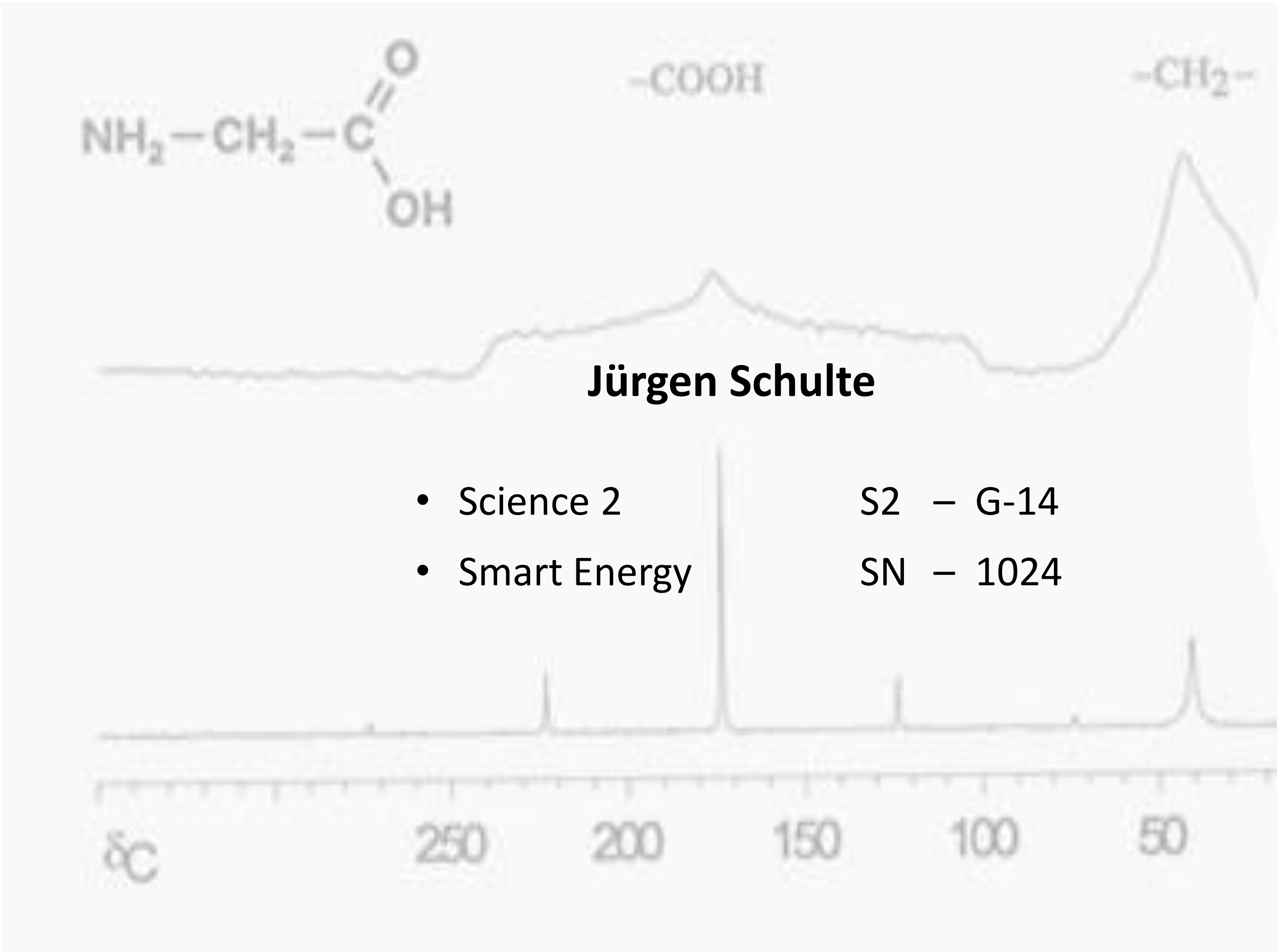
Solids Techniques - NMR Spectroscopy



Jürgen Schulte

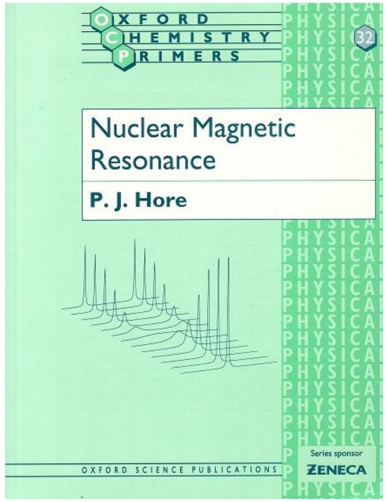
- Science 2 S2 – G-14
- Smart Energy SN – 1024

Topics:

- **Part I – Introduction**
  - **History of NMR**
  - **NMR Hardware**
- Part II – NMR Theory
  - Nuclei – Spin – Magnetic Moments
  - Shielding – Chemical Shifts
  - Coupling – Molecular Structure
  - Relaxation – Linewidth
- Part III NMR Experiments
  - Sample preparation
  - Solution vs. Solid State NMR
  - Techniques for optimizing Solid State NMR
  - Research Examples

Books for NMR Spectroscopy

general: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Nuclear Magnetic Resonance
P. J. Hore
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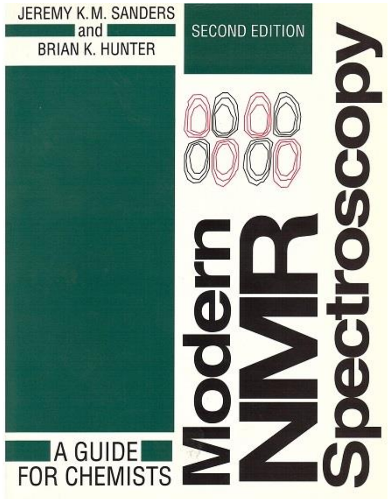
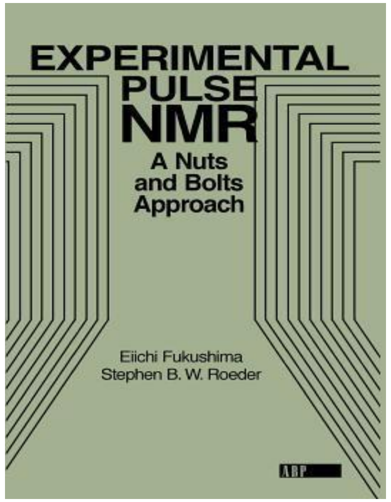
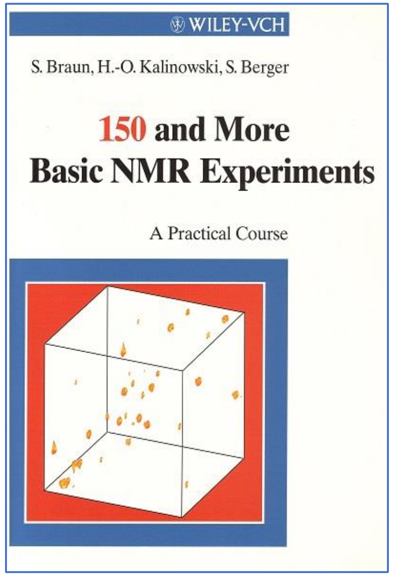
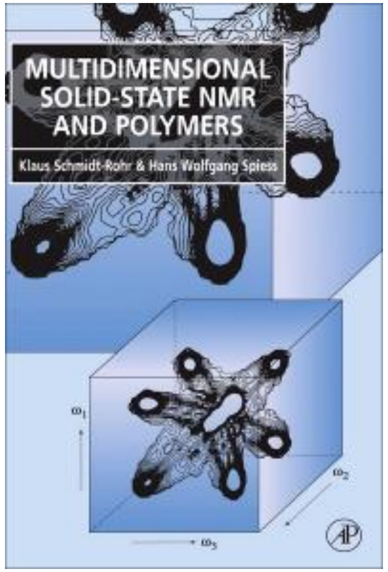
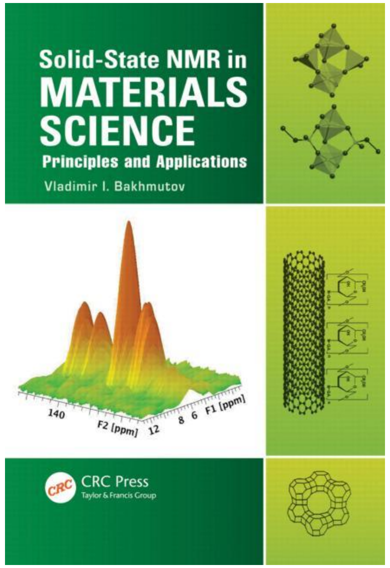

JEREMY K.M. SANDERS and BRIAN K. HUNTER
SECOND EDITION
Modern NMR Spectroscopy
A GUIDE FOR CHEMISTS


EXPERIMENTAL PULSE NMR
A Nuts and Bolts Approach
Eiichi Fukushima
Stephen B. W. Roeder
ABP

specialized:

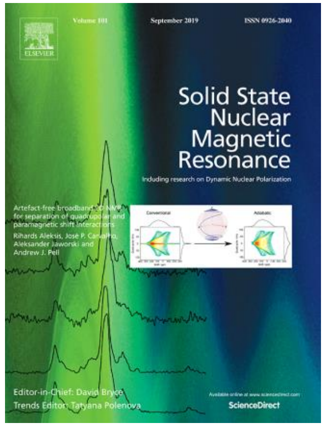

WILEY-VCH
S. Braun, H.-O. Kalinowski, S. Berger
150 and More Basic NMR Experiments
A Practical Course

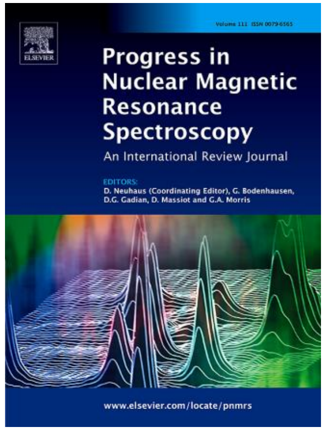

MULTIDIMENSIONAL SOLID-STATE NMR AND POLYMERS
Klaus Schmidt-Rohr & Hans Wolfgang Spiess
AP


Solid-State NMR in MATERIALS SCIENCE
Principles and Applications
Vladimir I. Bakhmutov
CRC Press
Taylor & Francis Group

Journals for NMR Spectroscopy

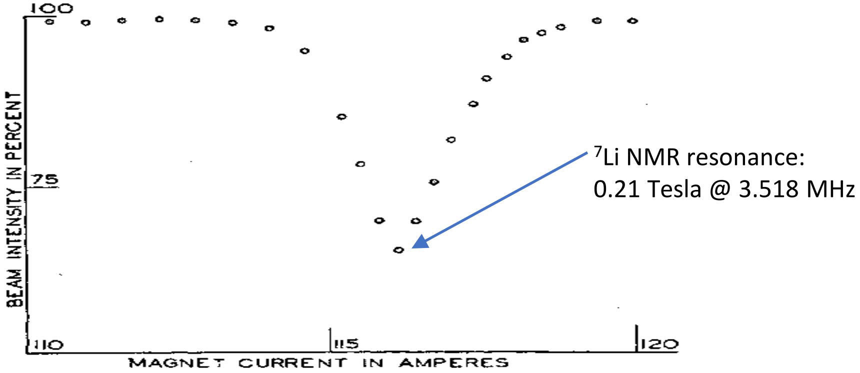
Journal of Magnetic Resonance
August 2, 2019 issue:
JMR's Golden Jubilee: Magnetic Resonance in the 21st Century
https://www.sciencedirect.com/journal/journal-of-magnetic-resonance/special-issue/10MNNC19J7V





NMR Milestones

- 1938 – NMR of LiCl molecular beams.
  Rabi (Columbia University)



^{7}Li NMR resonance:
0.21 Tesla @ 3.518 MHz

FIG. 1. Curve showing refocused beam intensity at various values of the homogeneous field. One ampere corresponds to about 18.4 gauss. The frequency of the oscillating field was held constant at 3.518×10^6 cycles per second.

- 1946 – NMR of Liquids and Solids.
  Purcell, Torrey, Pound (Harvard)
  Bloch, Hansen, Packard (CalTech)

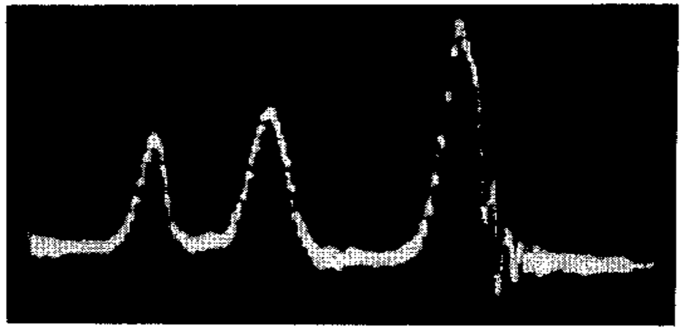


FIG. 1. Oscillograph trace of the nuclear induction signal from ethyl alcohol. The total trace is 75 milligauss wide and was traversed in 2 seconds. The peaks from left to right represent OH, CH_2, CH_3. (Packard, 1951)

1952 – First commercial NMR spectrometer

1962 – First Superconducting Magnet for NMR

1968 – First Pulse Fourier Transform NMR

1969 – First Concept of MRI Scanners

1971 – First two-dimensional NMR Experiment

1985 – First Protein Structure solved by NMR

2009 – First 1 Gigahertz NMR Spectrometer (23.5 T)

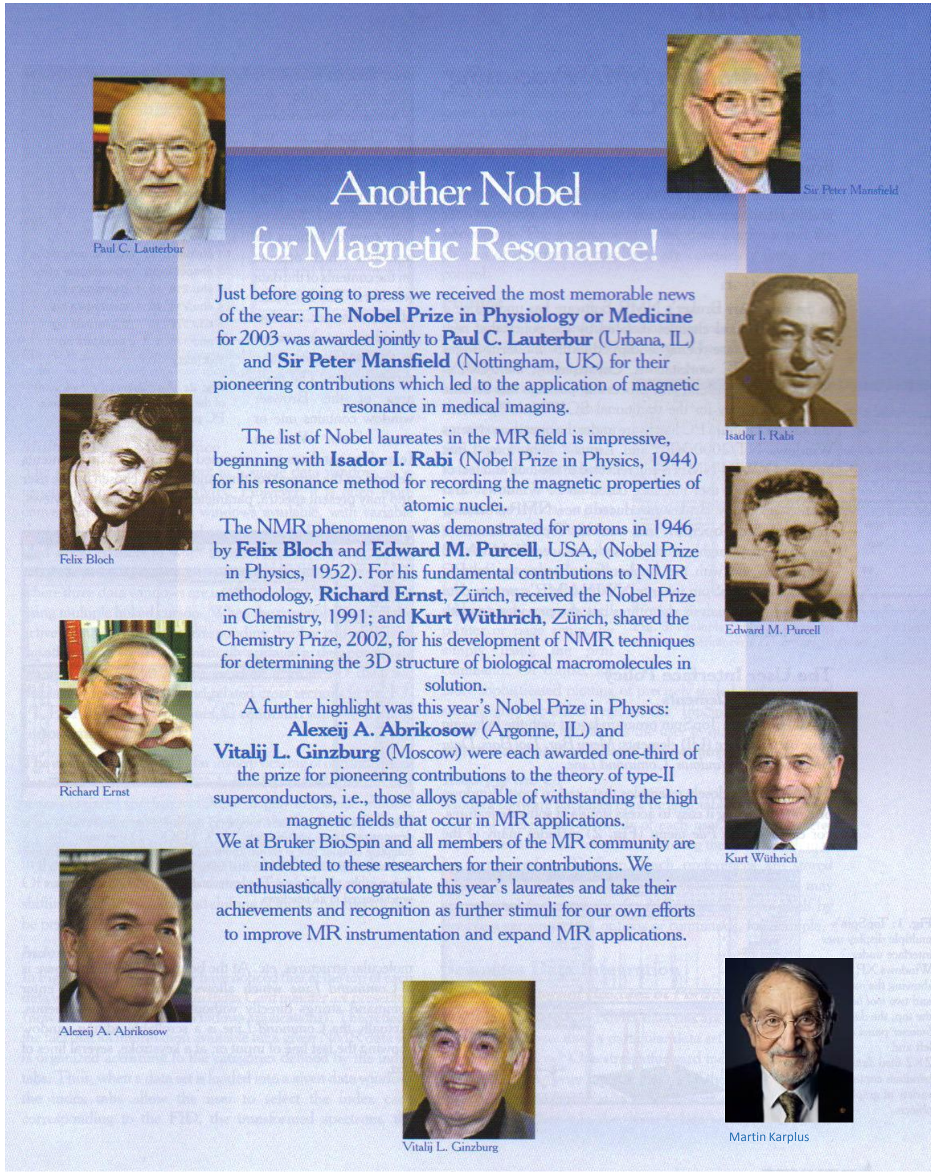
2019 – High Temperature Superconducting Magnets

1.1 GHz NMR, St. Jude, Memphis TN

1.2 GHz NMR, Florence, Italy

NMR Nobel Prize Winners

- 1944 (P) Isador Rabi
- 1952 (P) Felix Bloch
  Edward Purcell
- 1991 (C) Richard Ernst
- 2002 (C) Kurt Wüthrich
- 2003 (M) Paul Lauterbur
  Peter Mansfield
- 2013 (C) Martin Karplus
  (computational chemistry)



Paul C. Lauterbur

Sir Peter Mansfield

Another Nobel for Magnetic Resonance!

Just before going to press we received the most memorable news of the year: The **Nobel Prize in Physiology or Medicine** for 2003 was awarded jointly to **Paul C. Lauterbur** (Urbana, IL) and **Sir Peter Mansfield** (Nottingham, UK) for their pioneering contributions which led to the application of magnetic resonance in medical imaging.

