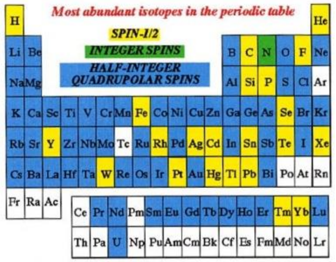
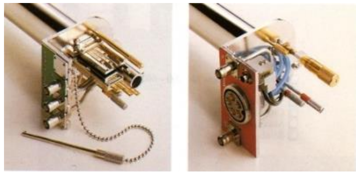
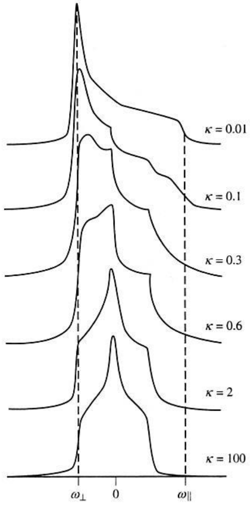




Nuclear Magnetic Resonance (NMR): solution, solid state, imaging



christian.bonhomme@upmc.fr

Christian BONHOMME, Professor

Laboratoire de Chimie de la Matière Condensée

UMR CNRS 7574 – Sorbonne Université, Paris

Spin: from 1925 to 2004

W. Pauli, Physics 1945

"for the discovery of the Exclusion Principle, also called the Pauli Principle"

G. Uhlenbeck, S. Goudsmit

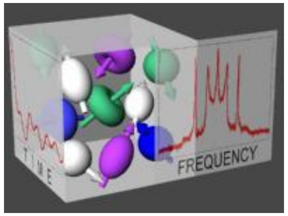
« fathers of the spin »

I. I. Rabi, Physique 1944

"for his resonance method for recording the magnetic properties of atomic nuclei"

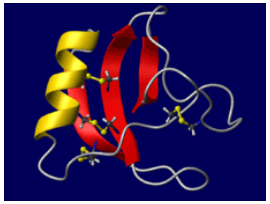
F. Bloch, E. M. Purcell, Physics 1952

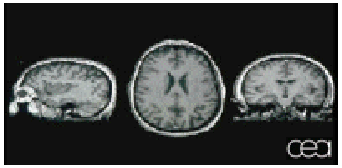
"for the development of new methods for nuclear magnetic precision measurements and discoveries in connection therewith"



K. Wüthrich, Chemistry 2002

"for his development of NMR spectroscopy for determining the three dimensional structure of biological macromolecules in solution"



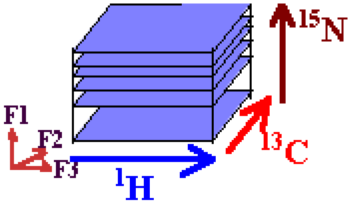


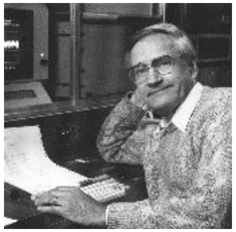
P. C. Lauterbur, P. Mansfield, Medicine 2003

"for their discoveries concerning magnetic resonance imaging"

R. R. Ernst, Chemistry 1991

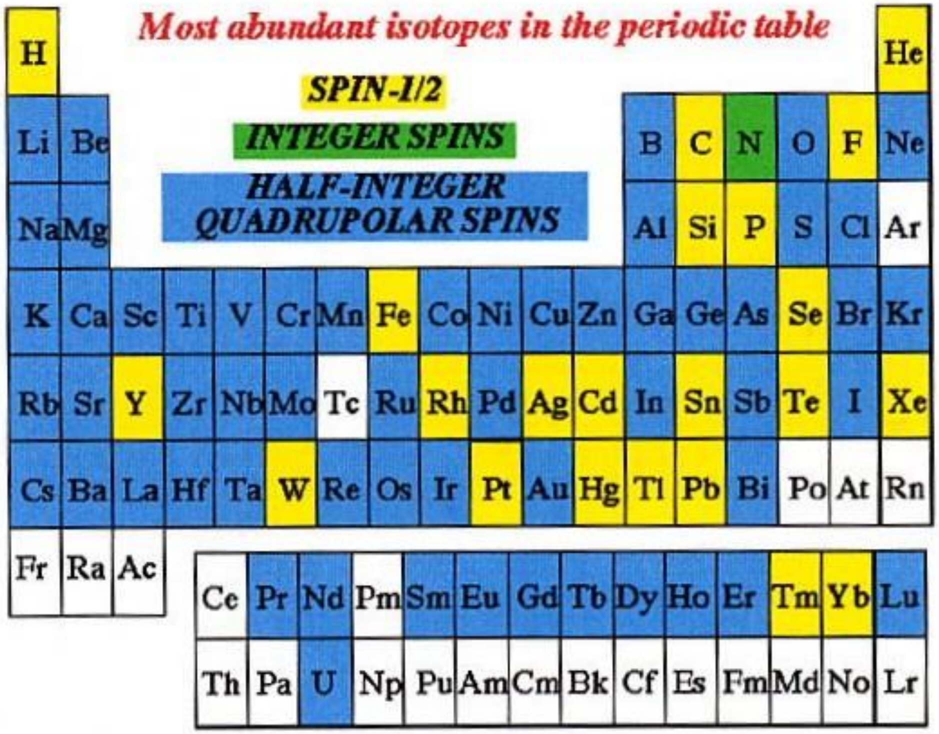
"for his contribution to the development of the methodology of high resolution NMR spectroscopy"





Spin quantum number I

$I \neq 0 \longrightarrow$ NMR…



Most abundant isotopes in the periodic table

SPIN-1/2

INTEGER SPINS

HALF-INTEGER QUADRUPOLAR SPINS

H																	He
Li	Be											B	C	N	O	F	Ne
Na	Mg											Al	Si	P	S	Cl	Ar
K	Ca	Sc	Ti	V	Cr	Mn	Fe	Co	Ni	Cu	Zn	Ga	Ge	As	Se	Br	Kr
Rb	Sr	Y	Zr	Nb	Mo	Tc	Ru	Rh	Pd	Ag	Cd	In	Sn	Sb	Te	I	Xe
Cs	Ba	La	Hf	Ta	W	Re	Os	Ir	Pt	Au	Hg	Tl	Pb	Bi	Po	At	Rn
Fr	Ra	Ac															
			Ce	Pr	Nd	Pm	Sm	Eu	Gd	Tb	Dy	Ho	Er	Tm	Yb	Lu	
			Th	Pa	U	Np	Pu	Am	Cm	Bk	Cf	Es	Fm	Md	No	Lr	

spin

electron 1/2

neutron 1/2

proton I=1/2

photon 1

intrinsic angular momentum

$I = n/2$

n: integer

identity card:

isotope ^{13}C

spin I (m_I)

natural abundance (%)

gyromagnetic ratio

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

receptivity :

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

^{13}C: I = ½ (1.1%)

^{12}C: I = 0 (98.9%)

$D^P(^1H) = 1$

$D^P(^{13}C) = 0.00017\ldots$!

Nuclear spins and ... magnetic fields

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

magnetic moment

gyromagnetic ratio

spin angular momentum

$\boxed{E = - \mu \cdot B}$

B_0 (~10T)

$\boxed{\Delta m_I = \pm 1}$

$m_I = -1/2$

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

$m_I = +1/2$

$\boxed{\nu_0 = \gamma B_0 / 2\pi}$

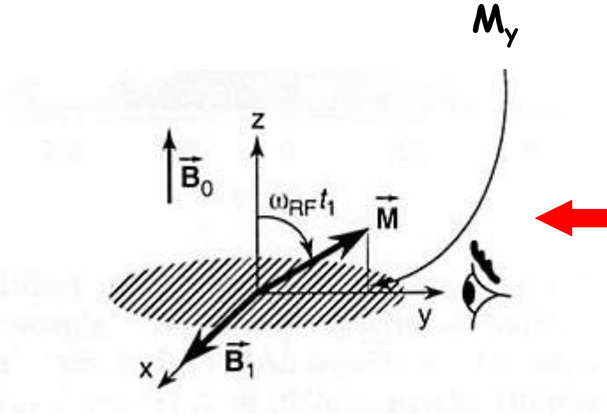
Larmor frequency !

Boltzmann equation

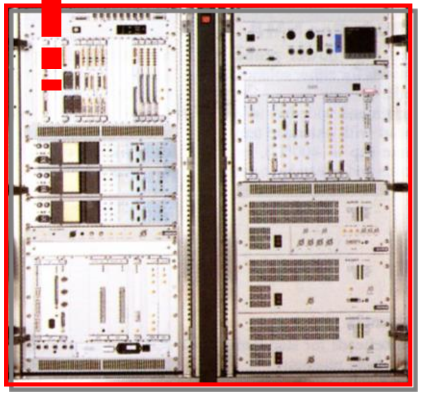
Curie's law

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

M



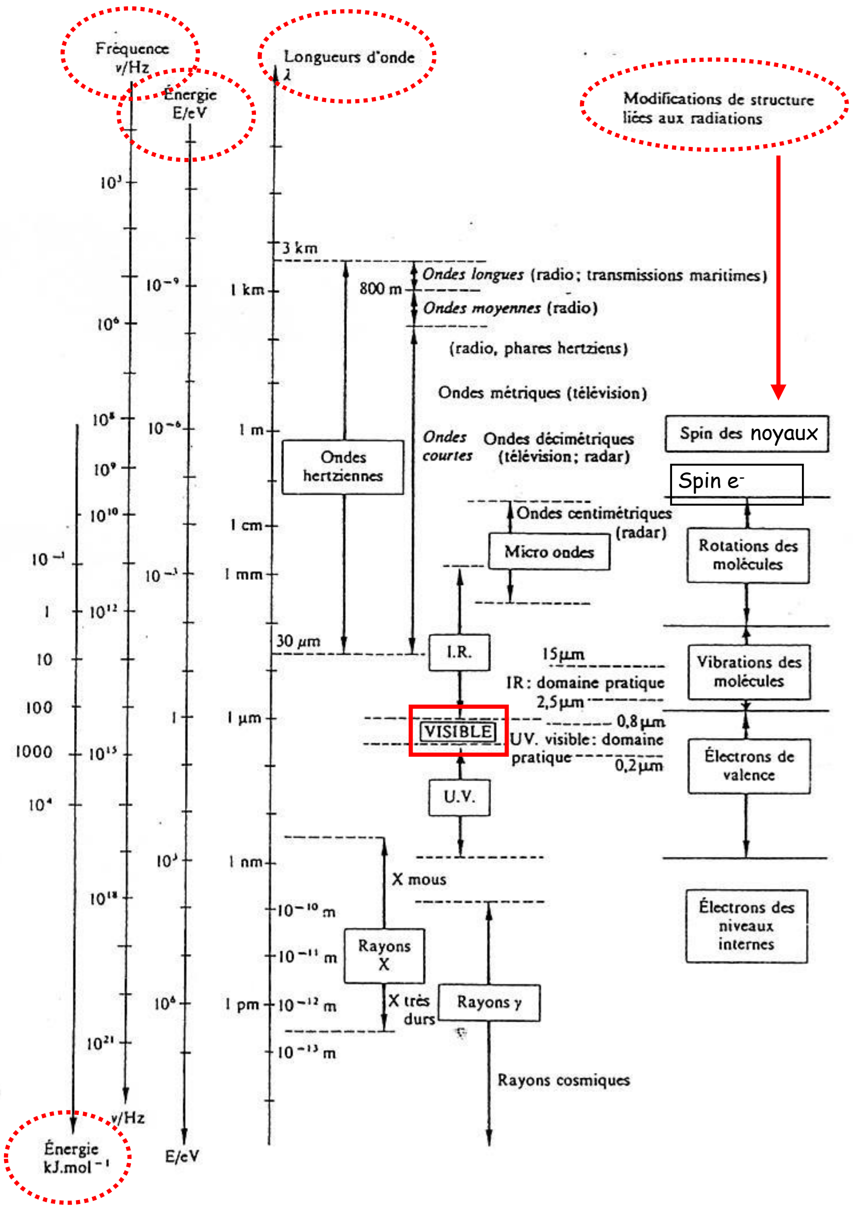
Man, Encyclopedia of analytical chemistry, 2000, 12228.



B_1(RF) "at resonance" !

order of magnitude : very small !...
sensitivity ?

Electromagnetic spectrum



Les radiations électromagnétiques.

frequency ν **(Hz)**

wave length λ = c/ν **(m)**

wave number $\bar{\nu}$ = 1/λ (cm^{-1})

energy hν **(J)**

units : eV, kJ.mol^{-1}, cm^{-1}

NMR

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

Electron Paramagnetic Resonance

The case of the proton

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

$\gamma \hbar = g_N \beta_N$

$g_N = 5{,}5855$

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

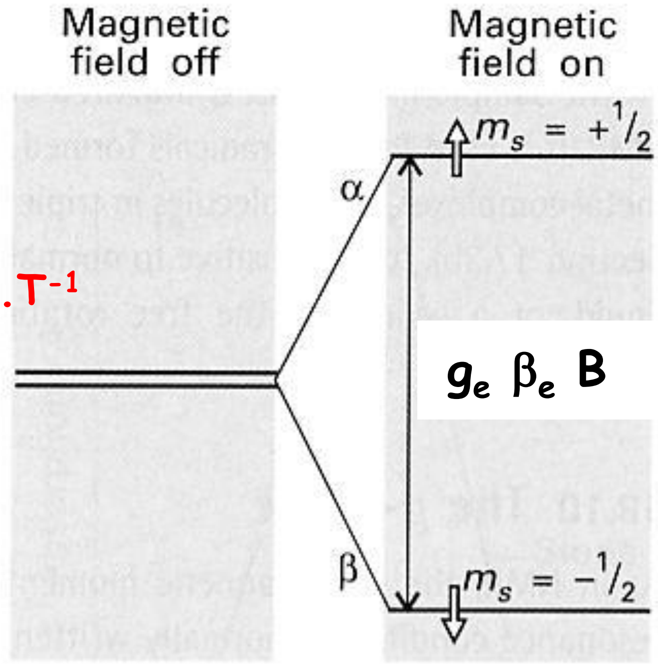
$= 5{,}051.10^{-27}$ J.T^{-1}

The case of the electron

$g_e = 2{,}0023$

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

$= 9{,}274.10^{-24}$ J.T^{-1}



Order of magnitude:

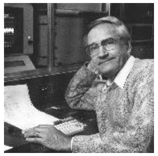
B ≈ 0,3 T

ν = 9 GHz = 9.10^9 Hz ; $\lambda \approx$ 3 cm

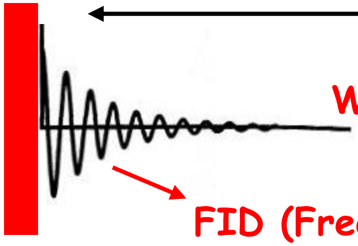
microwaves

Fourier transform NMR

« The idea » :

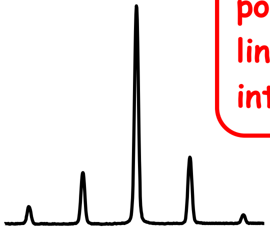


N times !



Wait... ~ 5 T_1

TF



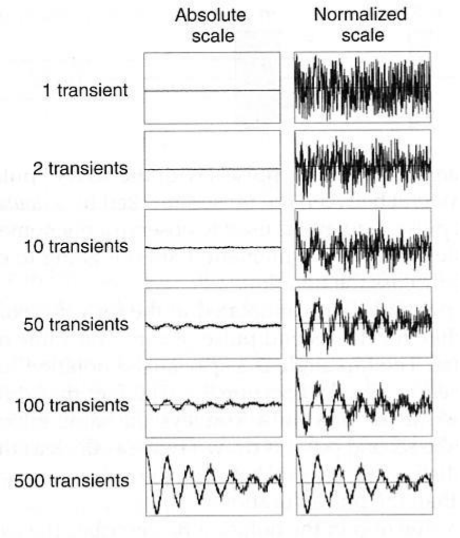
position (shift)
line width
intensity

RF pulse (B_1)

FID (Free Induction Decay)
(time domain)

spectrum
(frequency domain)

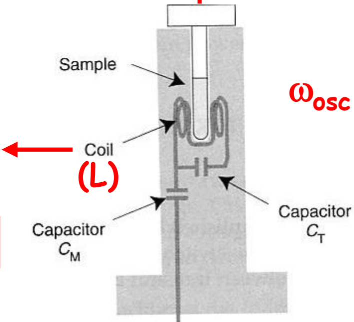
back to equilibrium



Signal/Noise ~ $\sqrt{N}$

Levitt, Spin dynamics, 2002.

B_0



$\omega_{osc}=(L\ C_T)^{-1/2}$

B_1 ← (L)

matching

tuning

RF

NMR signal

amplification

digitization

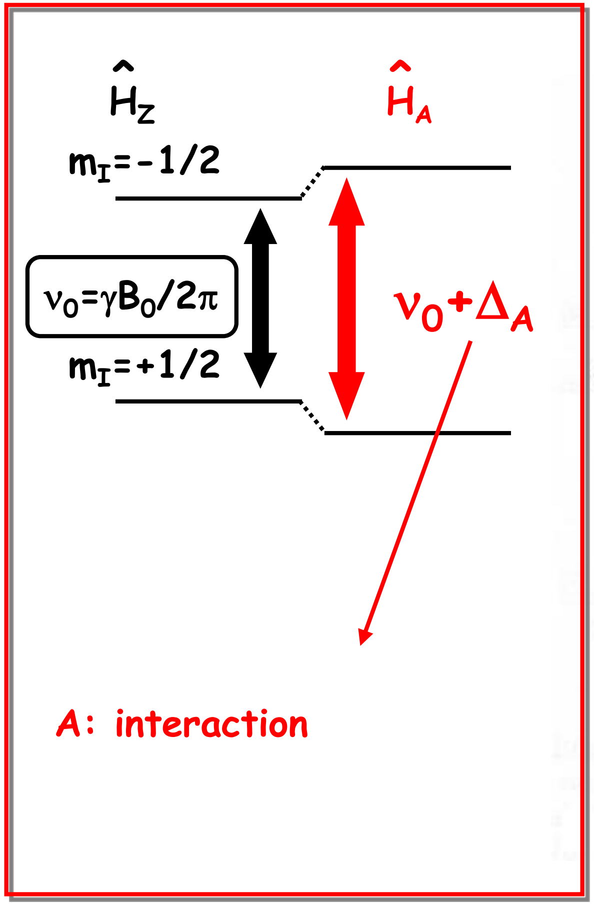
math. treatment

NMR and quantum mechanics

Towards quantum mechanics:

$\hat{H}_Z = -\gamma B_0 \hat{I}_z$

$\hat{H}_{RF} = -\gamma B_1 (\cos\omega_{ref} t) \hat{I}_x$



$\hat{H}_Z$

$\hat{H}_A$

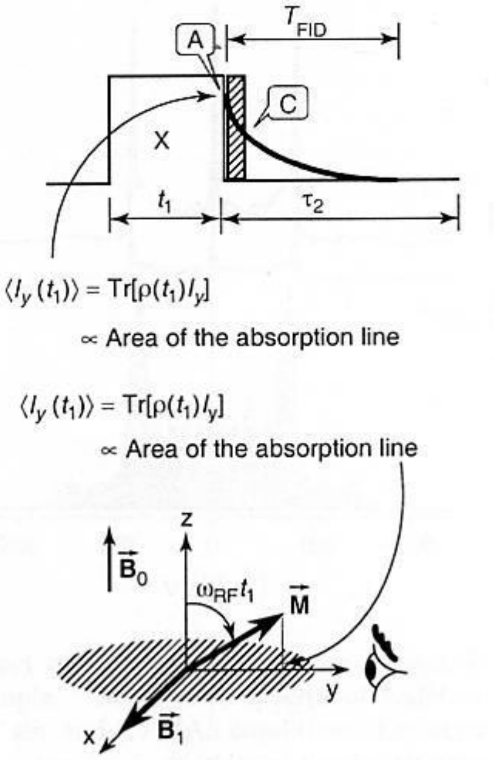
$m_I=-1/2$

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

$m_I=+1/2$

$\nu_0+\Delta_A$

A: interaction



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

$\propto$ Area of the absorption line

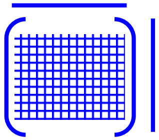
$\langle I_y(t_1)\rangle = \mathrm{Tr}[\rho(t_1)I_y]$

$\propto$ Area of the absorption line

10^{18} spins: density matrix

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

$\rho(t)$ =



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

Liouville-von Neumann equation

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

observable

ex: I_y

Man, Encyclopedia of analytical chemistry, 2000, 12228.

Interactions in NMR

2

dipole-dipole

(dipolar)

(INT)

3

electron-nucleus

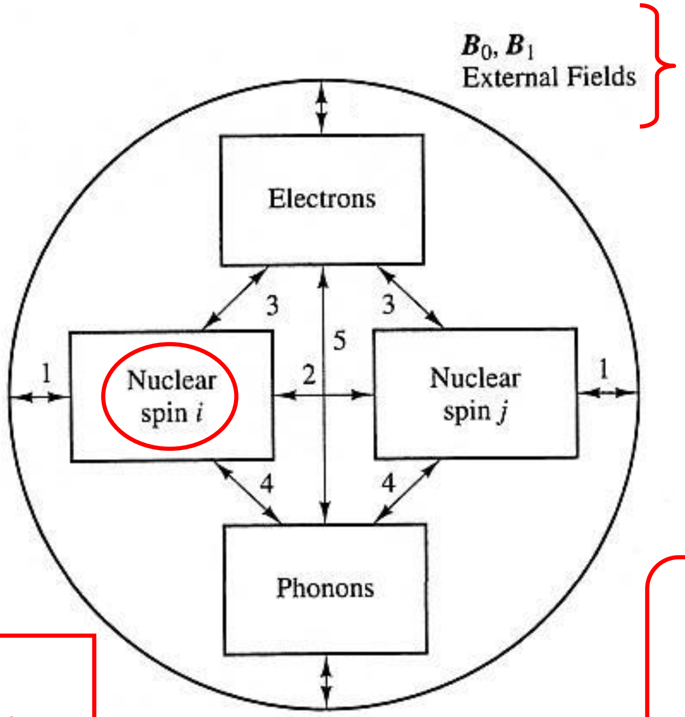
(chemical shift, quadrupolar, J, Knight shift)

(INT)

« spies » for structure elucidation

INT: internal

EXT: external



1

(EXT)

manipulation of the quantum states

4, 5

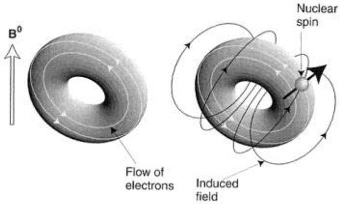
relaxation

back to equilibrium

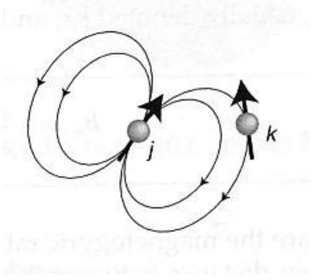
$$\hat{H} = \underbrace{\hat{H}_{ext}}_{(\hat{H}_0 + \hat{H}_{RF})} + \underbrace{\hat{H}_{int}}_{(\hat{H}_D + \hat{H}_{CS} + \hat{H}_Q \ldots)}$$

Mehring, High resolution NMR in solids, 1983, 8.

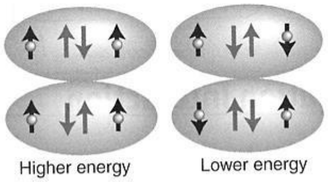
Fundamental interactions for chemists



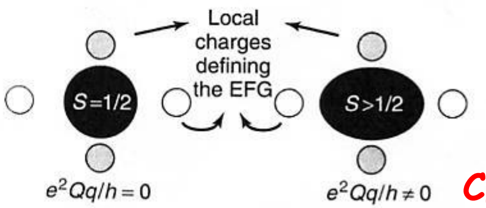
chemical shift : δ



dipolar interaction : 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

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

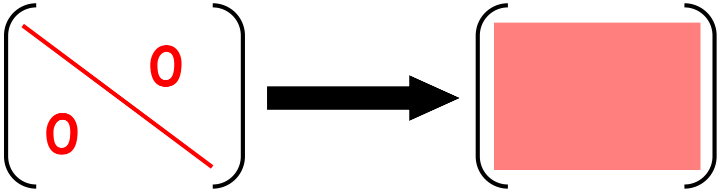
(CS, D, Q...)

nuclear spin operator

the interaction: a second rank tensor (symmetrical)

another spin operator or B_0...

anisotropy : why ?

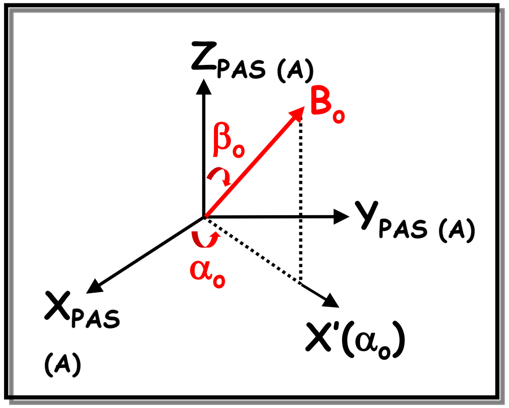


diagonal in the PAS (Principal Axes System)

LAB

Principal values A_{ii} – Ellipsoid representation

For each interaction A (CS, D, Q...)

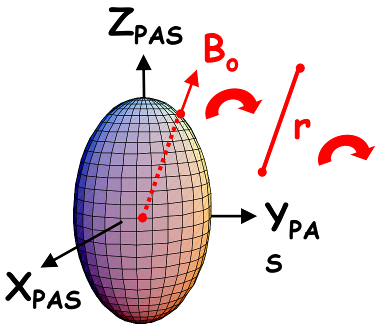


$$\begin{pmatrix} A_{11} & & 0 \\ & A_{22} & \\ 0 & & A_{33} \end{pmatrix}$$

... at the level of the nucleus ...

$$\begin{pmatrix} A_{xx} & A_{xy} & A_{xz} \\ A_{yx} & A_{yy} & A_{yz} \\ A_{zx} & A_{zy} & \boxed{A_{zz}} \end{pmatrix}_{LAB} = \begin{bmatrix} f(\alpha_0, \beta_0) \end{bmatrix}_{LAB}$$

« first order » perturbation



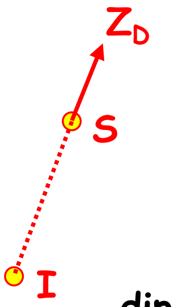
$r^{-2} \overset{!}{=} A_{ZZ}$

equation: $A_{11}X^2+A_{22}Y^2+A_{33}Z^2 = 1$

semi-axes: $(A_{ii})^{-1/2}$

the trace $TrA = \Sigma A_{ii}$ ou $A_{iso} = 1/3\ TrA$

ex: null trace : D, Q



$$[D]_{PAS} \propto D \begin{pmatrix} 1 & 0 & 0 \\ 0 & 1 & 0 \\ 0 & 0 & -2 \end{pmatrix}$$

dipolar constant

Interactions in solution state NMR

...a degenerated case : all interactions are averaged to their isotropic values...

Remember :

$\mathrm{Tr}(CS) \neq 0$

$\mathrm{Tr}(J) \neq 0$

!

$\mathrm{Tr}(D) = \mathrm{Tr}(Q) = 0$

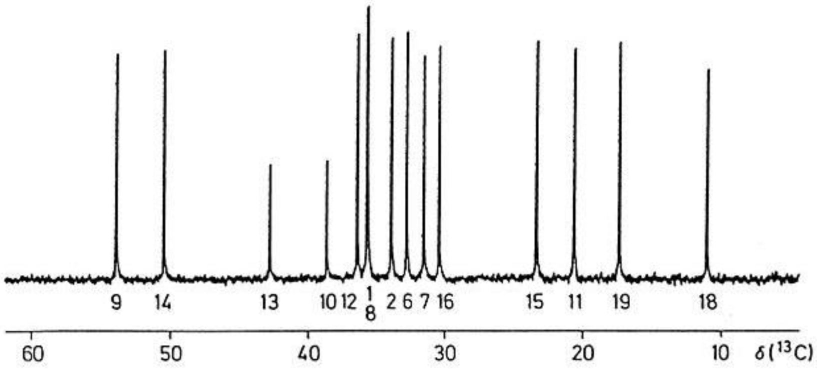
CS : "position of the lines", "fingerprints"

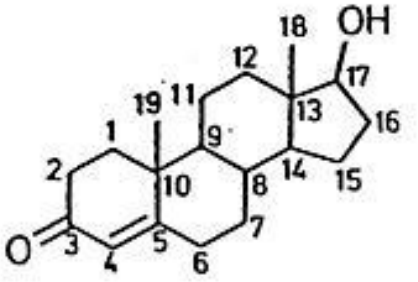
J : "multiplets", connectivity

(D and Q have a direct impact on relaxation...)

HIGH RESOLUTION NMR

^{13}C-$\{^{1}H\}$: a steroid



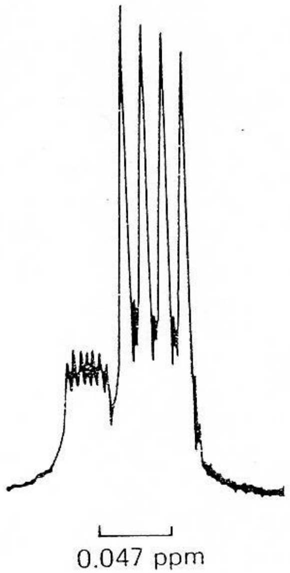


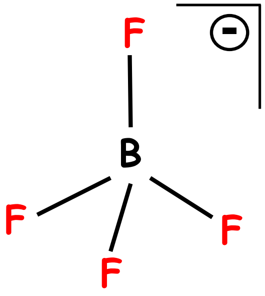
J couplings and multiplets

a spin J coupled to n spins I...

(2nI + 1) expected lines

ex: ^{19}F : BF_4^-

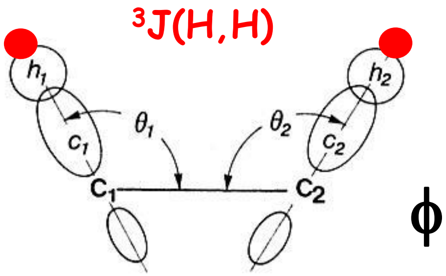


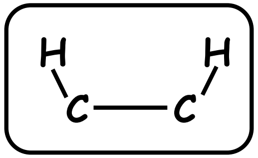


^{10}B (I=3): 7 lines (nat. ab. 20%)

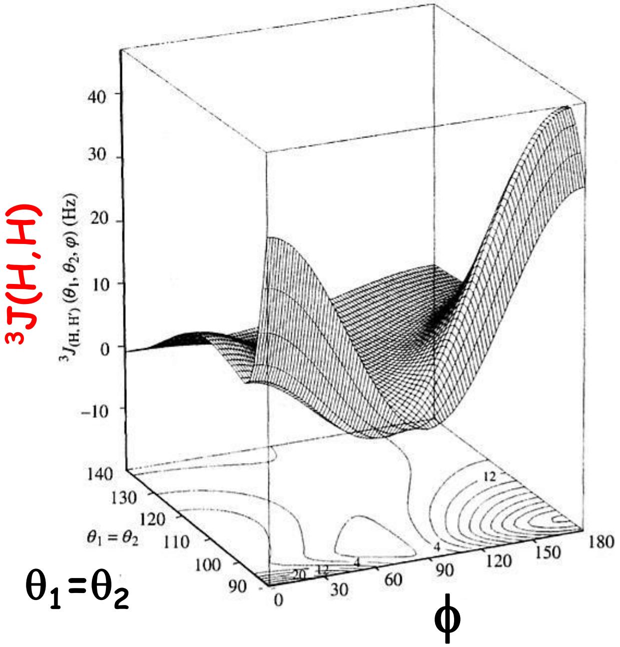
^{11}B (I=3/2) : 4 lines (nat. ab. 80%)

a tool for structural characterization



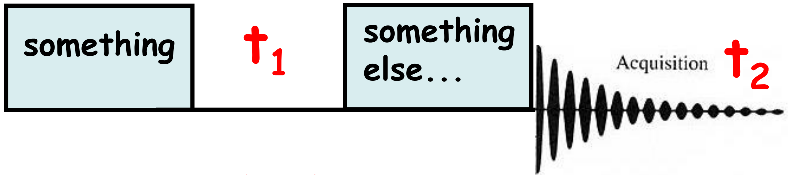


ϕ : dihedral angle

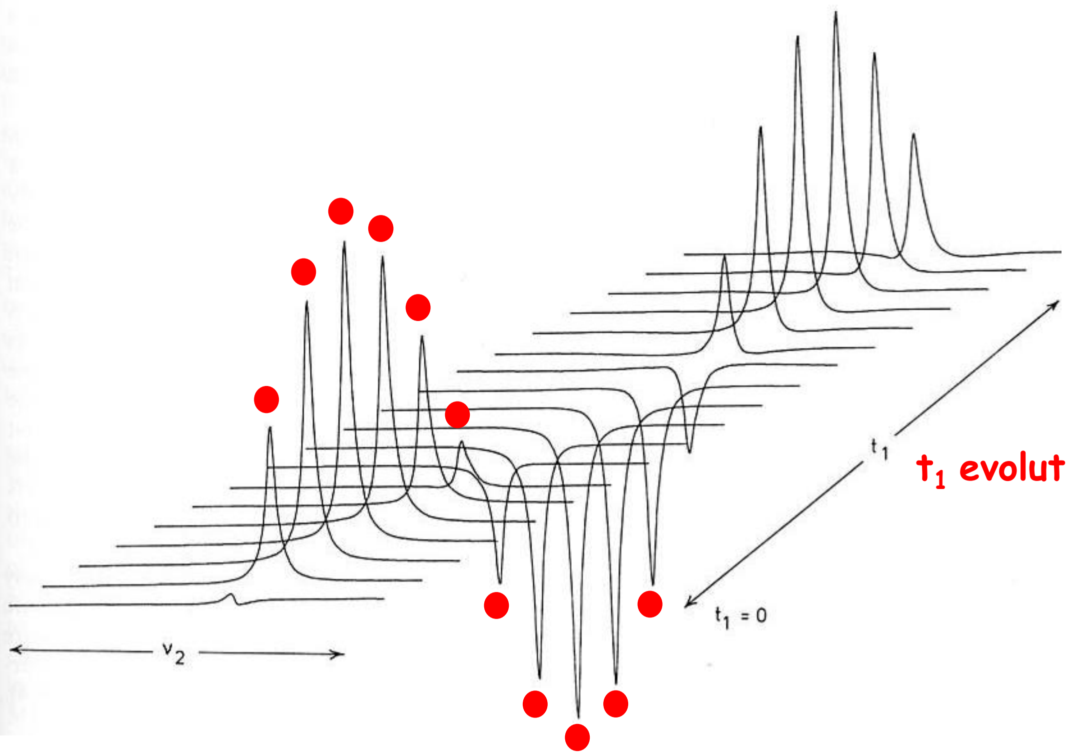


Barfield et al., J. Am. Chem. Soc., 1992, 114, 1574.

Combining dimensions…



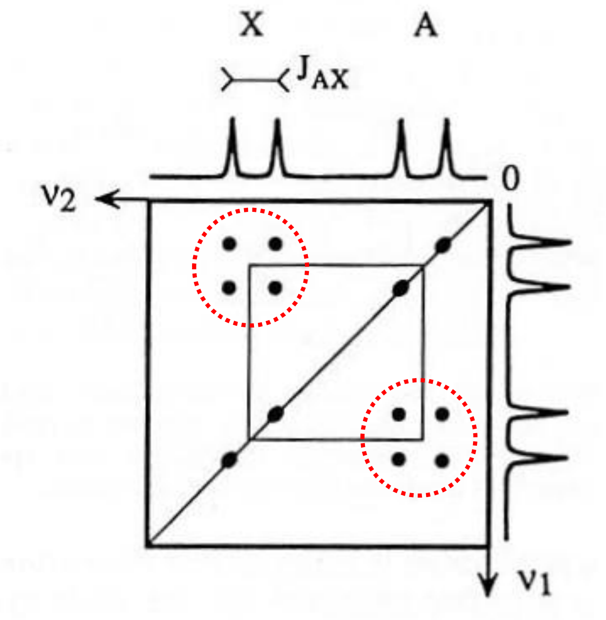
J.Jeener ~ 1971



t_1 evolution

Derome, Modern NMR techniques for chemistry research, 1991.

A–X system

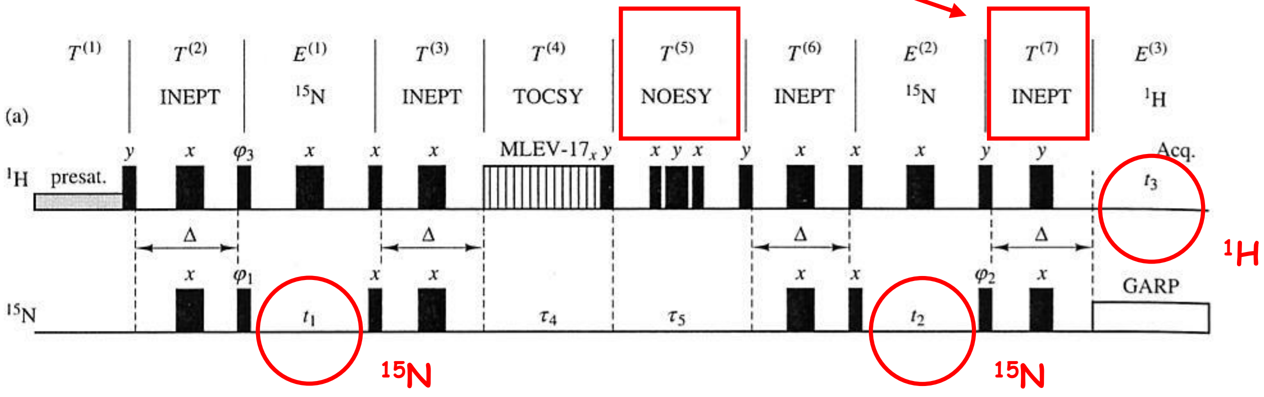


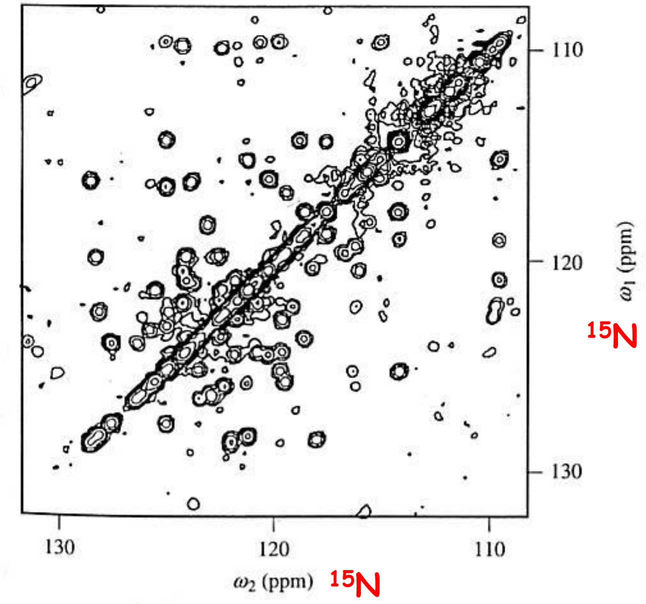
Canet, La RMN: concepts et méthodes, 1991.

Multidimensional NMR: solution state

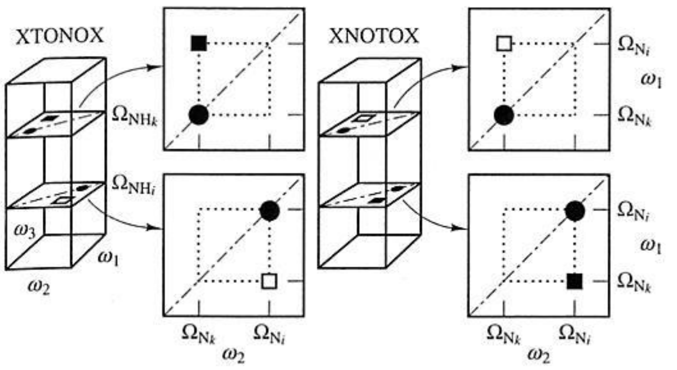
CS and J: selection, transfer, edition, correlation...(COSY, INEPT, HETCOR...)

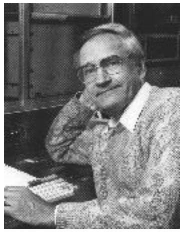
D: relaxation... (NOESY...)





99% ^{15}N-human ubiquitine





Ernst, Encyclopedia of NMR, 1996, 3130.

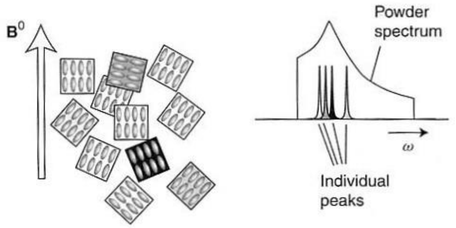
When powders are available !

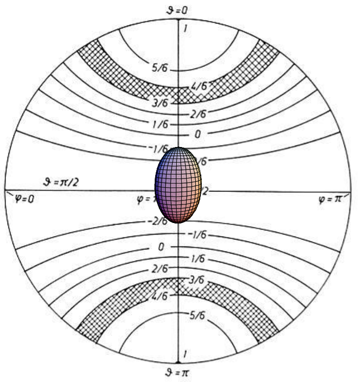
...how to build a CSA lineshape ?

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

$$\boxed{r^{-2} = \delta_{zz} = (\delta_{\perp}\,\mathrm{Sin}^2\beta_0 + \delta_{//}\,\mathrm{Cos}^2\beta_0)}$$

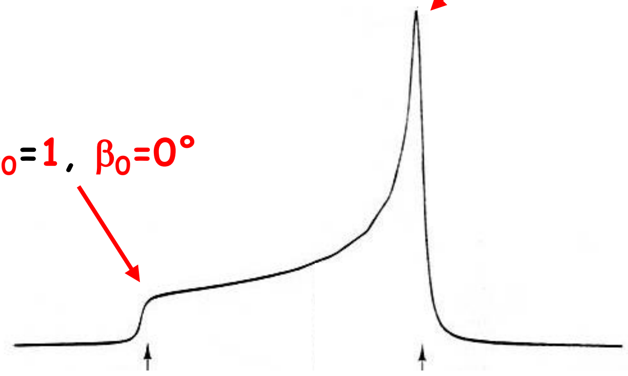
Ellipsoid of revolution !





Levitt, Spin dynamics, 2002.

Haeberlen, High resolution NMR in solids, selective averaging, 1976.

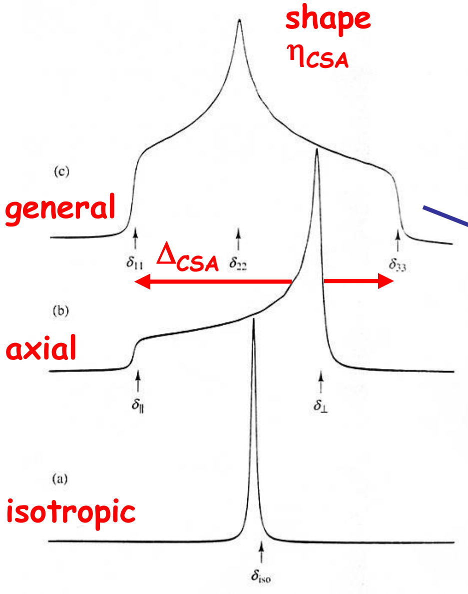


$\mathrm{Cos}^2\beta_0=0$, $\beta_0=90°$

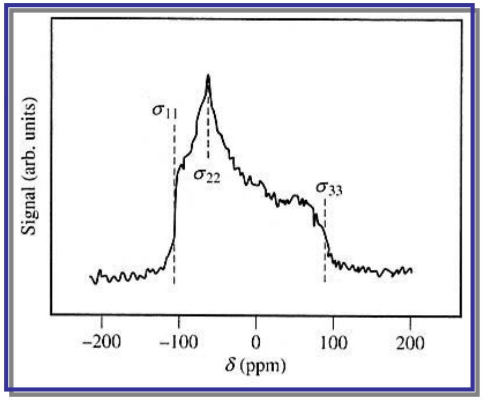
$\mathrm{Cos}^2\beta_0=1$, $\beta_0=0°$

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

shape η_{CSA}



^{19}F in fluoranil, $C_6F_4O_2$



shape: elliptic integrals

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

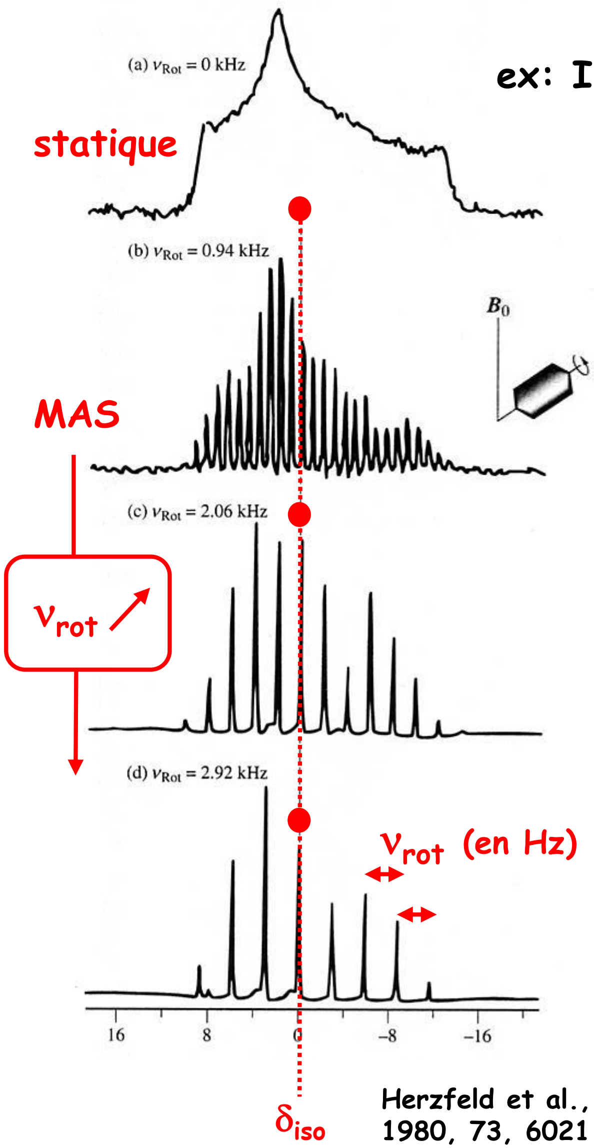
Mehring et al., J. Chem. Phys., 1971, 59, 746.

Magic Angle Spinning (MAS)

"explosion" of the spectrum in sharp rotation spinning sidebands

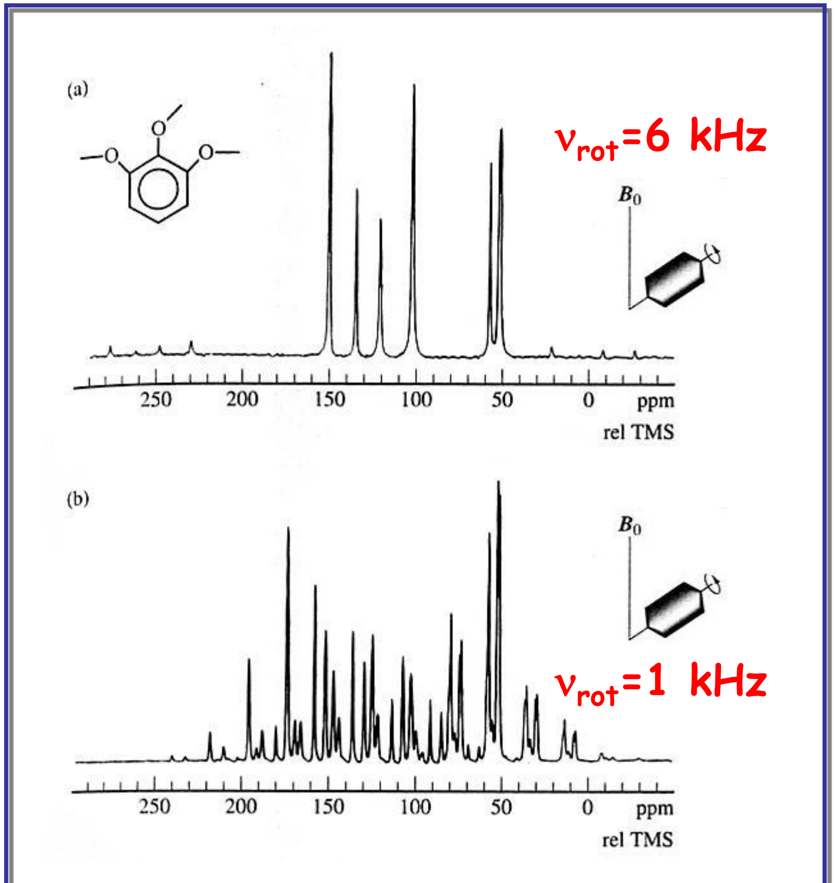
ex: I=1/2, A=CSA

^{31}P: dipalmitoylphosphatidylcholine



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

Spinning Spins
A Tribute to Raymond Andrew



Orendt, Encyclopedia of NMR, 1996, 1287.

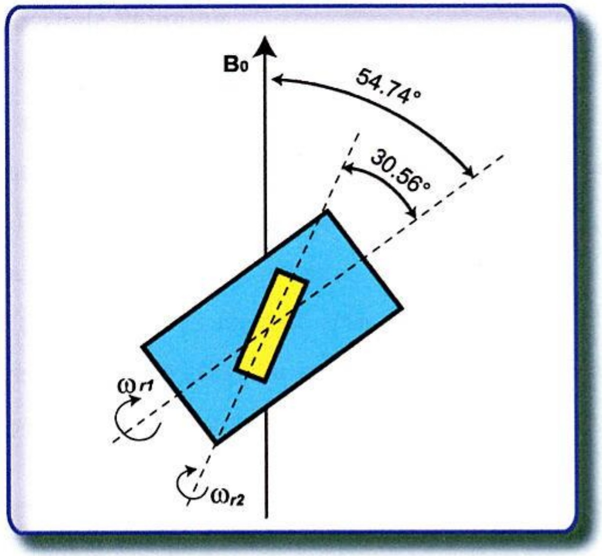
Quadrupolar nuclei and macroscopic rotations

MAS: « one degree of freedom" (1959)

we invent a new experiment involving 2 angles of reorientation !

DOR experiment (**DO**uble **R**otation)

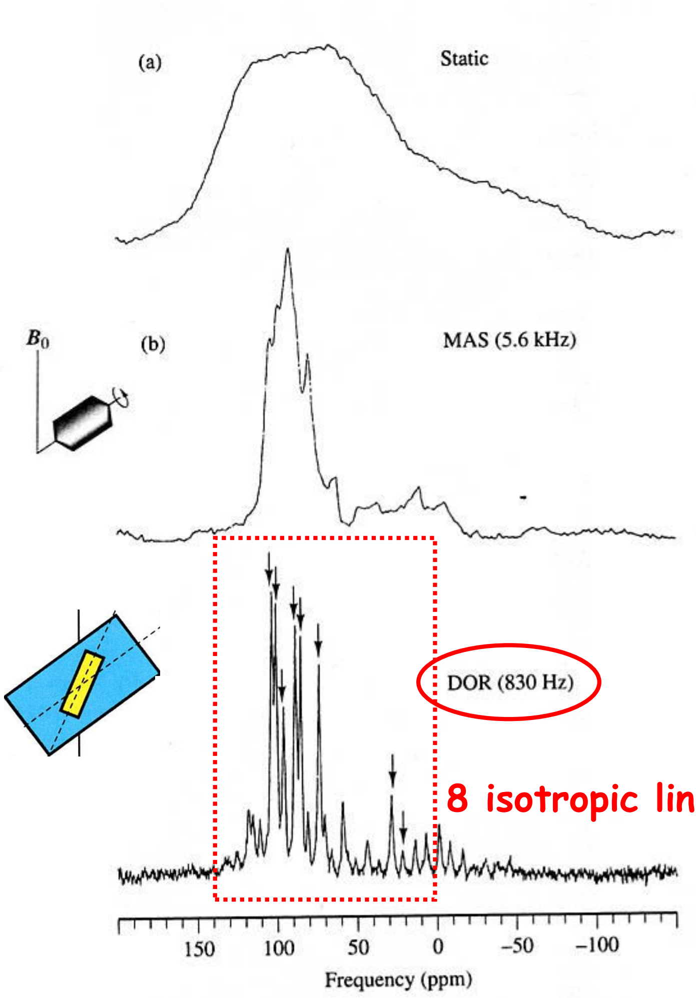
(Samoson, Pines, 1988)



Ziarelli, phD thesis.

1D experiment

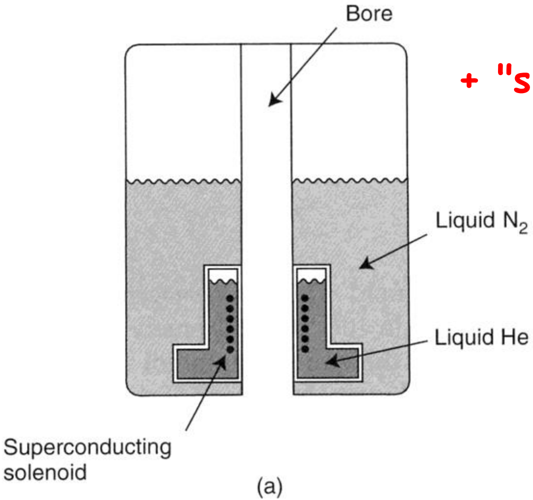
^{17}O (I=5/2) : $CaSiO_3$ wollastonite: 9 ^{17}O sites



8 isotropic lines

Wu, Encyclopedia of NMR, 1996, 1749.

B_0: homogeneous or not ?

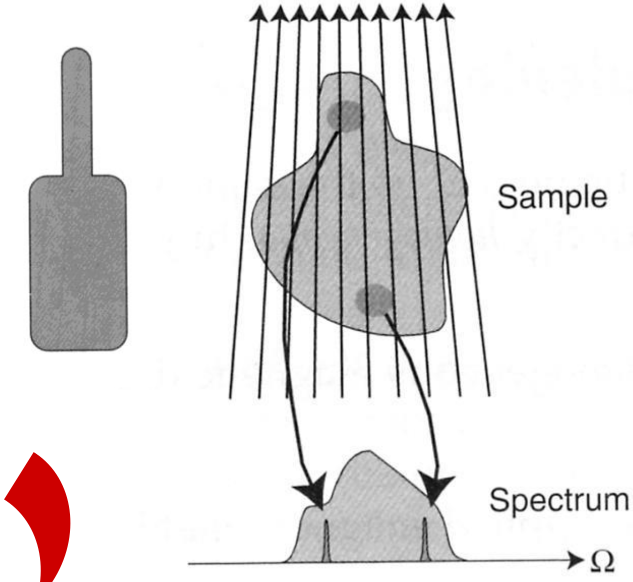


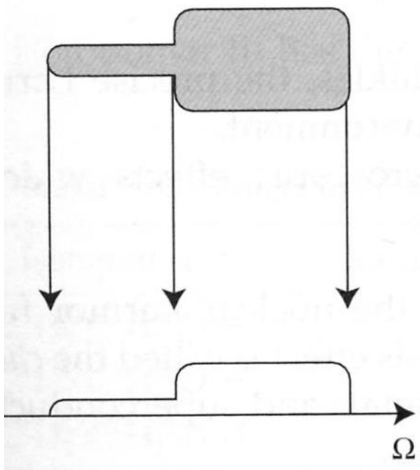
+ "shims" coils

Nb/Sn/...

