvironment and health topic**S**.

Spectroscopic and numerical approaches for synthetic and natural materials.



Nuclear Magnetic Resonance

The Nobel Prize in Physics 1944
Isidor Isaac Rabi

The Nobel Prize in Physics 1944
Isidor Isaac Rabi

Isidor Isaac Rabi

The Nobel Prize in Physics 1944 was awarded to Isidor Isaac Rabi *"for his resonance method for recording the magnetic properties of atomic nuclei"*.

→ atomic beams

The Nobel Prize in Physics 1952
Felix Bloch, E. M. Purcell

The Nobel Prize in Physics 1952
Felix Bloch
E. M. Purcell

Felix Bloch

Edward Mills Purcell

The Nobel Prize in Physics 1952 was awarded jointly to Felix Bloch and Edward Mills Purcell *"for their development of new methods for nuclear magnetic precision measurements and discoveries in connection therewith"*

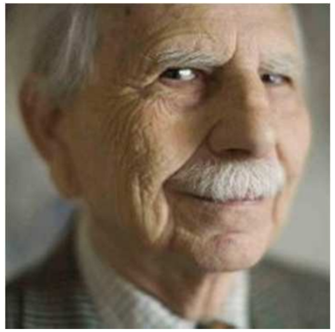
→ condensed matter

(high P gas, solutions, solids)

« … In this method, developed independently by two research groups headed respectively by F. Bloch and E. M. Purcell, the detection of the passage through the resonance is based on a modification *occuring at resonance* in the electromagnetic device itself that « drives » the resonant transition of interest… »

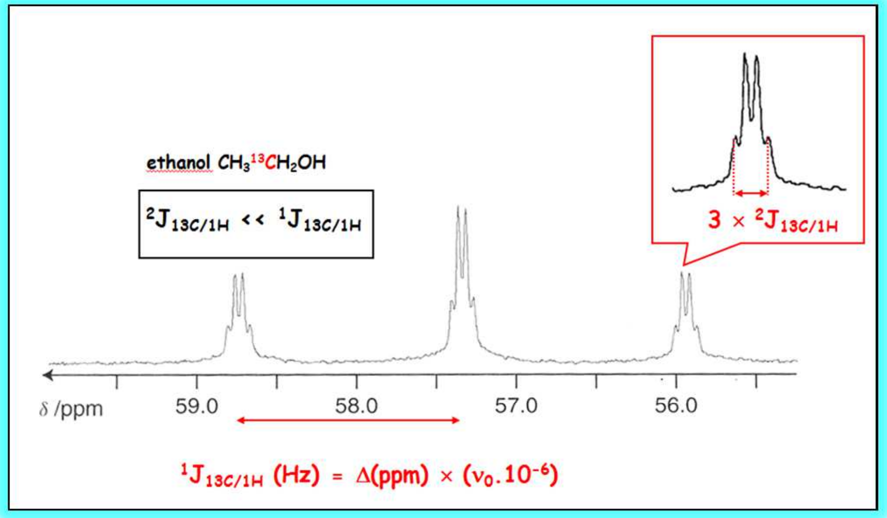
in: *Principles of Nuclear Magnetism*,

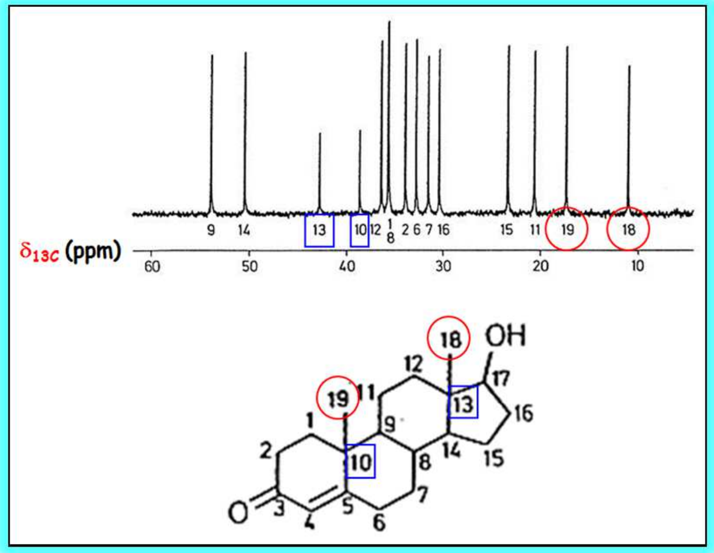
A. Abragam, 1961 (CEA, Collège de France)

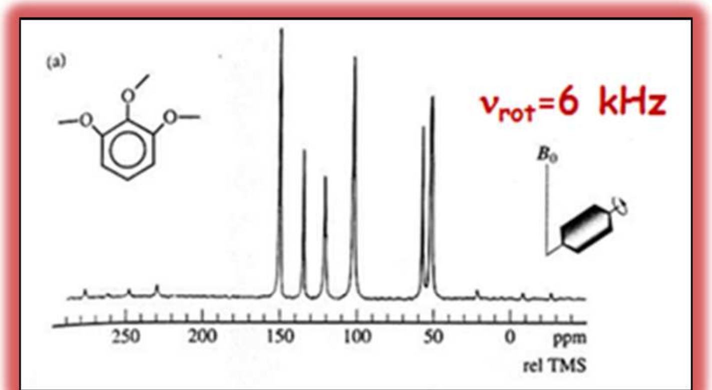


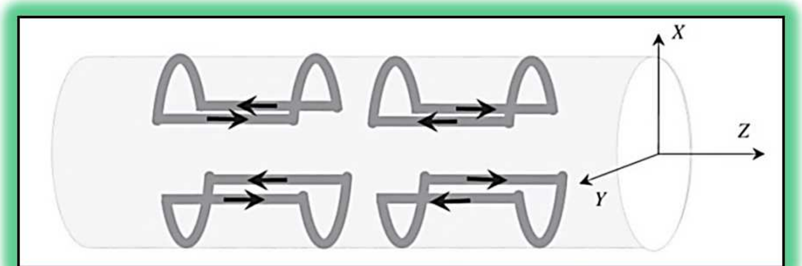
A. Abragam

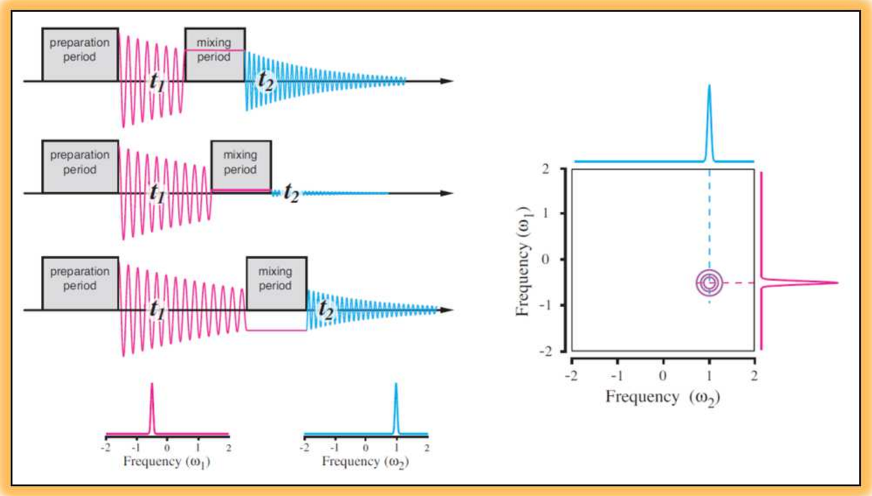
Nuclear Magnetic Resonance



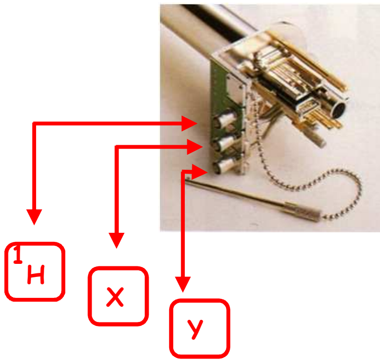


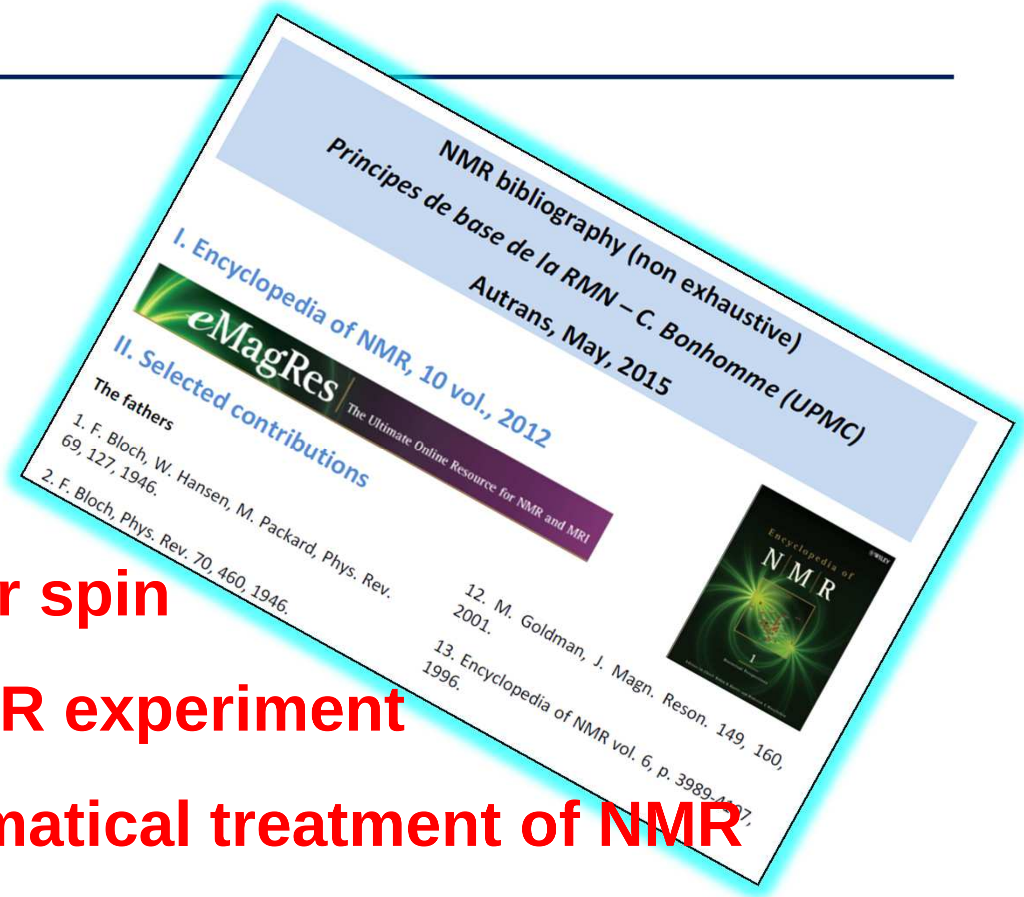






Outline




NMR bibliography (non exhaustive)
Principes de base de la RMN – C. Bonhomme (UPMC)
Autrans, May, 2015

I. Encyclopedia of NMR, 10 vol., 2012

eMagRes The Ultimate Online Resource for NMR and MRI

II. Selected contributions

The fathers

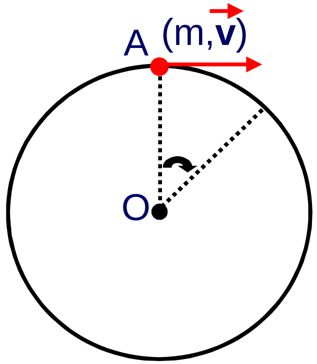
1. F. Bloch, W. Hansen, M. Packard, Phys. Rev. 69, 127, 1946.
2. F. Bloch, Phys. Rev. 70, 460, 1946.

12. M. Goldman, J. Magn. Reson. 149, 160, 2001.
13. Encyclopedia of NMR vol. 6, p. 3989-[illegible], 1996.

- **Nuclear spin**
- **the NMR experiment**
- **Mathematical treatment of NMR**
- **Multidimensional NMR**
- **Relaxation**
- **Solid State NMR**
- **Gradients and imaging**

Angular momentum

circular orbit



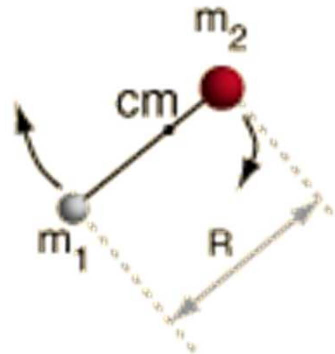
$\vec{L} = \vec{OA} \wedge m\vec{v}$

quantum mechanics: quantification

$L = [J(J+1)]^{1/2}\,\hbar$

$J = 0, 1, 2...$

$E_J = B\,J(J+1)$



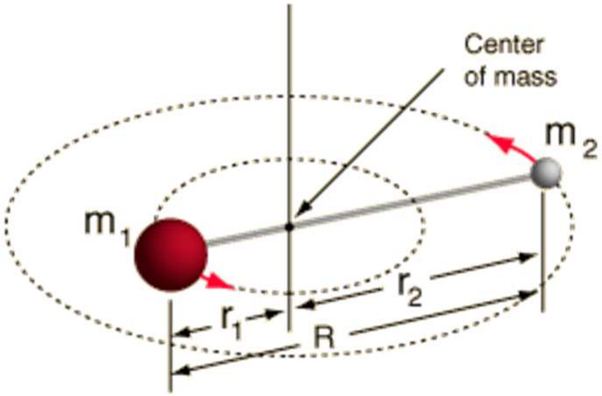
rotational constant

Planck's constant :

$h = 6.62608.\ 10^{-34}$ J.S

"in regognition of the services he rendered to the advancement of physics by his discovery of energy quanta",

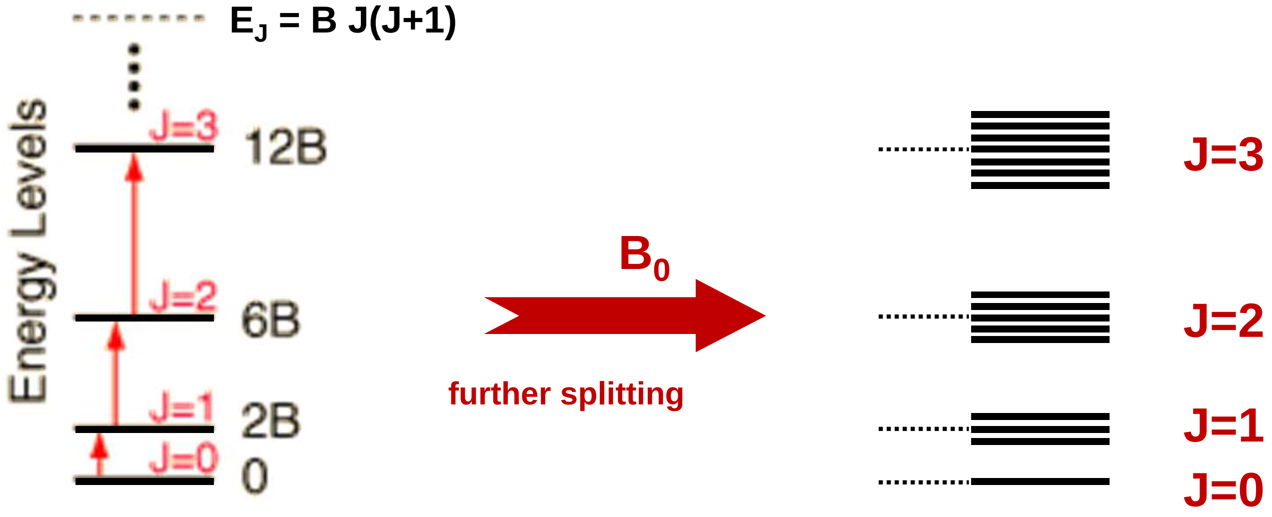
Physics, 1918



$M_J = -J, -J+1, ..., +J$

quantum number (azimuth)

Magnetic field – Zeeman effect



$B_0 = 0$

(2J+1) degenerated levels

$B_0 \neq 0$

"in recognition of the extraordinary services they rendered by the researches into the influence of magnetism upon radiation phenomena",

Physics, 1902 (with Lorentz)

Spin

angular momentum ⇒ intrinsic property

(p, n, e^-, photon, muon ....)

⇓

- $[I(I+1)]^{1/2}\hbar$
- deg.

(2I+1) levels

non deg.

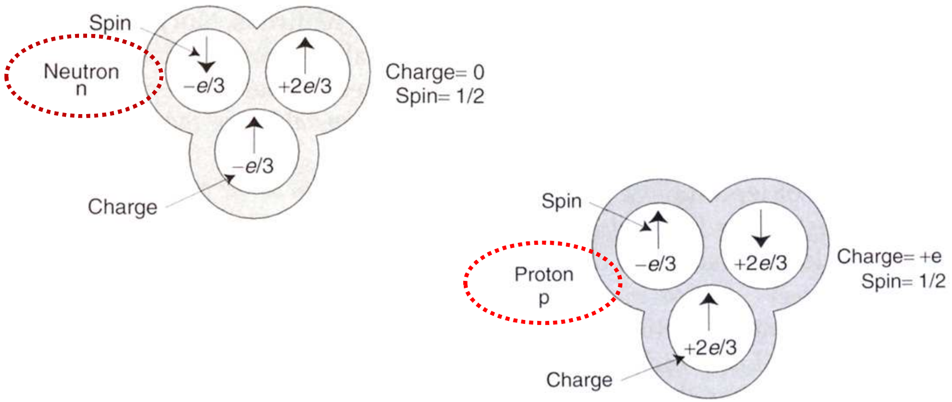
ex :

ORBITAL angular momentum ⟺ e^- ⟺ SPIN angular momentum

composition of J_1 and J_2

$$J_3 \in \begin{cases} |J_1 - J_2| \\ \vdots \\ |J_1 + J_2| \end{cases}$$

Atomic structure



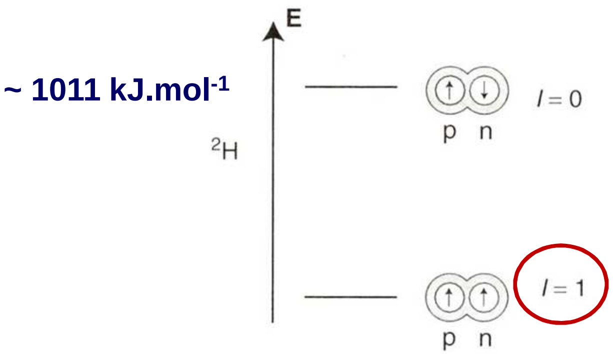
nucleons ⟷ n and p

atomic nucleus

- **atomic number: Z**
  (p)
- **mass number: A**
  (n+p)
  isotopes
- **spin number I**

<u>nuclear spin</u>:

"combination of p spin and n spin"



ex :

^{12}C = 6p + 6n (98.9%)

^{13}C = 6p + 7n (1.1%)

(^{14}C = 6p + 8n)

nuclear spin *of the ground state*

here : I = 1

Spin

angular momentum ⇒ intrinsic property

(p, n, e^-, photon, muon ....)

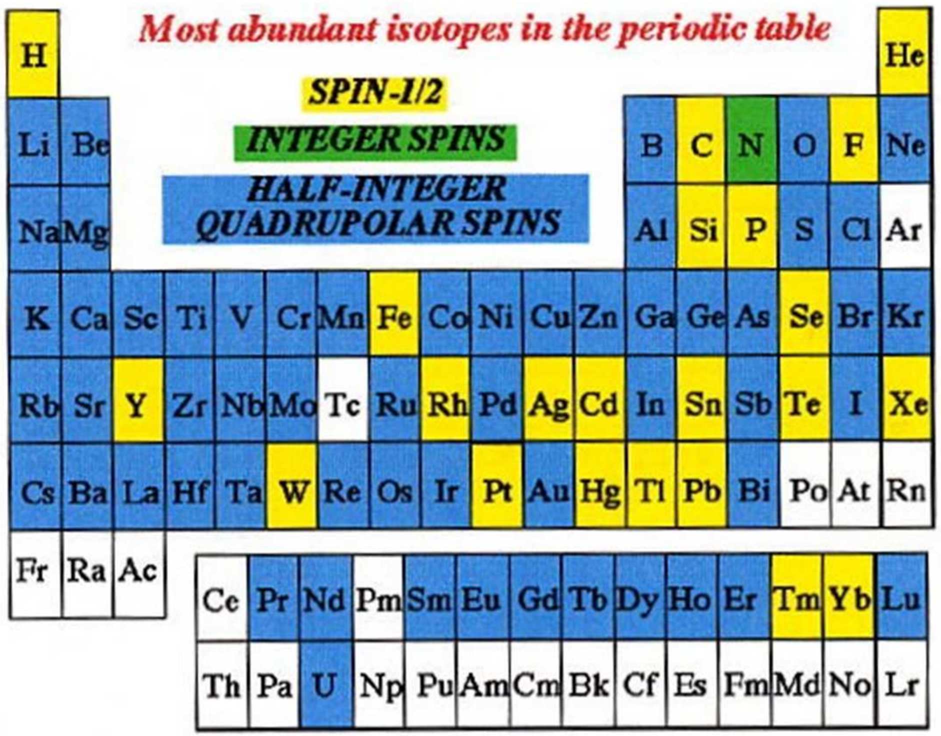
- $[I(I+1)]^{1/2}\hbar$ and $m_I = -I, -I+1, \ldots, +I$
- $\hbar$ is the quantum of angular momentum (sometimes $\hbar = 1$)
- deg.

(2I+1) levels

non deg.

Spin number I

$I \neq 0 \longrightarrow$ NMR …



odd A $\rightarrow$ half integer I

even A, even charge $\rightarrow$ I = 0

even A, odd charge $\rightarrow$ integer I

isotope ^{13}C

spin I (m_I)

natural abundance (%)

gyromagnetic ratio (rad s^{-1} T^{-1})

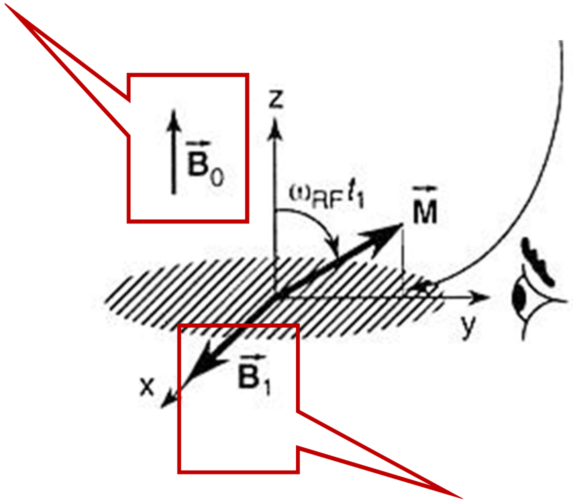
receptivity:

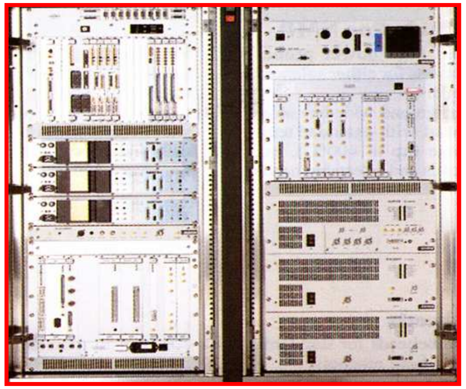
$$D_P = \frac{|\gamma_X|^3 \ (\%X) \ (I_X+1) \ I_X}{\gamma_{1H}^3 \ (\%^1H) \ (I_{1H}+1) \ I_{1H}}$$

^{13}C: I = ½ (1.1%)

$D_P(^{13}C)$ =0.00017… !

The NMR experiment





Static B_0 field – Larmor frequency

energy levels

$m_I = -1/2$

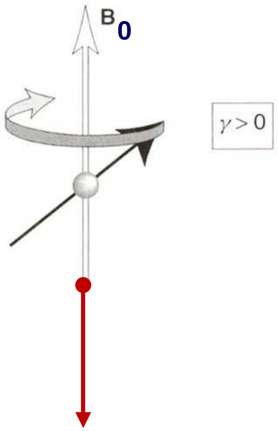
$\Delta E = |\gamma| h B_0 / 2\pi$

$m_I = +1/2$

$\nu_0 = |\gamma| B_0 / 2\pi$

LARMOR FREQUENCY

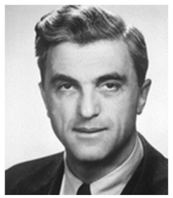
« mechanical » action of B_0



$$\vec{\omega}_0 = -\gamma \vec{B}_0$$

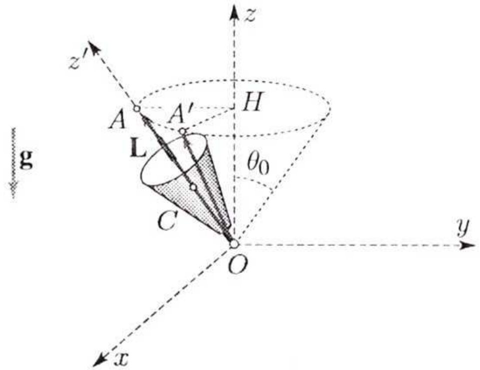
angular momentum theorem:

$$\frac{d\vec{\mu}}{dt} = \gamma\, \vec{\mu} \wedge \vec{B}_0$$



PRECESSION

mechanical analogy

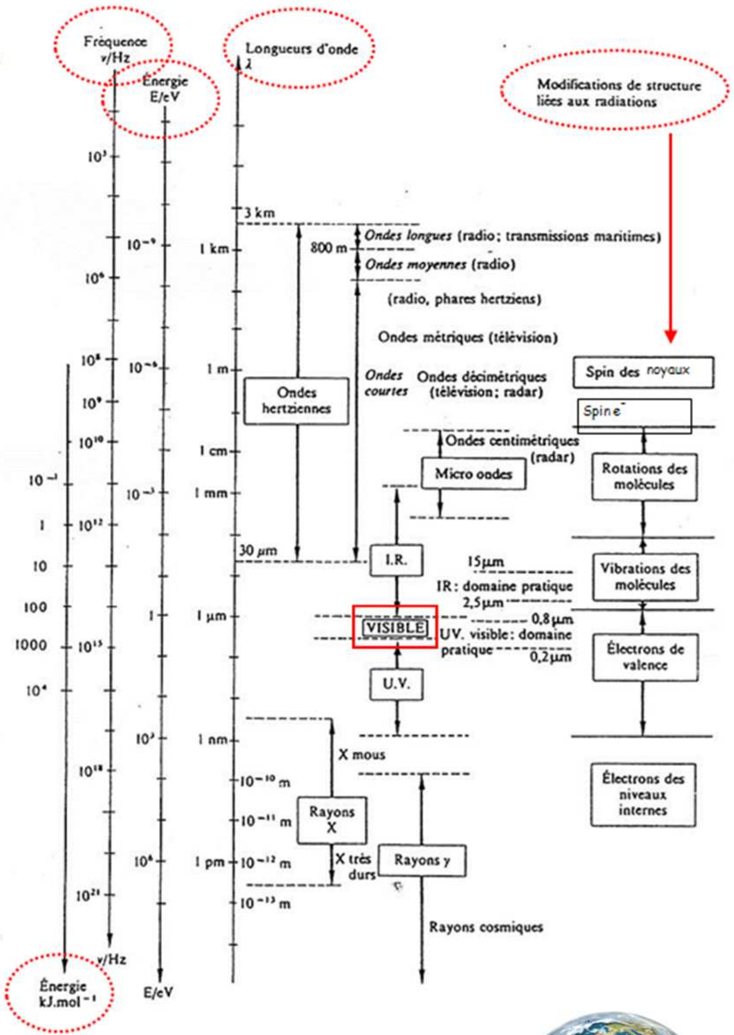


$$\frac{d\vec{L}}{dt} = \overrightarrow{OC} \wedge m\vec{g}$$

F. Bloch et coll., *Phys. Rev.*, 69, 127 (1946)

Order of magnitudes

B_0 (T)	ν_0 (^{1}H) (MHz)
7	300
14	600
21	900
23.3	1000



to « work on a: »

^{1}H : 400 MHz

^{13}C : 100 MHz

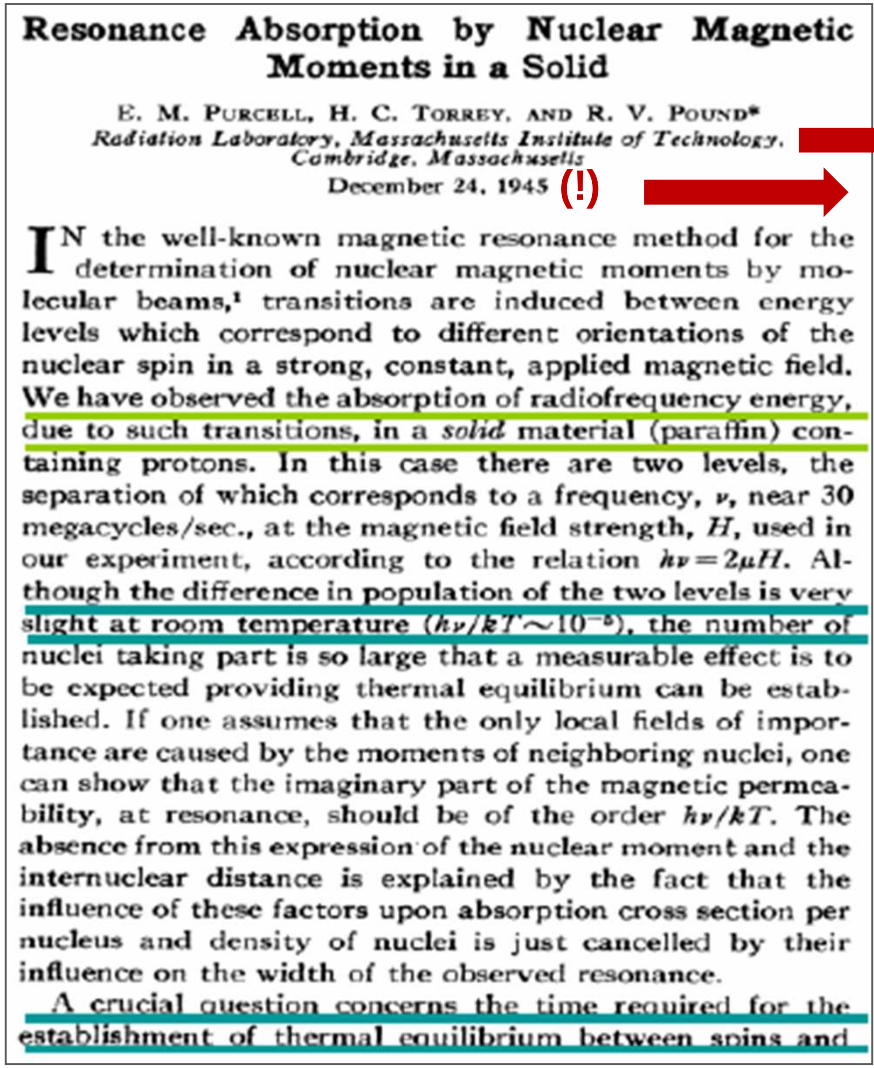
^{15}N : 40 MHz

.....

Earth magnetic field

~ 50 mT

Purcell's vision



Resonance Absorption by Nuclear Magnetic Moments in a Solid

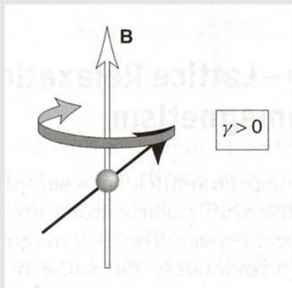
E. M. Purcell, H. C. Torrey, and R. V. Pound*
Radiation Laboratory, Massachusetts Institute of Technology, Cambridge, Massachusetts
December 24, 1945

In the well-known magnetic resonance method for the determination of nuclear magnetic moments by molecular beams,[1] transitions are induced between energy levels which correspond to different orientations of the nuclear spin in a strong, constant, applied magnetic field. We have observed the absorption of radiofrequency energy, due to such transitions, in a *solid* material (paraffin) containing protons. In this case there are two levels, the separation of which corresponds to a frequency, ν, near 30 megacycles/sec., at the magnetic field strength, H, used in our experiment, according to the relation $h\nu = 2\mu H$. Although the difference in population of the two levels is very slight at room temperature ($h\nu/kT \sim 10^{-5}$), the number of nuclei taking part is so large that a measurable effect is to be expected providing thermal equilibrium can be established. If one assumes that the only local fields of importance are caused by the moments of neighboring nuclei, one can show that the imaginary part of the magnetic permeability, at resonance, should be of the order $h\nu/kT$. The absence from this expression of the nuclear moment and the internuclear distance is explained by the fact that the influence of these factors upon absorption cross section per nucleus and density of nuclei is just cancelled by their influence on the width of the observed resonance.

A crucial question concerns the time required for the establishment of thermal equilibrium between spins and

(!)

« … There the snow lay around my doorstep – ***great heaps of protons quietly precessing in the Earth's magnetic field*.** To see the world for a moment as something rich and strange is the private reward of many discovery … »



in: *Spin Dynamics*, M. H. Levitt., 2002

NMR *vs* EPR

proton case

$\gamma\hbar = g_N \beta_N$

$g_N = 5.5855$

$\beta_N = e\hbar/(2m_p)$

$= 5.051\ 10^{-27}\ J.T^{-1}$

electron case

$g_e = 2.0023$

$\beta_e = e\hbar/(2m_e)$

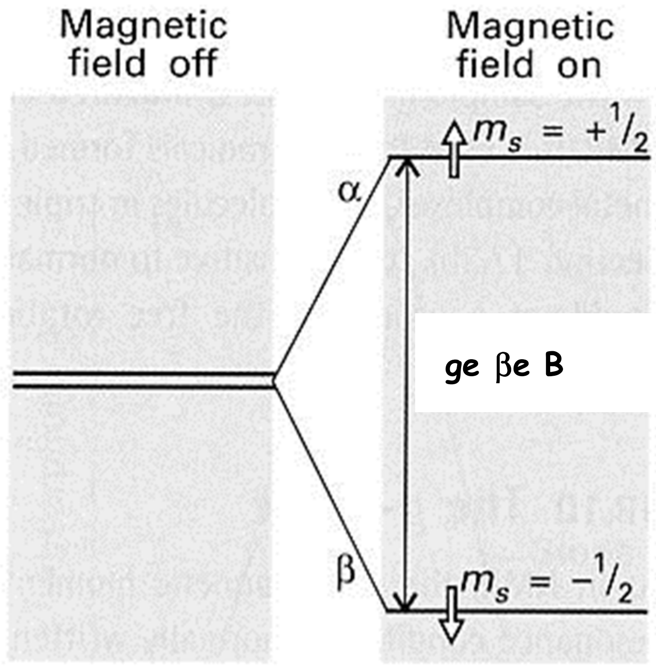
$= 9.274\ 10^{-24}\ J.T^{-1}$

Order of magnitude

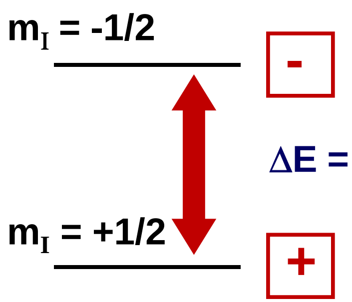
microwaves

B ≈ 0.3 T

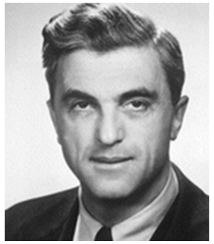
ν = 9 GHz = 9.109 Hz ; λ ≈ 3 cm



Macroscopic magnetization – T_1 relaxation



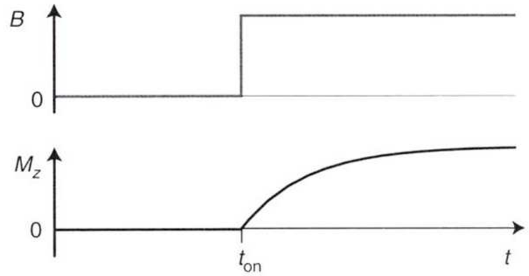
$\Delta E = |\gamma| h B_0 / 2\pi$



F. Bloch

$$\frac{P_-}{P_+} = \exp\left(-\frac{\Delta E}{kT}\right)$$

relaxation



$$M_z = M_{éq.} \left(1 - \exp\{-(t - t_{on})/T_1\} \right)$$

T_1 ~ s, min, h...

high T approximation

$$\frac{P_-}{P_+} \approx 1 - \frac{\gamma \hbar B_0}{kT}$$

^{1}H
B_0 = 9.4T
room T
≈ 6.10^{-5} !

k: Boltzmann constant

$1.3806\ 10^{-23}$ J.K^{-1}

Curie's law

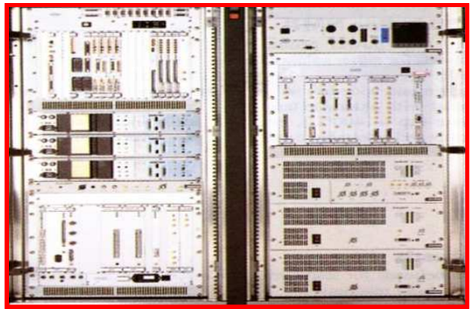
$$M_{éq.} = \frac{N \gamma^2 h^2 B_0 I(I+1)}{12 \pi^2 kT}$$

Méq.

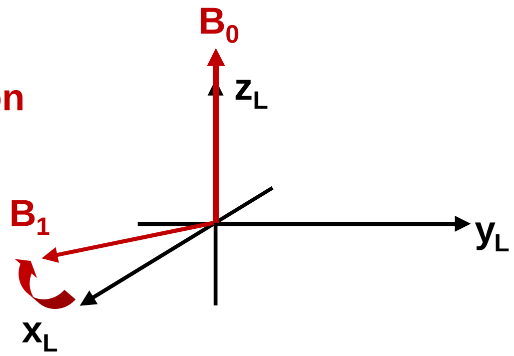
B_0: highest as possible !