The list of Nobel laureates in the MR field is impressive, beginning with **Isador I. Rabi** (Nobel Prize in Physics, 1944) for his resonance method for recording the magnetic properties of atomic nuclei.

The NMR phenomenon was demonstrated for protons in 1946 by **Felix Bloch** and **Edward M. Purcell**, USA, (Nobel Prize in Physics, 1952). For his fundamental contributions to NMR methodology, **Richard Ernst**, Zürich, received the Nobel Prize in Chemistry, 1991; and **Kurt Wüthrich**, Zürich, shared the Chemistry Prize, 2002, for his development of NMR techniques for determining the 3D structure of biological macromolecules in solution.

A further highlight was this year's Nobel Prize in Physics: **Alexeij A. Abrikosow** (Argonne, IL) and **Vitalij L. Ginzburg** (Moscow) were each awarded one-third of the prize for pioneering contributions to the theory of type-II superconductors, i.e., those alloys capable of withstanding the high magnetic fields that occur in MR applications.

We at Bruker BioSpin and all members of the MR community are indebted to these researchers for their contributions. We enthusiastically congratulate this year's laureates and take their achievements and recognition as further stimuli for our own efforts to improve MR instrumentation and expand MR applications.

Isador I. Rabi

Felix Bloch

Edward M. Purcell

Richard Ernst

Kurt Wüthrich

Alexeij A. Abrikosow

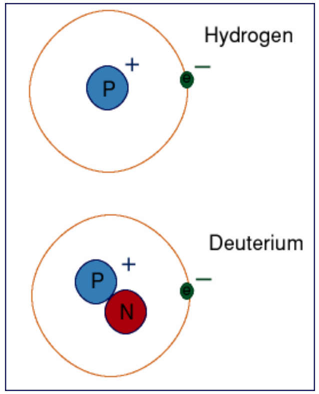
Vitalij L. Ginzburg

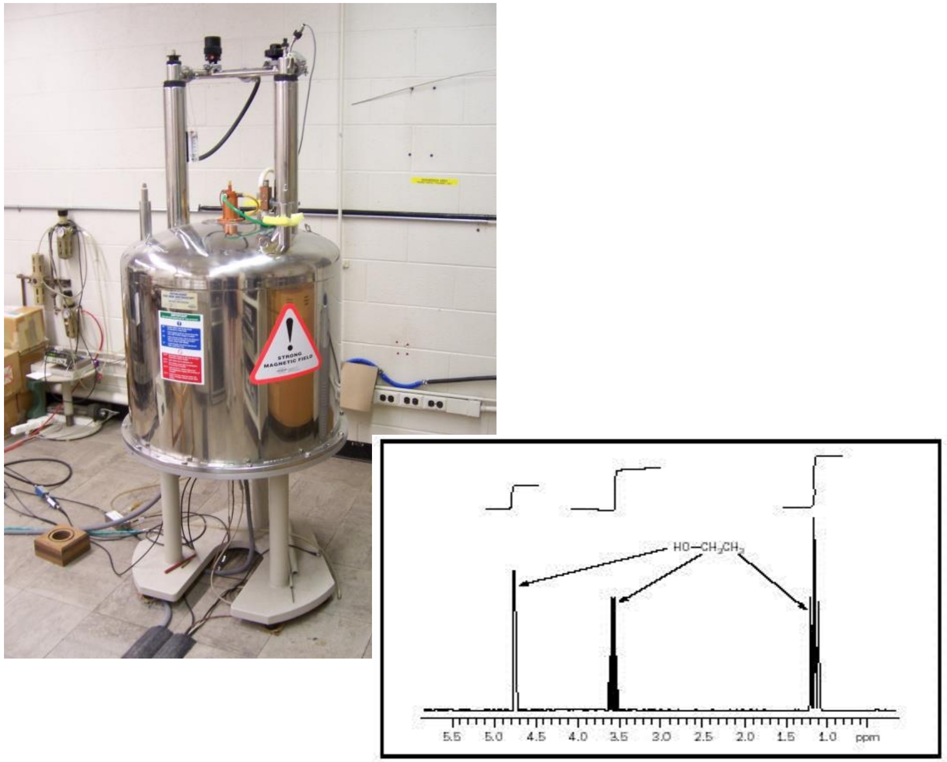
Martin Karplus

From: Bruker SpinReport, Vol 153

NMR Spectroscopy

- Nuclear
- Magnetic
- Resonance

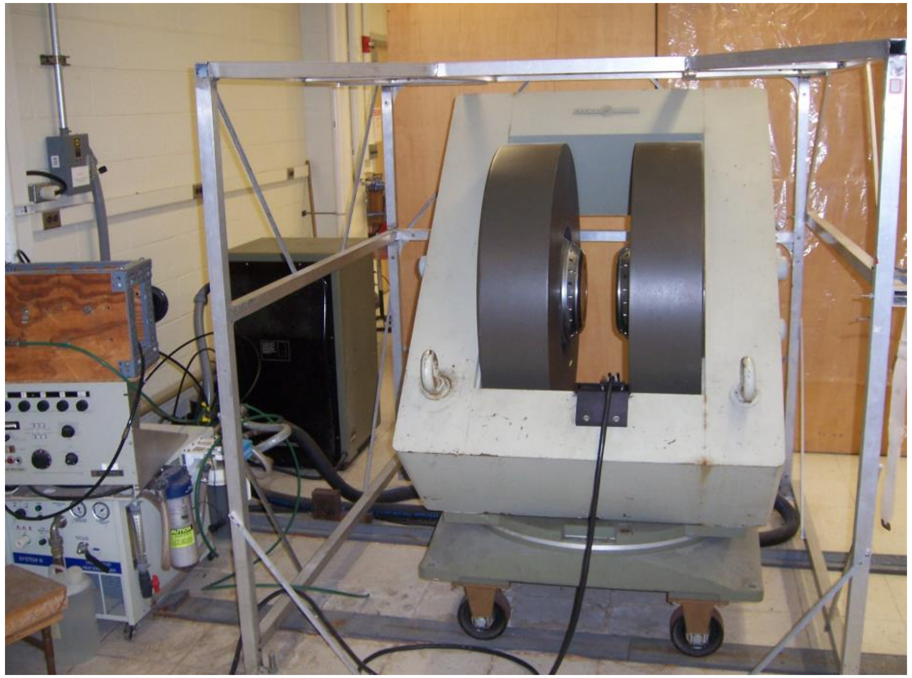


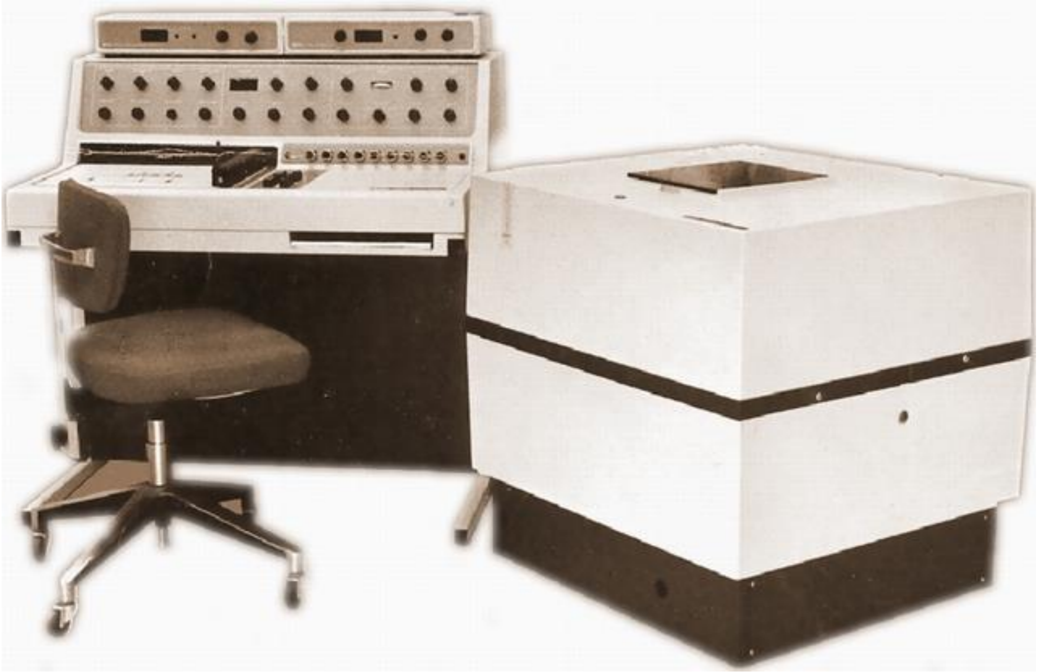


NMR Magnets

Magnet Types:

- Permanent Magnets: low fields (<2.5 Tesla)
- Electromagnets: high fields
  poor stability and homogeneity





NMR Magnets

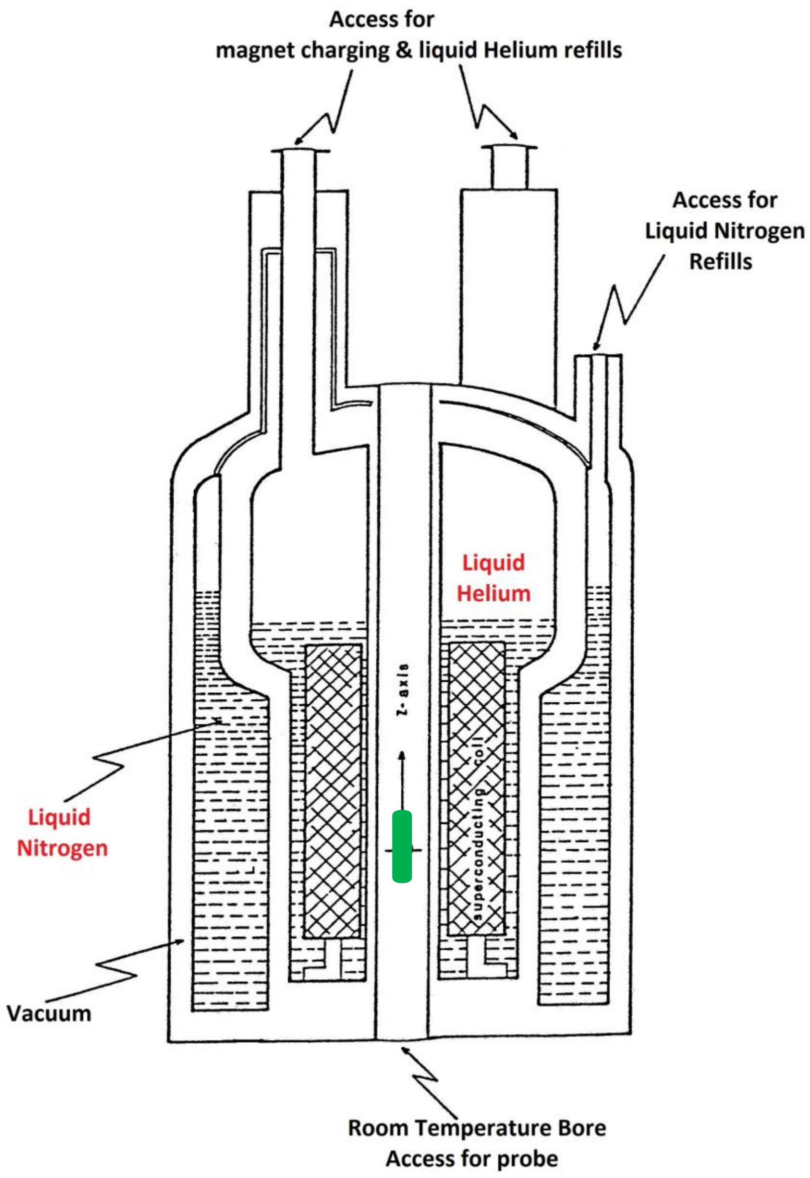
Magnet Types:

- Superconducting Magnets (aka. Cryomagnets): high, stable, and homogeneous fields

- Expensive to purchase, operate, and maintain.

Weekly Nitrogen refills (left) and monthly Helium refills (right) are required.

NMR Magnets



Cross section of a superconducting magnet:

The superconducting coil is cooled to 4 Kelvin in a bath of liquid Helium.

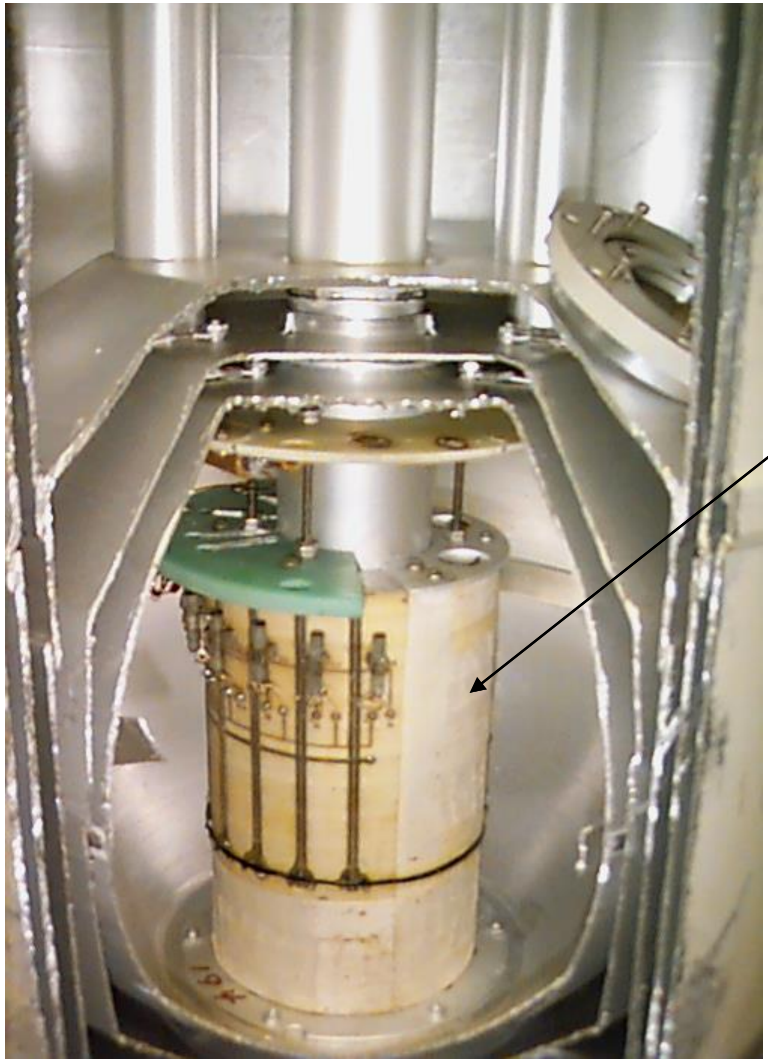
The Helium vessel is surrounded by a container of liquid Nitrogen (77K).

Helium and Nitrogen containers are separated and surrounded by vacuum.

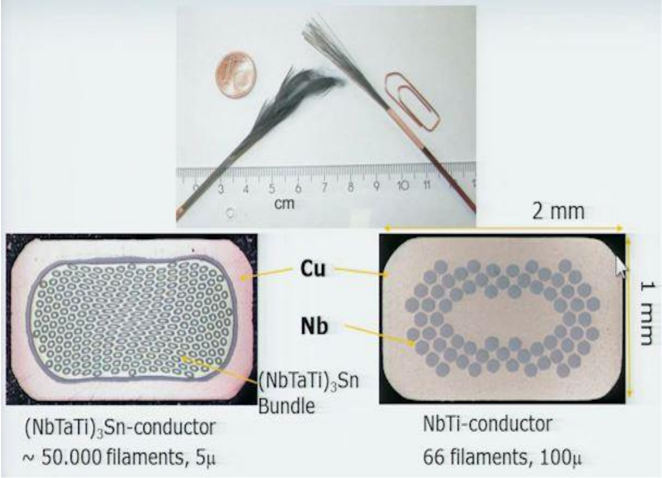
A probe is installed in the bottom of the magnet bore and samples can be inserted from the top of the magnet.