"standard" NMR: homogeneity ~ 10^{-9} !

Inhomogeneous magnetic field: B_0 (r)





Levitt, Spin dynamics, 2002.

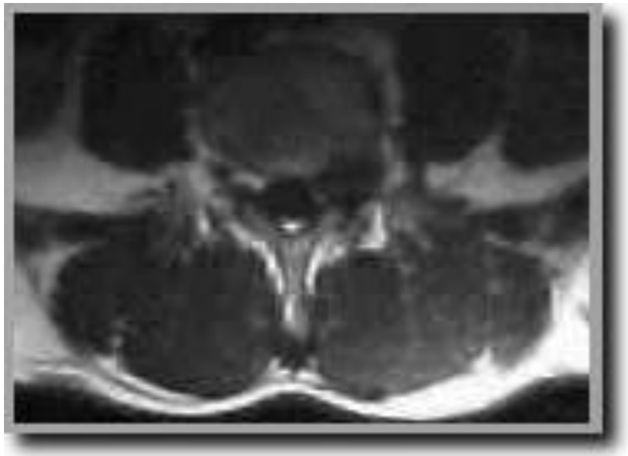
~ 1972

imaging

NMR imaging

brain

lungs

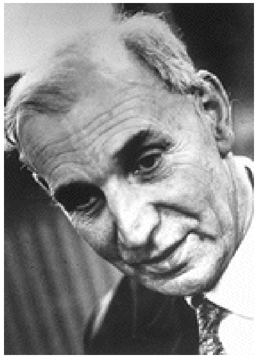


slipped disk

horizontal magnet: $B_0 \approx 2T$

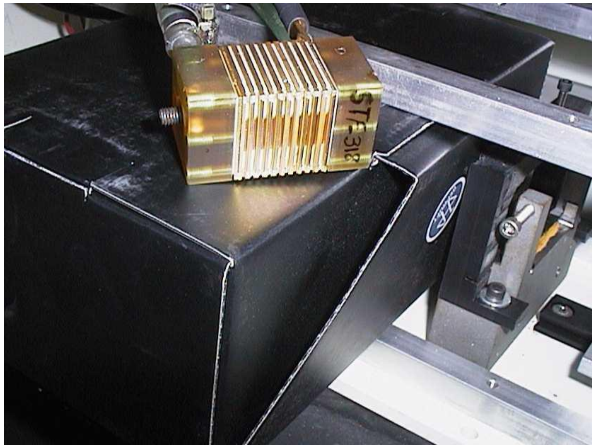
Imaging by hyperpolarization

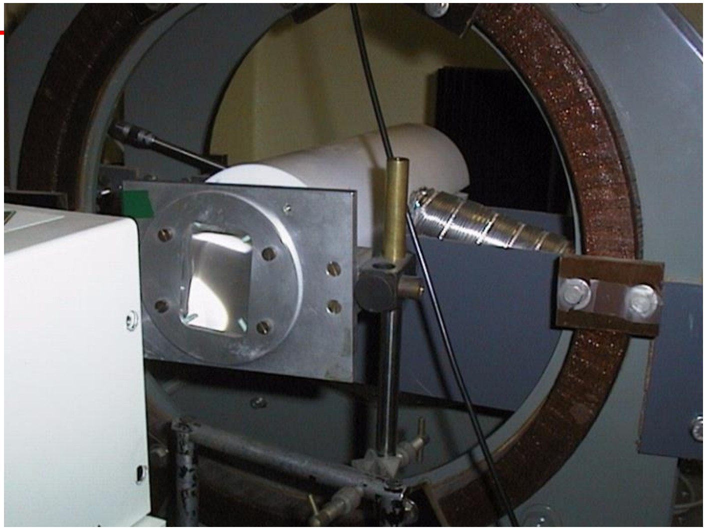
^{3}He, ^{17}O, ^{129}Xe...

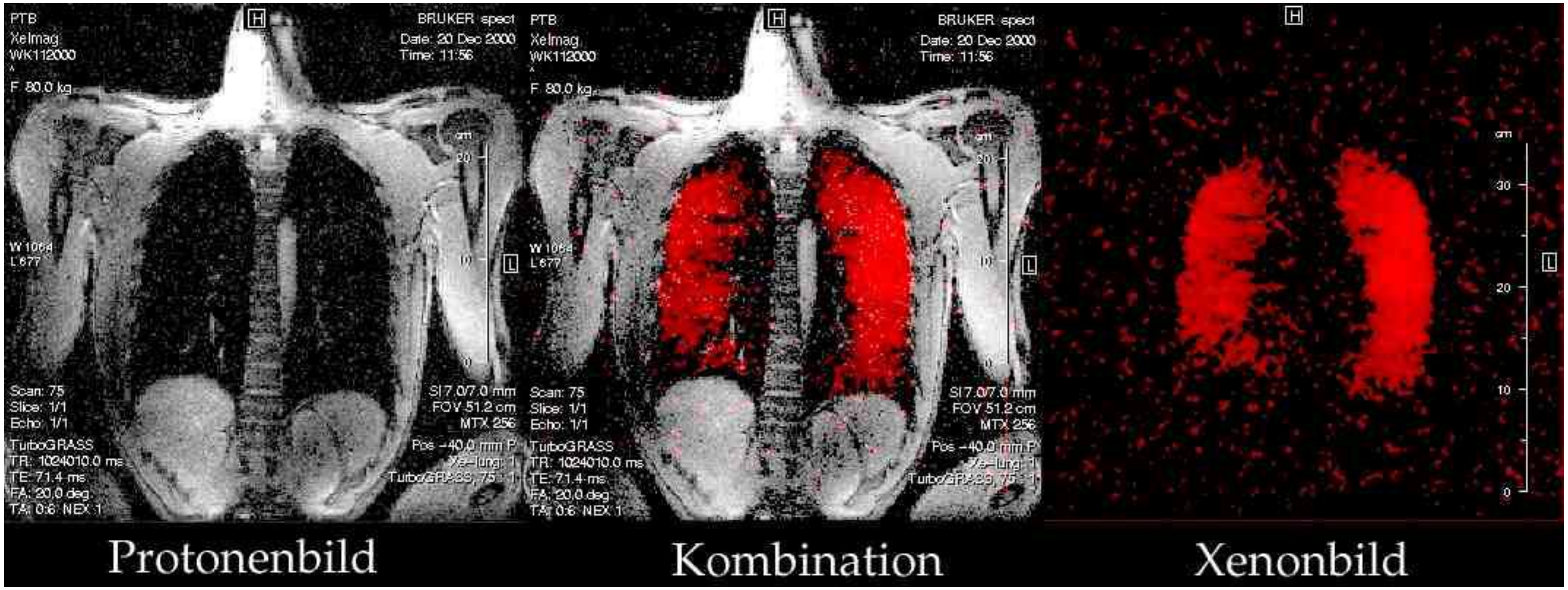


A. Kastler,

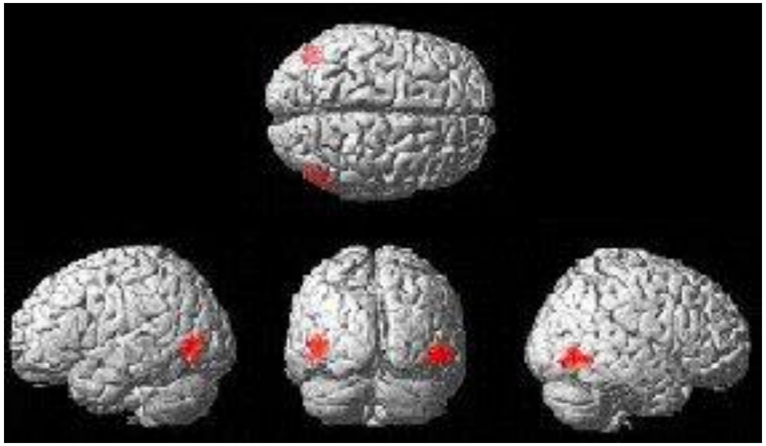
Physics, 1966

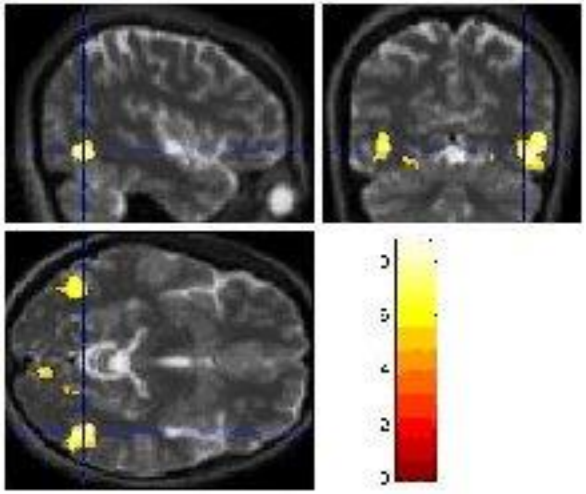


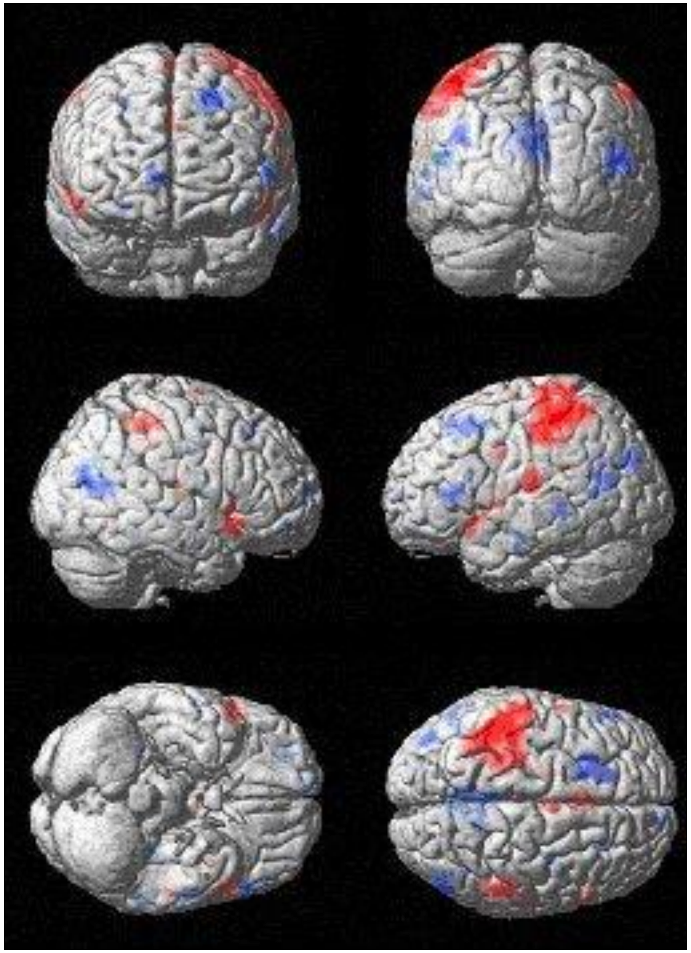




Functional imaging







Answers to stimuli: brain activity!

High Resolution Solid State NMR

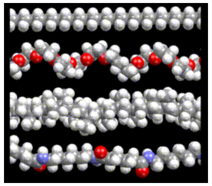
Christian BONHOMME, Professor

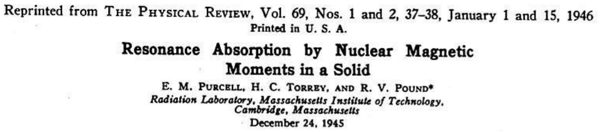
Laboratoire de Chimie de la Matière Condensée

UMR CNRS 7574 – Sorbonne Université, Paris

Some key experiments in sold state NMR

1) NMR of paraffin, 1946 (Purcell, Torrey, Pound)

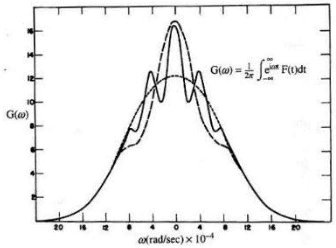




Reprinted from THE PHYSICAL REVIEW, Vol. 69, Nos. 1 and 2, 37–38, January 1 and 15, 1946
Printed in U. S. A.

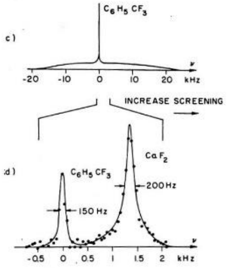
Resonance Absorption by Nuclear Magnetic Moments in a Solid

E. M. PURCELL, H. C. TORREY, AND R. V. POUND*
Radiation Laboratory, Massachusetts Institute of Technology, Cambridge, Massachusetts
December 24, 1945

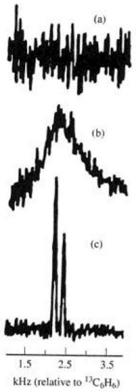


2) Magic Angle Spinning, MAS, 1959 (Andrew, Bradbury, Eades and Lowe)

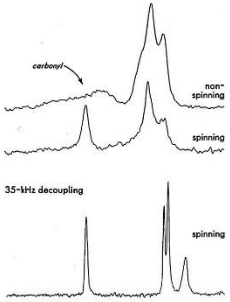
3) WAHUHA sequence, 1968 (Waugh, Huber, Haeberlen)



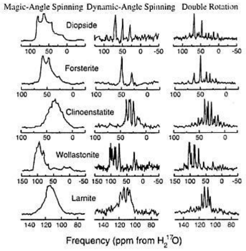
4) Cross Polarization (CP), 1962 (Hartmann, Hahn)



5) Indirect observation of dilute spins, 1972 (Pines, Gibby, Waugh)

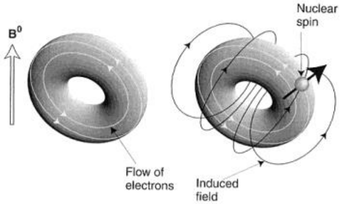


6) The CP MAS experiment, 1976 (Schaefer, Stejskal)

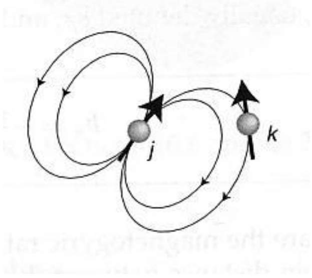


7) Quadrupolar nuclei: high resolution, 1988, 1995 (Virlet, Llor, Pines, Frydman)

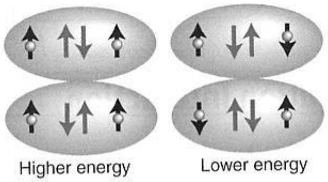
Fundamental interactions for chemists



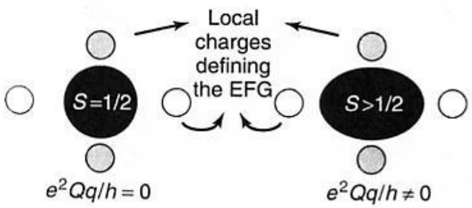
chemical shift :
δ



dipolar interaction : 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

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

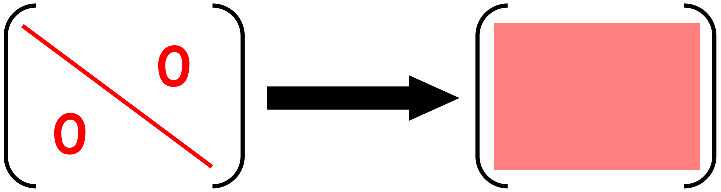
(CS, D, Q...)

nuclear spin operator

the interaction: a second rank tensor (symmetrical)

another spin operator or B_0...

anisotropy : why ?

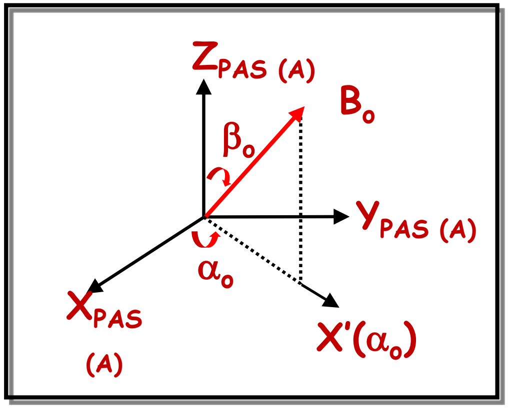


diagonal in the PAS (Principal Axes System)

LAB

Principal values A_{ii} – Ellipsoid representation

For *each* interaction A (CS, D, Q...)

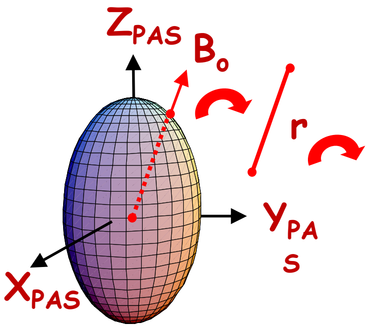


$$\begin{pmatrix} A_{11} & & 0 \\ & A_{22} & \\ 0 & & A_{33} \end{pmatrix}$$

... at the level of the nucleus ...

$$\begin{pmatrix} A_{xx} & A_{xy} & A_{xz} \\ A_{yx} & A_{yy} & A_{yz} \\ A_{zx} & A_{zy} & \boxed{A_{zz}} \end{pmatrix}_{LAB} = \begin{bmatrix} f(\alpha_0, \beta_0) \end{bmatrix}_{LAB}$$

« first order » perturbation



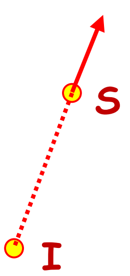
$$r^{-2} \overset{!}{=} A_{ZZ}$$

equation: $A_{11}X^2+A_{22}Y^2+A_{33}Z^2 = 1$

semi-axes: $(A_{ii})^{-1/2}$

the trace $TrA = \Sigma A_{ii}$ ou $A_{iso} = 1/3\ TrA$

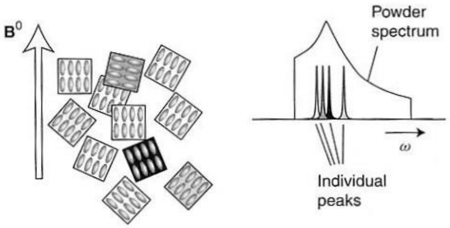
ex: null trace : D, Q

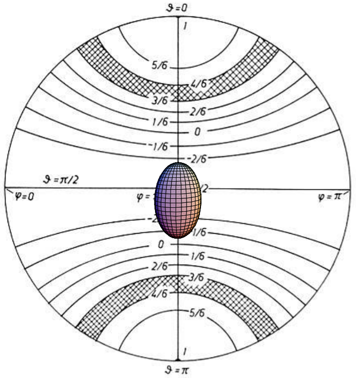


$$[D]_{PAS} \propto D \begin{bmatrix} 1 & 0 & 0 \\ 0 & 1 & 0 \\ 0 & 0 & -2 \end{bmatrix}$$

dipolar constant

When powders are available !





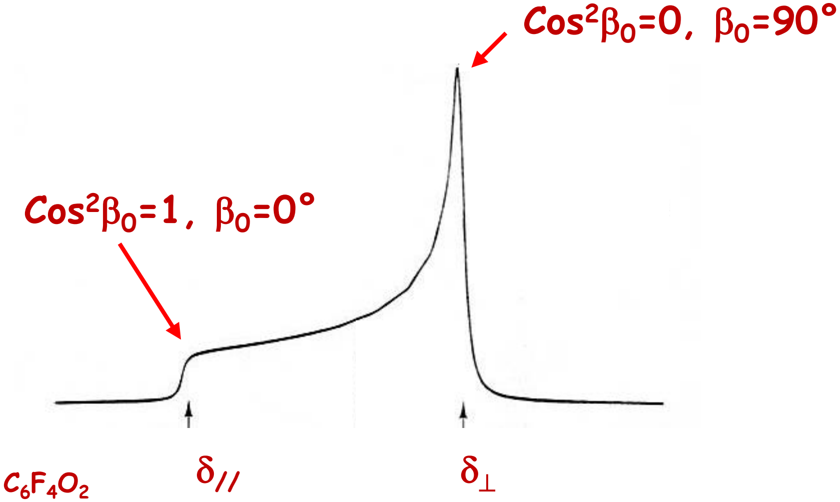
Levitt, Spin dynamics, 2002.
Haeberlen, High resolution NMR in solids, selective averaging, 1976.

...how to build a CSA lineshape ?

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

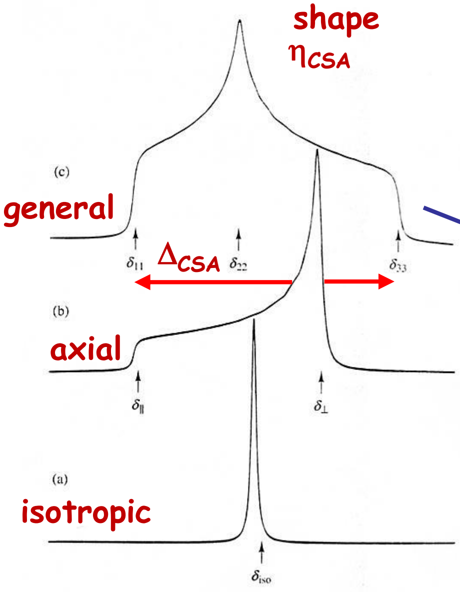
$$r^{-2}= \delta_{zz} =$$
$$(\delta_{\perp} \sin^2\beta_0+ \delta_{//} \cos^2\beta_0)$$

Ellipsoid of revolution !

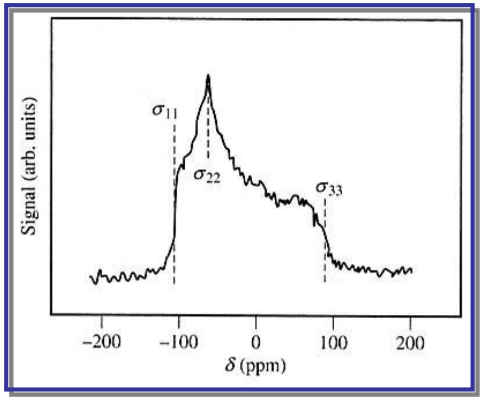

Cos$^2\beta_0$=0, β_0=90°

Cos$^2\beta_0$=1, β_0=0°

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



^{19}F in fluoranil, $C_6F_4O_2$

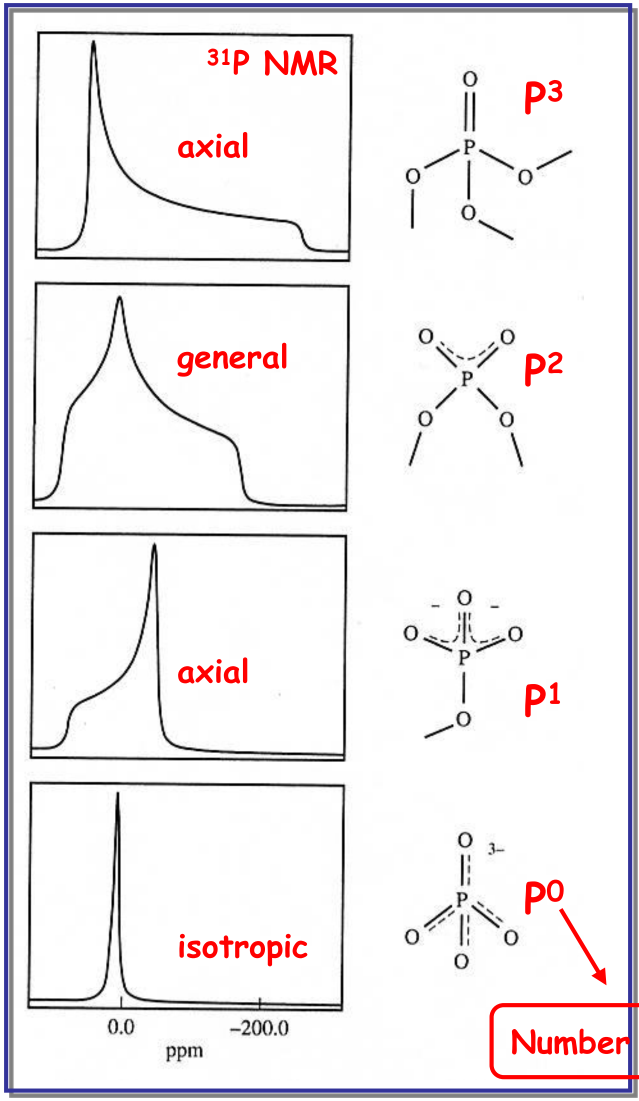


shape: elliptic integrals

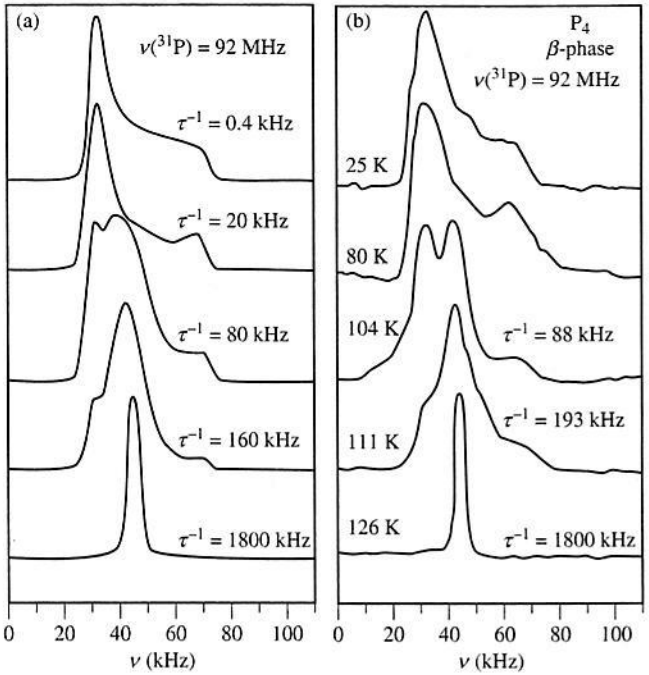
$$K(m)=\int_0^{\pi/2} d\varphi\ (1-m \sin^2\varphi)^{-1/2}$$

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

Local symmetry and molecular dynamics



Number of P-O-P bridges



simulation experiment

^{31}P NMR

Random jumps : tetrahedron

(τ^{-1}) (white phosphorus, β phase)

- Role of dynamics
- Average : $\tau^{-1} >> \Delta_A$

...NMR in time domain...

Back to ellipsoids !...

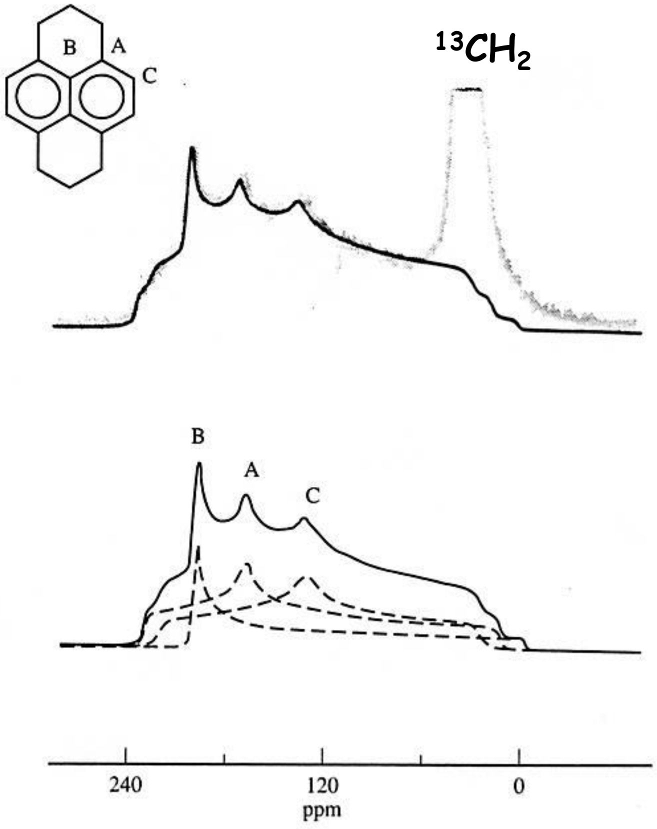
Eckert, Prog. Nucl. Magn. Reson., 1992, 24, 159.

Spiess et al., Chem. Phys., 1974, 6, 226.

Resolution in solid state NMR ?

an example...

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



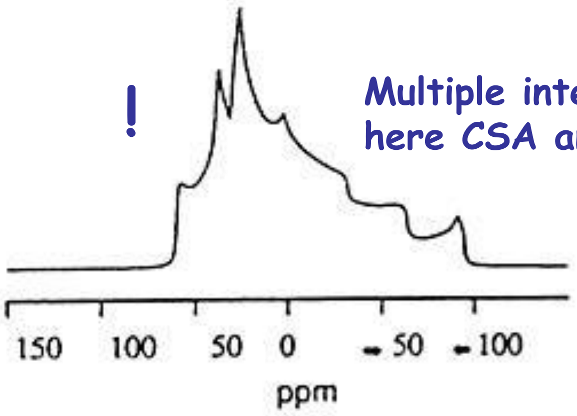
Sethi et al., Prep. Am. Chem. Soc., 1987, 32, 155.

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

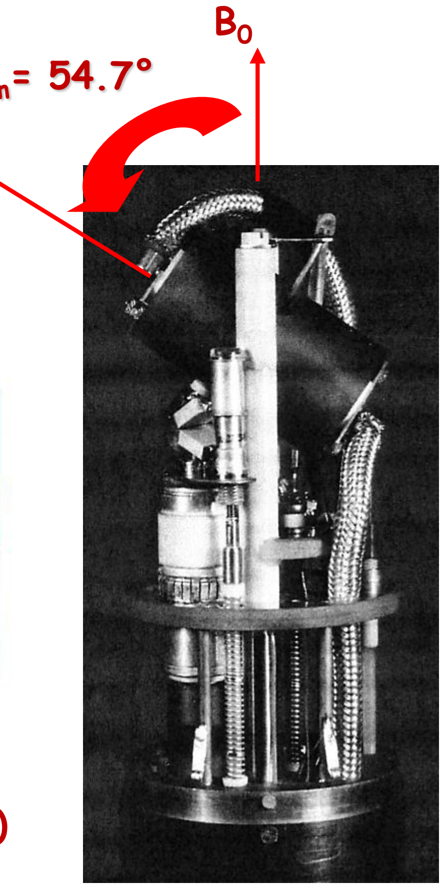
All crystallographically equivalent nuclei participate to the same lineshape

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



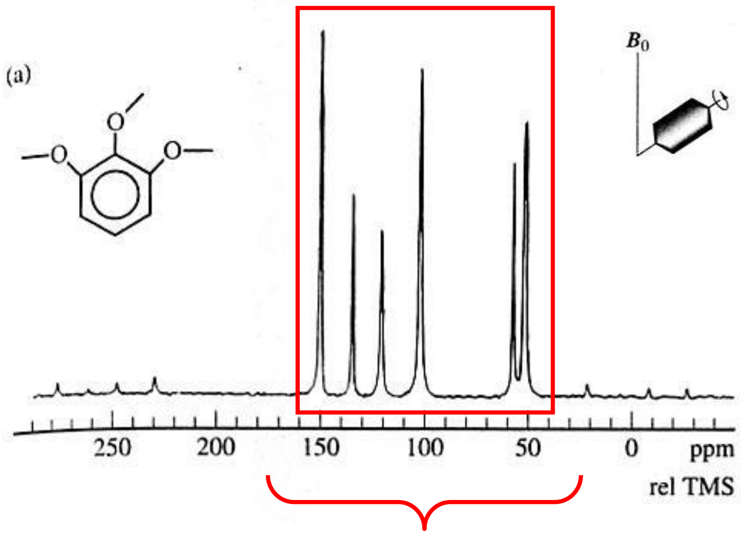
Multiple interactions : here CSA and D



↳ $P_2(\mathrm{Cos}\theta)$

Doty, Encyclopedia of NMR, 1996, 4477.

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



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

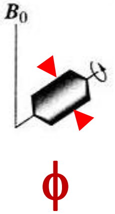
Orendt, Encyclopedia of NMR, 1996, 1287.

ϕ: 7mm ⟶ ... 6 kHz

ϕ: 4mm ⟶ ... 15 kHz

ϕ: 2,5mm ⟶ ... 35 kHz

ϕ: 1mm ⟶ ... 100 kHz



MAS at « infinite » frequency

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

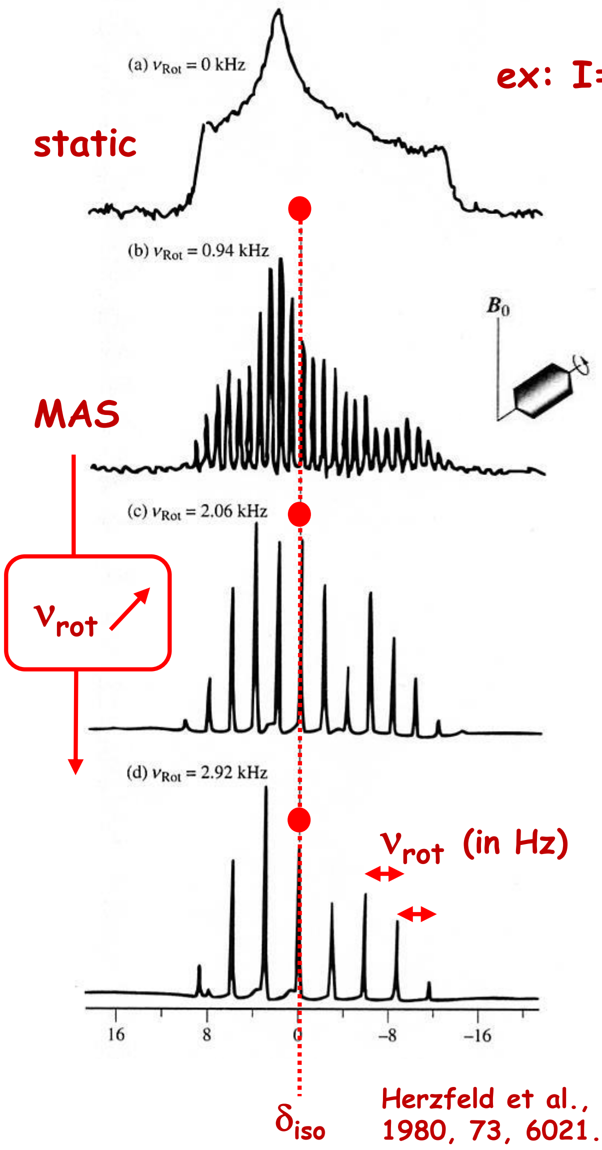
question: is it actually possible ?...

MAS at finite frequency

^{31}P: dipalmitoylphosphatidylcholine

ex: I=1/2, A=CSA

"explosion" of the spectrum in sharp spinning sidebands



static

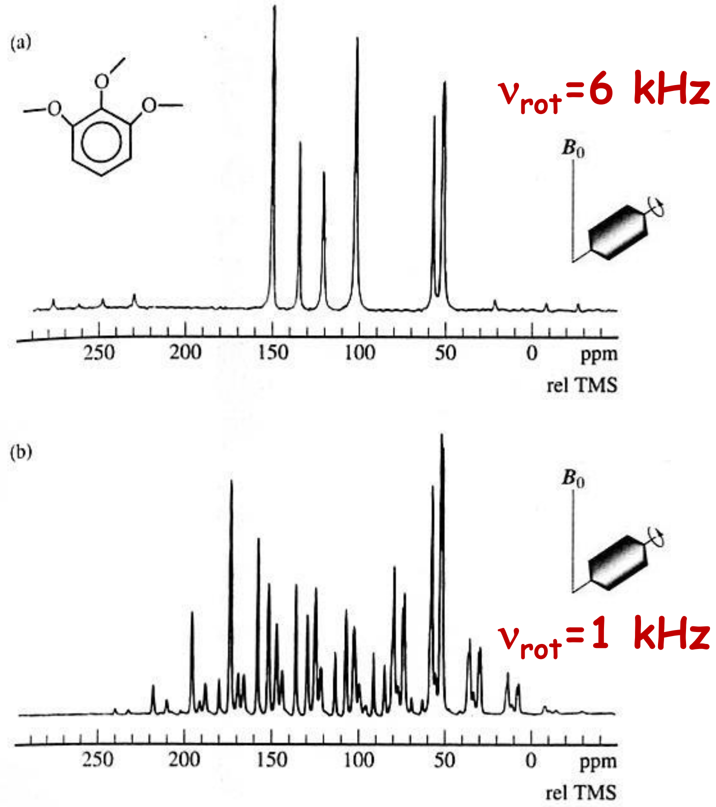
MAS

ν_{rot} ↗

ν_{rot} (in Hz)

δ_{iso}

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



ν_{rot}=6 kHz

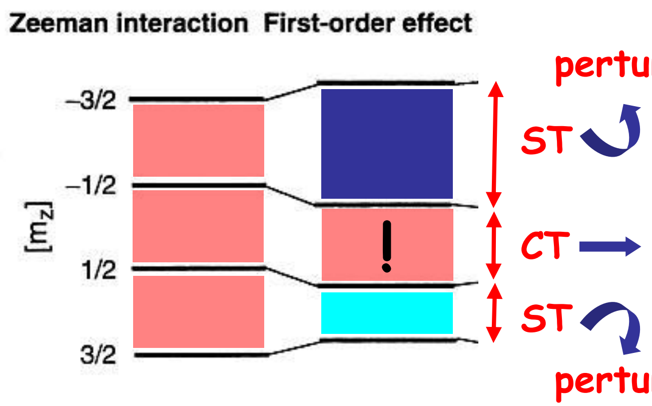
ν_{rot}=1 kHz

Orendt, Encyclopedia of NMR, 1996, 1287.

Quadrupolar interaction: first order effects

I > ½ (^{27}Al, ^{23}Na, ^{17}O...)

ex: I=3/2



perturbed !

non perturbed !

perturbed !

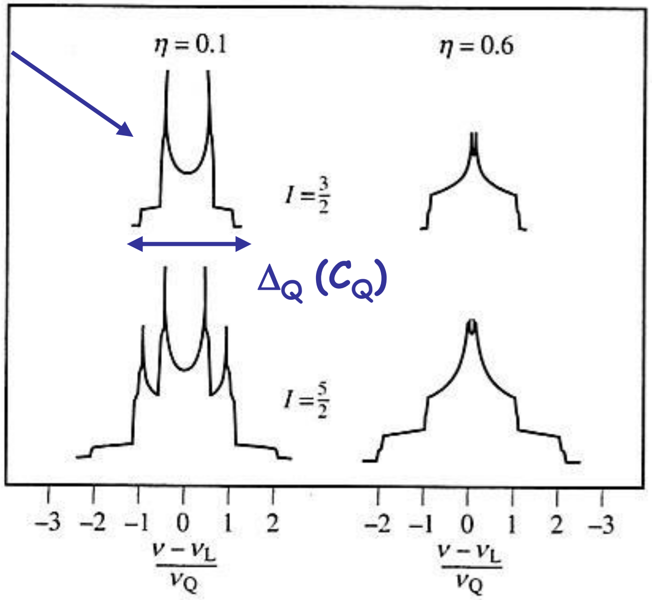
Multitransitions system

CT: central transition

ST: satellite transitions

shape η_Q

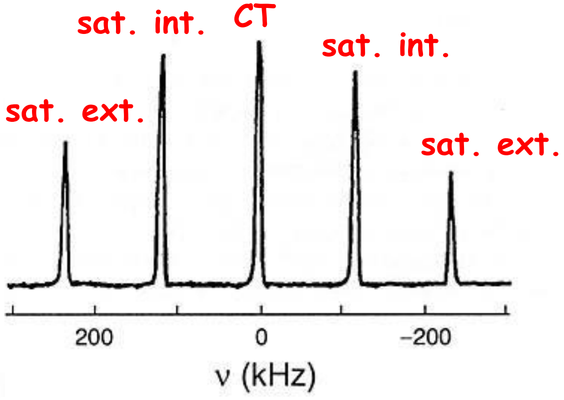
$C_Q=e^2qQ/h$



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

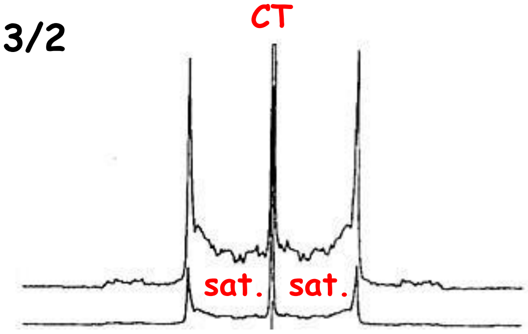
I = 5/2

^{27}Al in α-Al_2O_3
single crystal



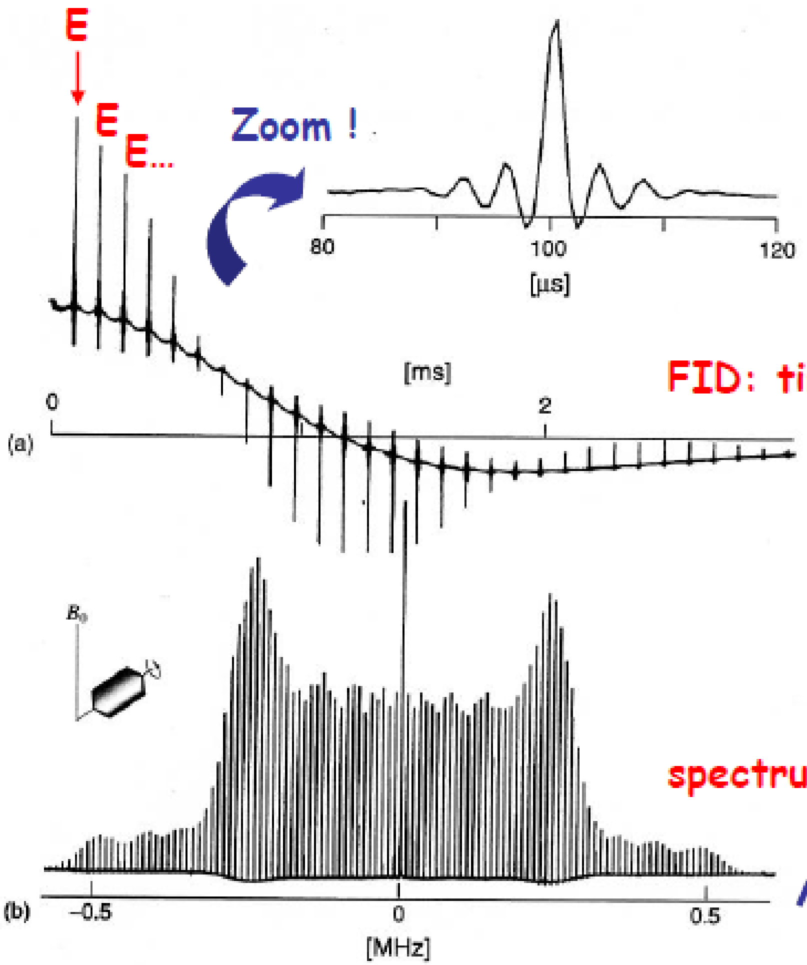
I = 3/2

^{23}Na in $NaNO_3$
powder



Man, Encyclopedia of analytical chemistry, 2000, 12229.

MAS and quadrupolar nuclei (1st order)



FID: time

spectrum: frequency

^{23}Na (I=3/2) in $NaNO_2$ - ν_{rot} = 10 KHz

Gan, Encyclopedia of NMR, supp. Vol., 135.

to set the magic angle...

$K^{81}Br$ (I=3/2)

$K^{127}I$ (I=5/2)

and maximize the number of echoes in the time domain (1 scan !)...

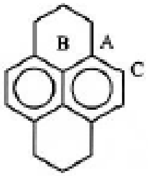
(but is it crucial ?...)

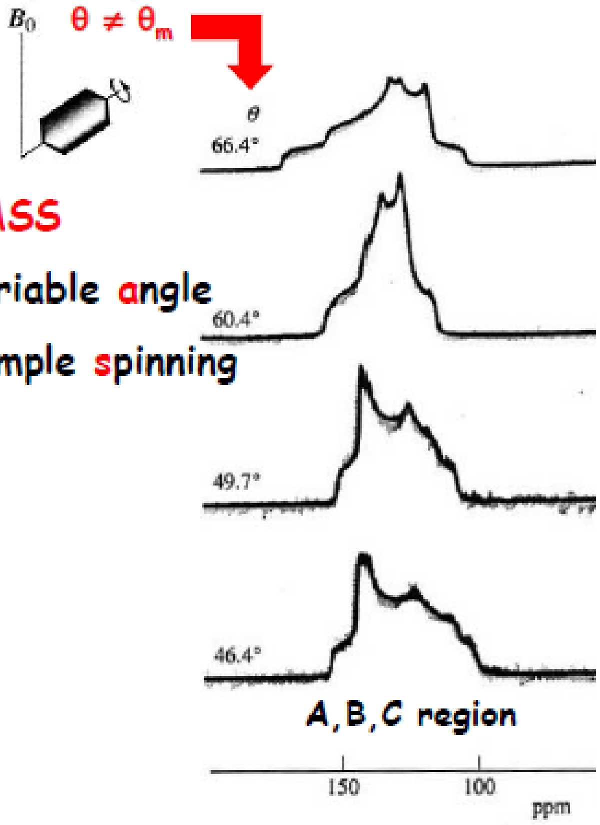
a huge number of SSB :

why ?!

Off MAS experiments

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





VASS

variable angle

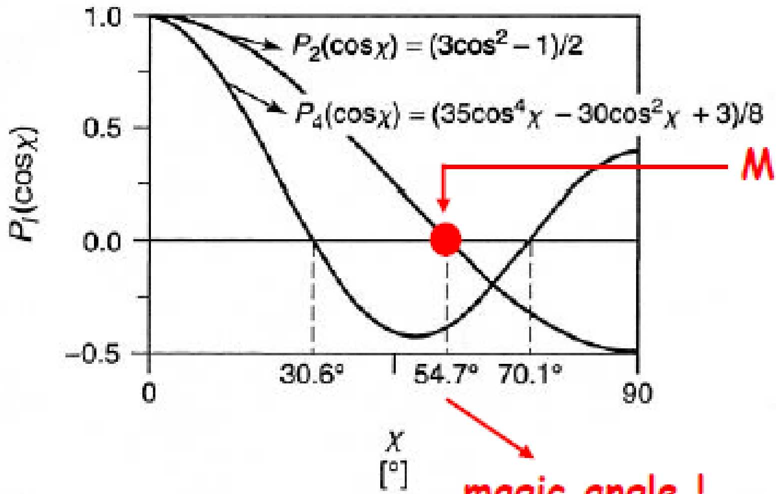
sample spinning

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

fast rotation at θ: scaling factor of Δ_A

$$\Delta_A\, P_2(\cos\theta) = \Delta_A\, \tfrac{1}{2}\, (3\cos^2\theta - 1)$$

Legendre polynomial !



MAS !

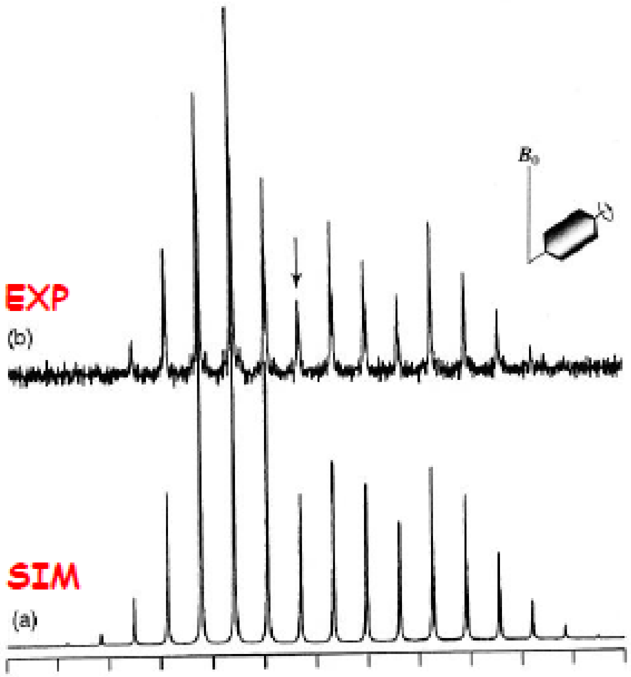
magic angle !

θ = θ$_m$= 54,7°

Information to extract from the set of spinning sidebands

ex: CS interaction I = 1/2

^{119}Sn MAS in: tin sulfate

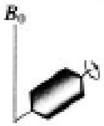


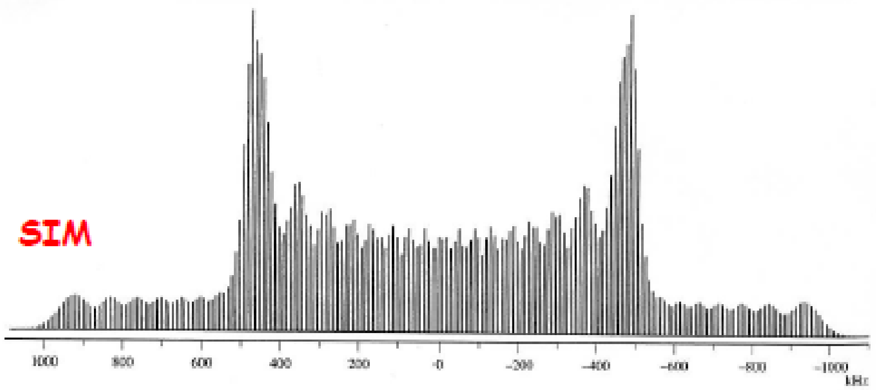
extracted data:

δ_{iso}, η_{CSA}, Δ_{CSA}

Harris et al., Encyclopedia of NMR, supp. Vol., 145.

ex: Q interaction I = 3/2





extracted data:

δ_{iso}, η_Q, C_Q

Jakobsen, Encyclopedia of NMR, 1996, 2374.

SIMulation programs:

DM2003 by Massiot

SIMPSON by Bak et al.

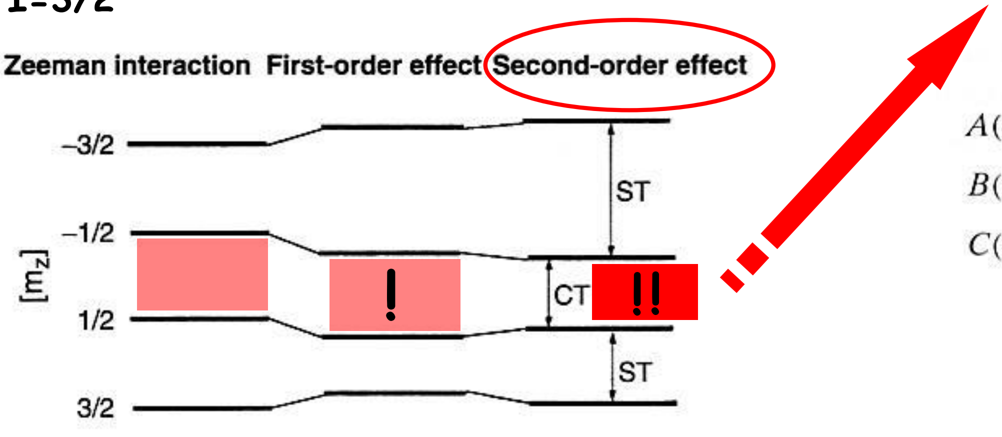
WEB !

DM2011

Strong quadrupolar nuclei

C_Q: 3 to 15 MHz...

I=3/2



$$w^{(2)\mathrm{static}}_{-1/2,1/2} = -\frac{1}{6w_L}\left[\frac{3e^2qQ}{2I(2I-1)\hbar}\right]^2\left\{I(I+1)-\frac{3}{4}\right\}$$

$$\times\{A(\alpha,\eta)\cos^4\beta + B(\alpha,\eta)\cos^2\beta + C(\alpha,\eta)\}$$

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

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

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

Man, Encyclopedia of analytical chemistry, 2000, 12229.

H_Q ~ H_{Zeeman}: second order perturbations

⬇

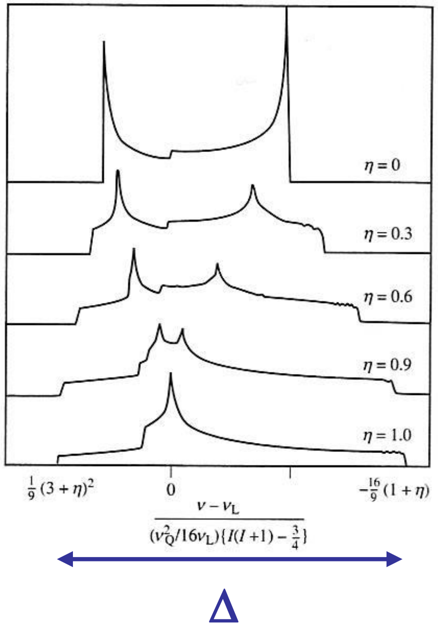
All transitions (ST and CT) are perturbed

Mathematical treatment...?

shape : η_Q

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

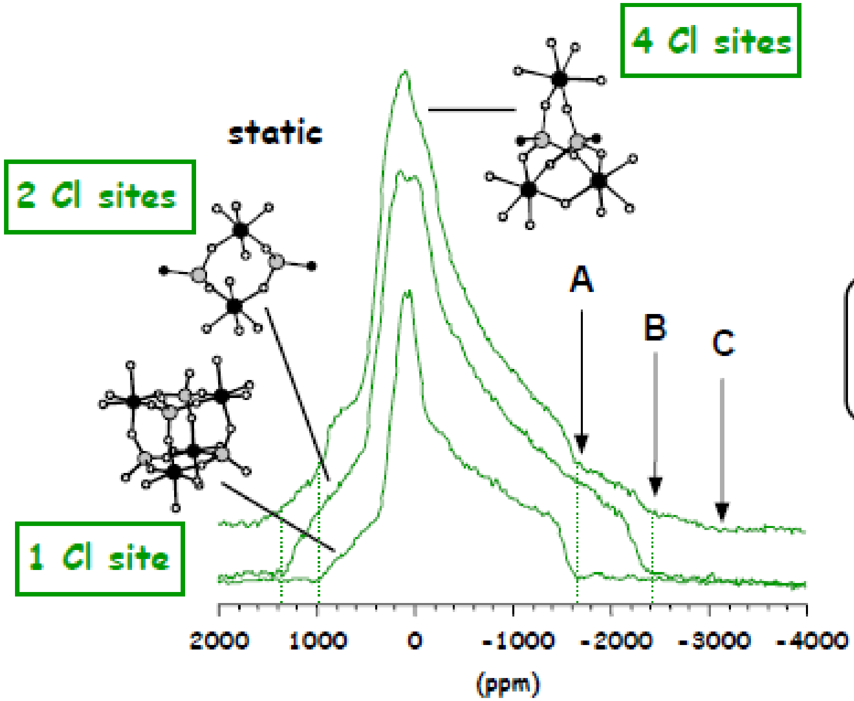
idea : B_0 ↗

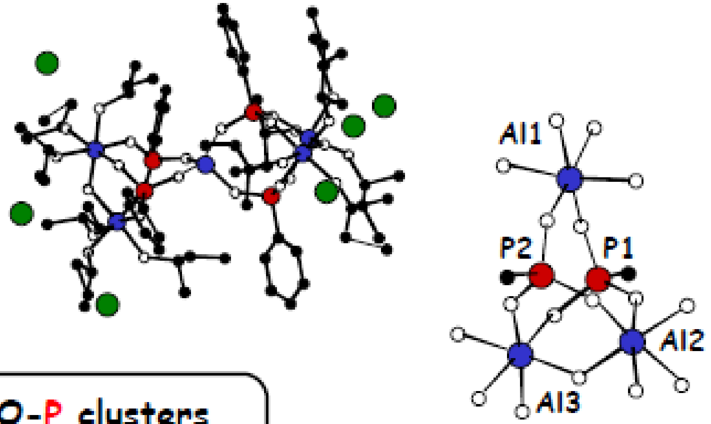


Freude et al., NMR Basic Princ. Prog., 1993, 29, 27.