B_1 RF field – rotating frame

	high resolution NMR	solid state NMR	clinical imaging
B_1 (Tesla)	$5\ 10^{-4}$	$2\ 10^{-3}$	10^{-5}



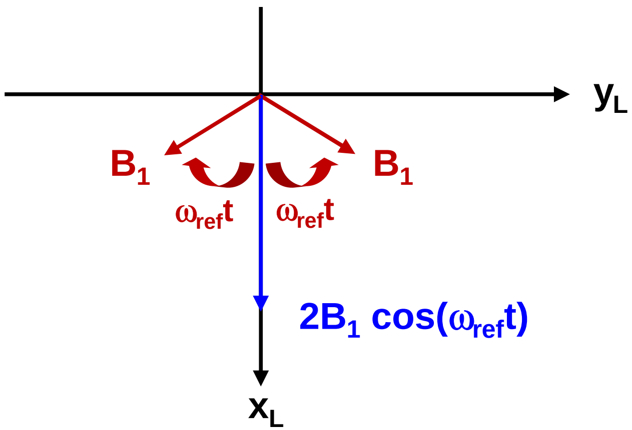
B_0 and B_1 action



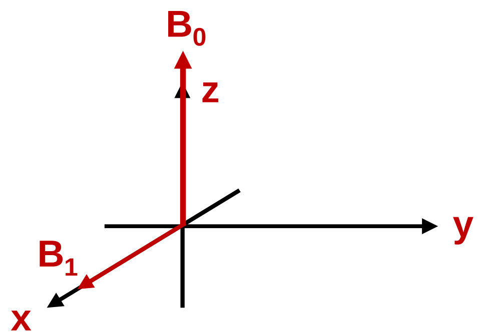
$$\frac{d\vec{\mu}}{dt} = \gamma\,\vec{\mu} \wedge \left[\vec{B}_0 + \vec{B}_1(t)\right]$$

oscillating field (along xL for instance)

amplitude $2B_1$, pulsation ω_{ref}



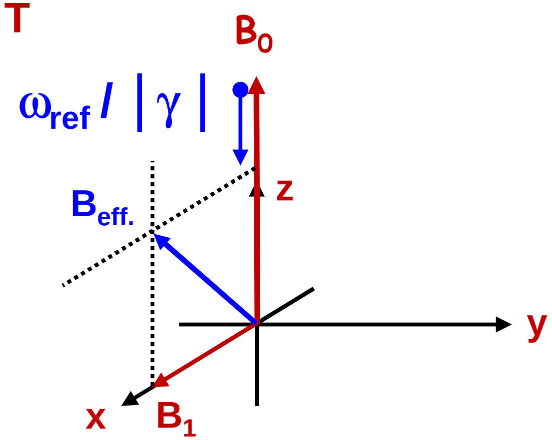
rotating frame T



$$\left(\frac{d\vec{\mu}}{dt}\right)_T = \gamma\,\vec{\mu} \wedge \left[\vec{B}_{eff.}\right]$$

Resonance

rotating frame T

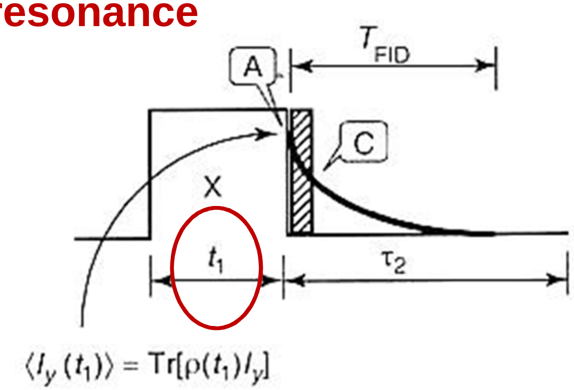


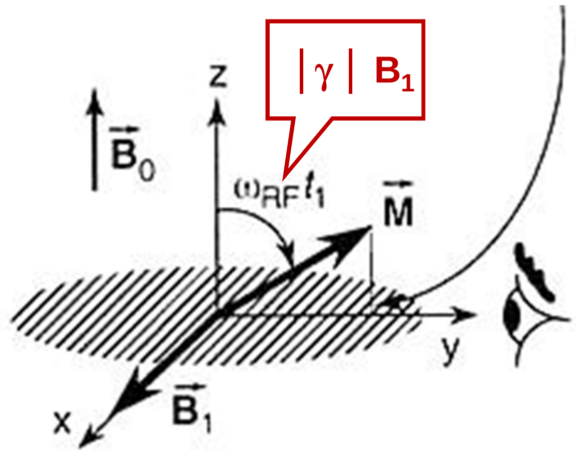
$$\left(\frac{d\vec{\mu}}{dt}\right)_T = \gamma\,\vec{\mu} \wedge \left[\vec{B}_{eff.}\right]$$

$$\vec{B}_{eff.} = (\vec{B}_0 - \frac{\omega_{ref}}{\gamma})\vec{z} + \vec{B}_1\,\vec{x}$$

nutation around B_{eff}

at resonance





$\Omega_0 = \omega_0 - \omega_{ref}$

rad s^{-1}

Summary

$\Delta m_I = \pm 1$

$$\hat{\mu} = \gamma \hbar \hat{I}$$

magnetic moment

gyromagnetic ratio

spin angular momentum

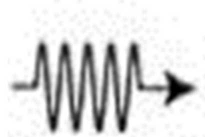
B_0 (~10T)

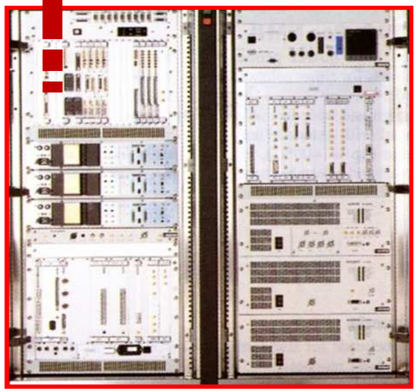
$m_I = -1/2$ [-]

$m_I = +1/2$ [+]

$\Delta E = |\gamma| hB_0 / 2\pi$

$$\frac{P_-}{P_+} = \exp\left(-\frac{\Delta E}{kT}\right)$$



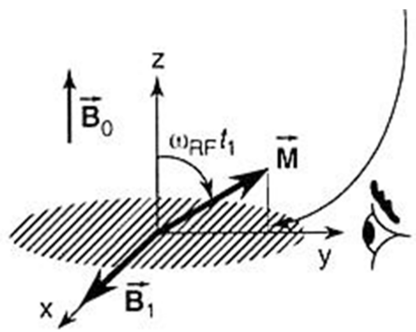


Curie's law

$$M_{\acute{e}q.} = \frac{N \gamma^2 h^2 B_0 I(I+1)}{12 \pi^2 kT}$$

Méq.

My



Man, Encyclopedia of analytical chemistry, 2000, 12228.

R. Ernst and W. Anderson: Fourier Transform NMR

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This Week's Citation Classic

CC/NUMBER 27
JULY 4, 1983

Ernst R R & Anderson W A. Application of Fourier transform spectroscopy to magnetic resonance. *Rev. Sci. Instr.* 37:93-102, 1966.
[Analytical Instrument Division, Varian Associates, Palo Alto, CA]

The Nobel Prize in Chemistry 1991
Richard R. Ernst

The Nobel Prize in Chemistry 1991
Nobel Prize Award Ceremony
Richard R. Ernst

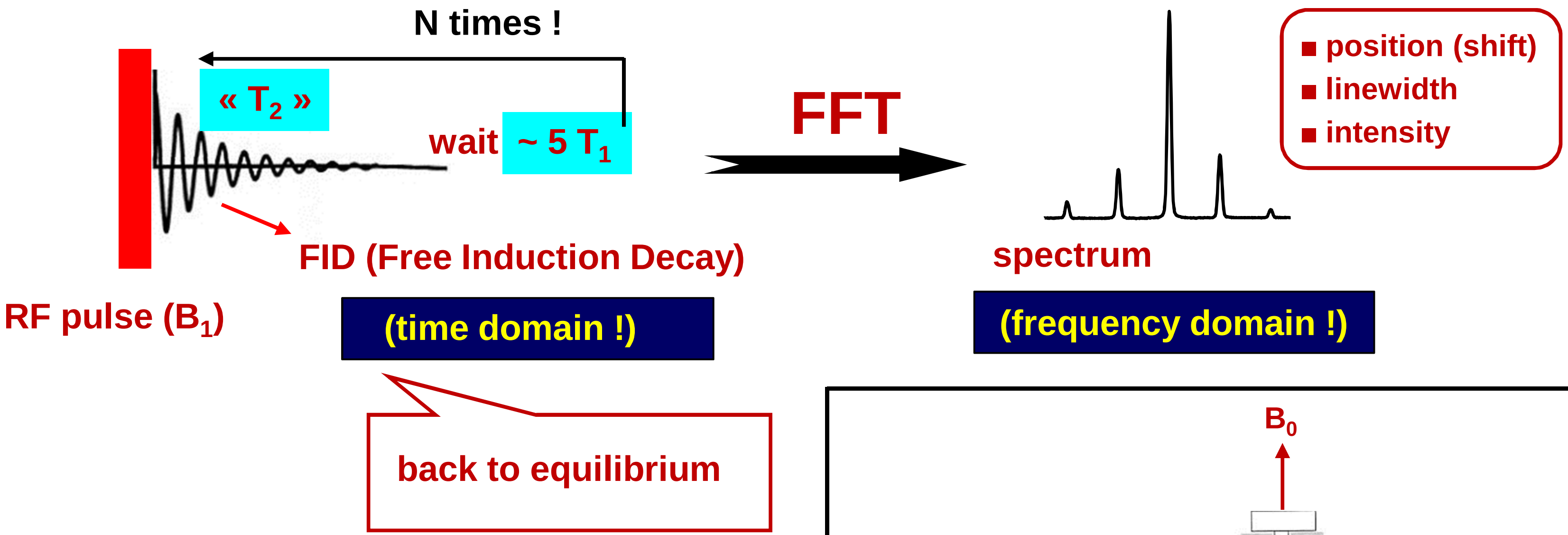
Richard R. Ernst

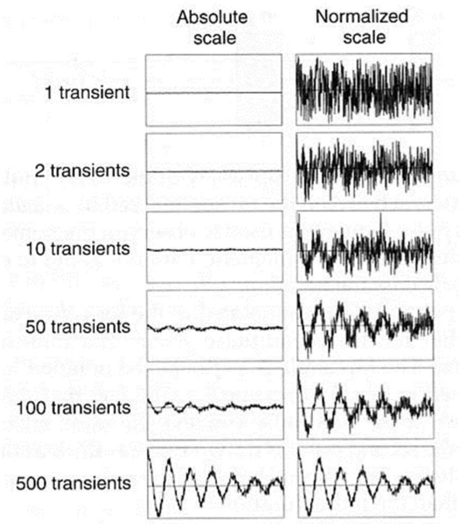
The Nobel Prize in Chemistry 1991 was awarded to Richard R. Ernst *"for his contributions to the development of the methodology of high resolution nuclear magnetic resonance (NMR) spectroscopy"*.

Fourier transform nuclear magnetic resonance (NMR) has become the accepted technique for recording NMR spectra in liquids and in solids. Both its superior sensitivity and its versatility have been essential for the remarkable success of NMR in numerous fields from physics to medicine. [The *SCI*® indicates that this paper has been cited in over 330 publications since 1966.]

"Looking back, it is not too astonishing that our paper got many citations. The message is simple and attractive. To the user it saves time and money and for the instrument companies it allowed them to increase returns by the development of new instruments."

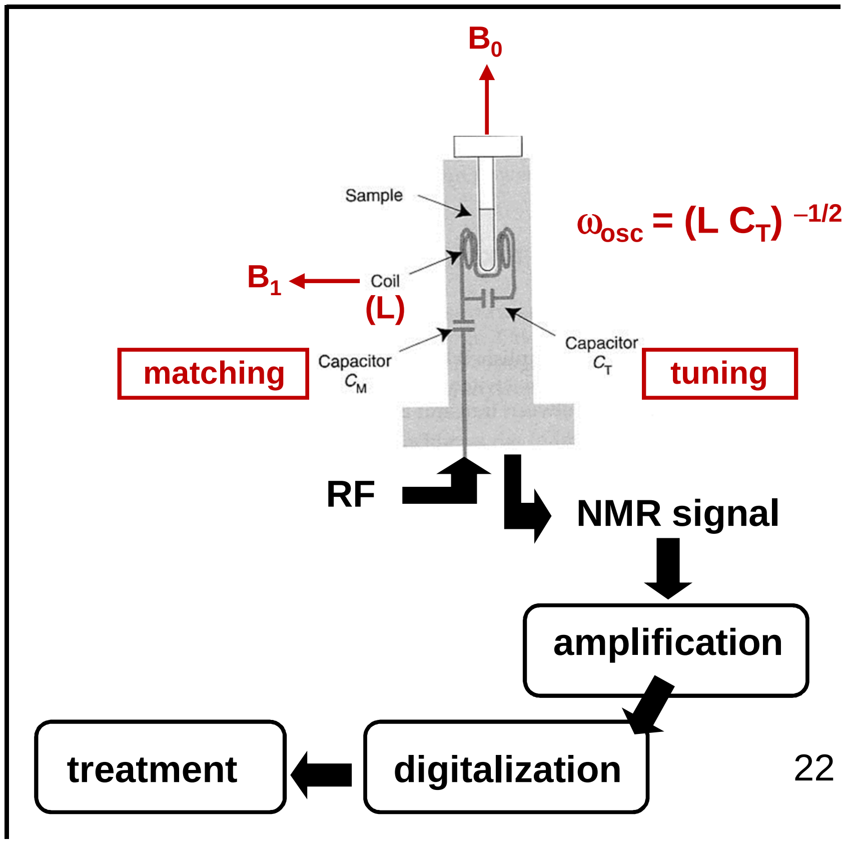
Fourier Transform NMR





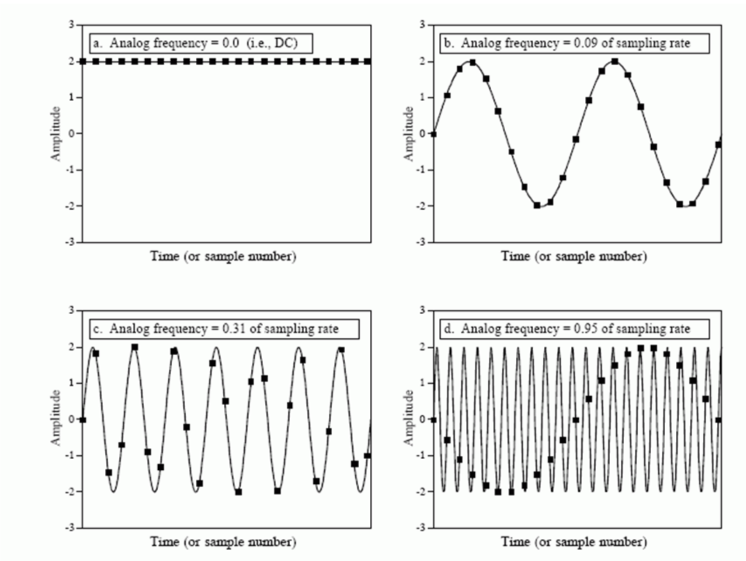
Signal/Noise ~ $\sqrt{N}$

Levitt, Spin dynamics, 2002.

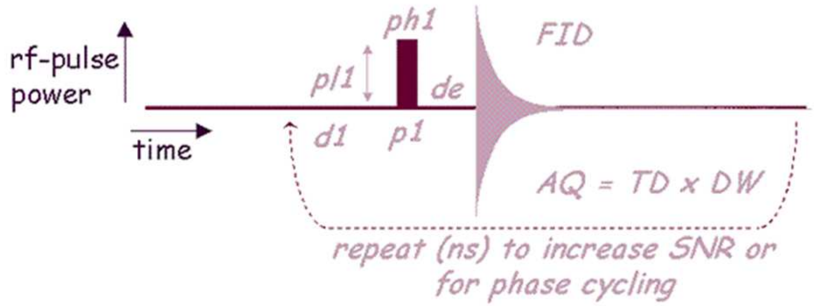


Fourier transformation and data processing

1° digitization



time domain (FID) → frequency (spectrum)



2° discrete FFT (1965, Princeton)

James Cooley　　John Tukey

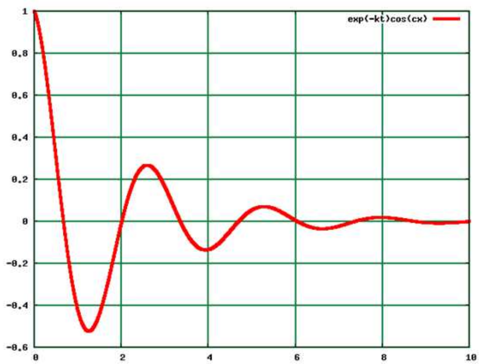
Time Duration		
Finite	Infinite	
Discrete FT (DFT) $X(k) = \sum_{n=0}^{N-1} x(n) e^{-j\omega_k n}$ $k = 0, 1, \ldots, N-1$	Discrete Time FT (DTFT) $X(\omega) = \sum_{n=-\infty}^{+\infty} x(n) e^{-j\omega n}$ $\omega \in [-\pi, +\pi)$	discr. time n
Fourier Series (FS) $X(k) = \frac{1}{P} \int_0^P x(t) e^{-j\omega_k t} dt$ $k = -\infty, \ldots, +\infty$	Fourier Transform (FT) $X(\omega) = \int_{-\infty}^{+\infty} x(t) e^{-j\omega t} dt$ $\omega \in (-\infty, +\infty)$	cont. time t
discrete freq. k	continuous freq. ω	

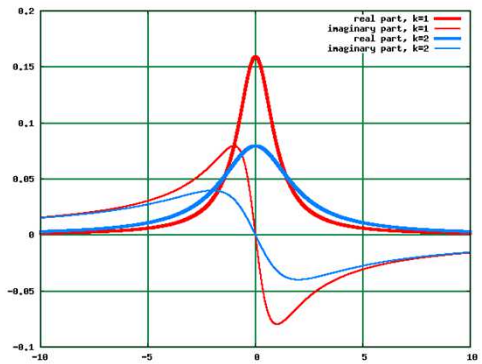
Cooley–Tukey FFT algorithm

Fourier transformation and data processing

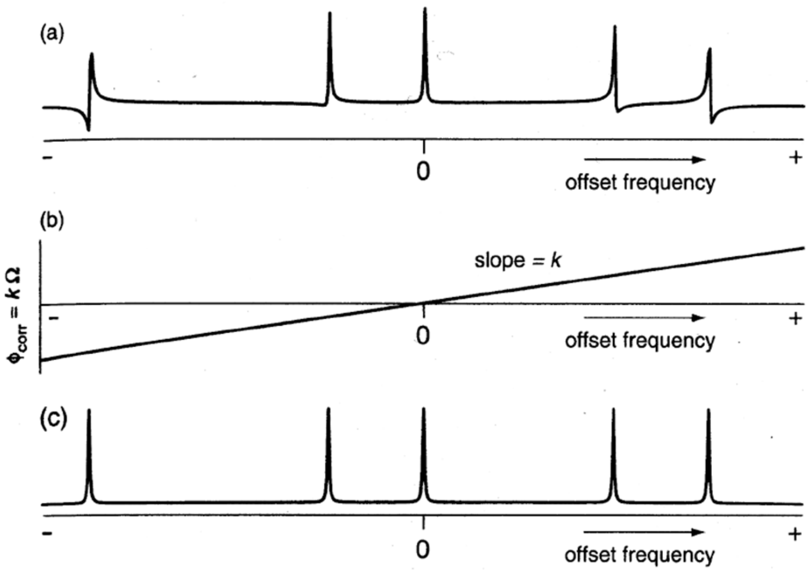
3° lineshape and phase

time domain (FID) → frequency (spectrum)



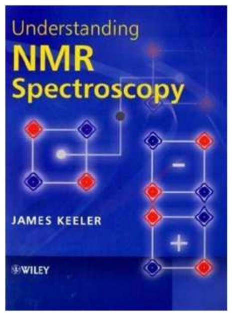


4° phase correction



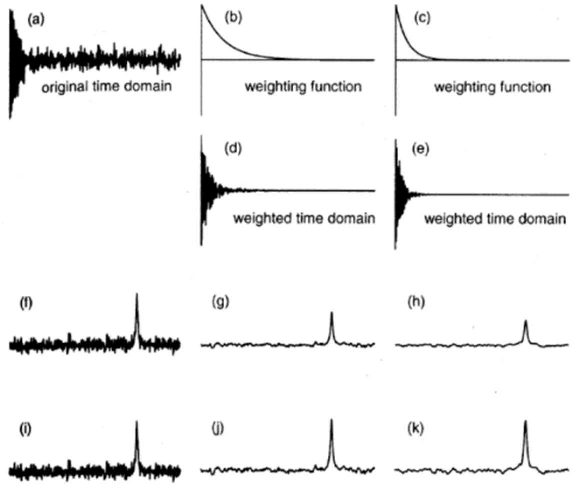
then … manipulate the FID ?

credits to

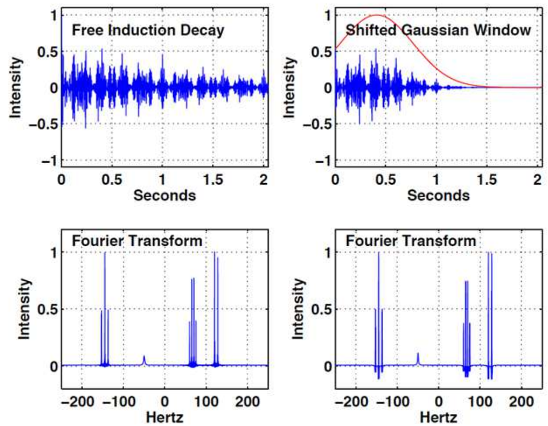


Manipulating the FID

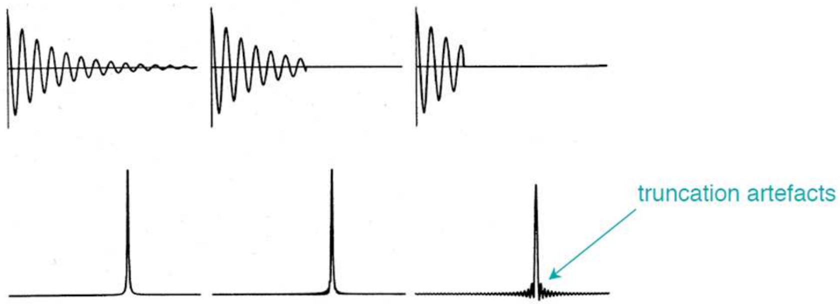
1° weighting funtions



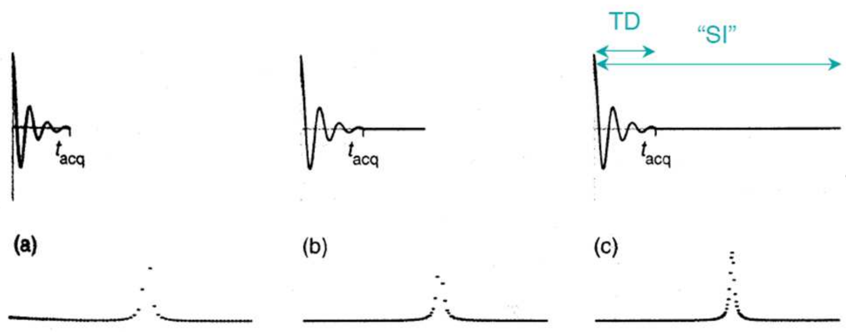
2° other weighting functions



3° truncation



4° zero filling

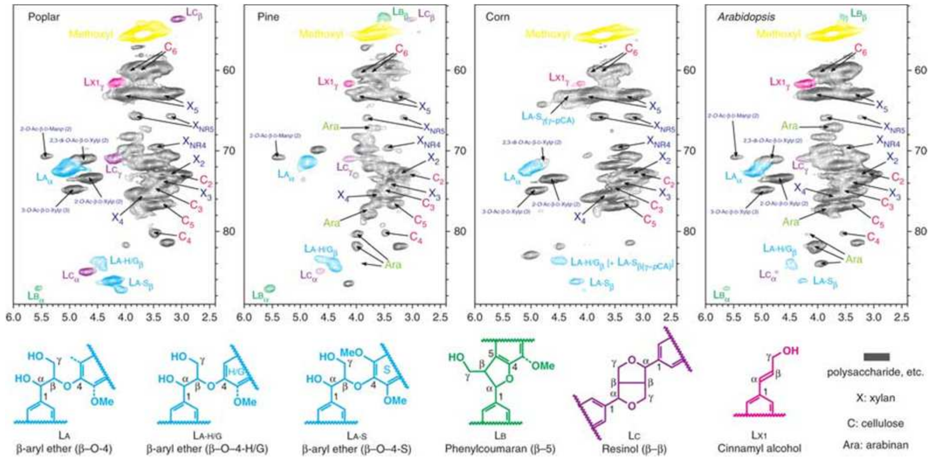


Processing NMR Data:
Window Functions

William D. Wheeler, Ph.D.

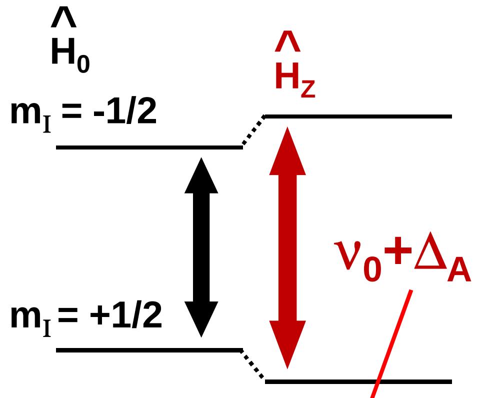
Outline

Nature Protocols, 2012



- **Nuclear spin – the NMR experiment**
- **Mathematical treatment of NMR**
- **Multidimensional NMR**
- **Relaxation**
- **Solid State NMR**
- **Gradients and imaging**

Quantum mechanics applied to NMR

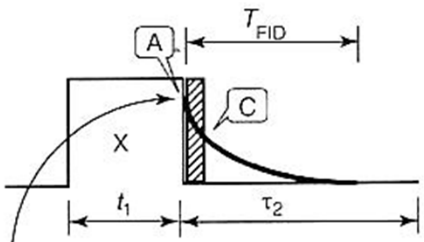


A: interaction

$\hat{\rho} = \overline{|\Psi\rangle\langle\Psi|}$

hermitian

$\hat{\rho} = \hat{\rho}^\dagger$

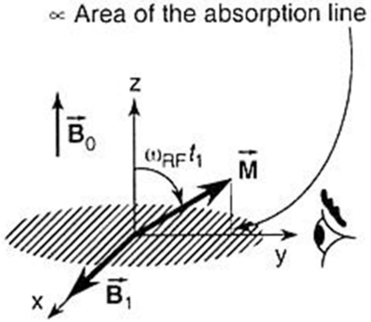


$\langle I_y(t_1)\rangle = \mathrm{Tr}[\rho(t_1)I_y]$

$\propto$ Area of the absorption line

$\langle I_y(t_1)\rangle = \mathrm{Tr}[\rho(t_1)I_y]$

$\propto$ Area of the absorption line

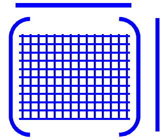


averages

~ 10^{18} spins: density matrix

$$\rho_{ml} = \sum_q p^{(q)} c_m^{(q)} c_l^{(q)*} = \overline{c_m c_l^*}.$$

$\hat{\rho}(t) =$



Liouville – von Neumann equation

$$\frac{d}{dt}\hat{\rho} = -i[\hat{H}, \hat{\rho}]$$

commutator

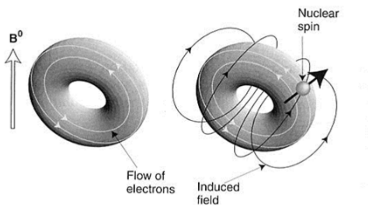
$$\langle A\rangle = \sum_{l,m=-j}^{j} \rho_{ml} A_{lm} = \mathrm{Tr}(\hat{\rho})(\hat{A}).$$

observable

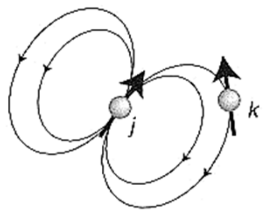
ex: $\hat{I}_y$

Man, Encyclopedia of analytical chemistry, 2000, 12228.

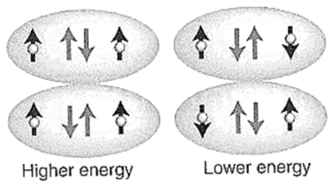
Internal interactions



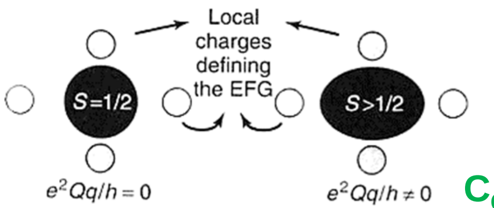
chemical shift : δ



dipolar coupling : D



indirect coupling : J



$C_Q \neq 0$

quadrupolar interaction (I > ½)

Levitt, Spin dynamics, 2002.
Frydman, Encyclopedia of NMR, supp. Vol., 263.

mathematical treatment

$$\hat{\mathcal{H}}_{int} = \hbar \hat{\boldsymbol{I}} \cdot \mathbf{A} \cdot \hat{X} = \hbar(\hat{I}_x \quad \hat{I}_y \quad \hat{I}_z) \begin{pmatrix} A_{xx} & A_{xy} & A_{xz} \\ A_{yx} & A_{yy} & A_{yz} \\ A_{zx} & A_{zy} & A_{zz} \end{pmatrix} \begin{pmatrix} \hat{X}_x \\ \hat{X}_y \\ \hat{X}_z \end{pmatrix}$$

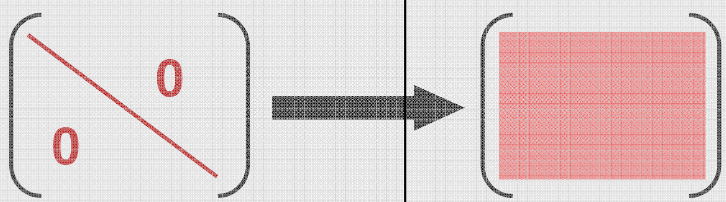
(CS, D, Q...)

nuclear spin operator

A: the interaction
second rank tensor
(assumed)

other spin operator or B_0...

anisotropy: why ?



diagonal in the PAS
(Principal Axes System)

LABO

Full NMR hamiltonians in the context of QM

"in recognition of the extraordinary services they rendered by the researches into the influence of magnetism upon radiation phenomena",

Physics, 1902 (with Lorentz)

external spin interactions

Zeeman interaction

$$\hat{H}_0 = -\gamma B_0 \hat{I}_z = -\Sigma \gamma^j B_0 \hat{I}_z^j$$

RF field: ex.

$$\hat{H}_{RF} = -\gamma B_1 \hat{I}_x \text{ for an } x \text{ pulse}$$

$$\hat{H}_{RF} = -\gamma B_1 (-\hat{I}_x) \text{ for an } -x \text{ pulse} \ldots$$

gradient field

$$\hat{H}_{grad}^{\,j} (r, t) = -\gamma^j G_x(t) x \hat{I}_z^j$$ for gradient G_x along x–axis

$$\hat{H}_{grad}^{\,j} (r, t) = -\gamma^j G_y(t) y \hat{I}_z^j$$ for gradient G_y along y–axis

$$\hat{H}_{grad}^{\,j} (r, t) = -\gamma^j G_z(t) z \hat{I}_z^j$$ for gradient G_z along z–axis

Full NMR hamiltonians in the context of QM

internal spin interactions

chemical shift

$$\hat{H}_{cs} = \gamma \hat{\vec{\mathbf{I}}} \boldsymbol{\sigma} \vec{\mathbf{B}}_0 = \gamma (\hat{I}_x \sigma_{xz}^{LF} + \hat{I}_y \sigma_{yz}^{LF} + \hat{I}_z \sigma_{zz}^{LF}) B_0 .$$

indirect J coupling

$$\hat{H}_J = 2\pi \, \hat{\mathbf{I}}_j \, J \, \hat{\mathbf{I}}_k$$

dipolar coupling

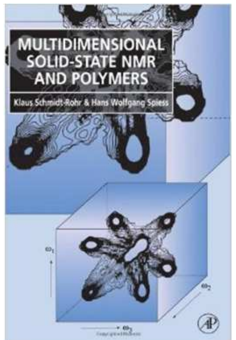
$$\hat{H}_D = -\frac{\mu_0}{4\pi} \hbar \sum\sum_{\text{all } j,k \text{ pairs}} \gamma_j \gamma_k \frac{3(\hat{\vec{\mathbf{I}}}^j \cdot \vec{\mathbf{r}}_{jk}/r_{jk})(\hat{\vec{\mathbf{I}}}^k \cdot \vec{\mathbf{r}}_{jk}/r_{jk}) - \hat{\vec{\mathbf{I}}}^j \cdot \hat{\vec{\mathbf{I}}}^k}{(r_{jk})^3}$$

$$=: \sum\sum_{\text{all } j,k \text{ pairs}} \hat{\vec{\mathbf{I}}}^j \mathbf{D}^{jk} \hat{\vec{\mathbf{I}}}^k$$

$$\omega_d := \frac{\mu_0}{4\pi} \hbar \frac{\gamma_1 \gamma_2}{(r_{1,2})^3} = 2\pi \ 122 \text{ kHz} \ \frac{\gamma_1}{\gamma^{^1\text{H}}} \frac{\gamma_2}{\gamma^{^1\text{H}}} \frac{1}{(r_{1,2}/1 \text{ Å})^3}$$

internuclear distance !

credits to



Full NMR hamiltonians in the context of QM

quadrupolar interaction

$$\hat{H}_Q = \frac{eQ}{2I(2I-1)\hbar}\,\hat{\mathbf{I}}\mathbf{V}\hat{\mathbf{I}}.$$

- CSA: it depends... .... $\propto B_0$
- D: up to ~ 30 kHz ! .... ind. B_0
- Q: up to MHz ! { ind. B_0. (1^{st}) ; $1/B_0$ (2^{nd}) }
- J: few 100^s Hz .... ind. B_0

Truncated NMR hamiltonians – secular parts

internal spin interactions

chemical shift

$$\hat{H}_{cs} = \gamma \hat{I}_z \sigma_{zz}^{LF} B_0$$

dipolar coupling

$$\hat{H}_D^{S,I} = \sum_j \sum_k \hat{I}_z^j (\mathbf{D}_{LF}^{jk})_{zz} \hat{S}_z^k$$

$$= -\frac{\mu_0}{4\pi} \hbar \sum_j \sum_k \frac{\gamma^I \gamma^S}{r_{jk}^3} \tfrac{1}{2}(3 \cos^2(\theta_{jk}) - 1)\ 2\hat{I}_z^j \hat{S}_z^k.$$

$$\hat{H}_D^{II} = \sum_j \sum_{k<j} \tfrac{1}{2}(\mathbf{D}_{LF}^{jk})_{zz} (3\hat{I}_z^j \hat{I}_z^k - \hat{\mathbf{I}}^j \cdot \hat{\mathbf{I}}^k)$$

$$= -\frac{\mu_0}{4\pi} \hbar \sum_j \sum_{k<j} \frac{\gamma^2}{r_{jk}^3} \tfrac{1}{2}(3 \cos^2(\theta_{jk}) - 1)(3\hat{I}_z^j \hat{I}_z^k - \hat{\mathbf{I}}^j \cdot \hat{\mathbf{I}}^k).$$

quadrupolar coupling

$$\hat{H}_Q = \frac{eQ}{2I(2I-1)\hbar} V_{zz}^{LF} \tfrac{1}{2}(3\hat{I}_z \hat{I}_z - \hat{\mathbf{I}} \cdot \hat{\mathbf{I}})$$

Action of hamiltonians: "pushing" the density operator !

- **density operator at equilibrium (high T approximation)**

$$\hat{\rho}_{eq} \sim \left(\hat{1} + \frac{\hbar\gamma B_0}{kT}\,\hat{I}_z\right)$$

- **Liouville – von Neumann equation**

$$\frac{d}{dt}\,\hat{\rho} = -i\,[\hat{H}, \hat{\rho}]$$

commutator

- **If… H independent of t**

$$\hat{\rho}(t) = e^{-i\hat{H}t}\hat{\rho}(0)\,e^{i\hat{H}t}$$

unitary operator

Nineteen Dubious Ways to Compute the Exponential of a Matrix, Twenty-Five Years Later*

Cleve Moler†
Charles Van Loan‡

SIAM Review
Vol. 45, No. 1, pp. 3–000

$$e^{tA} = I + tA + \frac{t^2A^2}{2!} + \cdots$$

$$e^{tB}e^{tC} = e^{t(B+C)} \Leftrightarrow BC = CB.$$

$$e^{B+C} = \lim_{m\to\infty}\left(e^{B/m}e^{C/m}\right)^m.$$

Exponential of a diagonal matrix

If A is diagonalizable then $A=PDP^{-1}$ and

$$e^{At} = I + tA + \frac{t^2A^2}{2!} + \ldots$$

$$= PP^{-1} + tPDP^{-1} + t^2\frac{PDP^{-1}PDP^{-1}}{2!} + \ldots$$

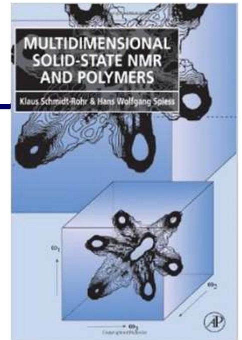
$$= P(I + tD + \frac{t^2D^2}{2!} + \ldots)P^{-1} = Pe^{Dt}P^{-1}$$

$$= P\begin{pmatrix} e^{\sigma_1 t} & 0.. & \ldots & \ldots \\ 0 & e^{\sigma_2 t} & \ldots & \ldots \\ \vdots & \vdots & \vdots & \vdots \\ \ldots & \ldots & \ldots & e^{\sigma_n t} \end{pmatrix} P^{-1}.$$

http://www.math.vt.edu/people/renardym/class_home/nova/bifs/node6.html

Matrices of spin operators

credits to



ex. I = ½ (Pauli spin matrices)

$$\hat{\mathbf{I}}_z = \tfrac{1}{2}\begin{bmatrix} 1 & 0 \\ 0 & -1 \end{bmatrix} \qquad \hat{\mathbf{I}}_x = \tfrac{1}{2}\begin{bmatrix} 0 & 1 \\ 1 & 0 \end{bmatrix} \qquad \hat{\mathbf{I}}_y = \tfrac{1}{2}\begin{bmatrix} 0 & -\mathrm{i} \\ \mathrm{i} & 0 \end{bmatrix}$$

hermitian matrices

$\hat{A} = \hat{A}^{\dagger}$

$$\tfrac{1}{4}\begin{bmatrix} 1 & 0 \\ 0 & 1 \end{bmatrix} =: \tfrac{1}{4}\hat{\mathbf{1}}$$

ex. I ≠ ½ → rules $(2I+1)\times(2I+1)$

$$(\mathbf{I}_z)_{m',m} = \langle m' \,|\, \hat{I}_z \,|\, m\rangle = \langle m' \,|\, m \,|\, m\rangle = m\delta_{m',m}$$

$$(\mathbf{I}_x \pm \mathrm{i}\mathbf{I}_y)_{m',m} = \langle m' \,|\, \hat{I}^{\pm} \,|\, m\rangle = \sqrt{I(I+1) - m(m\pm 1)}\;\delta_{m',m\pm 1}$$

$$\Rightarrow (\mathbf{I}_x)_{m',m} = (\pm \mathrm{i}\mathbf{I}_y)_{m',m} = \tfrac{1}{2}\sqrt{I(I+1) - m(m\pm 1)}\;\delta_{m',m\pm 1}$$

A first example of application

ex. I = ½ (Pauli spin matrices)

start → $\hat{\mathbf{H}} = \omega_0 \hat{\mathbf{I}}_z$ $\quad (\omega_0 = -\gamma B_0)$

$$\hat{\boldsymbol{\rho}}(0) = \hat{\mathbf{I}}_x = \tfrac{1}{2}\begin{bmatrix} 0 & 1 \\ 1 & 0 \end{bmatrix} \xrightarrow{\mathbf{H} = \begin{bmatrix} \frac{1}{2}\omega_0 & 0 \\ 0 & -\frac{1}{2}\omega_0 \end{bmatrix}}$$

$$\hat{\boldsymbol{\rho}}(t) = \tfrac{1}{2}\begin{bmatrix} 0 & 1 \cdot \mathrm{e}^{-\mathrm{i}\omega_0 t} \\ 1 \cdot \mathrm{e}^{\mathrm{i}\omega_0 t} & 0 \end{bmatrix} = \hat{\mathbf{I}}_x \cos \omega_0 t + \hat{\mathbf{I}}_y \sin \omega_0 t$$

$$\hat{\rho}(t) = \hat{I}_x \cos \omega_0 t + \hat{I}_y \sin \omega_0 t \quad \rightarrow \quad f(t) = \cos \omega_0 t + \mathrm{i} \sin \omega_0 t = \exp(\mathrm{i}\omega_0 t).$$

$$f(t) \sim \mathrm{tr}\{\boldsymbol{\rho}(t)\hat{\mathbf{I}}^+\}.$$

I > ½

ex. I = 1 (^{2}H, ^{14}N)

$$\hat{\mathbf{I}}_z = \begin{bmatrix} 1 & 0 & 0 \\ 0 & 0 & 0 \\ 0 & 0 & -1 \end{bmatrix} \quad \hat{\mathbf{I}}_x = \sqrt{\tfrac{1}{2}} \begin{bmatrix} 0 & 1 & 0 \\ 1 & 0 & 1 \\ 0 & 1 & 0 \end{bmatrix} \quad \hat{\mathbf{I}}_y = \sqrt{\tfrac{1}{2}} \begin{bmatrix} 0 & -\mathrm{i} & 0 \\ \mathrm{i} & 0 & -\mathrm{i} \\ 0 & \mathrm{i} & 0 \end{bmatrix}$$

$$\hat{\mathbf{H}}_Q = \frac{\omega_Q}{3}(3\hat{\mathbf{I}}_z\hat{\mathbf{I}}_z - I(I+1)\hat{\mathbf{1}}) = \frac{\omega_Q}{3}\left(3\begin{bmatrix} 1 & 0 & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 1 \end{bmatrix} - 2\begin{bmatrix} 1 & 0 & 0 \\ 0 & 1 & 0 \\ 0 & 0 & 1 \end{bmatrix}\right)$$

$$= \frac{\omega_Q}{3}\begin{bmatrix} 1 & 0 & 0 \\ 0 & -2 & 0 \\ 0 & 0 & 1 \end{bmatrix}$$

where the prefactor of the matrix is given by:

$$\frac{\omega_Q}{3} = \frac{eQeq}{4\hbar}\tfrac{1}{2}(3\cos^2\theta - 1 - \eta_Q \sin^2\theta \cos 2\phi)$$

$$\hat{\boldsymbol{\rho}}(0) = \hat{\mathbf{I}}_x = \sqrt{\tfrac{1}{2}}\begin{bmatrix} 0 & 1 & 0 \\ 1 & 0 & 1 \\ 0 & 1 & 0 \end{bmatrix} \xrightarrow{\hat{\mathbf{H}}_Q}$$

$$\hat{\boldsymbol{\rho}}(t) = \sqrt{\tfrac{1}{2}}\begin{bmatrix} 0 & \exp(-\mathrm{i}\omega_Q t) & 0 \\ \exp(\mathrm{i}\omega_Q t) & 0 & \exp(\mathrm{i}\omega_Q t) \\ 0 & \exp(-\mathrm{i}\omega_Q t) & 0 \end{bmatrix}$$

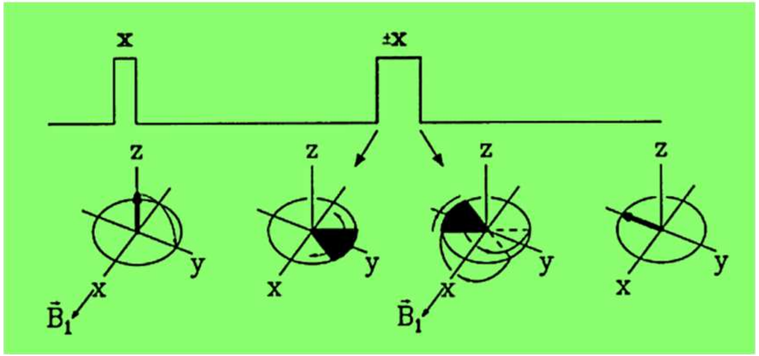
$$\hat{\boldsymbol{\rho}}(t) = \hat{\mathbf{I}}_x \cos \omega_Q t - \mathrm{i}\,\frac{\hat{\mathbf{r}}_1}{\omega_Q} \sin \omega_Q t$$

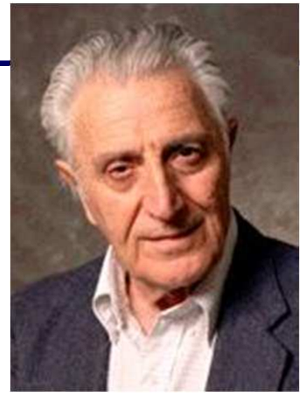
$$f(t) \sim \mathrm{tr}\{\boldsymbol{\rho}(t)\hat{\mathbf{I}}^+\}$$

$$\cos(\omega_Q t) = \tfrac{1}{2}\exp(\mathrm{i}\omega_Q t) + \tfrac{1}{2}\exp(-\mathrm{i}\omega_Q t) \overset{\mathrm{FT}}{\rightarrow} \tfrac{1}{2}\delta(\omega - \omega_Q) + \tfrac{1}{2}\delta(\omega + \omega_Q)$$

2 spectral lines !