NMR Magnets

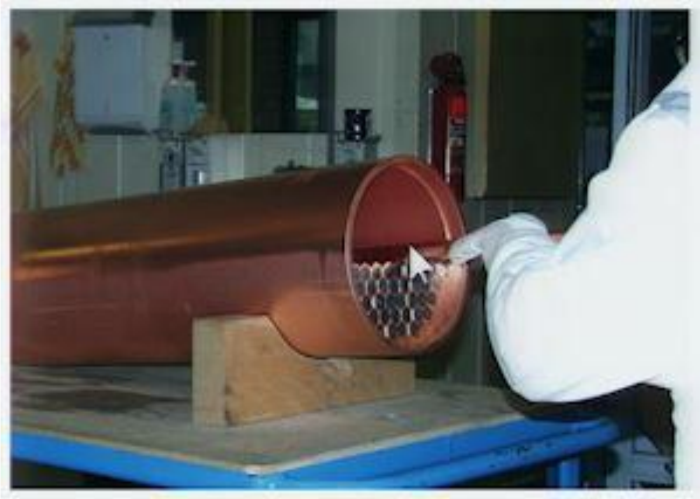
Inside a superconducting magnet

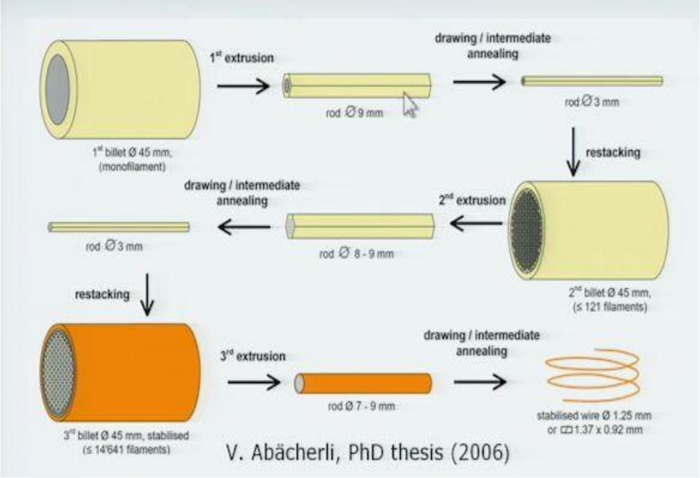


Bundled wires with superconducting filaments



Manufacturing superconducting wires





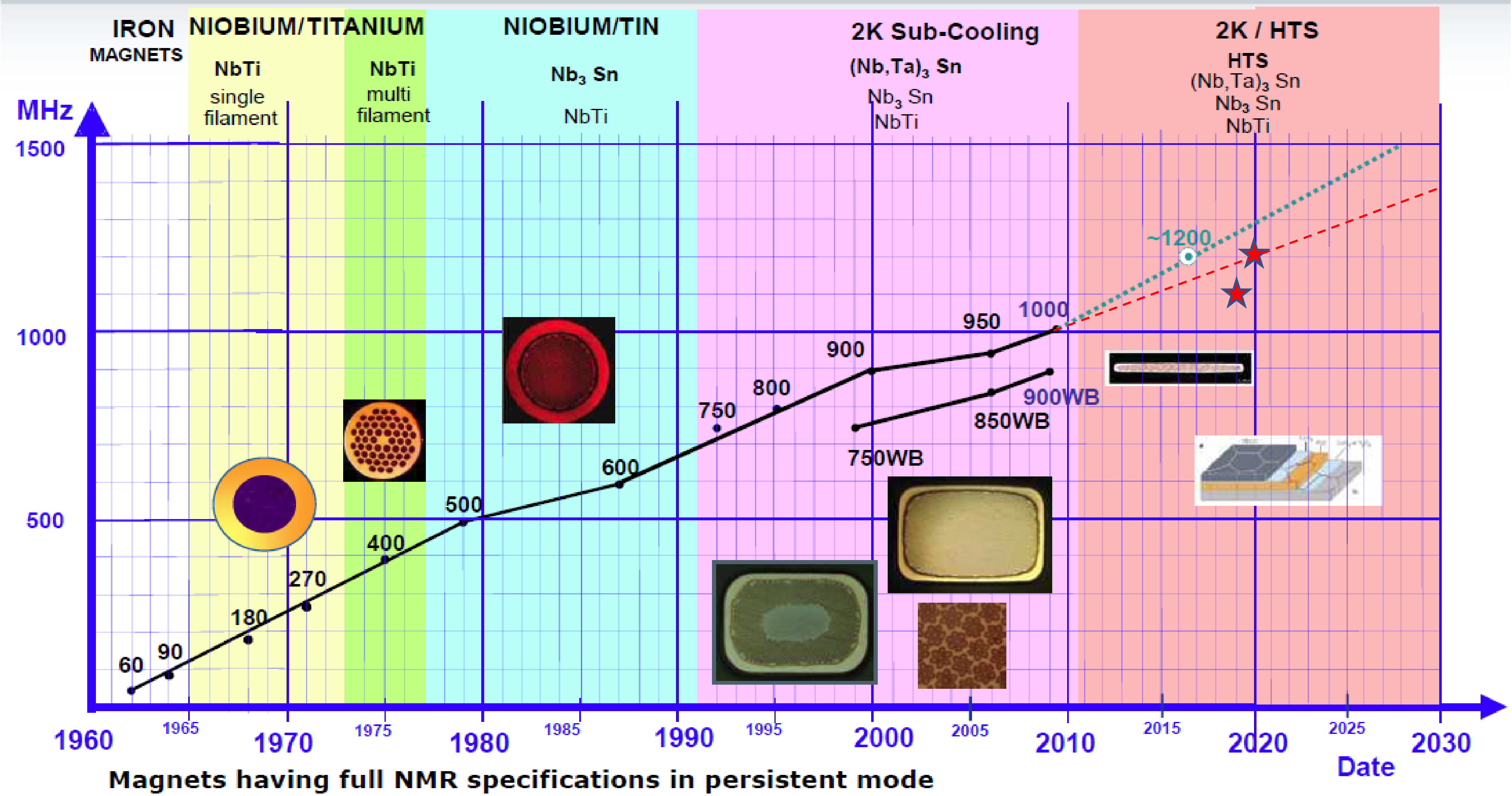
V. Abächerli, PhD thesis (2006)

NMR Magnets

High Field NMR Milestones

Empirical Law: ***5 years per 100 MHz step***

BRUKER



Magnets having full NMR specifications in persistent mode

NMR Magnets

BU presently has five NMR Spectrometers:

							Pharm.:
Magnet Field:	B_0	=	2.35 T	7.05 T	9.4 T	14.1 T	9.4 T
^{1}H Frequency:	ν_0	=	100 MHz	300 MHz	400 MHz	600 MHz	400 MHz
Location:			S2	S2	SN	SN	CE
liquid/solid:			Liquids	L&S	L&S	L&S	Liquids

All our instruments have superconducting magnets.

Dangers:

- High magnetic fields
  - may cause pacemakers, insulin pumps, and other electronic medical devices to fail,
  - may erase hard disks, credit cards, and your BU ID,
  - will attract ferromagnetic objects and turn them into dangerous projectiles.

- Cryogens (liquid Nitrogen and Helium)
  - will cause burns when contacting eyes or skin,
  - will displace breathable air in case of a magnet quench.
  - https://www.youtube.com/watch?v=d-G3Kg-7n_M
  - https://www.youtube.com/watch?v=6-sxe79Y5Nc
  - https://www.youtube.com/watch?v=Pu7eY8tRE_c

NMR Magnets

Magnet quench:

An energized magnet can fail when a segment of the superconducting wire becomes resistive due to localized heating.

The entire energy (Mega Joules) stored in the magnet coil is released instantaneously and vaporizes the entire volume of liquid Helium within minutes.

14.1 Tesla magnet quench

Coil current: 183 Amperes

Energy: 774 kJ

NMR Magnets

Accidents:

FLASHBACK

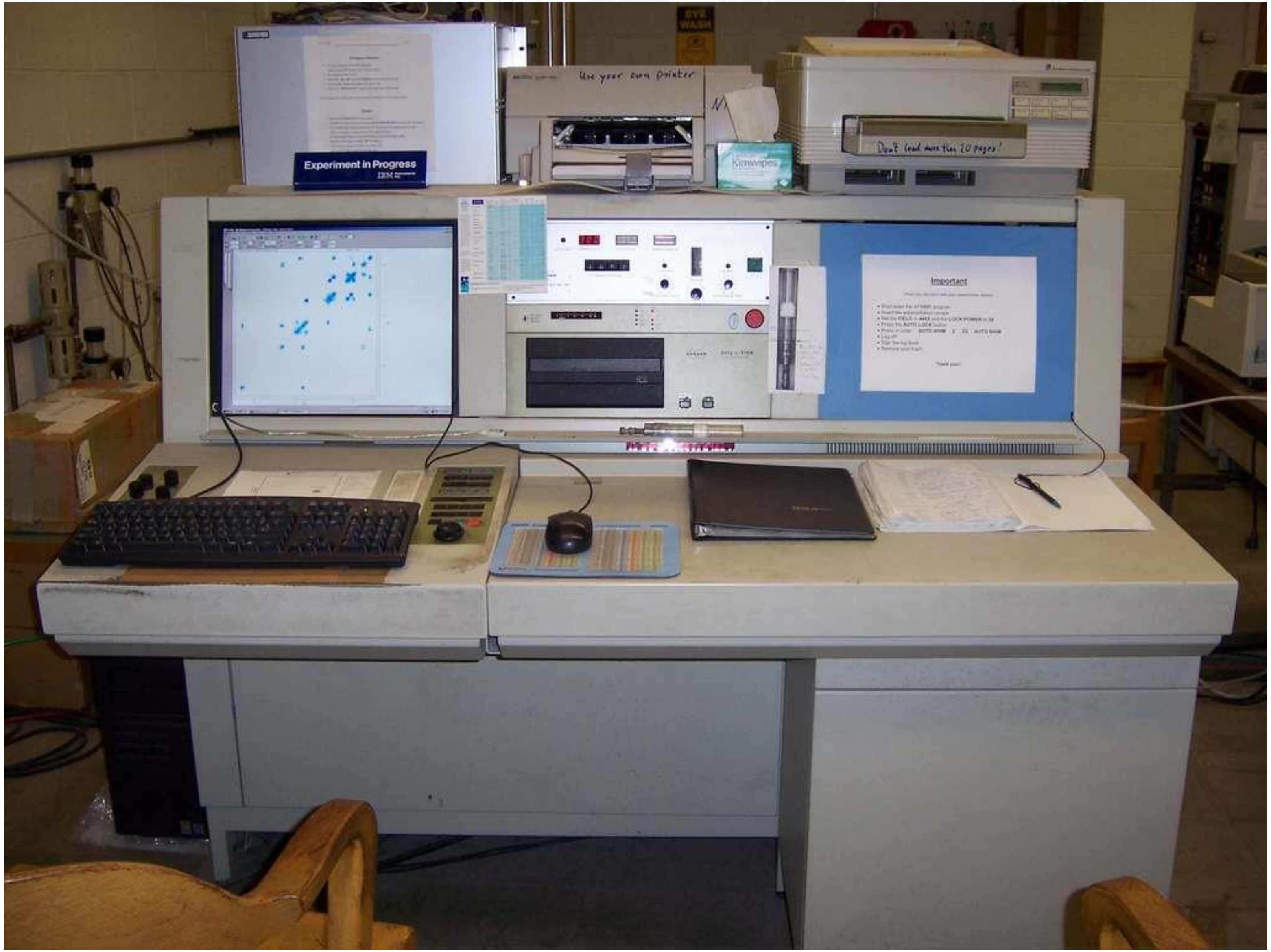
Mirror's November 11, 2014, exclusive report on the accident

Mumbai Mirror

50 DAYS TO NEW YEAR'S

TWO STUCK TO MRI MACHINE FOR 4 HRS

NMR Consoles



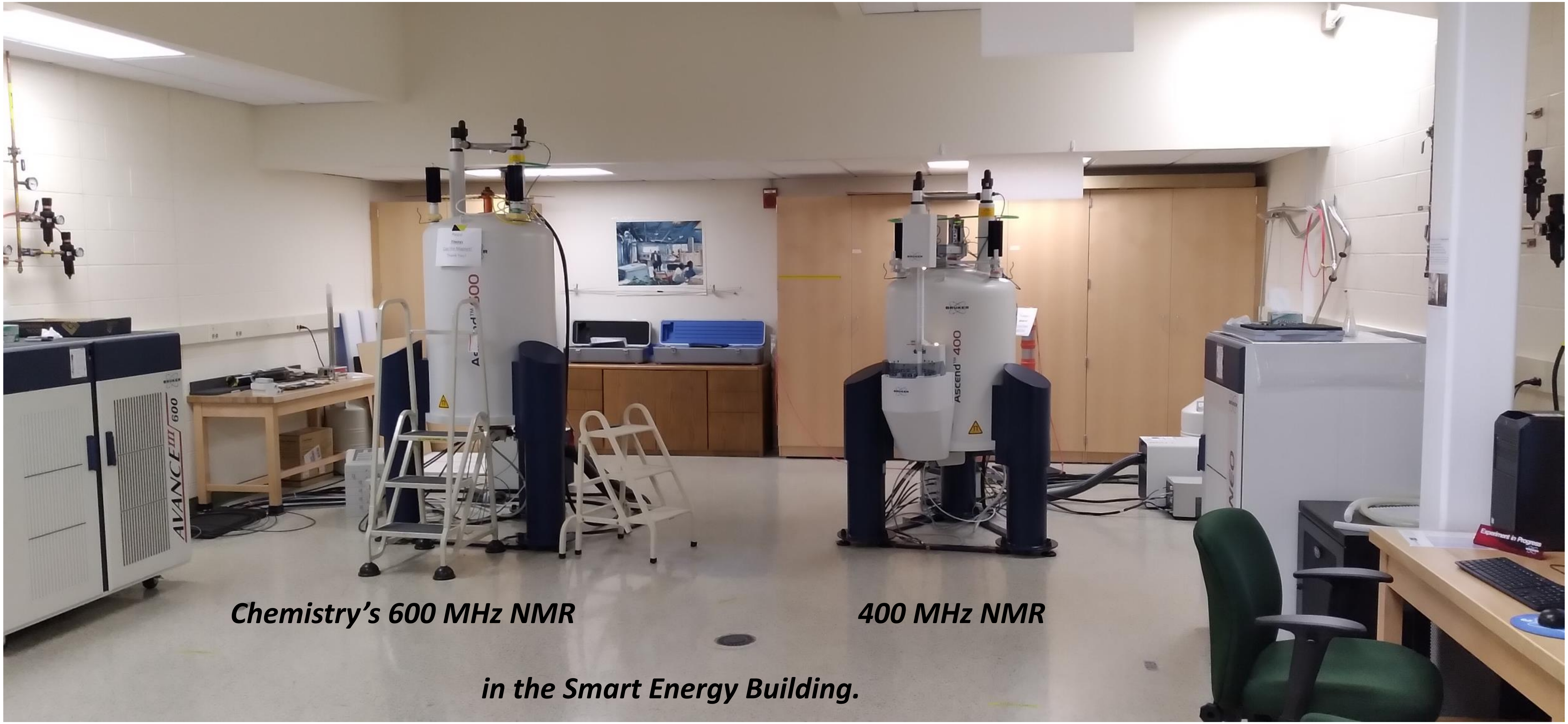
NMR Manufacturers:

BRUKER (DE,CH)

VARIAN Agilent Technologies (US)

JEOL Stability · Performance · Productivity (Japan)

Modern NMR Spectrometers

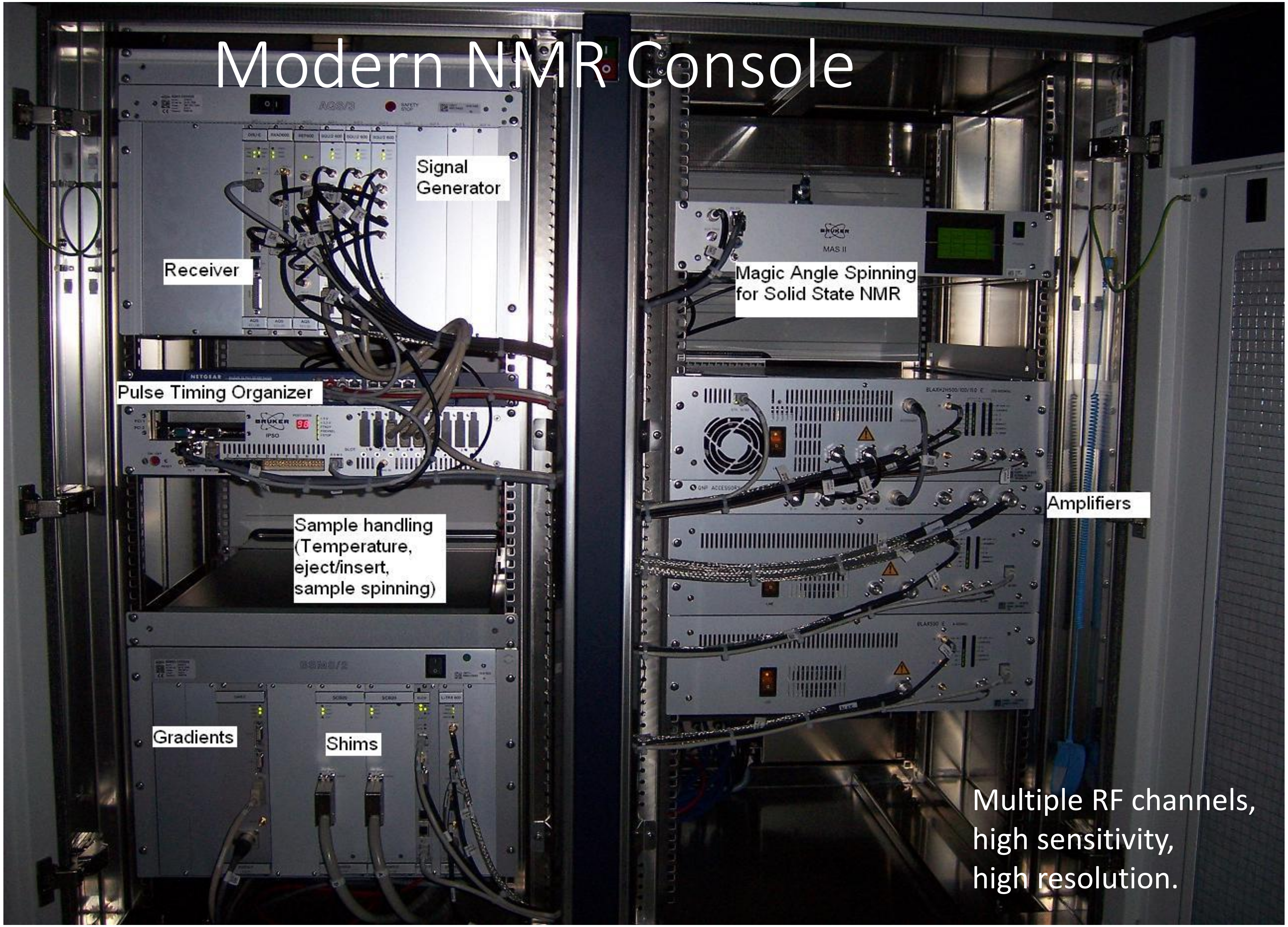


Chemistry's 600 MHz NMR

400 MHz NMR

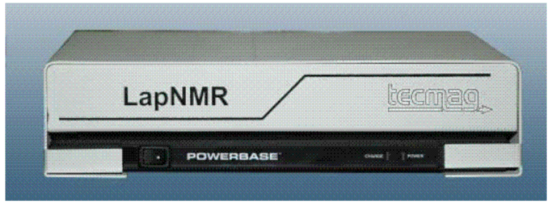
in the Smart Energy Building.