Examples: ^{35}Cl solid state NMR

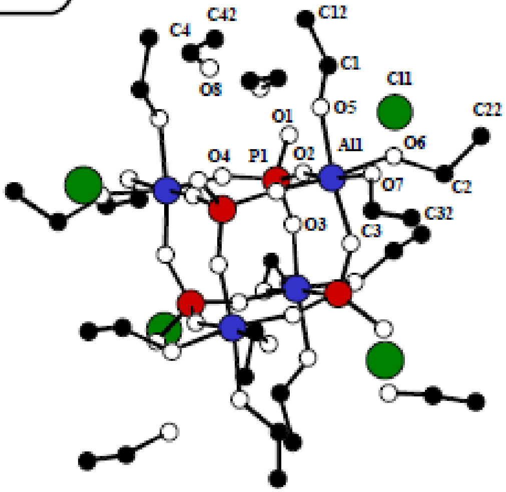
^{35}Cl: I=3/2

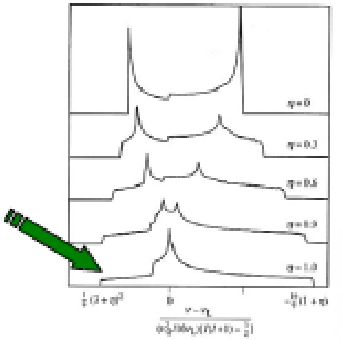




Al-O-P clusters

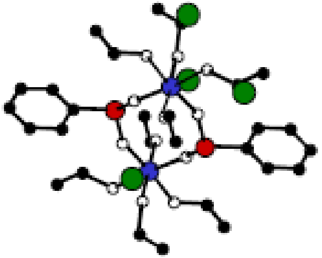
Cl⁻ as counter ions





η_Q ~ 1

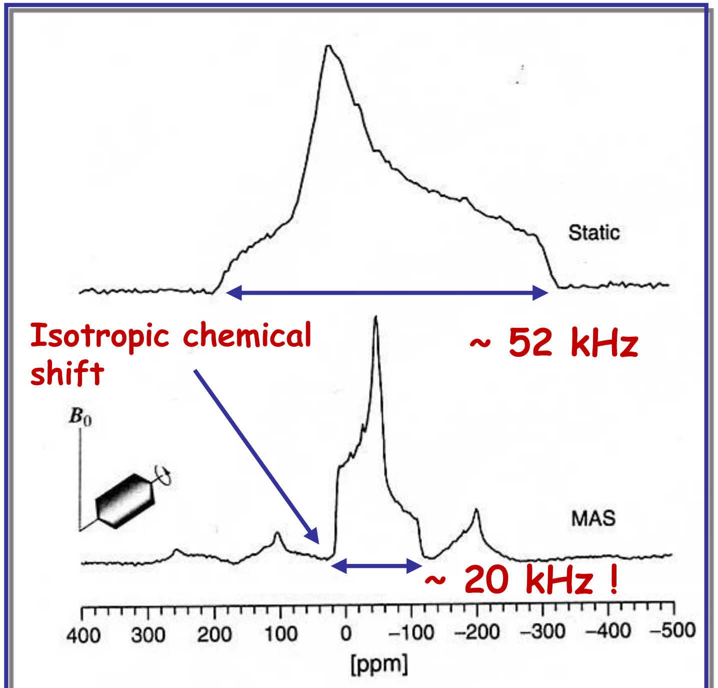
C_Q ~ 6-8 MHz



Azaïs et al., Solid State NMR, 2003, 23, 14.

Quadrupolar nuclei (2^{nd} order) and MAS rotation

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



Isotropic chemical shift

~ 52 kHz

~ 20 kHz !

^{87}Rb in $LiRbSO_4$

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

even at « infinite » MAS frequency !

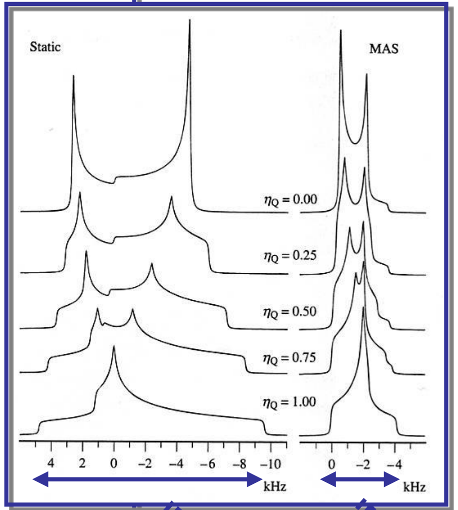
WHY ? (without any calculation)

MAS rotation: efficient for

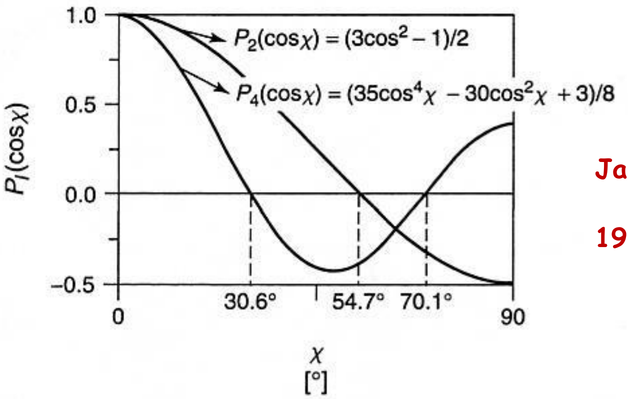
- ♦ ellipsoids
- ♦ $Cos^2(\alpha_0,\beta_0)$
- ♦ $P_2(Cos\theta)$

... 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 !!

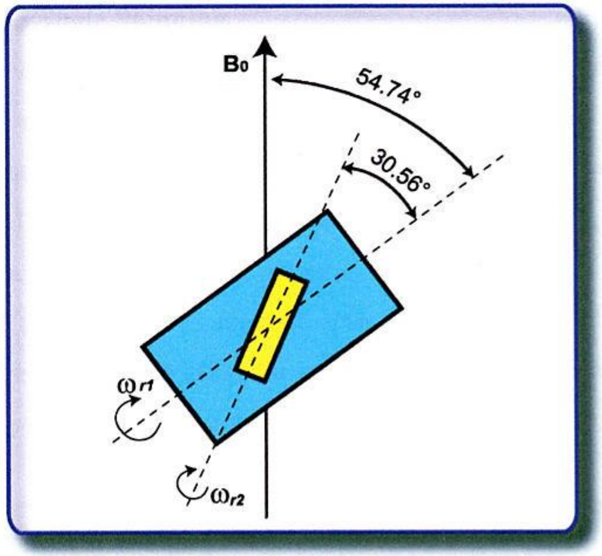
Quadrupolar nuclei and macroscopic reorientations

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

Let us invent an experiment with 2 angles of reorientation !

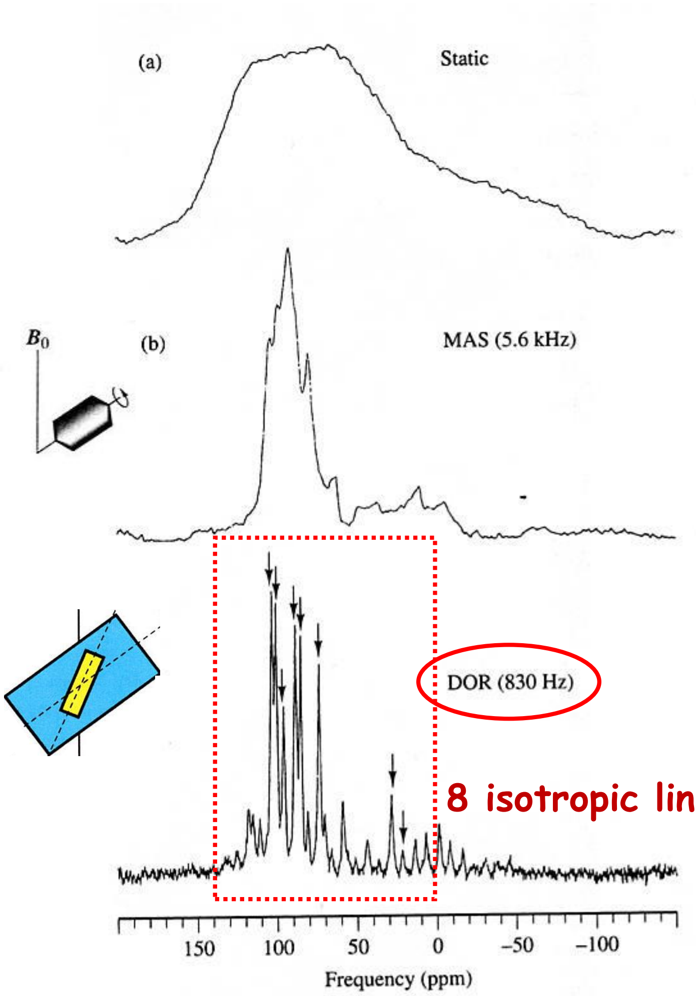
DOR experiment (DOuble Rotation)

(Samoson, Pines, 1988)



1D experiment

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



8 isotropic lines

Wu, Encyclopedia of NMR, 1996, 1749.

DAS approach: Dynamic Angle Spinning

Another way to involve 2 angles

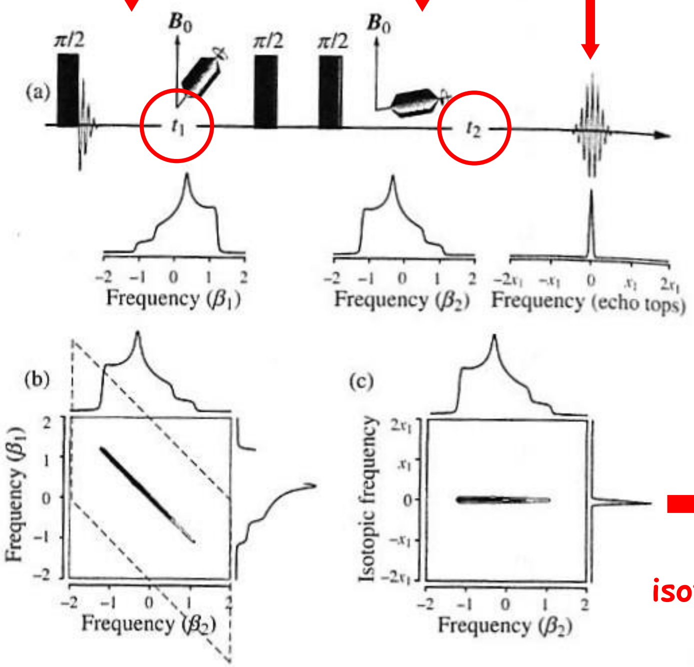
DAS experiment (Dynamic Angle Spinning)

(Llor, Virlet, 1988)

1^{er} angle, β_1

$2^{ème}$ angle, β_2

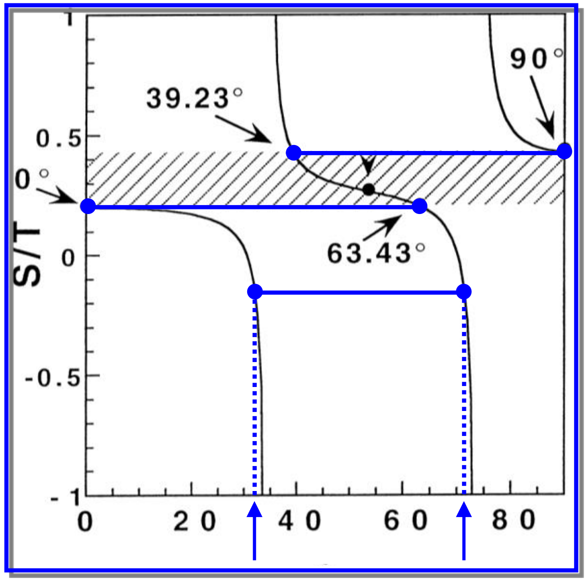
ECHO !



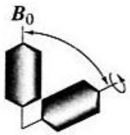
isotropic

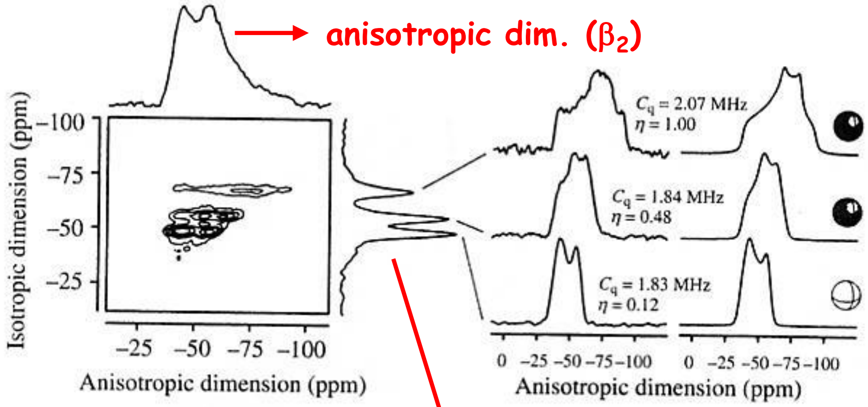
Grandinetti, Encyclopedia of NMR, 1996, 1770.

DAS angles pairs



β_1 β_2





anisotropic dim. (β_2)

^{87}Rb : $RbNO_3$

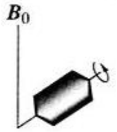
3 isotropic lines

Rotation around a unique angle: MQ-MAS !

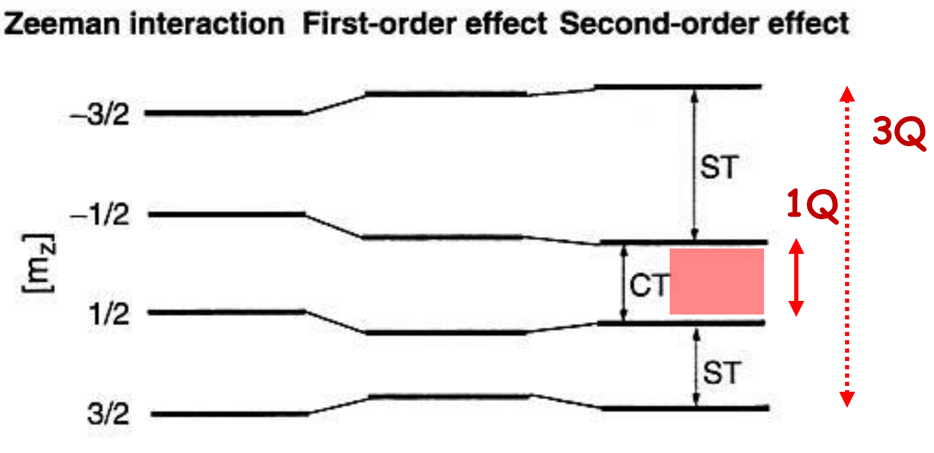
DAS and DOR: 1 transition (CT) et 2 angles...

MQ-MAS (Multiple Quantum MAS)

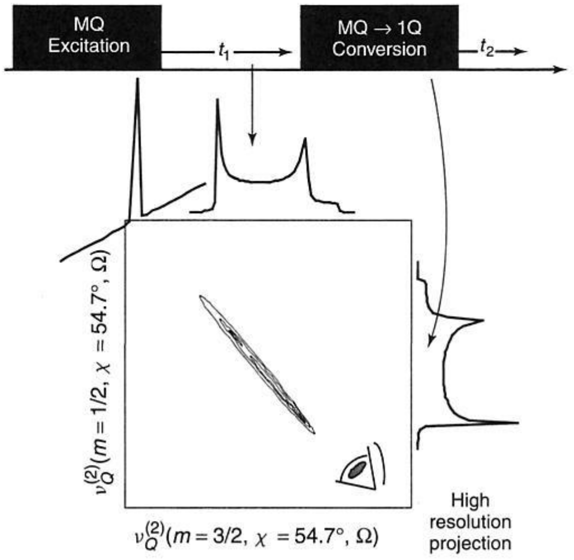
(Frydman, 1995)



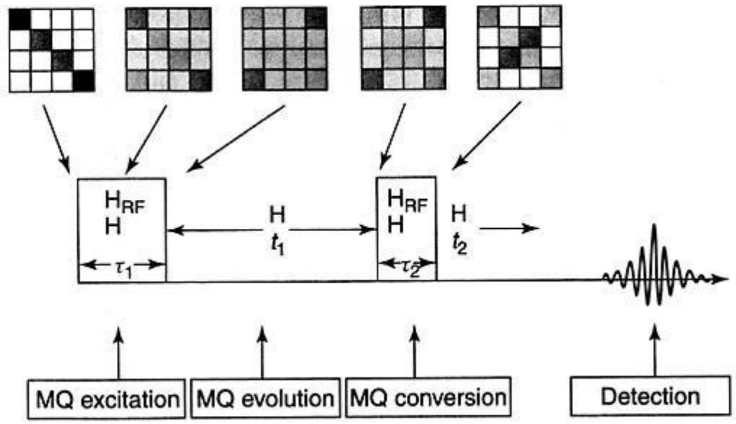
2 transitions (CT/MQ) and 1 angle (MAS) !



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



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

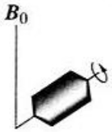


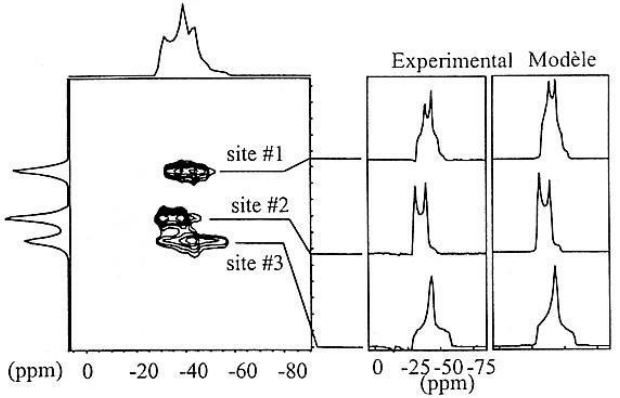
Amoureux *et al.*, Encyclopedia of NMR, supp. Vol., 230.

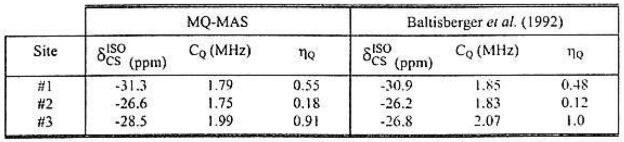
MQ-MAS: examples

DAS and DOR: demanding techniques

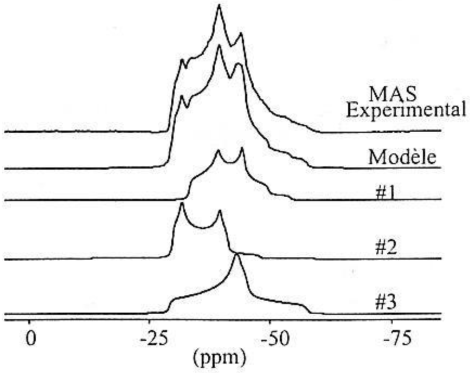
MQ-MAS: much easier (...)





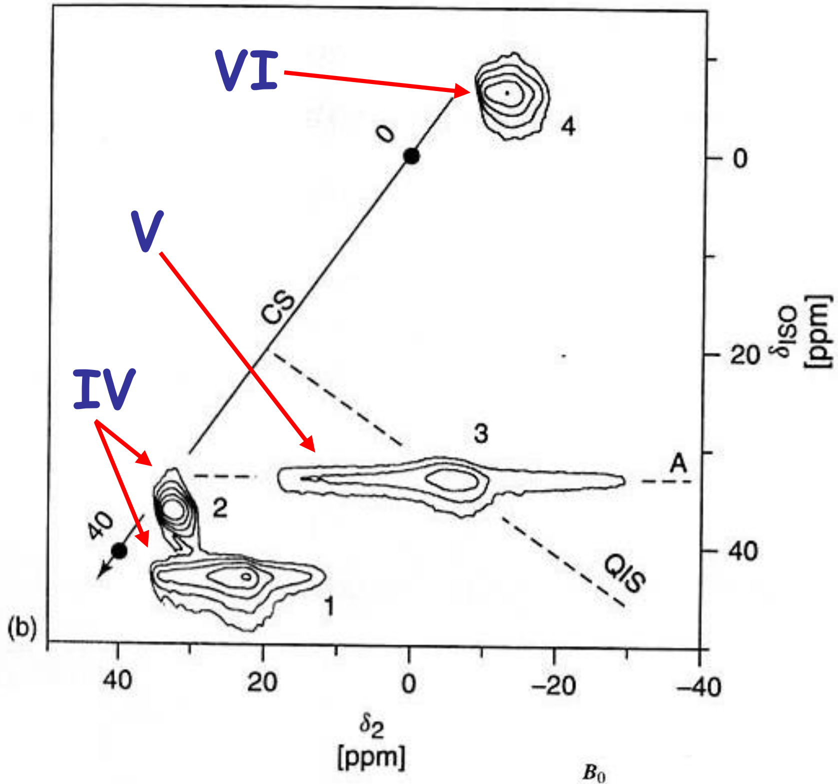


	MQ-MAS			Baltisberger *et al.* (1992)		
Site	δ_{CS}^{ISO} (ppm)	C_Q (MHz)	η_Q	δ_{CS}^{ISO} (ppm)	C_Q (MHz)	η_Q
#1	-31.3	1.79	0.55	-30.9	1.85	0.48
#2	-26.6	1.75	0.18	-26.2	1.83	0.12
#3	-28.5	1.99	0.91	-26.8	2.07	1.0



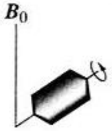
^{87}Rb : RbNO$_3$

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.

^{1}H solid state NMR: another challenge

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

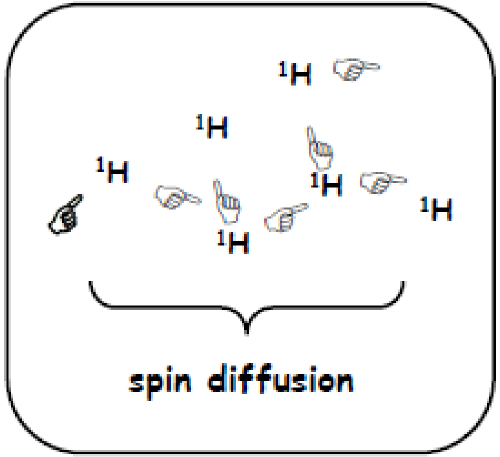
remember:

$$\boxed{D_{II} \sim \gamma^2/r_{II}^3}$$

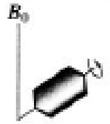
high for ^{1}H

up to 30 kHz...

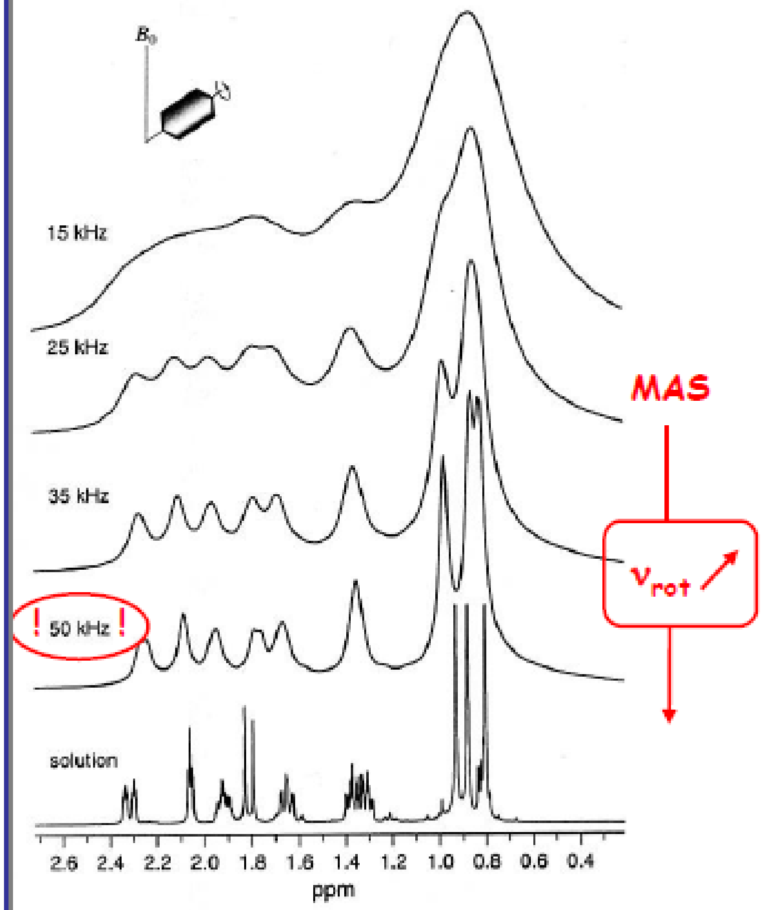
rather small



question: is the MAS reorientation efficient ?



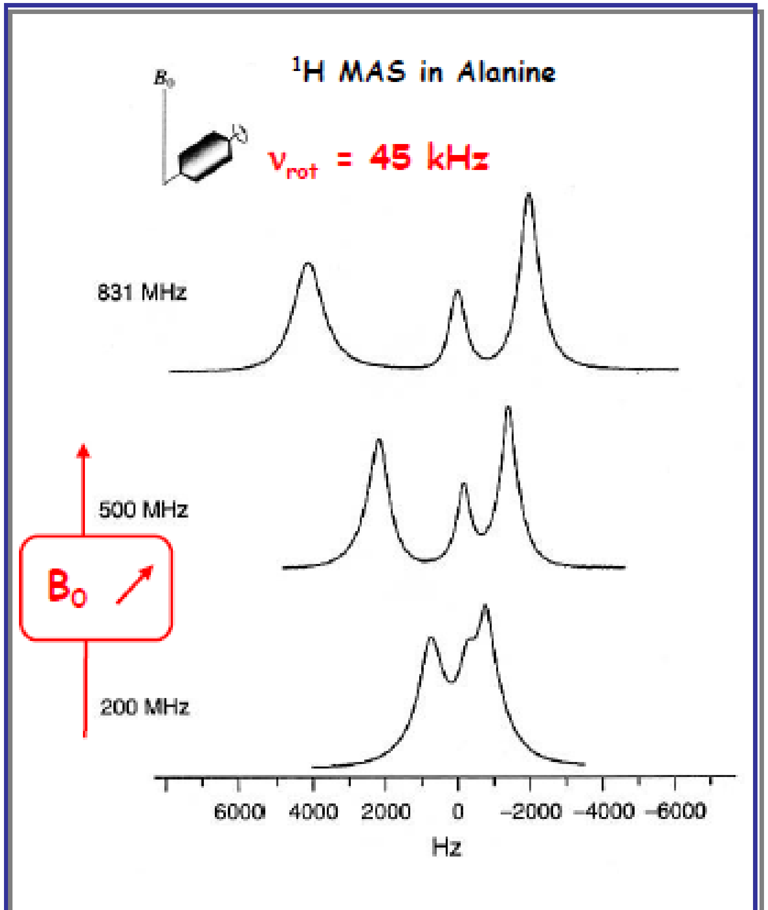
^{1}H MAS in Camphor (500MHz)



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

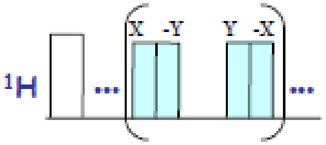
Two different approaches

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

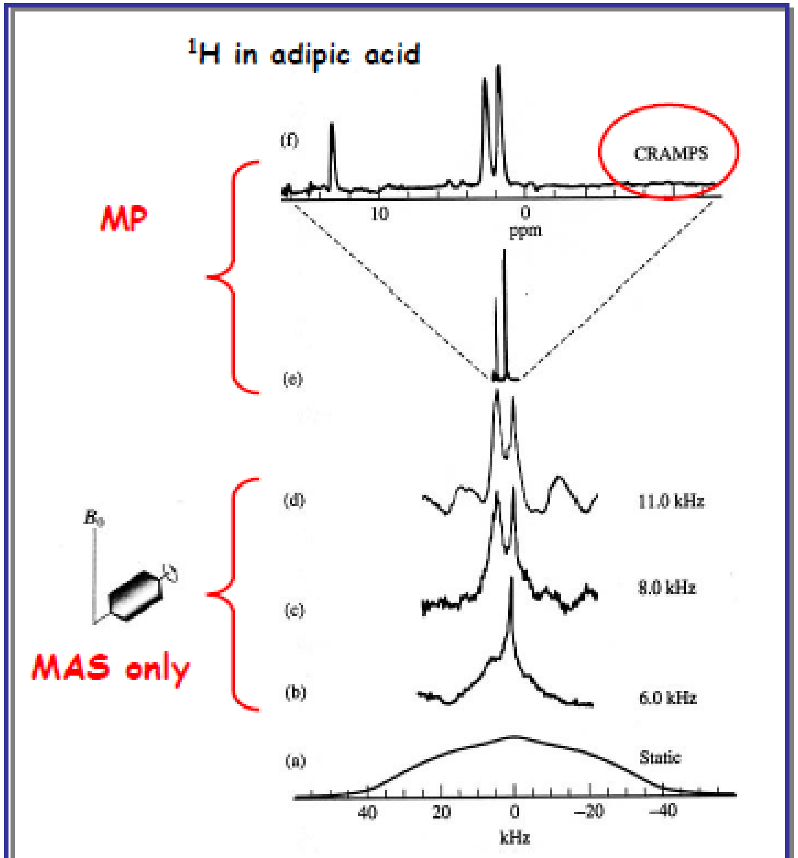


Samoson, Encyclopedia of NMR, supp. Vol., 63.

second idea: rotations in spin space !

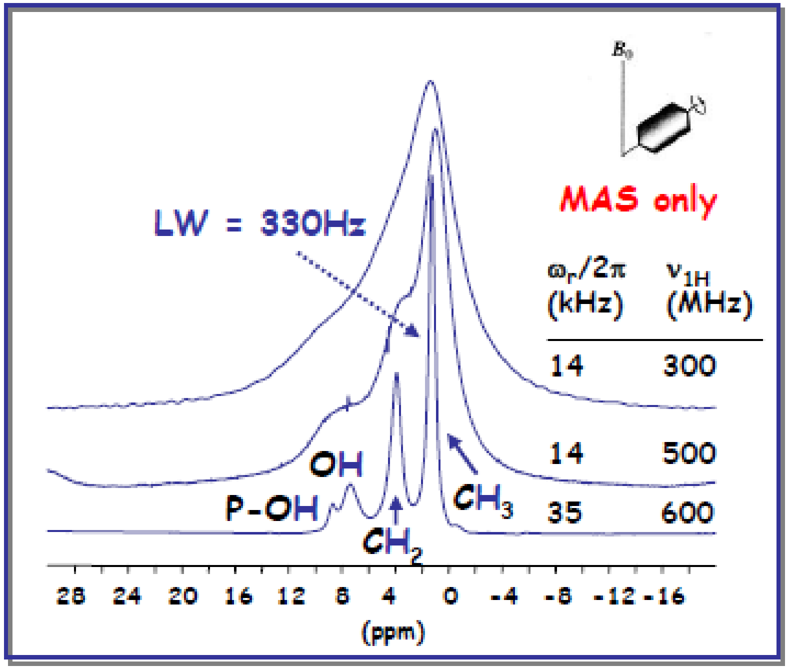


multiple pulses (MP)



Gerstein, Encyclopedia of NMR, 1996, 1502.

Comparison of techniques

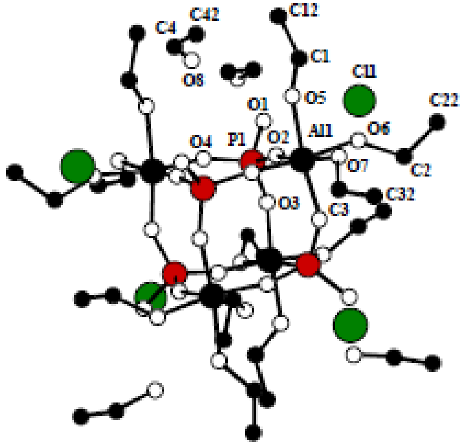


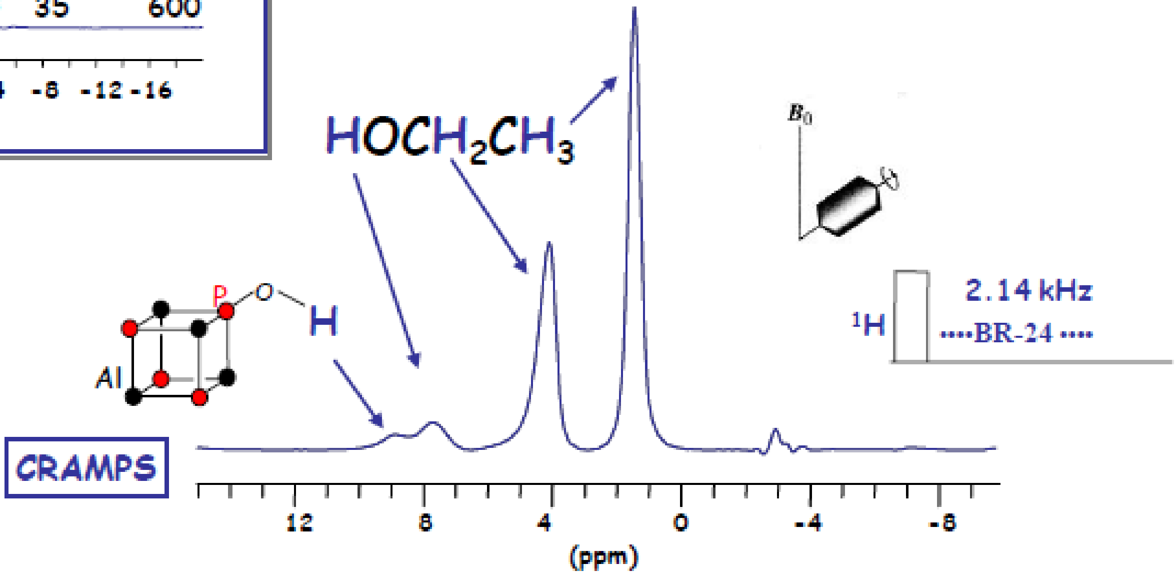
$\omega_r/2\pi$ (kHz)	ν_{1H} (MHz)
14	300
14	500
35	600

... what is the limit of resolution in ^1H solid state NMR !?

don't forget the role of molecular motion !...

CRAMPS: Combined Rotation And Multiple Pulses Spectroscopy

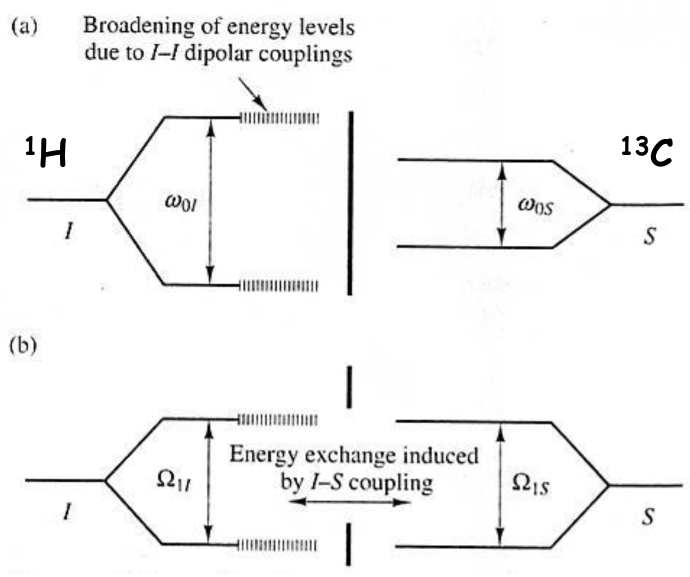




Azaïs, phD thesis.

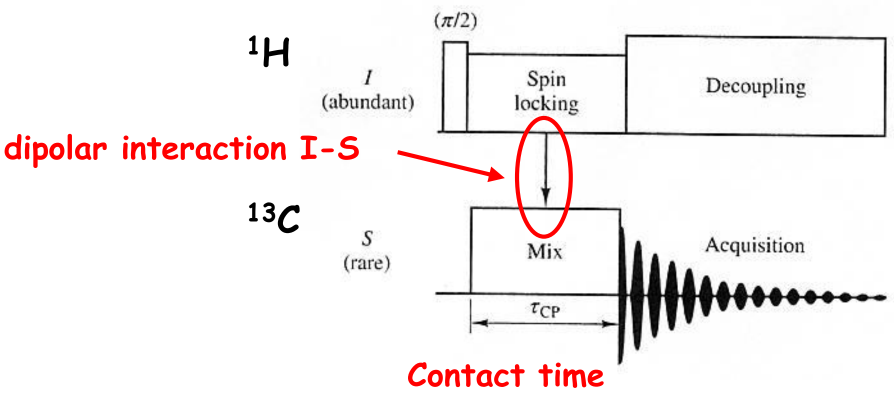
Cross Polarization (CP): a simplified description

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



Engelke, Encyclopedia of NMR, 1996, 1530.

the most popular sequence



Hartmann and Hahn (1962):

NO in the LAB frame mais YES in the rotating frame

advantages:

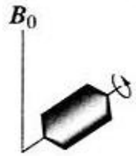
- gain: $M_S (\gamma_{1H}/|\gamma_S|) \longrightarrow$ 4 for ^{13}C, 10 for ^{15}N !
- τ_{CP} ~ ms !
- $T_1(^1H) << T_1(^{13}C)$
- ^{13}C FID with ^1H decoupling

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

Hartmann-Hahn condition on B_1(RF) fields

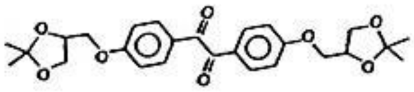
How to manage the ^{13}C CSA interaction ?

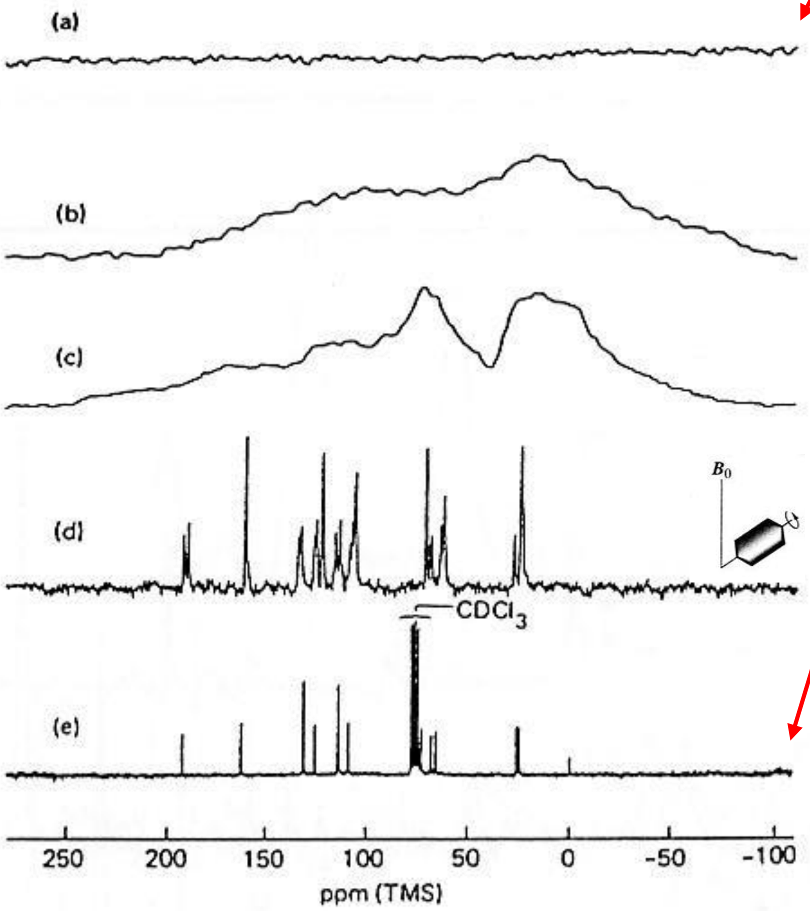
idea...



The CP MAS experiment

^{13}C in





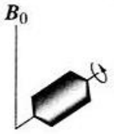
(a) solid (solution state conditions)

(b) CP (low power decoupling)

(c) CP (high power decoupling)

(d) CP MAS (high power decoupling)

(e) solution (low power decoupling)



$$\overbrace{\Omega_{1I} = \Omega_{1S}}^{\text{RF}} \pm n \overbrace{\Omega_{rot}}^{\text{MAS}}$$

with n = 1, 2

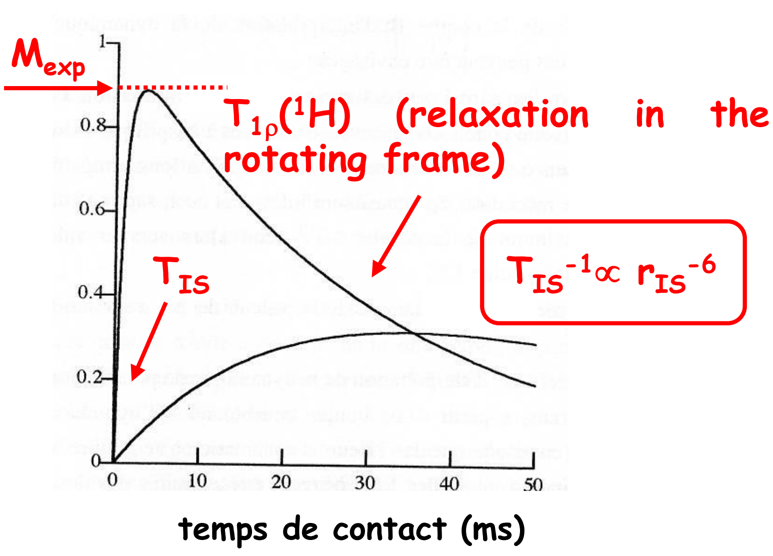
modified Hartmann-Hahn conditions

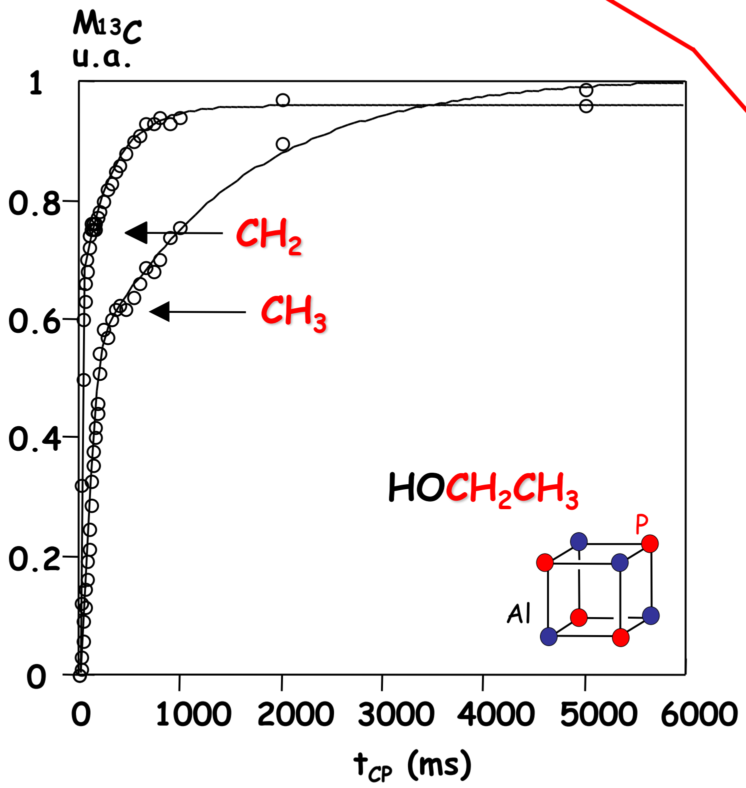
CP dynamics: quantitative approach

exponantial build-up of the magnetization

$$M_S^{CP}(t_c) = \frac{\gamma_I}{\gamma_S} M_S \frac{1}{1-\lambda}\left[\exp\left(-\frac{t_c}{T_{1\rho}^{I}}\right) - \exp\left(-\frac{t_c}{T_{IS}}\right)\right]$$

gain ! loss ! gain !





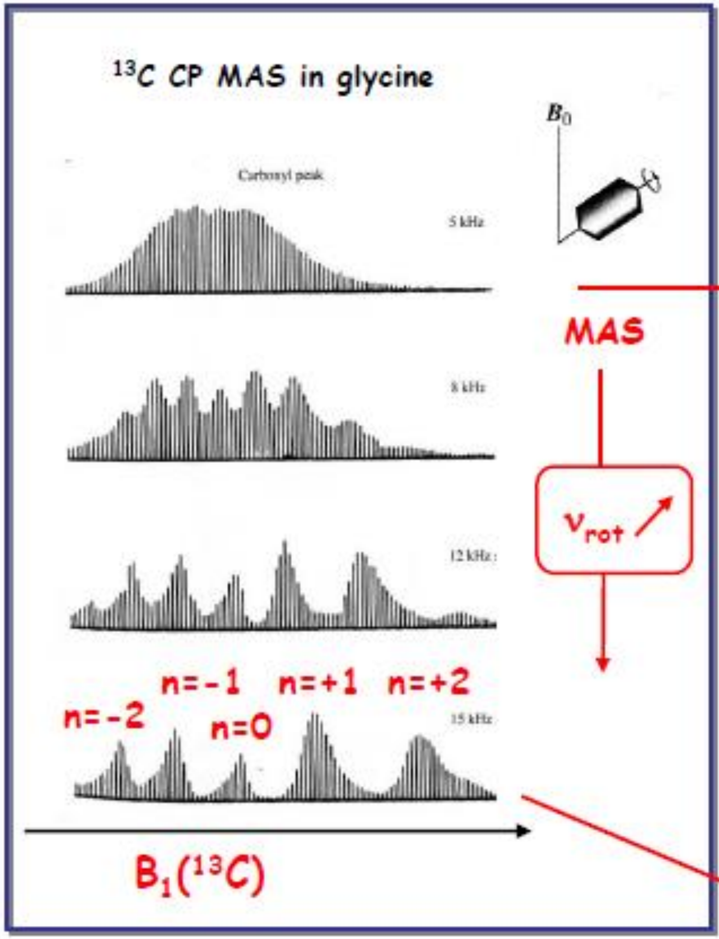
$T_{CH}(^{13}CH_2) < T_{CH}(^{13}CH) << T_{CH}(^{13}C_{quat})$

$^{13}C_{quat}$ are underestimated at short contact time

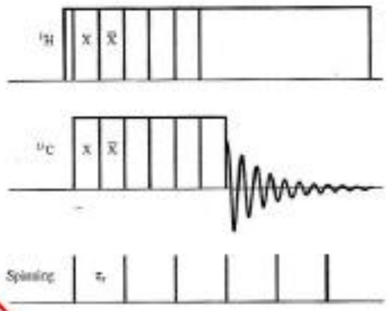
$\lambda = T_{CH}/T_{1\rho}(^1H)$ influence M_{exp}

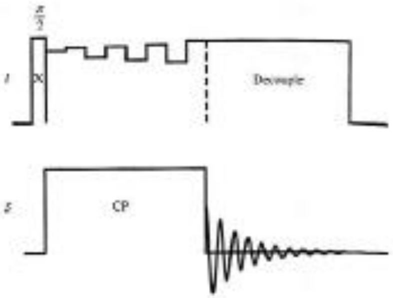
Care must be taken with materials involving several $T_{1\rho}(^1H)$!

CP and MAS

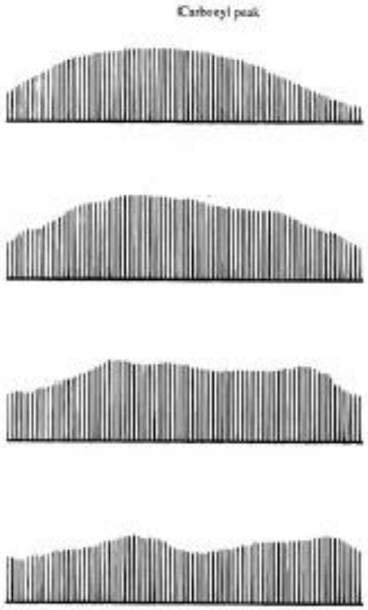


solutions...





variable amplitude
during the contact



Burum, Encyclopedia of NMR, 1996, 1539.

Distance measurement by CP MAS experiments

why distances ?...

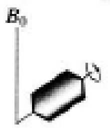
remember: $D_{IS} \sim \gamma_I\gamma_S/r_{IS}^3$

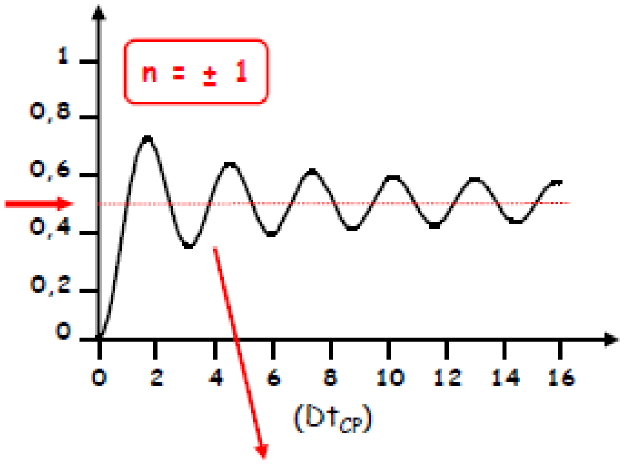
$\Downarrow$

CP transfer !

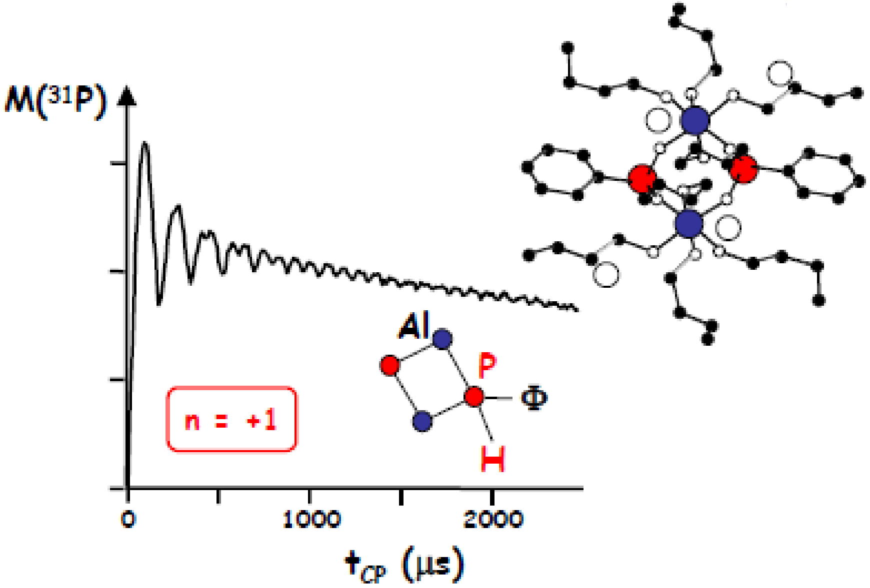
for a spin pair I-S at

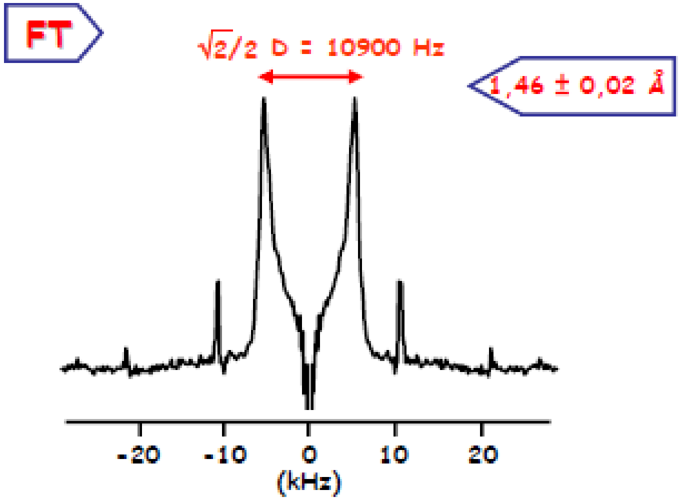
$$\Omega_{1I} = \Omega_{1S} \pm n\ \Omega_{rot}$$





the frequency of the oscillations gives D_{IS} !

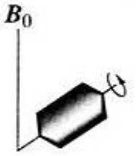




Azaïs et al., Inorg. Chem., 2002, 41, 981.