Effect of RF pulses – Hahn echo (1950)





$\hat{P} = e^{i\pi\hat{S}_x}$

$$\hat{P}\exp(\hat{A})\hat{P}^{-1} = \exp(\hat{P}\hat{A}\hat{P}^{-1})$$

start ↓

$$\hat{\rho}(t) = \hat{U}(t)\hat{\rho}(0)\hat{U}^{-1}(t).$$

$$\hat{U}(2t_e) = \underset{\text{precess}}{e^{-i\omega\hat{S}_z t_e}}\ \underset{\text{pulse}}{e^{i\pi\hat{S}_x}}\ \underset{\text{precess}}{e^{-i\omega\hat{S}_z t_e}}$$

$$= e^{-i\omega\hat{S}_z t_e}\underbrace{e^{i\pi\hat{S}_x}\ e^{-i\omega\hat{S}_z t_e}\overbrace{\exp(-i\pi\hat{S}_x)}^{}}_{\exp(-i\omega\{-\hat{S}_z\}t_e)}\overbrace{\ \exp(i\pi\hat{S}_x)}^{\hat{1}\text{ inserted}}$$

$$= \underbrace{e^{-i\omega\hat{S}_z t_e}\ e^{i\omega\hat{S}_z t_e}}_{=\hat{1}}\ e^{i\pi\hat{S}_x} = e^{i\pi\hat{S}_x}$$

$$\hat{\rho}(2t_e) = \hat{\rho}(0)$$

Product operators (PO) formalism

PRODUCT OPERATOR FORMALISM FOR THE DESCRIPTION OF NMR PULSE EXPERIMENTS

O. W. SØRENSEN, G. W. EICH, M. H. LEVITT, G. BODENHAUSEN and R. R. ERNST
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1. INTRODUCTION

In recent years, an astonishing variety of pulse techniques has been developed with the aim of enhancing the information content or the sensitivity of NMR spectra in both solution and solid phases.[1–39] For the design and analysis of new techniques two approaches have been pursued in the field of "spin engineering". Many of the original concepts were based on simplified *classical or semiclassical vector models* which have inherently severe limitations for describing more sophisticated techniques; for example, those involving multiple quantum coherence. On the other hand, for a full analysis of arbitrarily complex pulse experiments applied to large spin systems, the heavy machinery of *density operator theory* has been put into action, often at the expense of physical intuition.

We present here an approach which follows a middle course. It is founded on density operator theory but retains the intuitive concepts of the classical or semiclassical vector models. The formalism systematically uses product operators to represent the state of the spin system.

Finally, we treat in Sections 12–15 some examples involving coherence transfer such as two-dimensional correlation spectroscopy, relayed magnetization transfer, multiple quantum filters, 2D exchange spectroscopy, and systems with non-uniform spin temperature in the context of flip angle effects.

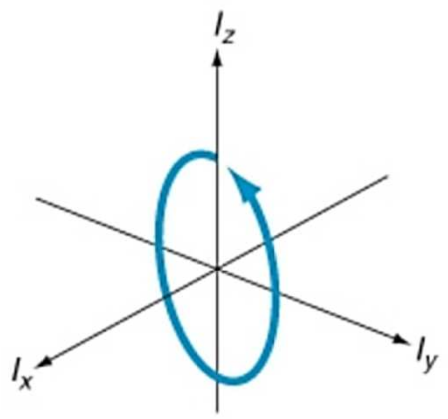
Progress in NMR Spectroscopy, Vol. 16, pp. 163–192, 1983.

- **complete QM approach**
- **clear physical meaning of operators**
- **geometrical rotations**
- **can be implemented in**

weak coupling – very short RF pulses – clear distinction between RF and free precession – no relaxation – I = ½ (or not …)

Product operators (PO) formalism

ex. one-spin system



$$\hat{I}_z \xrightarrow{\beta \hat{I}_x} \hat{I}_z \cos(\beta) - \hat{I}_y \sin(\beta)$$

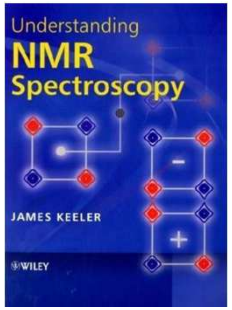
$$\hat{I}_z \xrightarrow{\beta \hat{I}_y} \hat{I}_z \cos(\beta) + \hat{I}_x \sin(\beta)$$

chemical shift

$$\hat{I}_x \xrightarrow{\omega_I t \hat{I}_z} \hat{I}_x \cos(\omega_I t) + \hat{I}_y \sin(\omega_I t)$$

$$\hat{I}_y \xrightarrow{\omega_I t \hat{I}_z} \hat{I}_y \cos(\omega_I t) - \hat{I}_x \sin(\omega_I t)$$

credits to



Product operators (PO) formalism

ex. two-spins system or more …

$\hat{I}_z$ – longitudinal magnetization of I
$\hat{I}_x$ – in-phase x-magnetization of I
$\hat{I}_y$ – in-phase y-magnetization of I
$\hat{S}_z$ – longitudinal magnetization of S
$\hat{S}_x$ – in-phase x-magnetization of S
$\hat{S}_y$ – in-phase y-magnetization of S
$2\hat{I}_x\hat{S}_z$ – x-magnetization of I antiphase with respect to S
$2\hat{I}_y\hat{S}_z$ – y-magnetization of I antiphase with respect to S
$2\hat{I}_z\hat{S}_x$ – x-magnetization of S antiphase with respect to I
$2\hat{I}_z\hat{S}_y$ – y-magnetization of S antiphase with respect to I
$2\hat{I}_x\hat{S}_x$ – two spin coherence
$2\hat{I}_x\hat{S}_y$ – two spin coherence
$2\hat{I}_y\hat{S}_x$ – two spin coherence
$2\hat{I}_y\hat{S}_y$ – two spin coherence
$2\hat{I}_z\hat{S}_z$ – longitudinal two-spin order
$4\hat{I}_x\hat{J}_z\hat{S}_z$ – x-magnetization of spin I in antiphase with respect to spins J and S
$4\hat{I}_x\hat{J}_x\hat{S}_z$ - two-spin coherence of spins I and J in antiphase with respect to spin S
$4\hat{I}_x\hat{J}_x\hat{S}_x$ - three-spin coherence
$4\hat{I}_z\hat{J}_z\hat{S}_z$ - longitudinal three-spin order
$\hat{E}/2$ – unity operator

indirect J coupling

$$\hat{I}_x \xrightarrow{(\pi J t)\hat{I}_z\hat{S}_z} \hat{I}_x\cos(\pi J t) + \hat{I}_y\hat{S}_z\sin(\pi J t)$$

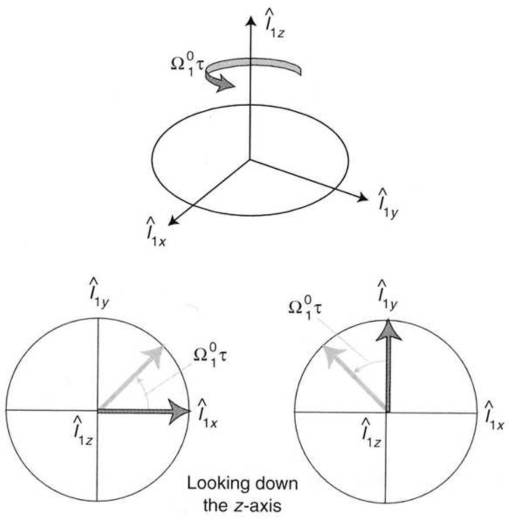
evolution under … **target**

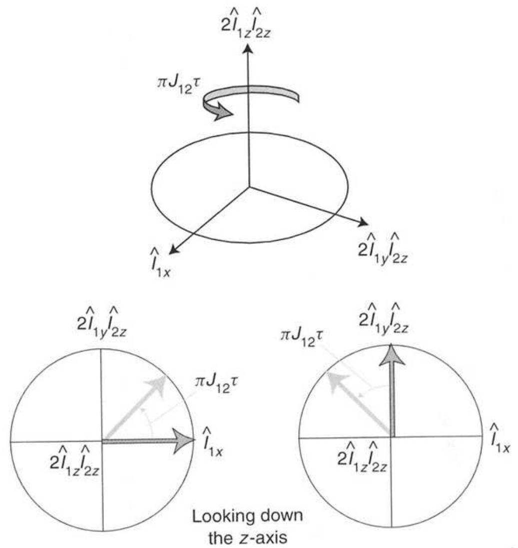
	$\hat{I}_z$	$\hat{I}_x$	$\hat{I}_y$	$\hat{S}_z$	$\hat{S}_y$	$\hat{S}_y$	$2\hat{I}_z\hat{S}_z$
$\hat{I}_z$		$-\hat{I}_y$	$\hat{I}_x$				
$\hat{I}_x$	$\hat{I}_y$		$-\hat{I}_z$				$2\hat{I}_y\hat{S}_z$
$\hat{I}_y$	$-\hat{I}_x$	$\hat{I}_z$					$-2\hat{I}_x\hat{S}_z$
$\hat{S}_z$					$-\hat{S}_y$	$\hat{S}_x$	$\hat{E}/2$
$\hat{S}_x$				$\hat{S}_y$		$-\hat{S}_z$	$2\hat{I}_z\hat{S}_y$
$\hat{S}_y$				$-\hat{S}_x$	$\hat{S}_z$		$-2\hat{I}_z\hat{S}_x$
$\hat{I}_z\hat{S}_z$		$-2\hat{I}_y\hat{S}_z$	$2\hat{I}_x\hat{S}_z$		$2\hat{I}_z\hat{S}_y$	$2\hat{I}_z\hat{S}_x$	
$2\hat{I}_x\hat{S}_z$	$2\hat{I}_y\hat{S}_z$		$-2\hat{I}_z\hat{S}_z$		$-2\hat{I}_x\hat{S}_y$	$2\hat{I}_x\hat{S}_x$	$\hat{I}_y$
$2\hat{I}_y\hat{S}_z$	$-2\hat{I}_x\hat{S}_z$	$\hat{I}_z\hat{S}_z$			$-2\hat{I}_y\hat{S}_y$	$2\hat{I}_y\hat{S}_x$	$-\hat{I}_x$
$2\hat{I}_z\hat{S}_x$		$-2\hat{I}_x\hat{S}_x$	$2\hat{I}_x\hat{S}_x$	$2\hat{I}_z\hat{S}_y$		$-2\hat{I}_z\hat{S}_z$	$\hat{S}_y$
$2\hat{I}_z\hat{S}_y$		$-2\hat{I}_y\hat{S}_y$	$2\hat{I}_x\hat{S}_y$	$-2\hat{I}_z\hat{S}_x$	$\hat{I}_z\hat{S}_z$		$-\hat{S}_y$
$2\hat{I}_x\hat{S}_x$	$2\hat{I}_y\hat{S}_x$		$-2\hat{I}_z\hat{S}_x$	$2\hat{I}_x\hat{S}_y$		$-2\hat{I}_x\hat{S}_z$	
$2\hat{I}_x\hat{S}_y$	$2\hat{I}_y\hat{S}_y$		$-2\hat{I}_z\hat{S}_y$	$-2\hat{I}_x\hat{S}_x$	$2\hat{I}_x\hat{S}_z$		
$2\hat{I}_y\hat{S}_x$	$-2\hat{I}_x\hat{S}_x$	$2\hat{I}_z\hat{S}_x$		$2\hat{I}_y\hat{S}_y$	$\hat{E}/2$	$-2\hat{I}_y\hat{S}_z$	
$2\hat{I}_y\hat{S}_y$	$-2\hat{I}_x\hat{S}_y$	$2\hat{I}_z\hat{S}_y$		$-2\hat{I}_y\hat{S}_x$	$2\hat{I}_y\hat{S}_z$		

start

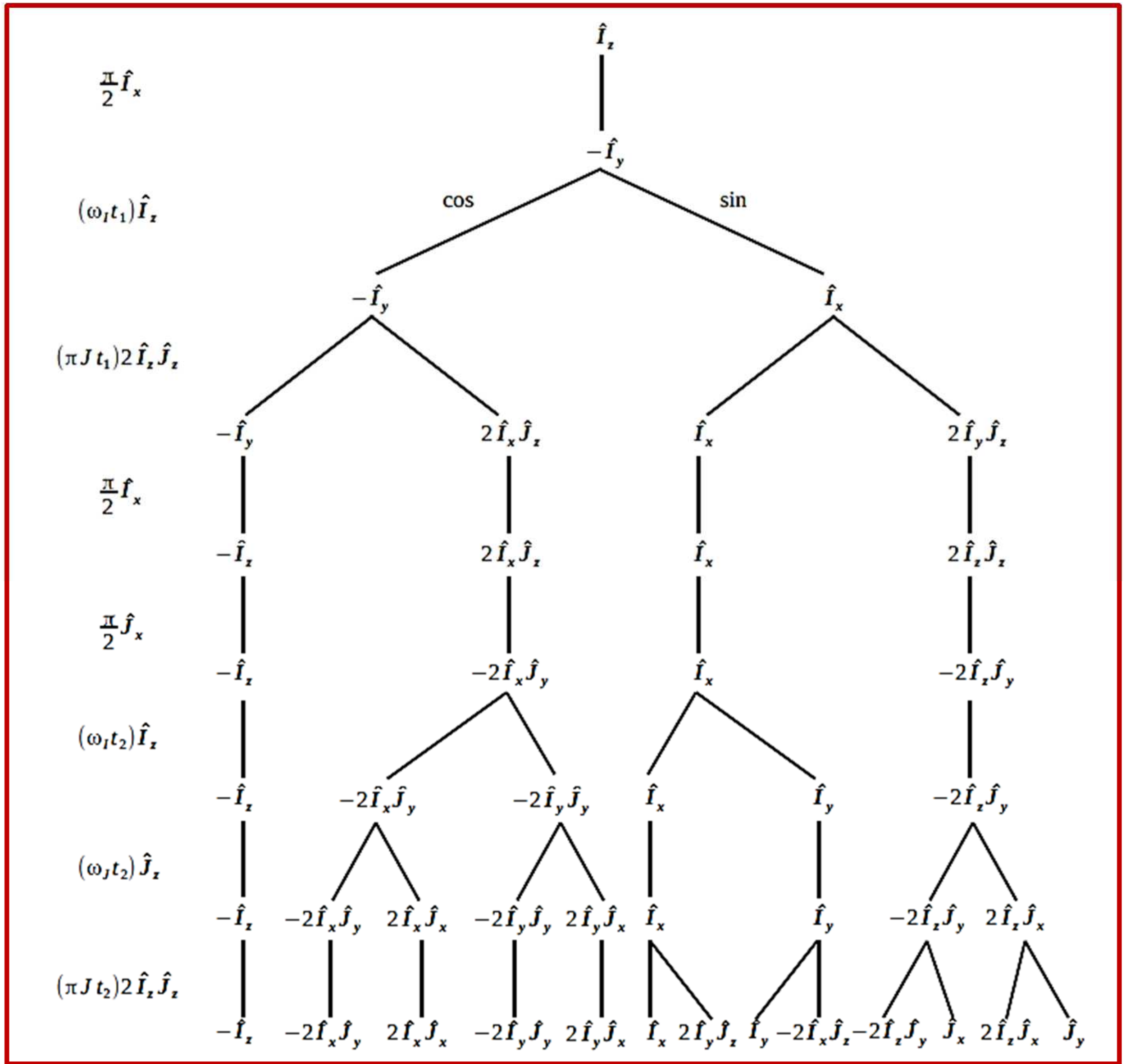
Product operators (PO) formalism

geometrical description





Product operators tree: speeding things up …



Fundamental blocks in NMR

credits to

55th Experimental Nuclear Magnetic Resonance Conference
Boston, 2014

The Basic Building Blocks of NMR Pulse Sequences

James Keeler

generation of anti-phase terms

$$\hat{I}_{1x} \xrightarrow{2\pi J_{12}\tau \hat{I}_{1z}\hat{I}_{2z}} \cos(\pi J_{12}\tau)\,\hat{I}_{1x} + \sin(\pi J_{12}\tau)\,2\hat{I}_{1y}\hat{I}_{2z}$$

$$\tau = 1/(2J_{12})$$

back in phase

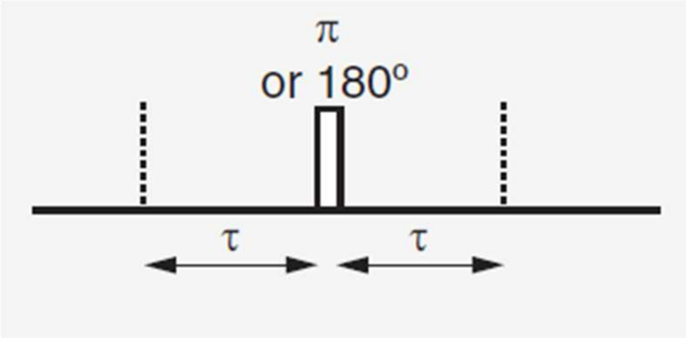
$$2\hat{I}_{1y}\hat{I}_{2z} \xrightarrow{2\pi J_{12}\tau \hat{I}_{1z}\hat{I}_{2z}} \cos(\pi J_{12}\tau)\,2\hat{I}_{1y}\hat{I}_{2z} - \sin(\pi J_{12}\tau)\,\hat{I}_{1x}$$

coherence transfer

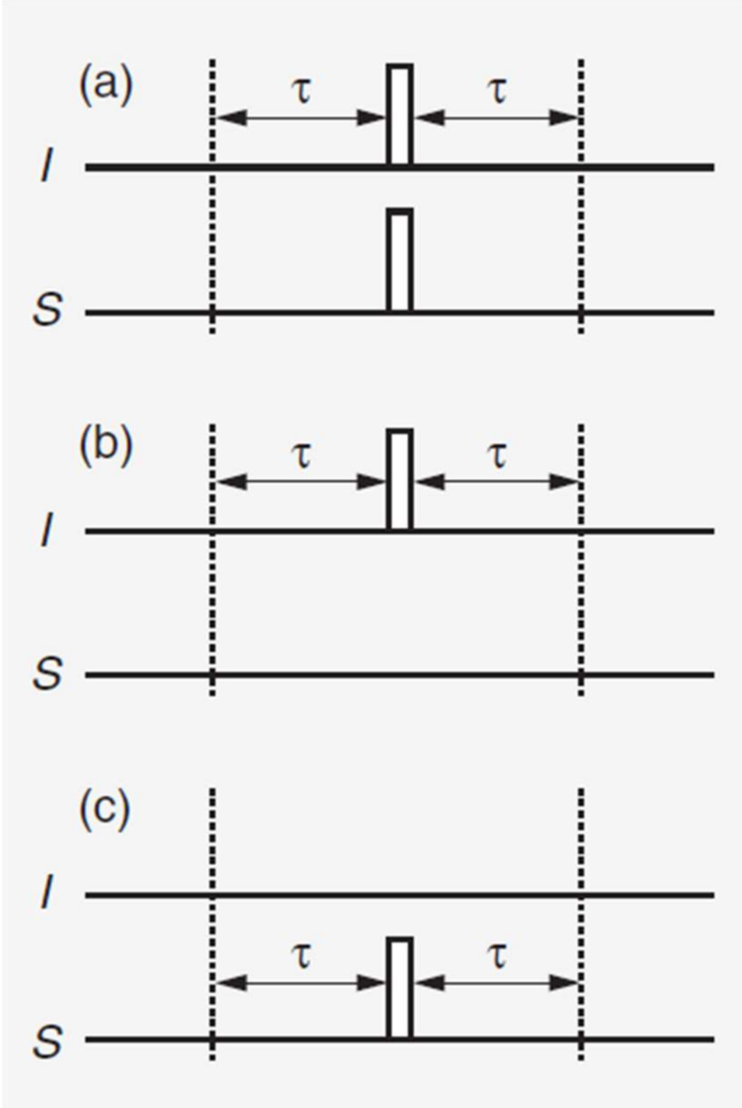
$$\underbrace{2\hat{I}_{1y}\hat{I}_{2z}}_{\text{on spin 1}} \xrightarrow{(\pi/2)\hat{I}_{1x}} 2\hat{I}_{1z}\hat{I}_{2z} \xrightarrow{(\pi/2)\hat{I}_{2x}} \underbrace{-2\hat{I}_{1z}\hat{I}_{2y}}_{\text{on spin 2}}$$

echoes

homonuclear spin system

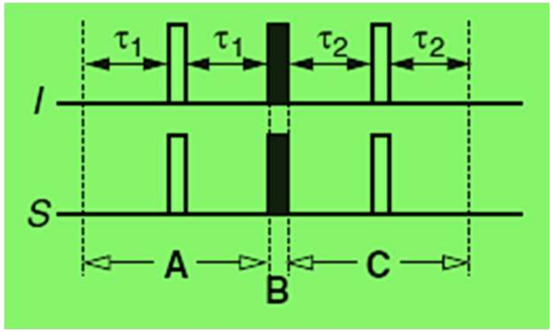


heteronuclear spin system



Fundamental blocks in NMR

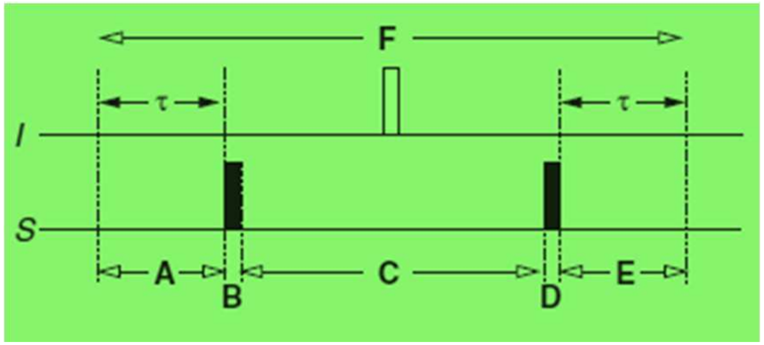
heteronuclear coherence transfer using INEPT



$$\hat{I}_x \xrightarrow{\text{INEPT}} \sin(2\pi J_{IS}\tau_2)\sin(2\pi J_{IS}\tau_1)\,\hat{S}_x$$

maximum transfer when $\tau_1 = 1/(4J_{IS})$ and $\tau_2 = 1/(4J_{IS})$

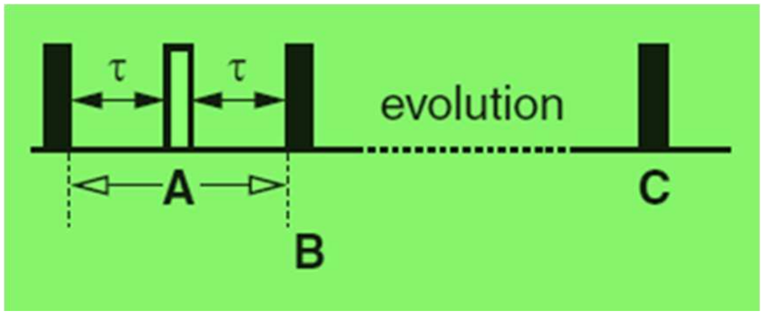
coherence transfer using HMQC



$$\hat{I}_x \xrightarrow{\text{HMQC transfer}} \text{mod. from } S\text{-spin} \times \sin^2(\pi J_{IS}\tau)\,\hat{I}_x$$

optimum delay τ is $1/(2J_{IS})$

generation of multiple quantum (MQ) coherences



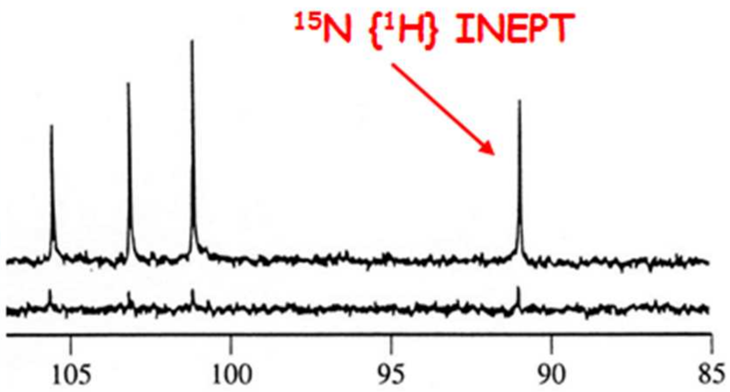
$$\underbrace{2\hat{I}_{1x}\hat{I}_{2z}}_{\text{anti-phase on spin 1}} \xrightarrow{(\pi/2)(\hat{I}_{1x}+\hat{I}_{2x})} \underbrace{-2\hat{I}_{1x}\hat{I}_{2y}}_{\text{MQC}}$$

INEPT

$gain_{INEPT} \propto |\gamma(^1H)/\gamma(X)|$

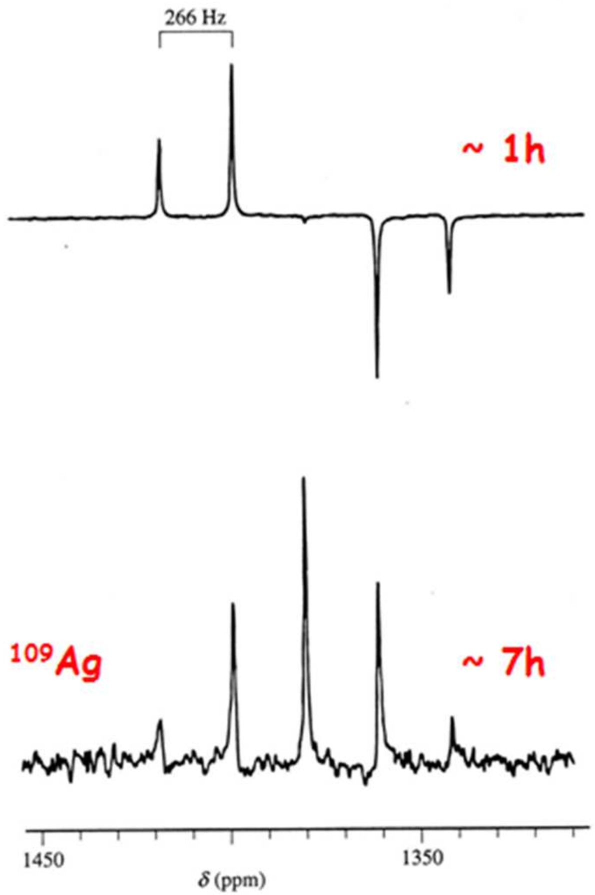
ex : ≈ 10 for ^{15}N !

$T_1(^1H) < T_1(^{15}N)$



^{15}N : gramicidin S

^{109}Ag {^{31}P} INEPT

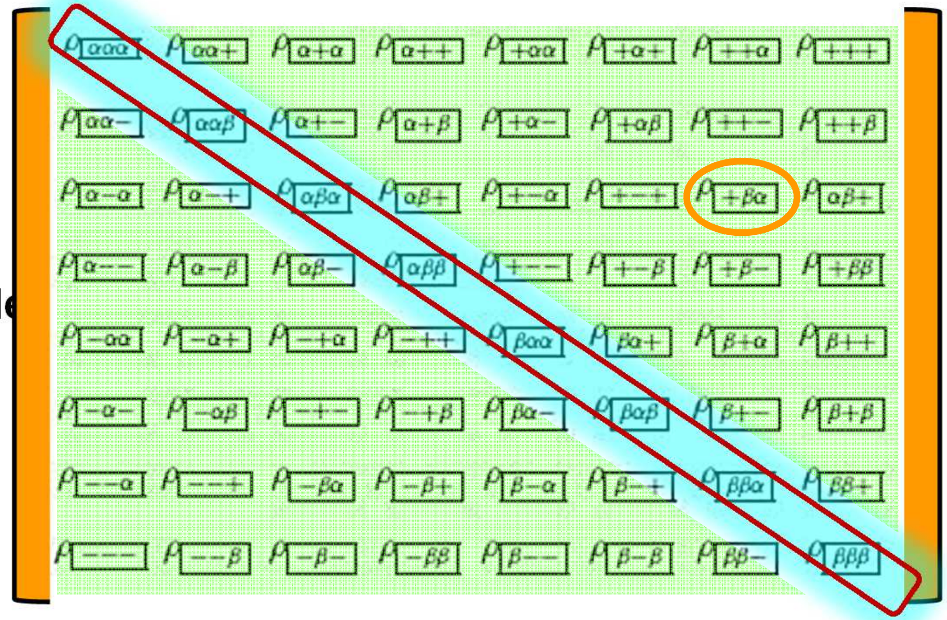


^{109}Ag : $[Ag(dppe)_2]NO_3$,
dppe=bisdiphenylphosphinoethane

The physical content of the density operator

- populations
- coherences
- coherence order $\rho_{+\beta\alpha}$
- combination coherences & le… coherences
- coherence frequencies
- observable coherences (simple –1Q)

$\hat{\rho} =$



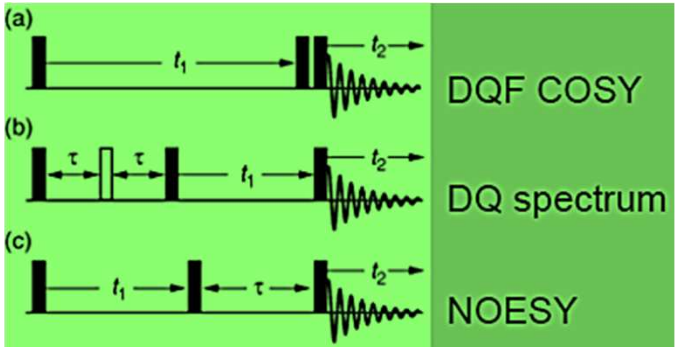
$\hat{I}_{+} = \hat{I}_{x} + \hat{I}_{y}$ $\hat{I}_{-} = \hat{I}_{x} - i\,\hat{I}_{y}$

$\hat{\rho} = \overline{|\Psi\rangle\langle\Psi|}$

product operator	double-quantum part	zero-quantum part
$2\hat{I}_{1x}\hat{I}_{2x}$	$\frac{1}{2}(\hat{I}_{1+}\hat{I}_{2+} + \hat{I}_{1-}\hat{I}_{2-})$	$\frac{1}{2}(\hat{I}_{1+}\hat{I}_{2-} + \hat{I}_{1-}\hat{I}_{2+})$
$2\hat{I}_{1x}\hat{I}_{2y}$	$\frac{1}{2i}(\hat{I}_{1+}\hat{I}_{2+} - \hat{I}_{1-}\hat{I}_{2-})$	$\frac{1}{2i}(-\hat{I}_{1+}\hat{I}_{2-} + \hat{I}_{1-}\hat{I}_{2+})$
$2\hat{I}_{1y}\hat{I}_{2x}$	$\frac{1}{2i}(\hat{I}_{1+}\hat{I}_{2+} - \hat{I}_{1-}\hat{I}_{2-})$	$\frac{1}{2i}(\hat{I}_{1+}\hat{I}_{2-} - \hat{I}_{1-}\hat{I}_{2+})$
$2\hat{I}_{1y}\hat{I}_{2y}$	$-\frac{1}{2}(\hat{I}_{1+}\hat{I}_{2+} + \hat{I}_{1-}\hat{I}_{2-})$	$\frac{1}{2}(\hat{I}_{1+}\hat{I}_{2-} + \hat{I}_{1-}\hat{I}_{2+})$

operator	definition
$\hat{DQ}_x$	$(2\hat{I}_{1x}\hat{I}_{2x} - 2\hat{I}_{1y}\hat{I}_{2y})$
$\hat{DQ}_y$	$(2\hat{I}_{1x}\hat{I}_{2y} + 2\hat{I}_{1y}\hat{I}_{2x})$
$\hat{ZQ}_x$	$(2\hat{I}_{1x}\hat{I}_{2x} + 2\hat{I}_{1y}\hat{I}_{2y})$
$\hat{ZQ}_y$	$(2\hat{I}_{1y}\hat{I}_{2x} - 2\hat{I}_{1x}\hat{I}_{2y})$

Phase cycling



rules

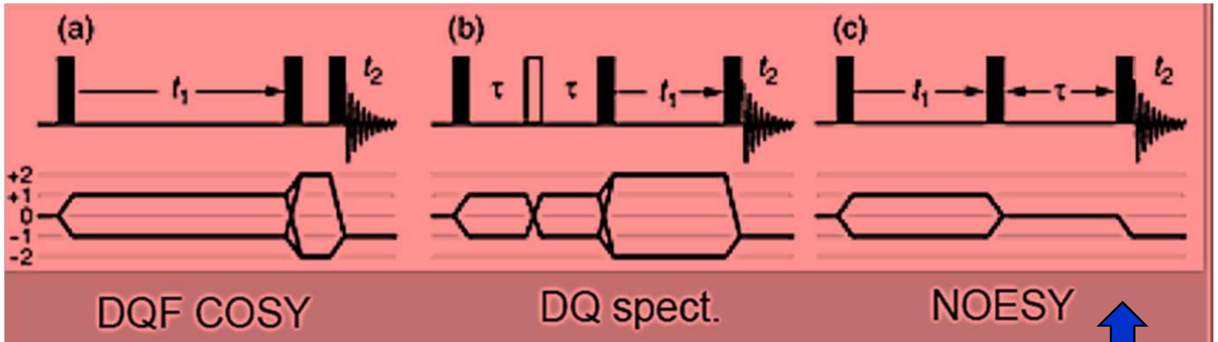
- **coherence order, p**

$$\hat{\rho}^{(p)} \xrightarrow{\text{rotate by } \varphi \text{ about } z} \hat{\rho}^{(p)} \times \exp(-\mathrm{i}p\varphi)$$

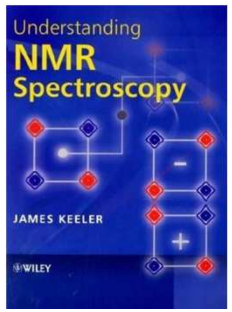
phase acquired is $-p\varphi$

- **only p = –1 is observable**
- **±N for N spins (I = ½)**

coherence transfer pathway

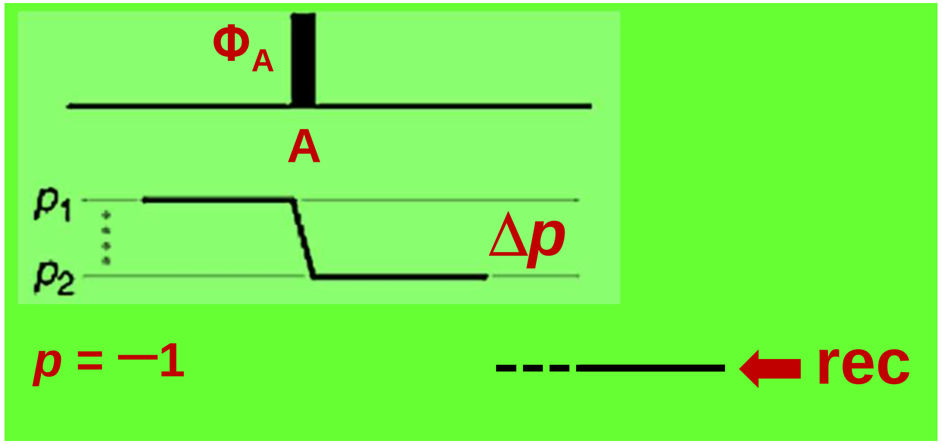


credits to

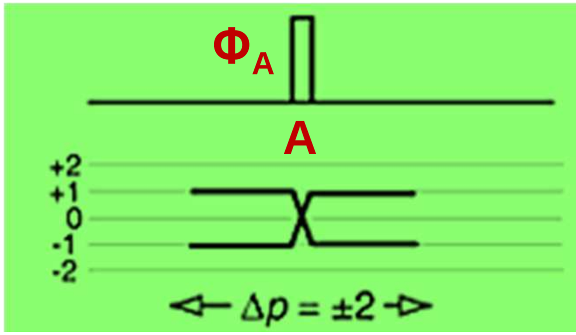


Phase cycling

- phase of the pulses (Φ_A, Φ_B …)
- phase of the receiver (Φ_{rec})