Modern NMR Console

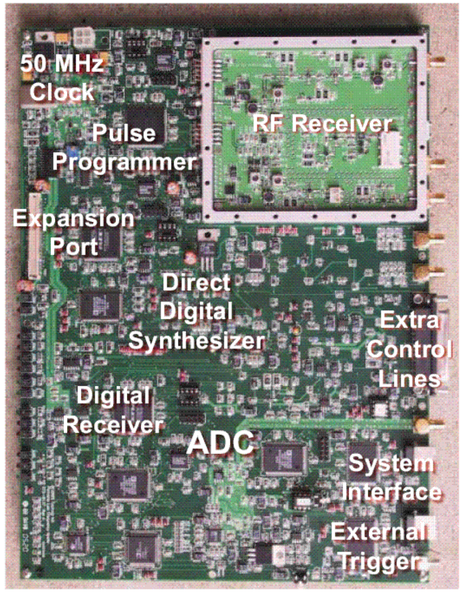


Multiple RF channels,
high sensitivity,
high resolution.

Benchtop NMR Systems



LapNMR with battery, enclosure and AC power adapter for portable usage



… can use existing magnets.

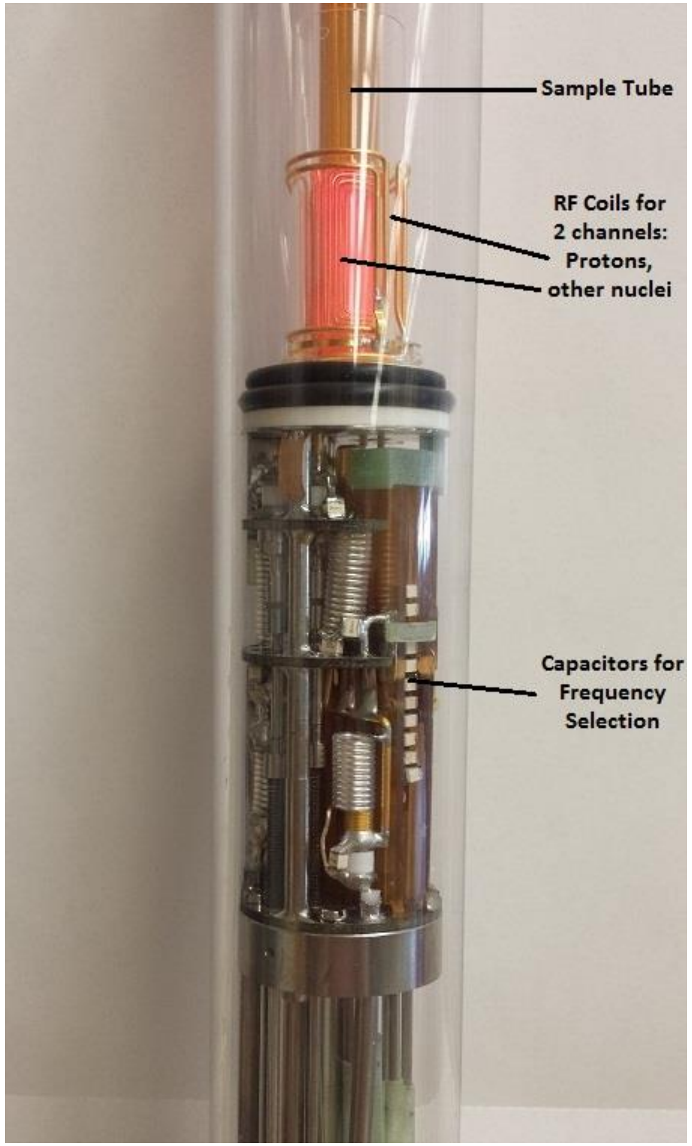
^{1}H typically 60-100 MHz
(1.4 – 2.3 T permanent magnet)

Nuclei: ^{1}H (+ 1 option: C, P, or F)
Low resolution,
Low sensitivity,
Low power.

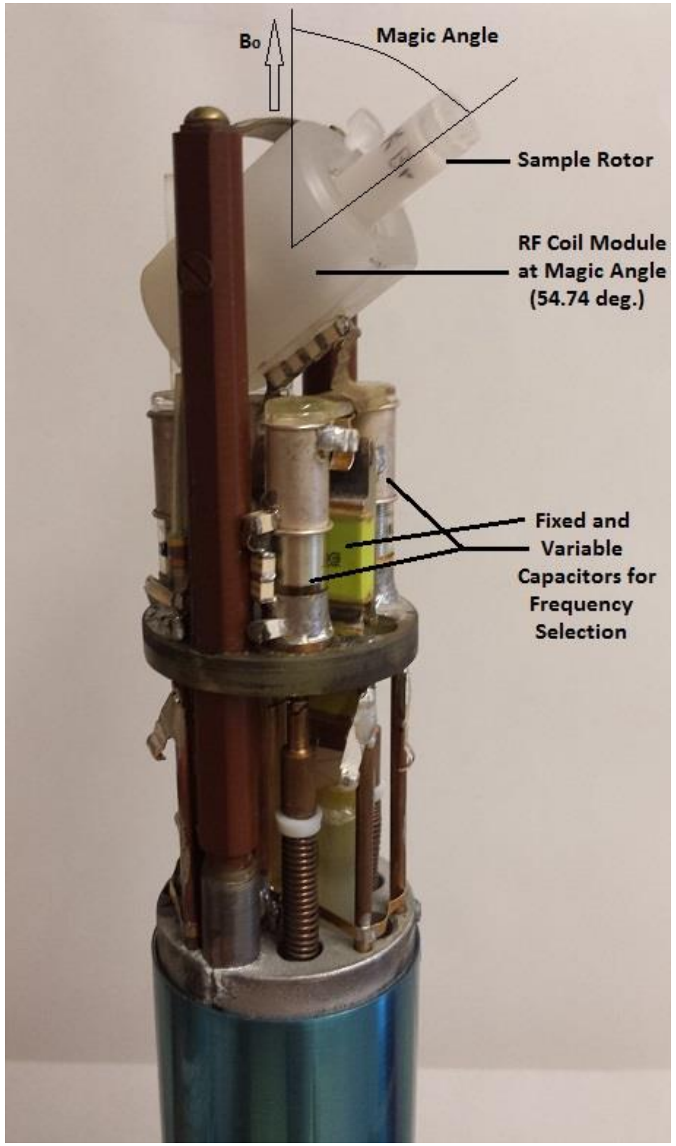
Suitable for teaching labs.
Limited usefulness for research.

NMR Probes …

Liquids



Solids



… and

Samples

Recent NMR Progress

2016: First 23.5 Tesla magnet (1 GHz)
Bayreuth University, Germany.

2019: First 1.1 GHz NMR
St. Jude Hospital, Memphis TN.

2020: First 1.2 GHz NMR
Florence University, Italy

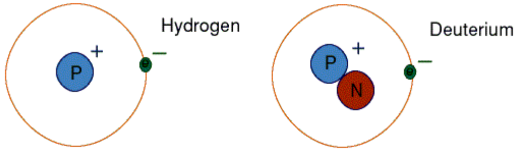
Nine 1.2 GHz NMRs have currently been ordered (in Europe).

Topics:

- Part I – Introduction
  - History of NMR
  - NMR Hardware
- **Part II – NMR Theory**
  - **Nuclei – Spin – Magnetic Moments**
  - **Shielding – Chemical Shifts**
  - **Coupling – Molecular Structure**
  - **Relaxation – Linewidth**
- Part III NMR Experiments
  - Sample preparation
  - Solution vs. Solid State NMR
  - Techniques for optimizing Solid State NMR
  - Research Examples

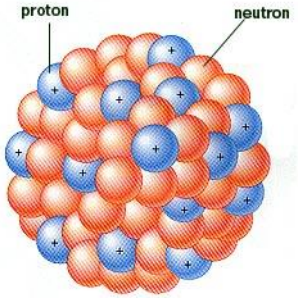
Nuclear Spin Quantum Number (I)

- Nuclei must possess a "non-zero spin" to be NMR active. Can we calculate I?
- Nucleus = Protons + Neutrons
  Mass m = p + n



Recap:
(mass) m z (charge)
(atomic #) p X a (# of atoms)

- Even p + even n → **I = 0 → no NMR signals** (^{12}C, ^{16}O)
- Odd p + odd n → **integer I**
  I = 1: ^{2}H, ^{14}N
  I = 3: ^{10}B
  I = 6: ^{50}V

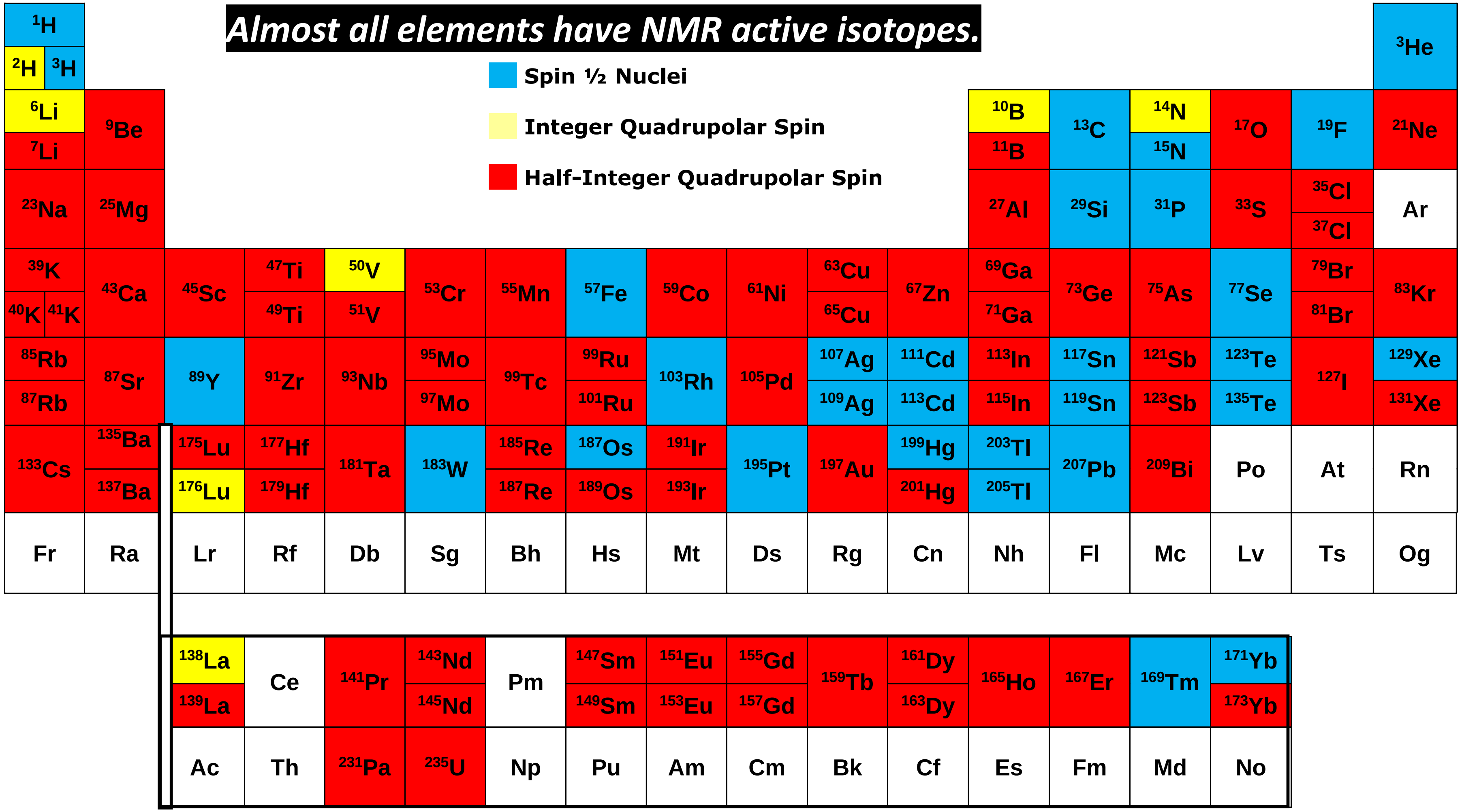


- All other nuclei: **half-integer I** (1/2, 3/2, 5/2, …)
  I = 7/2: ^{51}V
  I = 5/2: ^{17}O, ^{27}Al
  I = 3/2: ^{11}B, ^{23}Na
  I = 1/2: ^{1}H, ^{13}C, ^{15}N, ^{19}F, ^{29}Si, ^{31}P, ^{119}Sn

○ Isotopes with near 100 % natural abundance

- Nuclei with **I = ½** will produce the sharpest signals (high resolution NMR).
  Nuclei with **I > ½** are called **quadrupolar nuclei**, as they possess an electrical quadrupole.
  ➔ broad signals

Periodic Table of the NMR Isotopes



Almost all elements have NMR active isotopes.

🟦 **Spin ½ Nuclei**

🟨 **Integer Quadrupolar Spin**

🟥 **Half-Integer Quadrupolar Spin**

I	II	III	IV	V	VI	VII	VIII	IX	X	XI	XII	XIII	XIV	XV	XVI	XVII	XVIII
^{1}H ^{2}H ^{3}H																	^{3}He
^{6}Li ^{7}Li	^{9}Be											^{10}B ^{11}B	^{13}C	^{14}N ^{15}N	^{17}O	^{19}F	^{21}Ne
^{23}Na	^{25}Mg											^{27}Al	^{29}Si	^{31}P	^{33}S	^{35}Cl ^{37}Cl	Ar
^{39}K ^{40}K ^{41}K	^{43}Ca	^{45}Sc	^{47}Ti ^{49}Ti	^{50}V ^{51}V	^{53}Cr	^{55}Mn	^{57}Fe	^{59}Co	^{61}Ni	^{63}Cu ^{65}Cu	^{67}Zn	^{69}Ga ^{71}Ga	^{73}Ge	^{75}As	^{77}Se	^{79}Br ^{81}Br	^{83}Kr
^{85}Rb ^{87}Rb	^{87}Sr	^{89}Y	^{91}Zr	^{93}Nb	^{95}Mo ^{97}Mo	^{99}Tc	^{99}Ru ^{101}Ru	^{103}Rh	^{105}Pd	^{107}Ag ^{109}Ag	^{111}Cd ^{113}Cd	^{113}In ^{115}In	^{117}Sn ^{119}Sn	^{121}Sb ^{123}Sb	^{123}Te ^{135}Te	^{127}I	^{129}Xe ^{131}Xe
^{133}Cs	^{135}Ba ^{137}Ba	^{175}Lu ^{176}Lu	^{177}Hf ^{179}Hf	^{181}Ta	^{183}W	^{185}Re ^{187}Re	^{187}Os ^{189}Os	^{191}Ir ^{193}Ir	^{195}Pt	^{197}Au	^{199}Hg ^{201}Hg	^{203}Tl ^{205}Tl	^{207}Pb	^{209}Bi	Po	At	Rn
Fr	Ra	Lr	Rf	Db	Sg	Bh	Hs	Mt	Ds	Rg	Cn	Nh	Fl	Mc	Lv	Ts	Og
		^{138}La ^{139}La	Ce	^{141}Pr	^{143}Nd ^{145}Nd	Pm	^{147}Sm ^{149}Sm	^{151}Eu ^{153}Eu	^{155}Gd ^{157}Gd	^{159}Tb	^{161}Dy ^{163}Dy	^{165}Ho	^{167}Er	^{169}Tm	^{171}Yb ^{173}Yb		
		Ac	Th	^{231}Pa	^{235}U	Np	Pu	Am	Cm	Bk	Cf	Es	Fm	Md	No		

Notes: Elements ***without naturally occurring*** NMR-active isotopes are left uncolored.
Most Spin-½ isotopes are preferred over quadrupolar (I > ½) isotopes.
In Solid State NMR, half-integer spins are preferred over integer spins.

Adapted from: Harris RK, Becker ED, Cabral de Menezes SM, Goodfellow R, Granger P: NMR Nomenclature. Nuclear Spin Properties and Conventions for Chemical Shifts (IUPAC Recommendations 2001). Pure Appl Chem 2001; 73:1795-1818.

Nuclear Spin Quantum Number (I)

- High natural abundance is desirable, but …

  … "Spin-½" nuclei are preferred because they produce the sharpest signals. (Linewidth: few Hz in liquids)
  … Quadrupolar Nuclei (I > ½) have extremely broad signals. (Linewidth: kHz/MHz)
  … Elements with less abundant isotopes may be chemically or biologically important, i.e. ^{13}C, ^{15}N, ^{17}O.

Isotope	Spin I	Nat. Abundance	Sensitivity (Receptivity)	Techniques
^{1}H	½	99.98 %	5700	Direct Observation
^{12}C	0	98.89 %	0	No Signal
^{13}C	½	1.11 %	1	Direct & Indirect Observation
^{14}N	1	99.63 %	2.1	Direct Observation (large molecules are "invisible")
^{15}N	½	0.37 %	0.02	Isotopic Labeling, Indirect Observation

  The sensitivity of "Spin-½" nuclei can be increased either chemically (isotopic enrichment) or by special NMR techniques, i.e. Polarization Transfer (Cross Polarization, DEPT, INEPT, HETCOR), indirect detection through ^{1}H (HSQC, HMBC).