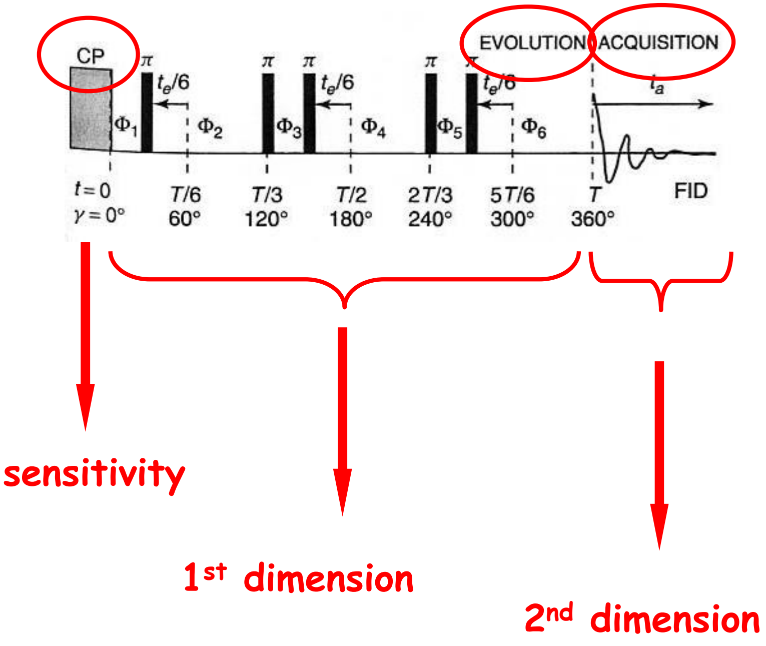
2D experiments: isotropic / anisotropic data

general idea: 2D corrélations between isotropic δ and anisotropies



si the interaction must be reintroduced

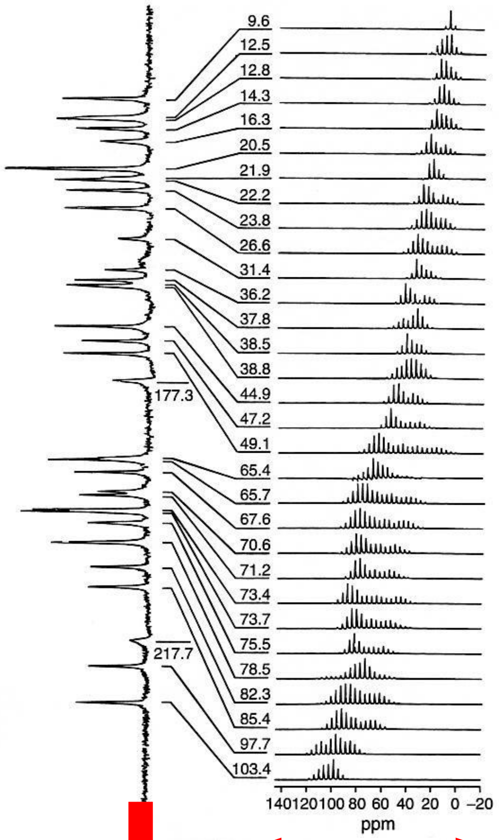
ex: δ_{iso} vs Δ_{CSA} – Magic Angle Turning



sensitivity

1st dimension

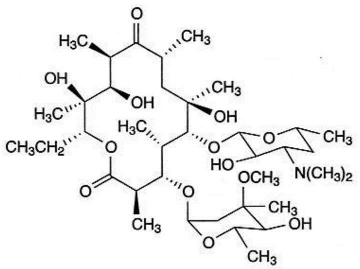
2nd dimension

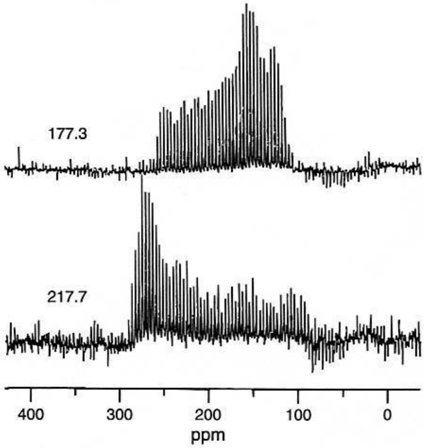


isotropic dim.

CSA dim.

^{13}C : erythromicine A

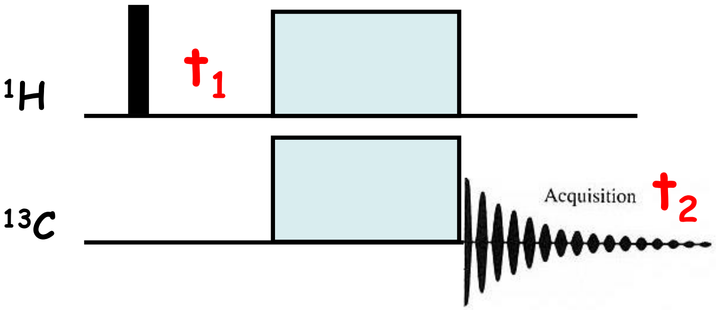




Alderman et al., Mol. Phys., 1998, 95, 113.

Heteronuclear 2D HETCOR correlation

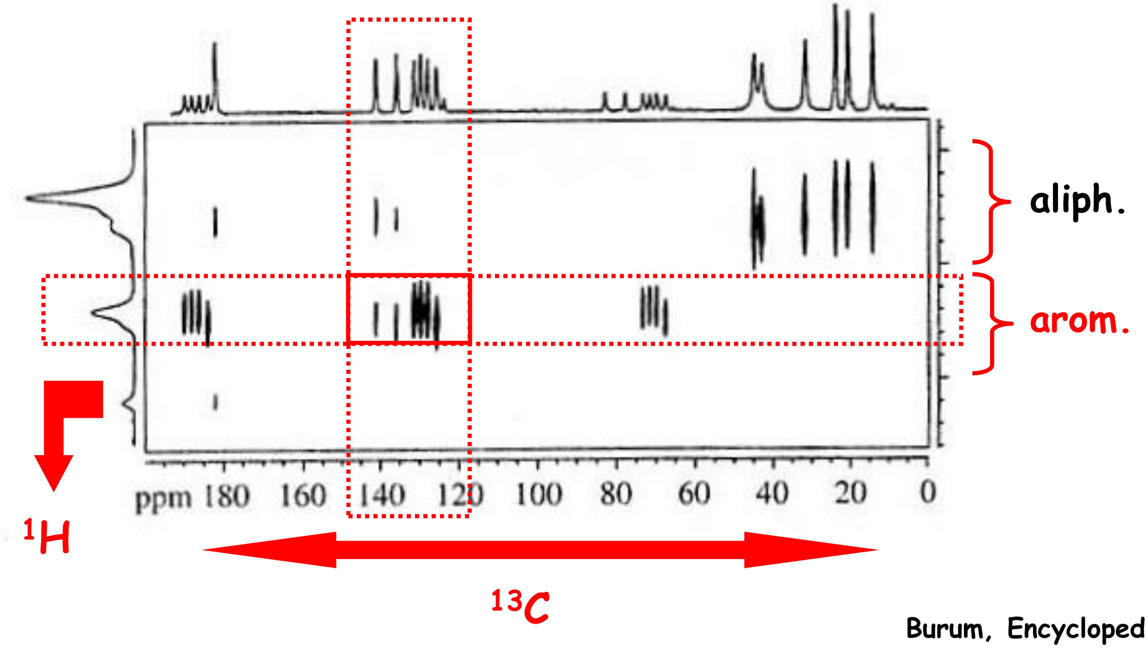
general idea: evolution of ^{1}H evolves during t_1 and is transferred to ^{13}C by CP.



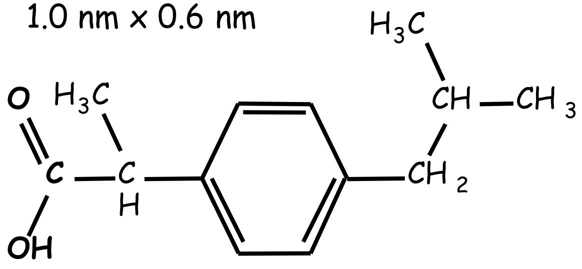
dipolar correlation peaks

short distances

^{13}C-^{1}H HETCOR for ibuprofene



1.0 nm x 0.6 nm



ibuprofene

Burum, Encyclopedia of NMR, 1996, 1542.

Solid State Nuclear Magnetic Resonance:

Applications to Materials

Christian BONHOMME
christian.bonhomme@upmc.fr

Laboratoire de Chimie de la Matière Condensée de Paris
UMR CNRS 7574 – Sorbonne Université, Paris, France

Topics

Solid state
NMR basics

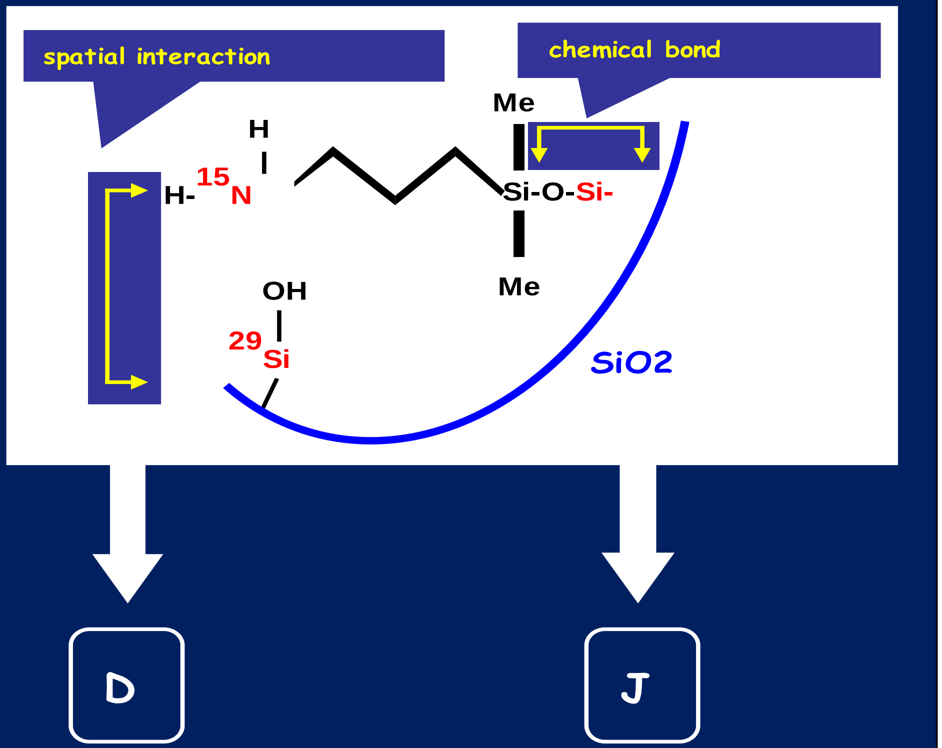
Applications

- OI hybrids
- interfaces
- calcium phosphates

Sensitivity

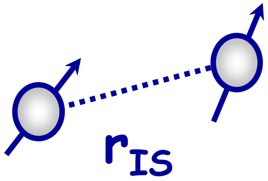
♦ Organic Inorganic Hybrid Materials - Part I

«playing» with the dipolar D and scalar J interactions...



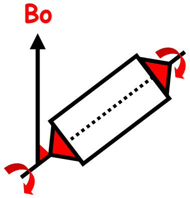
- connectivities in hybrids
- chemical grafting on nanoparticles
- H bonding ...

◆ DIPOLAR INTERACTION D

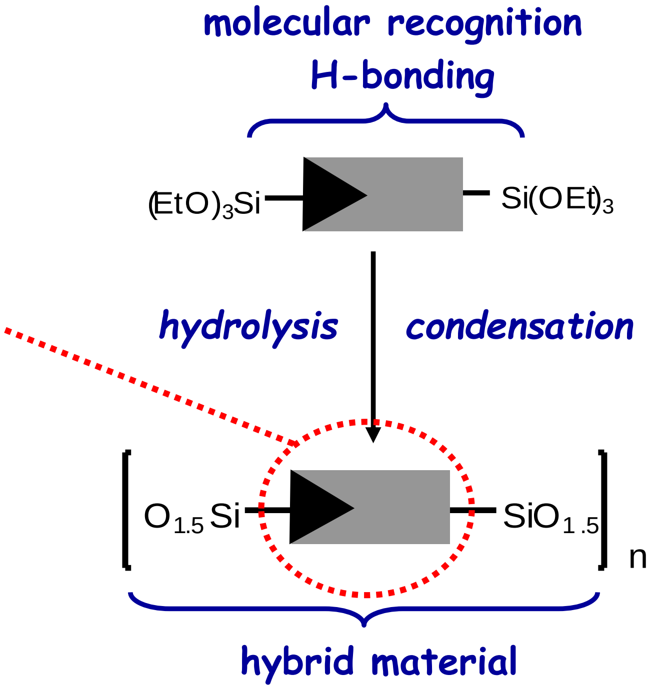


$$D \propto \frac{1}{r_{IS}^3}$$

CEMHTI,
Orléans



fast-, ultra fast MAS



molecular recognition
H-bonding

$(EtO)_3Si$ — $Si(OEt)_3$

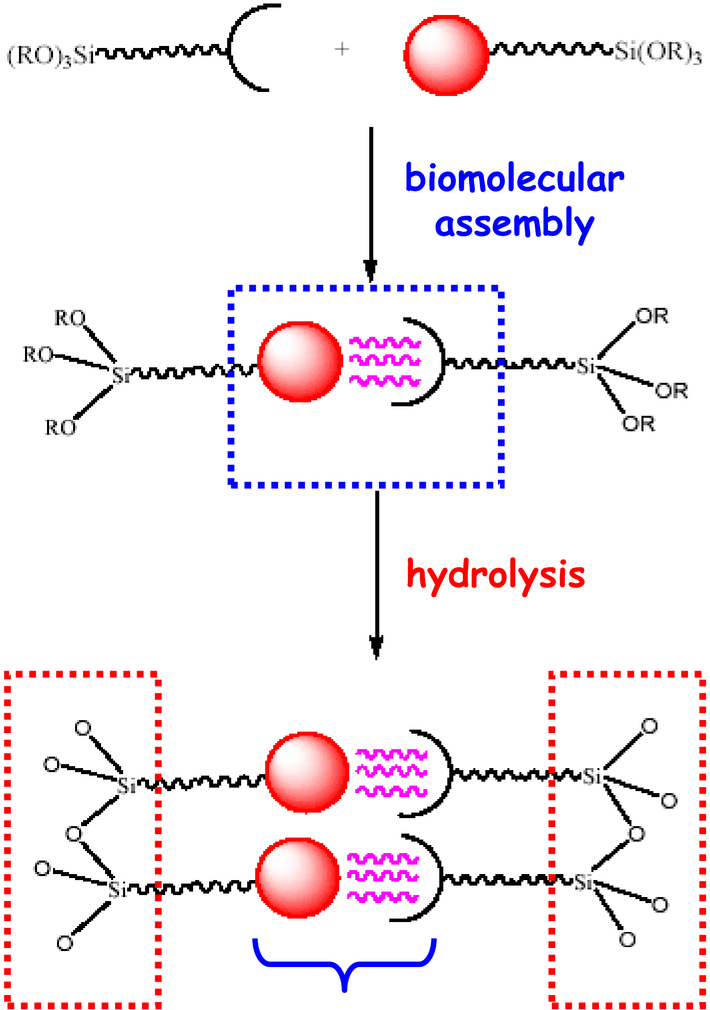
hydrolysis *condensation*

$\left[O_{1.5}Si — SiO_{1.5} \right]_n$

hybrid material

- ^1H-^1H dipolar interaction
- ureidopyrimidinone models
- bio-inspired materials

Ureidopyrimidinone based systems

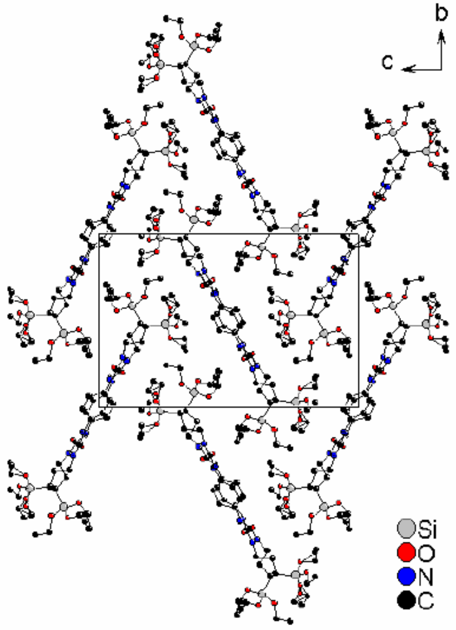


biomolecular assembly

hydrolysis

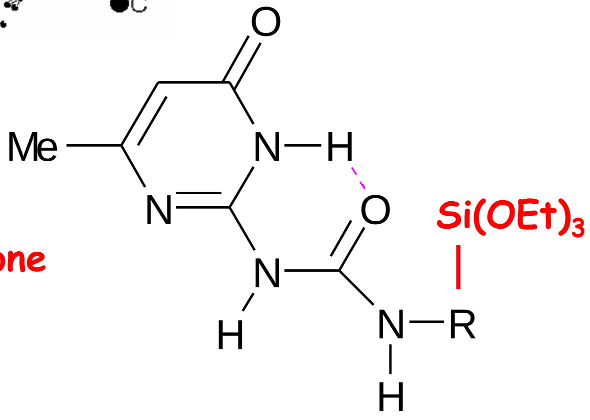
H-bonding

inorganic pillars



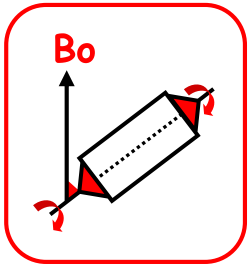
MONOCLINIC
P 21/n
a = 9.0372 Å
b = 15.5020 Å
c = 23.3873 Å
β = 92.837 °

XRD of precursors

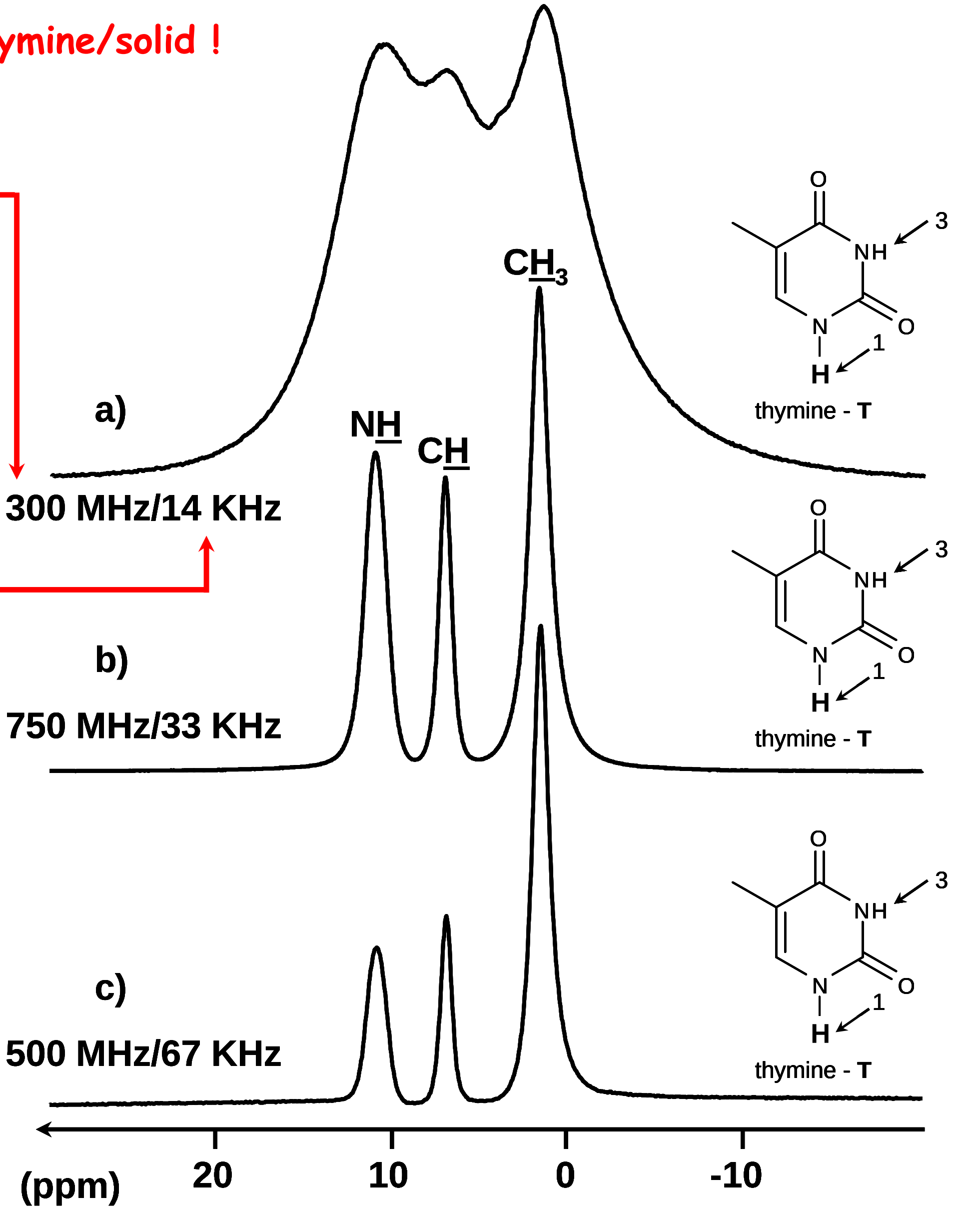


ureidopyrimidinone derivatives

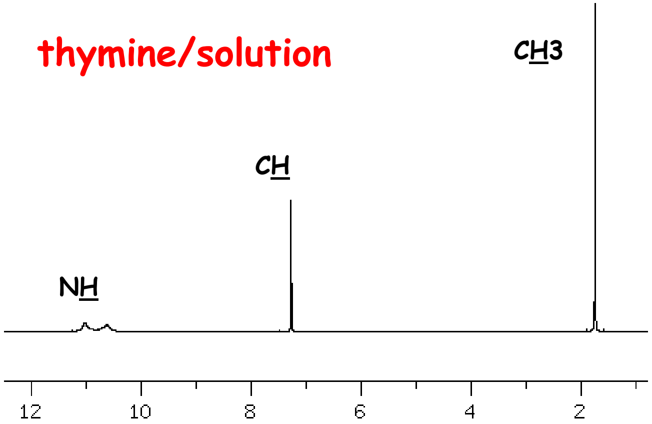
^{1}H high resolution solid state NMR



thymine/solid !

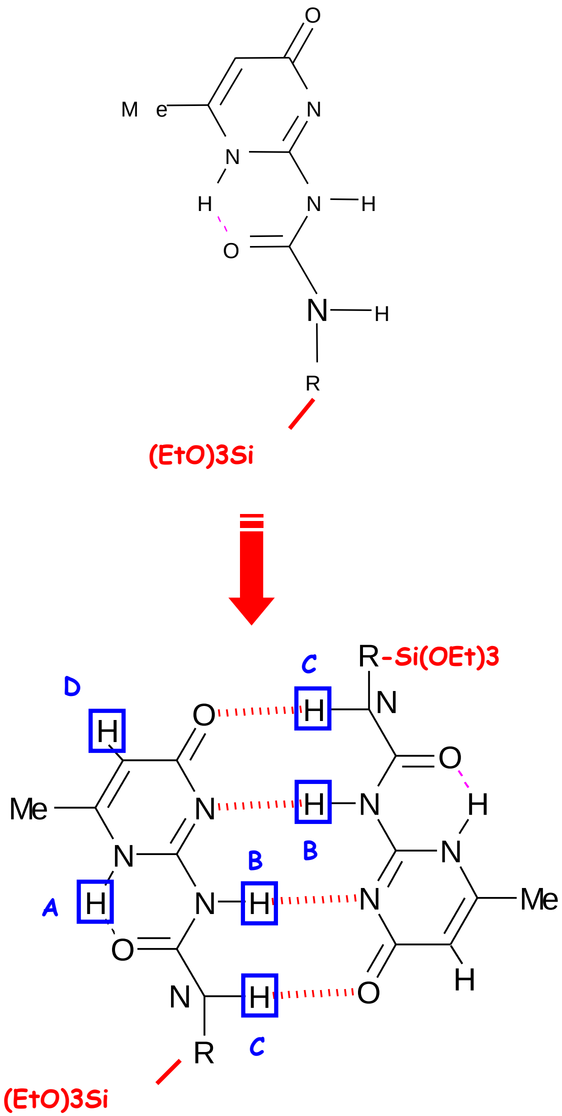


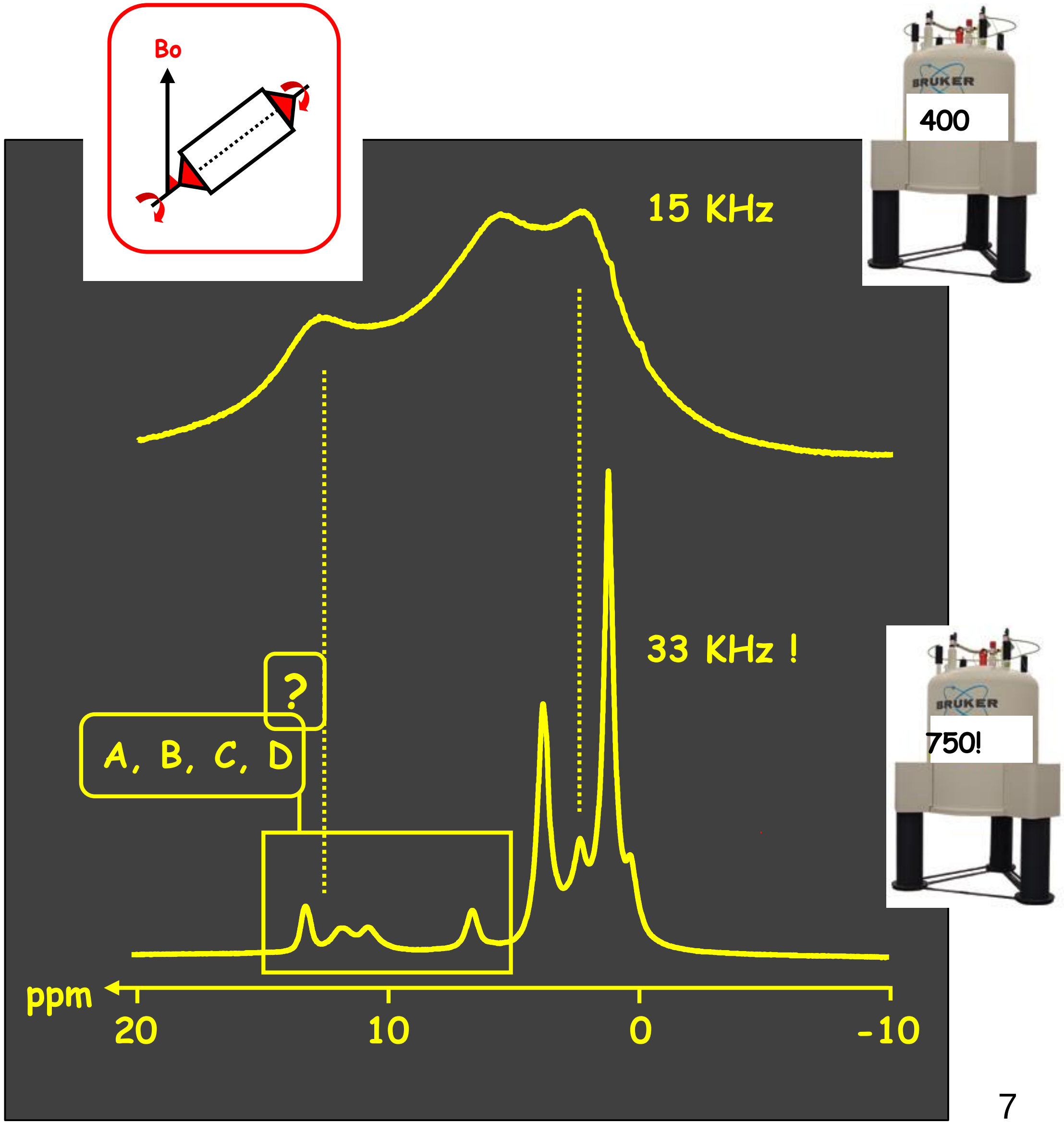
thymine/solution



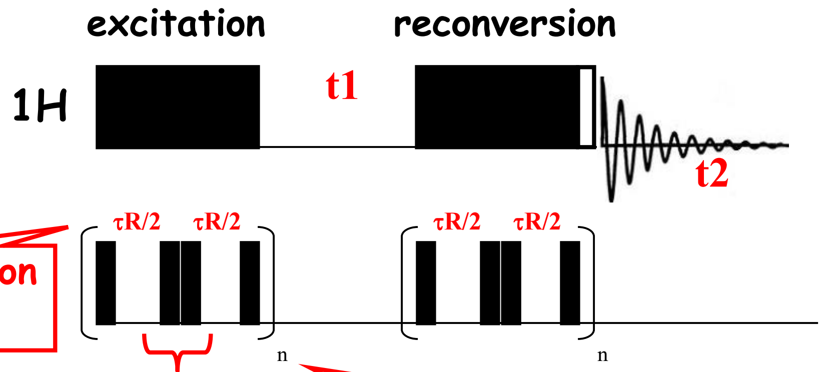
G. Arrachart et al., J. Mater. Chem. 18 (2008) 392

Ureidopyrimidinones: ^{1}H high resolution solid state NMR





Spatial connectivities: DQ ^{1}H fast MAS spectroscopy



synchronization with MAS

BAck to BAck

2Q hamiltonian !

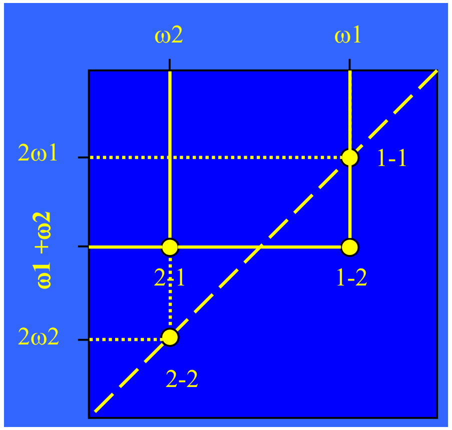
DHH ∝ $1/r^3$

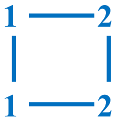
^{1}H .... ^{1}H
r

I=1/2 I=1/2

DQ

<++| ⇔ |-->





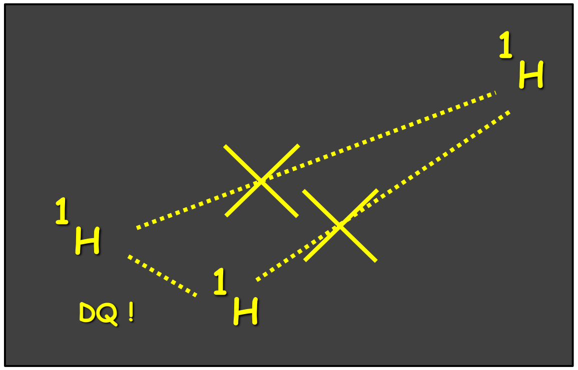
dipolar «links»

DQ dim.

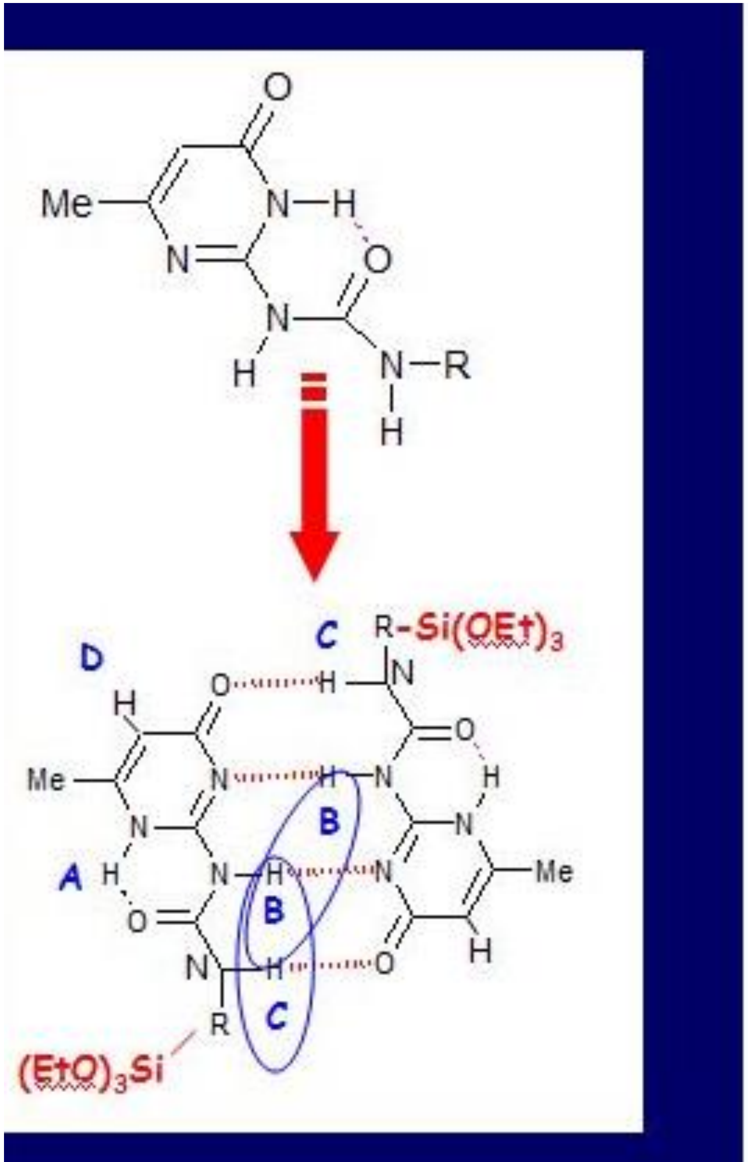
SQ dim.

δ_{iso}.: very fast MAS, very high B_0!

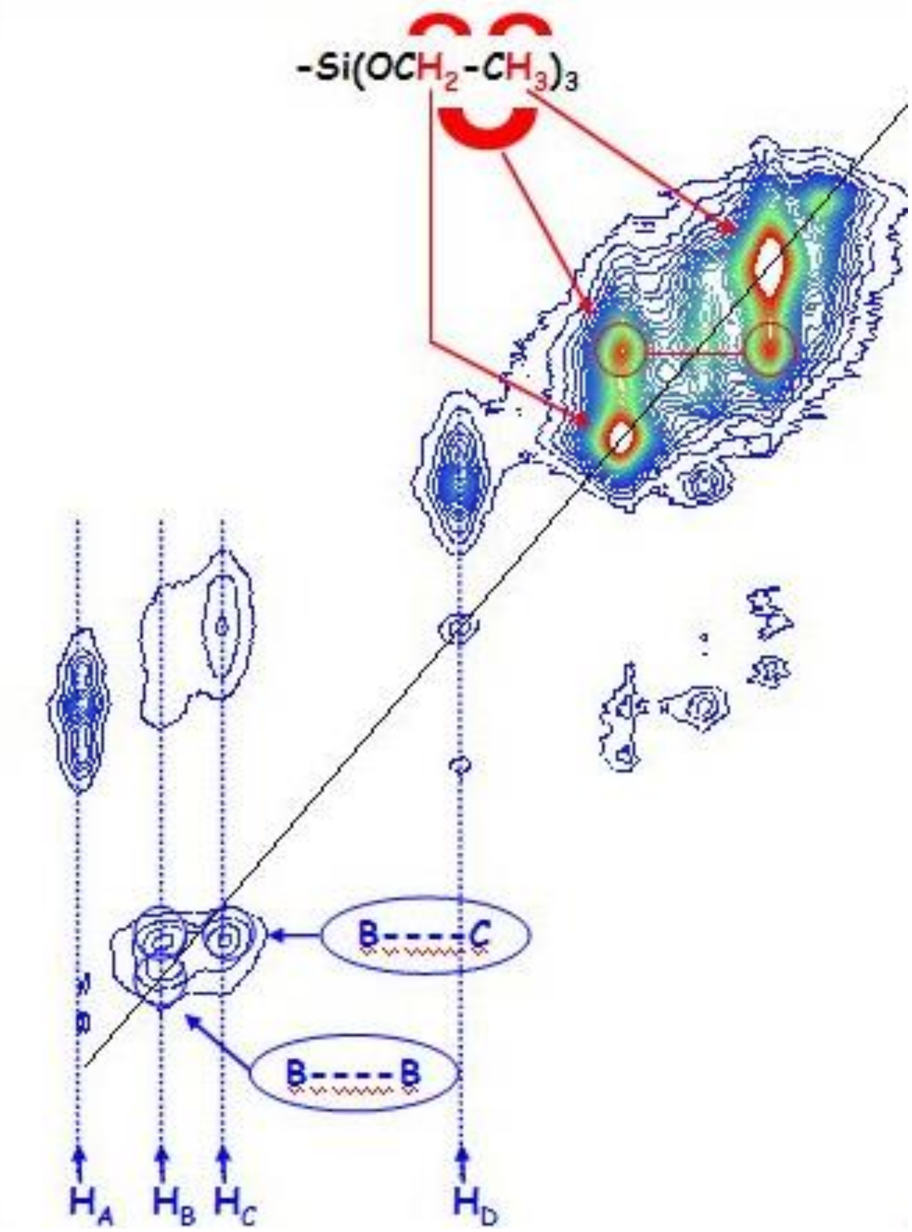
selectivity



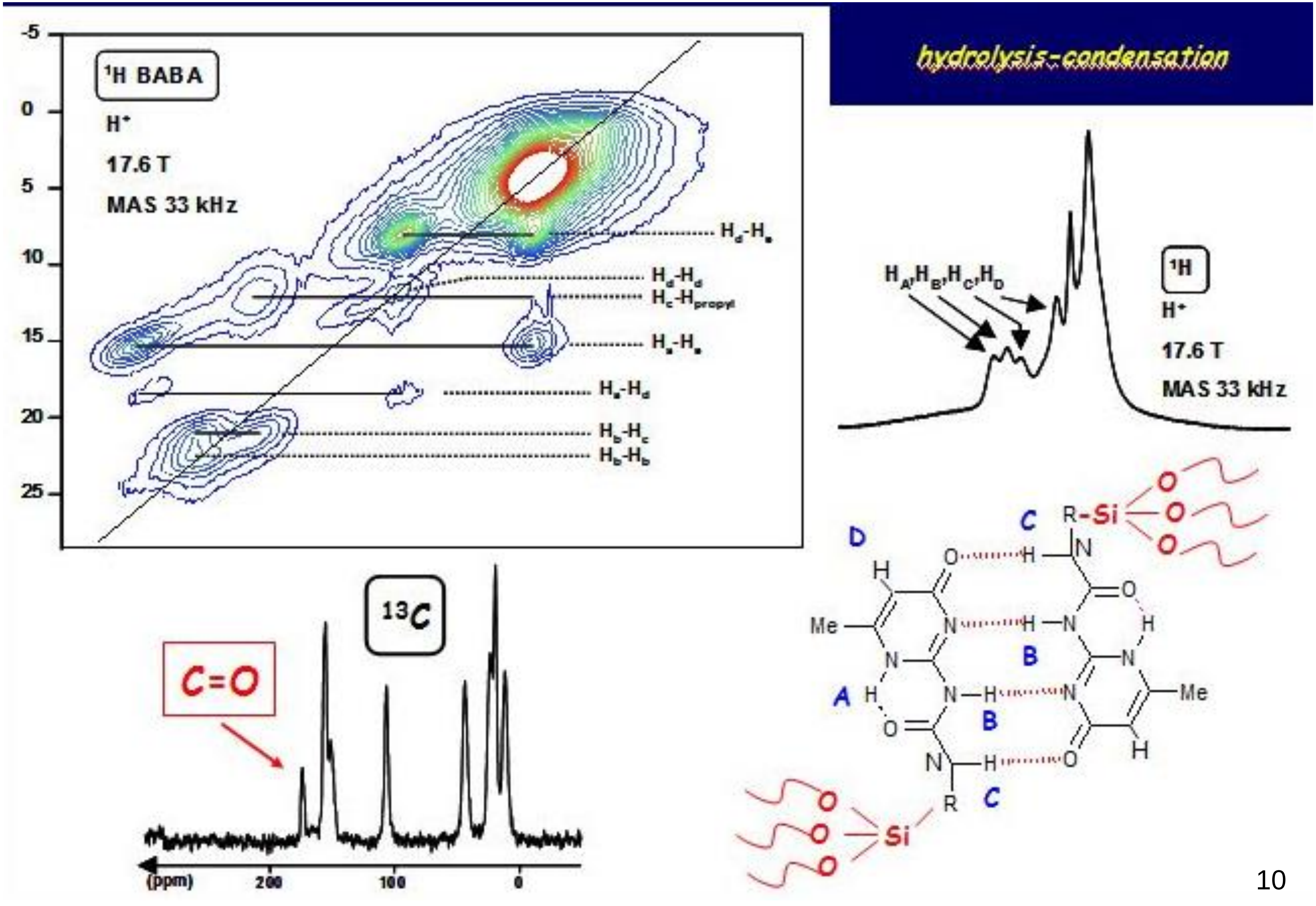
Application to ureidopyrimidinone precursors



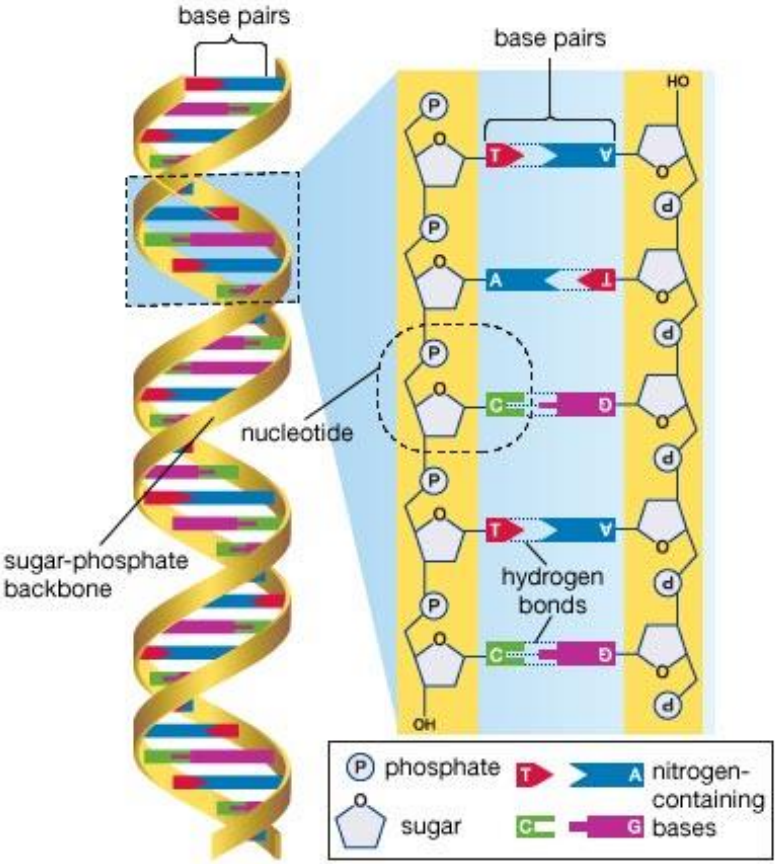
C. Bonhomme et al. Chem. Eur. J. (2008)



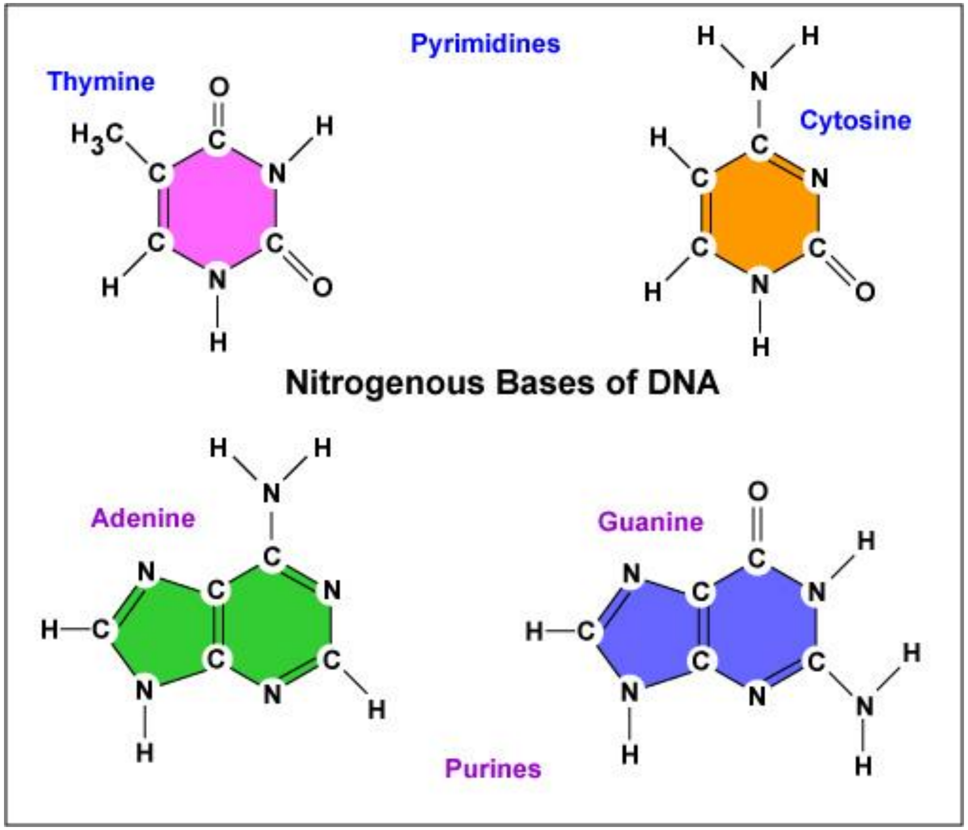
Application to ureidopyrimidinone derived materials: hybrid silica



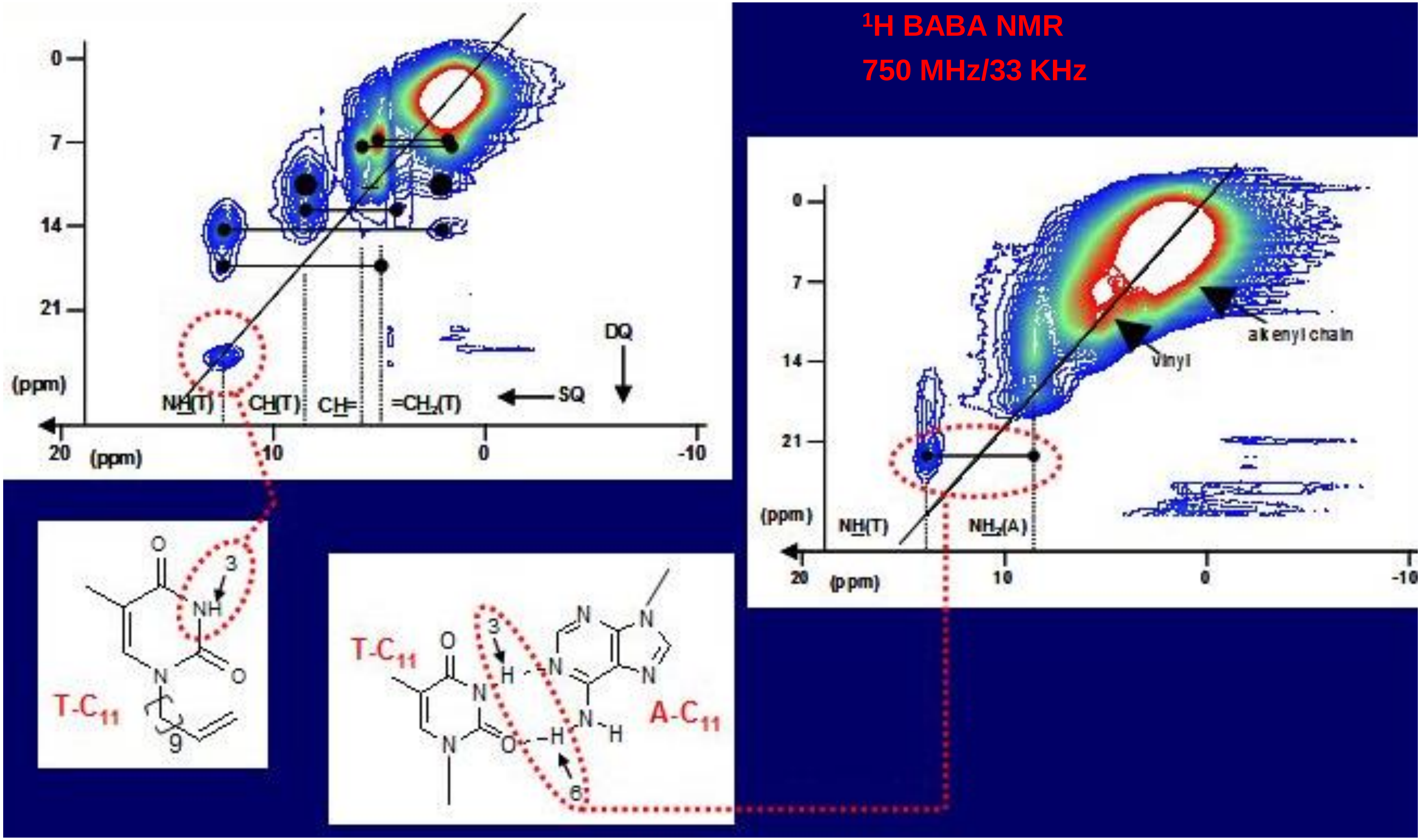
Motivations



© 2007 Encyclopædia Britannica, Inc.



Towards bio-inspired materials: adenine (A) and thymine (T) derivatives



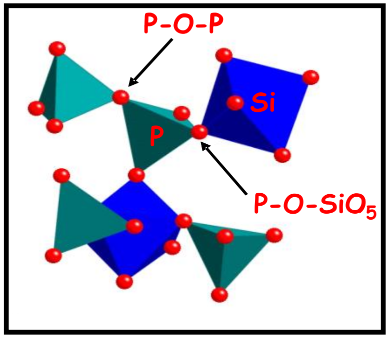
^{1}H BABA NMR

750 MHz/33 KHz

G. Arrachart et al., J. Mater. Chem. 18 (2008) 392

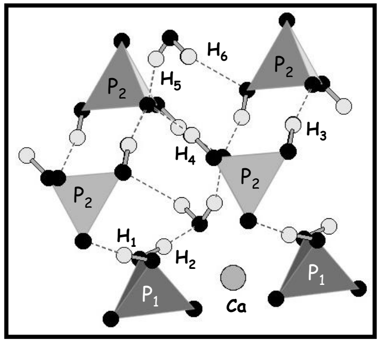
Materials - Part II

$Si_5O(PO_4)_6$
SiP_2O_7
monoclinic 1
monoclinic 2
...

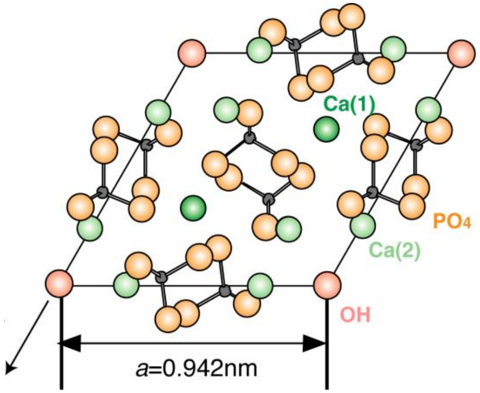


- silicophosphates

Brushite, $CaHPO_4.2H_2O$
MCPM, $Ca(H_2PO_4)_2.H_2O$
β- and γ-$Ca(PO_3)_2$
$Ca_4P_2O_9$
...