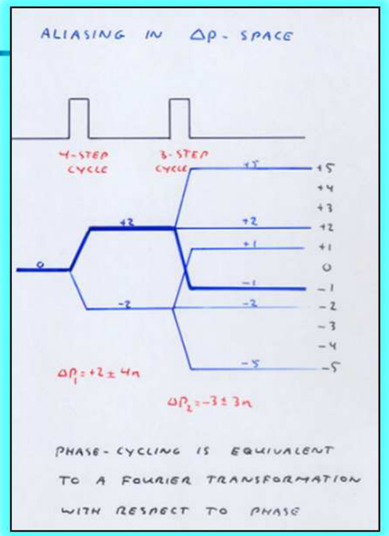


$$\Delta p_A \, \Phi_A + \Delta p_B \, \Phi_B + \ldots + \Phi_{rec} = 0$$



Φ_A [0°, 90°, 180°, 270°]

Φ_{rec} $\Delta p = \pm 2$: [0°, 180°, 0°, 180°]



Historical Perspective

Reflections of pathways: A short perspective on 'Selection of coherence transfer pathways in NMR pulse experiments'

Geoffrey Bodenhausen *

J. Magn. Reson., 2011.

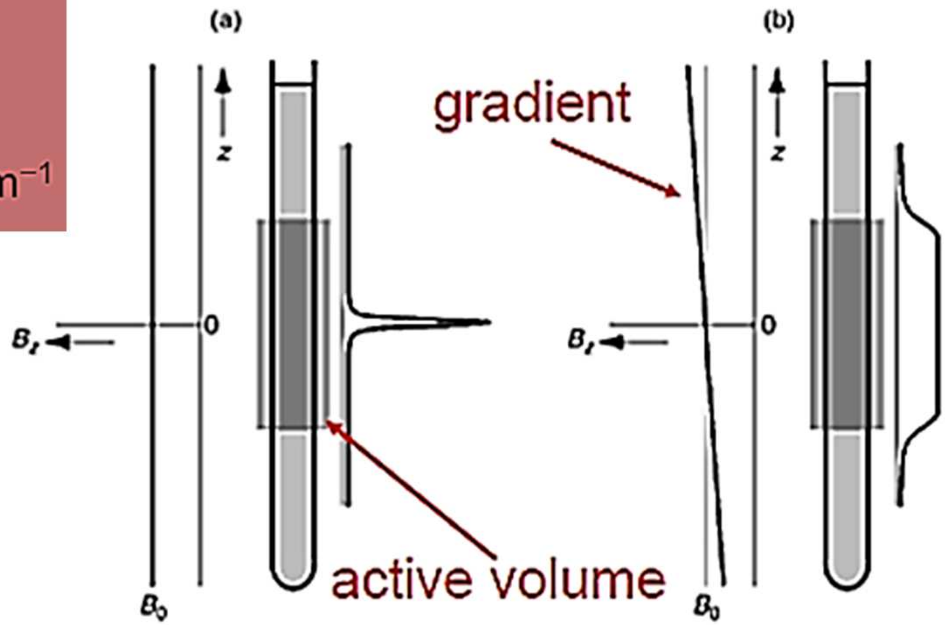
Field gradient pulses (*G*)

- **coherences dephase**
- **subsequent *G* may rephase some coherences**

$$\varphi(z) = -p \times \gamma\, G\, z\, t$$

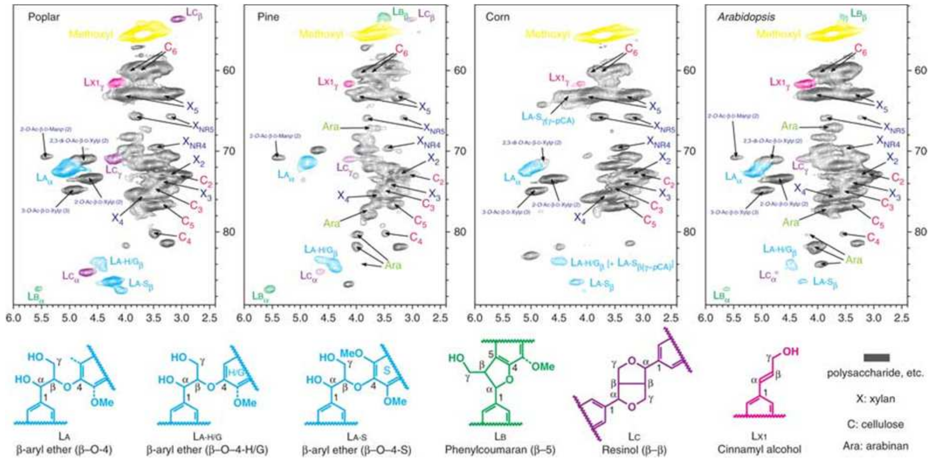
gyromagnetic ratio (γ)

gradient strength, G cm^{-1} (G)



Outline

Nature Protocols, 2012



- Nuclear spin – the NMR experiment
- Mathematical treatment of NMR
- Multidimensional NMR
- Relaxation
- Solid State NMR
- Gradients and imaging

J. Jeener and R. Ernst : 2 dimensional (2D) Fourier Transform NMR

The unpublished Baško Polje (1971) lecture notes about two-dimensional NMR spectroscopy

J. Jeener

Faculté des Sciences (CPI-232), Campus Plaine, Université Libre de Bruxelles, B-1050 Brussels, Belgium

Abstract. — The main part of this paper is a reproduction of (previously unpublished) lecture notes, which were circulated in 1971, and which are often cited as the initiation of two-dimensional NMR spectroscopy. A brief discussion follows, about the way of handling dates and durations in time-dependent quantum mechanics, and about the use of diagrams in NMR pulse spectroscopy in the usual or the superoperator formalisms.

The Nobel Prize in Chemistry 1991
Richard R. Ernst

The Nobel Prize in Chemistry 1991

Nobel Prize Award Ceremony

Richard R. Ernst

Richard R. Ernst

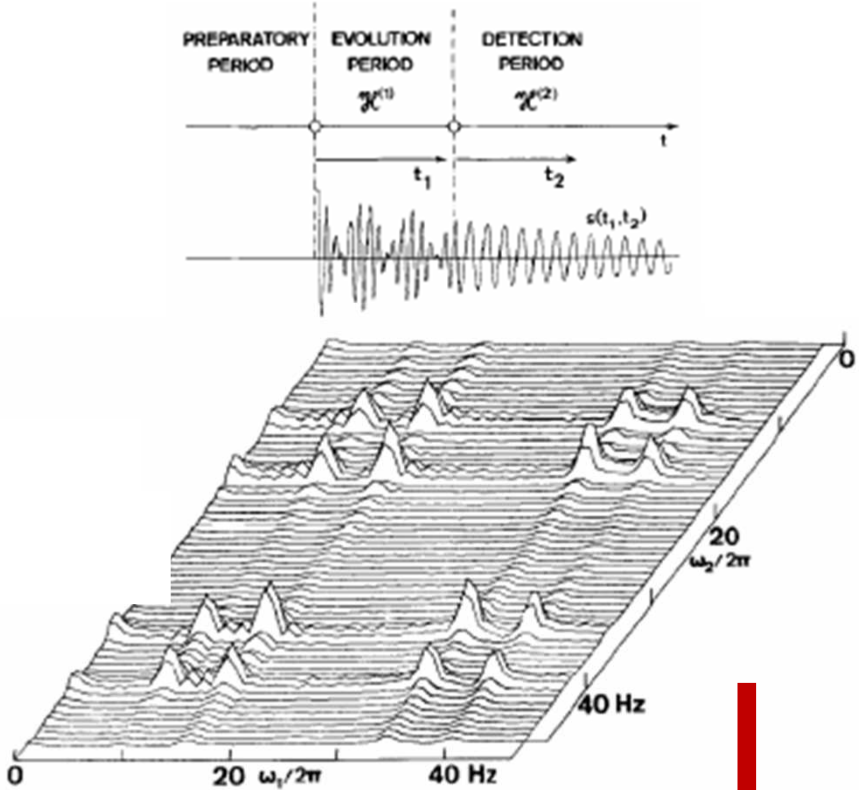
The Nobel Prize in Chemistry 1991 was awarded to Richard R. Ernst *"for his contributions to the development of the methodology of high resolution nuclear magnetic resonance (NMR) spectroscopy"*.

Two-dimensional spectroscopy. Application to nuclear magnetic resonance

W. P. Aue, E. Bartholdi, and R. R. Ernst

Laboratorium für physikalische Chemie, Eidgenössische Technische Hochschule, 8006 Zürich, Switzerland

(Received 13 November 1975)

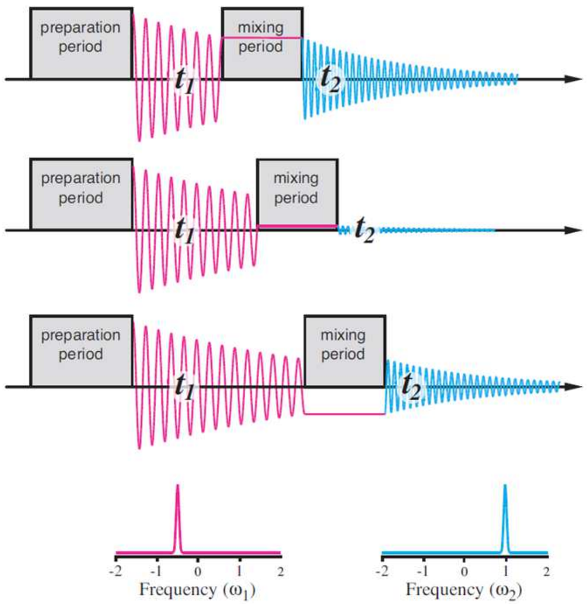


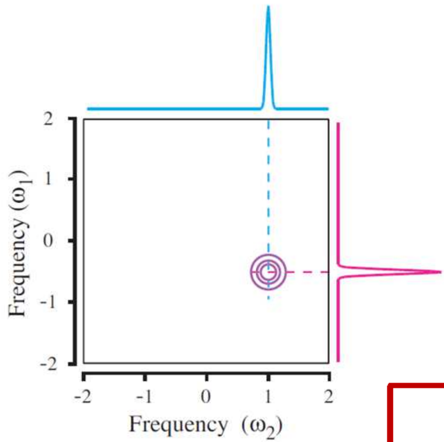
Discrete Fourier transform

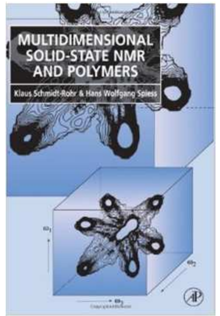
Uniform sampling

2D NMR

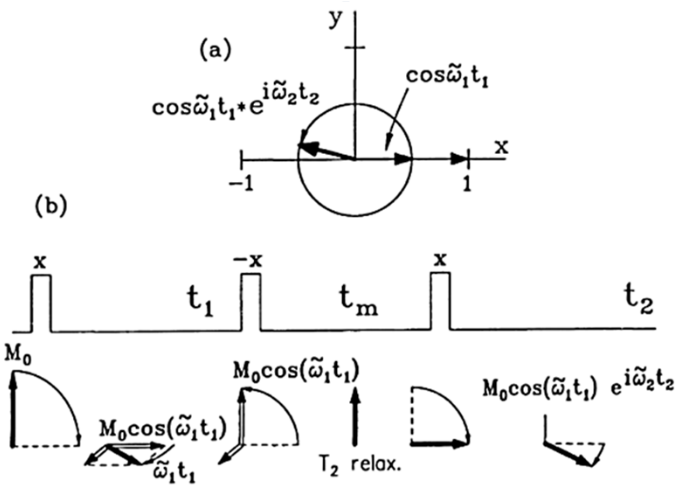
credits to: P. Grandinetti, NMR course, sept. 5, 2013



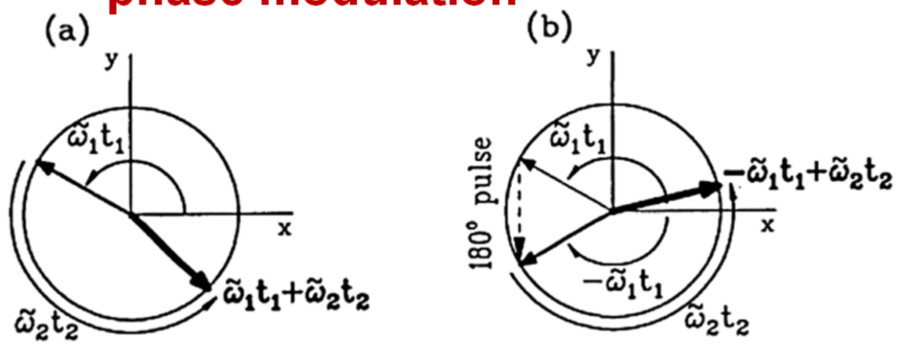




amplitude modulation

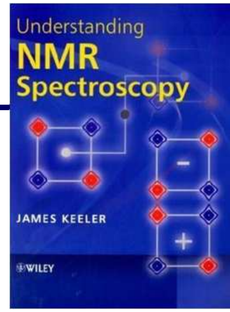


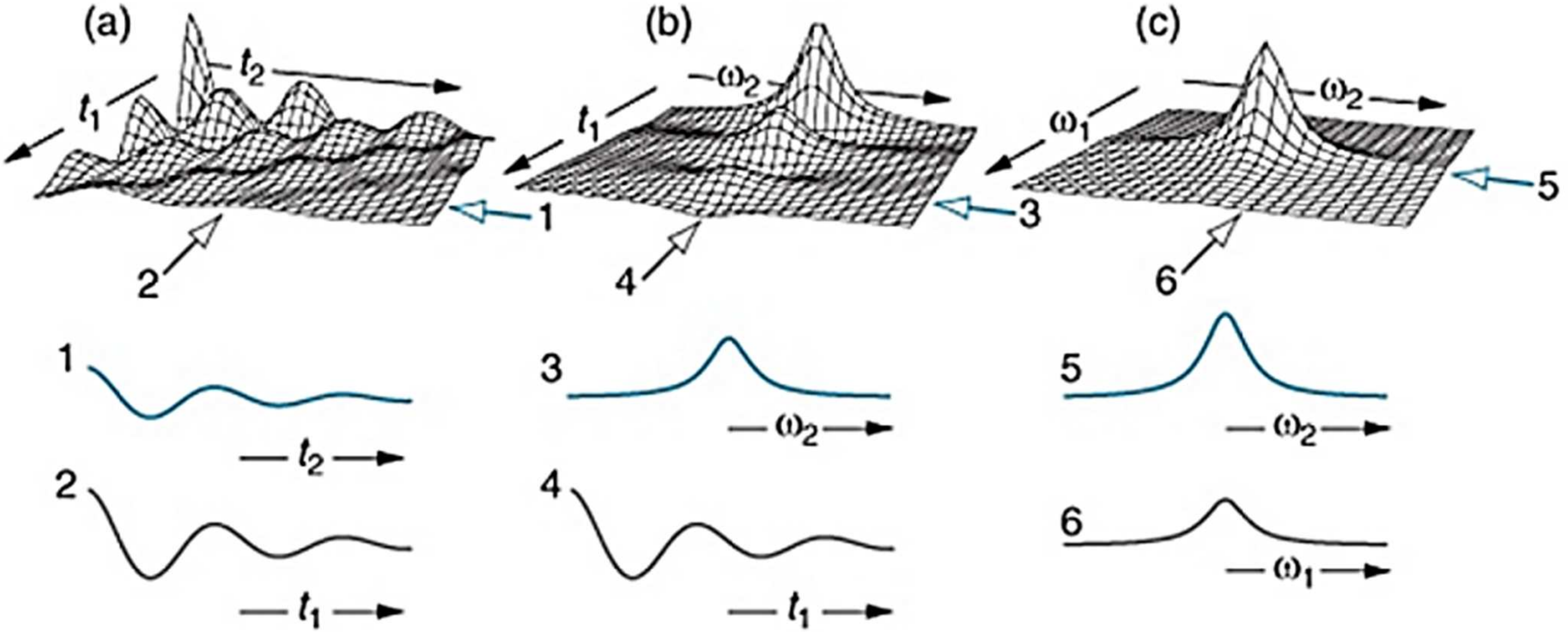
phase modulation



2D NMR – double FT

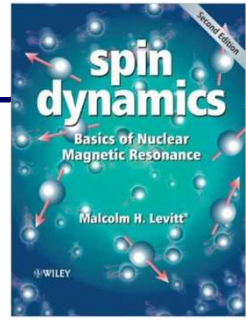
credits to



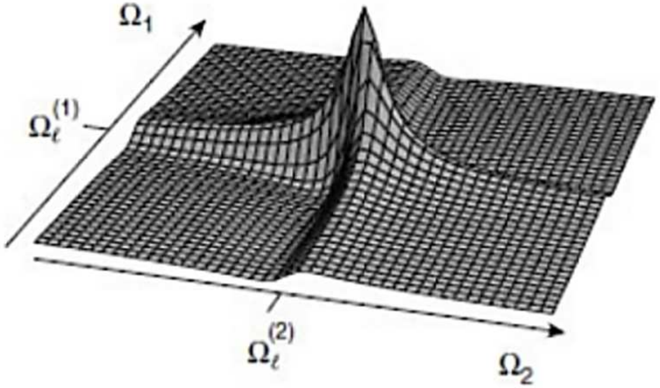


Pure absorption 2D spectra

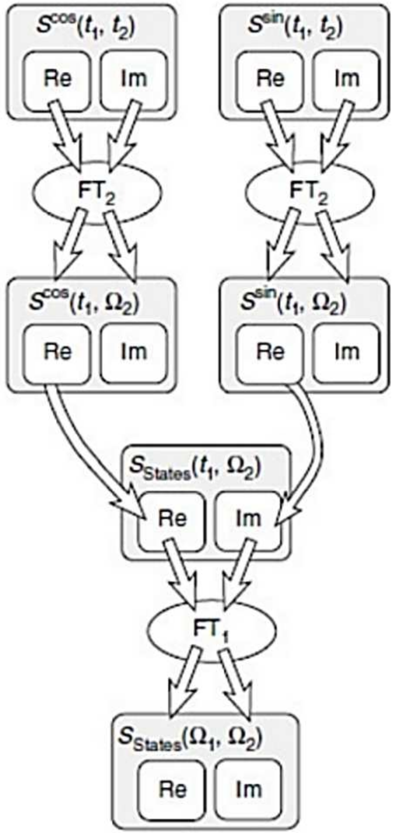
credits to



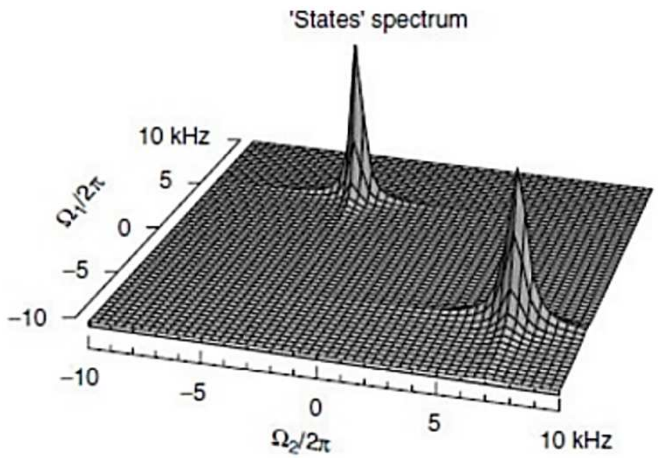
phase twist



States procedure

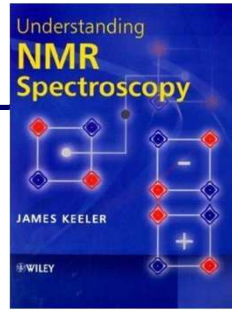


pure absorption mode

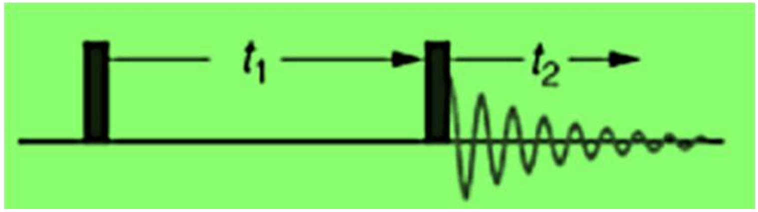


Essential 2D experiments

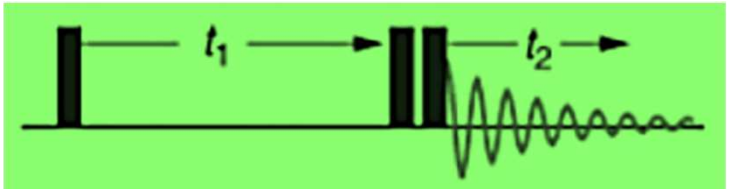
credits to

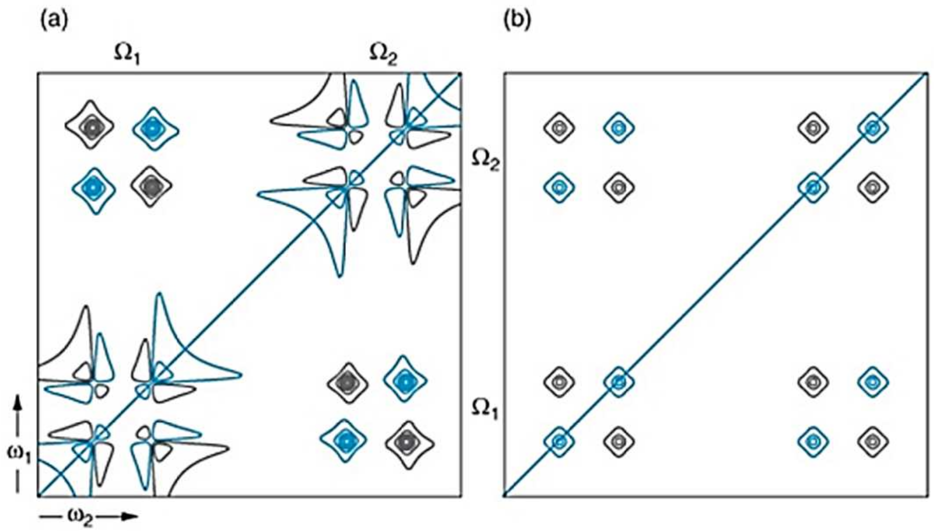


COSY

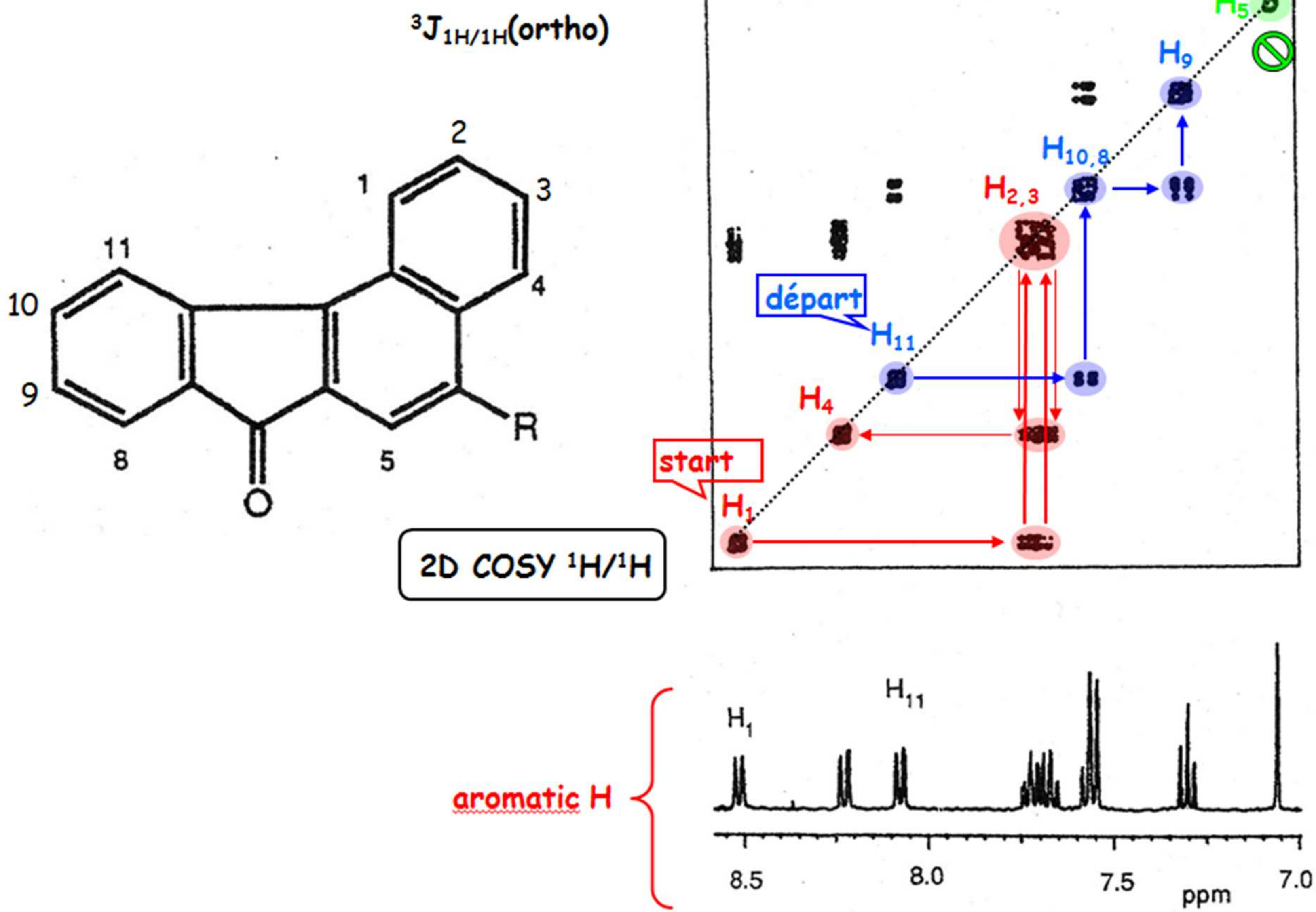


COSY DQF (double quantum filtered)



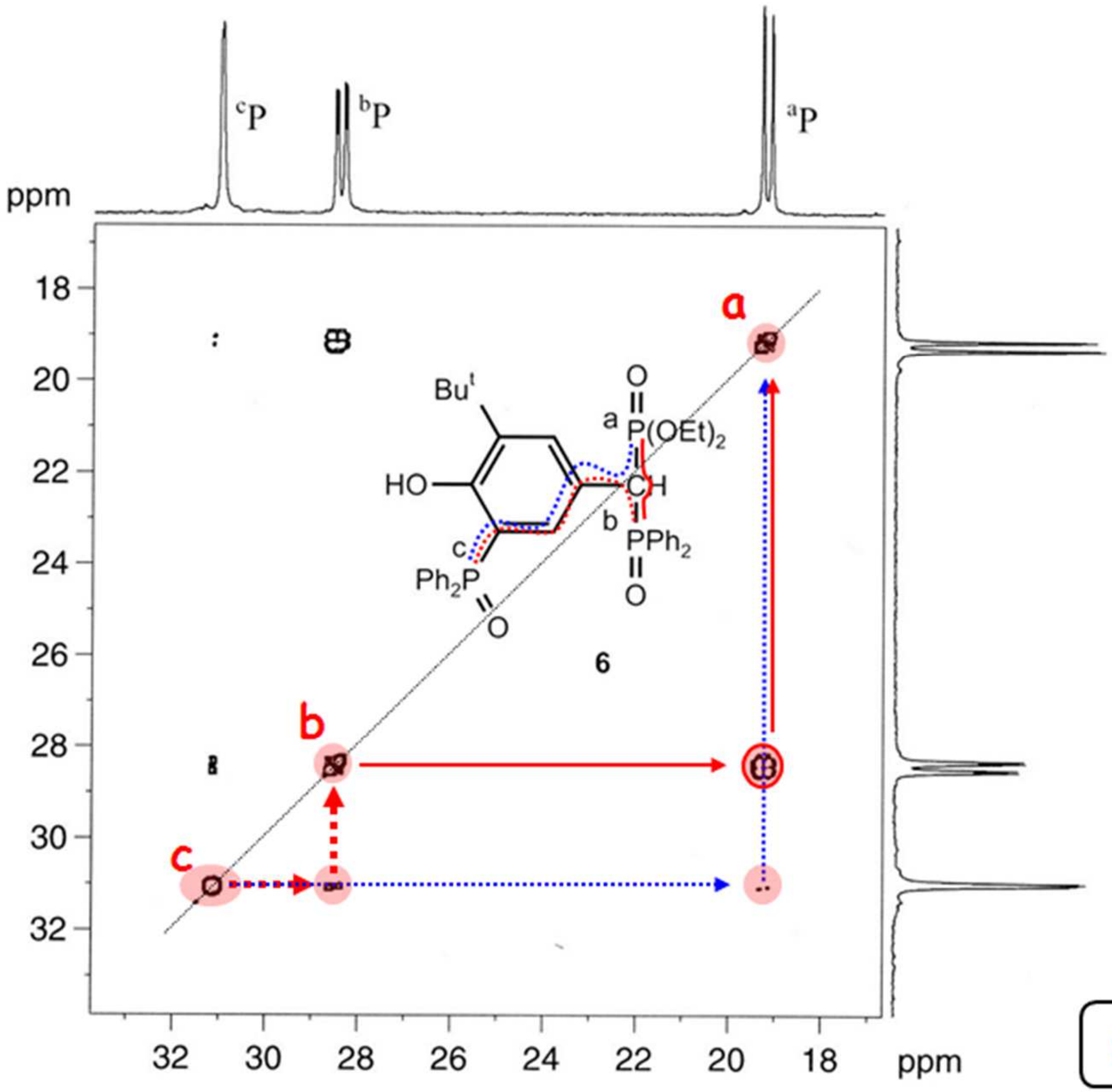


COSY



$^{3}J_{1H/1H}$(ortho)
1
2
3
4
5
8
9
10
11
R
O
2D COSY $^{1}H/^{1}H$
H_5
H_9
$H_{10,8}$
$H_{2,3}$
départ
H_{11}
H_4
start
H_1
aromatic H
H_1
H_{11}
8.5
8.0
7.5
7.0
ppm

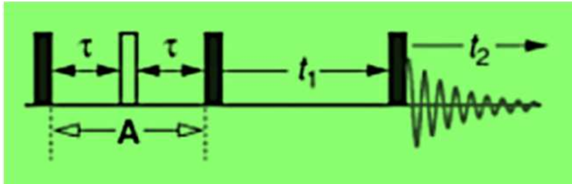
COSY



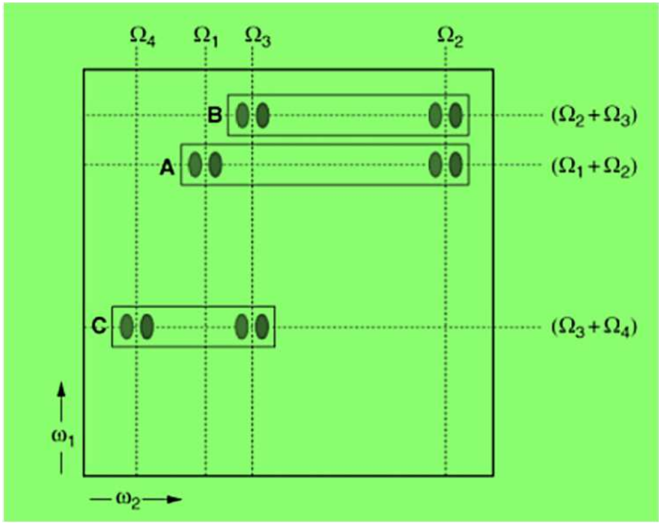
2D COSY $^{31}P/^{31}P$

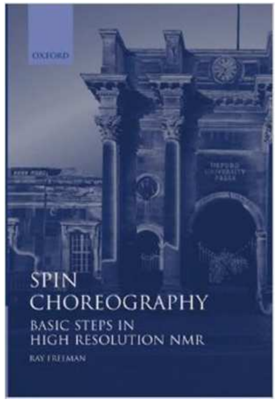
Essential 2D experiments

DQ spectroscopy

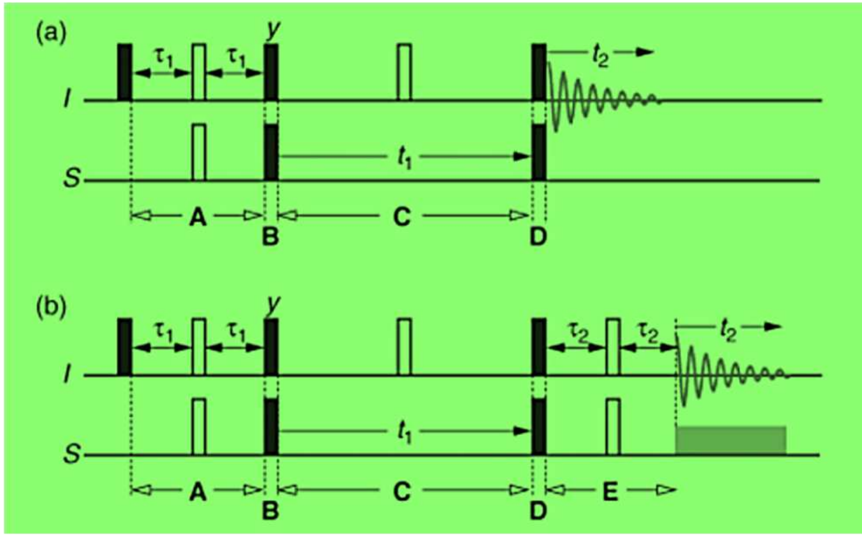


INADEQUATE

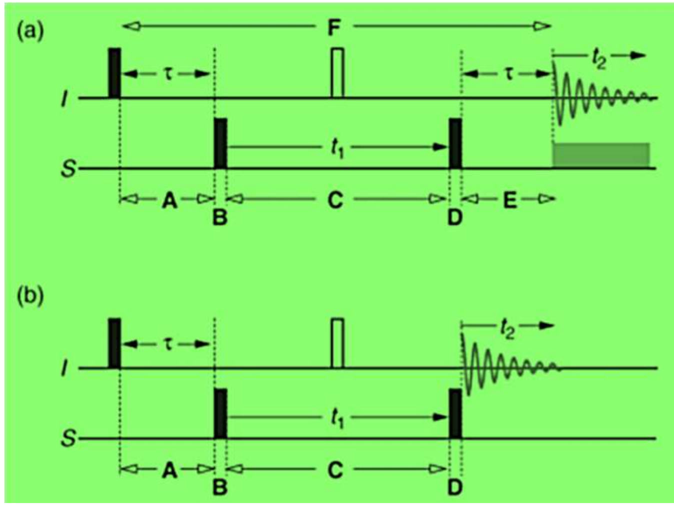




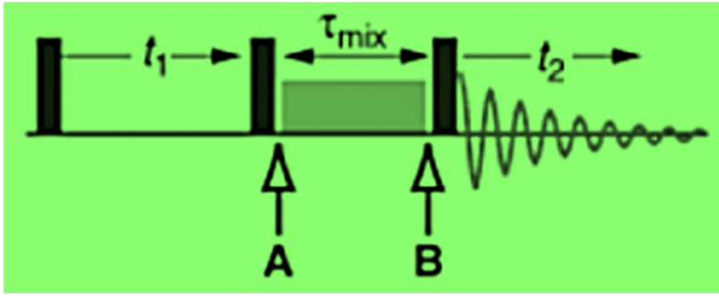
HSQC



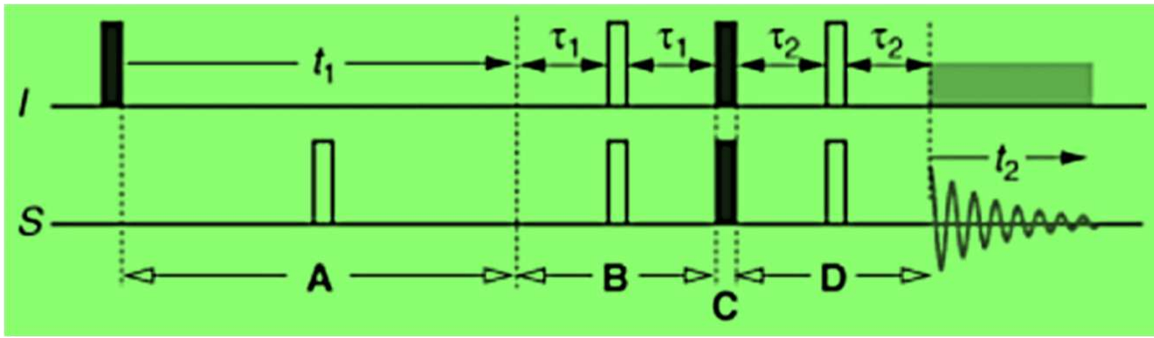
HMBC



TOCSY

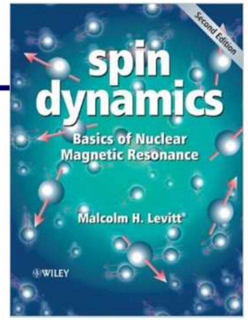


HETCOR

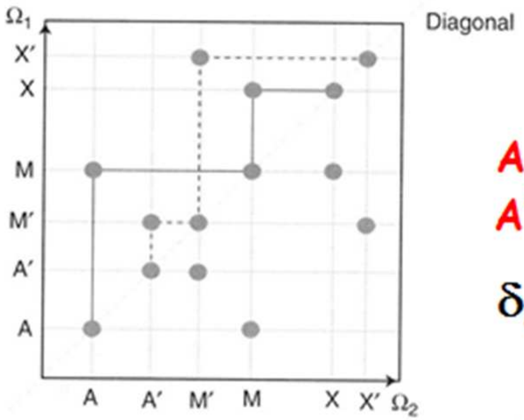


TOCSY

credits to



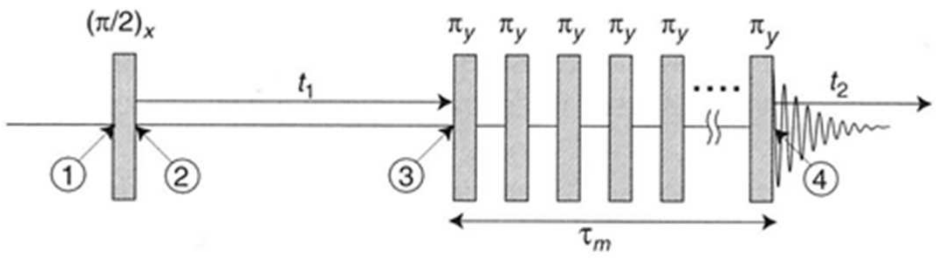
TOtal Correlation SpectroscopY



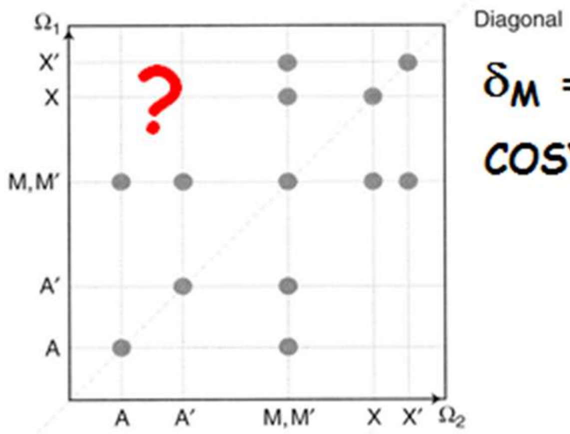
A-M-X
A'-M'-X'

$\delta_M \neq \delta_{M'}$

spin lock

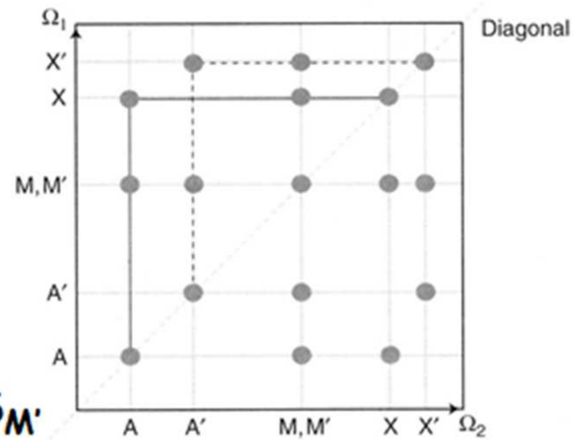


mixing time τ_m



$\delta_M = \delta_{M'}$

COSY

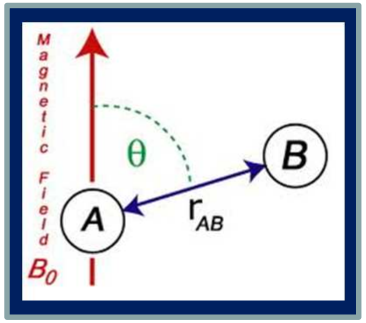


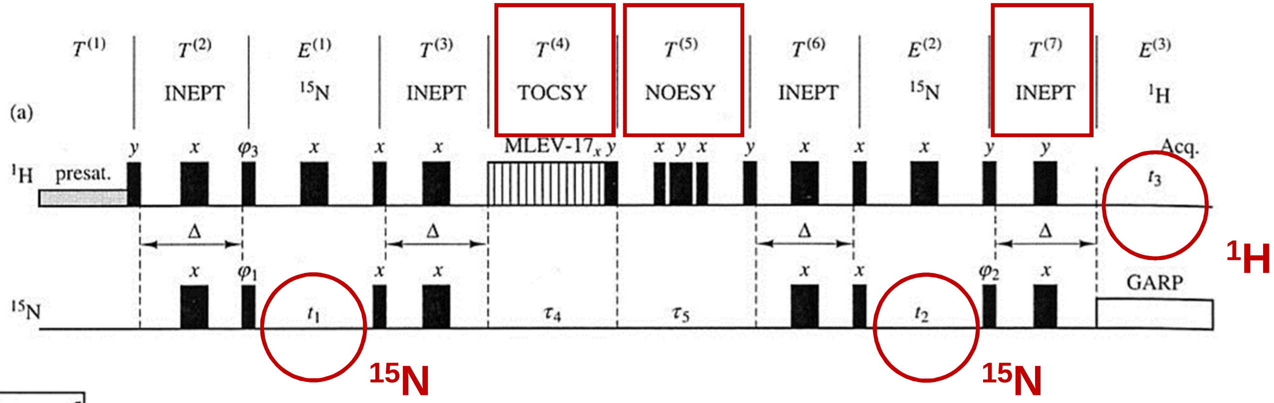
TOCSY

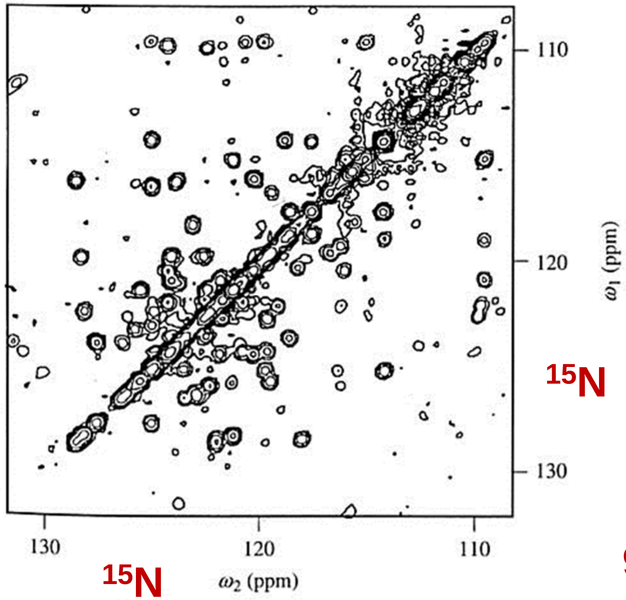
$\delta_M = \delta_{M'}$

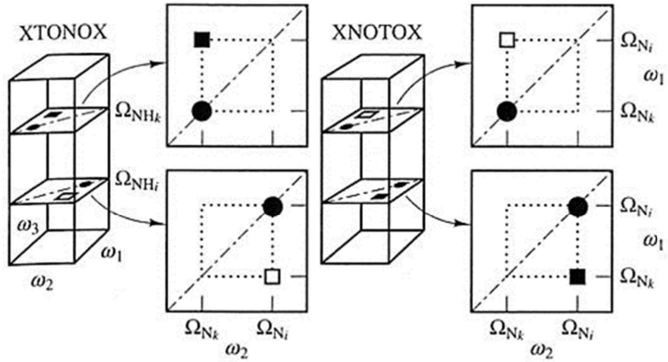
δ and J : selection, transfer, edition, correlation ... (COSY, INEPT, HETCOR...)