- Solids NMR spectra of "Spin-½" nuclei *can* produce sharp peaks. (tens/hundreds of Hz)

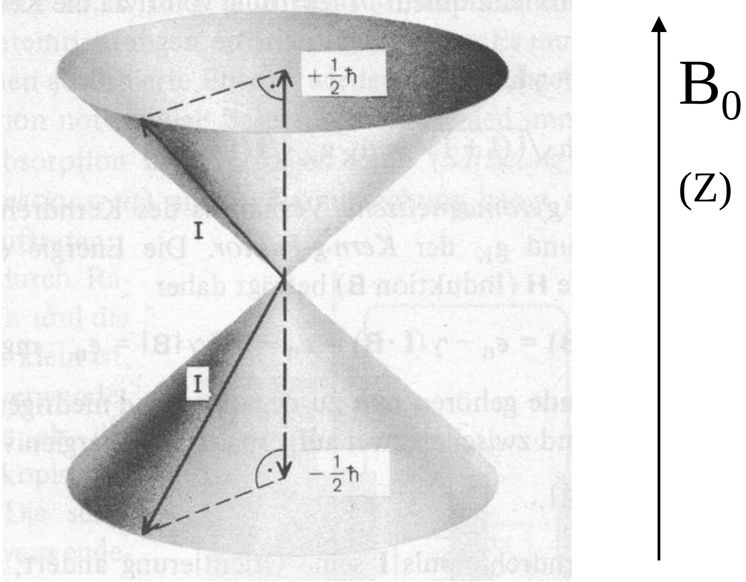
- Solids NMR spectra of half-integer-spin quadrupolar nuclei have
  a moderately broad central transition (kHz) and extremely broad satellite transitions (MHz).

- Solids NMR spectra of integer-spin quadrupolar nuclei have broad satellite transitions (MHz) and no central transition.

- In Solid State NMR "broad" does not equal "bad"!
  Line width and signal shape can contain a wealth of structural and dynamic information about the molecule or material.

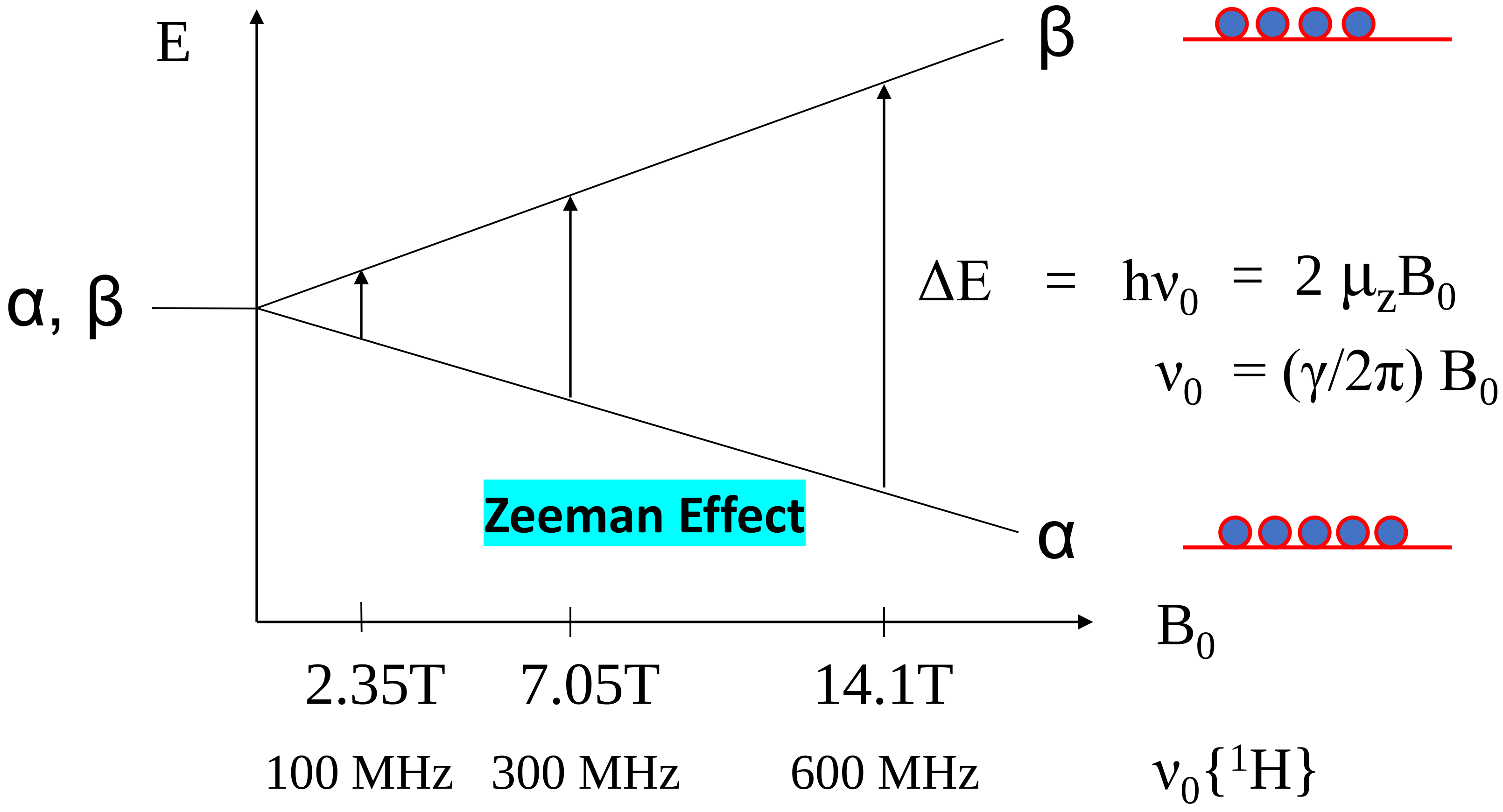
Magnetic Spin Quantum Number (M)

- General condition: **<u>2I + 1</u>** spin states
  $M_I = I, I-1, I-2, \ldots, -I$ i.e.: $I=2$, $M= 2,1,0,-1,-2$
- "Spin ½" case ^{1}H:
  - $M_I = +\frac{1}{2}$ (α) and $M_I = -\frac{1}{2}$ (β)
- Magnetic Moments (Z components) are quantized:
  $\mu_Z = \gamma\hbar M_I = \pm\gamma\hbar I = \pm\frac{1}{2}\gamma\hbar$



Spins in a Magnetic Field

- The α and β states possess the same energies (are degenerate) unless placed into a magnetic field:



$$\Delta E = h\nu_0 = 2\,\mu_z B_0$$

$$\nu_0 = (\gamma/2\pi)\,B_0$$

Magnetic Spin Quantum Number (M)

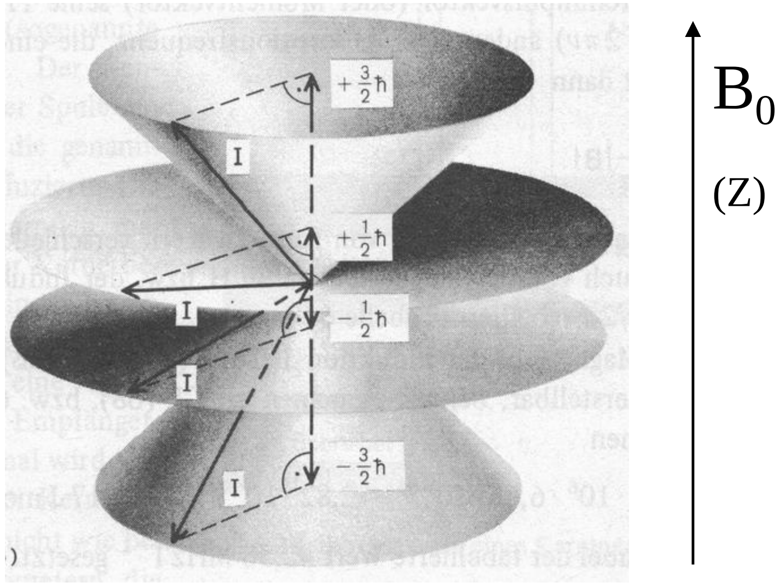
- General condition: **2I + 1** spin states

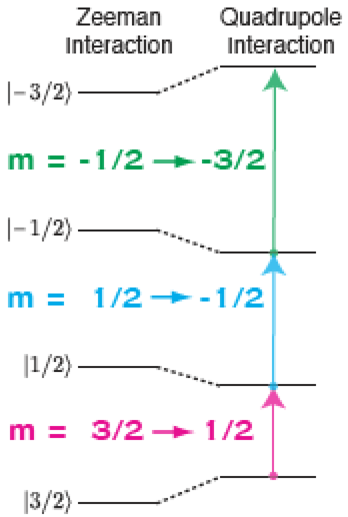
  $M_I = I, I-1, I-2, \ldots, -I$

- "Spin 3/2" case ^{11}B:
  - $M_I = +3/2,\ +1/2,\ -1/2,\ -3/2.$

- Magnetic Moment (Z component):

  $\mu_Z = \gamma\hbar M_I = \pm\gamma\hbar I = \pm\tfrac{1}{2}\gamma\hbar\ ,\ \pm 3/2\,\gamma\hbar$



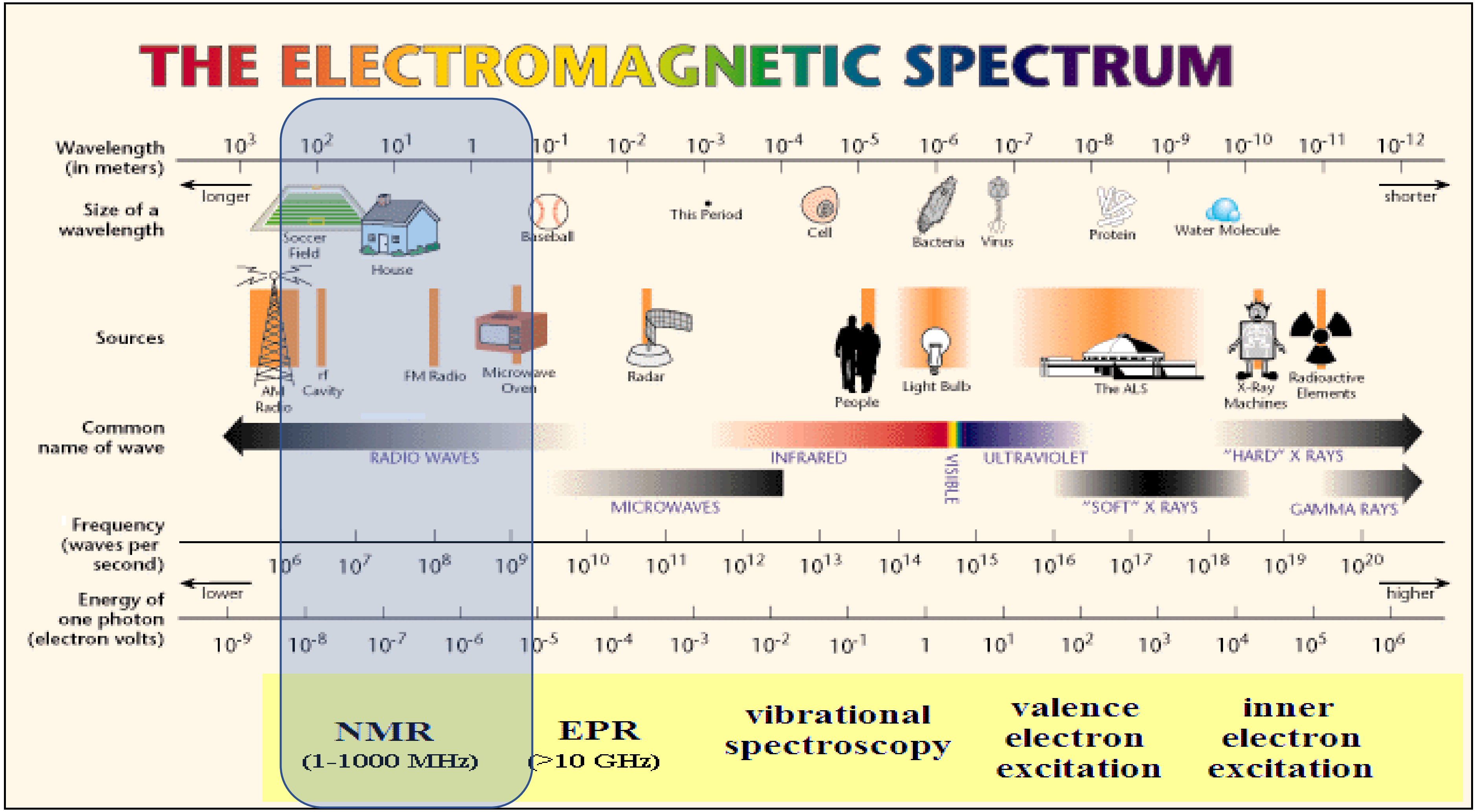


Satellite Transition

Central Transition

Satellite Transition

$$\nu_q = \frac{3Cq}{2I(2I-1)}$$



Boltzmann factor:

$$\frac{N_\alpha}{N_\beta} = exp\left(\frac{-\Delta E}{kT}\right) = 1.00002$$

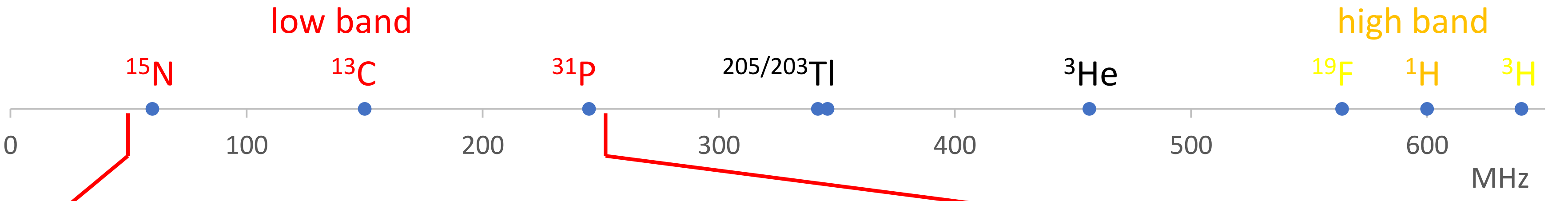
(at 100 MHz)

Only 0.001% of all spins are detected.

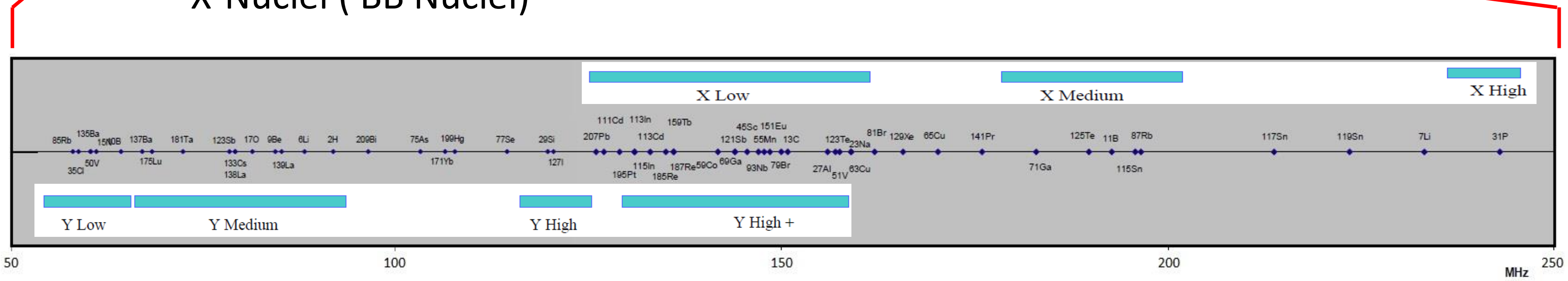
NMR has a very low sensitivity compared to other techniques!