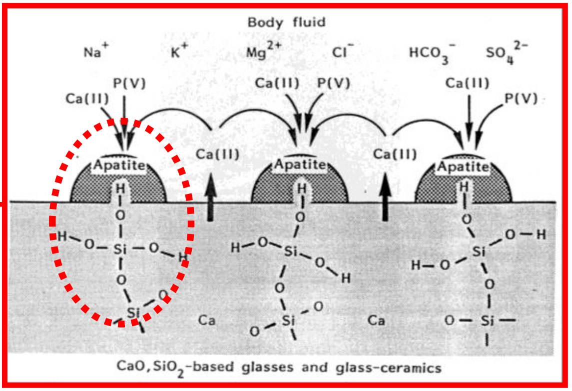
- calcium phosphates

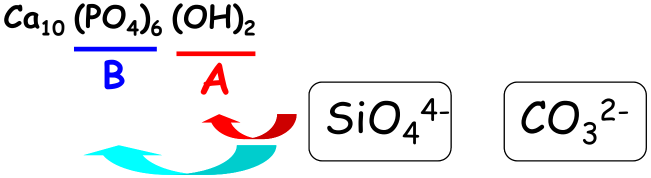


$Ca_{10} (PO_4)_6 (OH)_2$

- hydroxyapatite (HAp)

biocompatibility and bioactivity of complex systems

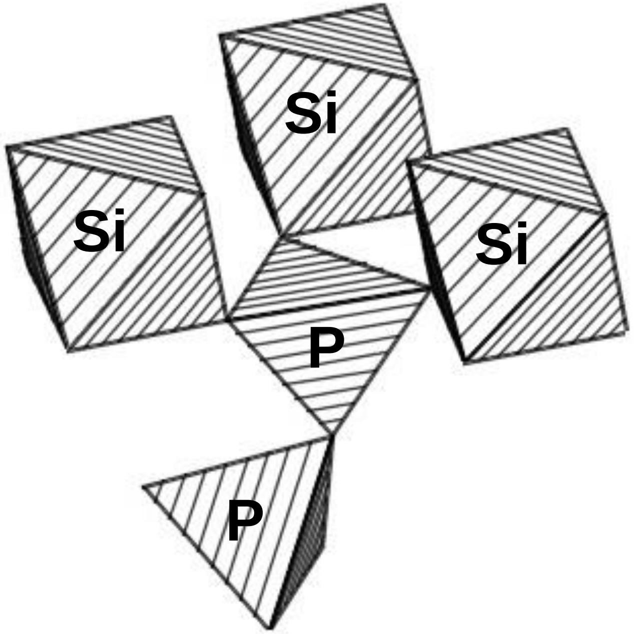


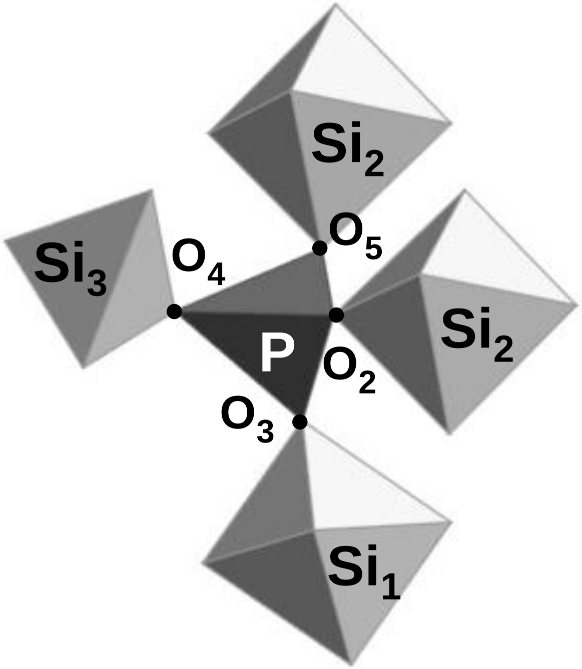


$Ca_{10} (\underbrace{PO_4)_6}_{B} \underbrace{(OH)_2}_{A}$

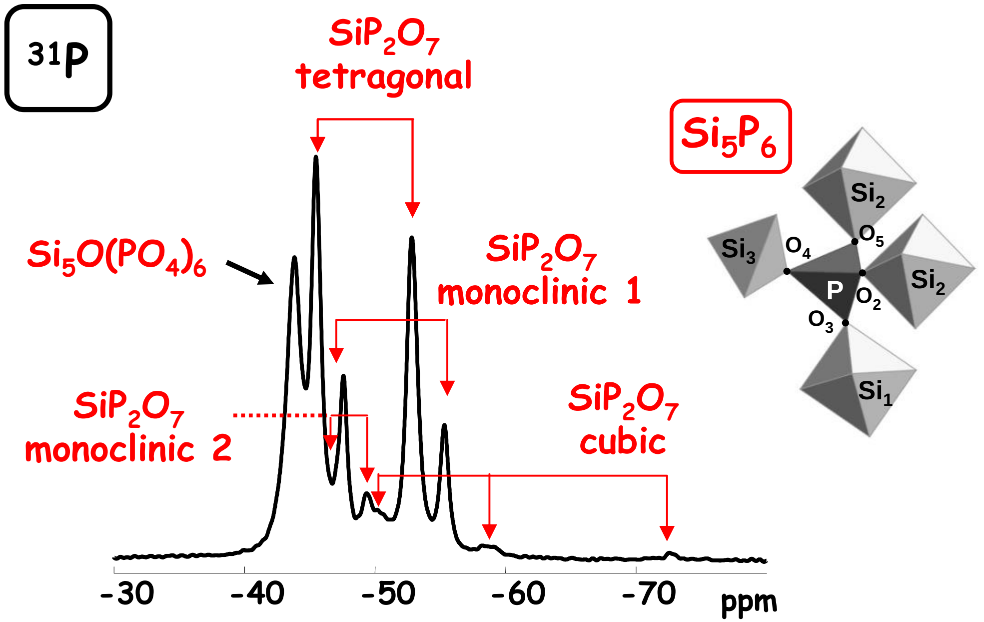
$\boxed{SiO_4^{4-}}$ $\boxed{CO_3^{2-}}$

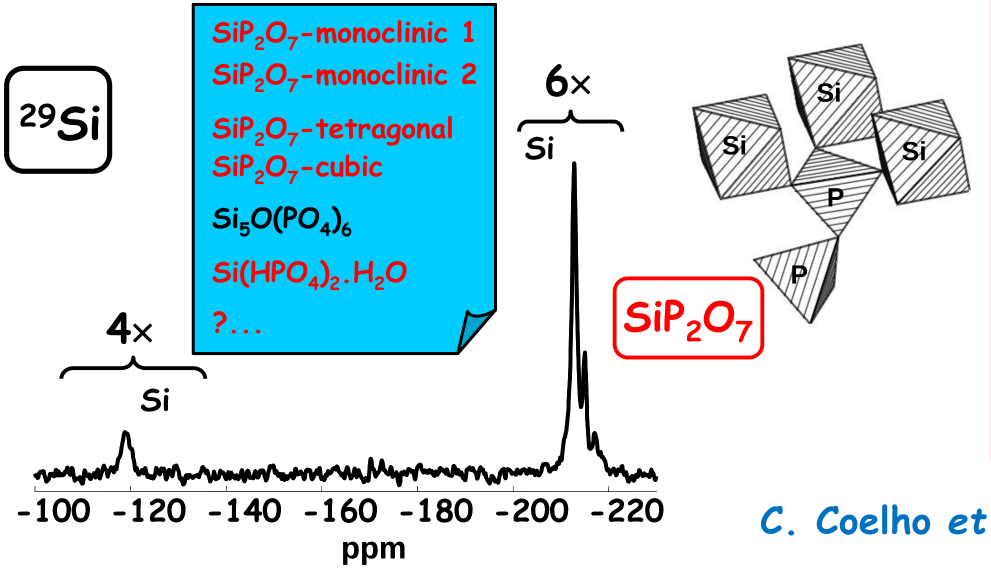
- silicophosphates





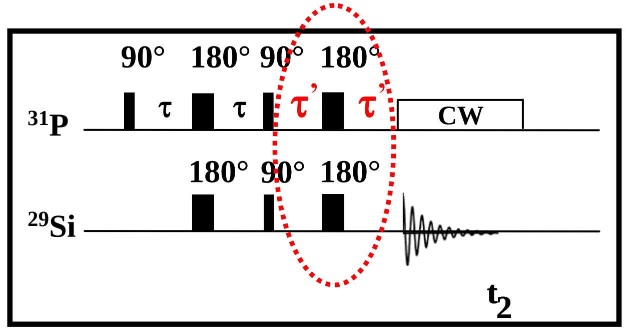
Crystalline silicophosphates: $Si_5O(PO_4)_6$ and SiP_2O_7 polymorphs

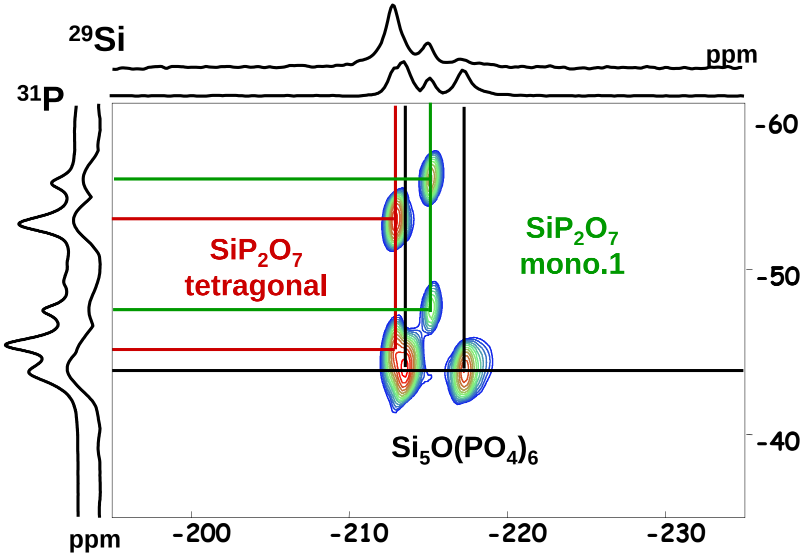




SiP_2O_7-monoclinic 1
SiP_2O_7-monoclinic 2
SiP_2O_7-tetragonal
SiP_2O_7-cubic
$Si_5O(PO_4)_6$
$Si(HPO_4)_2.H_2O$
?...

$^{31}P \rightarrow {}^{29}Si$ MAS-J-INEPT

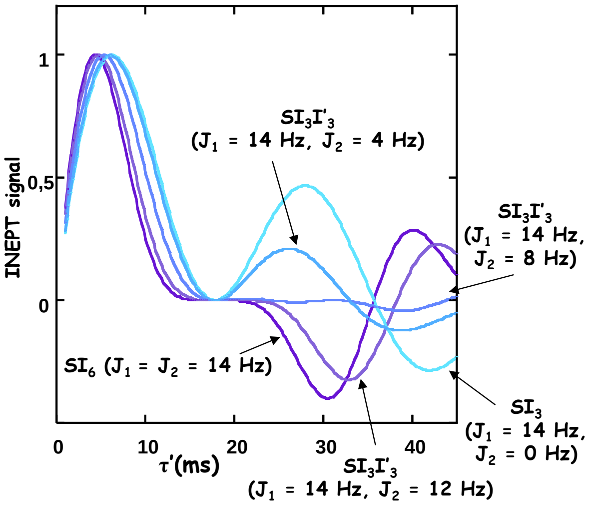


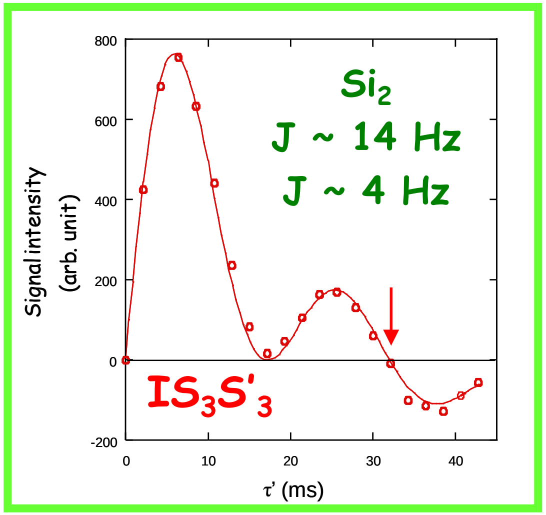


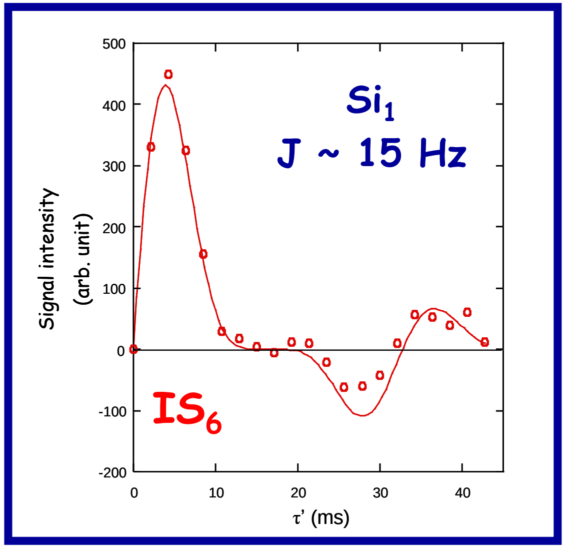
C. Coelho et al., *Inorg. Chem.* 46 (2007) 1379.

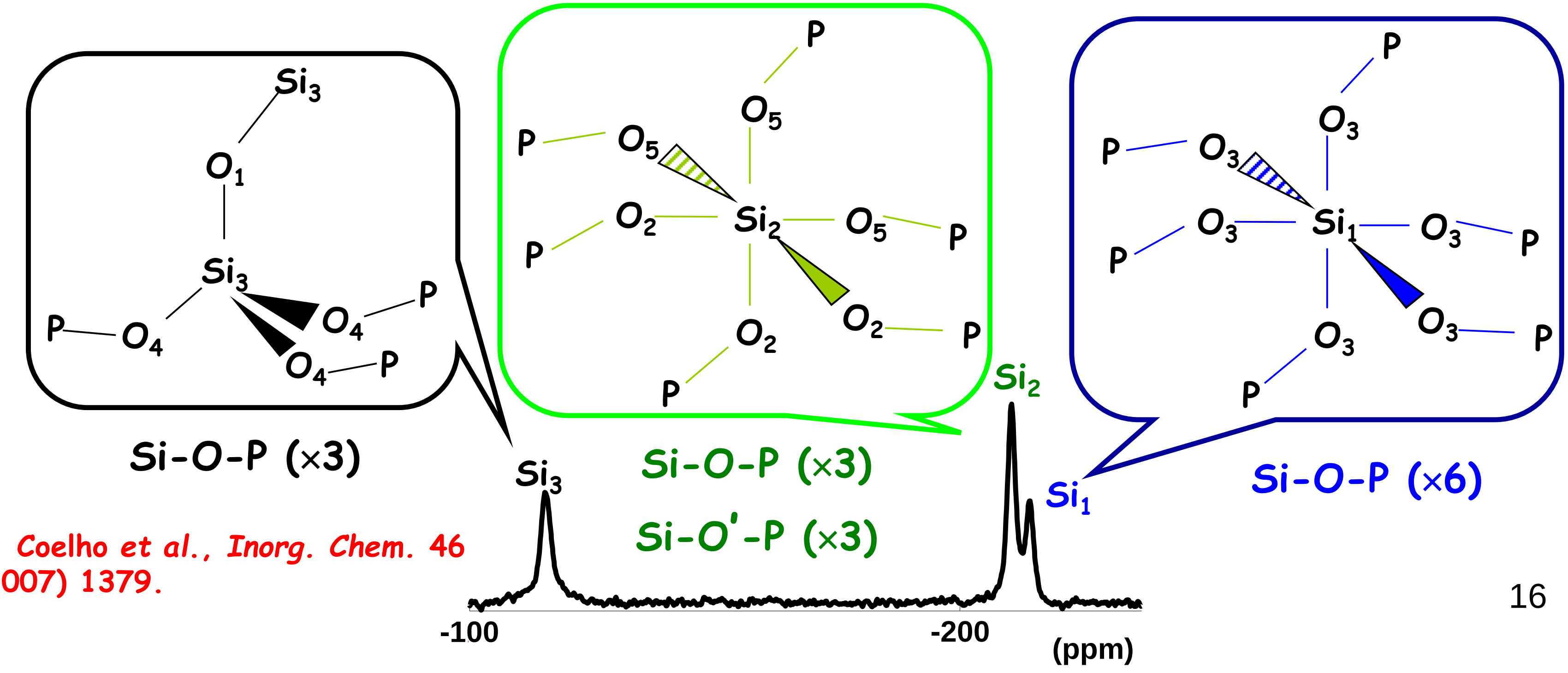
C. Coelho et al., *J. Magn. Reson.*, 179 (2006) 106.

$^{31}P \rightarrow {}^{29}Si$ MAS-J-INEPT curves: $Si_5O(PO_4)_6$









C. Coelho et al., Inorg. Chem. 46 (2007) 1379.

First principles calculations: the GIPAW approach

Pickard, Mauri, *Phys. Rev. B* (2001)

DFT
periodic systems
all-electron hamiltonians

GIPAW

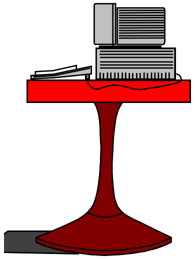
evaluation of $j^{(1)}(r')$ using pseudopotentials

$$B_{in}^{(1)}(r) = 1/c \int d^3r'\; j^{(1)}(r') \times \frac{r-r'}{|r-r'|^3}$$

CSA

EFG

J



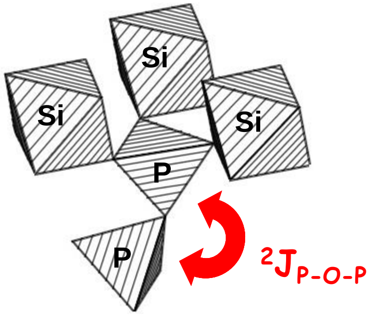
IDRIS

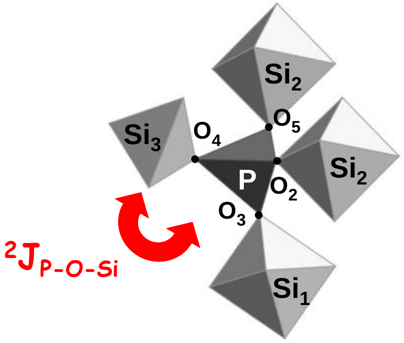
Gervais et al., Magn. Reson. Chem. 42 (2004) 445.

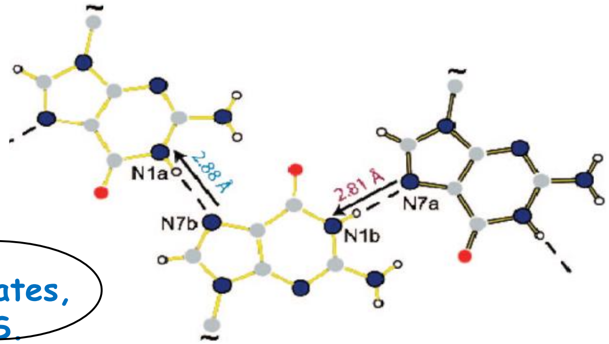
Gervais et al., J. Phys. Chem. A 109 (2005) 6960.

Bonhomme et al., J. Magn. Reson. 2007, *Chem. Mater.* 2008, *J. Am. Chem. Soc.* 2009, 2010

inorganic and organic derivatives...



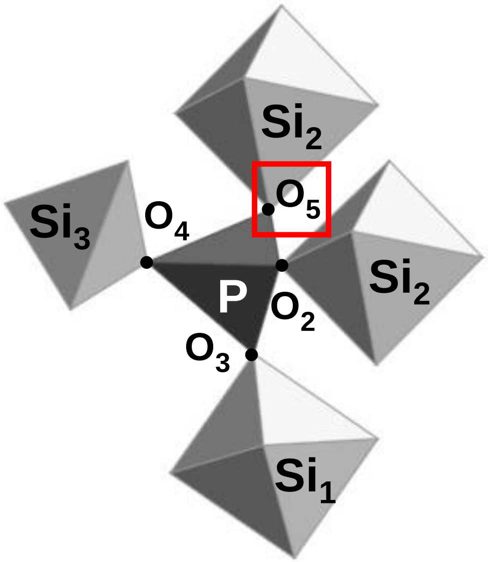




S. Joyce, J. Yates, C. Pickard, S. Brown, *J. Am. Chem. Soc.* (2008)

$J_{(N-N)}$

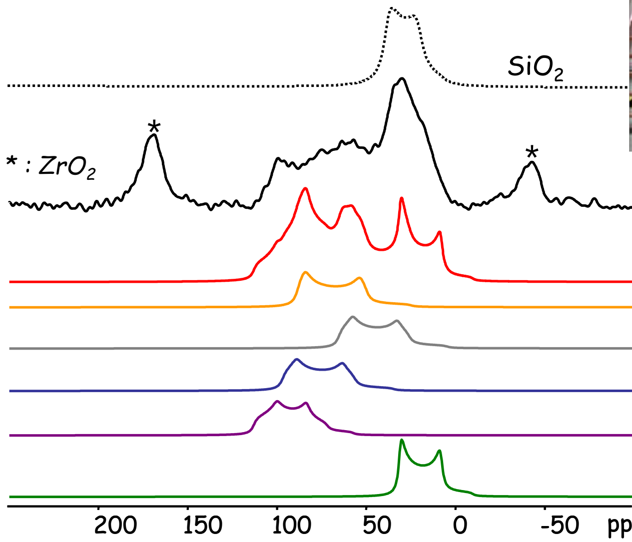
^{17}O data

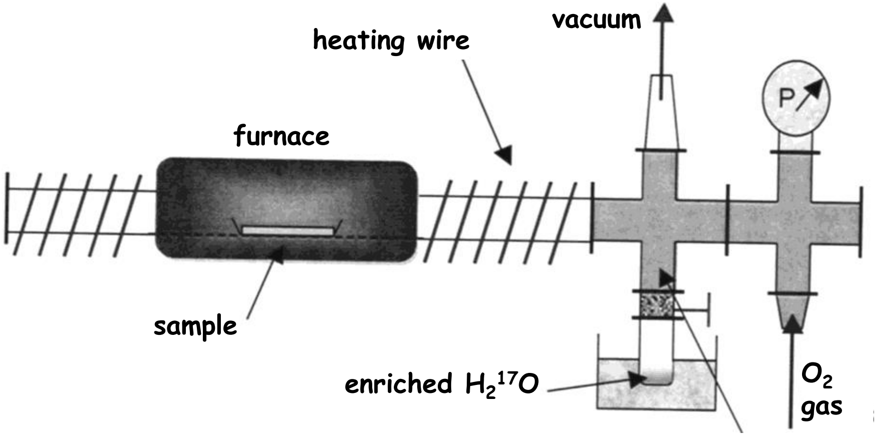


PAW

Q

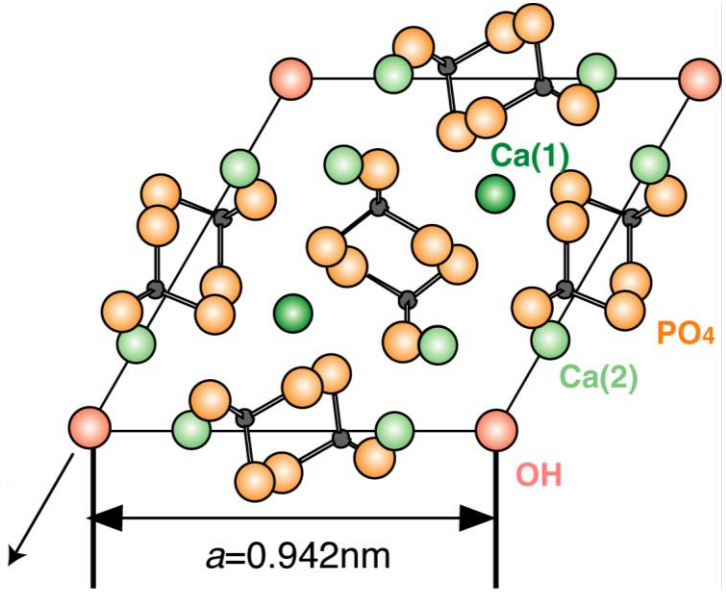
N.A. ^{17}O MAS experiment

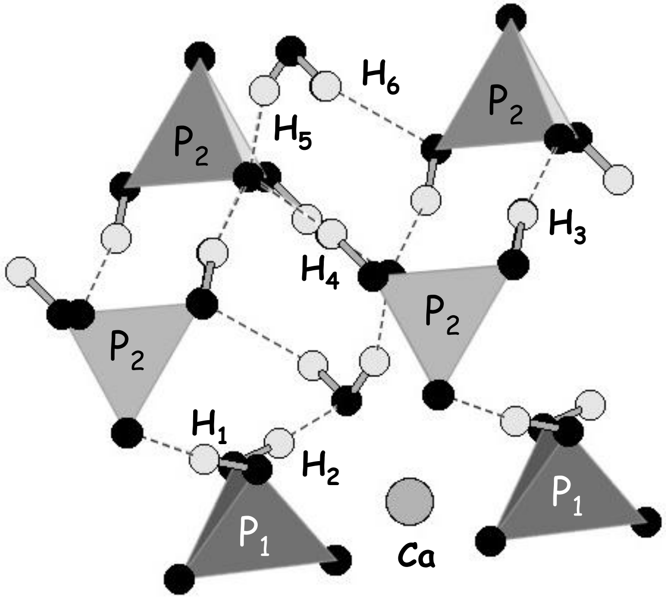




A. Flambart, L. Montagne, L. Delevoye, Chem. Commun. (2006) 3426

♦ Calcium phosphates and HAp structures





Biocompatible calcium phosphates

Brushite, $CaHPO_4.2H_2O$

MCPM, $Ca(H_2PO_4)_2.H_2O$

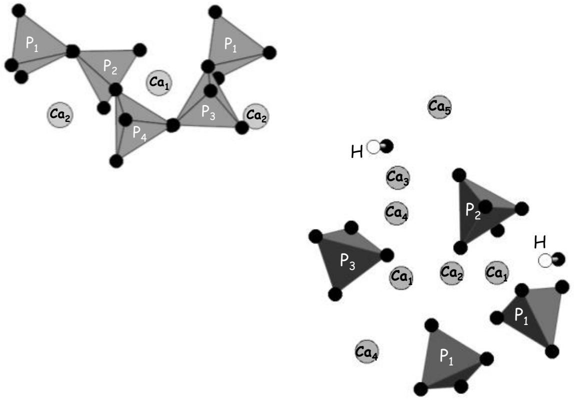
β- and γ-$Ca(PO_3)_2$

$Ca_4P_2O_9$

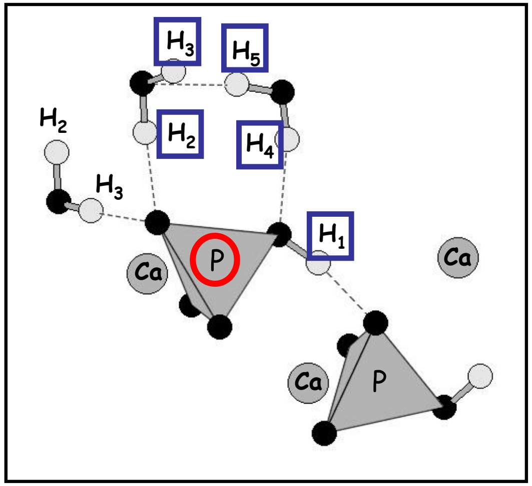
$Ca_{10}(PO_4)_6(OH)_2$ (HAp)

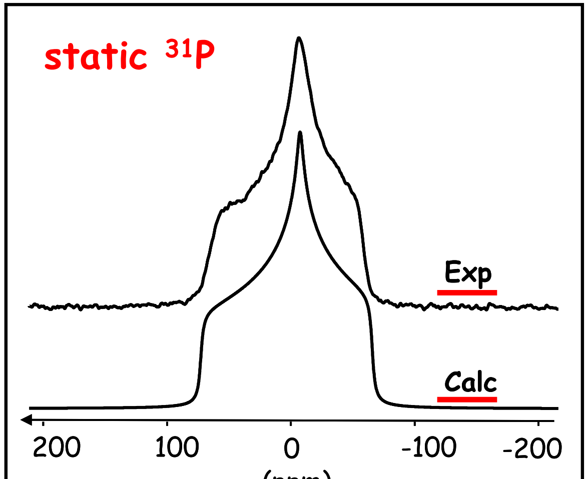
...

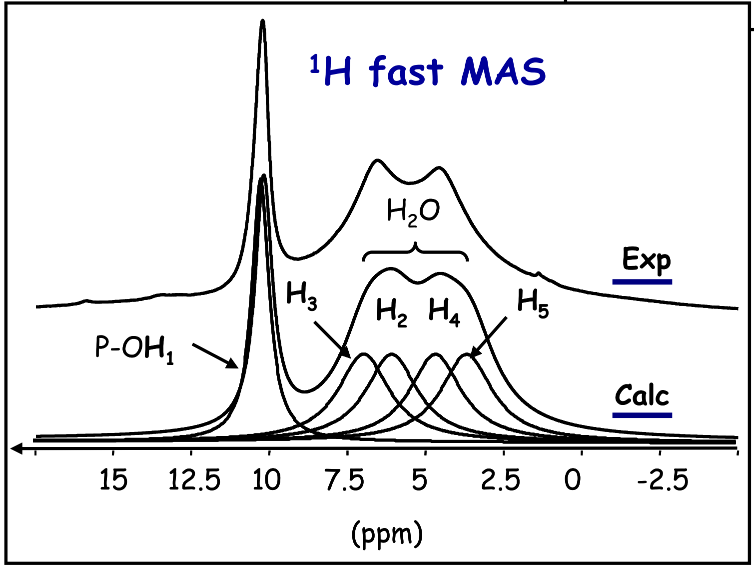
hydrated, dehydrated, and hydroxylated structures



Brushite: the GIPAW approach (^{31}P, ^{1}H)





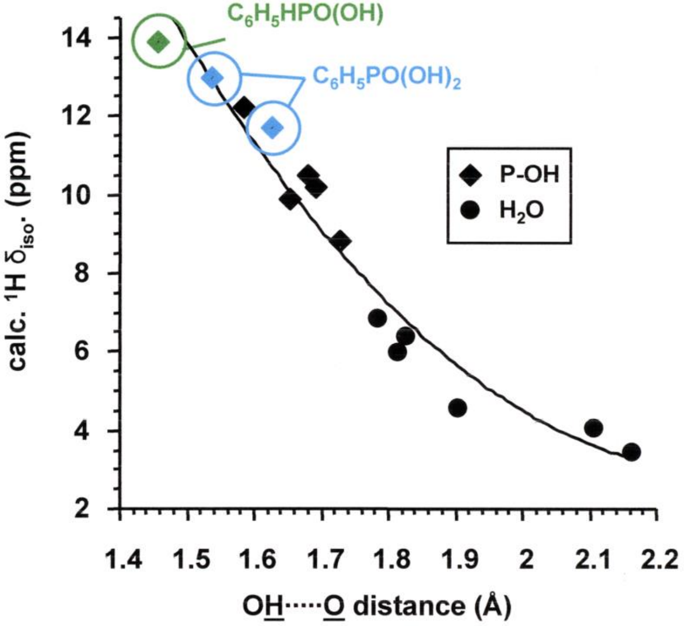


B. Alonso, D. Massiot, CEMHTI, Orléans, France

F. Pourpoint et al., Appl. Magn. Reson. 32 (2007) 435.

More from ^1H GIPAW data: H-bonding and CSA tensors

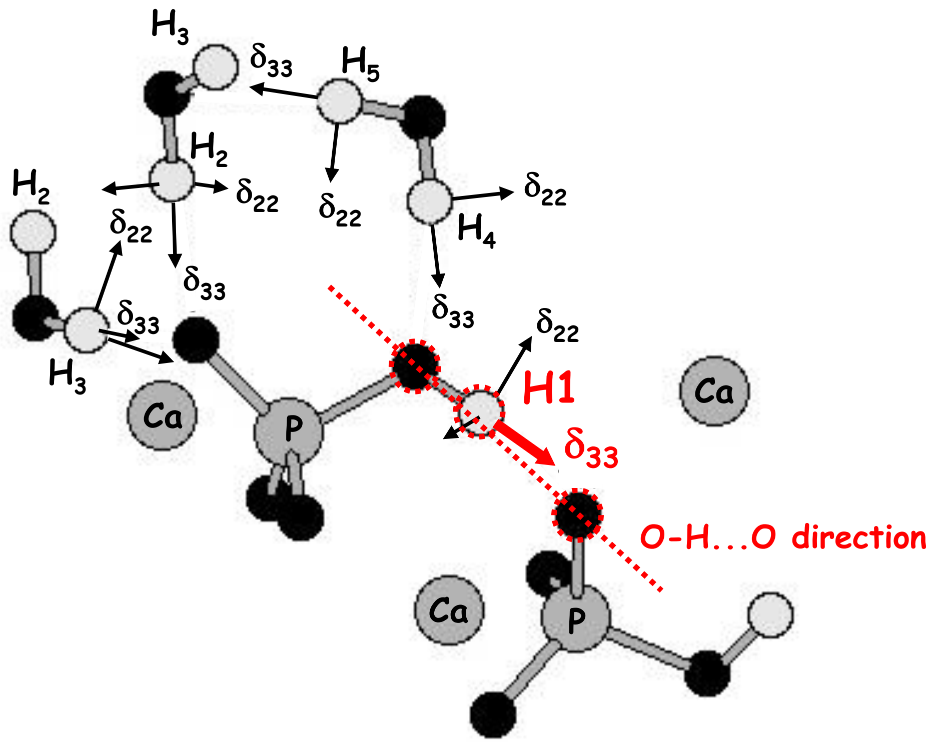
^1H *isotropic* chemical shifts



H-bonding in calcium phosphates and phosphonic acids

C. Gervais *et al.*, *J. Magn. Reson.* 187 (2007) 181.

Brushite: $CaHPO_4.2H_2O$

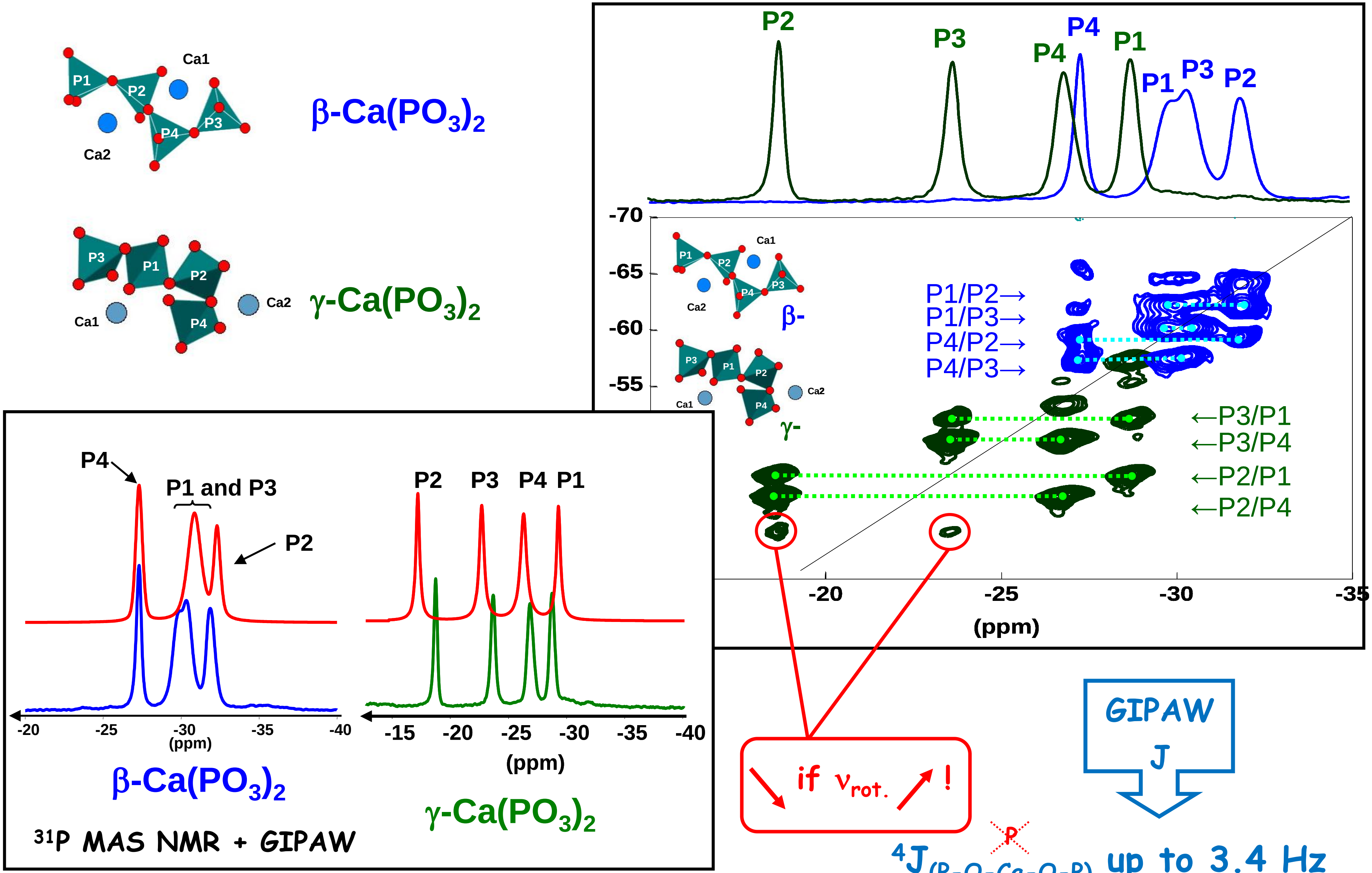


^1H CSA tensors and orientations

F. Pourpoint *et al.*, *Appl. Magn. Reson.* 32 (2007) 435.

β- and γ-$Ca(PO_3)_2$

2D ^{31}P MAS-J-INADEQUATE



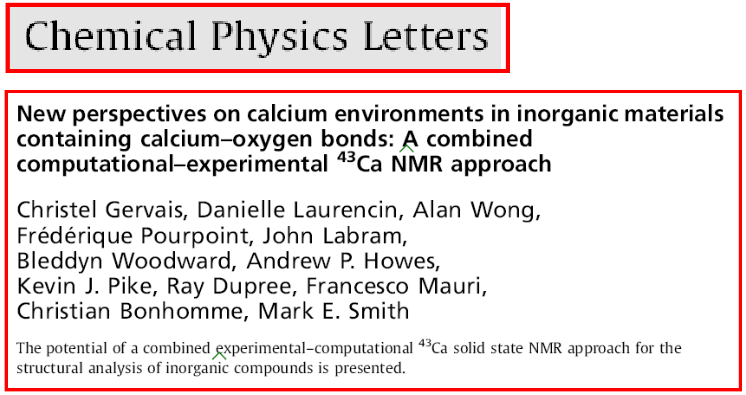
^{31}P MAS NMR + GIPAW

↘ if $\nu_{rot.}$ ↗ !

$^4J_{(P-O-Ca-O-P)}$ up to 3.4 Hz

F. Pourpoint *et al.* , *Chem. Mater.* 19 (2007) 6367

^{43}Ca NMR spectroscopy

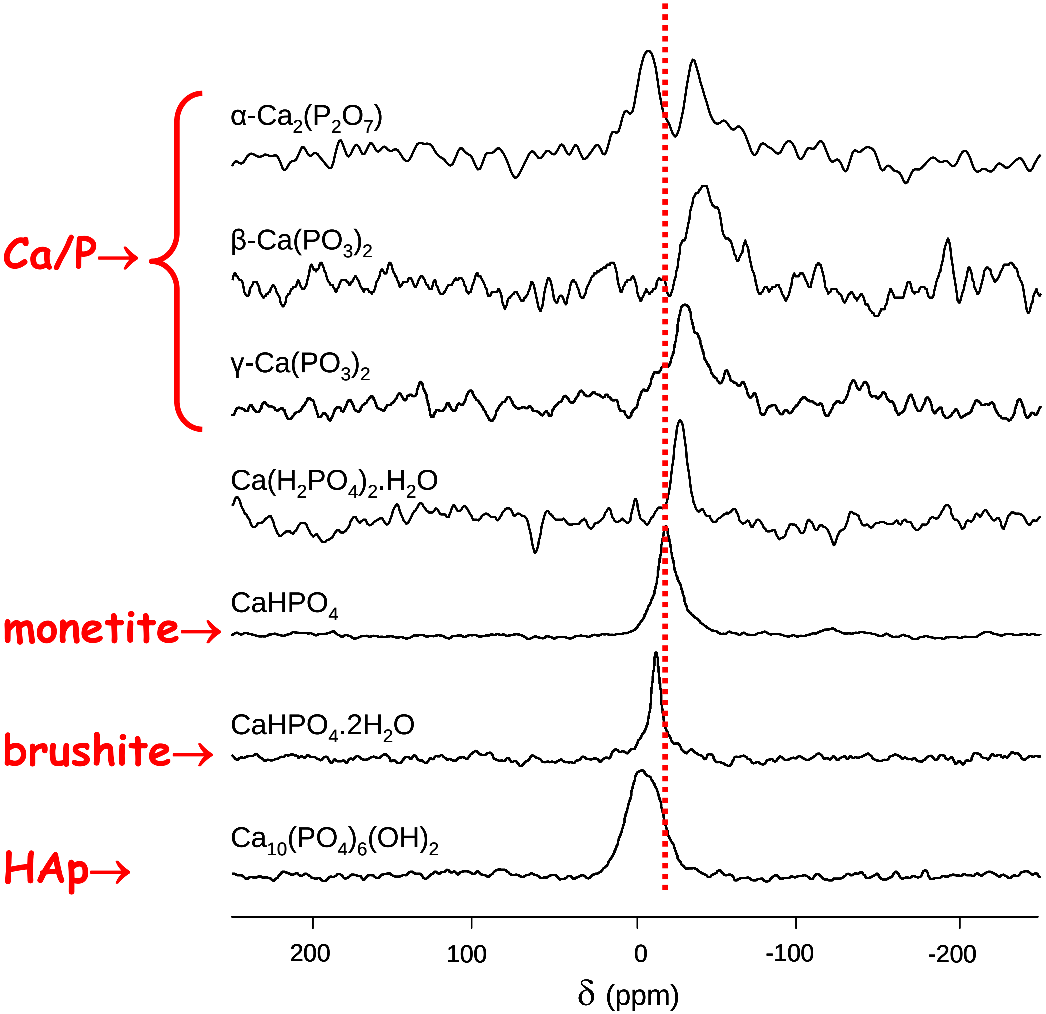


Chemical Physics Letters

New perspectives on calcium environments in inorganic materials containing calcium–oxygen bonds: A combined computational–experimental ^{43}Ca NMR approach

Christel Gervais, Danielle Laurencin, Alan Wong, Frédérique Pourpoint, John Labram, Bleddyn Woodward, Andrew P. Howes, Kevin J. Pike, Ray Dupree, Francesco Mauri, Christian Bonhomme, Mark E. Smith

The potential of a combined experimental–computational ^{43}Ca solid state NMR approach for the structural analysis of inorganic compounds is presented.

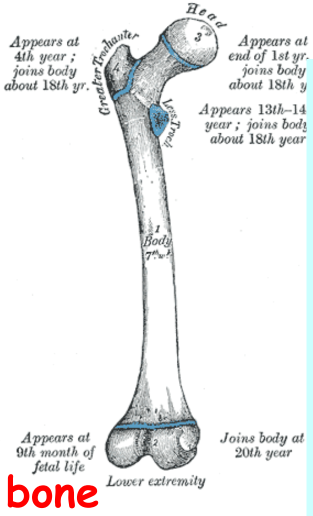


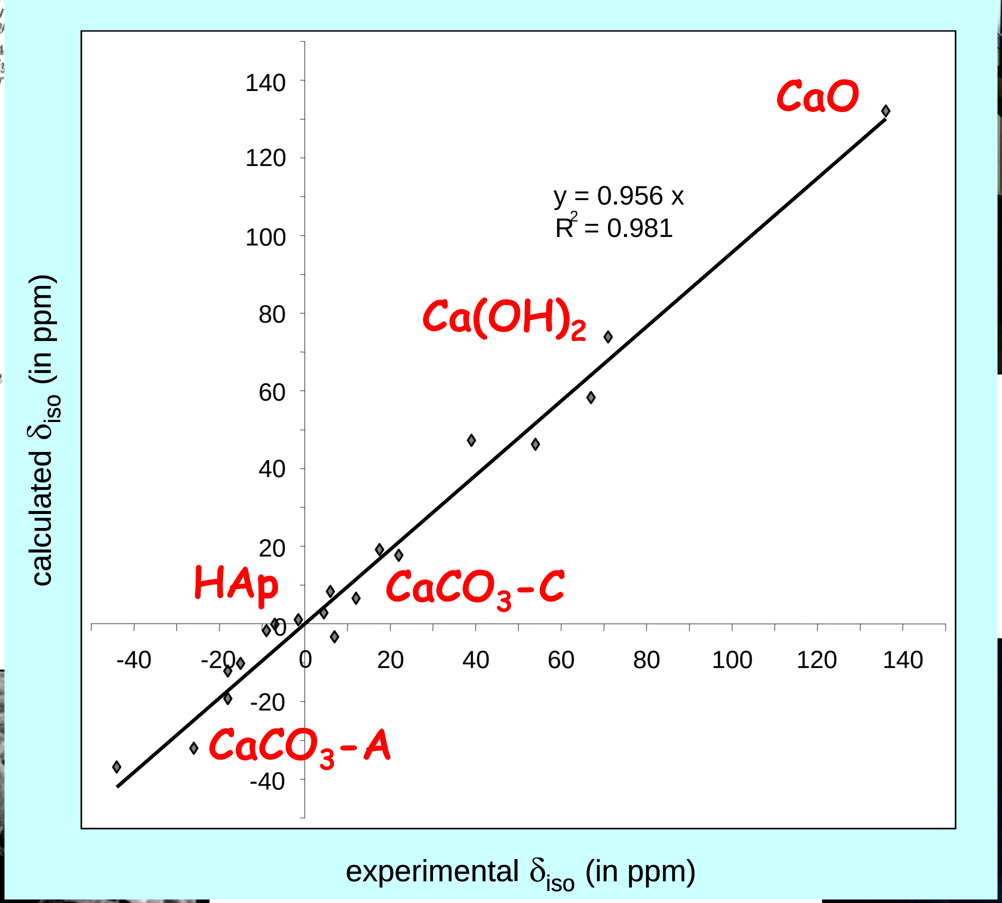
large volume MAS rotor (∅ 9.5mm)

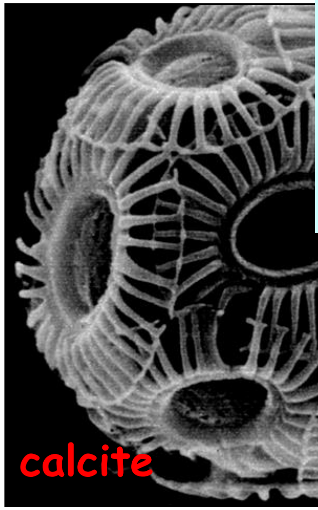
multi field experiments (up to 18.8 T)

natural abundance (0.14 %) ^{43}Ca MAS NMR

^{43}Ca CSA/Q GIPAW calculations

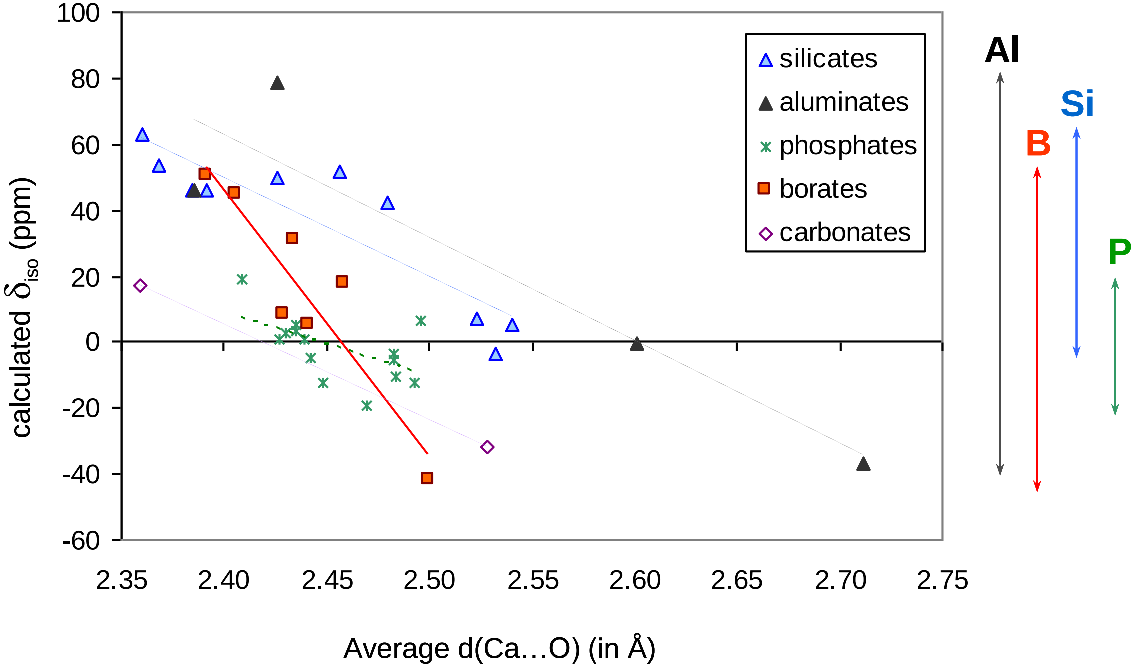




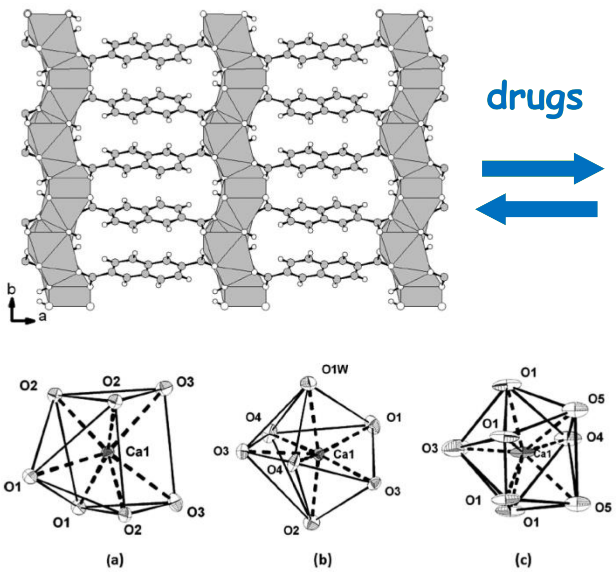


see also: Bryce *et al.*, *J. Am. Chem. Soc.* 130 (2008) 9282

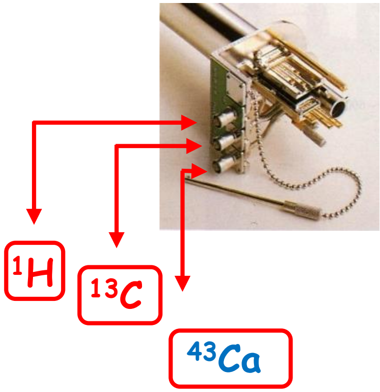
^{43}Ca NMR: a stuctural tool



Ca based Metal Organic Frameworks



C. Volkringer *et al.*, *Cryst. Growth & Design* 8 (2008) 685

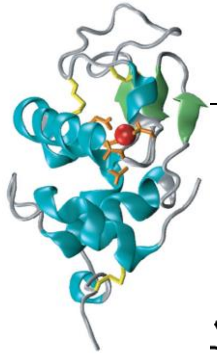


D. Laurencin *et al.*, *J. Am. Chem. Soc.* 130 (2008) 2412

D. Laurencin, C. Bonhomme *et al.* *J. Am. Chem. Soc.* (2009)

Towards $^{1}H/^{13}C/^{43}Ca$ triple resonance experiments

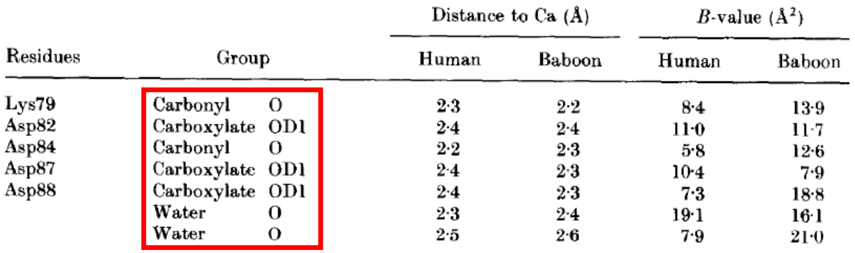
some structural key questions:



Acharya, 1991, Bushmarina, 2005

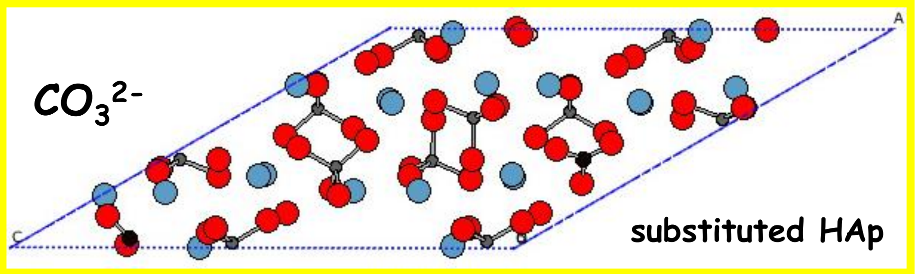
CALcium MODULated proteIN
α-Lactalbumin

calcium ligands in human and baboon α-lacs



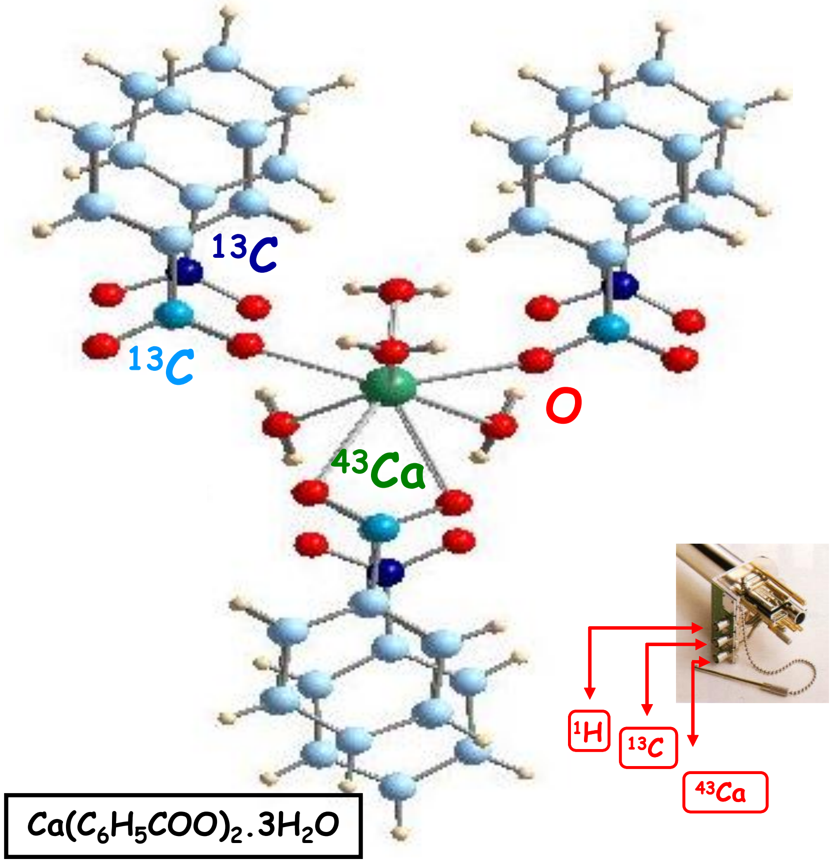
			Distance to Ca (Å)		B-value (Å^2)	
Residues	Group		Human	Baboon	Human	Baboon
Lys79	Carbonyl	O	2·3	2·2	8·4	13·9
Asp82	Carboxylate	OD1	2·4	2·4	11·0	11·7
Asp84	Carbonyl	O	2·2	2·3	5·8	12·6
Asp87	Carboxylate	OD1	2·4	2·3	10·4	7·9
Asp88	Carboxylate	OD1	2·4	2·3	7·3	18·8
	Water	O	2·3	2·4	19·1	16·1
	Water	O	2·5	2·6	7·9	21·0

- Ca/protein interactions



- carbonated HAp

calcium benzoate: a model compound (^{43}Ca: 60% ; ^{13}C: 100% or natural abundance)



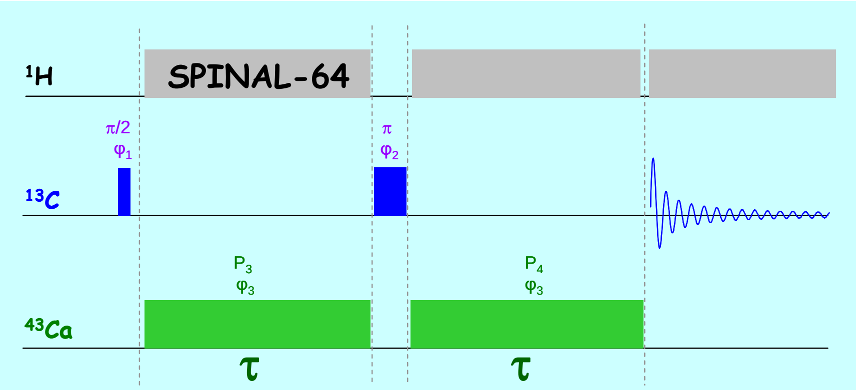
$Ca(C_6H_5COO)_2.3H_2O$

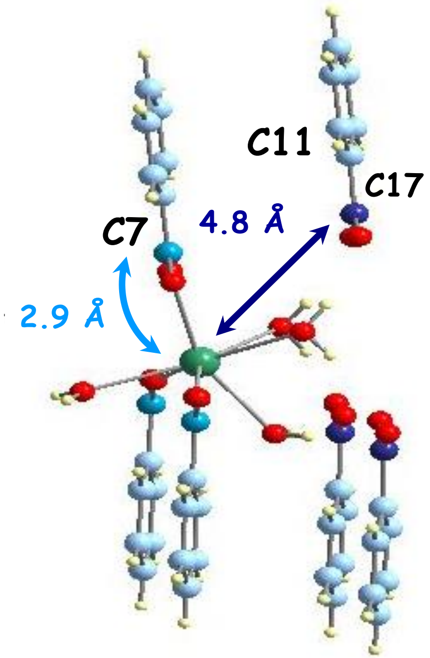
D. Laurencin, C. Bonhomme *et al.*, *J. Am. Chem. Soc.* 2009

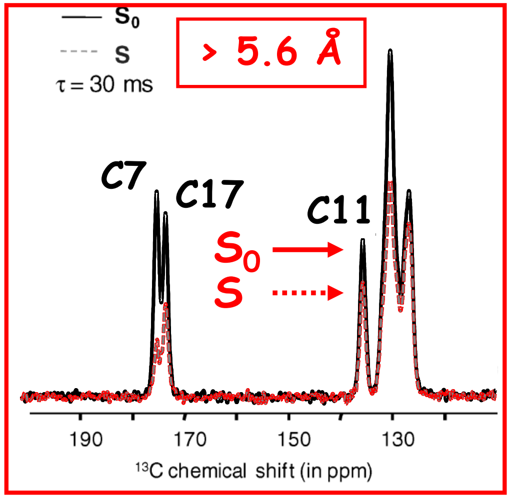
Dipolar MAS experiments: ^{43}Ca – ^{13}C proximities