D : relaxation ... (NOESY...)

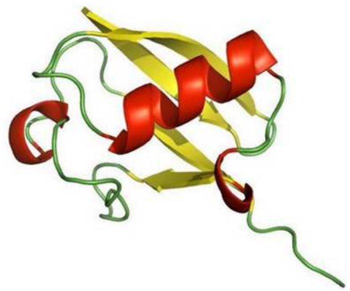








99% ^{15}N-human ubiquitin



Structural representation of human ubiquitin based on the crystal structure by Vijay-Kumar, S., Bugg, C.E. and Cook, W.J. (PDB-ID:1UBQ)

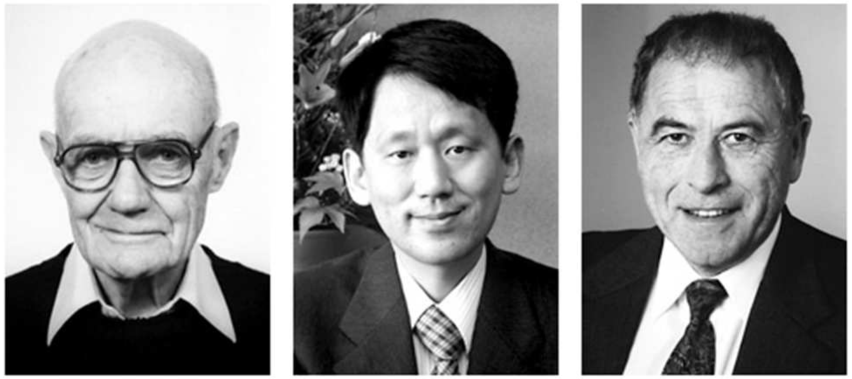
University of Cambridge

The Jackson Laboratory Research

NMR of proteins

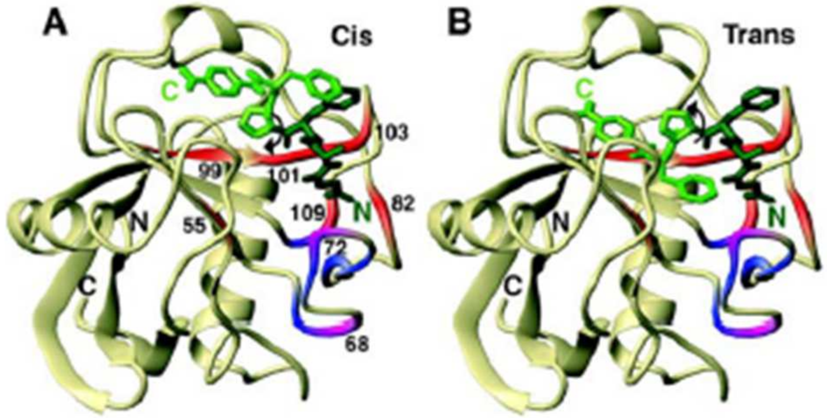
The Nobel Prize in Chemistry 2002
John B. Fenn, Koichi Tanaka, Kurt Wüthrich

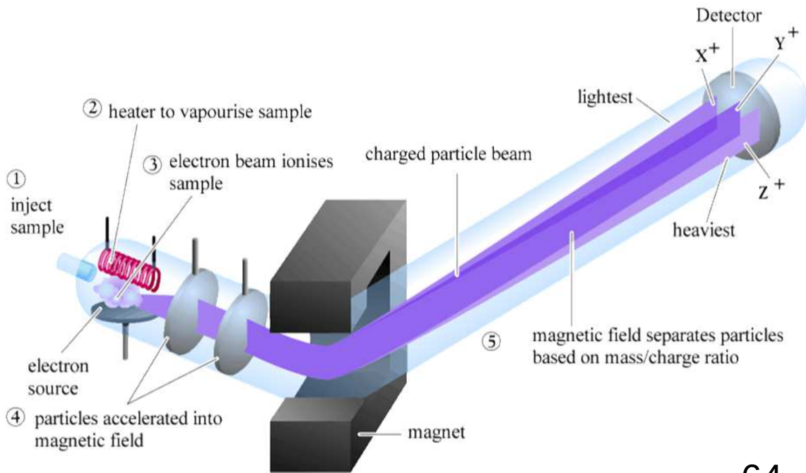
The Nobel Prize in Chemistry 2002
Nobel Prize Award Ceremony
John B. Fenn
Koichi Tanaka
Kurt Wüthrich



John B. Fenn | Koichi Tanaka | Kurt Wüthrich

The Nobel Prize in Chemistry 2002 was awarded *"for the development of methods for identification and structure analyses of biological macromolecules"* with one half jointly to John B. Fenn and Koichi Tanaka *"for their development of soft desorption ionisation methods for mass spectrometric analyses of biological macromolecules"* and the other half to Kurt Wüthrich *"for his development of nuclear magnetic resonance spectroscopy for determining the three-dimensional structure of biological macromolecules in solution"*.

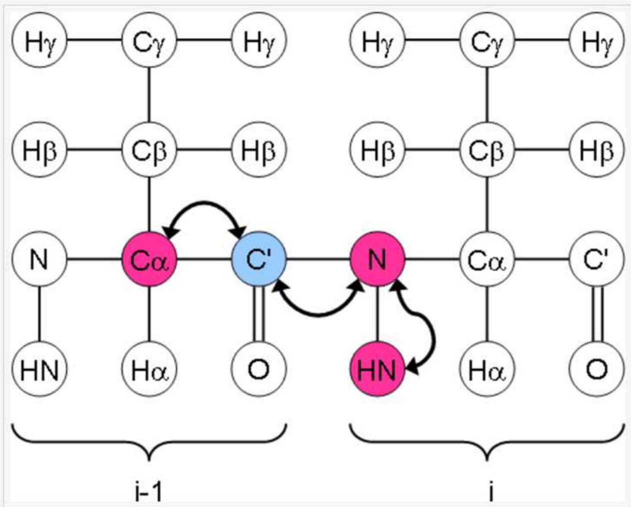




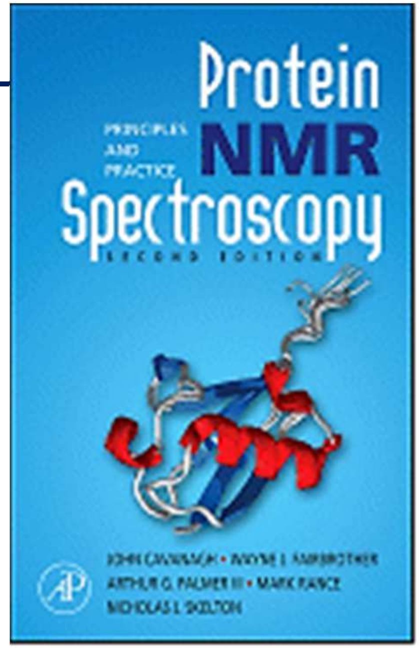
www.mhhe.com/physsci/chemistry/carey/student/

NMR of proteins

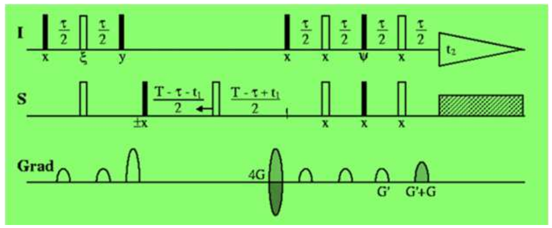
- isotope labeling
- restraints
- modeling
- structure …



1H-15N HSQC
HNCO
HN(CA)CO
HNCA
HN(CO)CA
CBCA(CO)NH / HN(CO)CACB
CBCANH / HNCACB
CC(CO)NH
H(CCO)NH
HBHA(CO)NH
HCCH-TOCSY
HCCH-COSY
15N-TOCSY-HSQC
13C-HMQC
1H-1H NOESY
15N-NOESY-HSQC
13C-NOESY-HSQC
13C-HMQC-NOESY



TROSY



HN(CO)CA

References:
A. Bax and M. Ikura (1991) *J. Biomol. NMR* **1** 99-104. (Link to Article)
S. Grzesiek and A. Bax (1992) *J. Magn. Reson.* **96** 432-440. (Link to Article)

Minimum labelling: ^{15}N, ^{13}C

Dimensions: 3

Methods Mol Biol. 2012;831:133-40. doi: 10.1007/978-1-61779-480-3_8.

NMR studies of large protein systems.

Tzeng SR[1], Pai MT, Kalodimos CG.

Author information

Abstract
Over the recent years, there has been increased interest in applying NMR spectroscopy for the characterization of proteins and protein complexes of large molecular weight. The combination of multidimensional NMR, novel pulse sequences allowing for the selection of slowly relaxing coherence pathways, and the development of a range of labeling techniques has enabled high-resolution NMR analyses of supramolecular systems of even megadalton size. Here, we describe how NMR can be used to obtain structural information in large systems by using as an example the recent structure determination of SecA ATPase (204 kDa) in complex with a signal peptide.

Applications: relaxation and dynamics of proteins

local flexibility ⌂

relaxation T_1, T_2 ⌂

collective motions ⌂

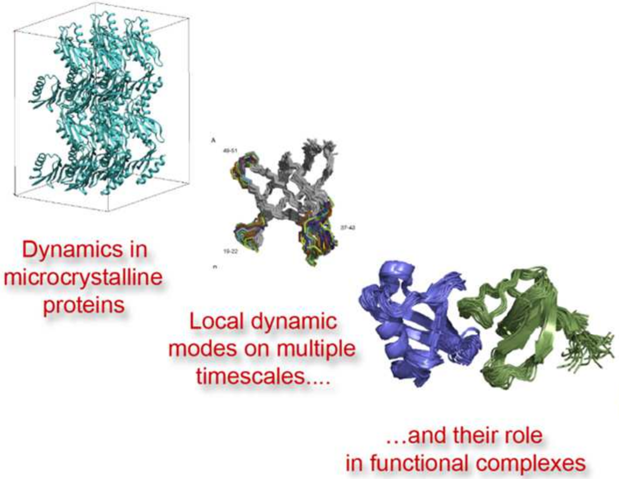
relaxation $T_{1\rho}$, CPMG ⌂

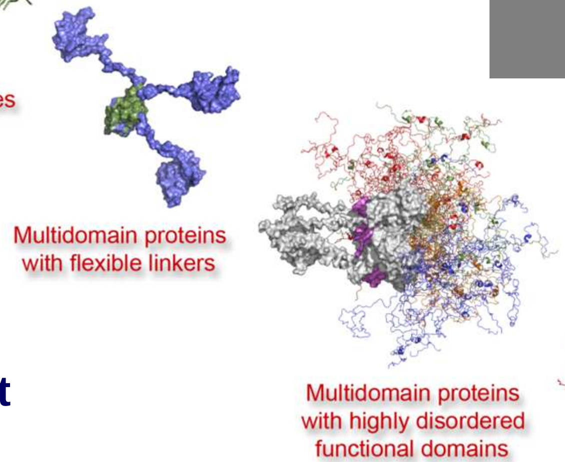
lineshape analysis ⌂

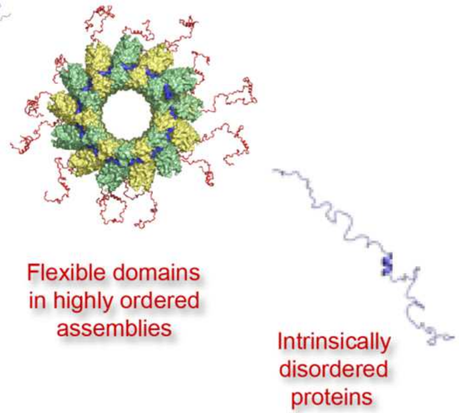
NOESY ⌂

H/D exchange ⌂

labeling schemes … ⌂





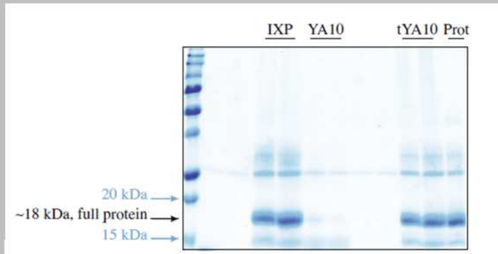


- ⌂ **proteins ARE dynamic**
- ⌂ **ps to s timescales**
- → **static models are not sufficient**
- ⌂ **conformational flexibility**
- ⌂ **folding**

…

www.ibs.fr/groups/protein-dynamics-and-flexibility

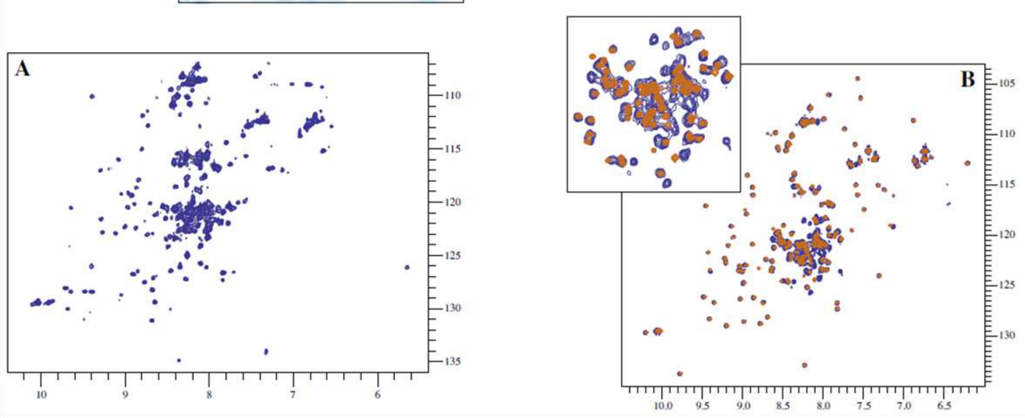
Applications: relaxation and dynamics of proteins



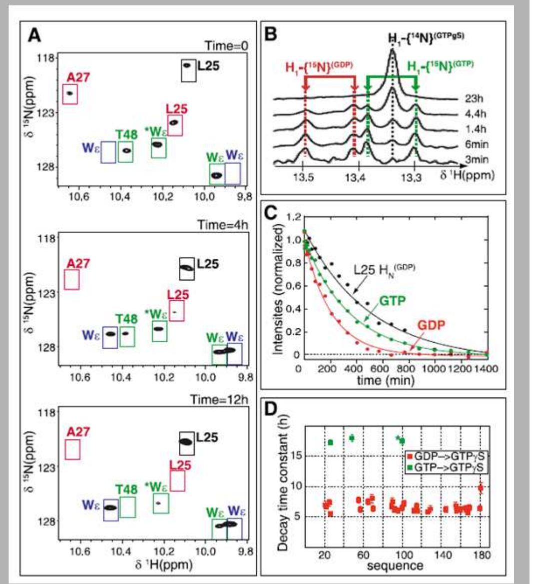
Robust and low cost uniform ^{15}N-labeling of proteins expressed in *Drosophila* S2 cells and *Spodoptera frugiperda* Sf9 cells for NMR applications

Annalisa Meola[a,b,c,1], Célia Deville[a,1], Scott A. Jeffers[b,c], Pablo Guardado-Calvo[b,c], Ieva Vasiliauskaite[b,c], Christina Sizun[a], Christine Girard-Blanc[d], Christian Malosse[e,f], Carine van Heijenoort[a], Julia Chamot-Rooke[e,f], Thomas Krey[b,c], Eric Guittet[a], Stéphane Pêtres[d], Félix A. Rey[b,c], François Bontems[a,b,c,*]

J. Struct. Biol. *188* (**2014**) 71-78



Carine Van Heijenoort, ICSN, Gif/Yvette, France



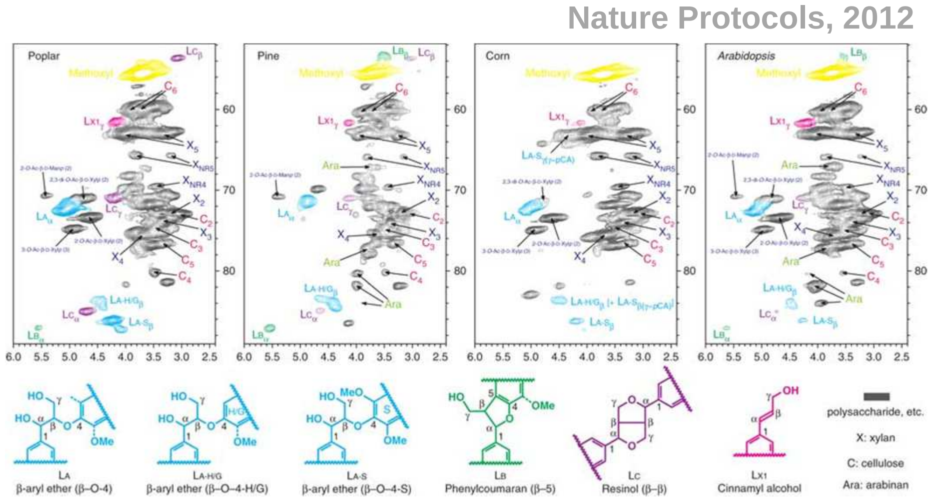
Insight into the Role of Dynamics in the Conformational Switch of the Small GTP-binding Protein Arf1*

Received for publication, April 15, 2010, and in revised form, September 14, 2010 Published, JBC Papers in Press, September 21, 2010, DOI 10.1074/jbc.M110.134445

Vanessa Buosi[‡], Jean-Pierre Placial[‡], Jean-Louis Leroy[‡], Jacqueline Cherfils[§1], Éric Guittet[‡2], and Carine van Heijenoort[‡3]

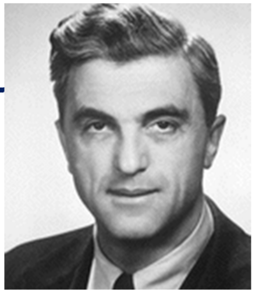
THE JOURNAL OF BIOLOGICAL CHEMISTRY VOL. 285, NO. 49, pp. 37987–37994, December 3, 2010

Outline



- **Nuclear spin – the NMR experiment**
- **Mathematical treatment of NMR**
- **Multidimensional NMR**
- **Relaxation**
- **Solid State NMR**
- **Gradients and imaging**

Bloch equations (Phys. Rev. 70, 1946, 460-474)



in the rotating frame T

$$\frac{d^*\mathbf{M}(t)}{dt} = \boldsymbol{\omega}_{\text{eff}}(t) \times \mathbf{M}(t) - [\mathbf{R}]\{\mathbf{M}(t) - \mathbf{M}_{\text{eq}}\},$$

$$\boldsymbol{\omega}_{\text{eff}}(t) = \boldsymbol{\omega}(t) - \boldsymbol{\omega}_{\text{rot}}.$$

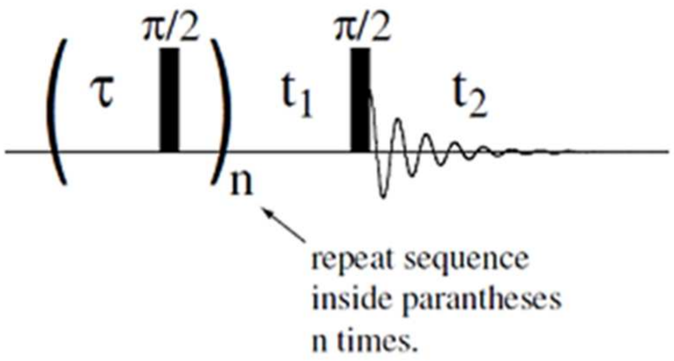
$$\begin{pmatrix} M_x^*(t) \\ M_y^*(t) \\ M_z^*(t) \end{pmatrix} = \begin{pmatrix} \left[M_x^*(0)\cos\Omega t - M_y^*(0)\sin\Omega t\right] e^{-t/T_2} \\ \left[M_y^*(0)\cos\Omega t + M_x^*(0)\sin\Omega t\right] e^{-t/T_2} \\ M_z^*(0)e^{-t/T_1} + M_{\text{eq}}(1 - e^{-t/T_1}) \end{pmatrix}$$

limitations of the Bloch equations

credits to: P. Grandinetti, NMR course, sept. 5, 2013

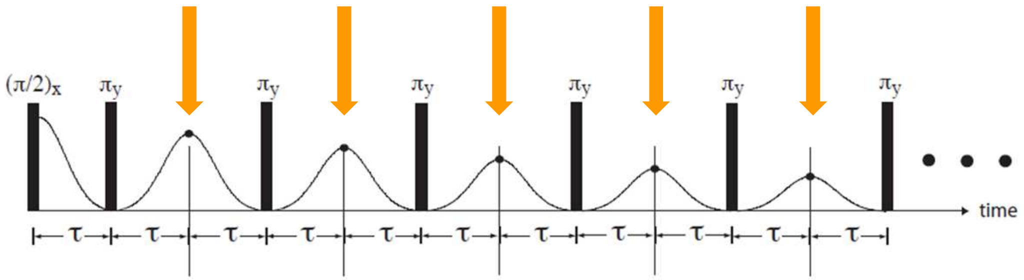
Measurements of T_1 and T_2

saturation recovery experiment (T_1)



$$M_z(t_1) = M_{eq}(1 - e^{-t_1/T_1}).$$

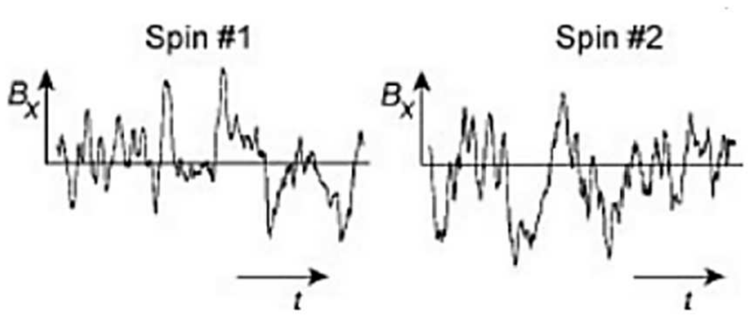
Carr–Purcell Meiboom–Gill (T_2)



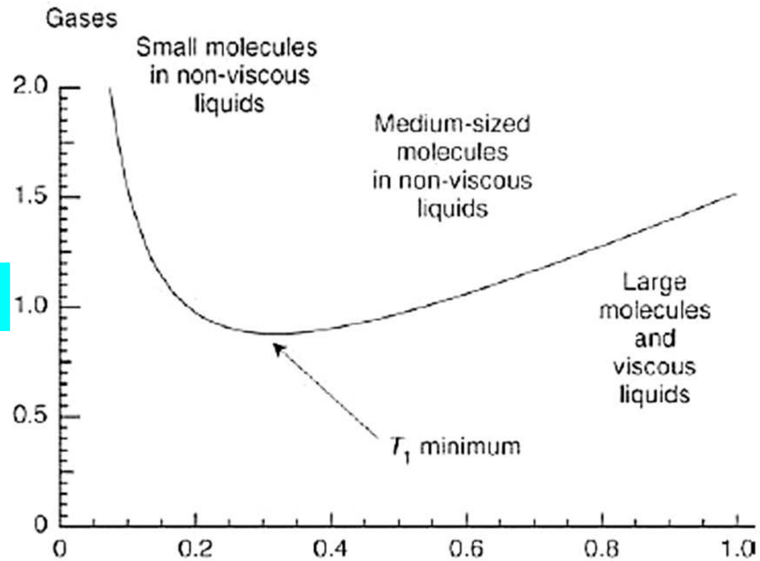
In principle one can obtain T_2 by taking half the inverse of the full width at half height of a resonance in an NMR spectrum. Unfortunately, the line widths of resonances in NMR are often dominated by the inhomogeneities in the magnetic field rather than T_2.

Introduction to relaxation theory

random field relaxation – fluctuating fields



fluctuations of B_x at two different spins



T_1 (s)

τ_C (ns)

B_0 = 11.7 T

^{1}H

$\langle B_x^2 \rangle = 10^{-8}\ T^2$

autocorrelation functions and τ_C

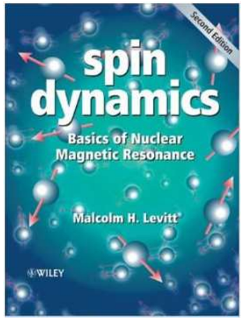
- autocorrelation function $$G(\tau) = \langle B_x(t)\, B_x(t+\tau) \rangle \neq 0$$
- assumption $$G(\tau) = \langle B_x^2 \rangle\, e^{-|\tau| / \tau_C}$$
- normalized spectral density

FT

$$\mathcal{J}(\omega) = \mathcal{A}(\omega; 0, \tau_c^{-1}) = \frac{\tau_c}{1+\omega^2\tau_c^2}$$

credits to:

EUROMAR
Zürich, 2014
Introduction to Relaxation Theory
James Keeler



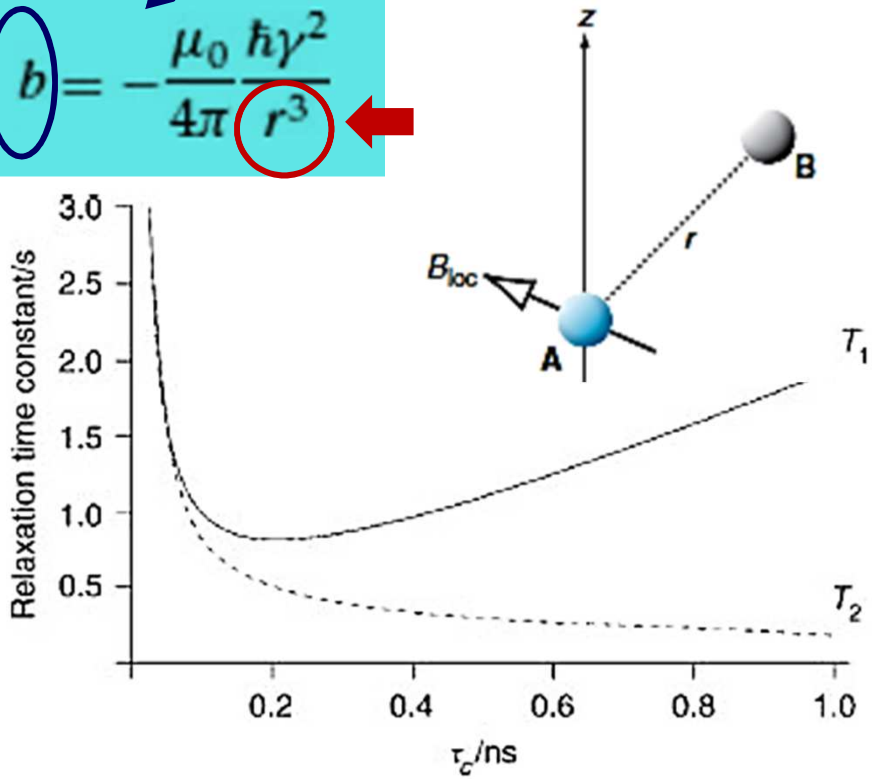
BPP theory (Bloembergen, Purcell, Pound, *Phys .Rev.* 1948)

ex.: dipole–dipole relaxation

$$T_2^{-1} = \frac{3}{20} b^2 \{3\mathcal{J}(0) + 5\mathcal{J}(\omega^0) + 2\mathcal{J}(2\omega^0)\}$$

$$T_1^{-1} = \frac{3}{10} b^2 \{\mathcal{J}(\omega^0) + 4\mathcal{J}(2\omega^0)\}$$

$$b = -\frac{\mu_0}{4\pi}\frac{\hbar\gamma^2}{r^3}$$



The Nobel Prize in Physics 1952
Felix Bloch, E. M. Purcell

The Nobel Prize in Physics 1952
Felix Bloch
E. M. Purcell


Felix Bloch | Edward Mills Purcell

The Nobel Prize in Physics 1952 was awarded jointly to Felix Bloch and Edward Mills Purcell *"for their development of new methods for nuclear magnetic precision measurements and discoveries in connection therewith"*

The Nobel Prize in Physics 1981



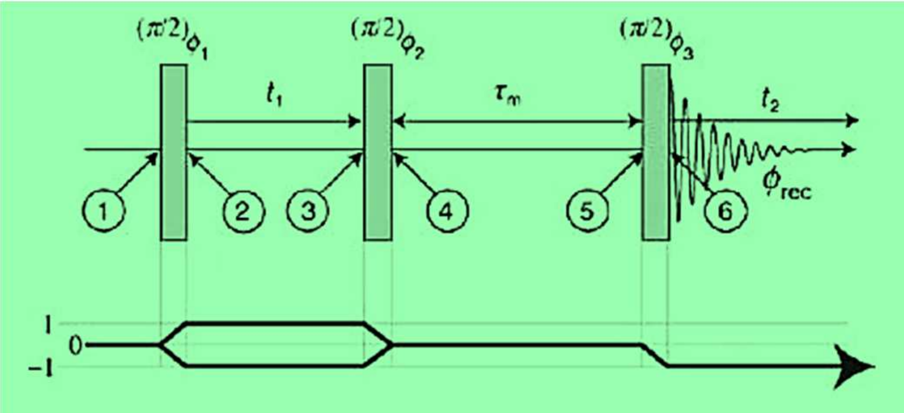
Nicolaas Bloembergen
Prize share: 1/4

Arthur Leonard Schawlow
Prize share: 1/4

Kai M. Siegbahn
Prize share: 1/2

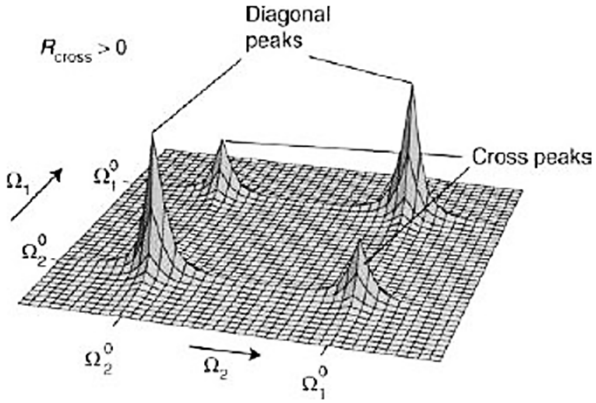
The Nobel Prize in Physics 1981 was divided, one half jointly to Nicolaas Bloembergen and Arthur Leonard Schawlow *"for their contribution to the development of laser spectroscopy"* and the other half to Kai M. Siegbahn *"for his contribution to the development of high-resolution electron spectroscopy"*.

NOESY… finally



Solomon equations

$$\frac{d}{dt}\begin{pmatrix}\langle \hat{I}_{1z}\rangle \\ \langle \hat{I}_{2z}\rangle\end{pmatrix} = \begin{pmatrix}-R_{auto} & R_{cross} \\ R_{cross} & -R_{auto}\end{pmatrix}\begin{pmatrix}\langle \hat{I}_{1z}\rangle \\ \langle \hat{I}_{2z}\rangle\end{pmatrix}$$



$a_{cross} \sim r^{-6}$

Progress in Nuclear Magnetic Resonance Spectroscopy

Volume 78, April 2014, Pages 1–46

The nuclear Overhauser effect from a quantitative perspective

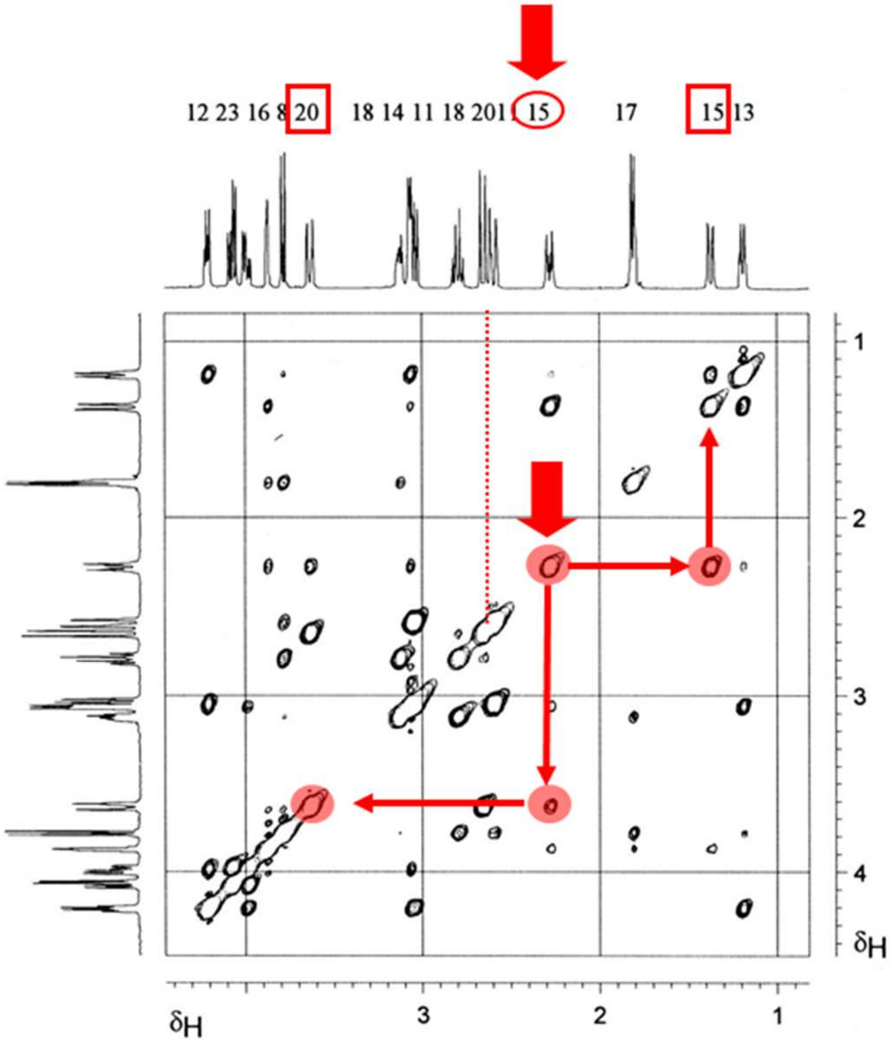
Beat Vögeli

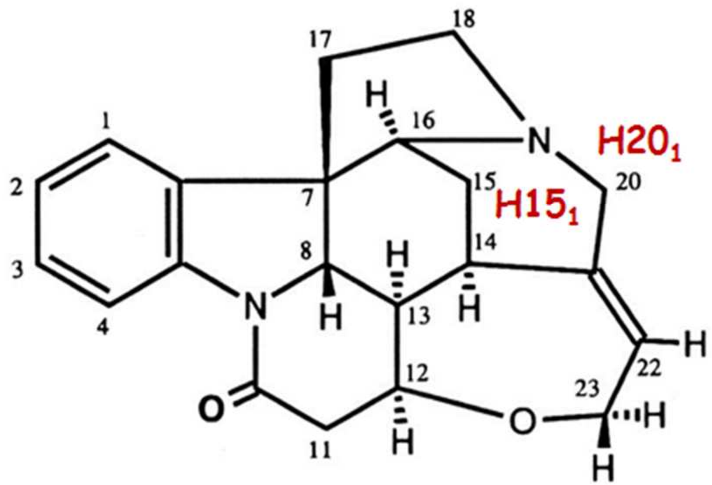
Abstract

The nuclear Overhauser enhancement or effect (NOE) is the most important measure in liquid-state NMR with macromolecules. Thus, the NOE is the subject of numerous reviews and books. Here, the NOE is revisited in light of our recently introduced measurements of exact nuclear Overhauser enhancements (eNOEs), which enabled the determination of multiple-state 3D protein structures. This review encompasses all relevant facets from the theoretical considerations to the use of eNOEs in multiple-state structure calculation. Important aspects include a detailed presentation of the relaxation theory relevant for the nuclear Overhauser effect, the estimation of the correction for spin diffusion, the experimental determination of the eNOEs, the conversion of eNOE rates into distances and validation of their quality, the distance-restraint classification and the protocols for calculation of structures and ensembles.