EM Spectrum

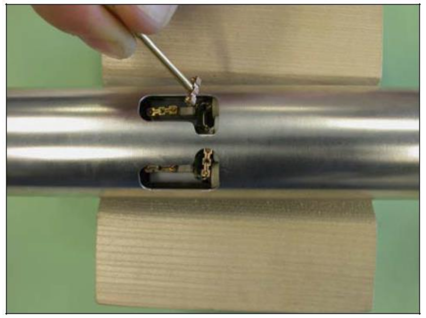
- NMR Frequency Range
  - Resonance Frequencies of Selected Nuclei at $B_0 = 14.1$ Tesla



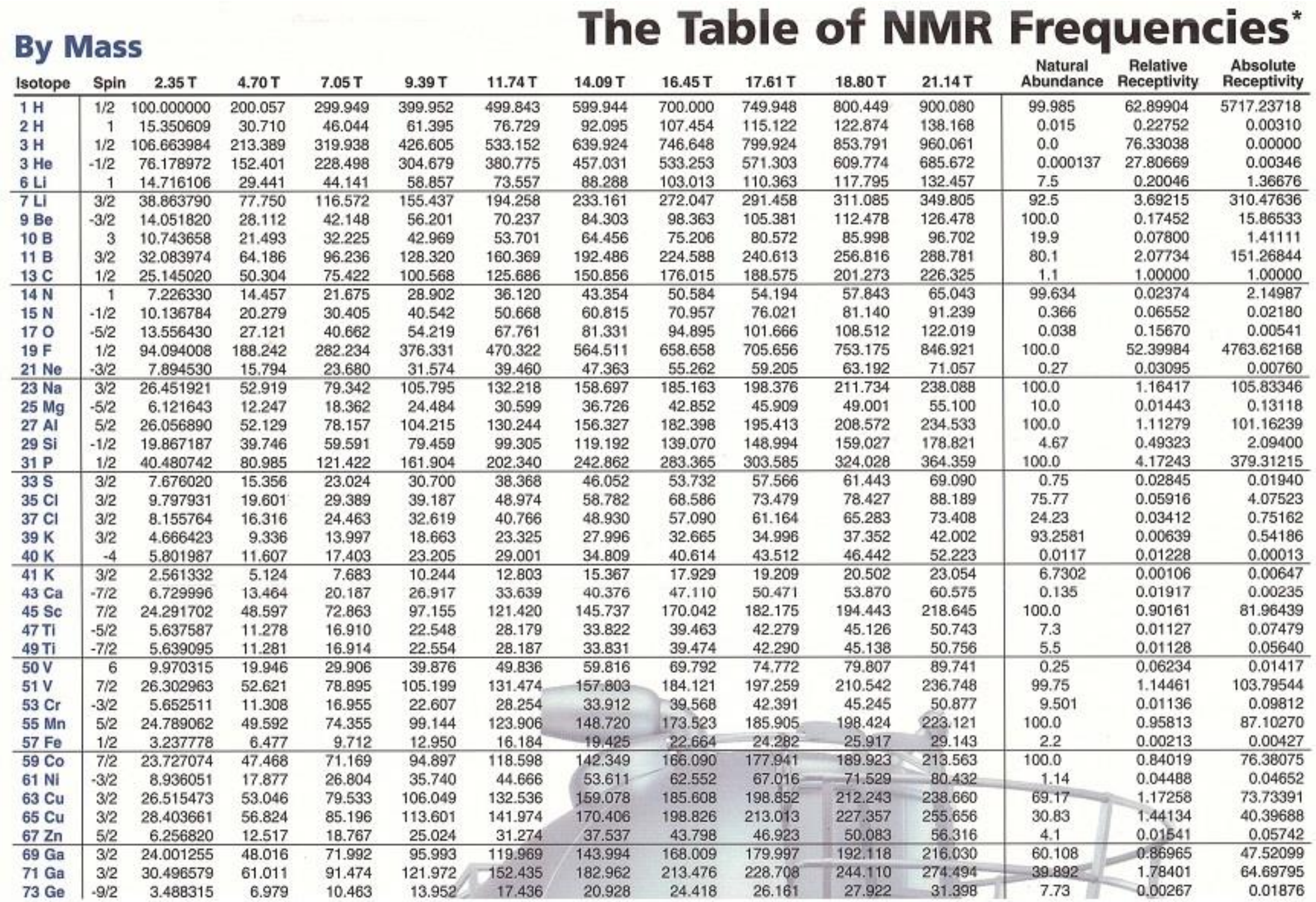
X-Nuclei (BB Nuclei)



Our 600 MHz Solids probe is a Triple-Nucleus probe (H,X,Y) with selectable tuning ranges for various nucleus combinations.



EM Spectrum

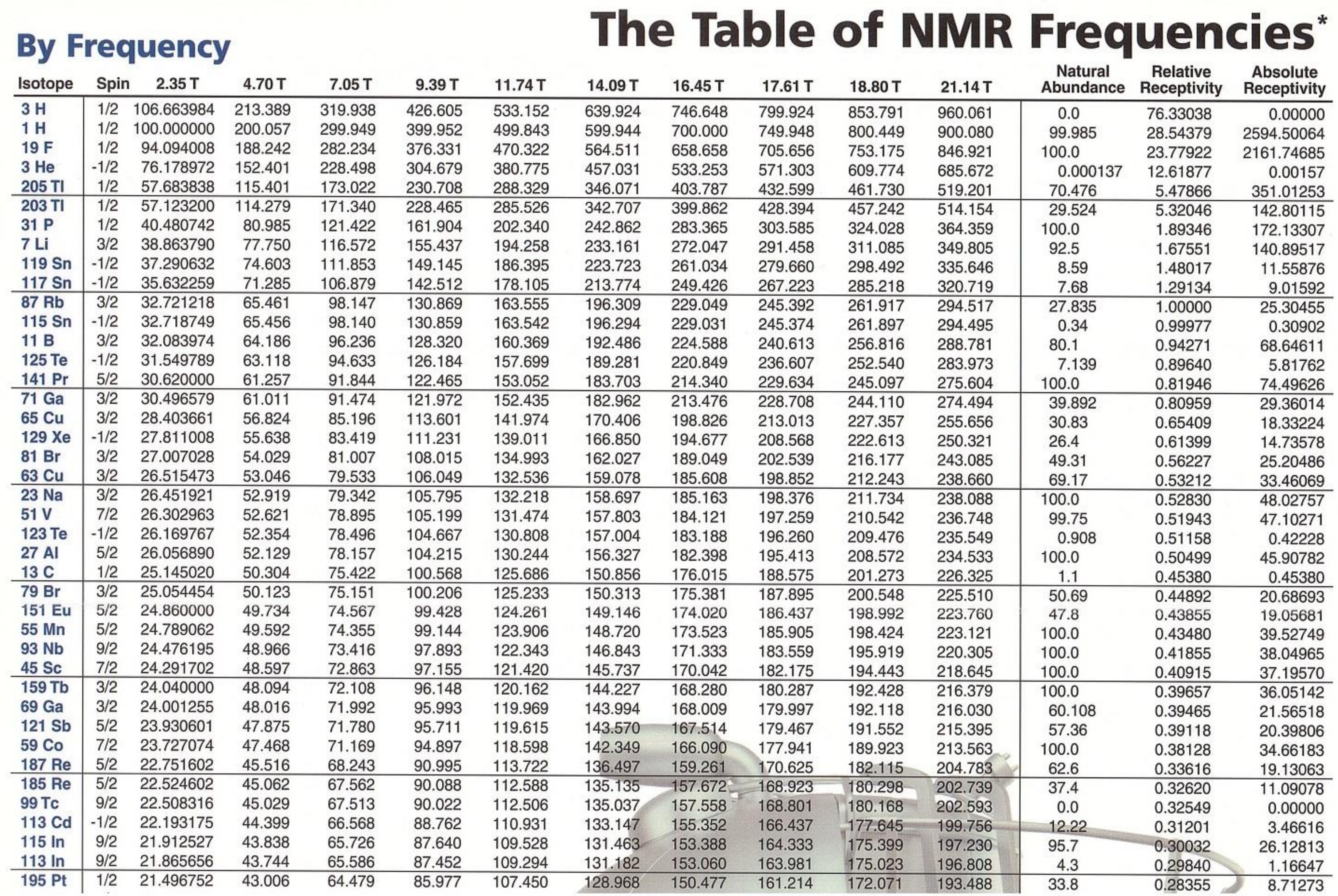


By Mass

The Table of NMR Frequencies*

Isotope	Spin	2.35 T	4.70 T	7.05 T	9.39 T	11.74 T	14.09 T	16.45 T	17.61 T	18.80 T	21.14 T	Natural Abundance	Relative Receptivity	Absolute Receptivity
1 H	1/2	100.000000	200.057	299.949	399.952	499.843	599.944	700.000	749.948	800.449	900.080	99.985	62.89904	5717.23718
2 H	1	15.350609	30.710	46.044	61.395	76.729	92.095	107.454	115.122	122.874	138.168	0.015	0.22752	0.00310
3 H	1/2	106.663984	213.389	319.938	426.605	533.152	639.924	746.648	799.924	853.791	960.061	0.0	76.33038	0.00000
3 He	-1/2	76.178972	152.401	228.498	304.679	380.775	457.031	533.253	571.303	609.774	685.672	0.000137	27.80669	0.00346
6 Li	1	14.716106	29.441	44.141	58.857	73.557	88.288	103.013	110.363	117.795	132.457	7.5	0.20046	1.36676
7 Li	3/2	38.863790	77.750	116.572	155.437	194.258	233.161	272.047	291.458	311.085	349.805	92.5	3.69215	310.47636
9 Be	-3/2	14.051820	28.112	42.148	56.201	70.237	84.303	98.363	105.381	112.478	126.478	100.0	0.17452	15.86533
10 B	3	10.743658	21.493	32.225	42.969	53.701	64.456	75.206	80.572	85.998	96.702	19.9	0.07800	1.41111
11 B	3/2	32.083974	64.186	96.236	128.320	160.369	192.486	224.588	240.613	256.816	288.781	80.1	2.07734	151.26844
13 C	1/2	25.145020	50.304	75.422	100.568	125.686	150.856	176.015	188.575	201.273	226.325	1.1	1.00000	1.00000
14 N	1	7.226330	14.457	21.675	28.902	36.120	43.354	50.584	54.194	57.843	65.043	99.634	0.02374	2.14987
15 N	-1/2	10.136784	20.279	30.405	40.542	50.668	60.815	70.957	76.021	81.140	91.239	0.366	0.06552	0.02180
17 O	-5/2	13.556430	27.121	40.662	54.219	67.761	81.331	94.895	101.666	108.512	122.019	0.038	0.15670	0.00541
19 F	1/2	94.094008	188.242	282.234	376.331	470.322	564.511	658.658	705.656	753.175	846.921	100.0	52.39984	4763.62168
21 Ne	-3/2	7.894530	15.794	23.680	31.574	39.460	47.363	55.262	59.205	63.192	71.057	0.27	0.03095	0.00760
23 Na	3/2	26.451921	52.919	79.342	105.795	132.218	158.697	185.163	198.376	211.734	238.088	100.0	1.16417	105.83346
25 Mg	-5/2	6.121643	12.247	18.362	24.484	30.599	36.726	42.852	45.909	49.001	55.100	10.0	0.01443	0.13118
27 Al	5/2	26.056890	52.129	78.157	104.215	130.244	156.327	182.398	195.413	208.572	234.533	100.0	1.11279	101.16239
29 Si	-1/2	19.867187	39.746	59.591	79.459	99.305	119.192	139.070	148.994	159.027	178.821	4.67	0.49323	2.09400
31 P	1/2	40.480742	80.985	121.422	161.904	202.340	242.862	283.365	303.585	324.028	364.359	100.0	4.17243	379.31215
33 S	3/2	7.676020	15.356	23.024	30.700	38.368	46.052	53.732	57.566	61.443	69.090	0.75	0.02845	0.01940
35 Cl	3/2	9.797931	19.601	29.389	39.187	48.974	58.782	68.586	73.479	78.427	88.189	75.77	0.05916	4.07523
37 Cl	3/2	8.155764	16.316	24.463	32.619	40.766	48.930	57.090	61.164	65.283	73.408	24.23	0.03412	0.75162
39 K	3/2	4.666423	9.336	13.997	18.663	23.325	27.996	32.665	34.996	37.352	42.002	93.2581	0.00639	0.54186
40 K	-4	5.801987	11.607	17.403	23.205	29.001	34.809	40.614	43.512	46.442	52.223	0.0117	0.01228	0.00013
41 K	3/2	2.561332	5.124	7.683	10.244	12.803	15.367	17.929	19.209	20.502	23.054	6.7302	0.00106	0.00647
43 Ca	-7/2	6.729996	13.464	20.187	26.917	33.639	40.376	47.110	50.471	53.870	60.575	0.135	0.01917	0.00235
45 Sc	7/2	24.291702	48.597	72.863	97.155	121.420	145.737	170.042	182.175	194.443	218.645	100.0	0.90161	81.96439
47 Ti	-5/2	5.637587	11.278	16.910	22.548	28.179	33.822	39.463	42.279	45.126	50.743	7.3	0.01127	0.07479
49 Ti	-7/2	5.639095	11.281	16.914	22.554	28.187	33.831	39.474	42.290	45.138	50.756	5.5	0.01128	0.05640
50 V	6	9.970315	19.946	29.906	39.876	49.836	59.816	69.792	74.772	79.807	89.741	0.25	0.06234	0.01417
51 V	7/2	26.302963	52.621	78.895	105.199	131.474	157.803	184.121	197.259	210.542	236.748	99.75	1.14461	103.79544
53 Cr	-3/2	5.652511	11.308	16.955	22.607	28.254	33.912	39.568	42.391	45.245	50.877	9.501	0.01136	0.09812
55 Mn	5/2	24.789062	49.592	74.355	99.144	123.906	148.720	173.523	185.905	198.424	223.121	100.0	0.95813	87.10270
57 Fe	1/2	3.237778	6.477	9.712	12.950	16.184	19.425	22.664	24.282	25.917	29.143	2.2	0.00213	0.00427
59 Co	7/2	23.727074	47.468	71.169	94.897	118.598	142.349	166.090	177.941	189.923	213.563	100.0	0.84019	76.38075
61 Ni	-3/2	8.936051	17.877	26.804	35.740	44.666	53.611	62.552	67.016	71.529	80.432	1.14	0.04488	0.04652
63 Cu	3/2	26.515473	53.046	79.533	106.049	132.536	159.078	185.608	198.852	212.243	238.660	69.17	1.17258	73.73391
65 Cu	3/2	28.403661	56.824	85.196	113.601	141.974	170.406	198.826	213.013	227.357	255.656	30.83	1.44134	40.39688
67 Zn	5/2	6.256820	12.517	18.767	25.024	31.274	37.537	43.798	46.923	50.083	56.316	4.1	0.01541	0.05742
69 Ga	3/2	24.001255	48.016	71.992	95.993	119.969	143.994	168.009	179.997	192.118	216.030	60.108	0.86965	47.52099
71 Ga	3/2	30.496579	61.011	91.474	121.972	152.435	182.962	213.476	228.708	244.110	274.494	39.892	1.78401	64.69795
73 Ge	-9/2	3.488315	6.979	10.463	13.952	17.436	20.928	24.418	26.161	27.922	31.398	7.73	0.00267	0.01876