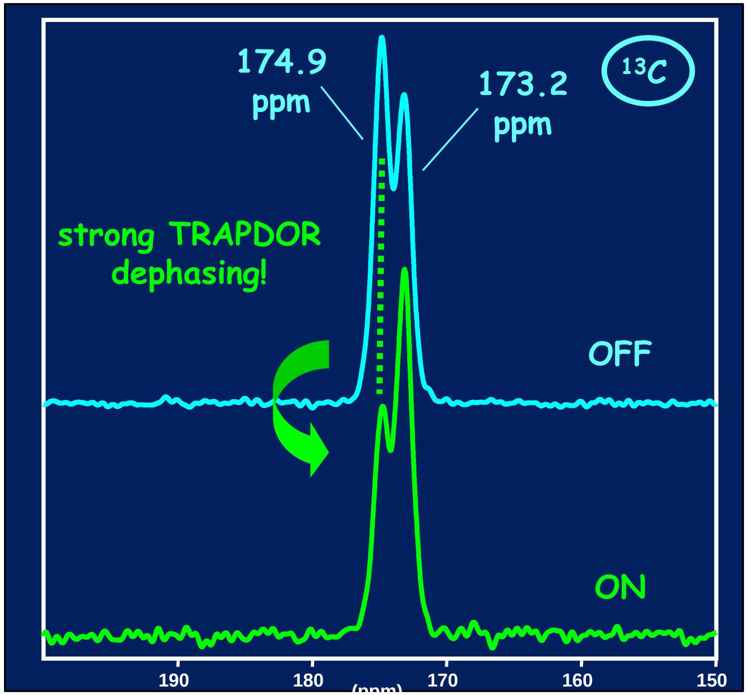
- $^{13}C/^{43}Ca$ TRAPDOR experiments

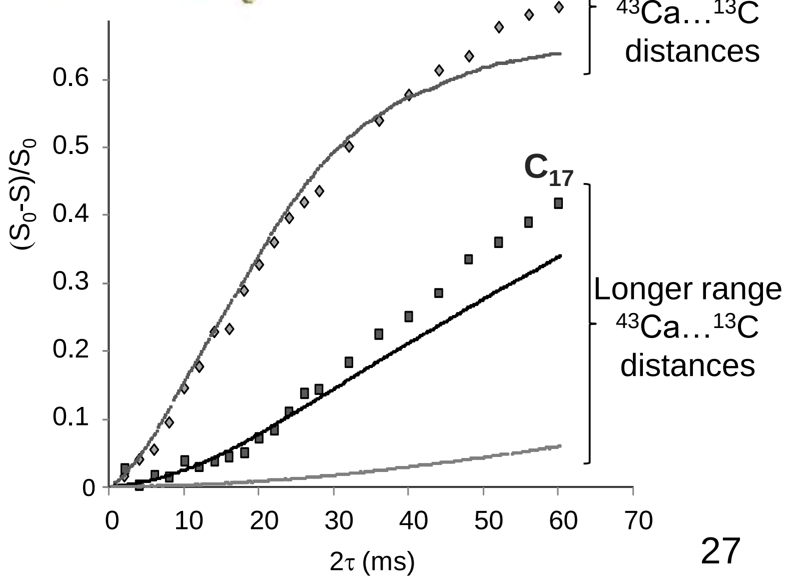
TRANsfer of Population in DOuble Resonance



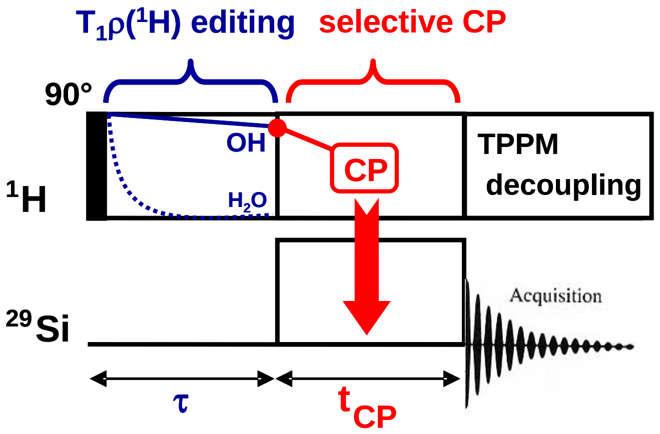


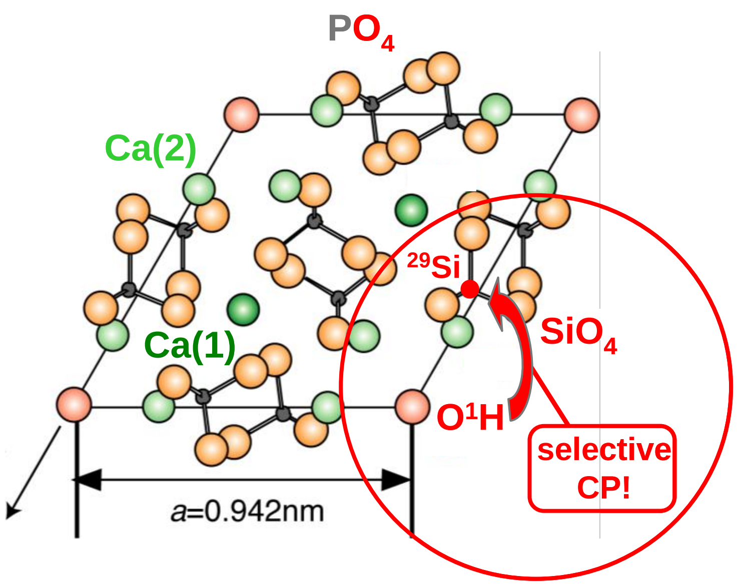


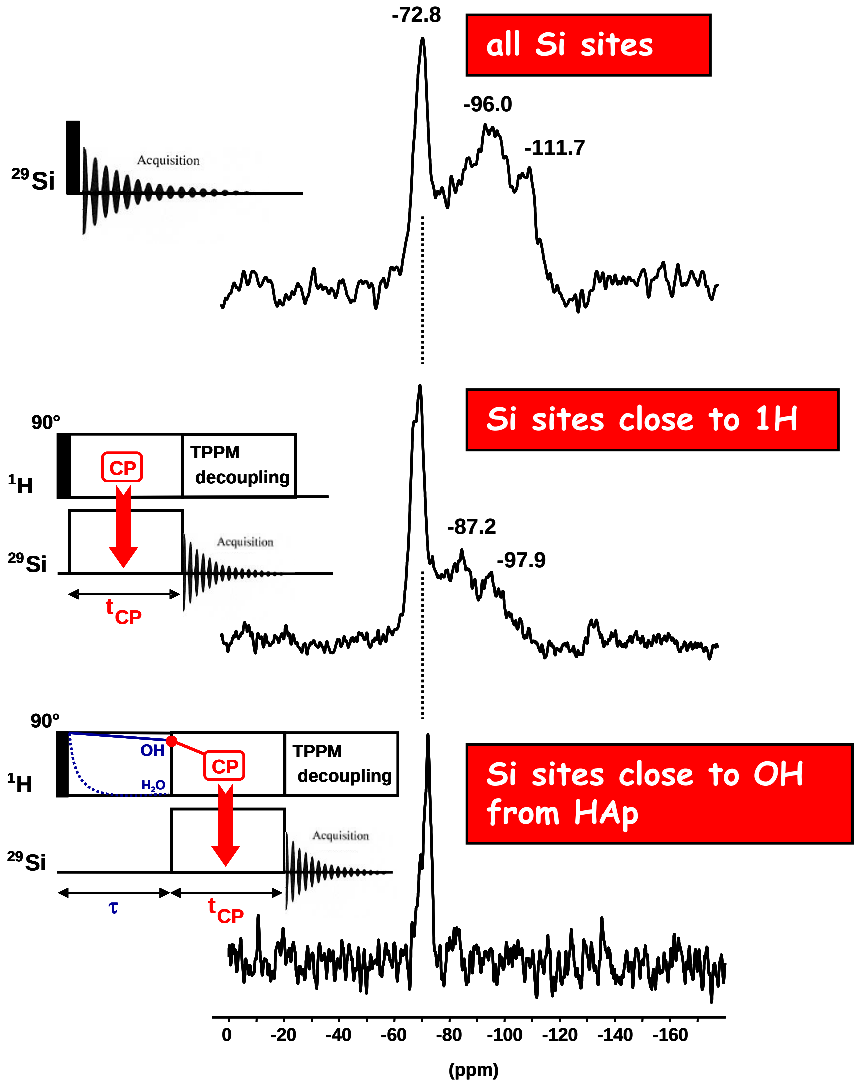




Silicate substituted HAp



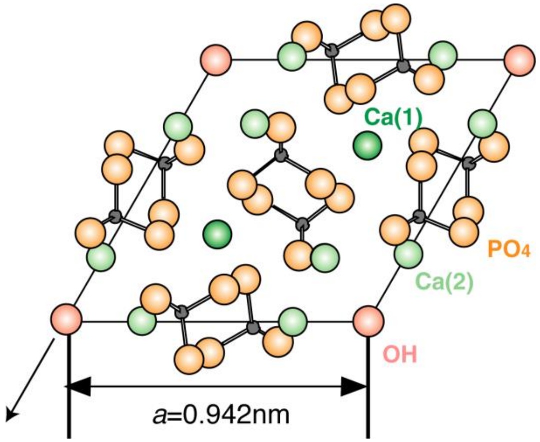




Gasquères et al., Magn. Reson. Chem., 46 (2008) 342

Si: 4.6 wt %

Substituted HAp structures

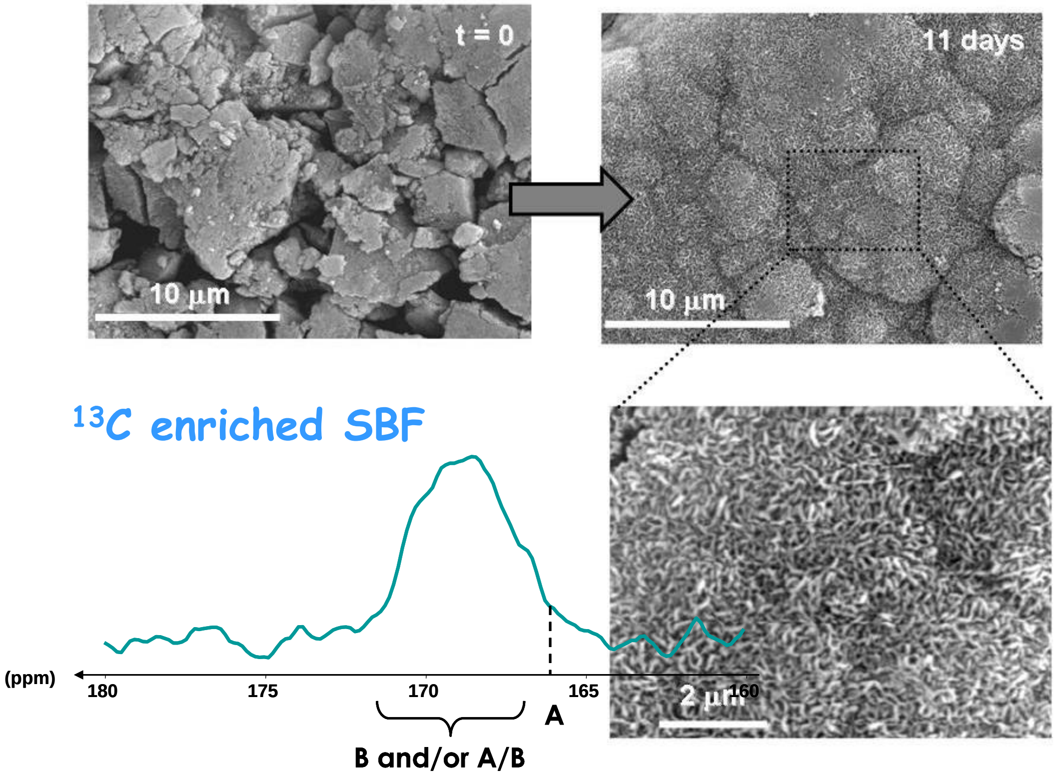


$Ca_{10}(PO_4)_6(OH)_2$

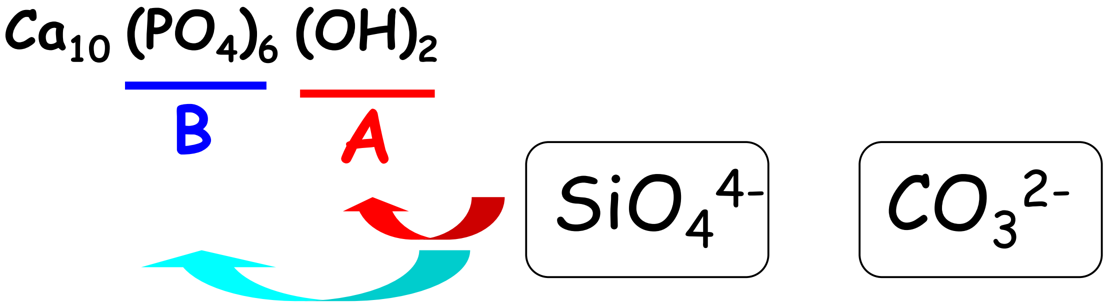
Mg^{2+}, Zn^{2+}, Na^{+}, K^{+} ...

SO_4^{2-}, CO_3^{2-}...

CO_3^{2-}, F^{-}, Cl^{-}...



^{13}C enriched SBF



$Ca_{10}(PO_4)_6(OH)_2$

B

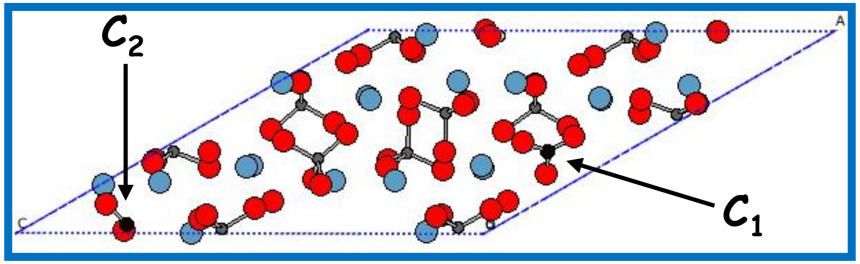
A

SiO_4^{4-}

CO_3^{2-}

F. Pourpoint, A. Salinas

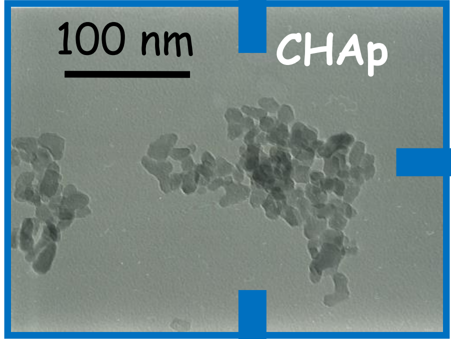
Models, 2D NMR, *ab initio* calculations: a combined approach

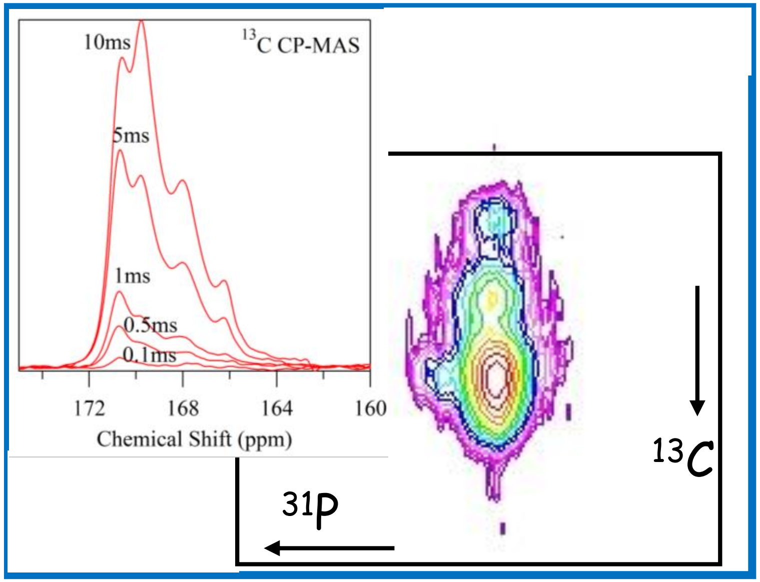


Astala et al., Chem. Mater. 2005

Peroos et al., Biomat. 2006

- **Modelling**





- **1D, 2D NMR experiments**

	δ (ppm)		δ (ppm)		δ (ppm)
P1	2.1	P7	1.9	C1	166.7
P2	0.1	P8	2.1	C2	165.7
P3	2.1	P9	1.8	H1	1.1
P4	3.3	P10	4.0	H2	1.1
P5	1.1	P11	3.3	H3	-0.7
P6	1.5				

- **first principles calculations**

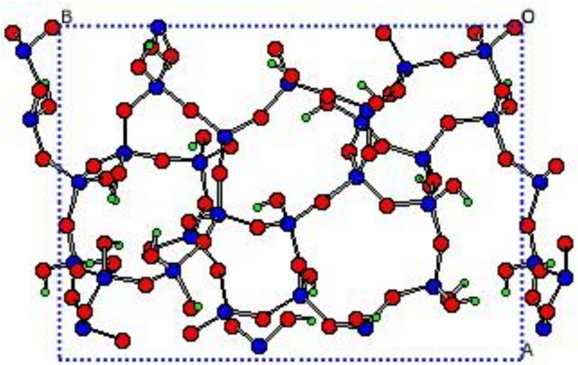
distribution of A-, B- and A/B sites...

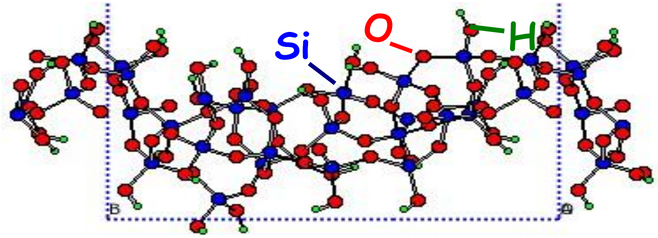
Hydroxylated silica surface: towards interfaces

VASP — ienna b-initio imulation ackage

amorphous slab

(~ 13Å × 18Å × 10Å)

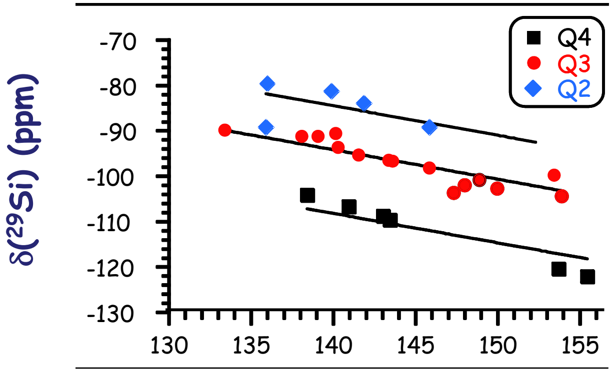




- ~ 6 OH/nm^2
- ~ 30% of geminal silanols
- ~ 40% involved in H-bonds

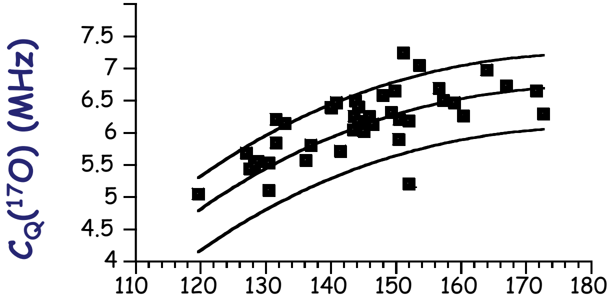
F. Tielens, C. Gervais et al., *Chem. Mater.* 20 (2008) 3336.

GIPAW calculations



^{29}Si NMR

Si-O-Si angle (°)

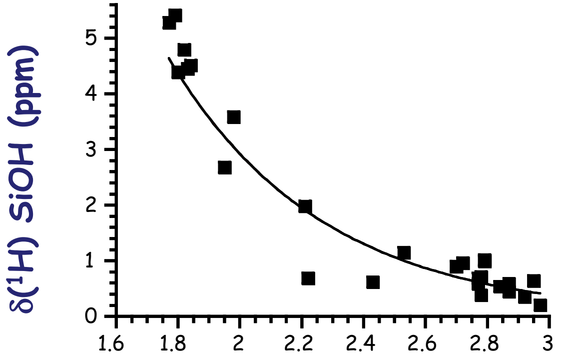


^{17}O NMR

Si-O-Si angle (°)

Clark et al., Solid State NMR 16 (2000) 55.

$C_Q = a\,(0.5 + \cos\alpha/(\cos\alpha-1))^b + m(d-d^0)$



^{1}H NMR

O<u>H</u> … <u>O</u> (Å)

Topics

Solid state
NMR basics

Applications

Sensitivity

- the key question
- the future!

Increasing the sensitivity in solid state NMR

"… the sensitivity of conventional NMR techniques is fundamentally limited by the ordinarily low spin polarization achievable in even the strongest NMR magnets…" in:
B. M. Goodson, *J. Magn. Reson.* 155 (2002) 157.

preparation

- optically pumped ^{129}Xe
- Dynamic Nuclear Polarization (DNP)

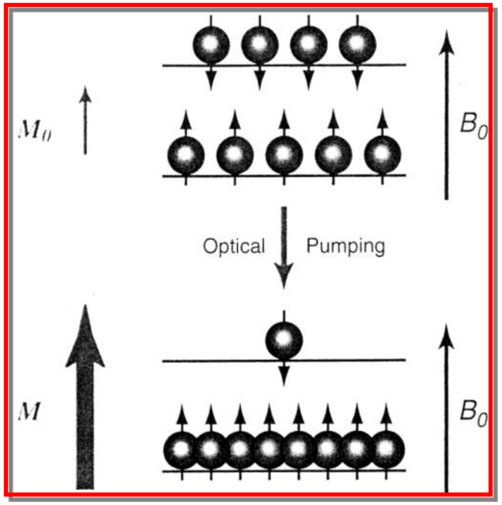
NMR equipment

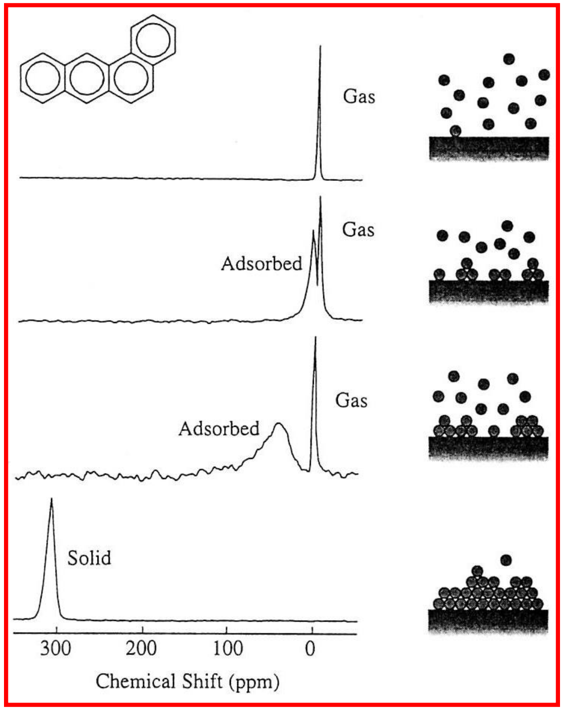
- microcoils
- Magic Angle Coil Spinning (MACS)

time domain NMR signal

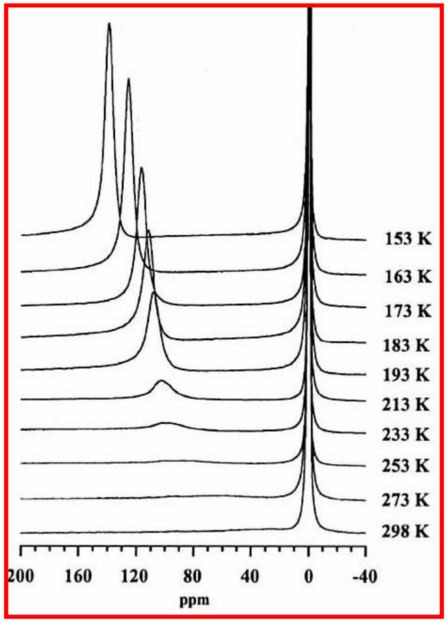
- Singular Value Decomposition (SVD)
- Harmonic Inversion
- Denoising

Surfaces and interfaces seen by hyperpolarized ^{129}Xe

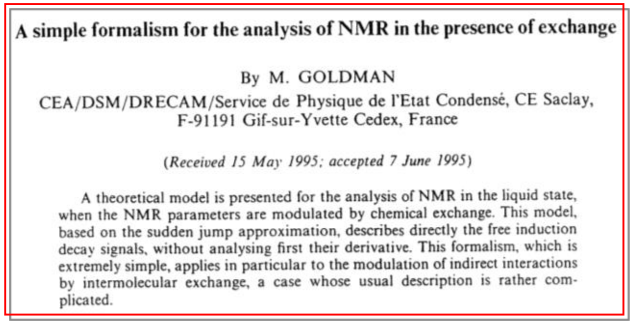




Raftery, Pines (1991)



Nossov (2002)



A simple formalism for the analysis of NMR in the presence of exchange

By M. GOLDMAN

CEA/DSM/DRECAM/Service de Physique de l'Etat Condensé, CE Saclay,
F-91191 Gif-sur-Yvette Cedex, France

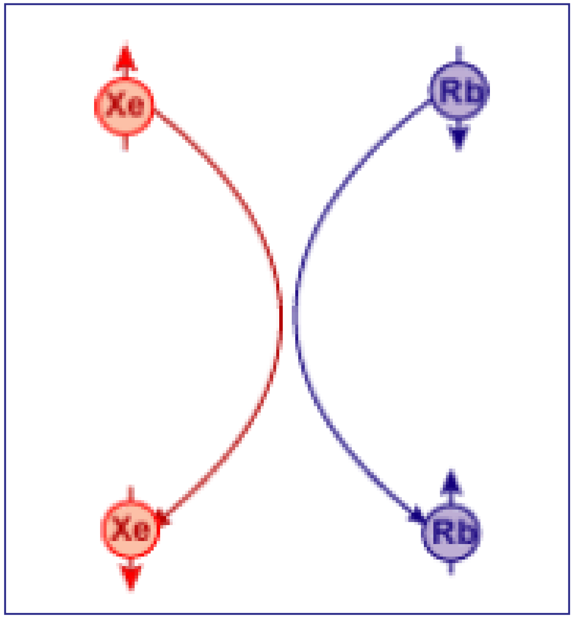
(*Received 15 May 1995; accepted 7 June 1995*)

A theoretical model is presented for the analysis of NMR in the liquid state, when the NMR parameters are modulated by chemical exchange. This model, based on the sudden jump approximation, describes directly the free induction decay signals, without analysing first their derivative. This formalism, which is extremely simple, applies in particular to the modulation of indirect interactions by intermolecular exchange, a case whose usual description is rather complicated.

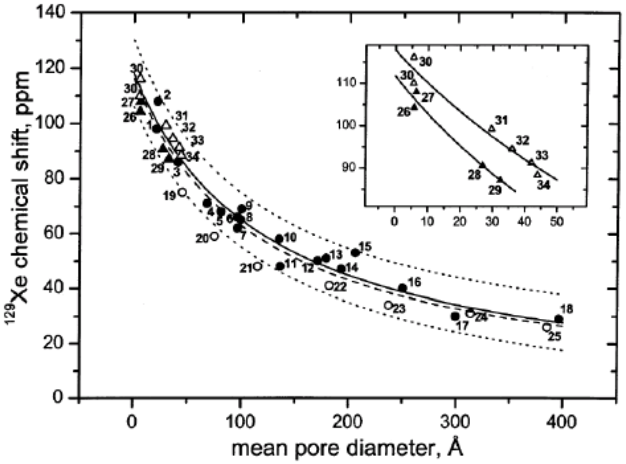
Goldman (1995)

Probing surfaces with ^{129}Xe NMR

- xenon: inert gas
- possible isotope: ^{129}Xe (spin ½, 26.4%)
- possibility to enhance its magnetization through optical pumping up to 25 000 times!!



δ(^{129}Xe) in various mesoporous silica



● Gels de silice ; ○Vycor/CPG ;▲ Organo-silicates

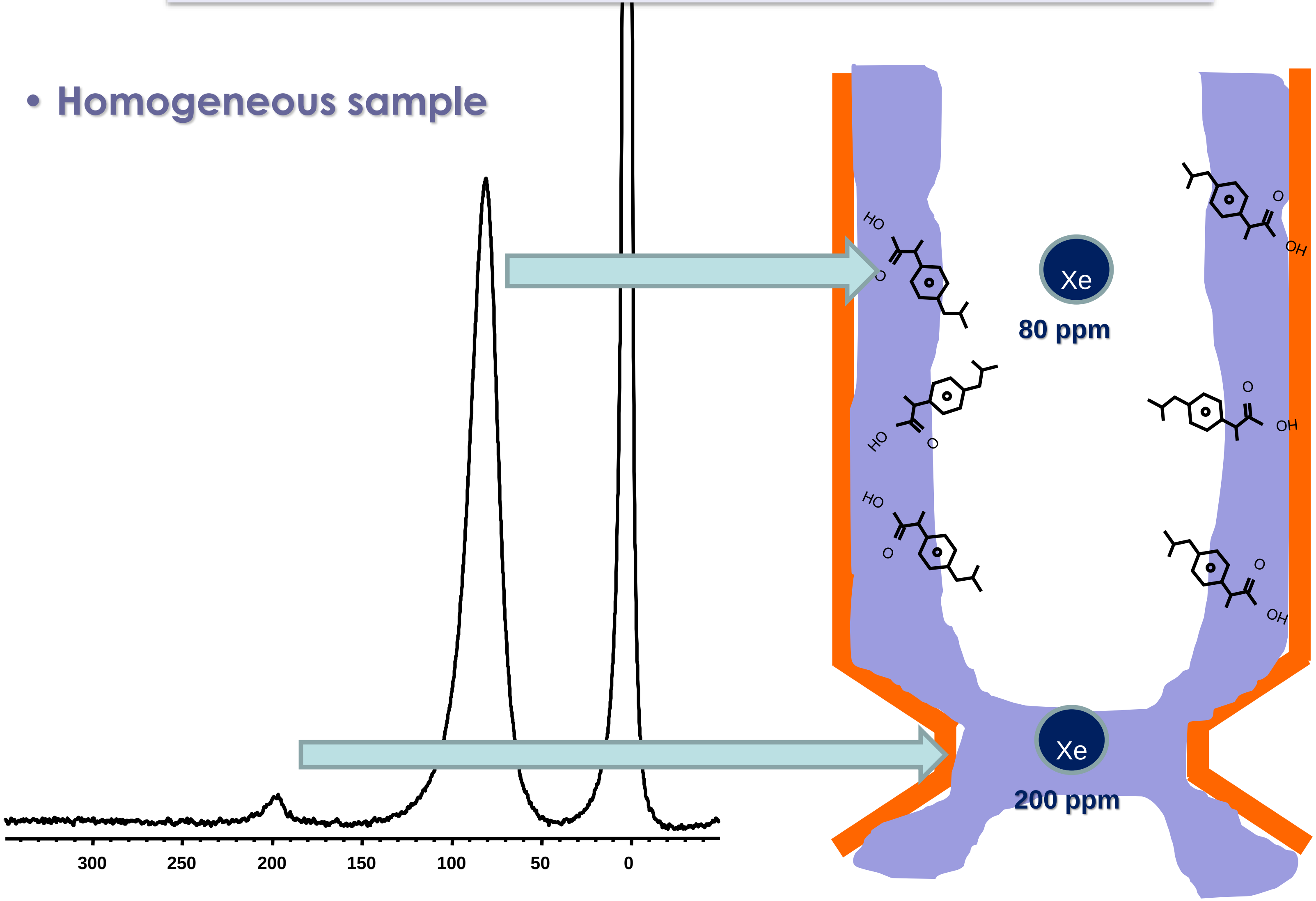
Terskikh et al., Langmuir 18 (2002) 5653

- δ(^{129}Xe) related to Ø

courtesy of Dr. T. Azaïs, LCMCP

Ibuprofen loaded MCM-41 100Å

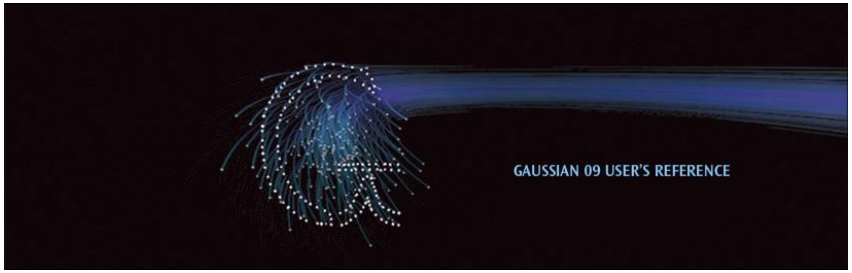
- **Homogeneous sample**



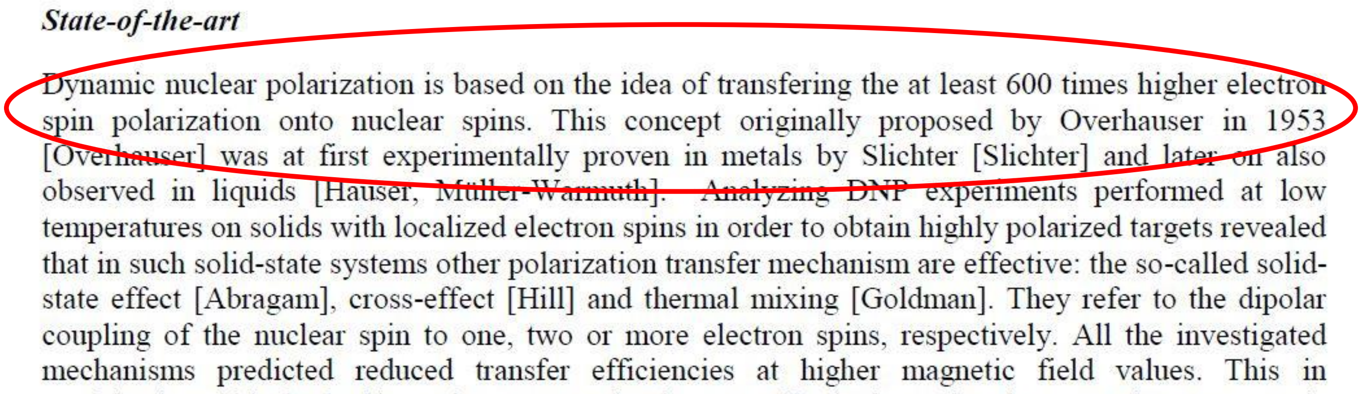
courtesy of Dr. T. Azaïs, LCMCP

To be done ...

- prediction/calculation of ^{129}Xe NMR shifts
- from a fundamental QM point of view: “dispersion forces” and DFT ?
- Hartree-Fock and post HF methods + GAUSSIAN -> chemical shifts
- a periodic approach by VASP ? GIPAW calculations ?
- what about the Xe (and other noble gases ...) pseudopotential ?
- another approach: ^{131}Xe (I = 3/2) -> calculation of EFG by Wien2k
- DYNAMICS ?



Dynamic Nuclear Polarization (DNP)



State-of-the-art

Dynamic nuclear polarization is based on the idea of transfering the at least 600 times higher electron spin polarization onto nuclear spins. This concept originally proposed by Overhauser in 1953 [Overhauser] was at first experimentally proven in metals by Slichter [Slichter] and later on also observed in liquids [Hauser, Müller-Warmuth]. Analyzing DNP experiments performed at low temperatures on solids with localized electron spins in order to obtain highly polarized targets revealed that in such solid-state systems other polarization transfer mechanism are effective: the so-called solid-state effect [Abragam], cross-effect [Hill] and thermal mixing [Goldman]. They refer to the dipolar coupling of the nuclear spin to one, two or more electron spins, respectively. All the investigated mechanisms predicted reduced transfer efficiencies at higher magnetic field values. This in combination with the lacking microwave technology to effectievly excite e

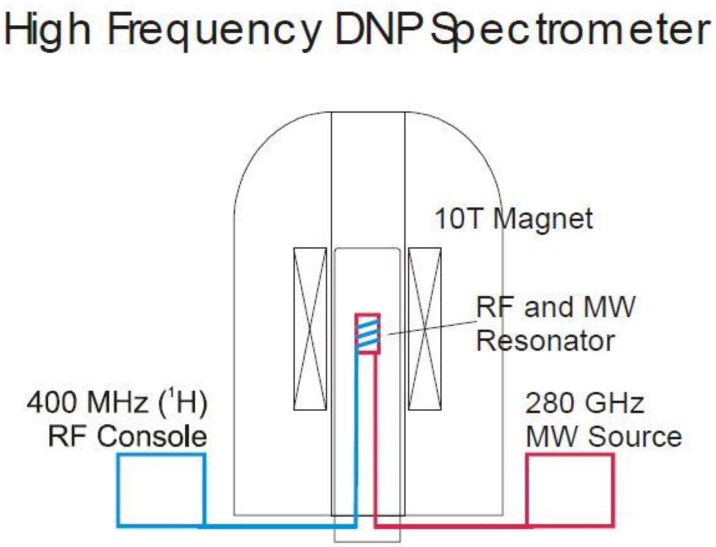
field values above 1 T turned DNP into an 'endangered species' while N

towards higher spectral resolution and higher magnetic fields [Wind, Yannon

20 years until breakthroughs of DNP at high magnetic fields were achievec

SS-MAS-DNP for structural biology applications [Griffin] and later on the A

the possibility to employ such polarized samples at very low temperatures foi



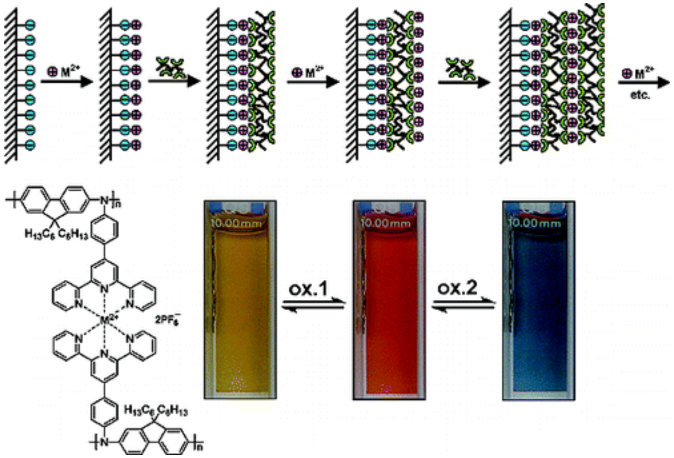
see for instance:

http://www.postgenomicnmr.net/NMRLife/docs/DynamicNuclearPolarization.pdf

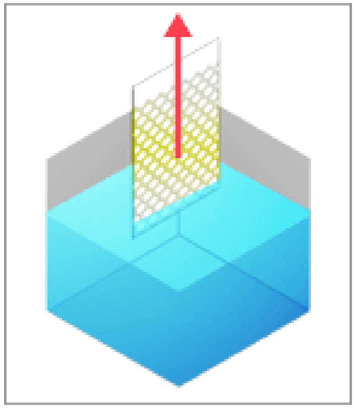
a revival:

- combination with MAS at low T -> Griffin's group (at MIT)
- applications to biosolids, inorganic materials, surfaces and grafted species ...

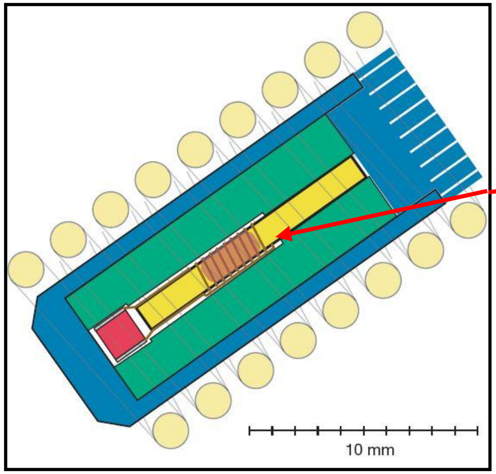
Towards μg experiments: MACS NMR



Maier et al., Chem. Mater. 2009



Magic Angle Coil Spinning



rotor at θ_m

μ-coil

static coil

D. Sakellariou *et al.*, *Nature*, 447, 2007.

P. Aguiar *et al.*, *J. Magn. Reson.*, 200, 2009

potential applications:

- **films**

S ~ 2 cm^2

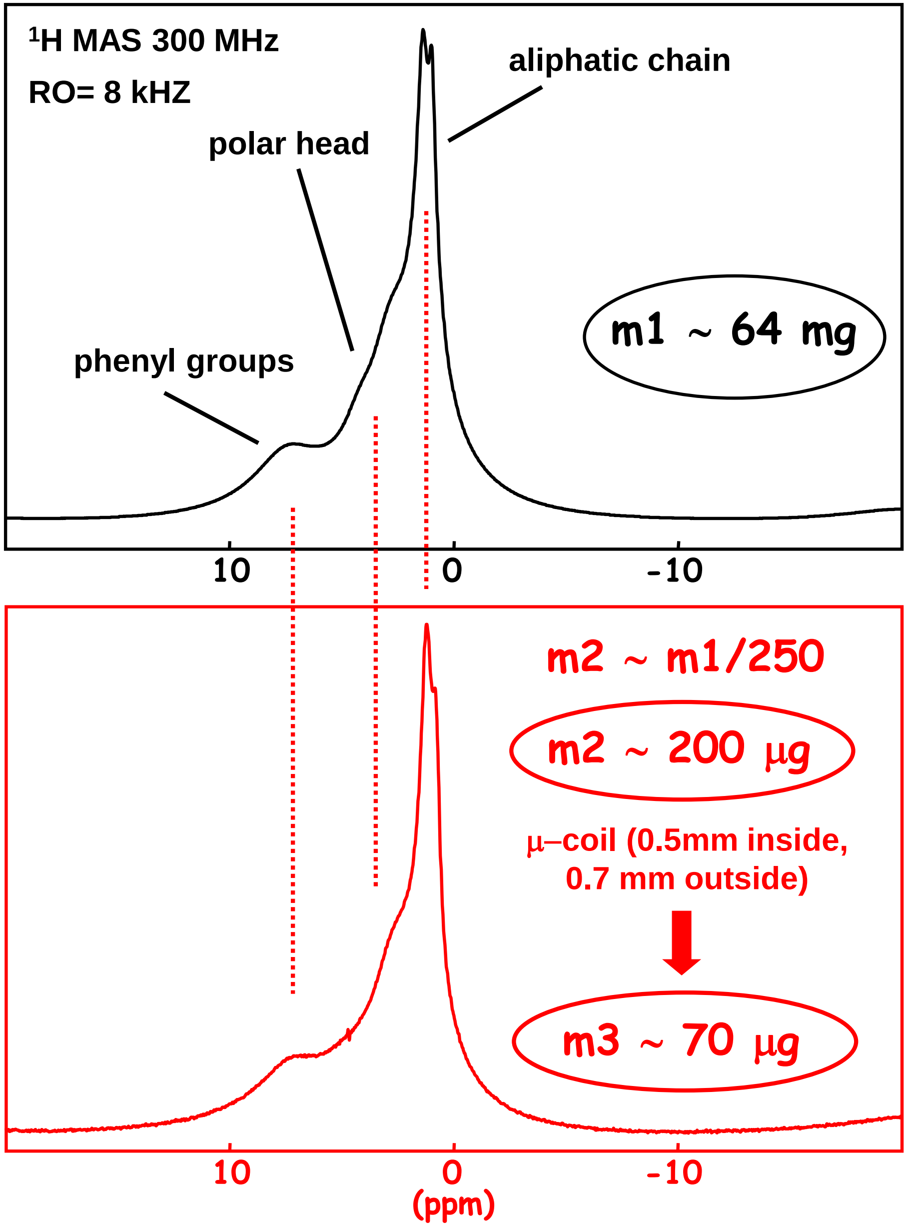
Th ~ 300 nm

m ~ 100 μg

^{1}H (but also ^{29}Si, ^{13}C …)

^{1}H MACS: mesoporous powder (CTAB / TEOS / PhSi(OEt)$_3$)

with P. Aguiar, D. Sakellariou - CEA - Saclay, France



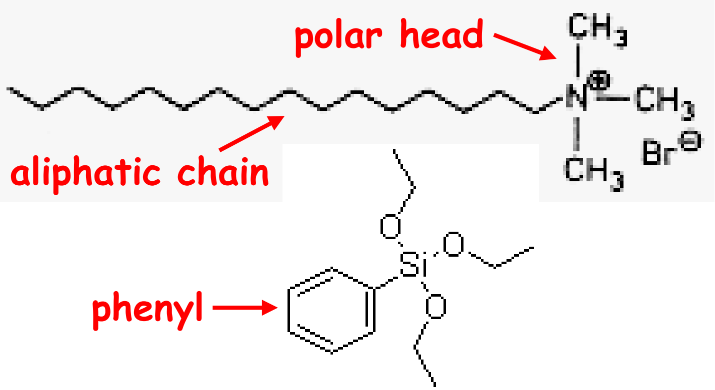
m1 ~ 64 mg

m2 ~ m1/250

m2 ~ 200 µg

µ–coil (0.5mm inside, 0.7 mm outside)

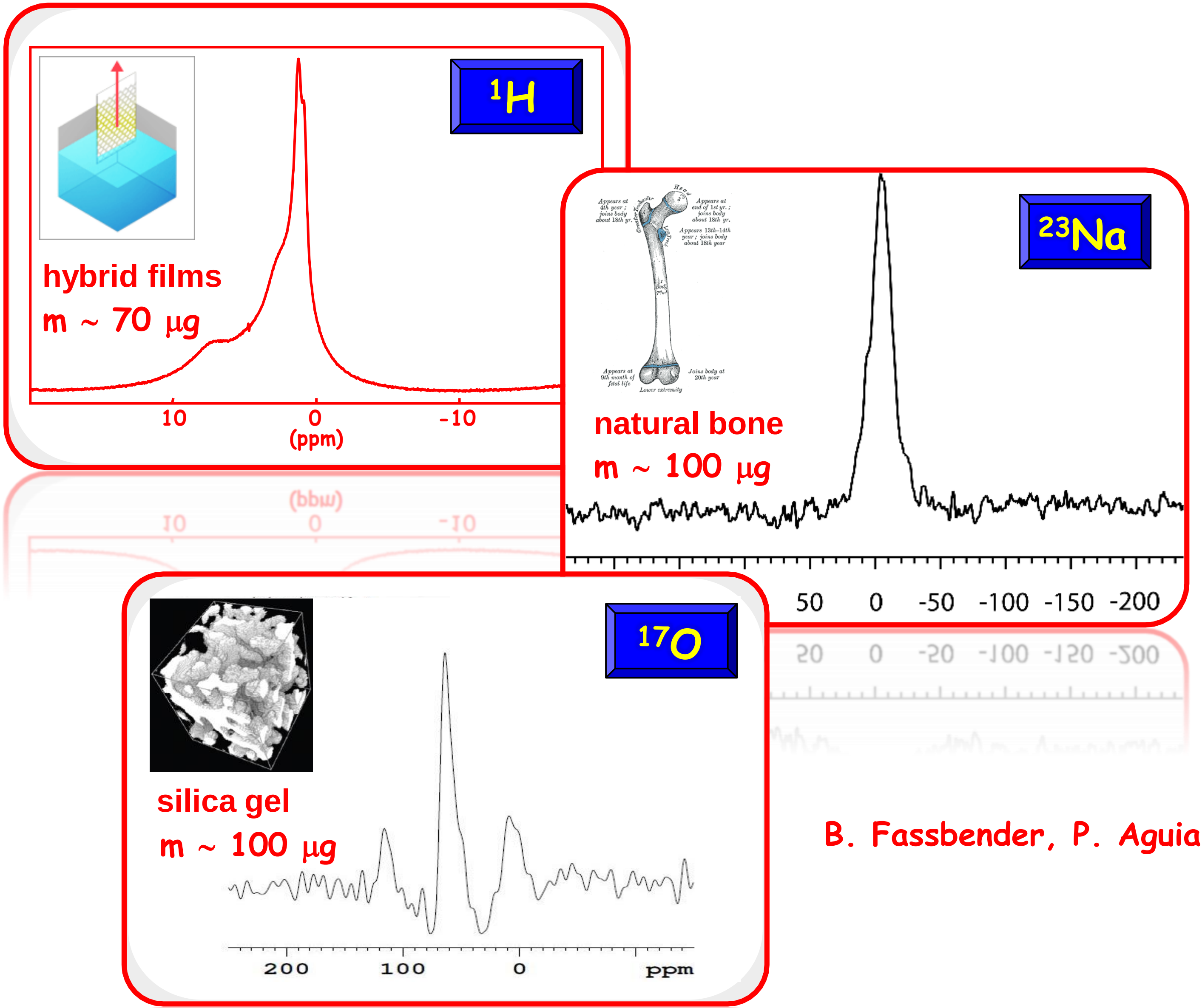
m3 ~ 70 µg



- ^{31}P in small biological samples, *i.e.* Randall plaque
- expensive isotopes: ^{29}Si, ^{43}Ca, ^{25}Mg …

3.2mm (24 kHz)

Magic Angle Coil Spinning

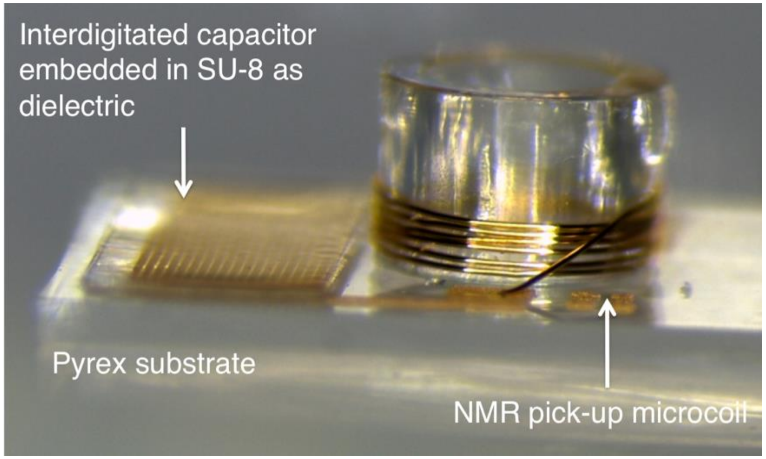


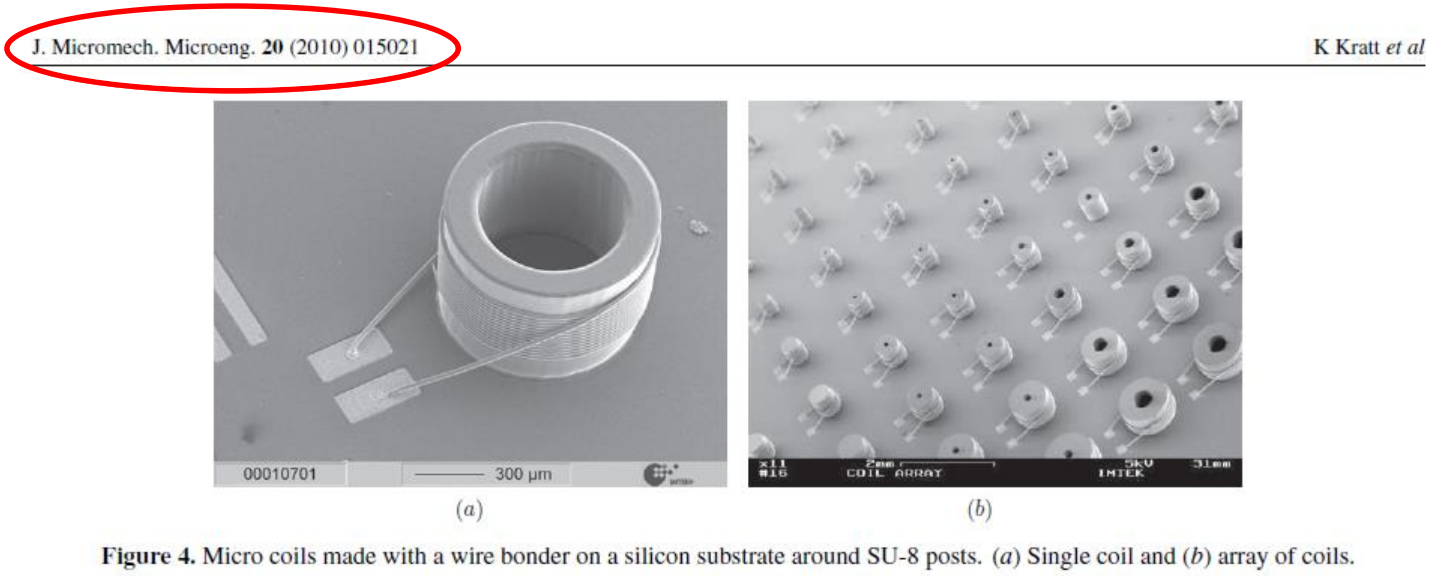
B. Fassbender, P. Aguiar, UPMC-CEA

MEMS approach

machine made micro-coils with reproducible enhancement factor (collaboration with Freiburg*, IMTEK, V. Badilita and CEA, D. Sakellariou)

MEMS compatible techniques

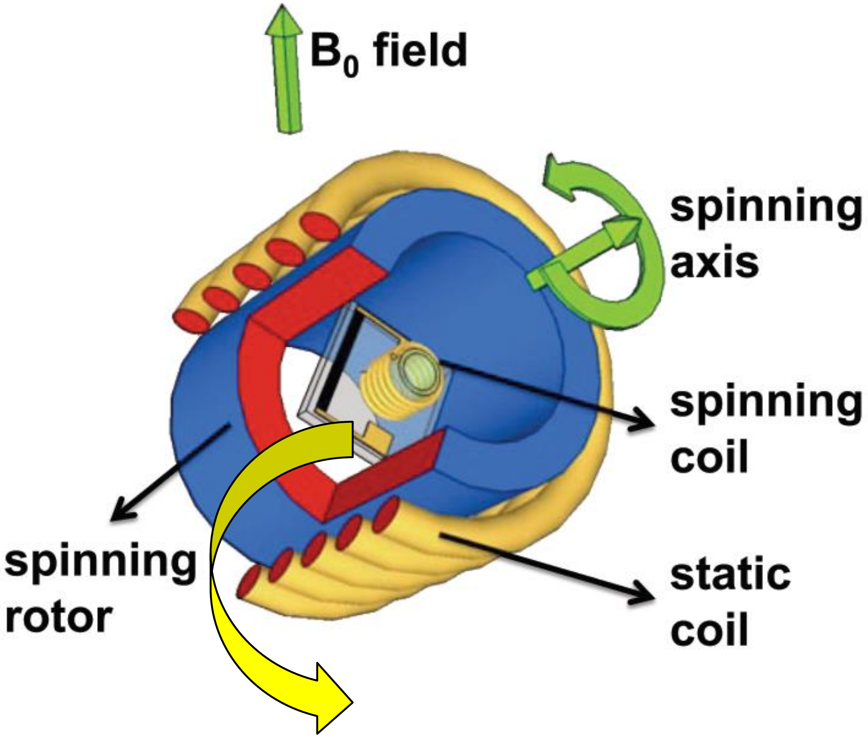


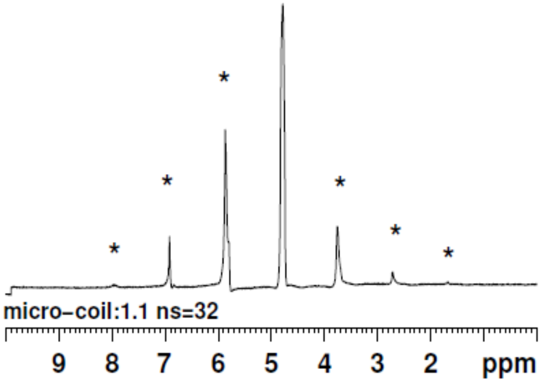

J. Micromech. Microeng. **20** (2010) 015021 K Kratt *et al*

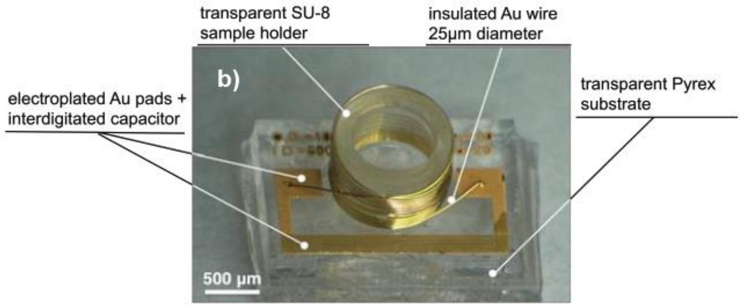
(*a*) (*b*)

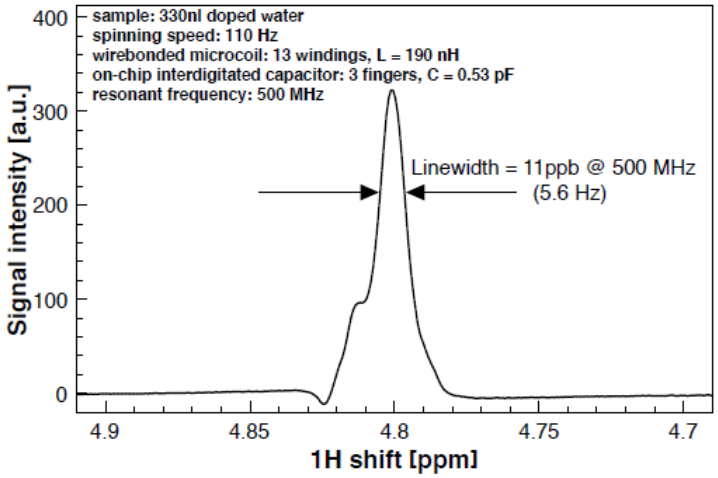
Figure 4. Micro coils made with a wire bonder on a silicon substrate around SU-8 posts. (*a*) Single coil and (*b*) array of coils.