An example

Nuclear Overhauser Effect SpectroscopY



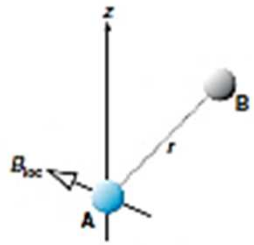


Other relaxation mecanisms

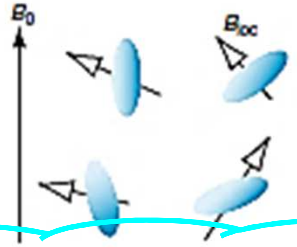
$$\frac{1}{T_1} = \left(\frac{1}{T_1}\right)_{\text{paramagnetic}} + \left(\frac{1}{T_1}\right)_{\text{quadrupole}} + \left(\frac{1}{T_1}\right)_{\text{dipole}} + \left(\frac{1}{T_1}\right)_{\text{chem. shift}} + \cdots .$$

Cross relaxation

- dipolar: local field goes as $\gamma_1 \gamma_2 / r^3$

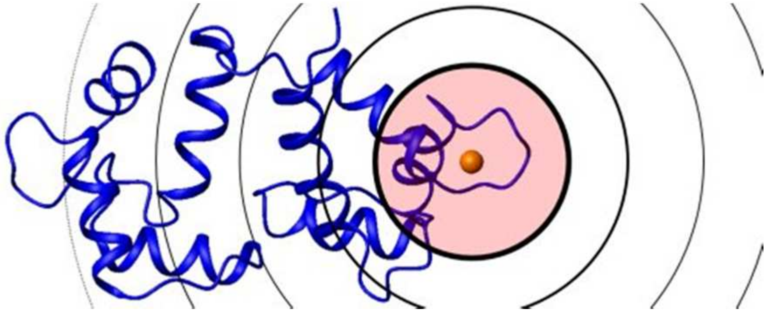


- chemical shift anisotropy (CSA): local field goes as B_0 and typically depends on shift range



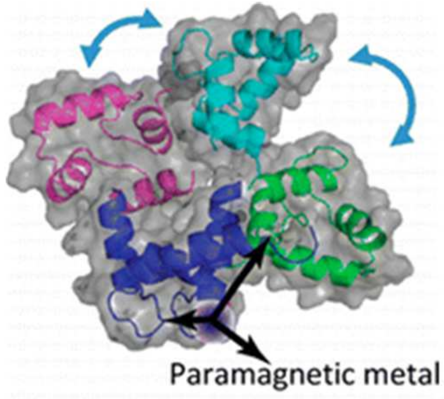
- paramagnetic species (e.g. dissolved oxygen)

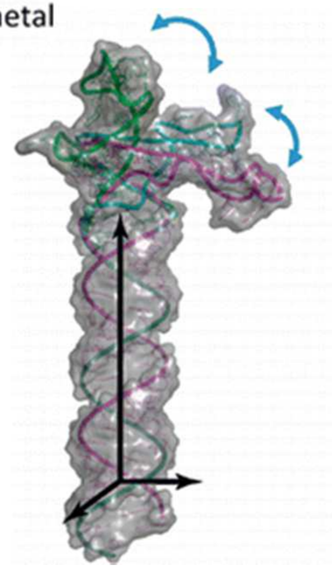
Applications: electronic paramagnetic relaxation for biological macromolecules dynamics



www.cerm.unifi.it/paramagnetism-assisted-nmr

Acc. Chem. Res., **2014**, *47* (10), pp 3118–3126





- ⌂ restraints for protein structure determination
- ⌂ probe/nucleus distance
- ⌂ dynamics
- ⌂ EPR & NMR

…

paramagnetic ion in a molecule ⌂

paramagnetic tag ⌂

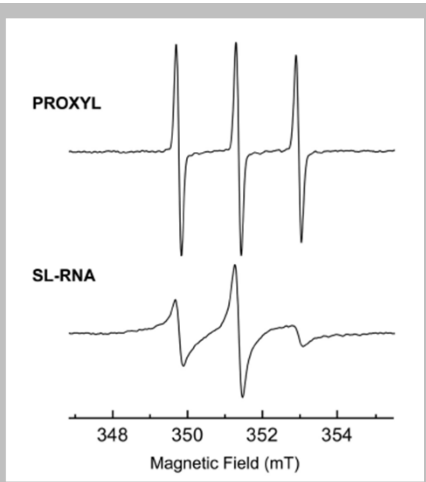
pseudocontact shift ⌂

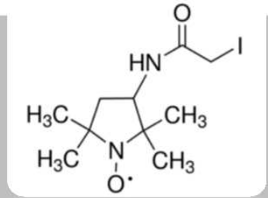
residual dipolar couplings ⌂

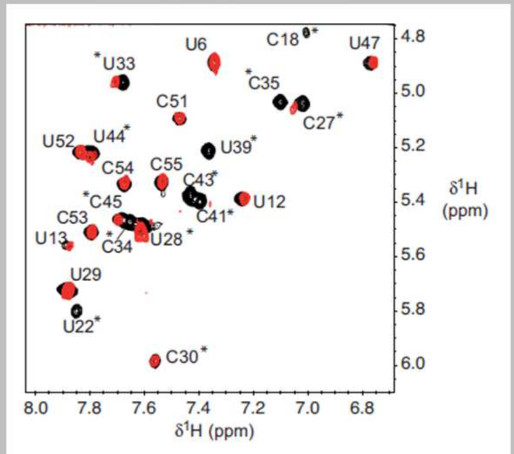
paramagnetic relaxation ⌂

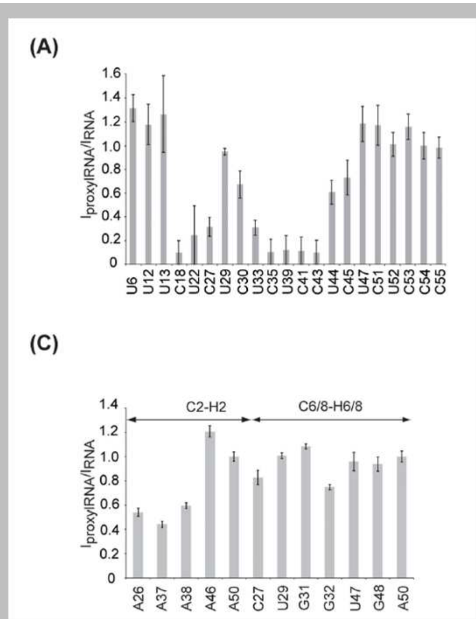
… ⌂

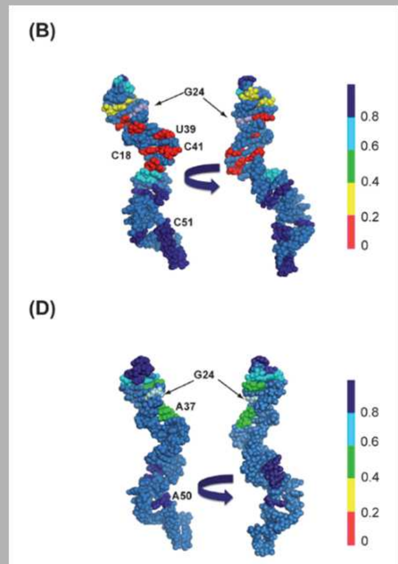
Applications: electronic paramagnetic relaxation for biological macromolecules dynamics











Bruno Kieffer, IGBMC, Strasbourg, France

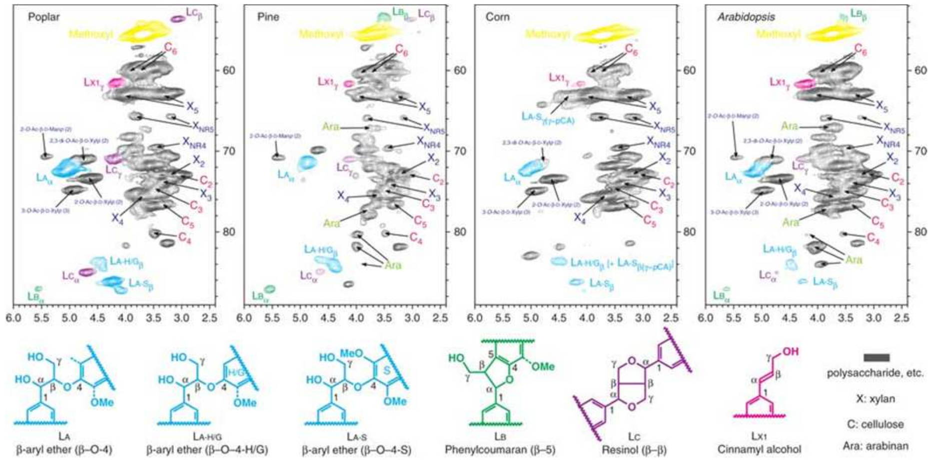
A fully enzymatic method for site-directed spin labeling of long RNA

Isabelle Lebars[1,*], Bertrand Vileno[2], Sarah Bourbigot[1], Philippe Turek[2], Philippe Wolff[3,4] and Bruno Kieffer[1]

Nucleic Acids Research, 2014, Vol. 42, No. 15 ***e117***
doi: 10.1093/nar/gku553

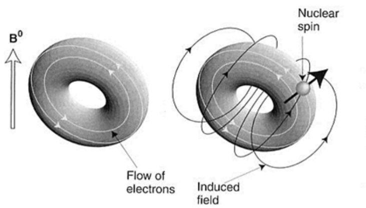
Outline

Nature Protocols, 2012

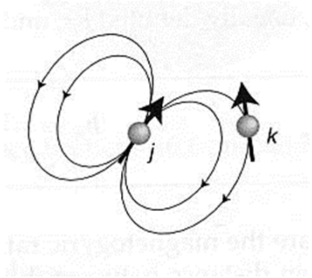


- **Nuclear spin – the NMR experiment**
- **Mathematical treatment of NMR**
- **Multidimensional NMR**
- **Relaxation**
- **Solid State NMR**
- **Gradients and imaging**

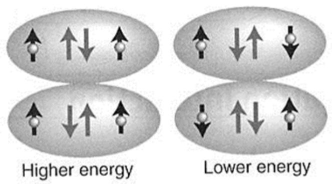
Internal interactions



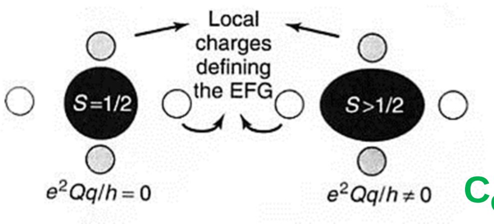
chemical shift : δ



dipolar coupling : D



indirect coupling : J



$C_Q \neq 0$

quadrupolar interaction (I > ½)

Levitt, Spin dynamics, 2002.

Frydman, Encyclopedia of NMR, supp. Vol., 263.

mathematical treatment

$$\hat{\mathcal{H}}_{\text{int}} = \hbar \hat{\boldsymbol{I}} \cdot \mathbf{A} \cdot \hat{X} = \hbar (\hat{I}_x \quad \hat{I}_y \quad \hat{I}_z) \begin{pmatrix} A_{xx} & A_{xy} & A_{xz} \\ A_{yx} & A_{yy} & A_{yz} \\ A_{zx} & A_{zy} & A_{zz} \end{pmatrix} \begin{pmatrix} \hat{X}_x \\ \hat{X}_y \\ \hat{X}_z \end{pmatrix}$$

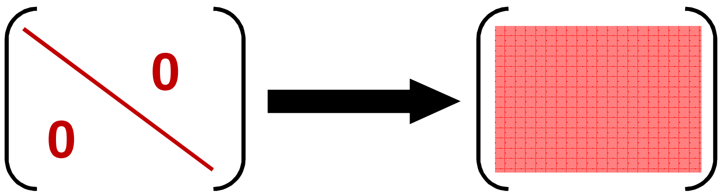
(CS, D, Q...)

nuclear spin operator

A: the interaction
second rank tensor
(assumed)

other spin operator or B_0...

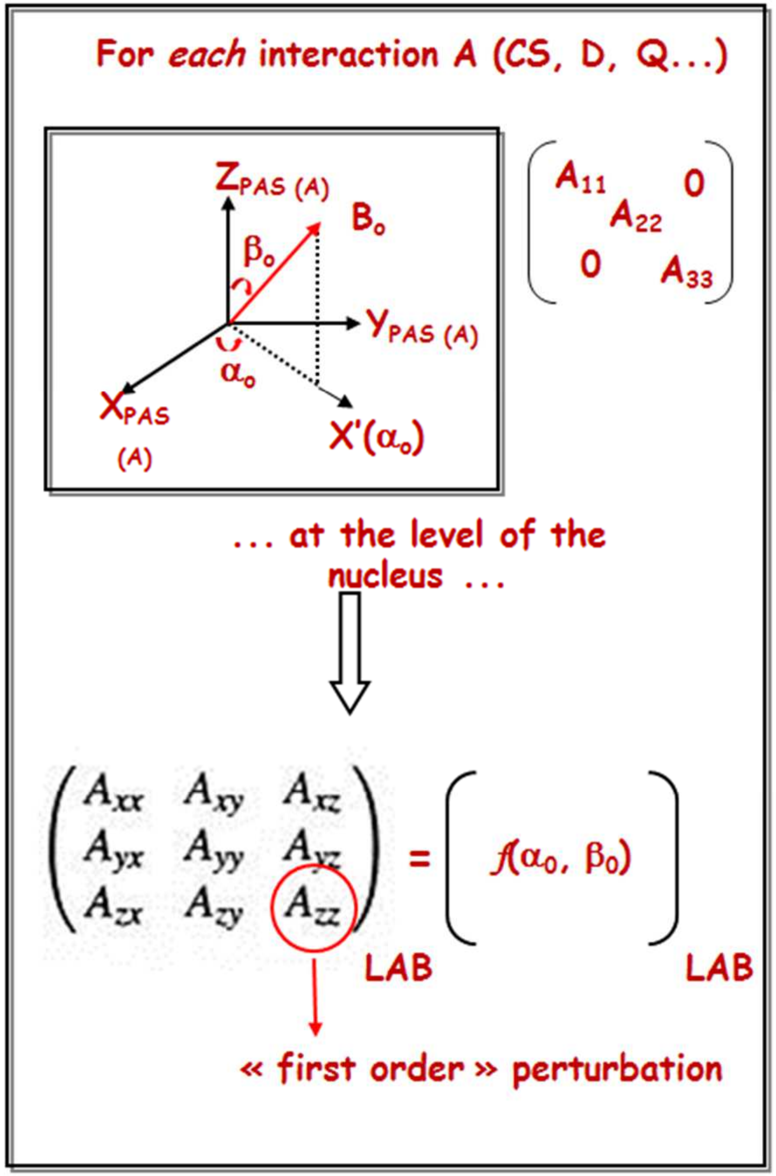
anisotropy: why ?

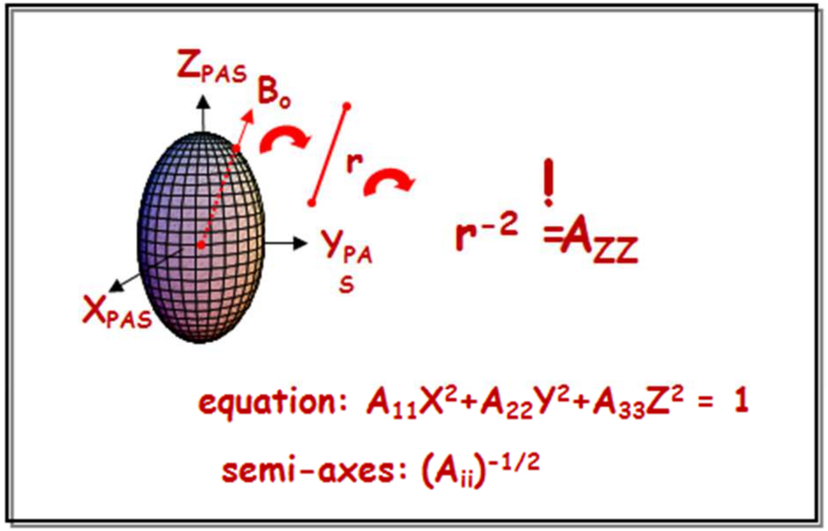


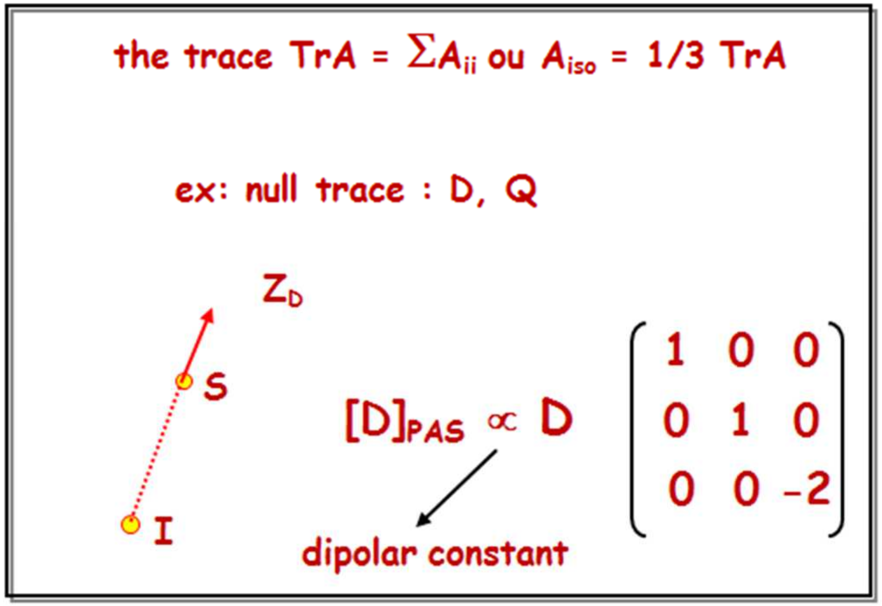
diagonal in the PAS
(Principal Axes System)

LABO

Principal values – ellipsoid representation

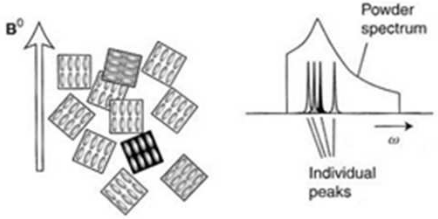


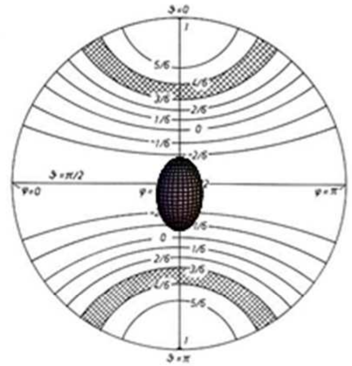




Powders available

...how to build a CSA lineshape ?





Levitt, Spin dynamics, 2002.
Haeberlen, High resolution NMR in solids, selective averaging, 1976.

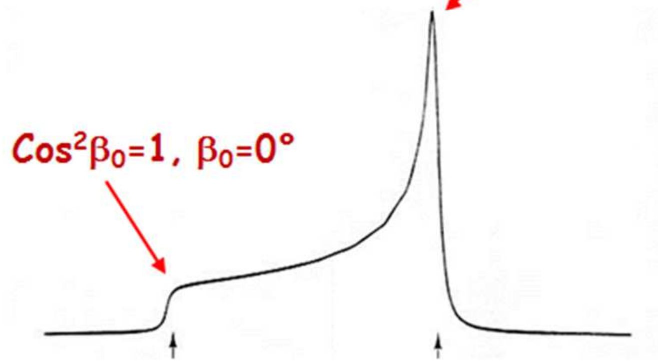
ex : $\delta_{11}=\delta_{22}=\delta_{\perp}$ and $\delta_{33}=\delta_{//}$

$$r^{-2}= \delta_{ZZ} = (\delta_{\perp} \sin^2\beta_0 + \delta_{//} \cos^2\beta_0)$$

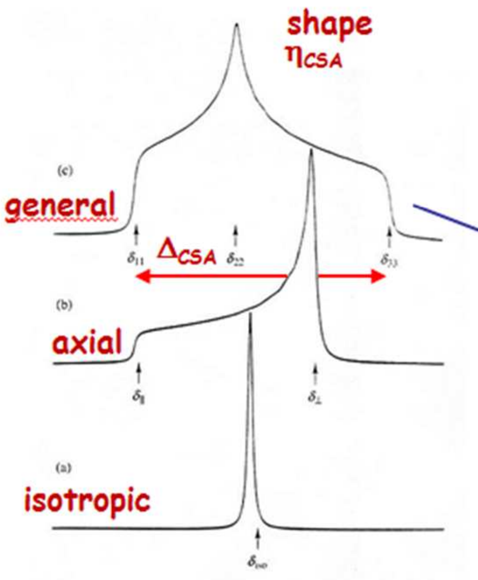
Ellipsoid of revolution !

$\cos^2\beta_0=0,\ \beta_0=90°$

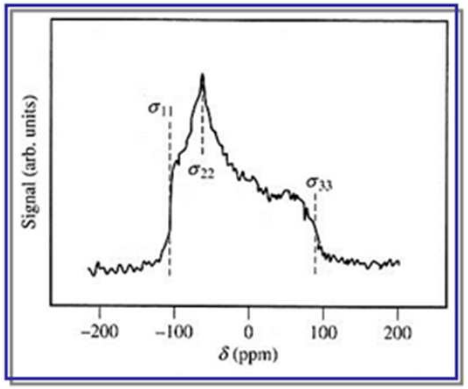
$\cos^2\beta_0=1,\ \beta_0=0°$



$\delta_{//}$ $\delta_{\perp}$



^{19}F in fluoranil, $C_6F_4O_2$



shape: elliptic integrals

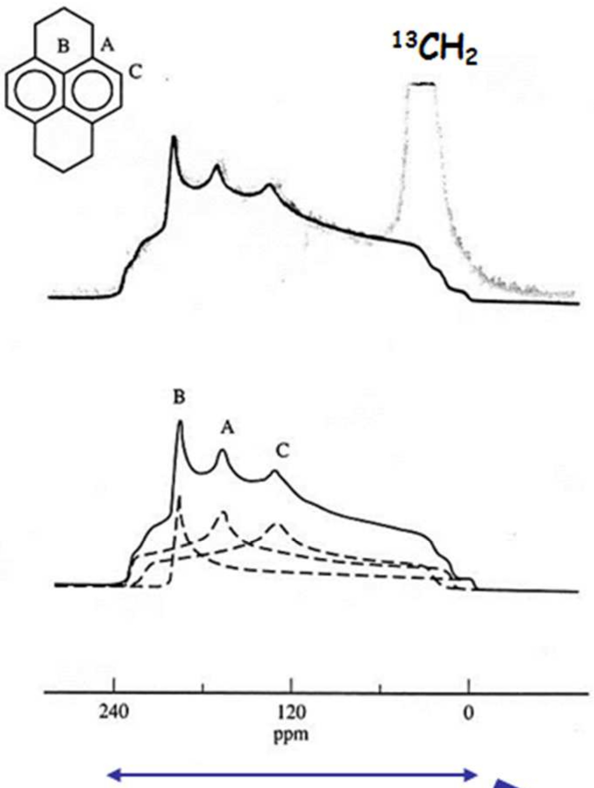
$$K(m)=\int_0^{\pi/2} d\varphi\ (1-m\ \sin^2\varphi)^{-1/2}$$

Mehring et al., J. Chem. Phys., 1971, 59, 746.

Resolution in solid state NMR

an example...

^{13}C: 1,2,3,6,7,8-hexahydropyrene

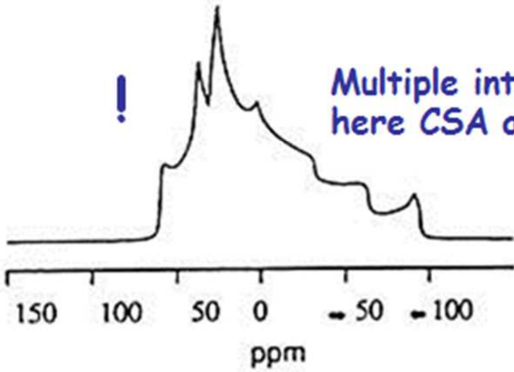


Sethi et al., Prep. Am. Chem. Soc., 1987, 32, 155.

All crystallographically equivalent nuclei participate to the same lineshape

All interactions broaden the lines

- CSA: it depends... .... $\propto B_0$
- D: up to ~ 30 kHz ! .... ind. B_0
- Q: up to MHz ! { ind. B_0. (1st) / $1/B_0$ (2nd) }
- J: few 100s Hz .... ind. B_0



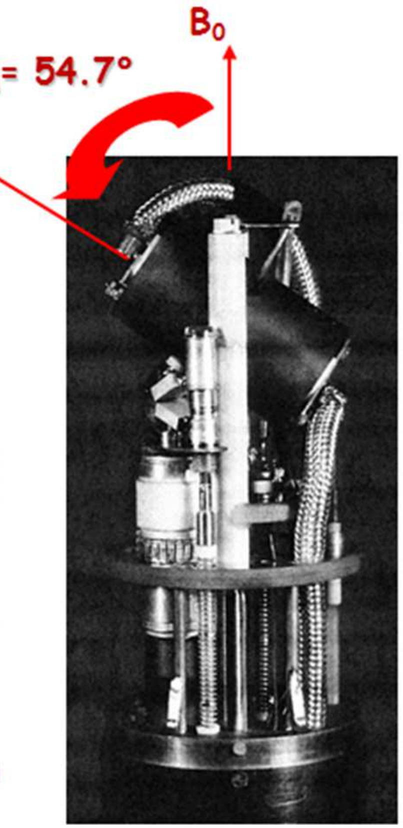
Multiple interactions : here CSA and D

Broadening over the whole ^{13}C chemical shift range !

Magic Angle Spinning (MAS): a kind …of miracle (Andrew *et al.* , Nature, 1959)

rotor axis

$\theta_m = 54.7°$

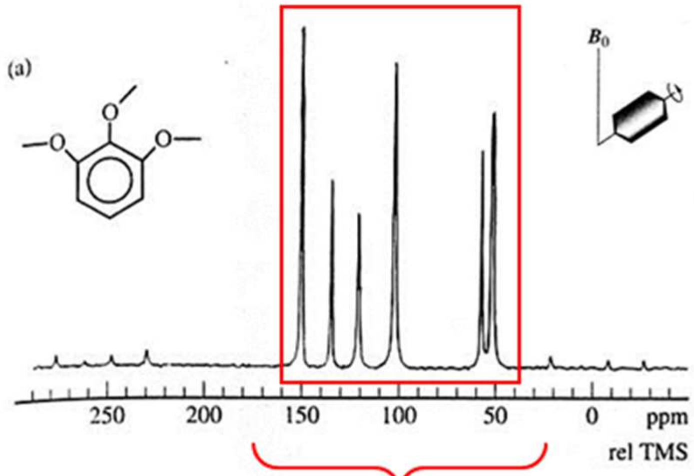


Spinning Spins
A Tribute to Raymond Andrew

→ $P_2(\cos\theta)$

Doty, Encyclopedia of NMR, 1996, 4477.

^{13}C: 1,2,3-trimethoxybenzene



Isotropic region : $\delta_{iso} = 1/3\ (\delta_{11} + \delta_{22} + \delta_{33})$

Orendt, Encyclopedia of NMR, 1996, 1287.

Free Induction Decays of Rotating Solids

I. J. Lowe
Phys. Rev. Lett. **2**, 285 – Published 1 April 1959

MAS at « infinite » frequency

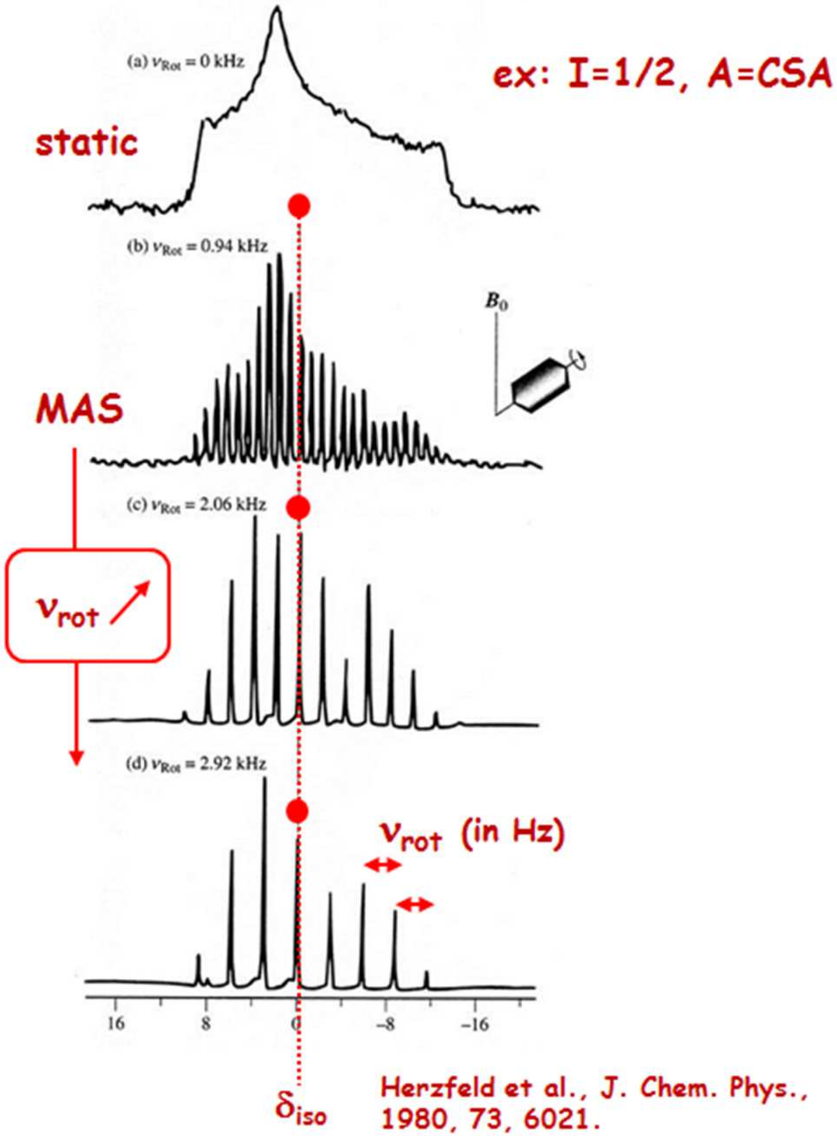
$\nu_{rot} > \Delta_A$ (A= CSA, D, Q…)

question: is it actually possible ?…

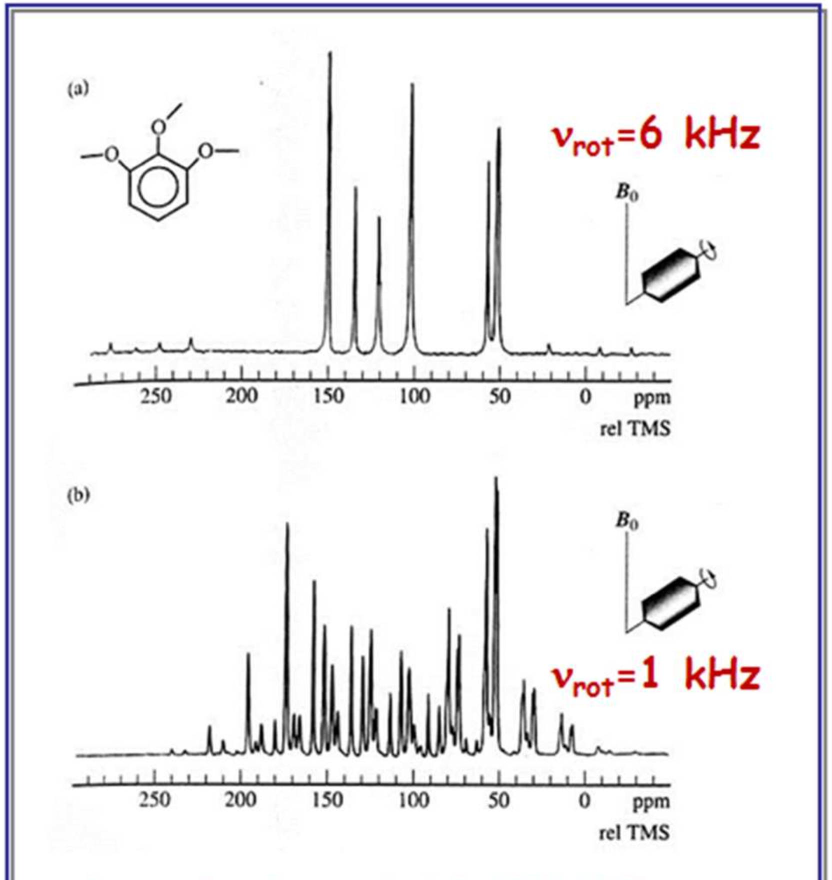
MAS at finite frequency

^{31}P: dipalmitoylphosphatidylcholine

"explosion" of the spectrum in sharp spinning sidebands



Herzfeld et al., J. Chem. Phys., 1980, 73, 6021.

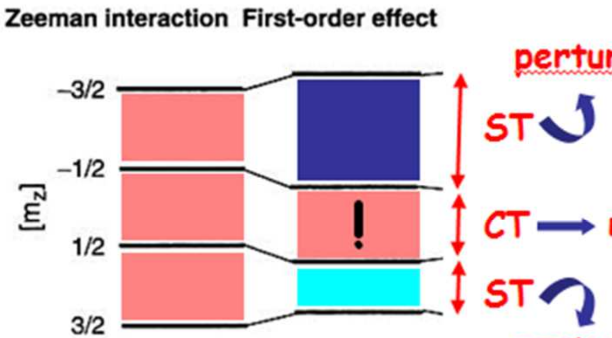


Orendt, Encyclopedia of NMR, 1996, 1287.

Quadrupolar interaction (I > ½): first order perturbation theory

I > ½ (^{27}Al, ^{23}Na, ^{17}O...)

ex: I=3/2



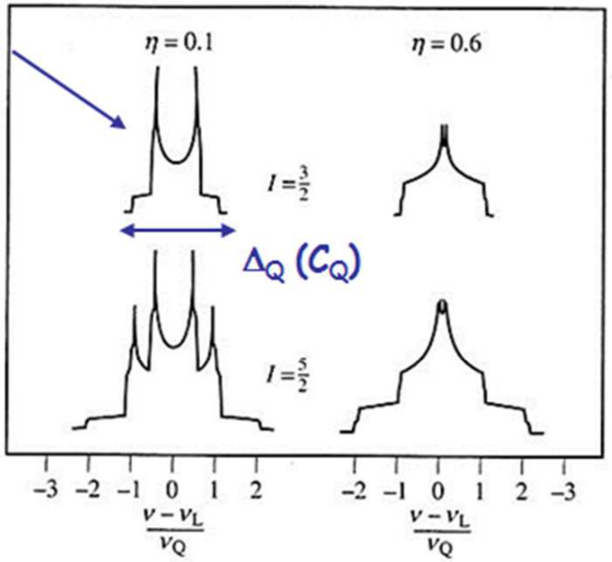
Multitransitions system

CT: central transition

ST: satellite transitions

shape η_Q

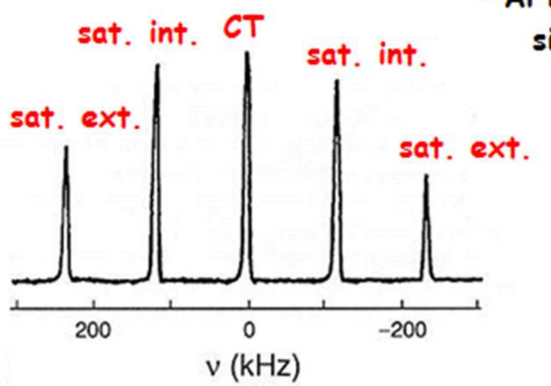
$C_Q = e^2qQ/h$



Freude et al., NMR Basic Princ. Prog., 1993, 29, 25.

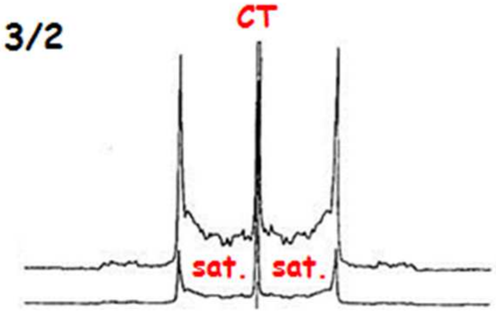
I = 5/2

^{27}Al in α-Al_2O_3 single crystal



I = 3/2

^{23}Na in $NaNO_3$ powder

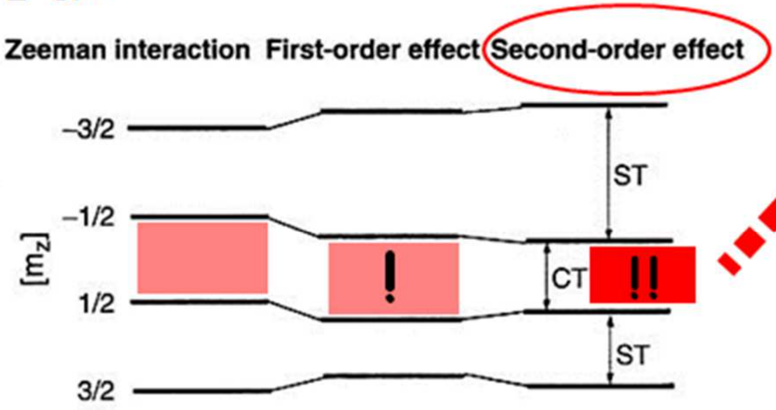


Man, Encyclopedia of analytical chemistry, 2000, 12229.