EM Spectrum



The Table of NMR Frequencies*

By Frequency

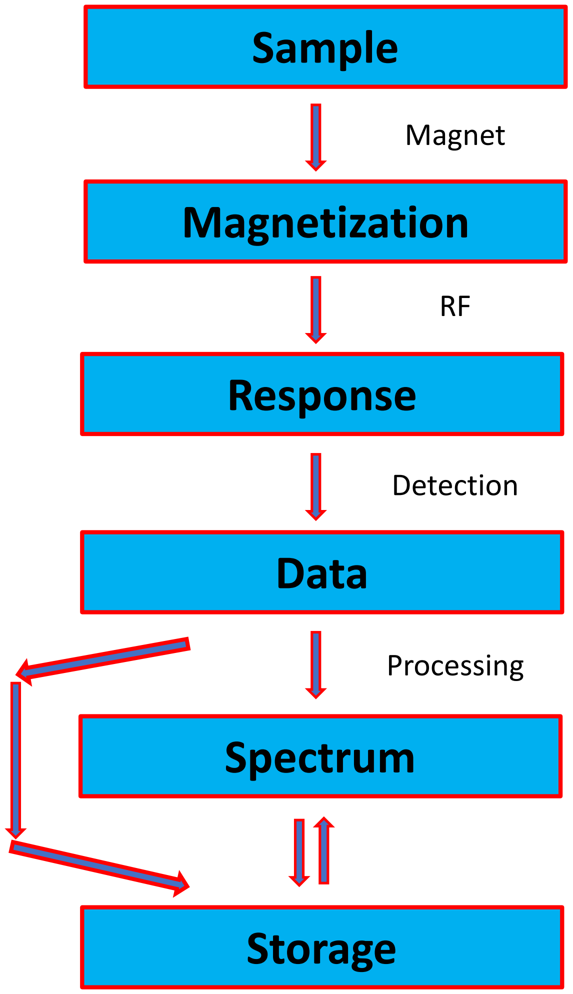
Isotope	Spin	2.35 T	4.70 T	7.05 T	9.39 T	11.74 T	14.09 T	16.45 T	17.61 T	18.80 T	21.14 T	Natural Abundance	Relative Receptivity	Absolute Receptivity
3 H	1/2	106.663984	213.389	319.938	426.605	533.152	639.924	746.648	799.924	853.791	960.061	0.0	76.33038	0.00000
1 H	1/2	100.000000	200.057	299.949	399.952	499.843	599.944	700.000	749.948	800.449	900.080	99.985	28.54379	2594.50064
19 F	1/2	94.094008	188.242	282.234	376.331	470.322	564.511	658.658	705.656	753.175	846.921	100.0	23.77922	2161.74685
3 He	-1/2	76.178972	152.401	228.498	304.679	380.775	457.031	533.253	571.303	609.774	685.672	0.000137	12.61877	0.00157
205 Tl	1/2	57.683838	115.401	173.022	230.708	288.329	346.071	403.787	432.599	461.730	519.201	70.476	5.47866	351.01253
203 Tl	1/2	57.123200	114.279	171.340	228.465	285.526	342.707	399.862	428.394	457.242	514.154	29.524	5.32046	142.80115
31 P	1/2	40.480742	80.985	121.422	161.904	202.340	242.862	283.365	303.585	324.028	364.359	100.0	1.89346	172.13307
7 Li	3/2	38.863790	77.750	116.572	155.437	194.258	233.161	272.047	291.458	311.085	349.805	92.5	1.67551	140.89517
119 Sn	-1/2	37.290632	74.603	111.853	149.145	186.395	223.723	261.034	279.660	298.492	335.646	8.59	1.48017	11.55876
117 Sn	-1/2	35.632259	71.285	106.879	142.512	178.105	213.774	249.426	267.223	285.218	320.719	7.68	1.29134	9.01592
87 Rb	3/2	32.721218	65.461	98.147	130.869	163.555	196.309	229.049	245.392	261.917	294.517	27.835	1.00000	25.30455
115 Sn	-1/2	32.718749	65.456	98.140	130.859	163.542	196.294	229.031	245.374	261.897	294.495	0.34	0.99977	0.30902
11 B	3/2	32.083974	64.186	96.236	128.320	160.369	192.486	224.588	240.613	256.816	288.781	80.1	0.94271	68.64611
125 Te	-1/2	31.549789	63.118	94.633	126.184	157.699	189.281	220.849	236.607	252.540	283.973	7.139	0.89640	5.81762
141 Pr	5/2	30.620000	61.257	91.844	122.465	153.052	183.703	214.340	229.634	245.097	275.604	100.0	0.81946	74.49626
71 Ga	3/2	30.496579	61.011	91.474	121.972	152.435	182.962	213.476	228.708	244.110	274.494	39.892	0.80959	29.36014
65 Cu	3/2	28.403661	56.824	85.196	113.601	141.974	170.406	198.826	213.013	227.357	255.656	30.83	0.65409	18.33224
129 Xe	-1/2	27.811008	55.638	83.419	111.231	139.011	166.850	194.677	208.568	222.613	250.321	26.4	0.61399	14.73578
81 Br	3/2	27.007028	54.029	81.007	108.015	134.993	162.027	189.049	202.539	216.177	243.085	49.31	0.56227	25.20486
63 Cu	3/2	26.515473	53.046	79.533	106.049	132.536	159.078	185.608	198.852	212.243	238.660	69.17	0.53212	33.46069
23 Na	3/2	26.451921	52.919	79.342	105.795	132.218	158.697	185.163	198.376	211.734	238.088	100.0	0.52830	48.02757
51 V	7/2	26.302963	52.621	78.895	105.199	131.474	157.803	184.121	197.259	210.542	236.748	99.75	0.51943	47.10271
123 Te	-1/2	26.169767	52.354	78.496	104.667	130.808	157.004	183.188	196.260	209.476	235.549	0.908	0.51158	0.42228
27 Al	5/2	26.056890	52.129	78.157	104.215	130.244	156.327	182.398	195.413	208.572	234.533	100.0	0.50499	45.90782
13 C	1/2	25.145020	50.304	75.422	100.568	125.686	150.856	176.015	188.575	201.273	226.325	1.1	0.45380	0.45380
79 Br	3/2	25.054454	50.123	75.151	100.206	125.233	150.313	175.381	187.895	200.548	225.510	50.69	0.44892	20.68693
151 Eu	5/2	24.860000	49.734	74.567	99.428	124.261	149.146	174.020	186.437	198.992	223.760	47.8	0.43855	19.05681
55 Mn	5/2	24.789062	49.592	74.355	99.144	123.906	148.720	173.523	185.905	198.424	223.121	100.0	0.43480	39.52749
93 Nb	9/2	24.476195	48.966	73.416	97.893	122.343	146.843	171.333	183.559	195.919	220.305	100.0	0.41855	38.04965
45 Sc	7/2	24.291702	48.597	72.863	97.155	121.420	145.737	170.042	182.175	194.443	218.645	100.0	0.40915	37.19570
159 Tb	3/2	24.040000	48.094	72.108	96.148	120.162	144.227	168.280	180.287	192.428	216.379	100.0	0.39657	36.05142
69 Ga	3/2	24.001255	48.016	71.992	95.993	119.969	143.994	168.009	179.997	192.118	216.030	60.108	0.39465	21.56518
121 Sb	5/2	23.930601	47.875	71.780	95.711	119.615	143.570	167.514	179.467	191.552	215.395	57.36	0.39118	20.39806
59 Co	7/2	23.727074	47.468	71.169	94.897	118.598	142.349	166.090	177.941	189.923	213.563	100.0	0.38128	34.66183
187 Re	5/2	22.751602	45.516	68.243	90.995	113.722	136.497	159.261	170.625	182.115	204.783	62.6	0.33616	19.13063
185 Re	5/2	22.524602	45.062	67.562	90.088	112.588	135.135	157.672	168.923	180.298	202.739	37.4	0.32620	11.09078
99 Tc	9/2	22.508316	45.029	67.513	90.022	112.506	135.037	157.558	168.801	180.168	202.593	0.0	0.32549	0.00000
113 Cd	-1/2	22.193175	44.399	66.568	88.762	110.931	133.147	155.352	166.437	177.645	199.756	12.22	0.31201	3.46616
115 In	9/2	21.912527	43.838	65.726	87.640	109.528	131.463	153.388	164.333	175.399	197.230	95.7	0.30032	26.12813
113 In	9/2	21.865656	43.744	65.586	87.452	109.294	131.182	153.060	163.981	175.023	196.808	4.3	0.29840	1.16647
195 Pt	1/2	21.496752	43.006	64.479	85.977	107.450	128.968	150.477	161.214	172.071	193.488	33.8	0.28355	8.71273

NMR Experiments

NMR Experiment Flowchart

__Solution NMR:__

All adjustments and calibrations are done with the test sample.



Sample

Magnet

Magnetization

RF

Response

Detection

Data

Processing

Spectrum

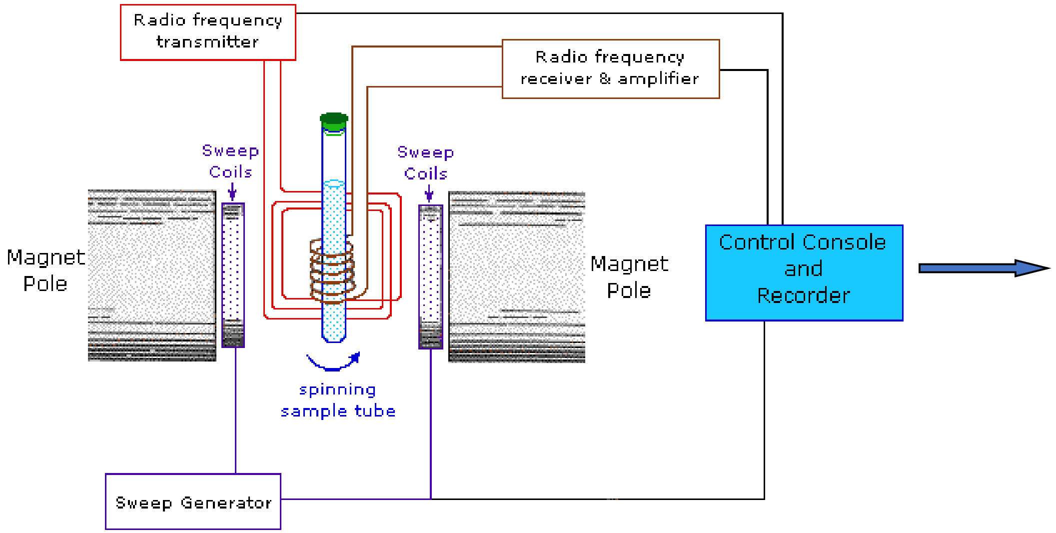
Storage

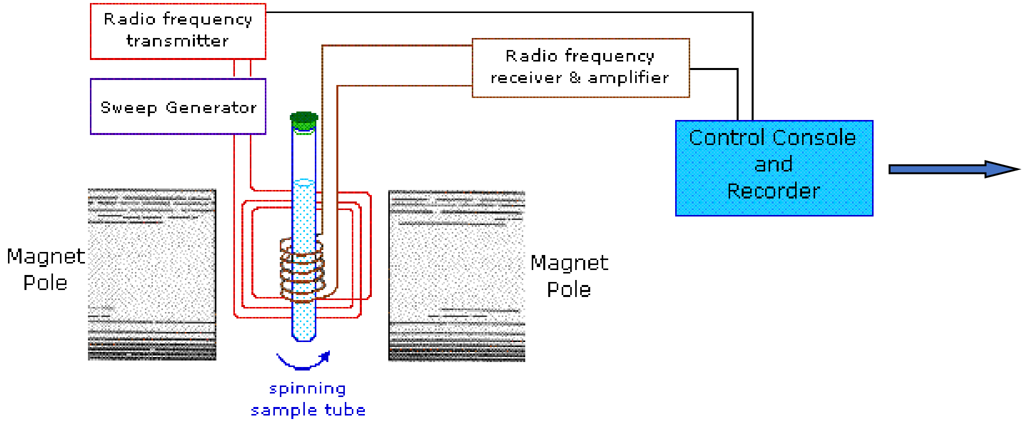
__Solid State NMR:__

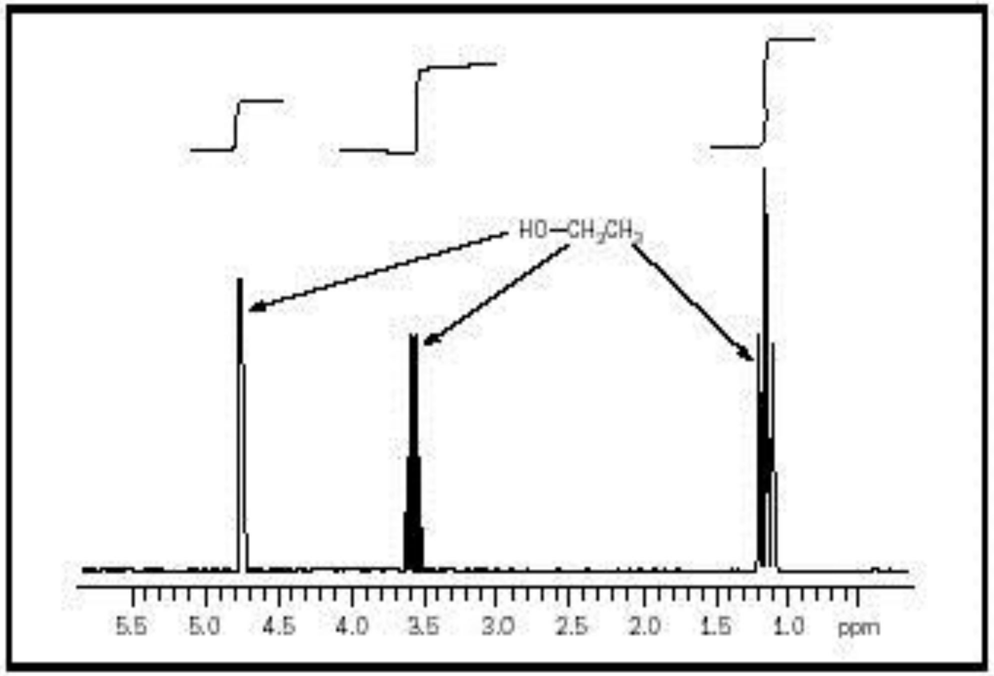
Repeat all steps with:
Adamantane – adjust shims
KBr – adjust magic angle
Reference – adjust RF match
Test sample – finally……

NMR Experiments – Continuous Wave NMR

CW Spectrometer







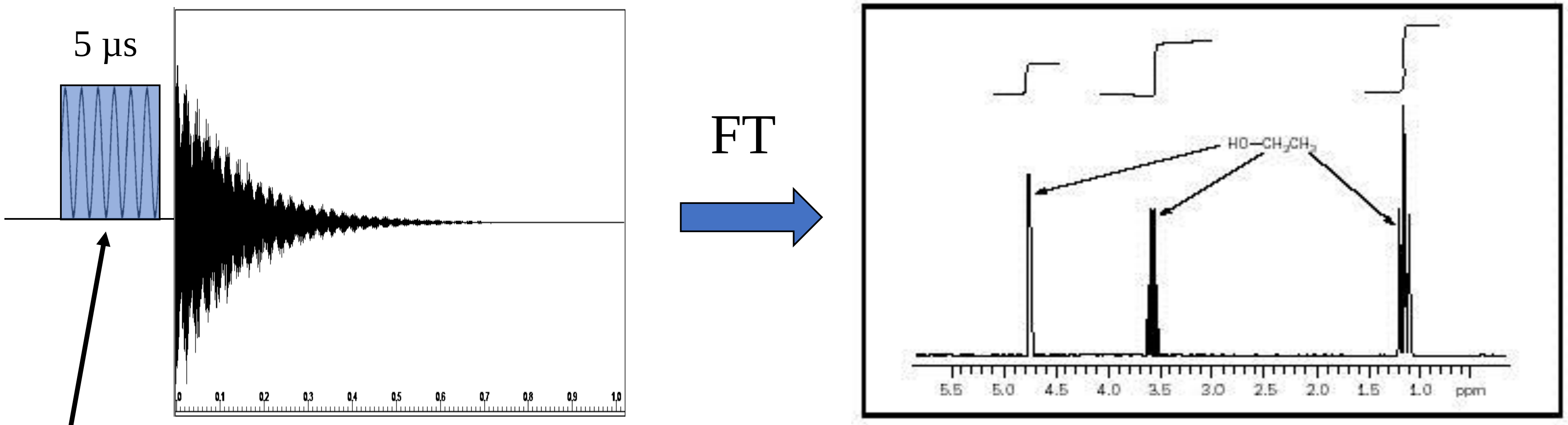
Frequency or field sweeps can be very time consuming.

(several minutes per scan for high resolution)

NMR Experiments – Pulse-Fourier Transform

Pulse Fourier Transform Spectrometer

(records time domain data after a radiofrequency pulse)

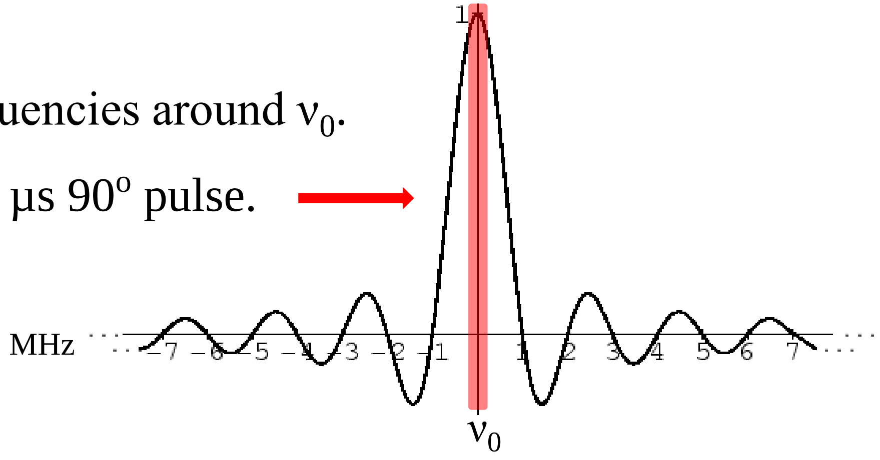


The FID (Free Induction Decay) is Fourier-Transformed into the spectrum.

A single RF pulse at the frequency ν_0 excites a band of frequencies around ν_0.

The RF power is adjusted to excite a 50 kHz range with a 5 μs 90^o pulse.

This is also called a "***50 kHz B$_1$ field*** ".



Spins – Calculation/Visualization

NMR Hamiltonians

$$\mathcal{H} = \mathcal{H}_Z + \mathcal{H}_{\text{r.f.}} + \mathcal{H}_{CS} + \mathcal{H}_Q + \mathcal{H}_{SR} + \mathcal{H}_D + \mathcal{H}_J$$

Zeeman Interaction	$\mathcal{H}_Z = \sum_i \omega_i I_{zi}$
RF Field	$\mathcal{H}_{\text{r.f.}} = B_1(t)\cos(\omega t + \phi(t)) \sum_i \gamma_i I_{xi}$
Chemical Shifts	$\mathcal{H}_{CS} = \hbar \sum_i \gamma^i \mathbf{I}_i \,.\, \sigma_i \,.\, \mathbf{B}$
Quadrupolar Interaction	$\mathcal{H}_Q = \sum_i \frac{eQi}{6I_i(2I_i-1)} \sum_{\alpha,\beta} V^i_{\alpha\beta}[\frac{3}{2}(I_{\alpha i}I_{\beta i} + I_{\beta i}I_{\alpha i}) - \delta_{\alpha\beta}(\mathbf{I}_i)^2]$
Spin Rotation	$\mathcal{H}_{SR} = \sum_m \sum_i \mathbf{I}_i \,.\, \mathbf{C}_{i,m} \,.\, \mathbf{J}_m$
Dipolar Interaction	$\mathcal{H}_D = \frac{1}{2}\sum_{j=1}^{N}\sum_{k=1}^{N}\left[\frac{\mu_j \,.\, \mu_k}{\mathbf{r}_{jk}^3} - \frac{3(\mu_j \,.\, \mathbf{r}_{jk})(\mu_k \,.\, \mathbf{r}_{jk})}{\mathbf{r}_{jk}^5}\right]$
Spin Coupling	$\mathcal{H}_J = \sum_{i<k} J_{ik}(I_{xi}I_{xk} + I_{yi}I_{yk} + I_{zi}I_{zk})$

Is this much detail needed?
What are we using NMR for?

Product Operators

Pulse:

$$I_z \xrightarrow{\phi I_x} I_z \cos\phi - I_y \sin\phi$$

$$I_z \xrightarrow{\phi I_y} I_z \cos\phi + I_y \sin\phi$$

$$I_x \xrightarrow{\phi I_x} I_x$$

$$I_x \xrightarrow{\phi I_y} I_x \cos\phi - I_z \sin\phi$$

$$I_y \xrightarrow{\phi I_x} I_y \cos\phi + I_z \sin\phi$$

$$I_y \xrightarrow{\phi I_y} I_y$$

Chemical Shift:

$$I_x \xrightarrow{(2\pi\delta\tau)\, I_z} I_x \cos(2\pi\delta\tau) + I_y \sin(2\pi\delta\tau)$$

$$I_y \xrightarrow{(2\pi\delta\tau)\, I_z} I_y \cos(2\pi\delta\tau) - I_x \sin(2\pi\delta\tau)$$

J-Couplings:

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

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

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

Spins – The Vector Model

Coherence

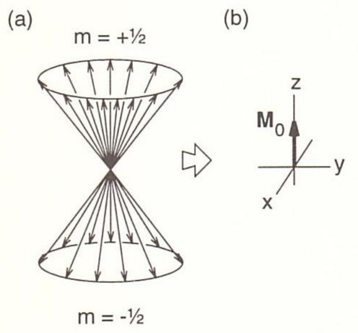


Fig. 6.3 Vector model of a collection of spin-$\frac{1}{2}$ nuclei at thermal equilibrium in a magnetic field along the *z* axis. (a) The magnetic moments of the individual spins: there is a slight excess of nuclei in the *m* = $+\frac{1}{2}$ state, which is lower in energy than the *m* = $-\frac{1}{2}$ state (for nuclides with positive gyromagnetic ratio). At equilibrium, the phases of the individual magnetic moments in the *xy* plane are random. (b) The net magnetic moment of a large number of spins.