First results at 700 MHz (^{1}H)





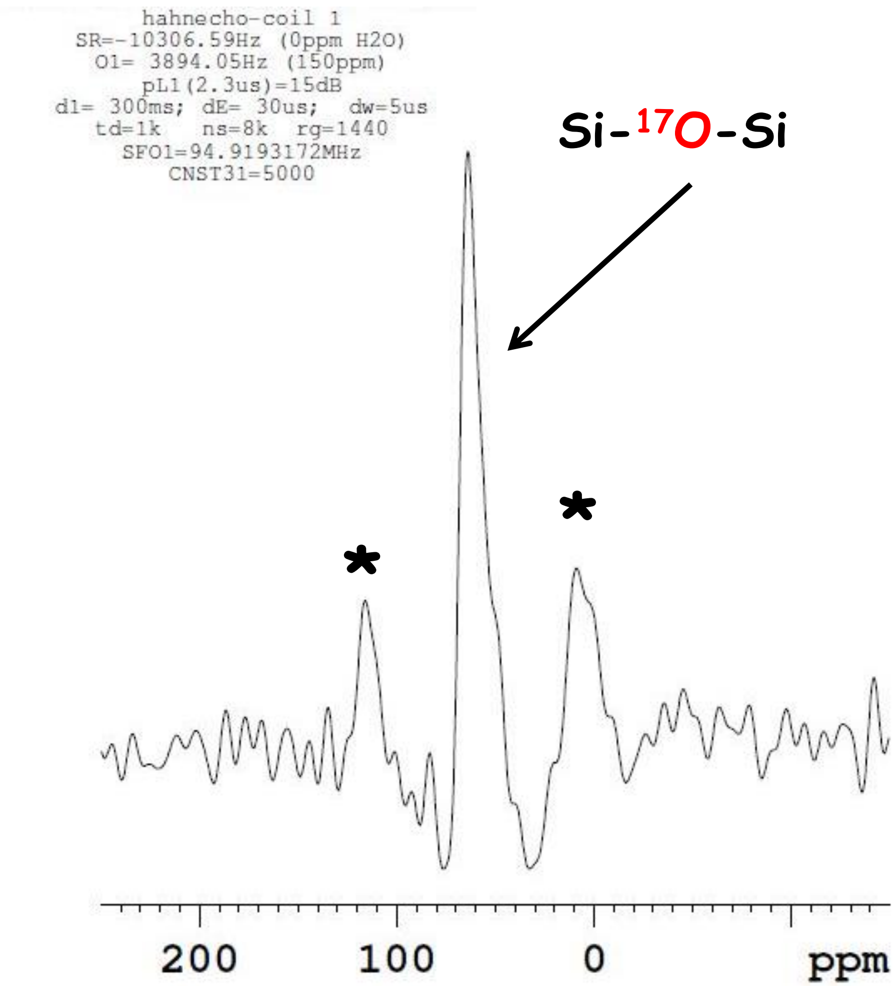




V. Badilita, D. Sakallariou, C. Bonhomme *et al., Lab. Chip* **2011**, submitted

The first ^{17}O MACS experiments – silicate hybrid gels

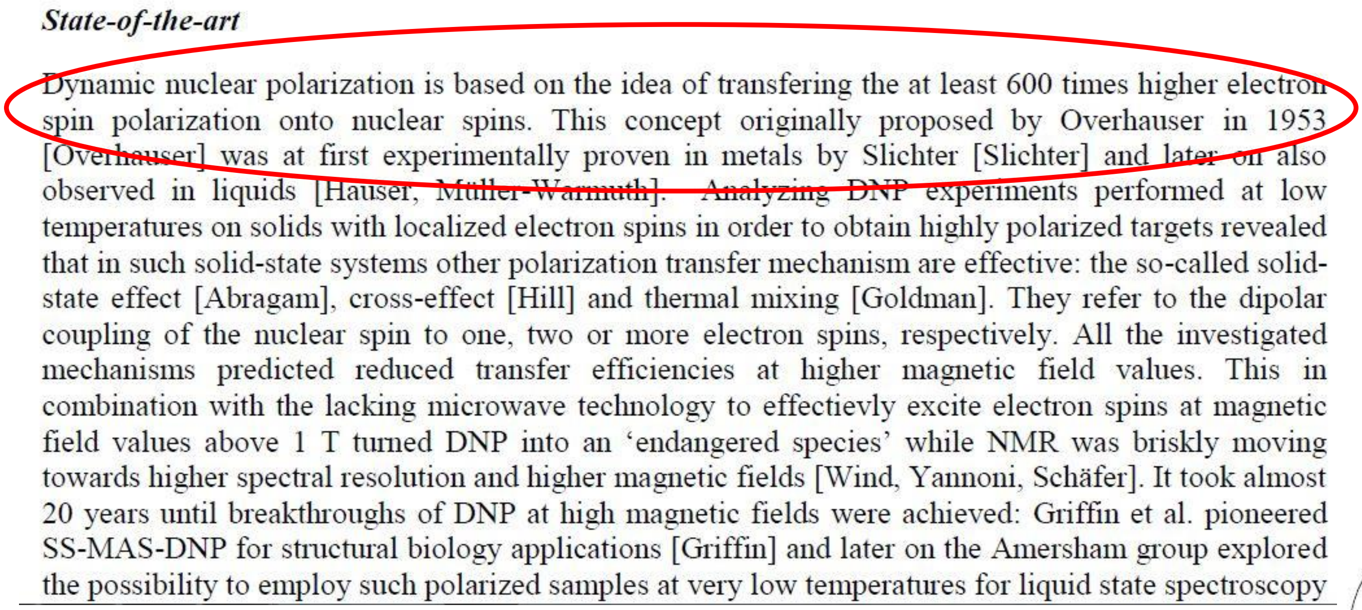
Micro-coil
16.3 T
5 kHz MAS
< 0.200 mg
40 min.



Birgit Fassbender

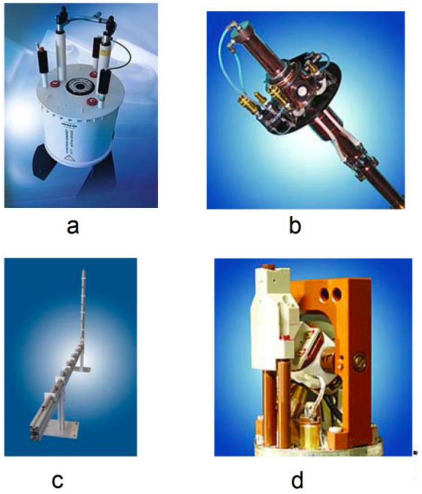
(LCMCP + CEA, CNano'IDF grant)

Dynamic Nuclear Polarization (DNP)

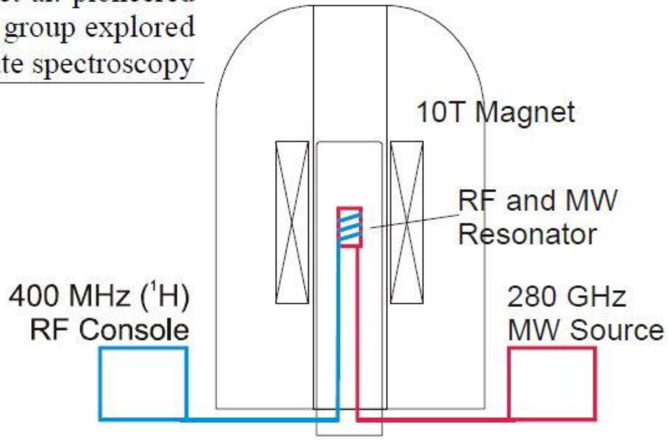


State-of-the-art

Dynamic nuclear polarization is based on the idea of transfering the at least 600 times higher electron spin polarization onto nuclear spins. This concept originally proposed by Overhauser in 1953 [Overhauser] was at first experimentally proven in metals by Slichter [Slichter] and later on also observed in liquids [Hauser, Müller-Warmuth]. Analyzing DNP experiments performed at low temperatures on solids with localized electron spins in order to obtain highly polarized targets revealed that in such solid-state systems other polarization transfer mechanism are effective: the so-called solid-state effect [Abragam], cross-effect [Hill] and thermal mixing [Goldman]. They refer to the dipolar coupling of the nuclear spin to one, two or more electron spins, respectively. All the investigated mechanisms predicted reduced transfer efficiencies at higher magnetic field values. This in combination with the lacking microwave technology to effectievly excite electron spins at magnetic field values above 1 T turned DNP into an 'endangered species' while NMR was briskly moving towards higher spectral resolution and higher magnetic fields [Wind, Yannoni, Schäfer]. It took almost 20 years until breakthroughs of DNP at high magnetic fields were achieved: Griffin et al. pioneered SS-MAS-DNP for structural biology applications [Griffin] and later on the Amersham group explored the possibility to employ such polarized samples at very low temperatures for liquid state spectroscopy



http://www.postgenomicnmr.net/NMRLife/docs/DynamicNuclearPolarization.pdf

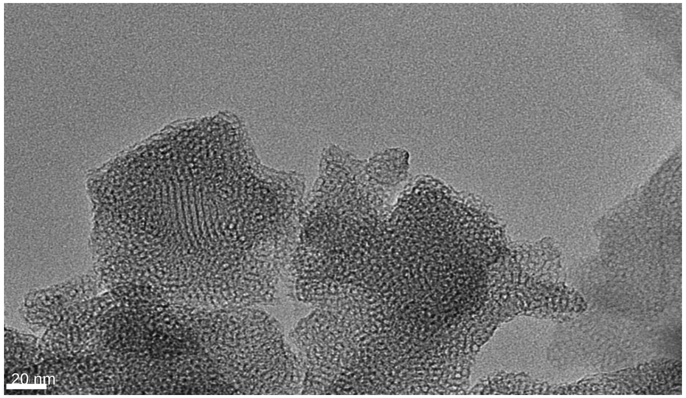


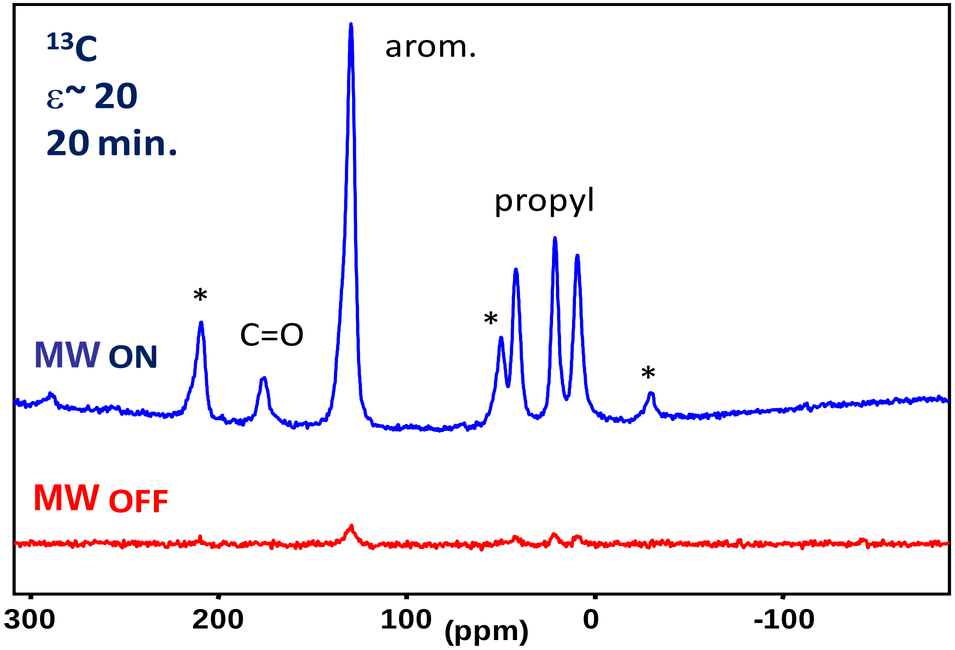
renewal:

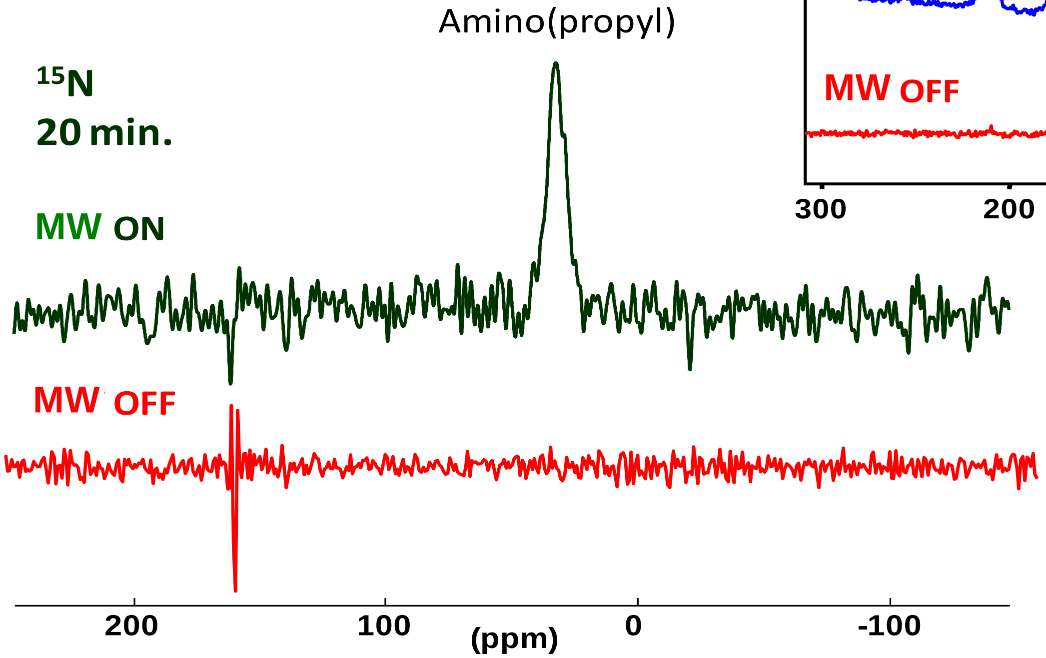
- high field, low T (90 K) MAS (10 kHz)
- applications : biosolids (B. Griffin, MIT), materials (Emsley, Bodenhausen)

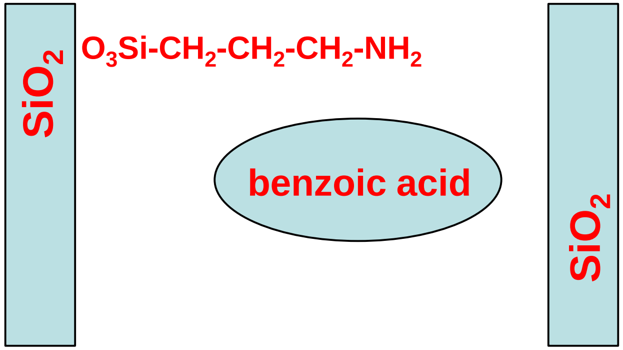
Application to functionnalized MCM-41 structures

Coll.: M. Caporini, G. Bodenhausen, EPFL, Lausanne

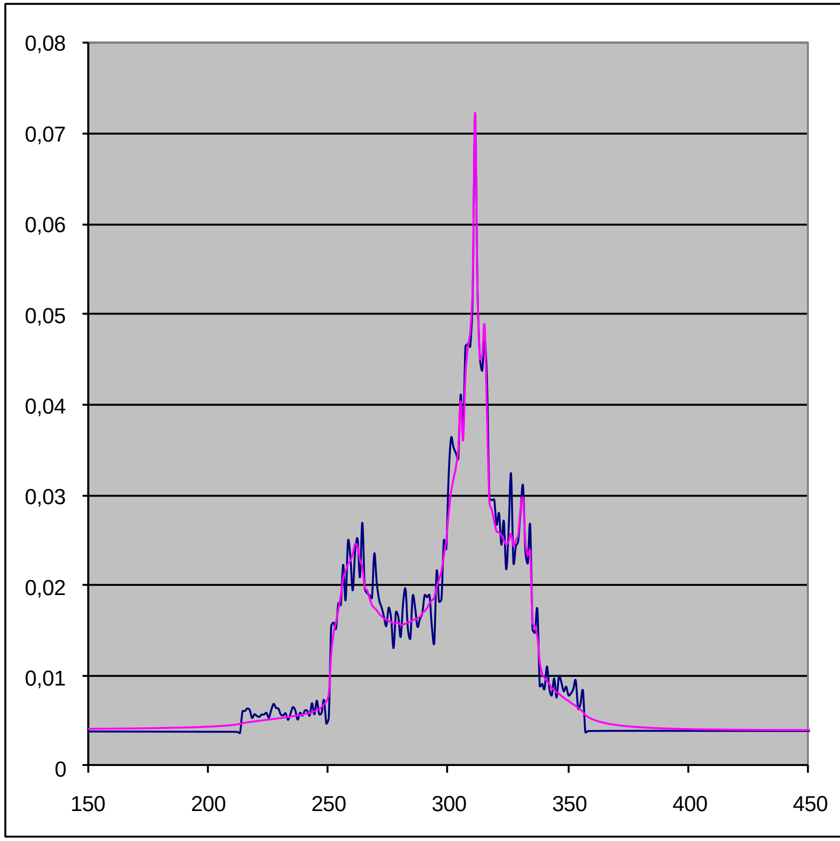


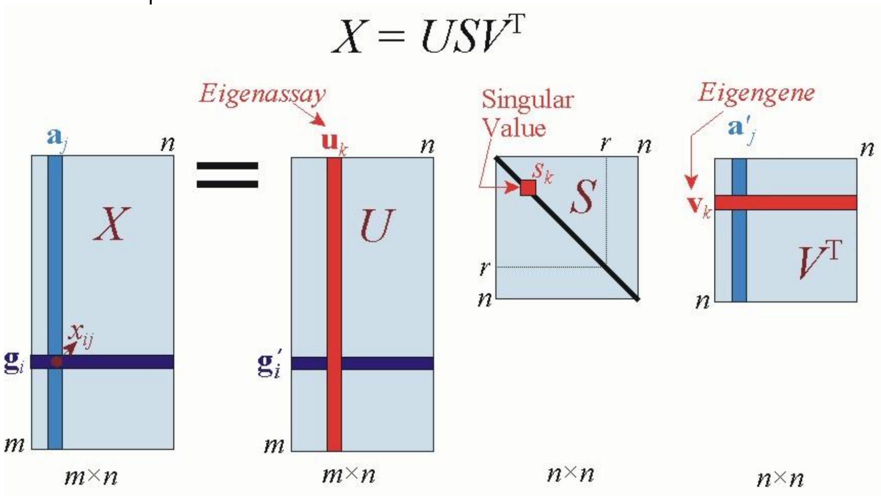


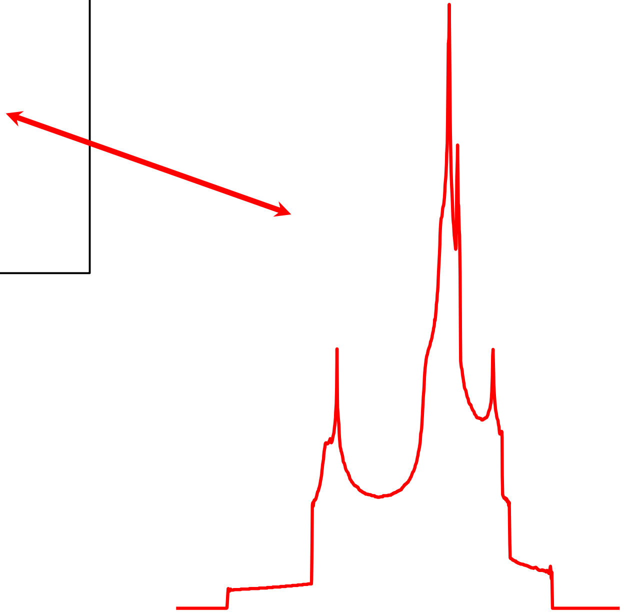




Denoising of the FID: post processing of the data







- **FID as a complex Hankel matrix**
- **Singular Value Decomposition**
- **Cadzow denoising**

Coll.: Pascal Man (UPMC)

Résonance Magnétique Nucléaire multidimensionnelle et multinucléaire en solution

Certaines illustrations sont extraites de :

Hore, Nuclear Magnetic Resonance, 1998.

Levitt, Spin dynamics, 2002.

Braun, 150 and more basic NMR experiments, 1998.

Derome, Modern NMR Techniques for Chemistry Research, 1991.

Christian BONHOMME, Professeur

Laboratoire de Chimie de la Matière Condensée

UMR CNRS 7574 – Sorbonne Université, Paris

Rappels

toutes les interactions sont moyennées à leur valeur isotrope...

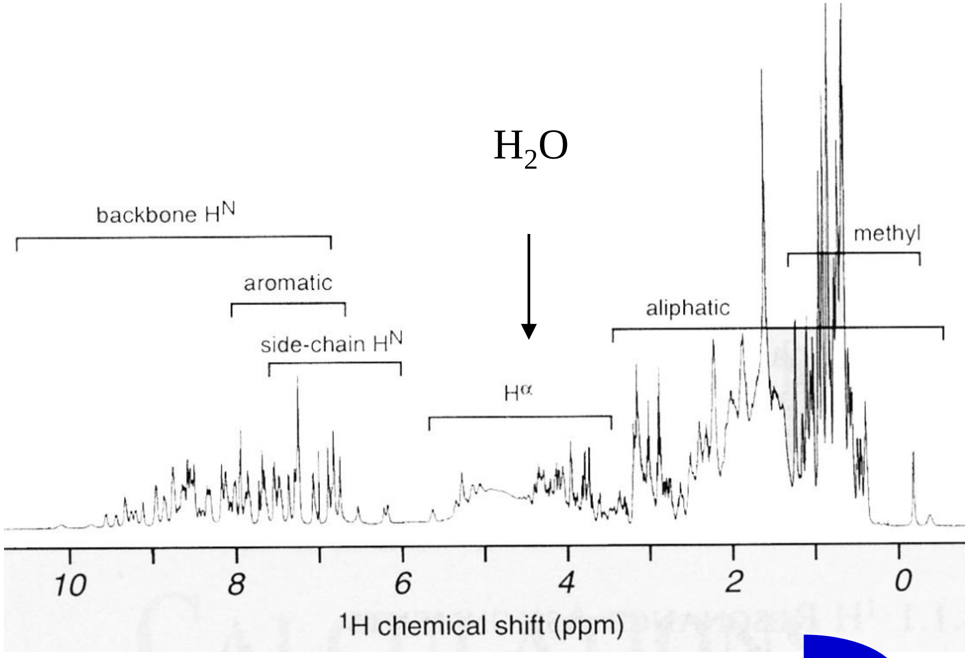
$\mathrm{Tr}(CS) \neq 0$

$\mathrm{Tr}(J) \neq 0$

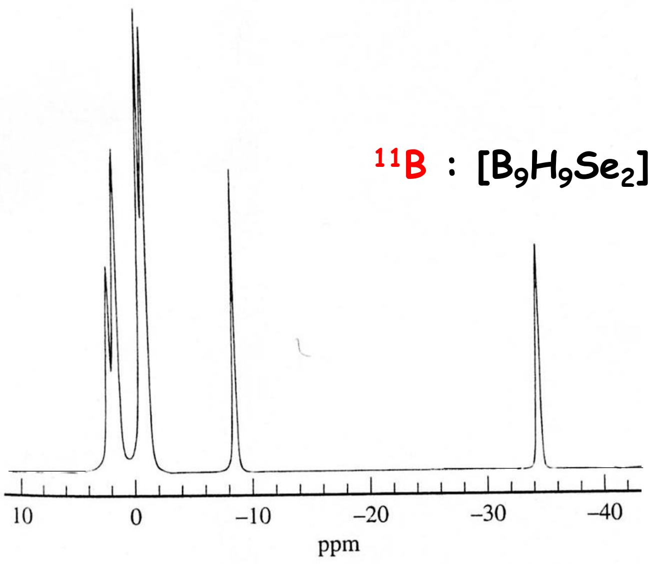
$\mathrm{Tr}(D) = \mathrm{Tr}(Q) = 0$

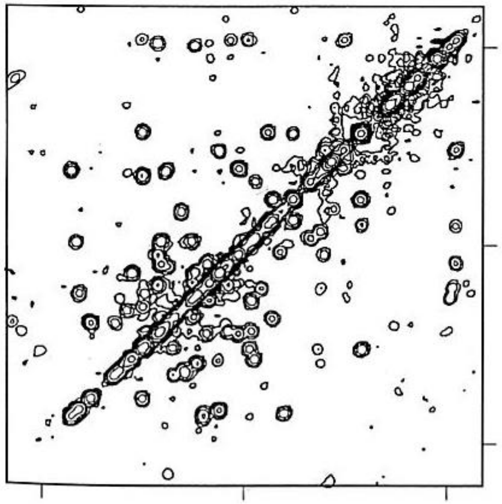
haute résolution

ex : RMN ^1H en solution ♦ peptides, protéines



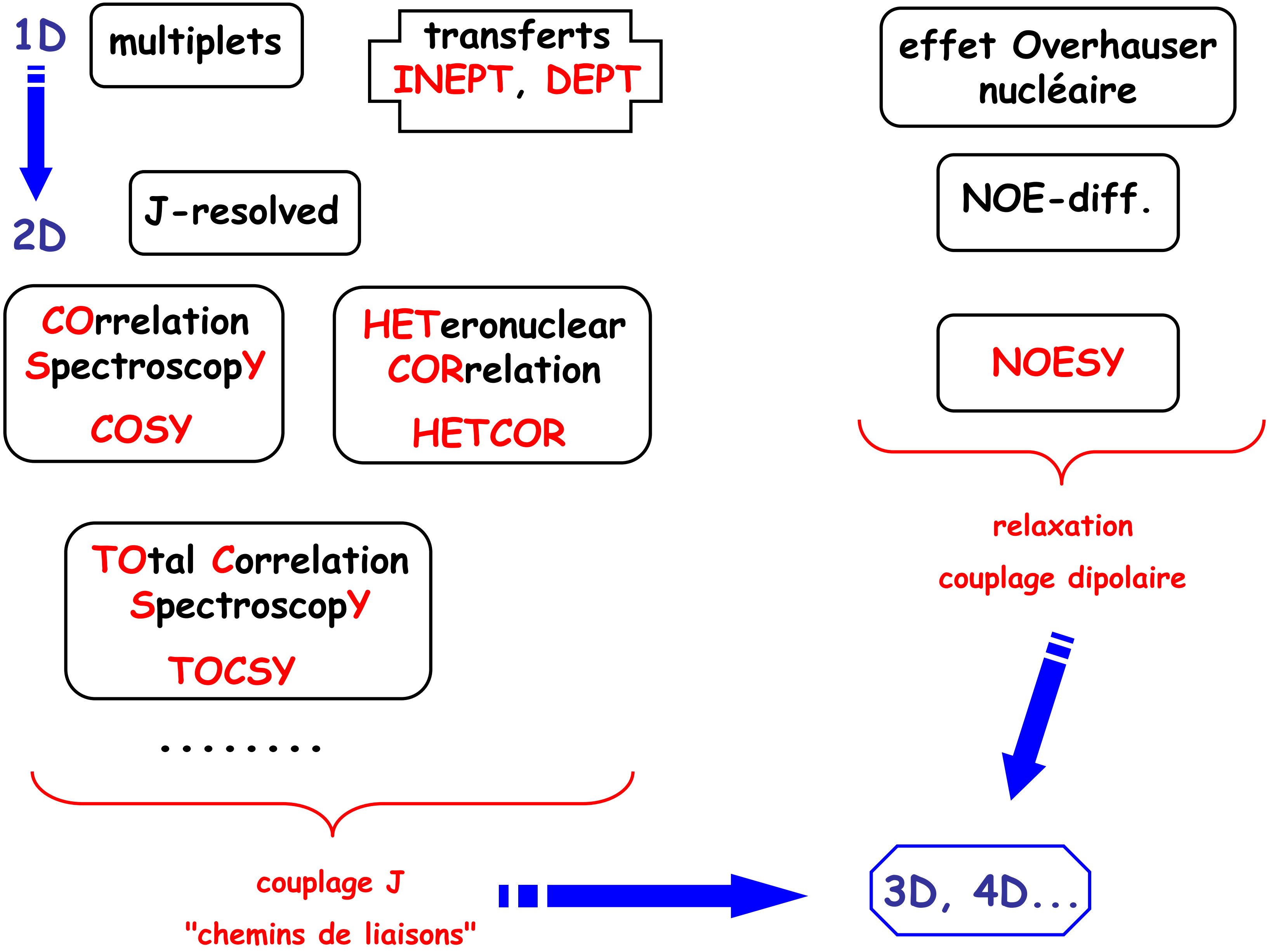
ex : RMN des noyaux quadripolaires





2D, 3D...

Déplacement chimique, couplage J - Relaxation



1D

2D

multiplets

transferts
INEPT, DEPT

J-resolved

COrrelation SpectroscopY
COSY

HETeronuclear CORrelation
HETCOR

TOtal Correlation SpectroscopY
TOCSY

. . . .

couplage J
"chemins de liaisons"

effet Overhauser nucléaire

NOE-diff.

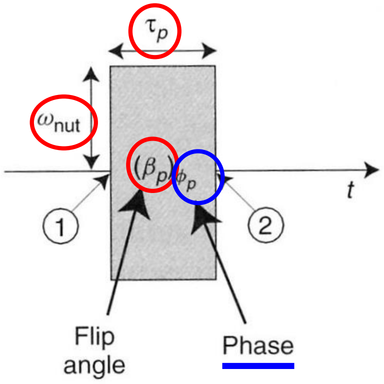
NOESY

relaxation
couplage dipolaire

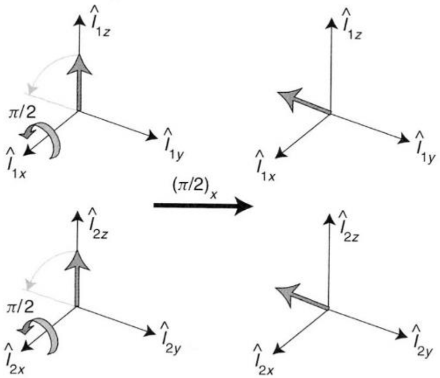
3D, 4D...

Approche quantique

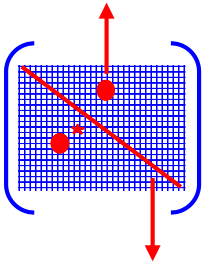
"action des impulsions ($\hat{I}_x$,$\hat{I}_y$) sur les opérateurs de spin" → **ROTATIONS**



β_p(rad.) $=\omega_{nut}.\tau_p=\gamma B_1.\tau_p$



$\rho(t)$ =



cohérence

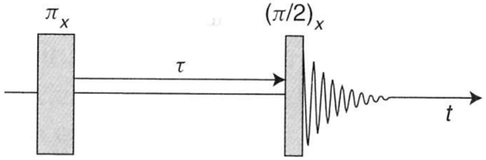
populations

ordre de cohérence :

<αβ> ↔ <ββ> : 1Q

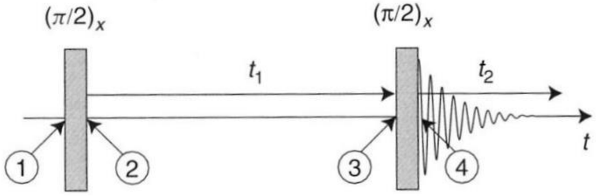
<αα> ↔ <ββ> : 2Q...

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

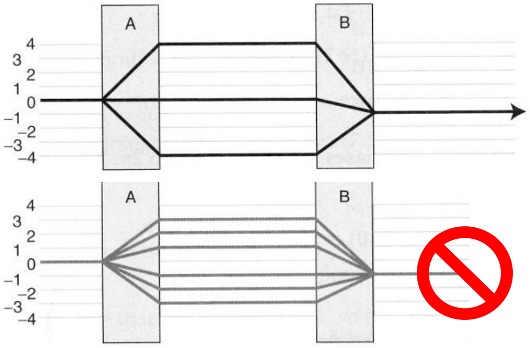


mesure de T_1

?



COSY



chemins de cohérence

impulsions

cyclage de phases

récepteur

Systèmes faiblement couplés : opérateurs produits (OP)

ex: système AX → 16 OP

construction

$$2\hat{I}_{1x}\hat{I}_{2z} = 2\,\frac{1}{2}\begin{pmatrix} 0 & 1 \\ 1 & 0 \end{pmatrix} \otimes \frac{1}{2}\begin{pmatrix} 1 & 0 \\ 0 & -1 \end{pmatrix}$$

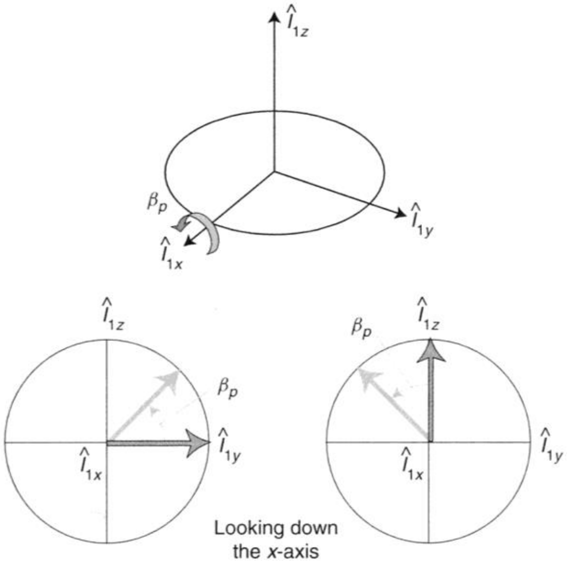
$$= \frac{1}{2}\begin{pmatrix} 0 & 1 \\ 1 & 0 \end{pmatrix} \otimes \begin{pmatrix} 1 & 0 \\ 0 & -1 \end{pmatrix}$$

$$= \frac{1}{2}\begin{pmatrix} 0\begin{pmatrix} 1 & 0 \\ 0 & -1 \end{pmatrix} & 1\begin{pmatrix} 1 & 0 \\ 0 & -1 \end{pmatrix} \\ 1\begin{pmatrix} 1 & 0 \\ 0 & -1 \end{pmatrix} & 0\begin{pmatrix} 1 & 0 \\ 0 & -1 \end{pmatrix} \end{pmatrix}$$

$$= \frac{1}{2}\begin{pmatrix} 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & -1 \\ 1 & 0 & 0 & 0 \\ 0 & -1 & 0 & 0 \end{pmatrix}$$

etc...

action des impulsions



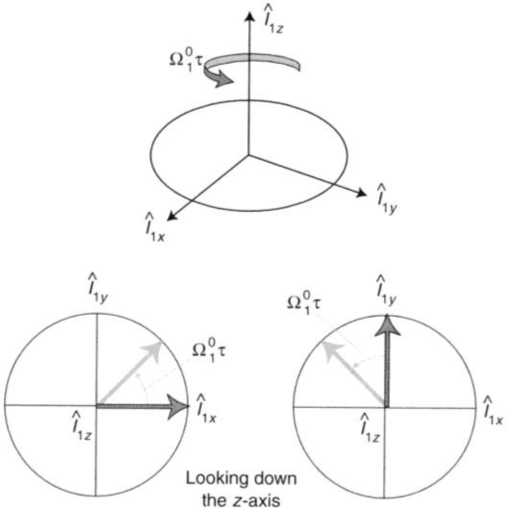
$$\frac{1}{2}\hat{\mathbb{1}}_1 \longrightarrow \frac{1}{2}\hat{\mathbb{1}}_1$$

$$\hat{I}_{1x} \longrightarrow \hat{I}_{1x}$$

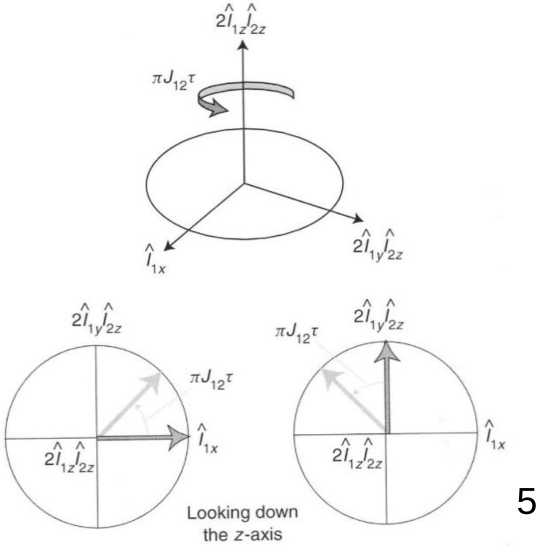
$$\hat{I}_{1y} \longrightarrow \hat{I}_{1y}\cos\beta_p + \hat{I}_{1z}\sin\beta_p$$

$$\hat{I}_{1z} \longrightarrow \hat{I}_{1z}\cos\beta_p - \hat{I}_{1y}\sin\beta_p$$

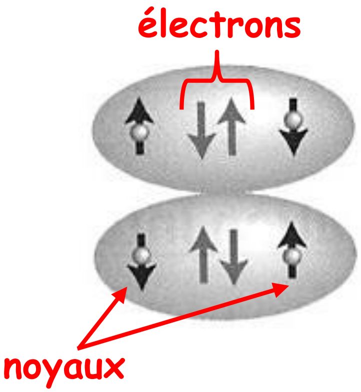
évolution sous δ

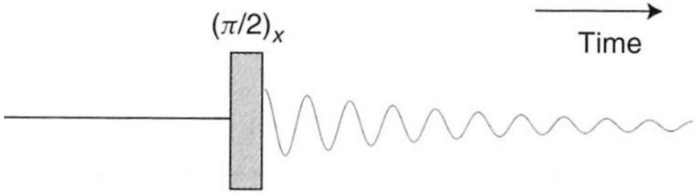


évolution sous J



Couplages J homonucléaires – Multiplets au 1er ordre





rappel :

un spin J couplé à n spins I...

↓

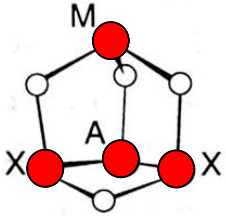
(2nI + 1) raies attendues

cas particulier (!) : I = 1/2

↳ (n + 1) raies, binôme de Newton

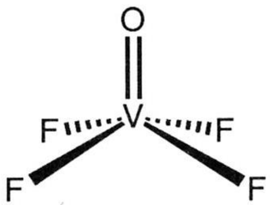
I = 1/2

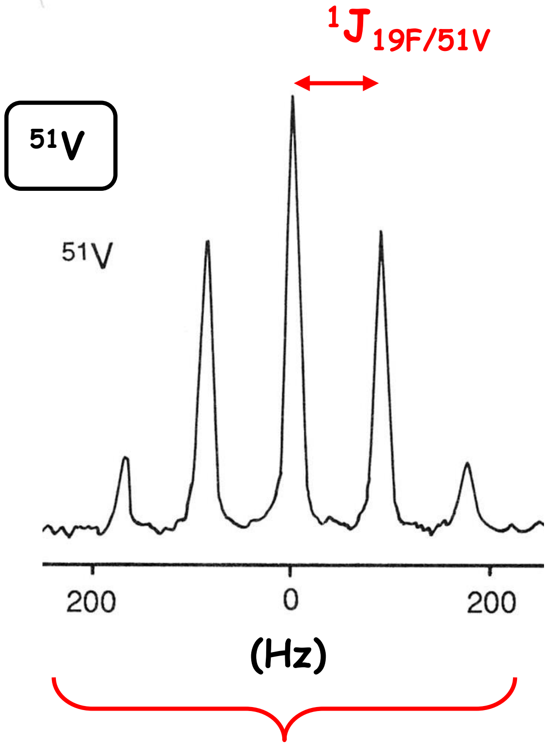
^{31}P : βP_4S_4

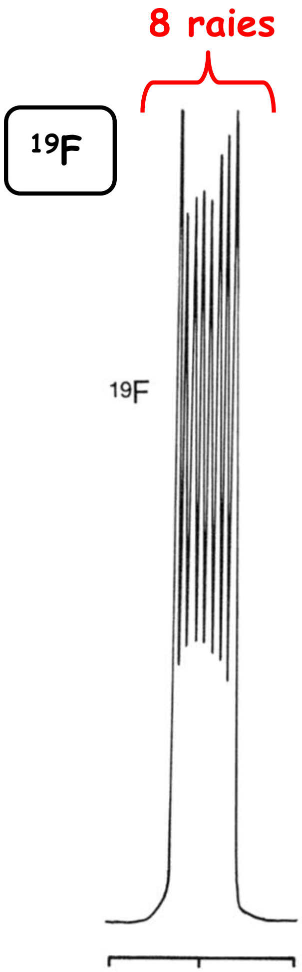


Couplages J : noyaux quadripolaires -1

^{19}F : I=1/2 100% D^P : 0,83 ^{51}V : I=7/2 99,8% D^P : 0,38



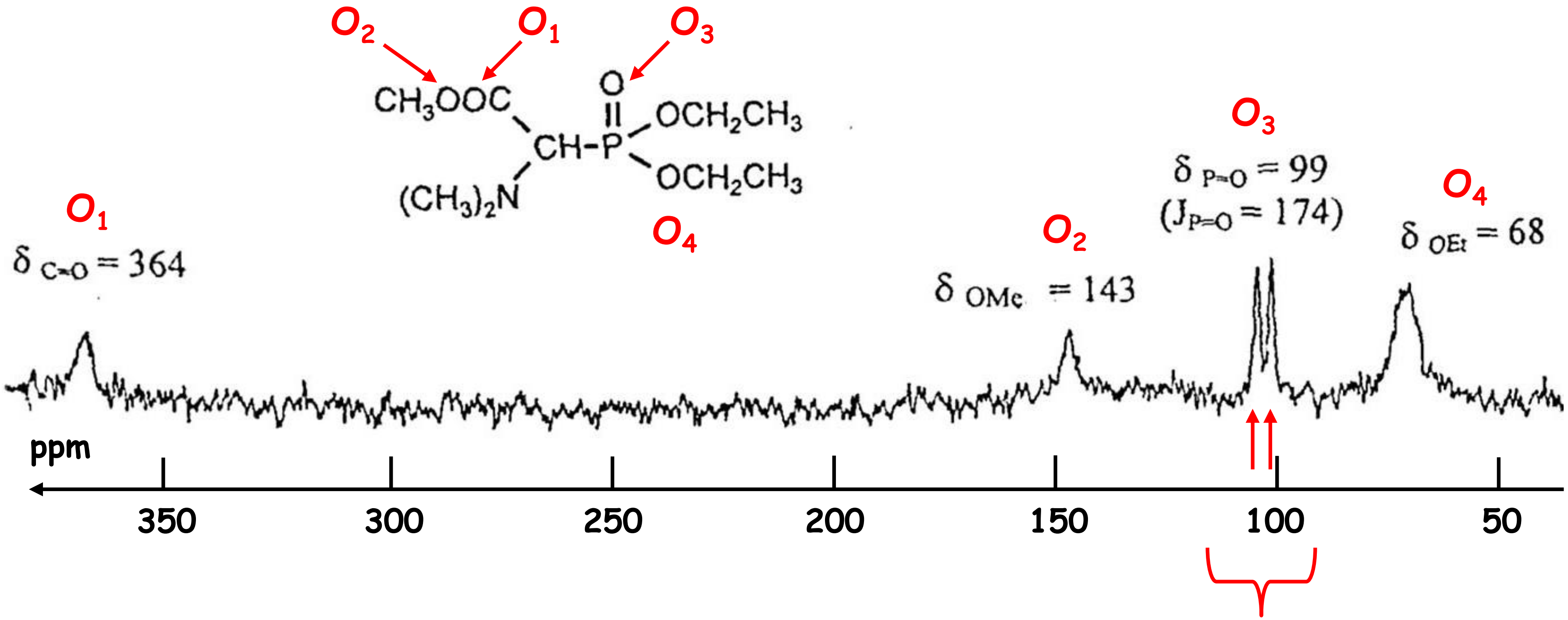




(Hz)

Couplages J : noyaux quadripolaires -2

^{17}O : I=5/2 0.037% D^P : 1.08 × 10^{-5}



doublet

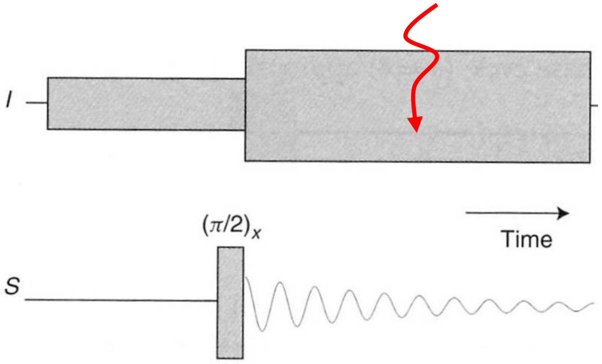
$^1J_{17O/31P}$ = 174 Hz

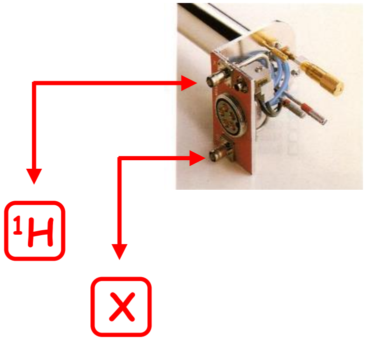
relaxation rapide

NS élevé

enrichissement isotopique possible via $H_2{}^{17}O$

Simplification des spectres : découplage hétéronucléaire

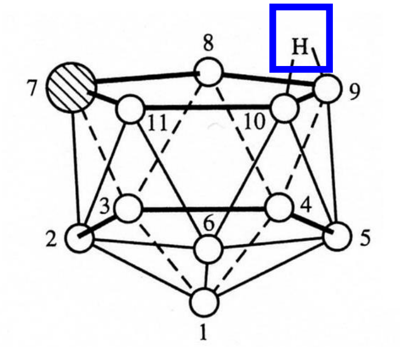




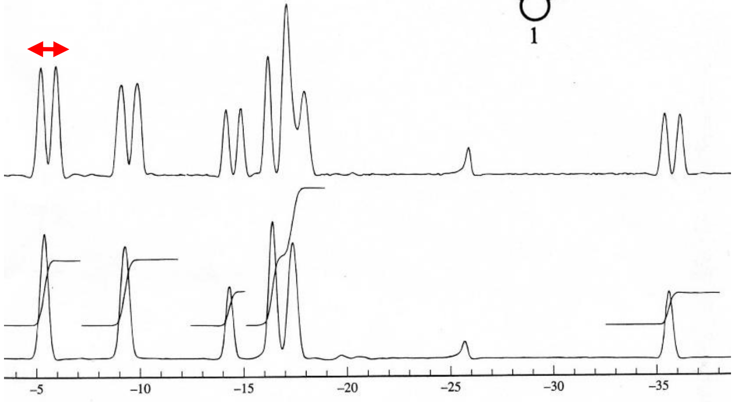
^1H

$[NEt_3H^+]$

^{11}B



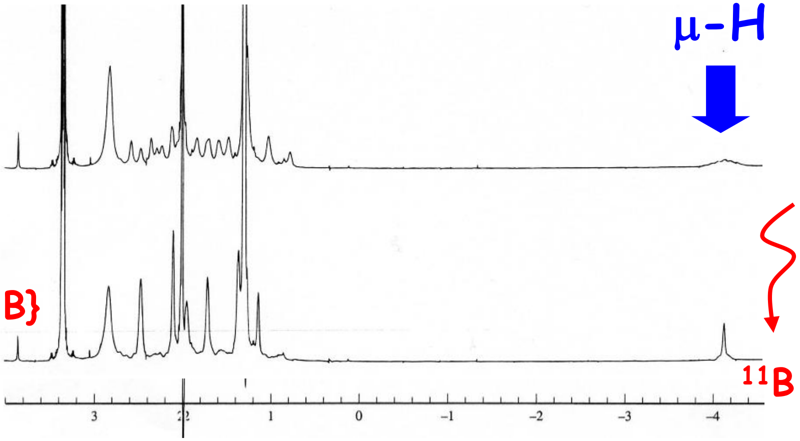
$^1J_{11B/1H}$ ~ 140 Hz



^{11}B

^{11}B-{^1H}

^1H



^1H

^1H-{^{11}B}

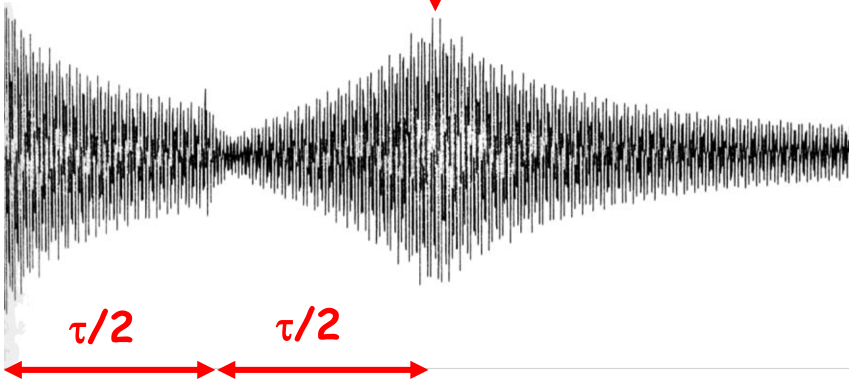
B–H site	$\delta(^{11}B)$	$\delta(^1H)$
8, 11	−9.2	2.05
2, 3	−16.3	1.67
9, 10	−17.6	1.26
		(also μ-H, −4.11)
4, 6	−5.6	2.37
1	−35.6	1.05
5	−14.6	1.83

attributions : $[B_{10}H_{11}Se^-]$

Echos de spins

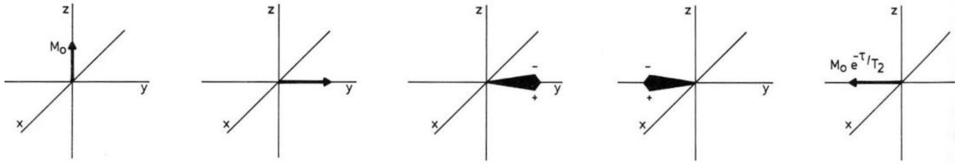
réponse du système de spins à 2 impulsions

top de l'écho



$\tau/2$ **$\tau/2$**

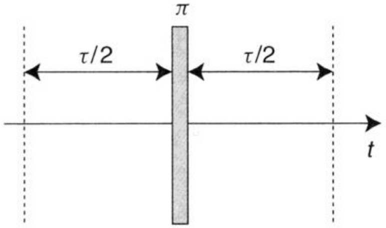
$(\pi/2)_x$ $(\pi)_x$

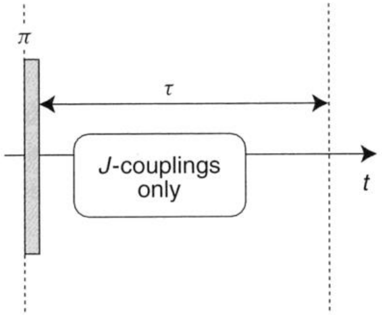


refocalisation au temps $\tau/2$

après l'impulsion π

systèmes homonucléaires :
effet de l'écho sur δ et J





refocalisation du déplacement chimique

couplage J uniquement...