Quadrupolar interaction (I > ½): second order perturbation theory

C_Q: 3 to 15 MHz...

I=3/2



$$w^{(2)\mathrm{static}}_{-1/2,1/2} = -\frac{1}{6w_L}\left[\frac{3e^2qQ}{2I(2I-1)\hbar}\right]^2 \left\{I(I+1)-\frac{3}{4}\right\} \times \{A(\alpha,\eta)\cos^4\beta + B(\alpha,\eta)\cos^2\beta + C(\alpha,\eta)\}$$

$$A(\alpha,\eta) = -\frac{27}{8} + \frac{9}{4}\eta\cos 2\alpha - \frac{3}{8}(\eta\cos 2\alpha)^2$$

$$B(\alpha,\eta) = \frac{30}{8} - \frac{1}{2}\eta^2 - 2\eta\cos 2\alpha + \frac{3}{4}(\eta\cos 2\alpha)^2$$

$$C(\alpha,\eta) = -\frac{3}{8} + \frac{1}{3}\eta^2 - \frac{1}{4}\eta\cos 2\alpha - \frac{3}{8}(\eta\cos 2\alpha)^2$$

Man, Encyclopedia of analytical chemistry, 2000, 12229.

$H_Q \sim H_{Zeeman}$: second order perturbations

⬇

All transitions (ST and CT) are perturbed

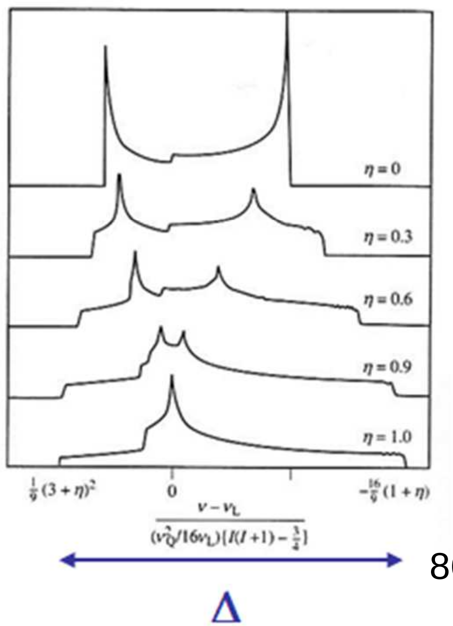
Mathematical treatment...?

shape : η_Q

$\Delta \sim C_Q^2/\nu_L$

↓

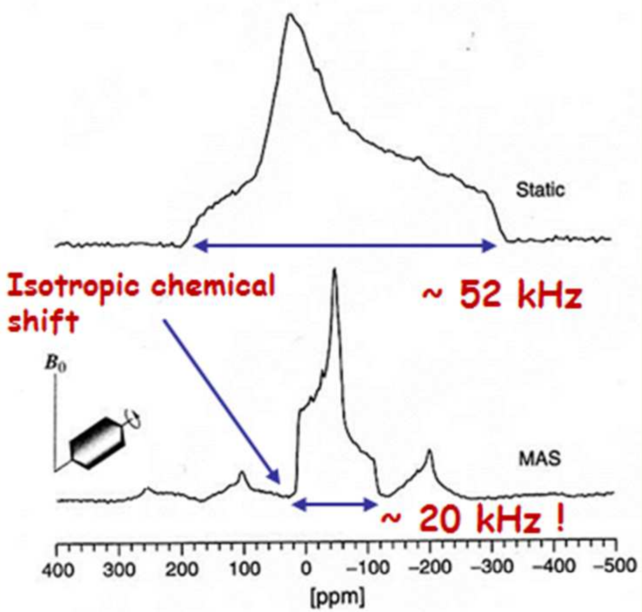
idea : B_0 ↗



Freude et al., NMR Basic Princ. Prog., 1993, 29, 27.

Quadrupolar interaction (second order): MAS

theorem: MAS has an effect... But the second order broadening effect is only partially averaged !



^{87}Rb in $LiRbSO_4$

Pruski, J. Magn. Reson., 2000, 147, 286.

even at « infinite » MAS frequency !

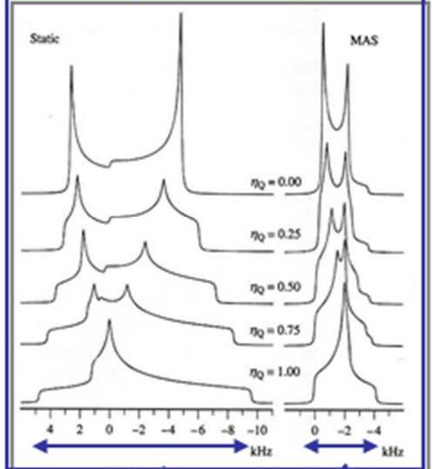
WHY ? (without any calculation)

MAS rotation: efficient for

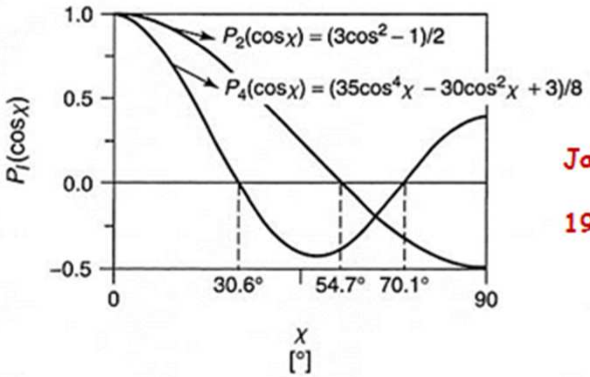
- ellipsoids
- $Cos^2(\alpha_0, \beta_0)$
- $P_2(Cos\theta)$

... But not for:

- quartics
- $Cos^4(\alpha_0, \beta_0)$, $Cos^2(\alpha_0, \beta_0)$
- $P_4(Cos\theta)$, $P_2(Cos\theta)$



Δ_{static} Δ_{MAS}



Jakobsen, Encyclopedia of NMR, 1996, 2371.

? $P_4(Cos\theta) = P_2(Cos\theta) = 0$?...NO !!

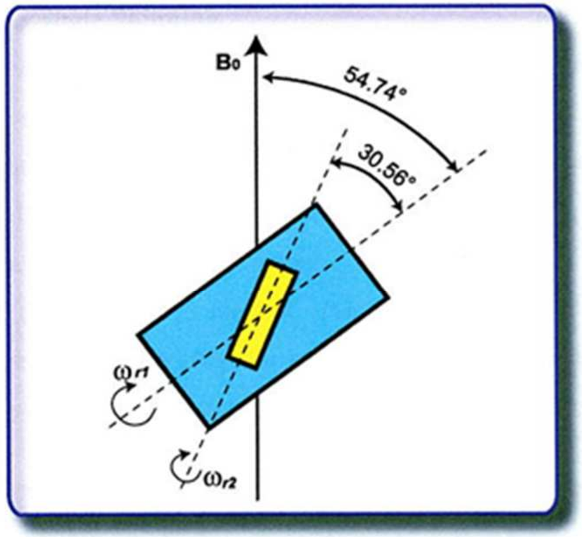
Quadrupolar nuclei and macroscopic reorientations

MAS: "one unique degree of freedom" (1959)

Let us invent an experiment with 2 angles of reorientation !

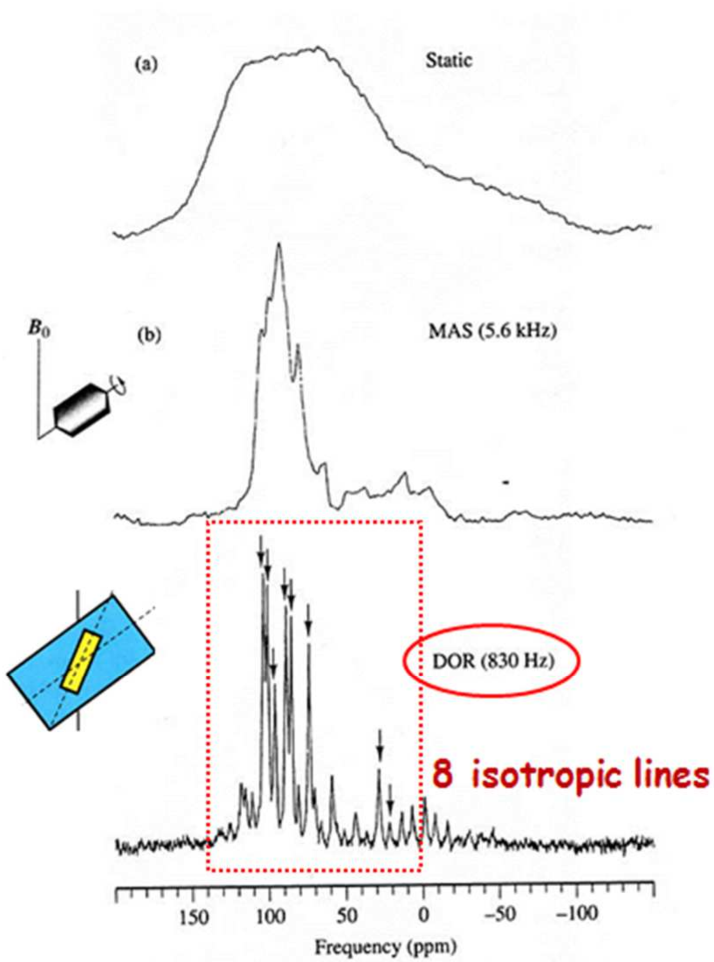
DOR experiment (DOuble Rotation)

(Samoson, Pines, 1988)



1D experiment

^{17}O (I=5/2) : $CaSiO_3$ wollastonite: 9 sites (^{17}O)

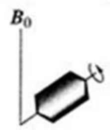


Wu, Encyclopedia of NMR, 1996, 1749.

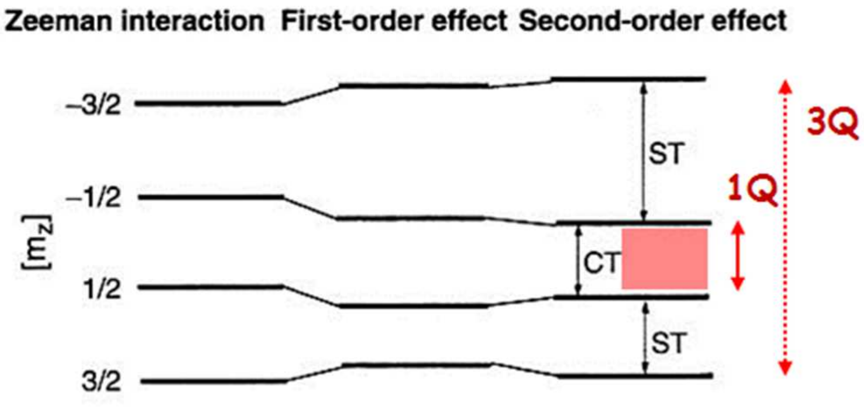
Rotation around a unique axis: MQ-MAS

DAS and DOR: 1 transition (CT) et 2 angles...

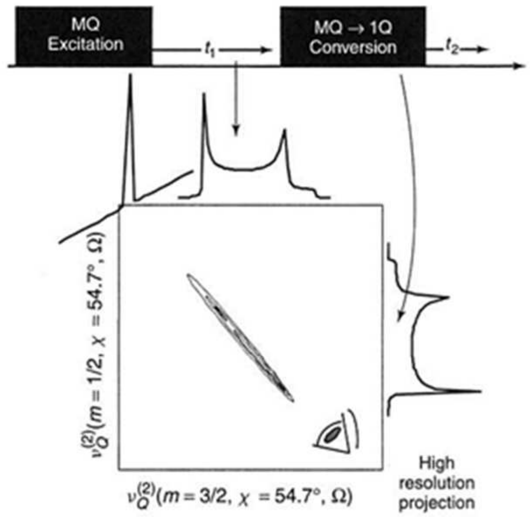
MQ-MAS (Multiple Quantum MAS)
(Frydman, 1995)



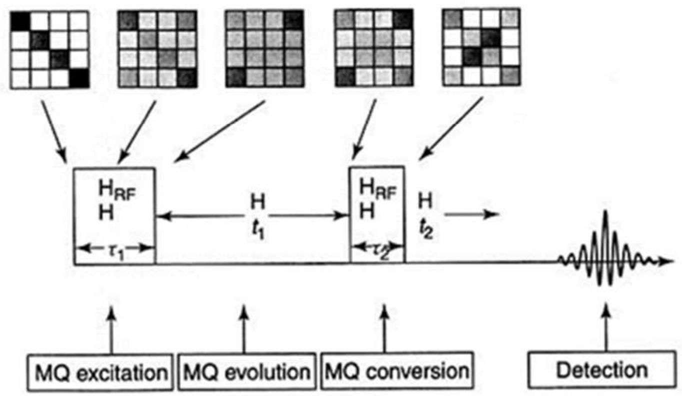
→ 2 transitions (CT/MQ) and 1 angle (MAS) !



idea: 1Q and 3Q correlation to give ... an ECHO !



Frydman, Encyclopedia of NMR, supp. Vol., 265.

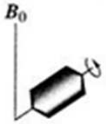


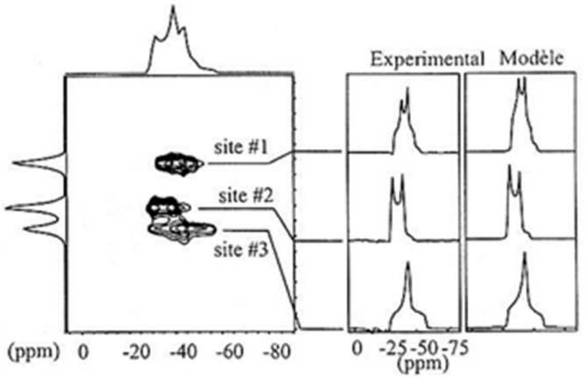
Amoureux *et al.*, Encyclopedia of NMR, supp. Vol., 230.

Applications of MQ-MAS

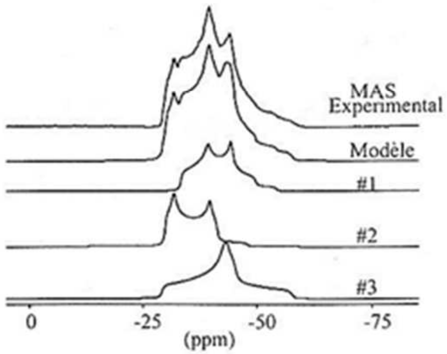
DAS and DOR: demanding techniques

MQ-MAS: much easier (...)



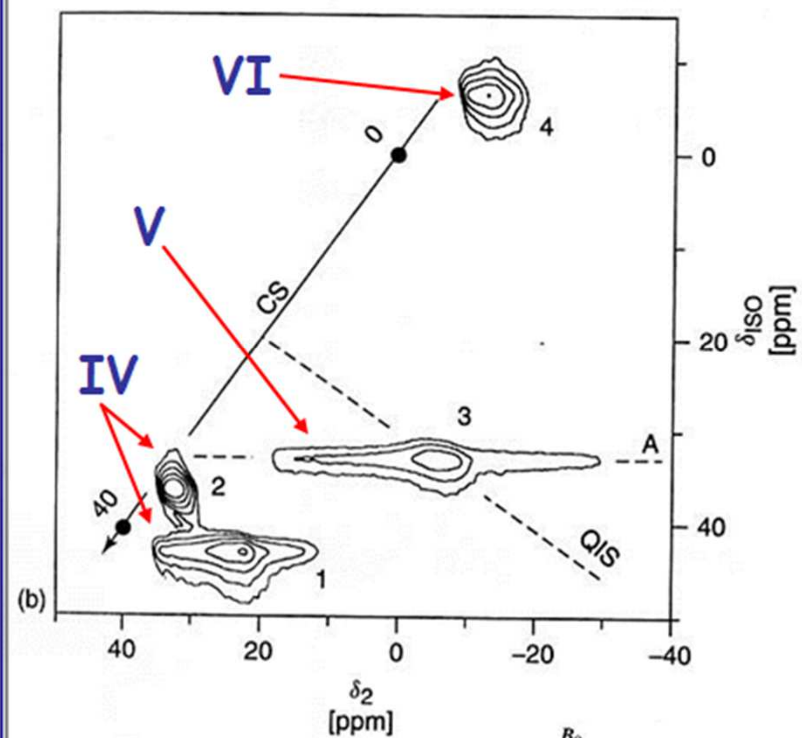


	MQ-MAS			Baltisberger *et al.* (1992)		
Site	δ_{CS}^{ISO} (ppm)	C_Q (MHz)	η_Q	δ_{CS}^{ISO} (ppm)	C_Q (MHz)	η_Q
#1	-31.3	1.79	0.55	-30.9	1.85	0.48
#2	-26.6	1.75	0.18	-26.2	1.83	0.12
#3	-28.5	1.99	0.91	-26.8	2.07	1.0



^{87}Rb : $RbNO_3$

Massiot, Ecole RMN des Houches, 1997.

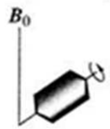


^{27}Al : $AlPO_4$-14

2 sites IV

1 site V

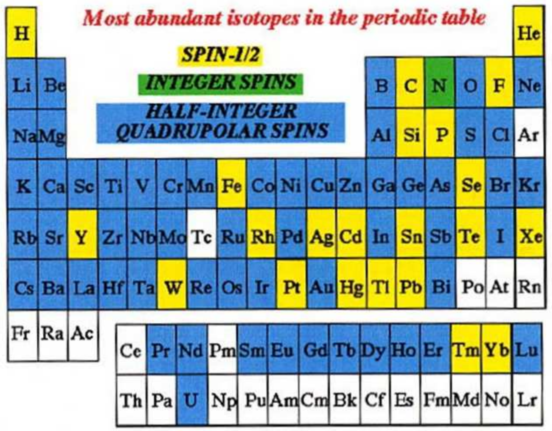
1 site VI



15 kHz

Amoureux et al., Encyclopedia of NMR, supp. Vol., 235.

Applications: NMR and materials



⌂ crystals (organic, inorganic) & glasses

⌂ polymers & soft materials

⌂ organic-inorganic hybrids

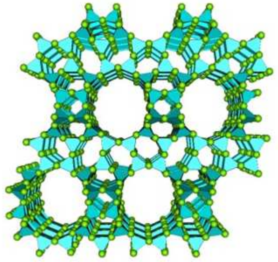
⌂ cements & pastes

⌂ ceramics

⌂ biomaterials

⌂ catalysts & zeolites

…



www.personal.utulsa.edu/~geoffrey-price/zeolite/

(almost) all nuclei in the periodic table ⌂

ultra high field and ultra fast MAS ⌂

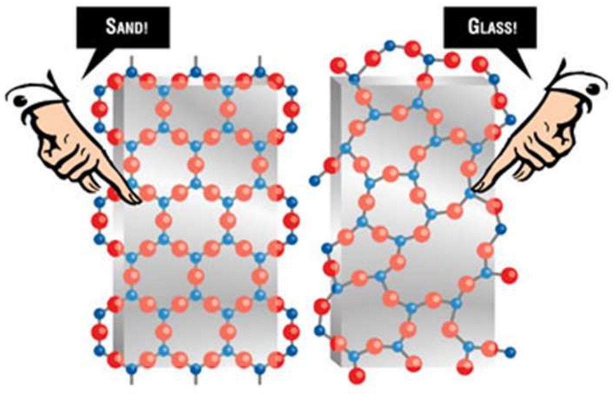
decoupling / recoupling under fast MAS ⌂

specific pulse schemes for Q nuclei ⌂

DAS, DOR, MQMAS ⌂

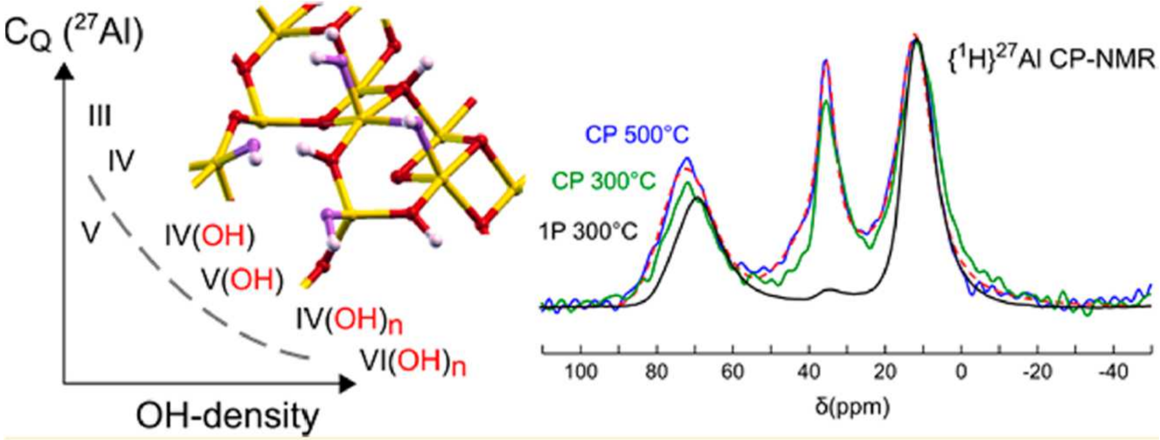
very low / high T ⌂

…



www.acmecompany.com/Pages/glass.html

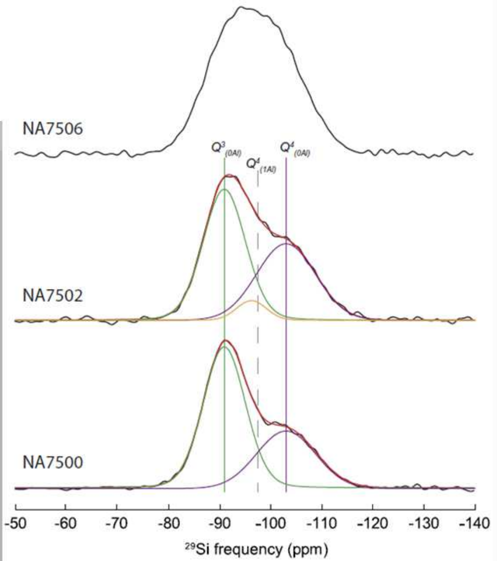
Applications: NMR and materials



Visibility of Al Surface Sites of γ-Alumina: A Combined Computational and Experimental Point of View

J. Phys. Chem. C, **2014**, *118* (28), pp 15292–15299

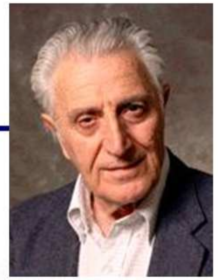
Pierre Florian, CEMHTI, Orléans, France



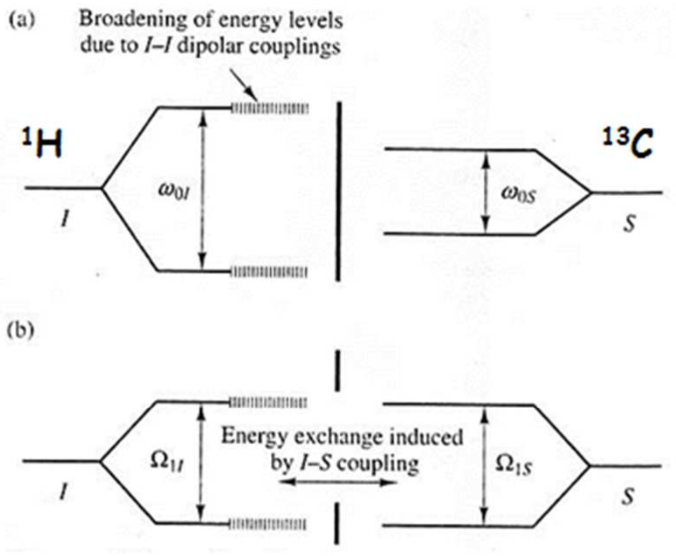
The role of Al^{3+} on rheology and structural changes in sodium silicate and aluminosilicate glasses and melts

Geochim. Cosmochim. Acta, *126* (**2014**) 495-517

Cross Polarization (CP) – Hartmann-Hahn condition



question: is it possible to transfer magnetization from ^1H to ^{13}C ?



Engelke, Encyclopedia of NMR, 1996, 1530.

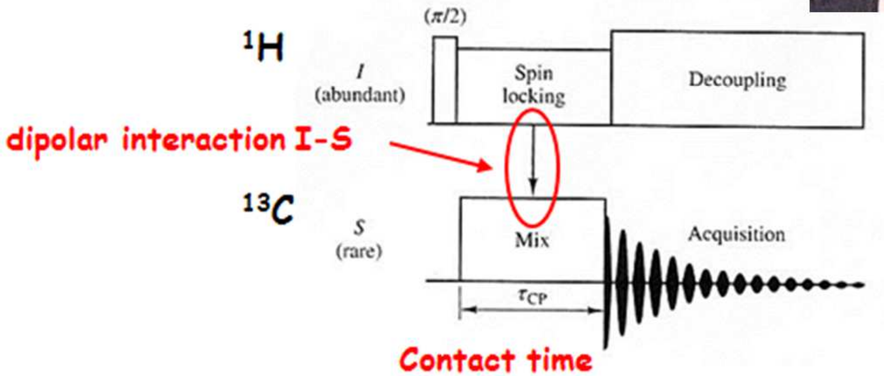
Hartmann and Hahn (1962):

NO in the LAB frame mais YES in the rotating frame

$$\Omega_{1I} = |\gamma_I| B_{1I} = \Omega_{1S} = |\gamma_S| B_{1S}$$

Hartmann-Hahn condition on B_1(RF) fields

the most popular sequence

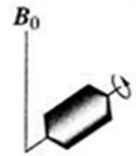


advantages:

- gain: $M_S (\gamma_{1H}/|\gamma_S|)$ → 4 for ^{13}C, 10 for ^{15}N !
- τ_{CP} ~ ms !
- $T_1(^1H) << T_1(^{13}C)$
- ^{13}C FID with ^1H decoupling

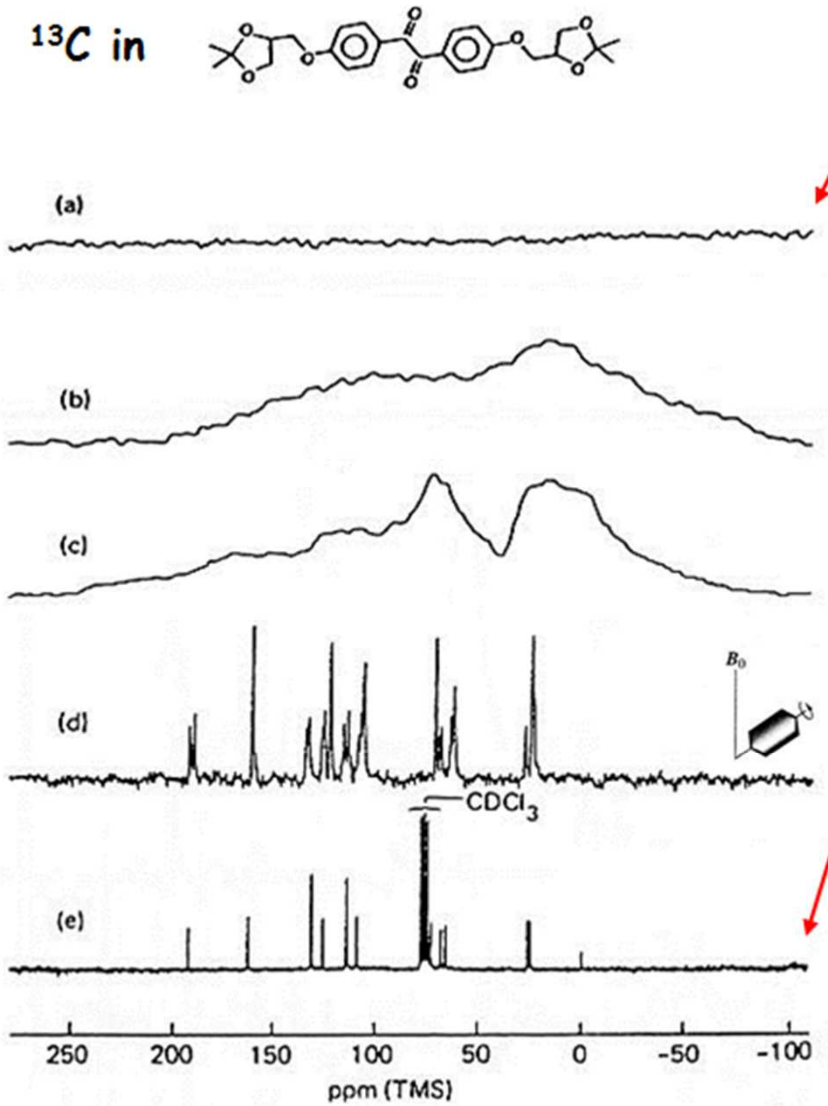
How to manage the ^{13}C CSA interaction ?

idea...



The CP MAS combination

	high resolution NMR	solid state NMR	clinical imaging
B_1 (Tesla)	$5\ 10^{-4}$	$2\ 10^{-3}$	10^{-5}



(a) solid (solution state conditions)

(b) CP (low power decoupling)

(c) CP (high power decoupling)

(d) CP MAS (high power decoupling)

(e) solution (low power decoupling)

RF MAS

$$\Omega_{1I} = \Omega_{1S} \pm n\ \Omega_{rot}$$

with n = 1, 2

modified Hartmann-Hahn conditions

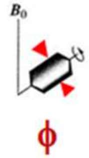
^{1}H solid state NMR

ϕ: 7mm ⟶ ... 6 kHz

ϕ: 4mm ⟶ ... 15 kHz

ϕ: 2,5mm ⟶ ... 35 kHz

ϕ: 1mm ⟶ ... 100 kHz



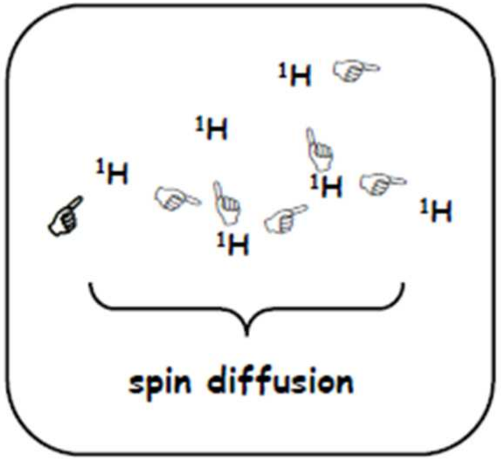
^{1}H: strongly coupled by the homonuclear dipolar interaction !

remember:

$D_{II} \sim \gamma^2/r_{II}^3$ up to 30 kHz...

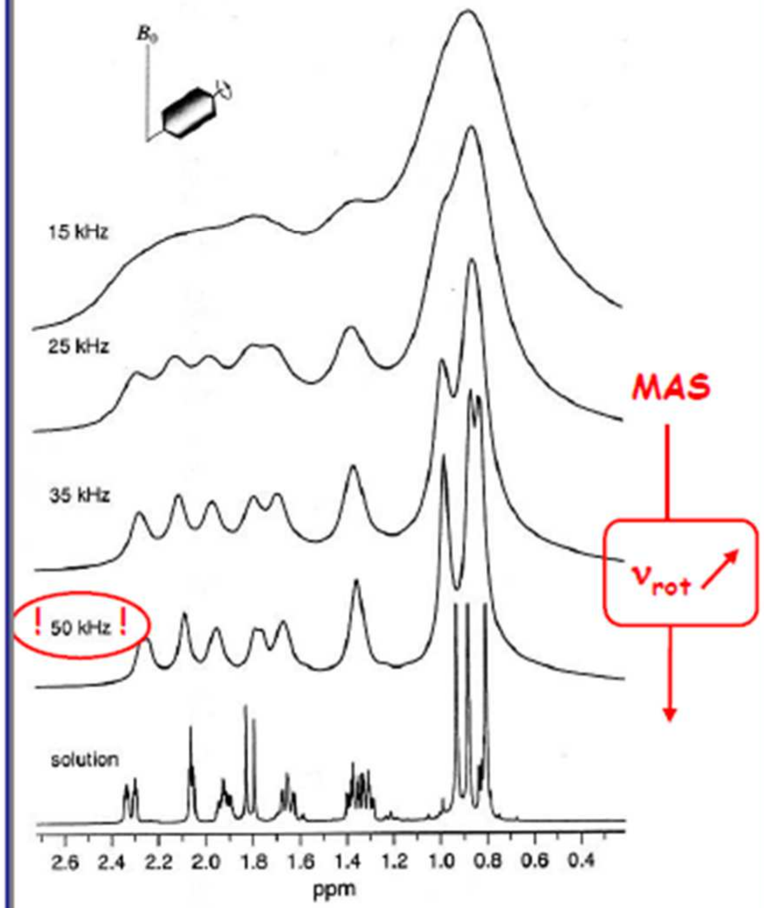
high for ^{1}H (γ)

rather small (r_{II})



question: is the MAS reorientation efficient ?

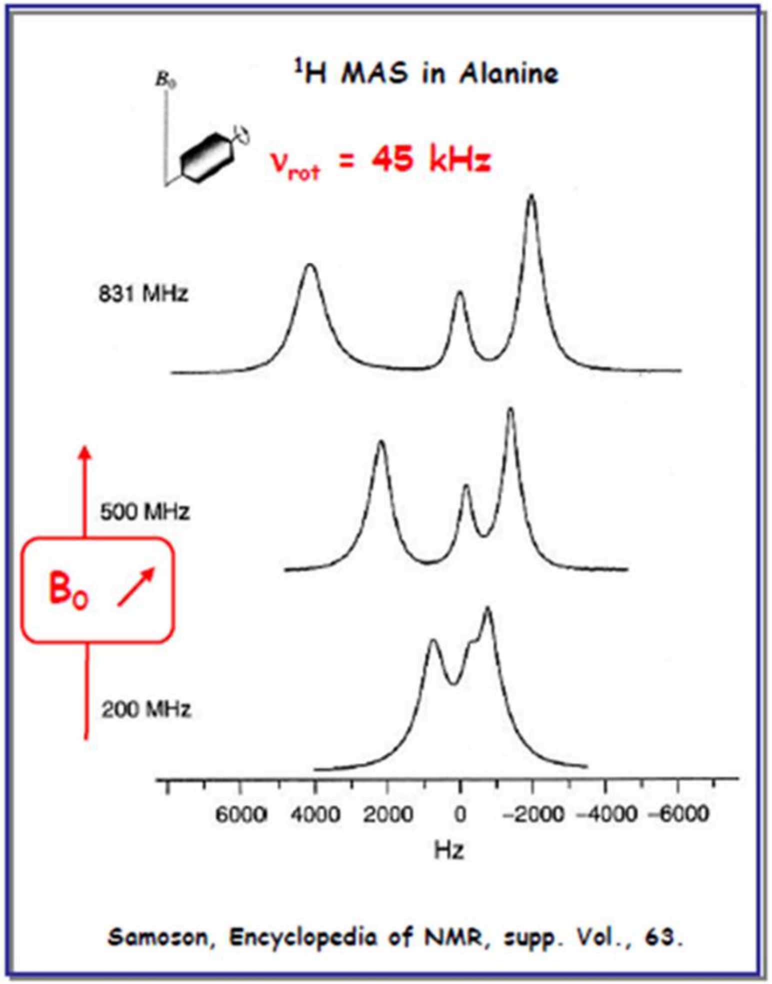
^{1}H MAS in Camphor (500MHz)



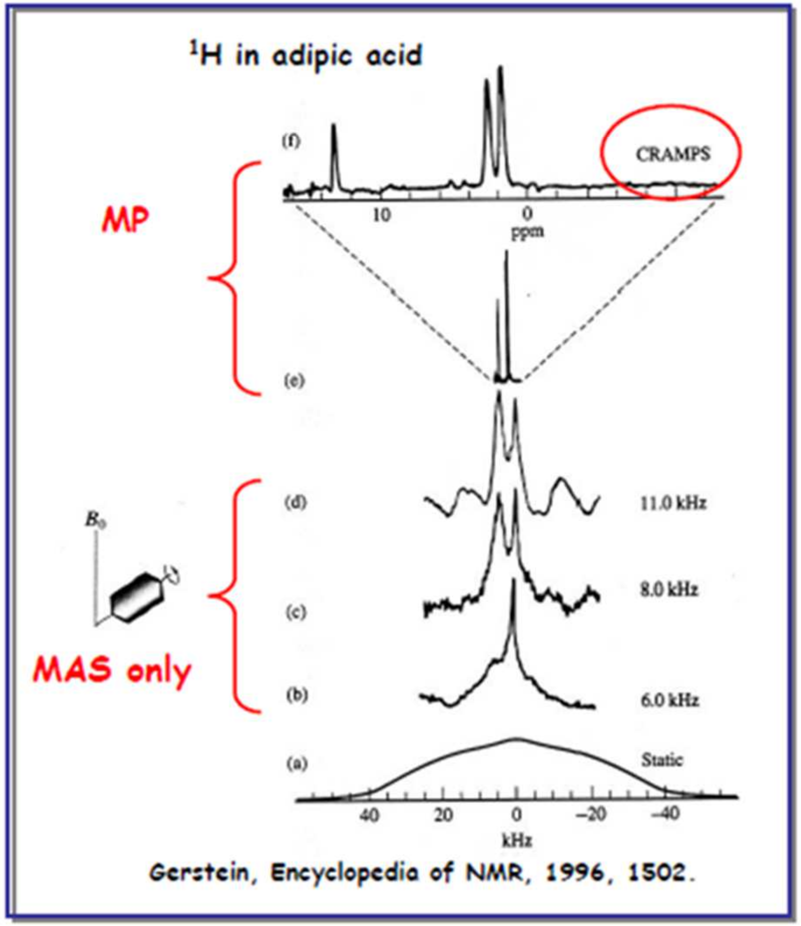
Samoson, Encyclopedia of NMR, supp. Vol., 63.

The combination of two averaging processes

first idea: highest B_0 and highest ν_{rot} !



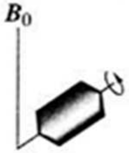
second idea: rotations in spin space !