$\underbrace{\qquad\qquad\qquad\qquad}$

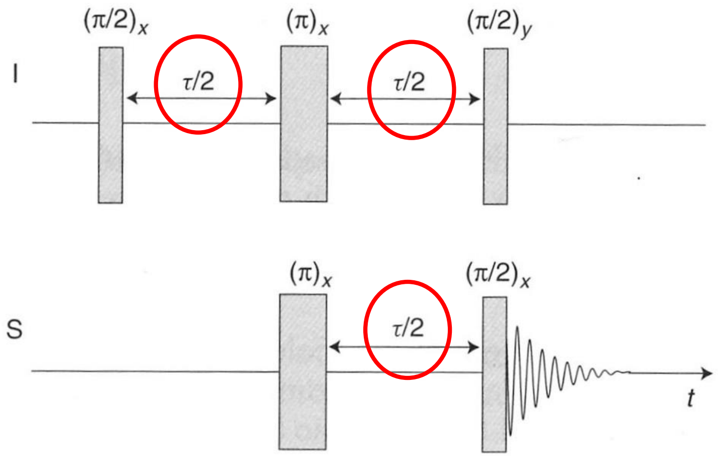
calculs quantiques simplifiés

efficacité accrue des séquences

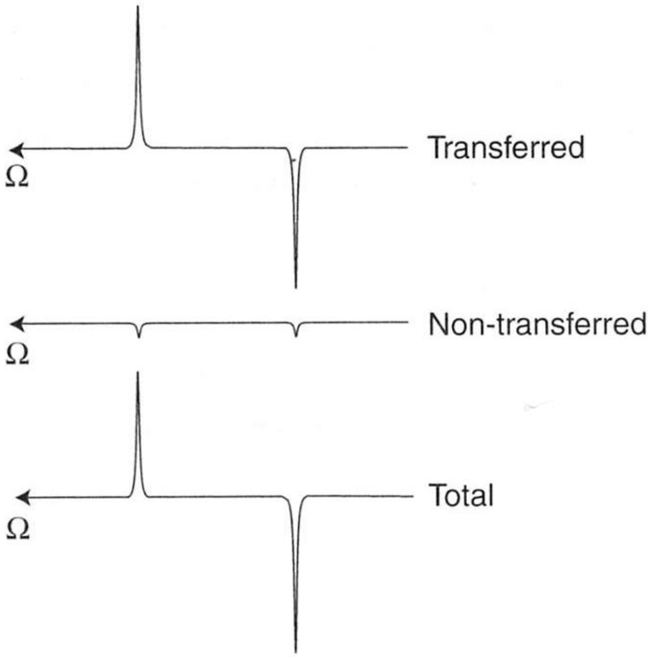
Transfert de polarisation : INEPT

Insensitive Nuclei Enhanced by Polarization Transfer

$$\boxed{\text{signal/bruit} \propto |\gamma|^{5/2}\ (B_0)^{3/2}}$$



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



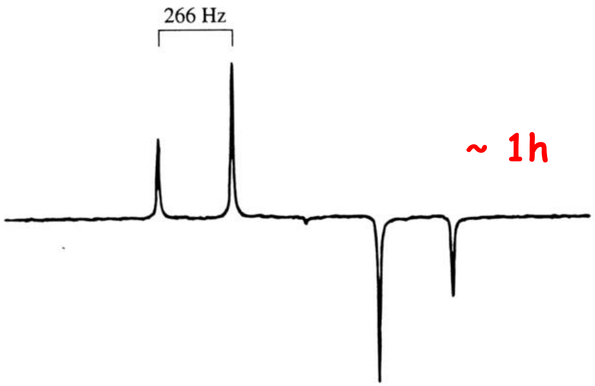
$$\boxed{\text{gain}_{\text{INEPT}} \propto |\gamma(^1H)/\gamma(X)|}$$

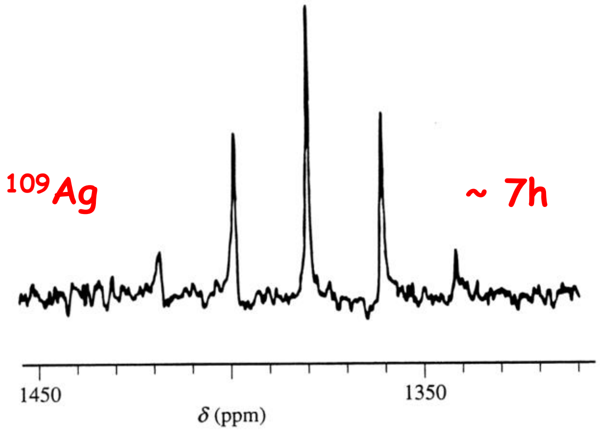
ex : ≈ 10 pour ^{15}N !

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

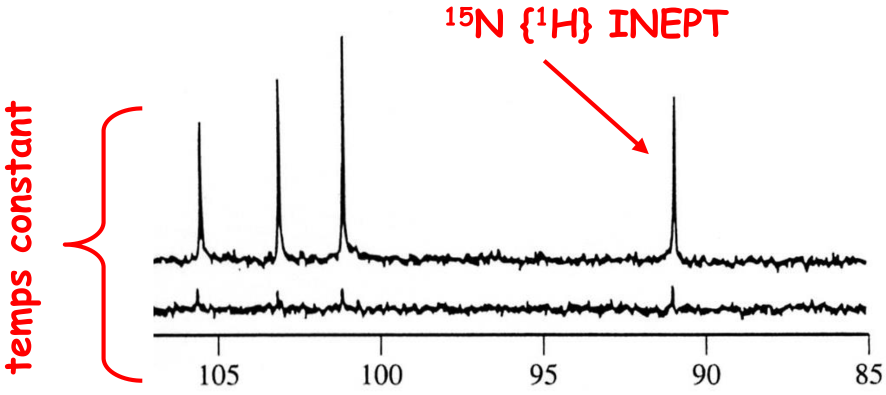
INEPT : exemples

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



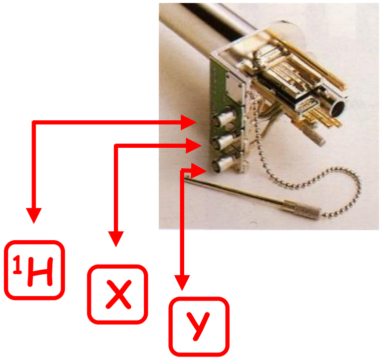


^{109}Ag : [Ag(dppe)$_2$]NO$_3$,
dppe=bisdiphenylphosphinoethane



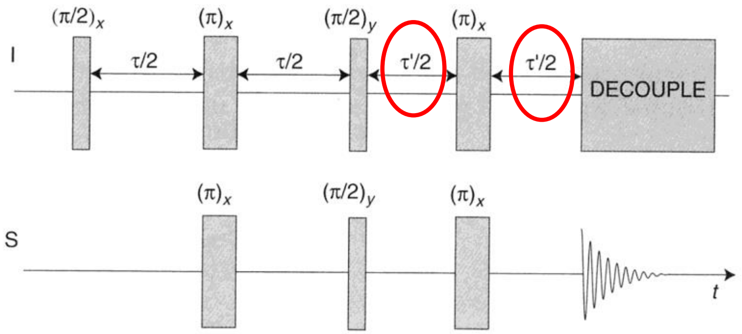
^{15}N : gramicidine S

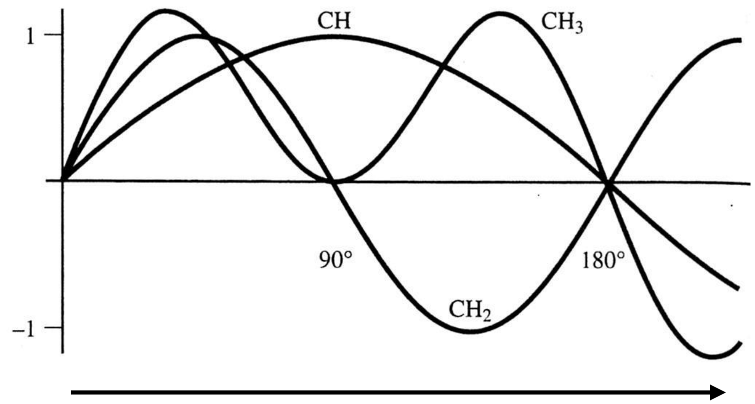
INEPT en version refocalisée



INEPT : édition spectrale

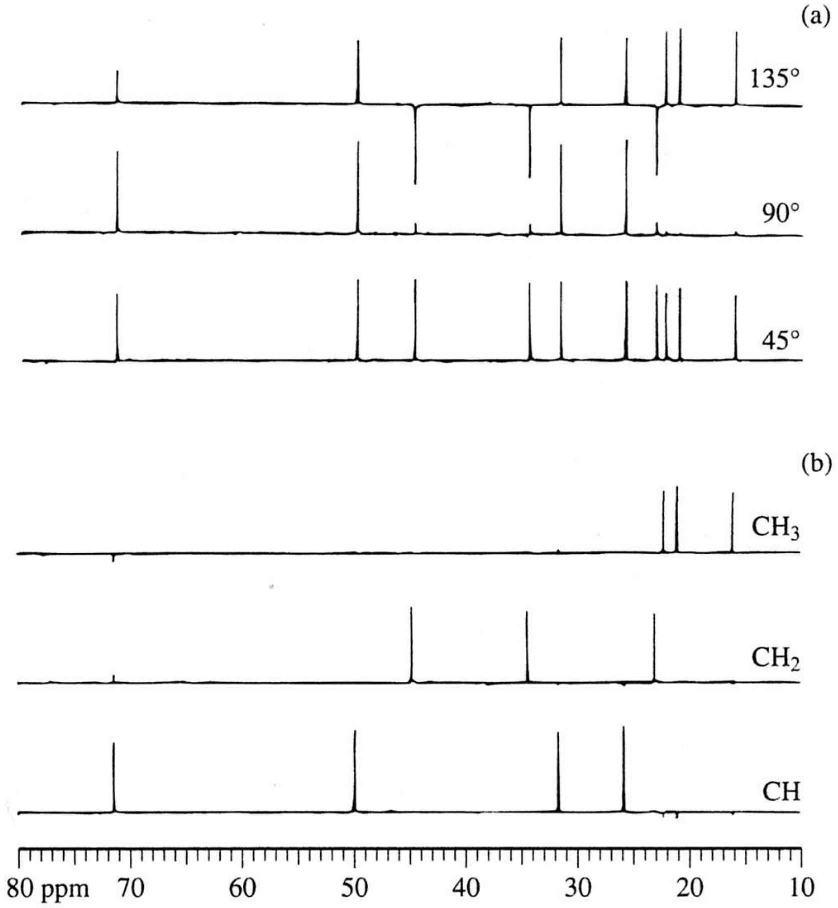
INEPT en version refocalisée





$^1J_{IS}$=125 Hz

$^{13}C\ \{^1H\}$ INEPT

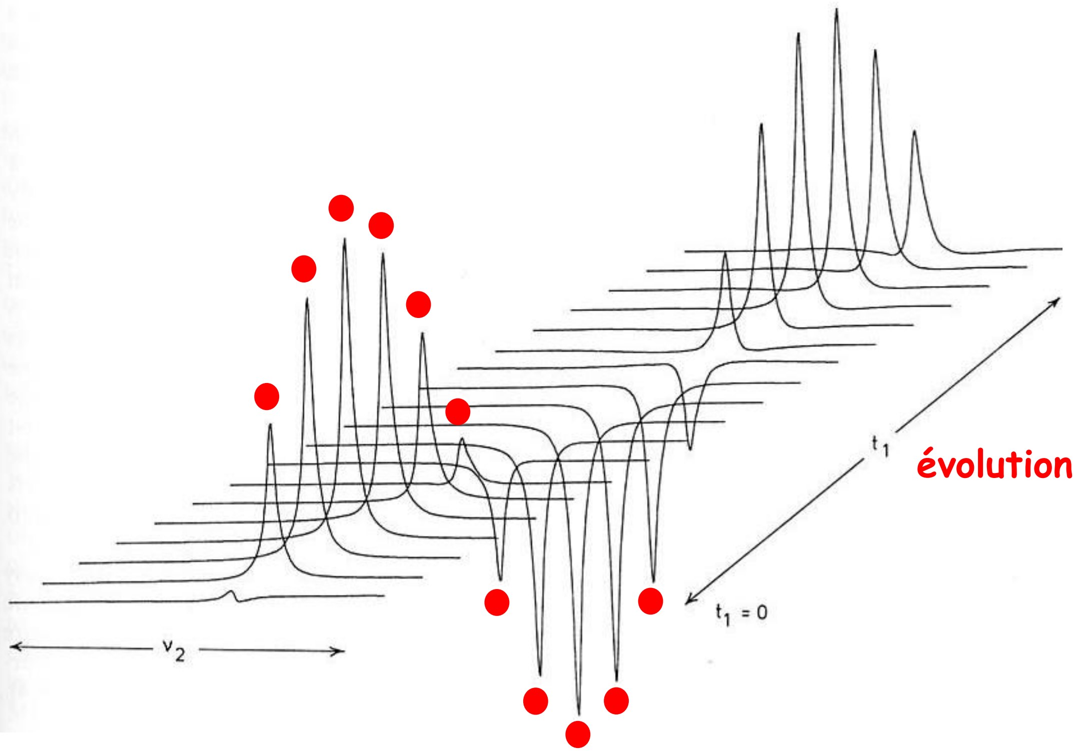


INEPT refocalisé : menthol
(2,4,6 ms)

Corrélations bidimensionnelles

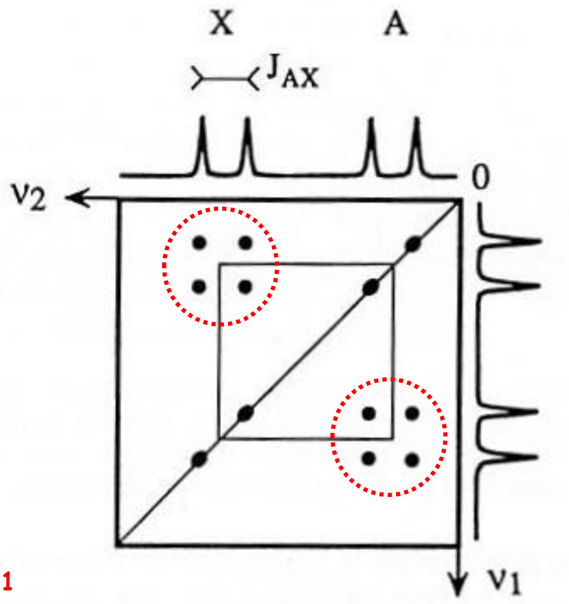
rappels :

J.Jeener ~ 1971



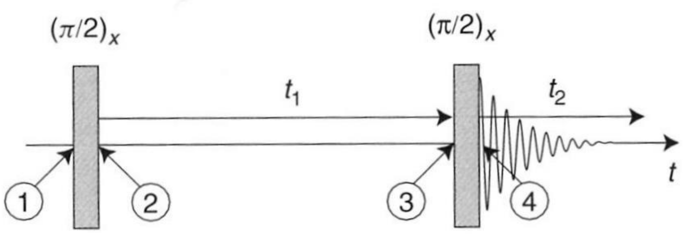
évolution en t_1

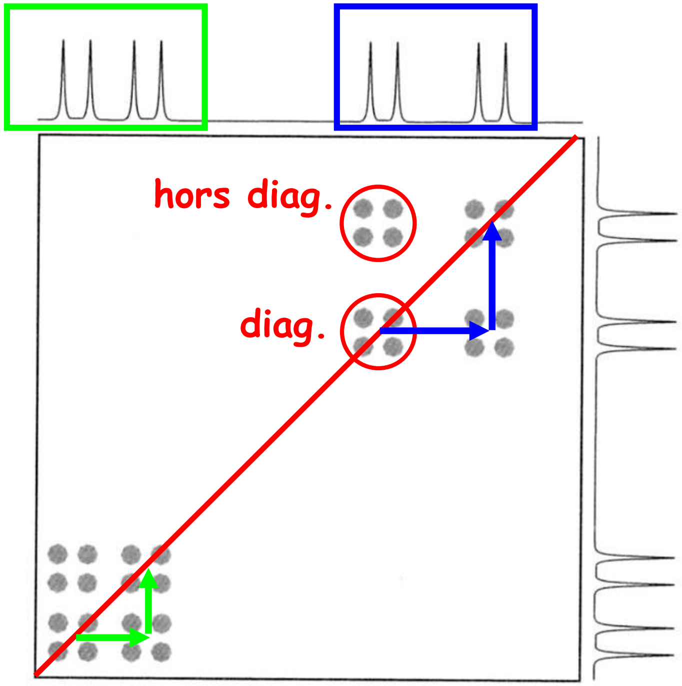
système A–X

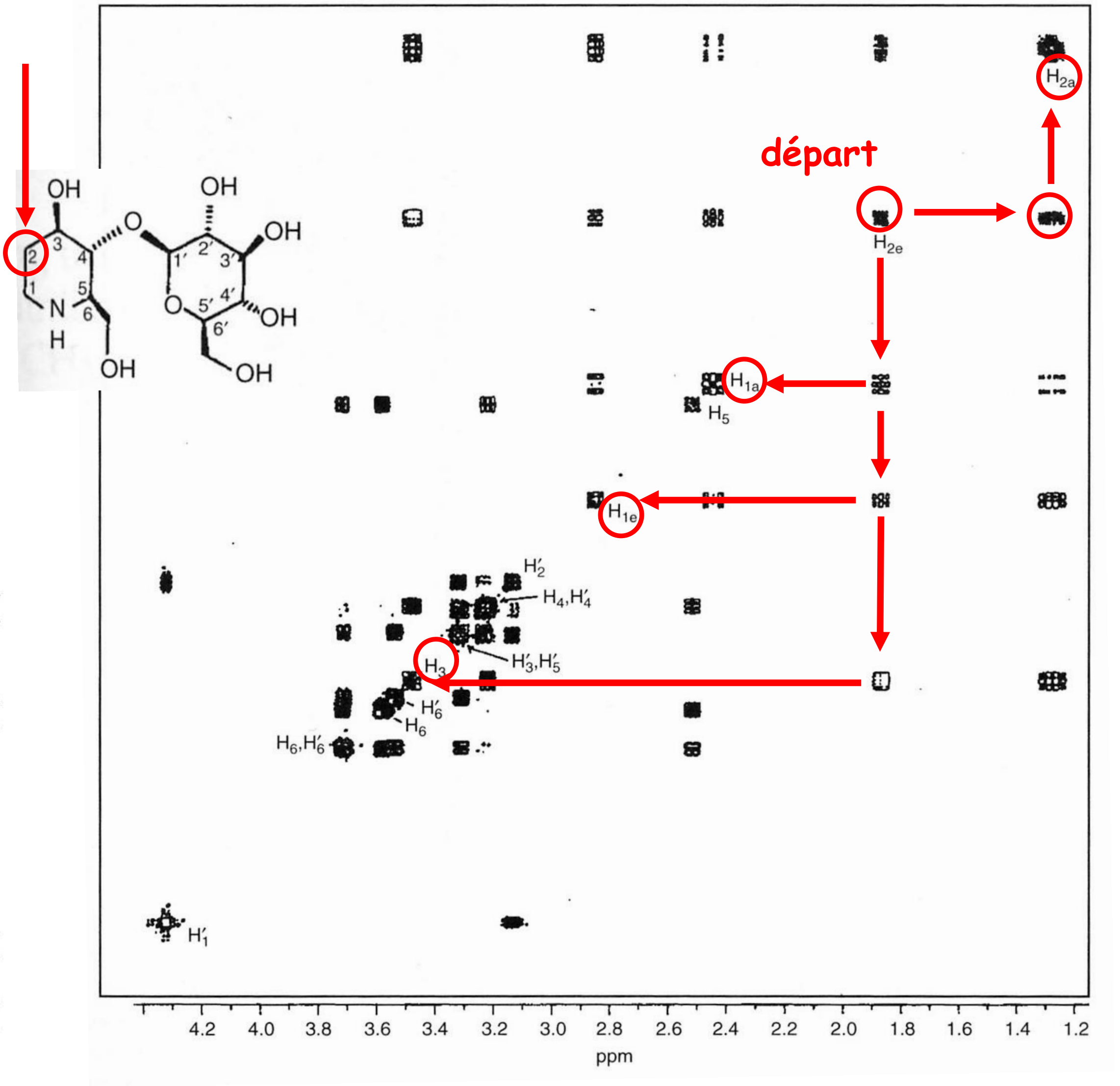


Corrélation 2D homonucléaire : COSY

COrrelation **S**pectroscop**Y**





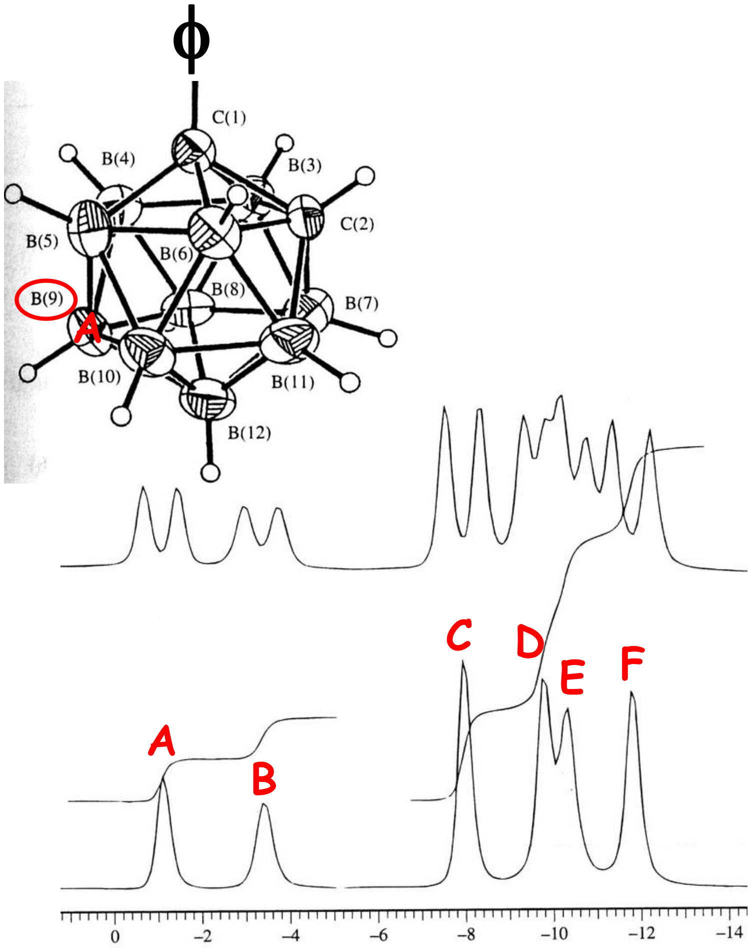


COSY $^1H/^1H$

Corrélation 2D homonucléaire : COSY quadripolaire

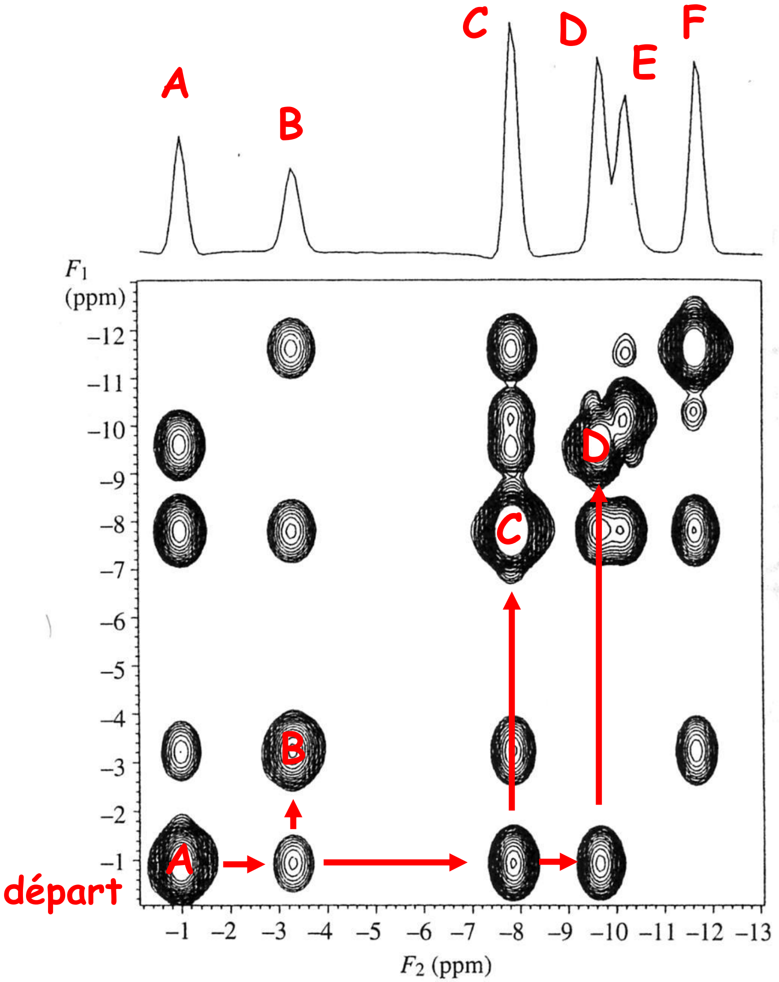
COSY $^{11}B/^{11}B$, déc.{^1H}

$^1J_{11B/11B}$ non observables en RMN 1D



$[1\text{-}Ph\text{-}1,2\text{-}C_2B_{10}H_{11}]$

plan de symétrie passant par :
C(1), C(2), B(9), B(12)

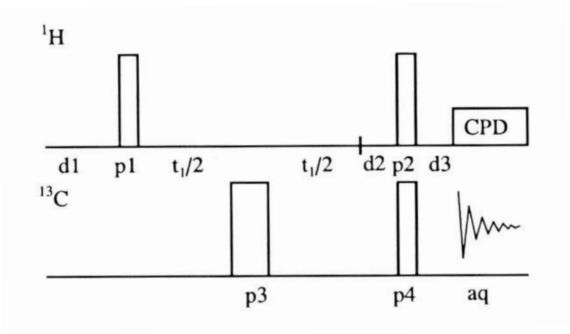


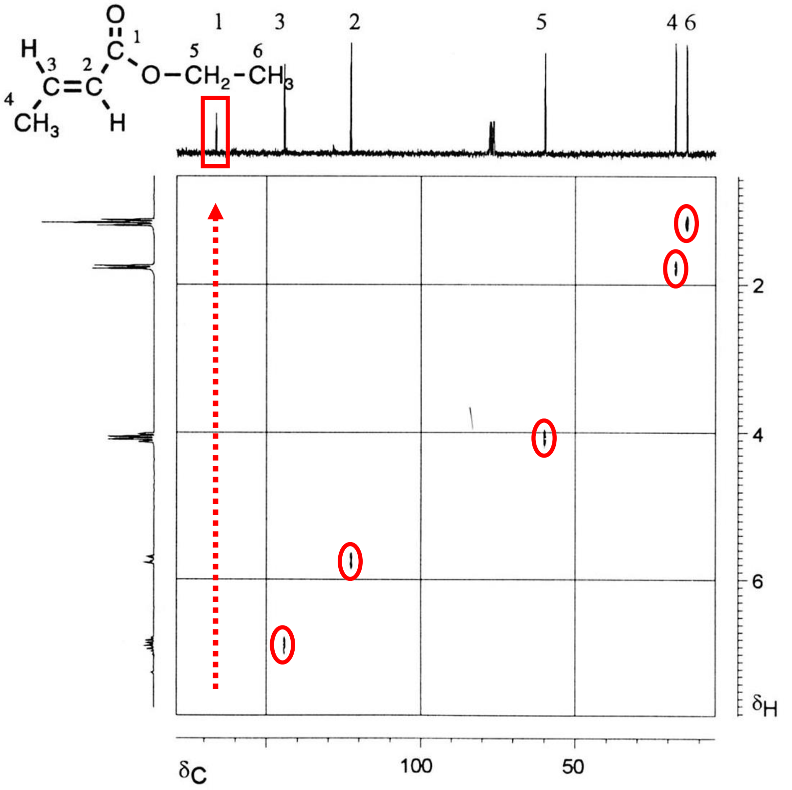
A≡B(9) B≡B(12) C≡B(8,10)

D≡B(4,5) E≡B(3,6) F≡B(7,11)

Transfert de polarisation hétéronucléaire : HETCOR

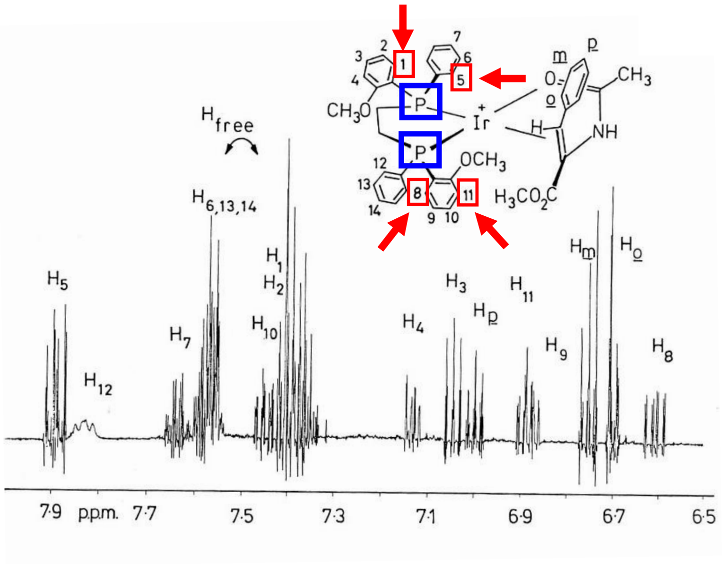
HETeronuclear **COR**relation



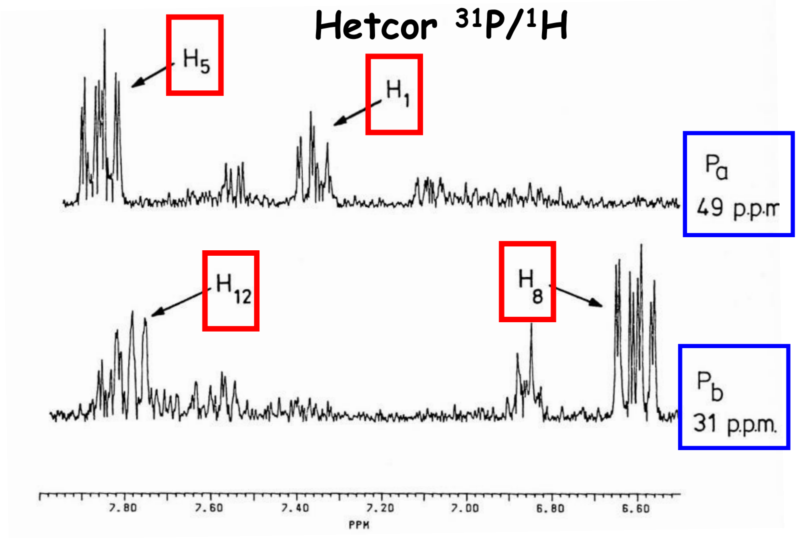


crotonate d'éthyle

Hetcor $^{13}C/^1H$



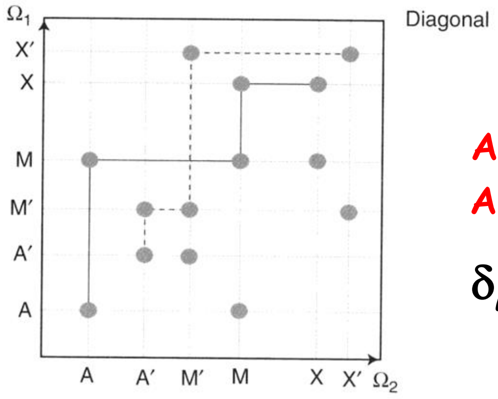
Hetcor $^{31}P/^1H$



ortho-H : 1,5,8,12

Corrélations complètes : TOCSY

TOtal **C**orrelation **S**pectroscop**Y**

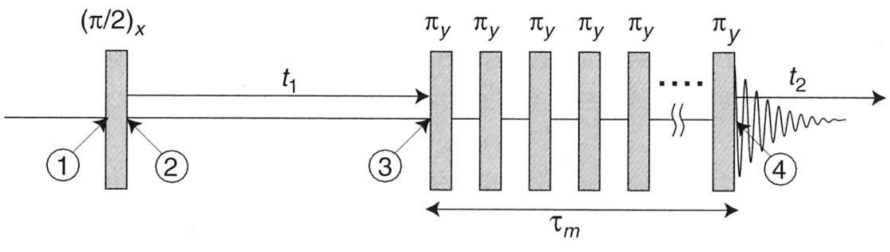


A-M-X

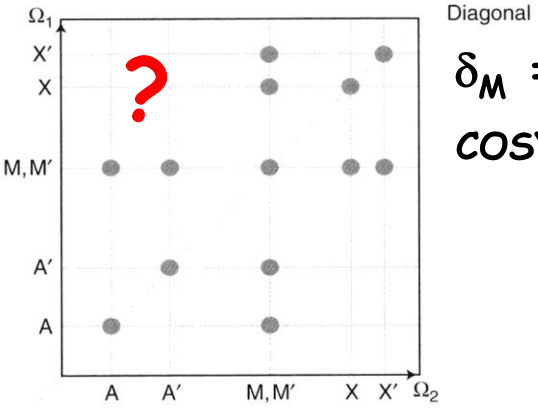
A'-M'-X'

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

spin lock



temps de mélange τ_m

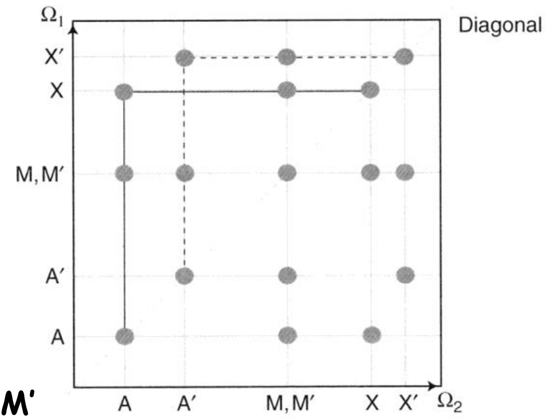


$\delta_M = \delta_{M'}$

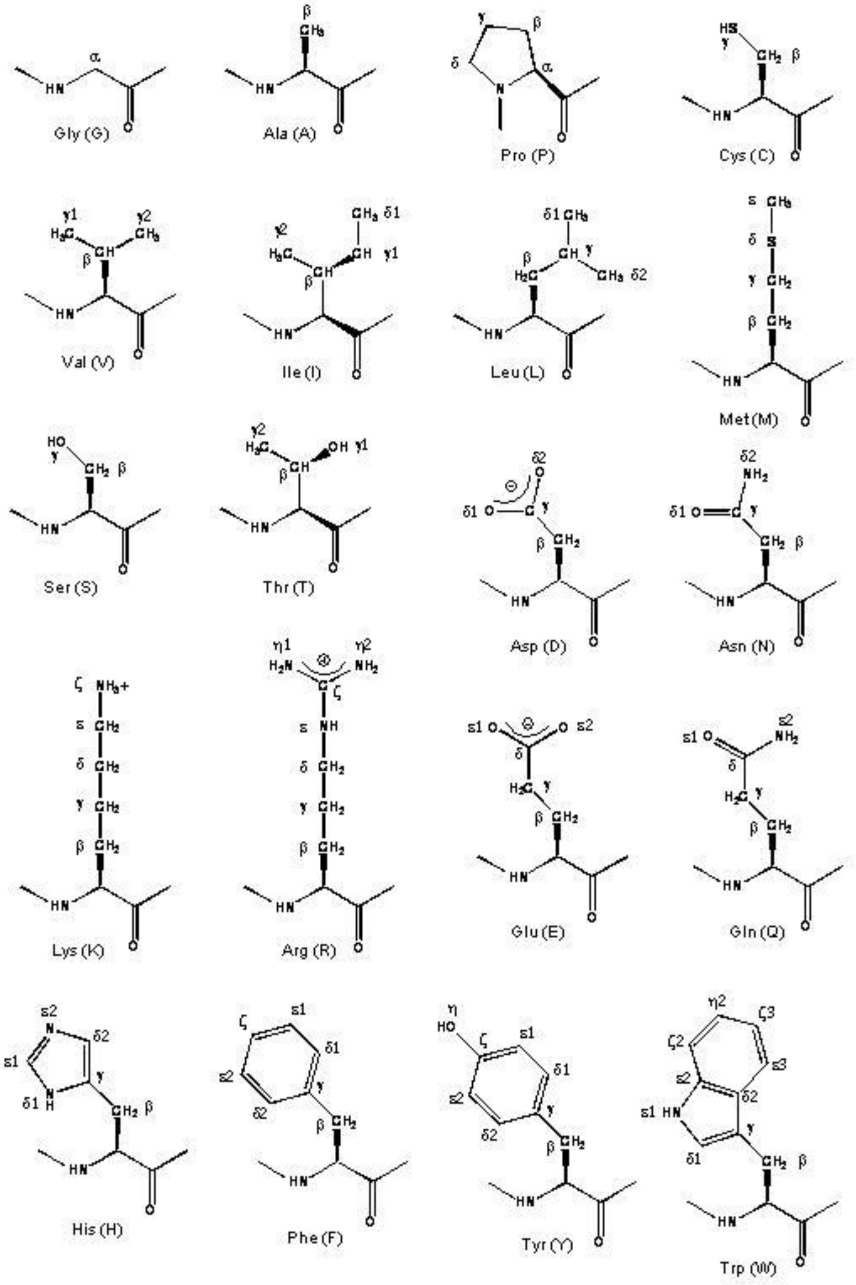
COSY

TOCSY

$\delta_M = \delta_{M'}$



TOCSY : application à l'étude des acides aminés -1



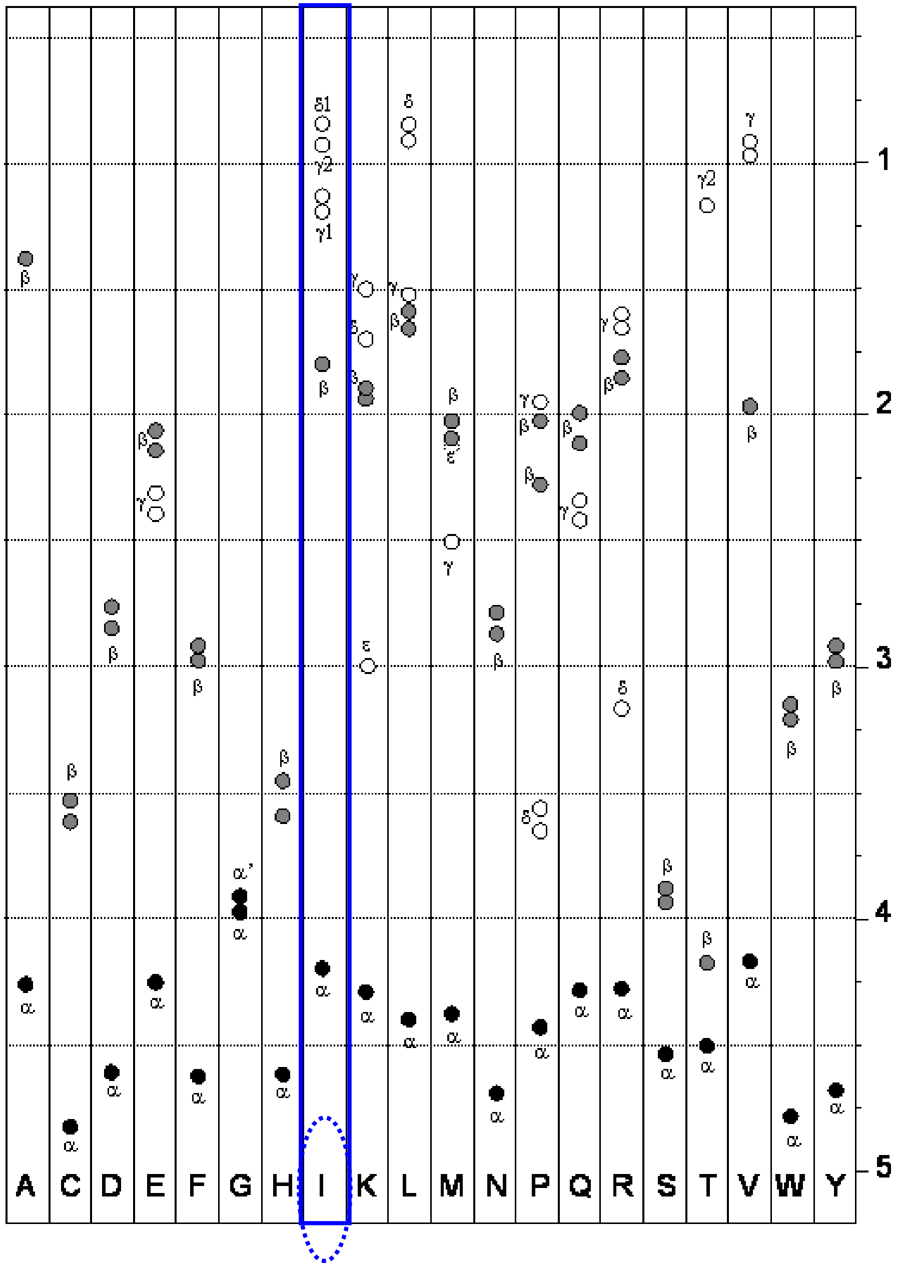
identification des systèmes de spins

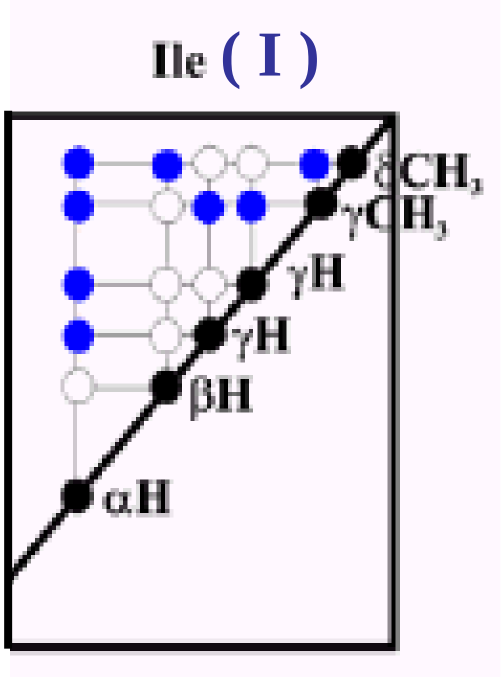
COSY
TOCSY

NH-H$^{\alpha}$-Hlat

O. Lequin, UPMC

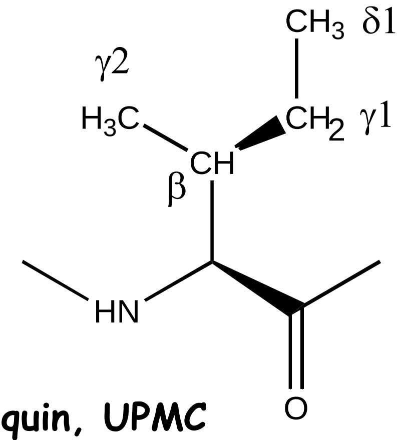
TOCSY : application à l'étude des acides aminés -2





○ **COSY**

● **TOCSY**

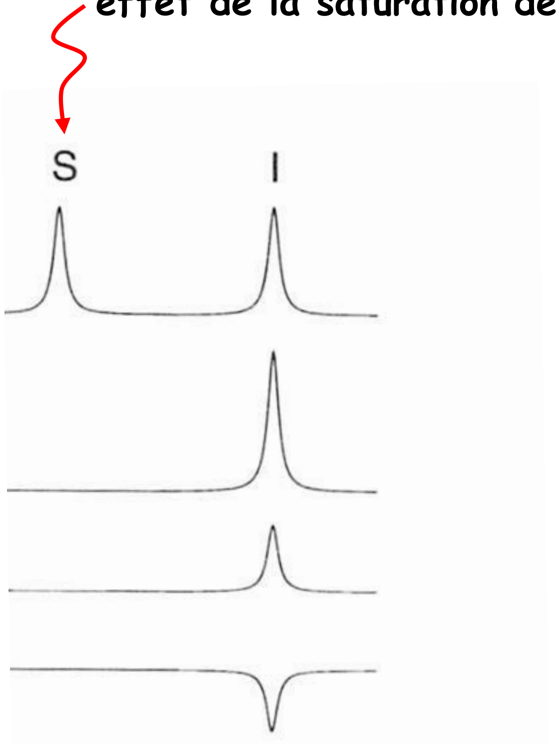


O. Lequin, UPMC

NOE

Nuclear Overhauser Effect

effet de la saturation de S



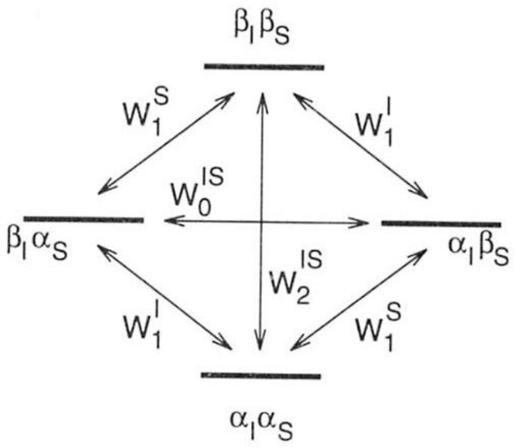
$W \propto r^{-6}$

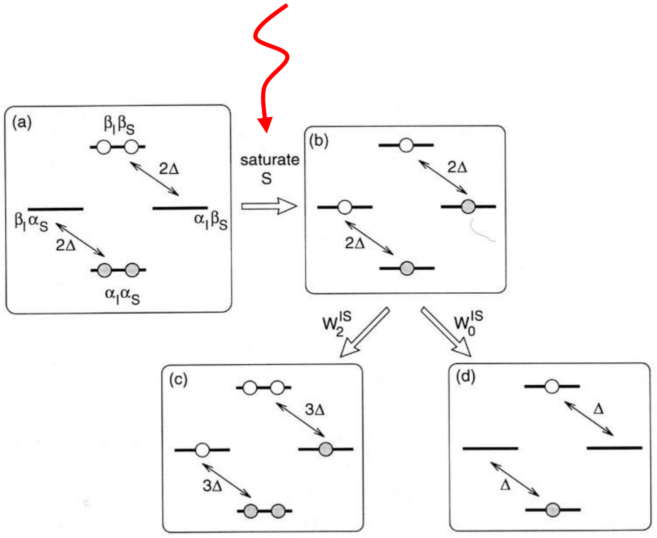
W_0, W_1, W_2 dépendent de τ_c

$\eta_{max} = 1/2\ \gamma_S/\gamma_I$

(paire, retrécissement extrême)

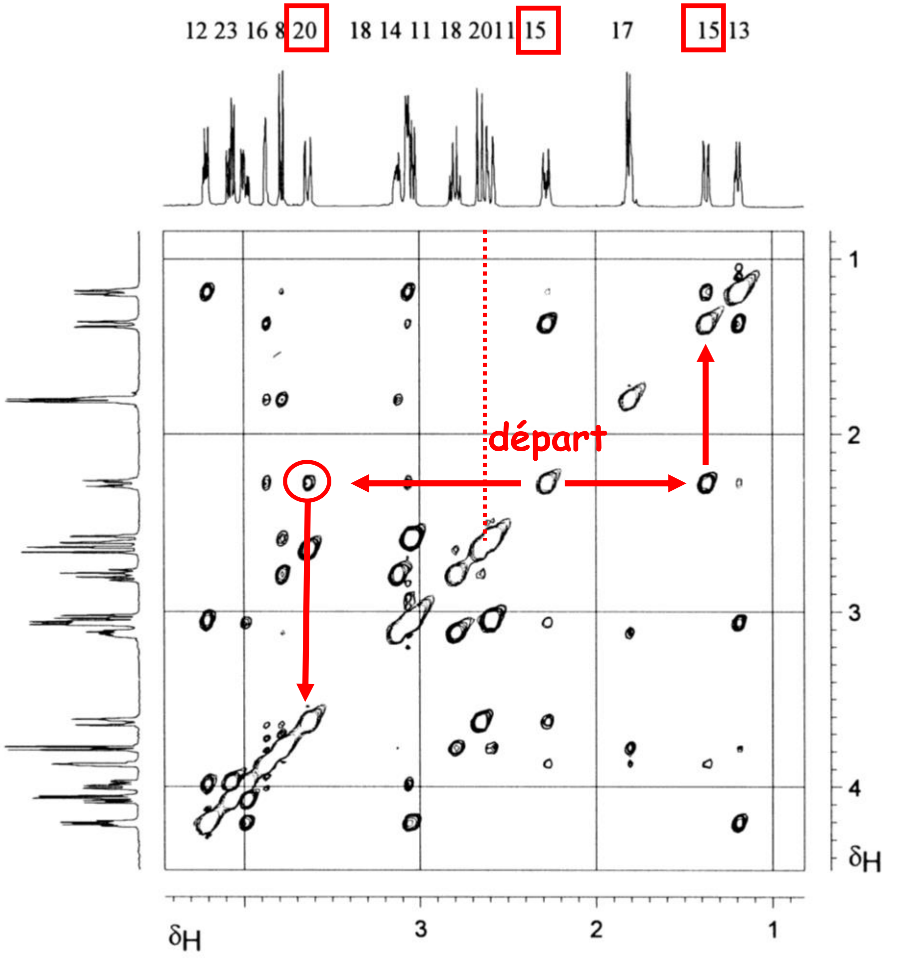
chemins de relaxation possibles pour un système IS (spins 1/2)

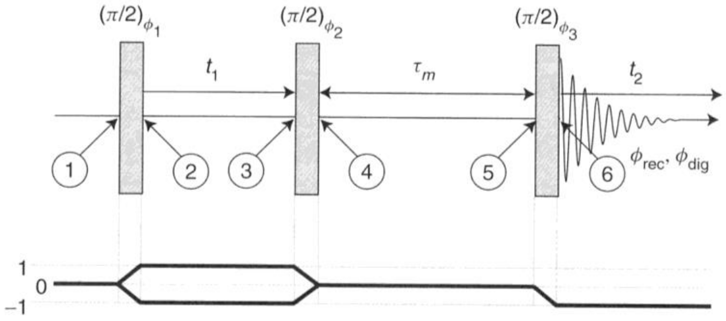


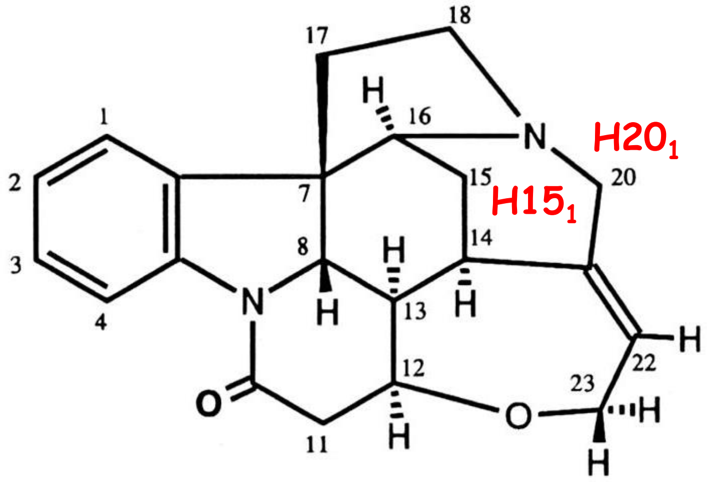


NOESY

Nuclear Overhauser Effect SpectroscopY







Structure des protéines

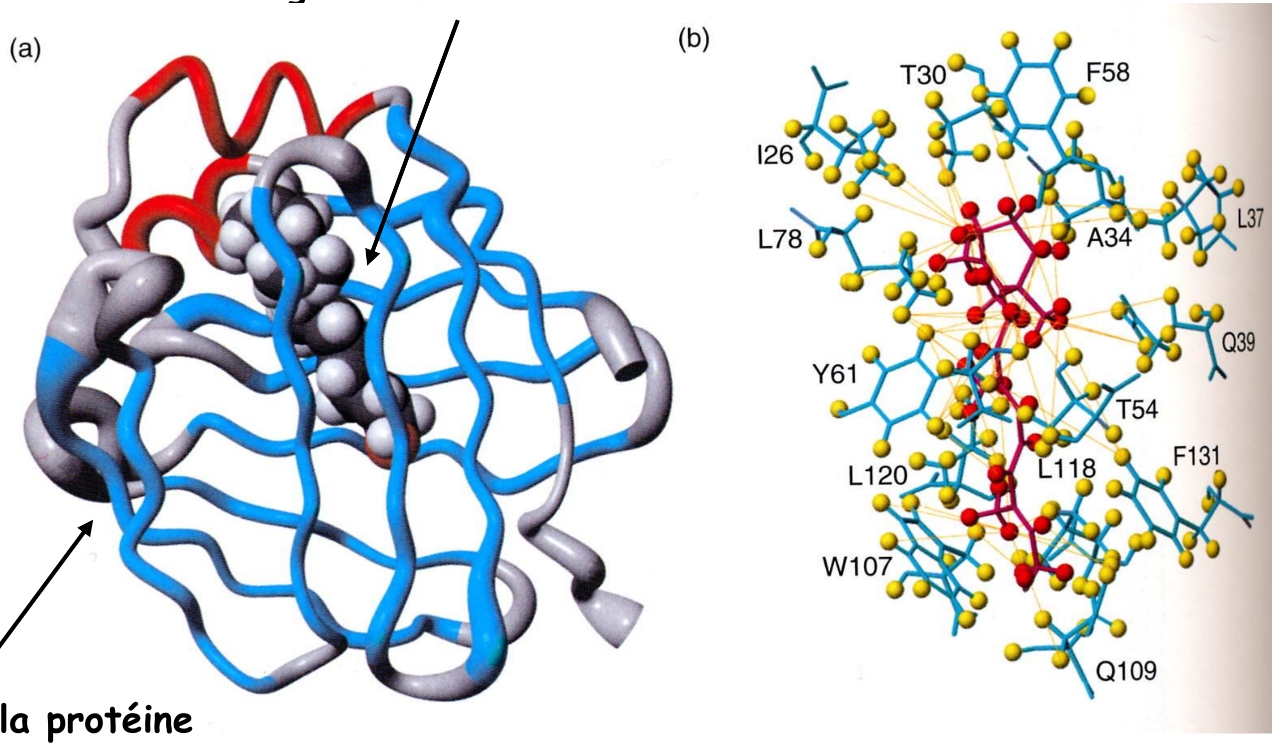
combinaison de :

DQ-COSY

TOCSY

NOESY ⟶ 3980 contraintes de distances

3D



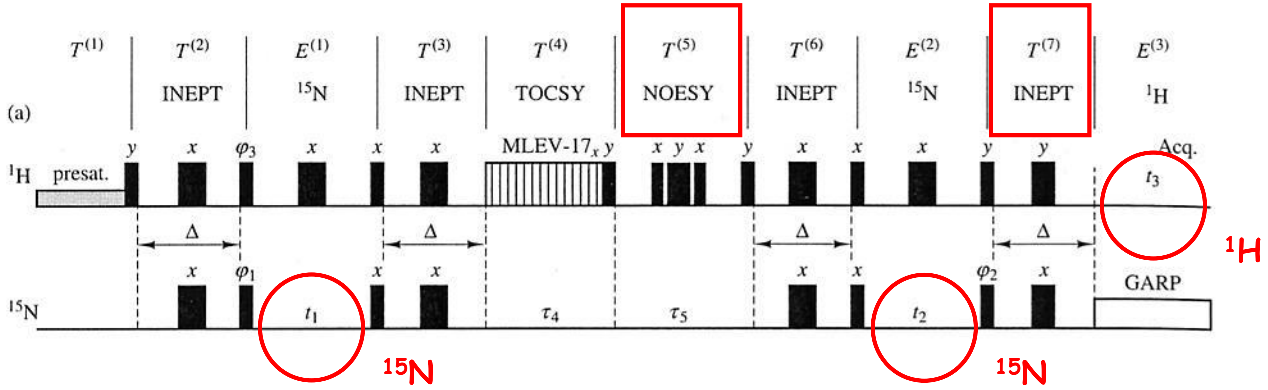
ligand rétinol

squelette de la protéine

cellular retinol binding protein II

RMN à 3 dimensions

rappel :



ex : COSY éditée par les corrélations $J_{C\text{-}H}$