Decoupling / recoupling in solid state NMR

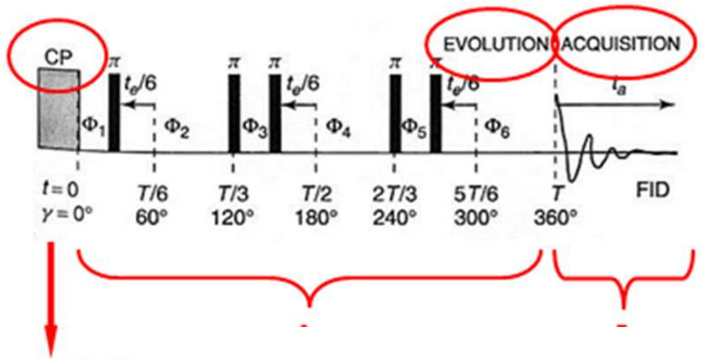
general idea: 2D corrélations between isotropic δ and anisotropies

if



the interaction must be reintroduced

ex: δ_{iso} vs Δ_{CSA} – Magic Angle Turning



sensitivity

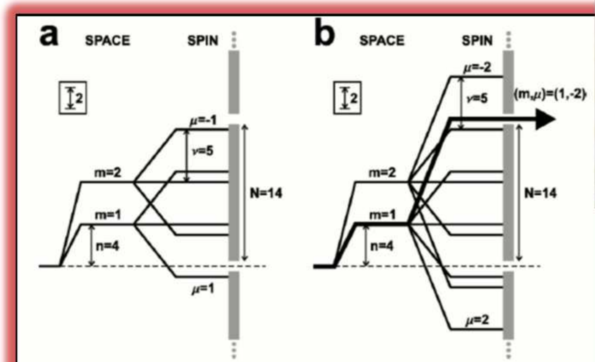
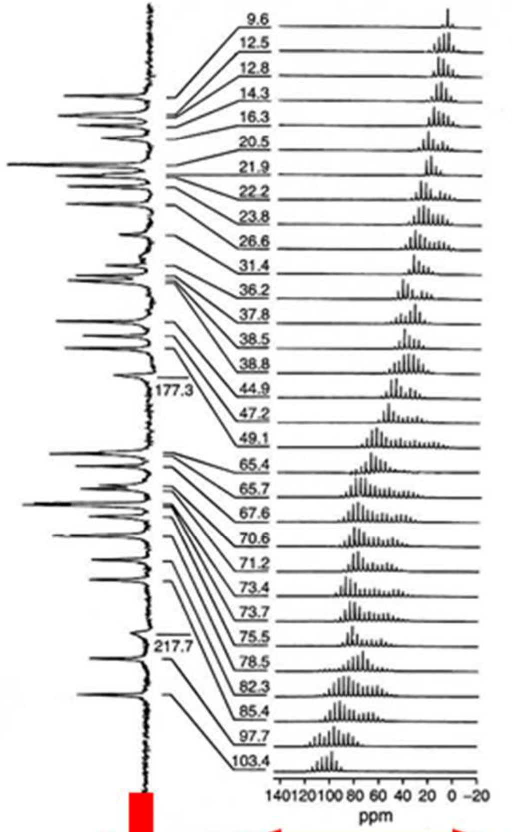


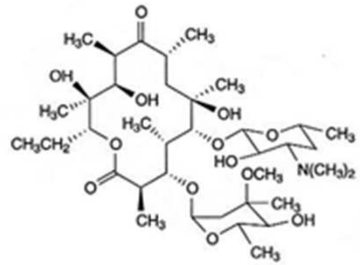
FIG. 3. Space-spin selection diagram (SSS diagram) for $C14_4^5$. (a) Suppression of all CSA modulation components. (b) Selection of a single 2Q dipole–dipole component, with quantum numbers $(m,\mu)=(1,-2)$. The vertical scale of this figure is one half that of Fig. 2. The mirror image pathways stemming from $m=-1$, $m=-2$ have been suppressed for simplicity.

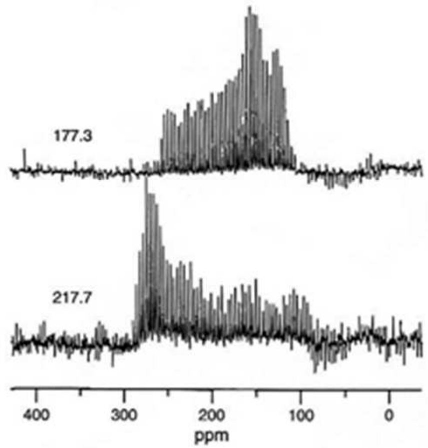


isotropic dim.

CSA dim.

^{13}C : erythromicine A





Applications: solid state NMR and biomolecules

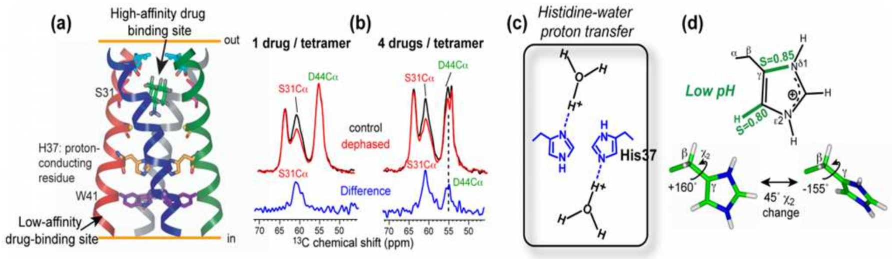
⌂ **proteins**

⌂ **role of water molecules**

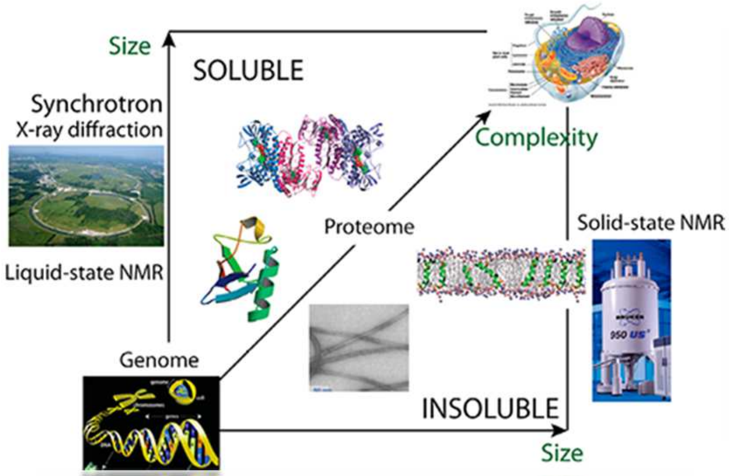
⌂ **polymorphism**

⌂ **molecules of pharmaceutical interest**

…



http://www.chem.iastate.edu/faculty/Mei_Hong/research



www.biokemi.org/biozoom

^{1}H, ^{13}C, ^{15}N (^{17}O, ^{31}P) ⌂

^{2}H ⌂

ultra high B_0 field, ultra fast MAS ⌂

high res. ^{1}H solid state NMR: methodology ⌂

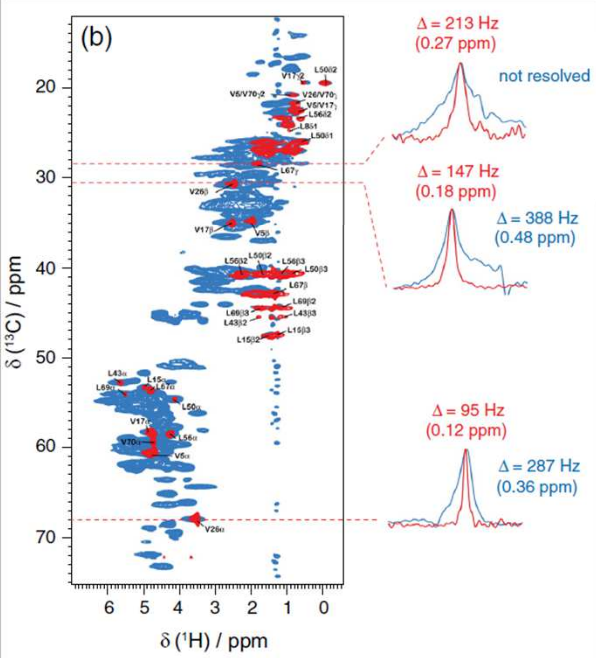
low power decoupling ⌂

sample preparation ⌂

hyperpolarization (DNP…) ⌂

…

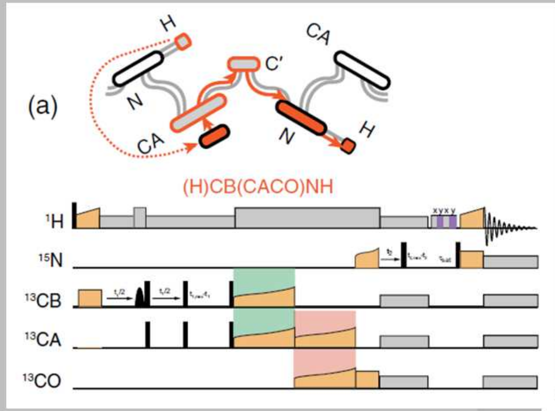
Applications: solid state NMR and biomolecules



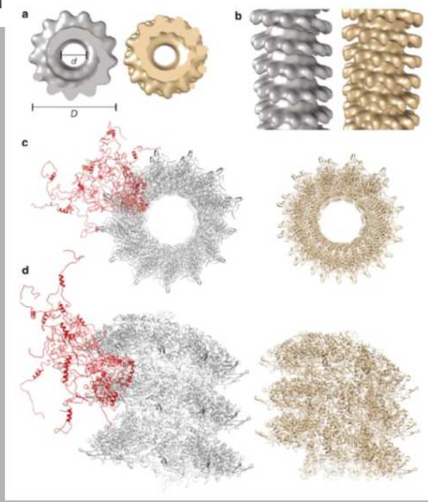
High-resolution proton-detected NMR of proteins at very fast MAS

Loren B. Andreas [a], Tanguy Le Marchand [a], Kristaps Jaudzems [b], Guido Pintacuda [a,*]

J. Magn. Reson, *253* (**2015**) 36-49



Guido Pintacuda, CRMN, Lyon, France



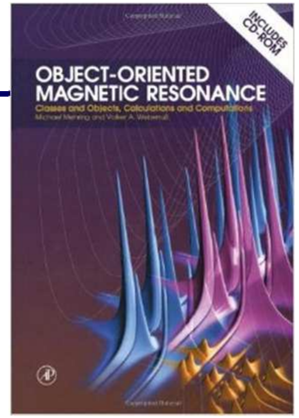
Insights into the Structure and Dynamics of Measles Virus Nucleocapsids by ^{1}H-detected Solid-state NMR

Emeline Barbet-Massin,[1] Michele Felletti,[1] Robert Schneider,[2] Stefan Jehle,[1] Guillaume Communie,[2,3] Nicolas Martinez,[3] Malene Ringkjøbing Jensen,[2] Rob W. H. Ruigrok,[3] Lyndon Emsley,[1] Anne Lesage,[1] Martin Blackledge,[2] and Guido Pintacuda[1,*]

Biophys. J., *107* (**2014**) 941-946

Mathematical tools for solid state NMR experiments

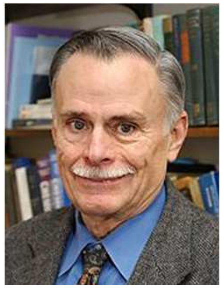
credits to



Average Hamiltonian theory (AHT)

$$\hat{U}(nt_c) = [\hat{U}(t_c)]^n, \quad \hat{U}(t_c) = \exp\left[-\frac{i}{\hbar} t_c \hat{\bar{\mathcal{H}}}(t_c)\right].$$

$$\hat{\bar{\mathcal{H}}}(t_c) = \hat{\bar{\mathcal{H}}}^{(0)} + \sum_{k=1}^{\infty} \hat{\bar{\mathcal{H}}}^{(k)}(t_c).$$



J. Waugh

Magnus expansion

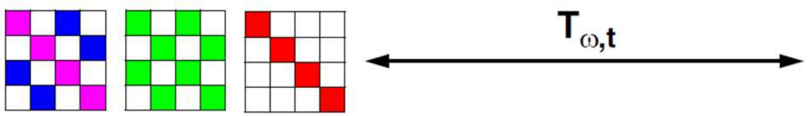
$$\hat{\bar{\mathcal{H}}}^{(0)} = \frac{1}{t_c}\int_0^{t_c} dt\, \hat{\mathcal{H}}(t),$$

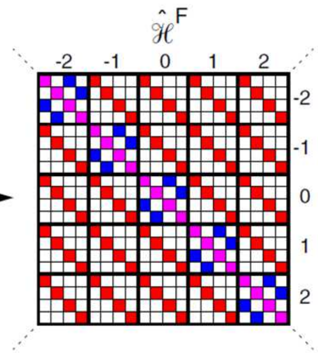
$$\hat{\bar{\mathcal{H}}}^{(1)}(t_c) = -\frac{i}{2\hbar t_c}\int_0^{t_c} dt_2 \int_0^{t_2} dt_1 \left[\hat{\mathcal{H}}(t_2), \hat{\mathcal{H}}(t_1)\right]_-,$$

$$\hat{\bar{\mathcal{H}}}^{(2)}(t_c) = -\frac{1}{6\hbar^2 t_c}\int_0^{t_c} dt_3 \int_0^{t_3} dt_2 \int_0^{t_2} dt_1 \Big([\hat{\mathcal{H}}(t_3), [\hat{\mathcal{H}}(t_2), \hat{\mathcal{H}}(t_1)]_-]_- + [\hat{\mathcal{H}}(t_1), [\hat{\mathcal{H}}(t_2), \hat{\mathcal{H}}(t_3)]_-]_-\Big) \quad \text{etc.}$$

Floquet approach

$$\hat{\mathcal{H}}(t) = \sum_{n=-\infty}^{\infty} {}^{(n)}\hat{\mathcal{H}} e^{in\omega_m t}$$

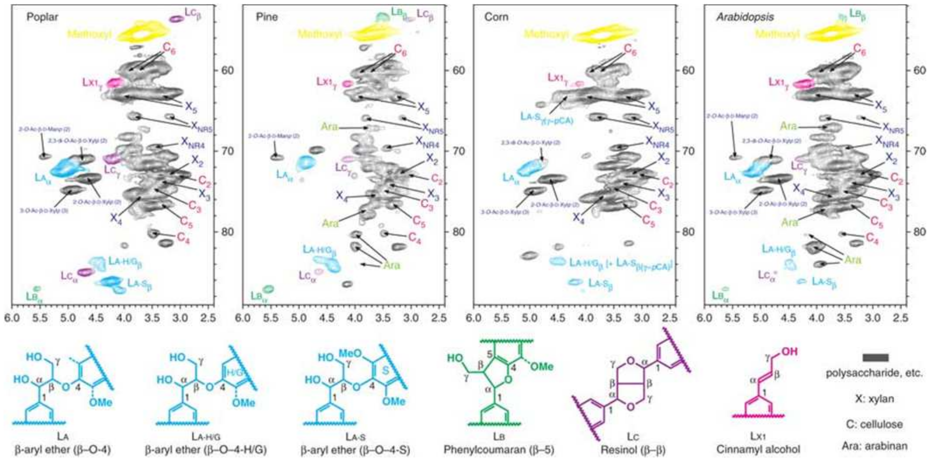




Matthias Ernst (maer@ethz.ch)
ETH Zürich, Switzerland

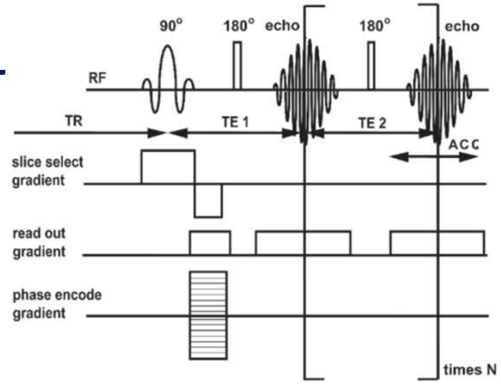
Outline

Nature Protocols, 2012



- **Nuclear spin – the NMR experiment**
- **Mathematical treatment of NMR**
- **Multidimensional NMR**
- **Relaxation**
- **Solid State NMR**
- **Gradients and imaging**

MRI



The Nobel Prize in Physiology or Medicine 2003
Paul C. Lauterbur, Sir Peter Mansfield

The Nobel Prize in Physiology or Medicine 2003

Nobel Prize Award Ceremony

Paul C. Lauterbur

Sir Peter Mansfield

Paul C. Lauterbur

Sir Peter Mansfield

The Nobel Prize in Physiology or Medicine 2003 was awarded jointly to Paul C. Lauterbur and Sir Peter Mansfield *"for their discoveries concerning magnetic resonance imaging"*

Journal of Insect Science

NMR imaging of the honeybee brain

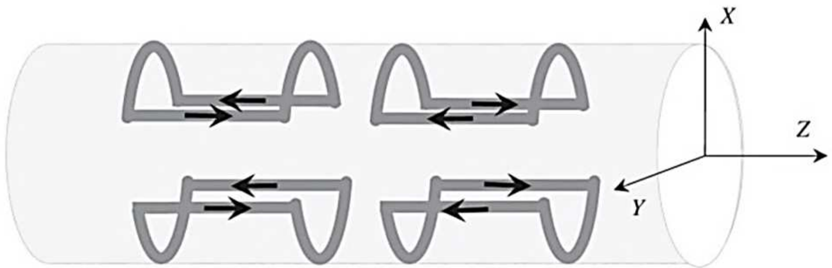
D. Haddad[1], F. Schaupp[2], R. Brandt[2], G. Manz[2], R. Menzel[2], A. Haase[1]

Introduction to gradients

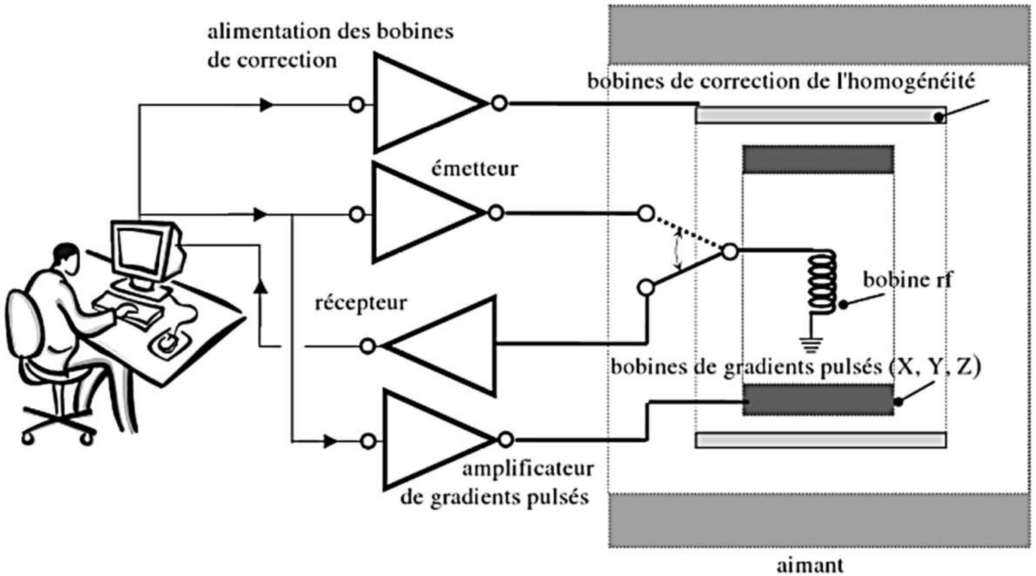
credits to

dedicated to:

- compensation of field inhomogeneities (shims)
- coherence selection
- space encoding for image acquisition

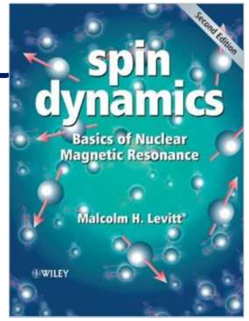


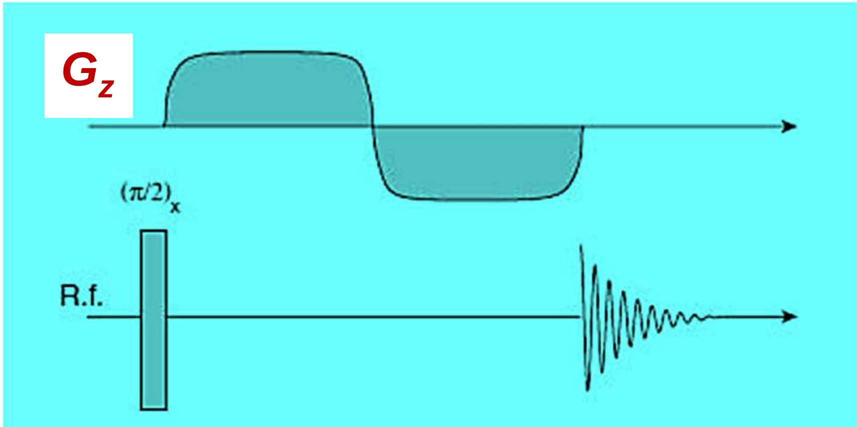
getting a G_x gradient



Gradient echoes

credits to

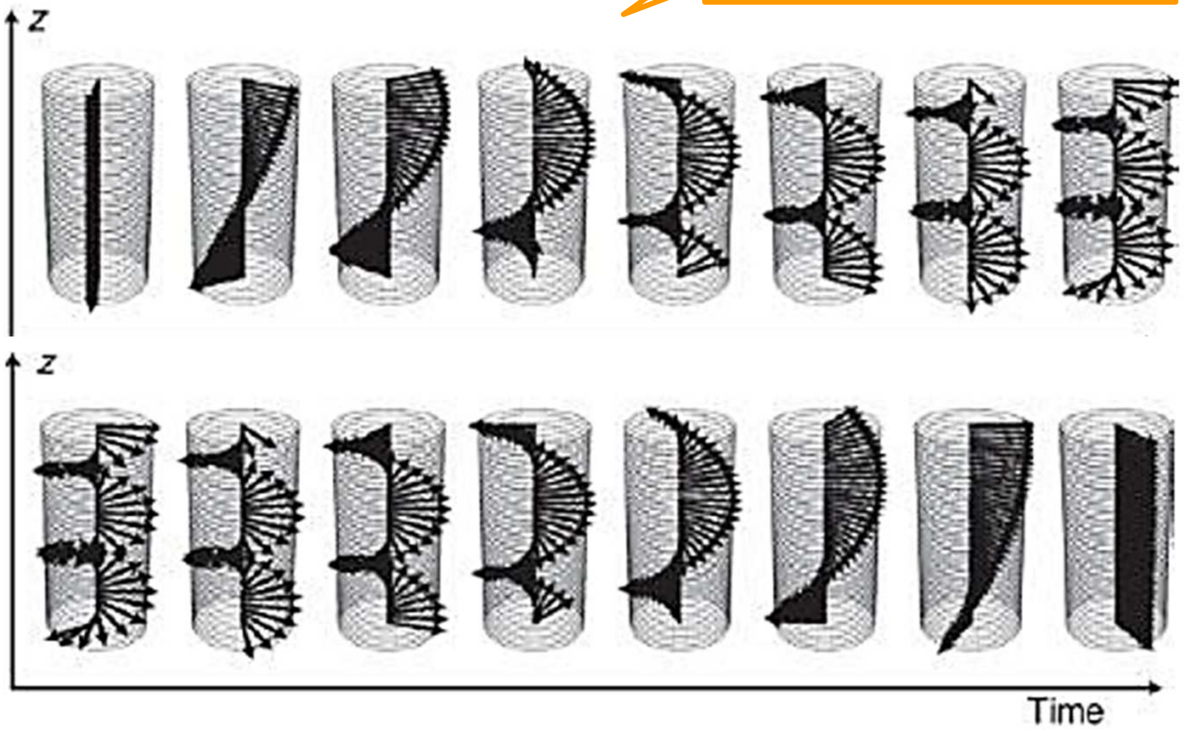




$B(\mathbf{r}) = B_0\, \mathbf{e_z} + G_z\, z\, \mathbf{e_z}$

magnetization helix

start



field gradient

G_z

echo

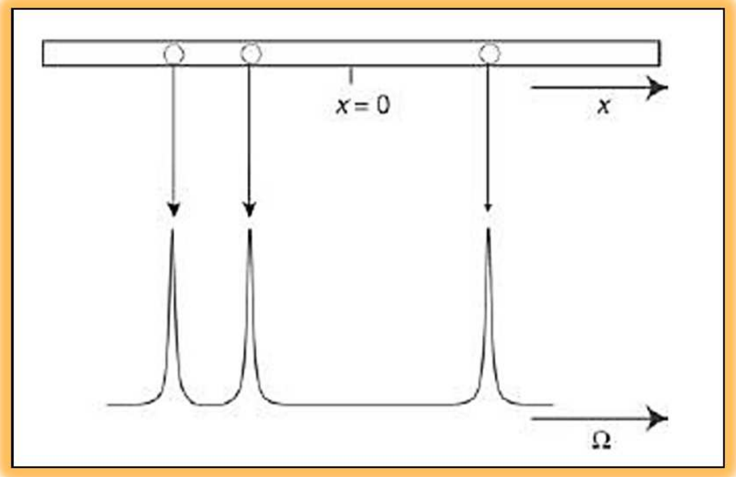
(shifted in phase)

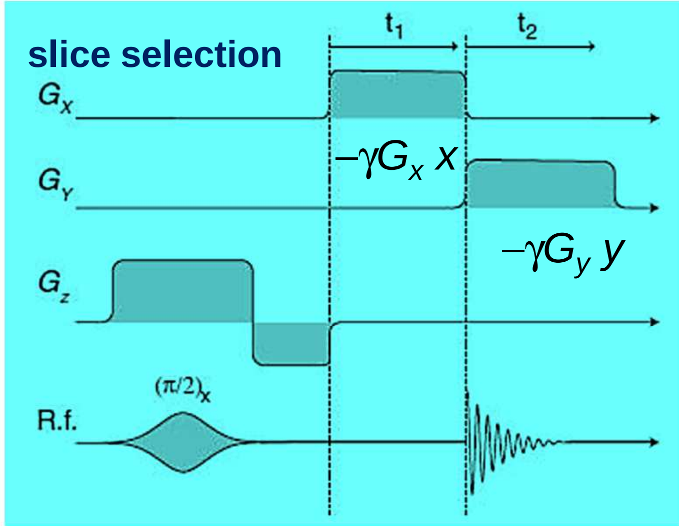
NMR imaging

$$\mathbf{B} = (B^0 + G_x x)\,\mathbf{e}_z$$

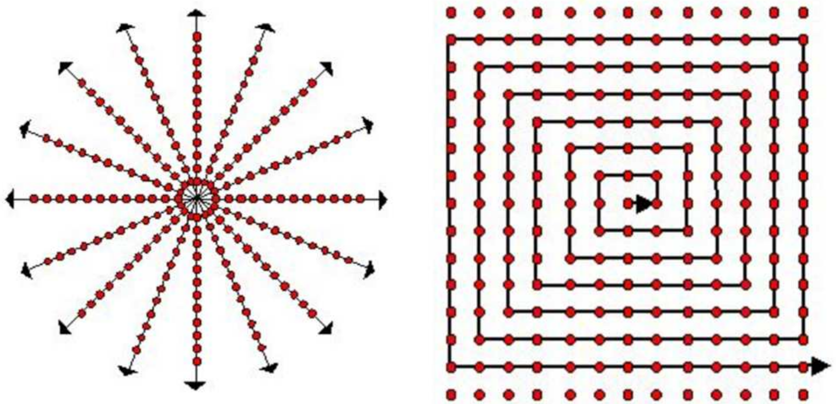
$$\omega^0(x) = -\gamma(B^0 + G_x x) = \omega^0(0) - \gamma G_x x$$

$$\Omega^0(x) = \omega^0(x) - \omega_{\text{ref}} = -\gamma G_x x$$





K-space charting strategies



k-Space Formalism

$$s(\vec{k}) = \int d^3r\, \rho(\vec{r}) \cdot \mathrm{e}^{2\pi i\, \vec{k}(t)\cdot\vec{r}},$$

$$\rho(\vec{r}) = \int d^3k\, s(\vec{k}) \cdot \mathrm{e}^{-2\pi i\, \vec{k}(t)\cdot\vec{r}}.$$

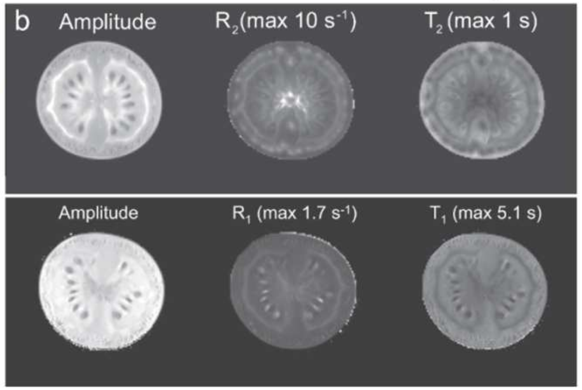
www.ebyte.it/library/educards/mri/K-SpaceMRI

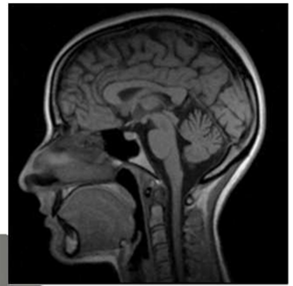
Applications: imaging and MRI

⌂ **field gradients**

⌂ **Magnetic Resonance Imaging (MRI)**

⌂ **functional imaging**





Magnetic Resonance Imaging of Plants: Water Balance and Water Transport in Relation to Photosynthetic Activity

Henk Van As[1,2*] and Carel W. Windt[1]

[1]Laboratory of Biophysics and [2]Wageningen NMR Centre, Wageningen University, Dreijenlaan 3, 6703 HA Wageningen, The Netherlands

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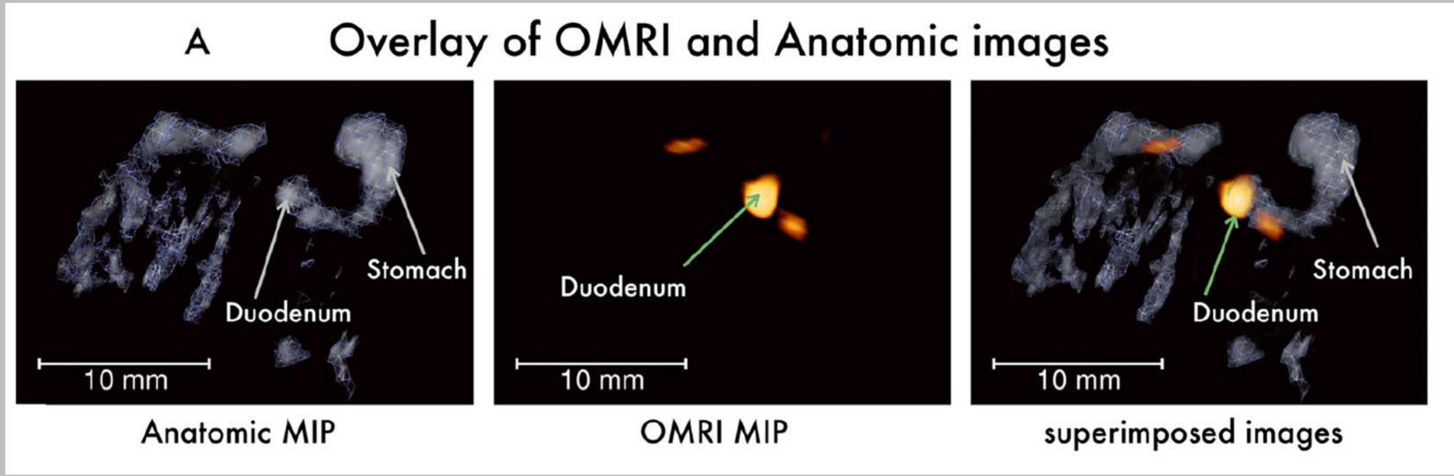
SNR ⌂

… ⌂

	high resolution NMR	solid state NMR	clinical imaging
B_1 (Tesla)	$5\ 10^{-4}$	$2\ 10^{-3}$	10^{-5}

Applications: imaging and MRI

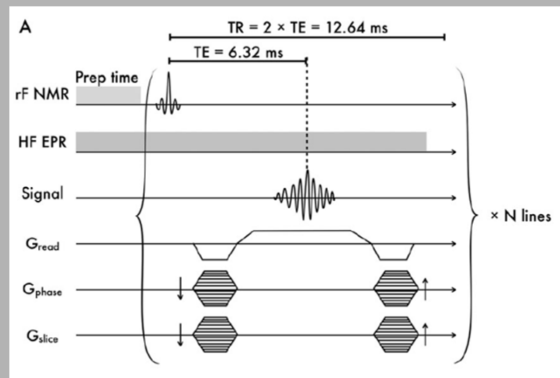


Elodie Parzy, RMSB, Bordeaux, France

In vivo Overhauser-enhanced MRI of proteolytic activity

Neha Koonjoo[a], Elodie Parzy[a], Philippe Massot[a], Matthieu Lepetit-Coiffé[a,b], Sylvain R. A. Marque[c], Jean-Michel Franconi[a], Eric Thiaudiere[a] and Philippe Mellet[a,d]*

Contrast Media Mol. Imaging **2014**, 9 363–371



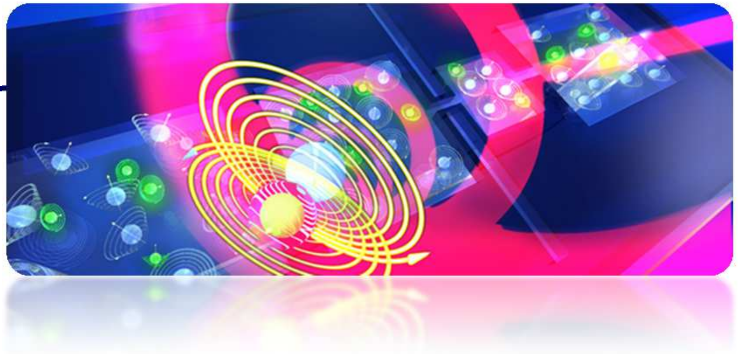
back to SENSITIVITY ! …

Applications: hyperpolarization

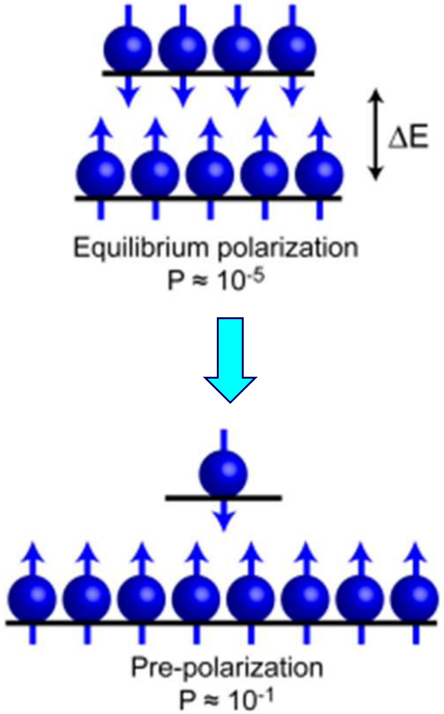
⌂ **NMR sensitivity: THE challenge !**

⌂ **from thermal equlibrium to …**

⌂ **non equilibrium polarization**



https://pines.berkeley.edu/research/hyperpolarization



http://www.chem.tamu.edu/rgroup/hilty

noble gas atoms: ^{129}Xe, ^{131}Xe, ^{83}Kr… ⌂

^{3}He ⌂

Dynamic Nuclear Polarization (DNP) ⌂

photochemical DNP ⌂

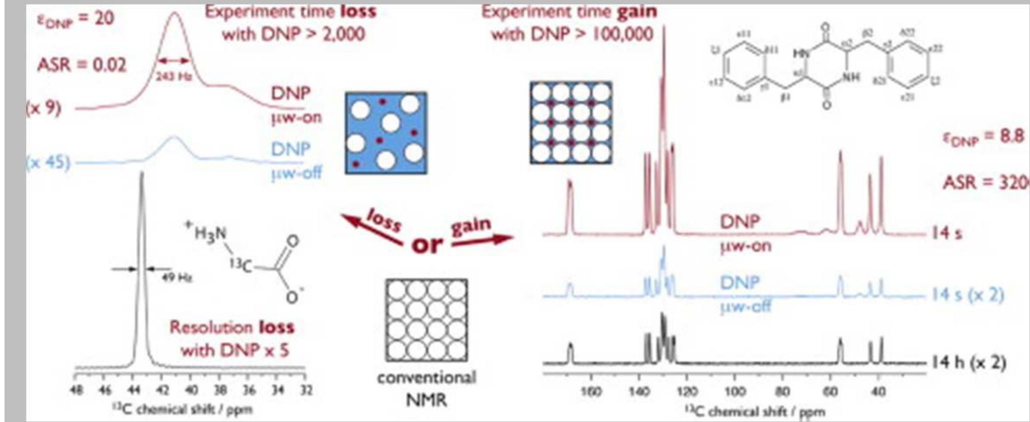
parahydrogen ⌂

optical excitation of NV^{-} center ⌂

hyperpolarized *singlet* MRI ⌂

…

Applications: hyperpolarization



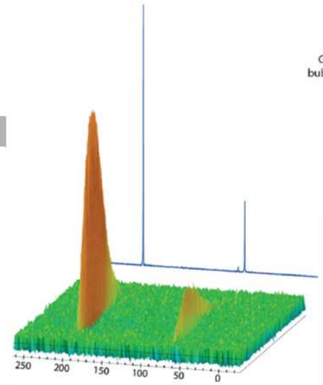
Is solid-state NMR *enhanced* by dynamic nuclear polarization?

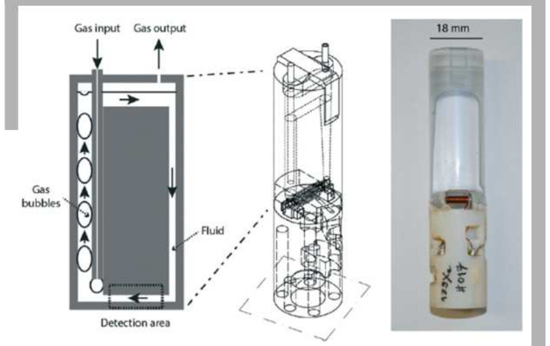
Daniel Lee [a,b,*], Sabine Hediger [a,b,c], Gaël De Paëpe [a,b]

Solid State NMR, *66-67* (**2015**) 6-20

CEA, Grenoble, France, Sabine Hediger

Patrick Berthault, CEA Saclay, France



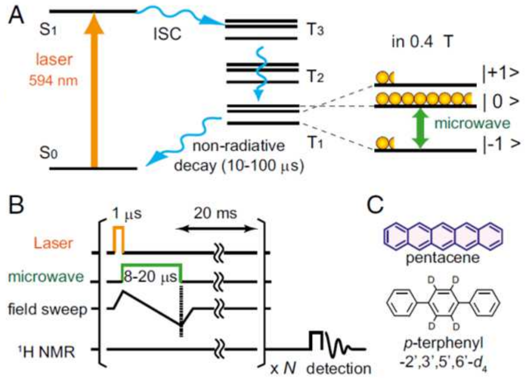


3D-printed system optimizing dissolution of hyperpolarized gaseous species for micro-sized NMR†

A. Causier,[ab] G. Carret,[b] C. Boutin,[b] T. Berthelot[a] and P. Berthault*[b]

Lab Chip, 2015, 15, 2049

As a conclusion: the NMR saga continues …



Science

AAAS

Nanoscale Nuclear Magnetic Resonance with a Nitrogen-Vacancy Spin Sensor

H. J. Mamin[1], M. Kim[1,2], M. H. Sherwood[1], C. T. Rettner[1], K. Ohno[3], D. D. Awschalom[3], D. Rugar[1,*]

Author Affiliations

*To whom correspondence should be addressed. E-mail: rugar@us.ibm.com

ABSTRACT

Extension of nuclear magnetic resonance (NMR) to nanoscale samples has been a longstandi… because of the insensitivity of conventional detection methods. We demonstrated the use… near-surface nitrogen-vacancy (NV) center in diamond as a sensor to detect proton N… located external to the diamond. Using a combination of electron spin echoes an… we showed that the NV center senses the nanotesla field fluctuations from th… …ain and spectroscopic NMR measurements on the nanomete…

Nuclear Magnetic Resonance Spectroscopy on a (5-Nanometer)^3 Sample Volume

T. Staudacher[1,2], F. Shi[3], S. Pezzagna[4], J. Meijer[4], J. Du[3], C. A. Meriles[5], F. Reinhard[1,*], J. Wrachtrup[1]

Author Affiliations

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ABSTRACT

Application of nuclear magnetic resonance (NM… …scale samples has remained an elusive goal, achieved only with great experi… …peratures. We demonstrated detection of NMR signals from a (5-nano… …id organic samples under ambient conditions. We used an ato… …ogen-vacancy defect center, embedded ~7 nanometers under… …ctra of various samples placed on the diamond surfa… …ins with a net magnetization of only 10²…

Room temperature hyperpolarization of nuclear spins in bulk

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