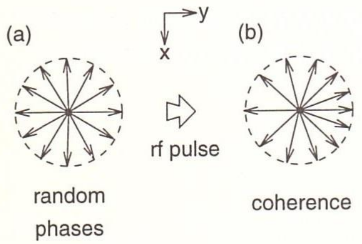


Fig. 6.7 The effect of a radiofrequency pulse on the magnetic moments of the individual spins in an NMR sample (looking down the *z* axis). Starting from the equilibrium state with random phases (a), a pulse along the *x* axis in the rotating frame causes the spins to 'bunch together' to some extent (b), producing a net *y* magnetization in the sample. This phase-correlation amongst the spins is known as *coherence*.

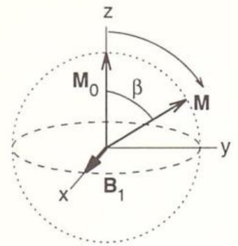
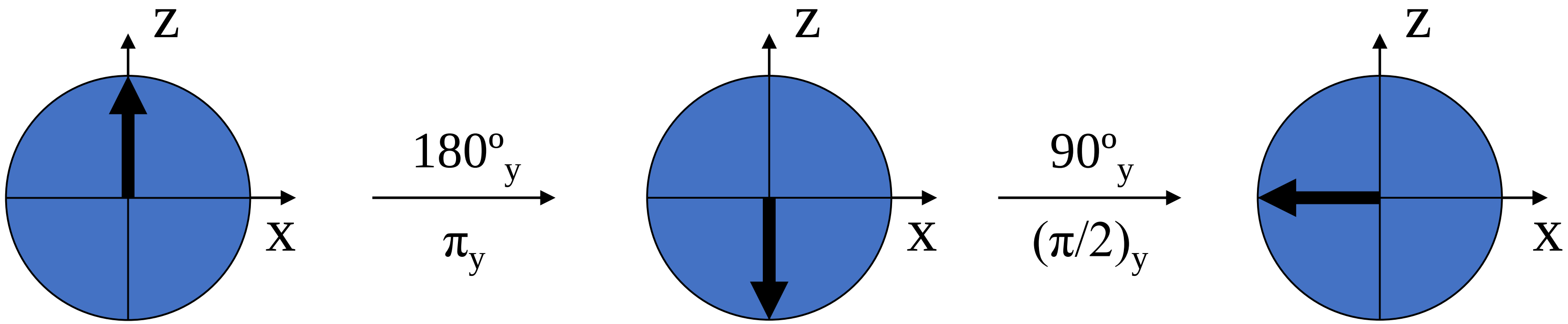


Fig. 6.6 The effect of a radiofrequency pulse on a collection of nuclear spins at equilibrium is to rotate the magnetization away from the *z* axis, around the direction of B_1, through an angle β (eqn 6.5).

Most NMR Experiments use combinations of
90º and 180º pulses
(π/2 and π pulses)
along the x or y axis.

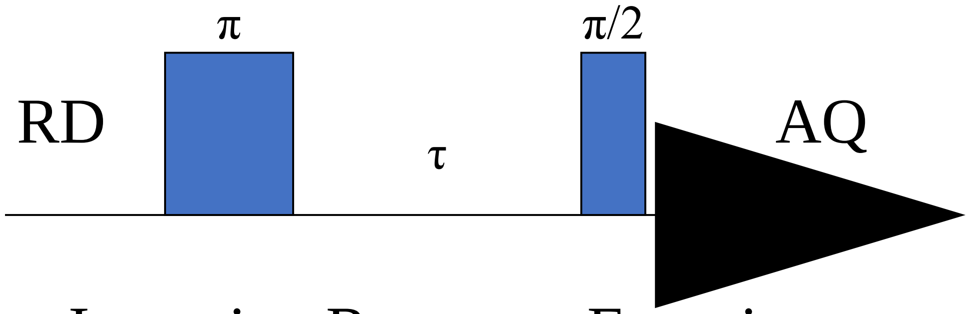
NMR Pulses / Pulse Sequences

Pulses are described by the angle (degree or radian) by which they turn the magnetization:



Only the magnetization in the X,Y plane is observable, Z magnetization is not.

Pulse Sequences consist of a series of pulses separated by delays:



Inversion Recovery Experiment

NMR Pulses / Pulse Sequences

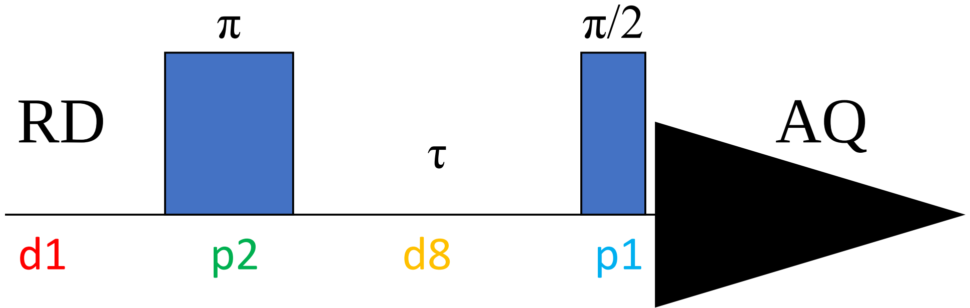
```
"p2=p1*2"
"d11=30m"
"acqt0=-p1*2/3.1416"

1 ze
2 d1            Relaxation Delay
  p2 ph1        Inversion Pulse
  d8            Recovery Delay
  p1 ph2        Detection Pulse
3 go=2 ph31     Detection Loop
  d11  wr #0  if #0
exit

ph1=0 2
ph2=0 0 2 2 1 1 3 3
ph31=0 0 2 2 1 1 3 3
```

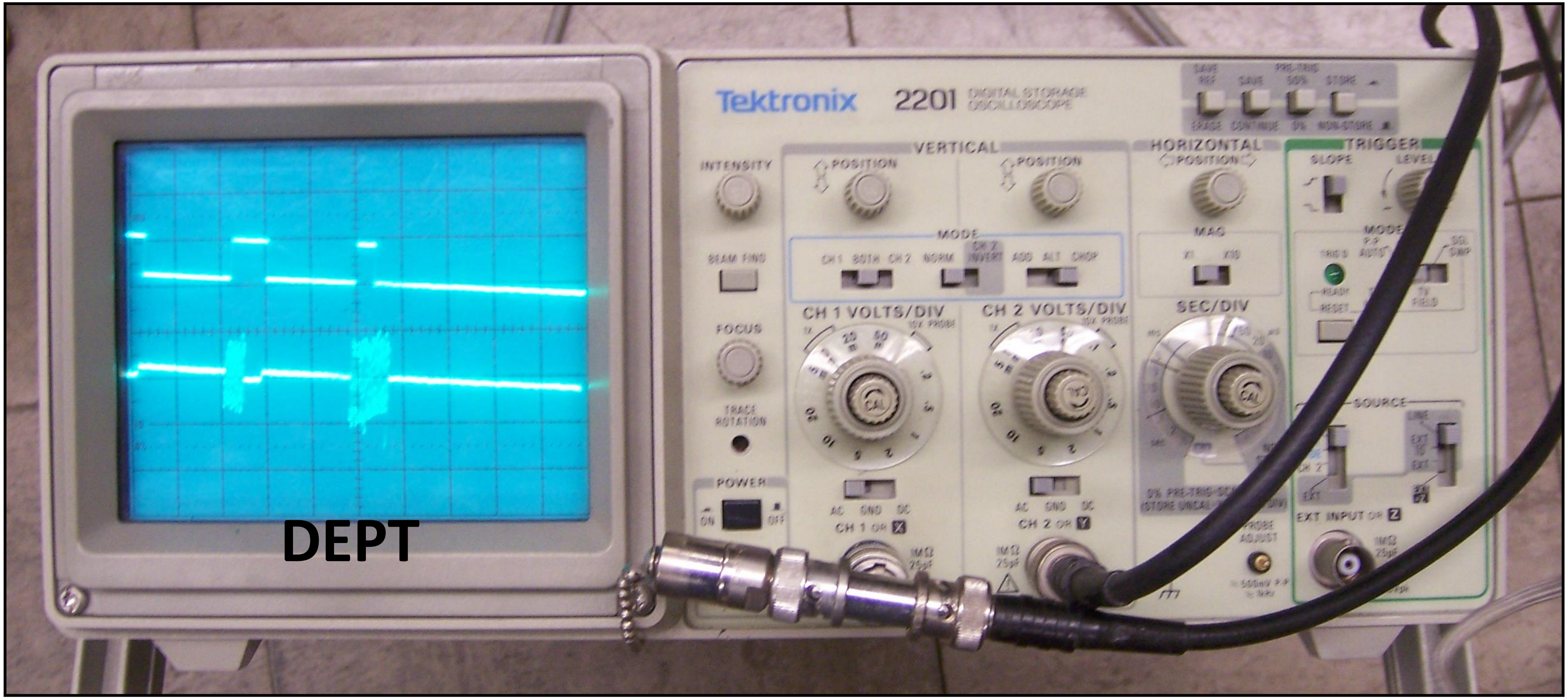
```
;t1ir
;avance-version (07/04/03)
;T1 measurement using inversion recovery


;pl1 : f1 channel - power level for pulse (default)
;p1 : f1 channel -  90 degree high power pulse
;p2 : f1 channel - 180 degree high power pulse
;d1 : relaxation delay; 1-5 * T1
;d11: delay for disk I/O                    [30 msec]
;d8 : recovery delay
;NS: 8 * n
;DS: 4
;td1: number of experiments
```

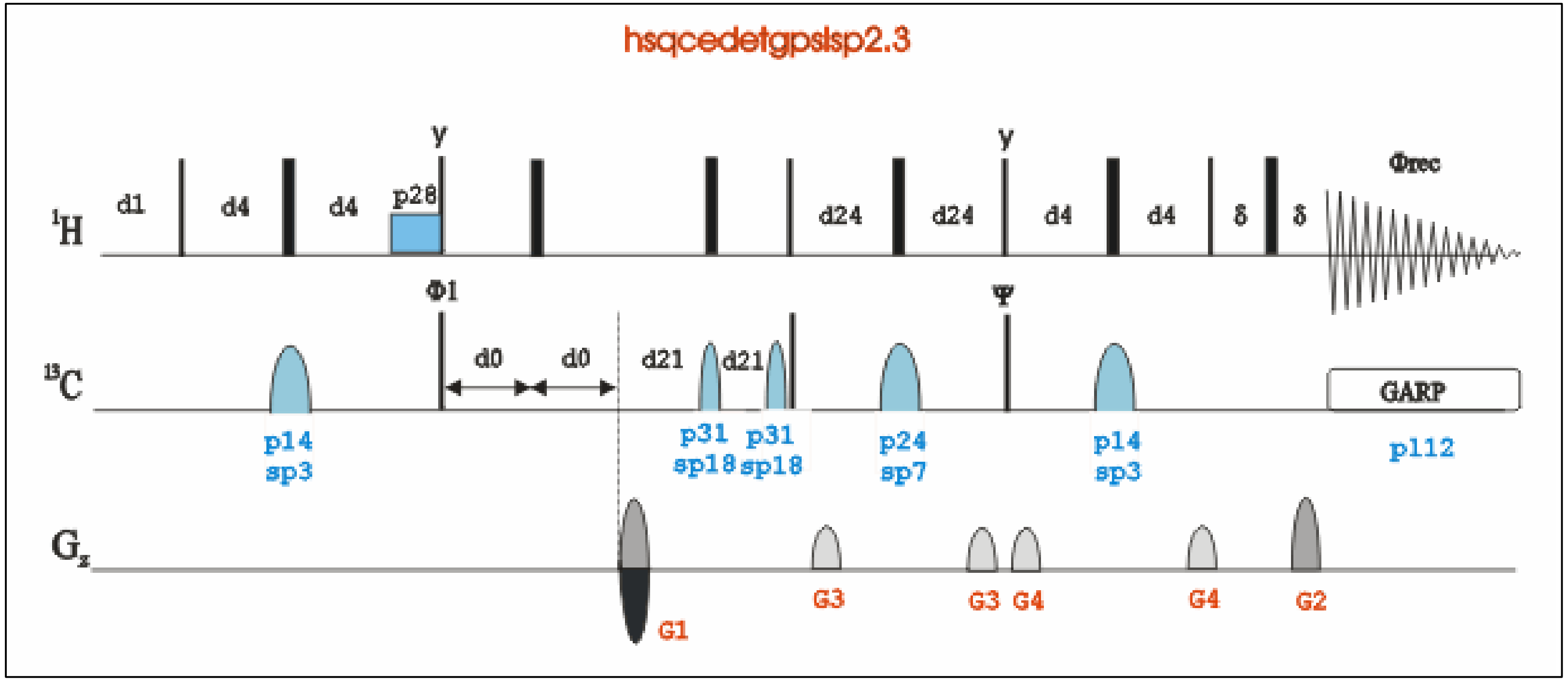


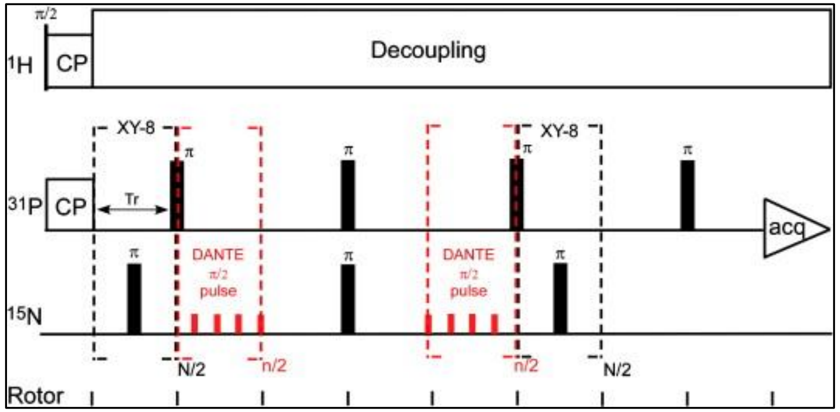
Inversion Recovery Experiment

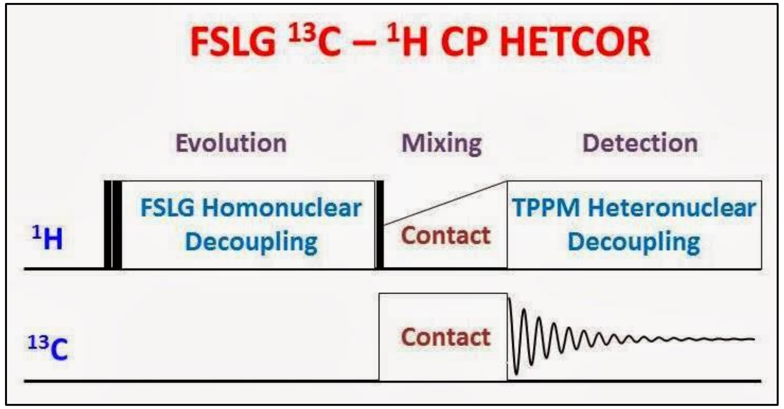
Pulse Sequences



Pulse Sequences can be very complicated





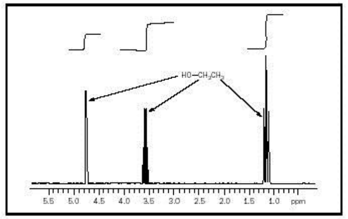


NMR Parameters - Shielding

The general resonance condition: $\nu_0 = (\gamma/2\pi)\, B_0 \longrightarrow$

This would mean that every proton spectrum would only have one signal.

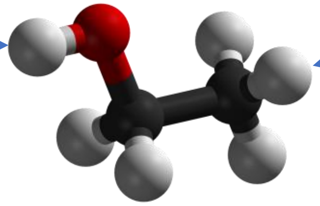
In reality we observe
separate signals for different protons.



An increased electron density will shield the nucleus and it will require a higher value of B_0 to achieve resonance:

$$B_{eff} = B_0 - \sigma\, B_0$$

lower
electron
density



higher
electron
density

(more shielded)

The resonance condition becomes: $\nu = (\gamma/2\pi)\, B_0\, (1 - \sigma)$

increasing field B_0 →
increasing shielding

downfield (less shielded)

upfield (more shielded)

These terms originate from the early days of NMR when the magnetic field was swept while transmitting a constant frequency.

Today’s NMR spectrometers usually have a fixed magnetic field and record frequencies. The direction of the frequency axis is inverted.

← increasing frequency
decreasing shielding

NMR Parameters - Chemical Shift

The resonance condition: $\nu = (\gamma/2\pi)\, B_0\, (1 - \sigma)$

The problem:

The absolute frequency ν is very large (MHz - GHz) and is B_0 dependent.
The range $\Delta\nu$ for most nuclei is very small (Hz - kHz).

i.e. a spectrum may have two proton signals at 60.000000 MHz and 60.000120 MHz.

The solution: Chemical Shift (δ)

Report a signal's position relative to a reference signal, i.e. tetramethylsilane (TMS), and normalize it to the reference frequency:

$$\delta(X) = 10^6 \; [\; \nu(X) \; - \; \nu(TMS) \;] \, / \; \nu(TMS)$$

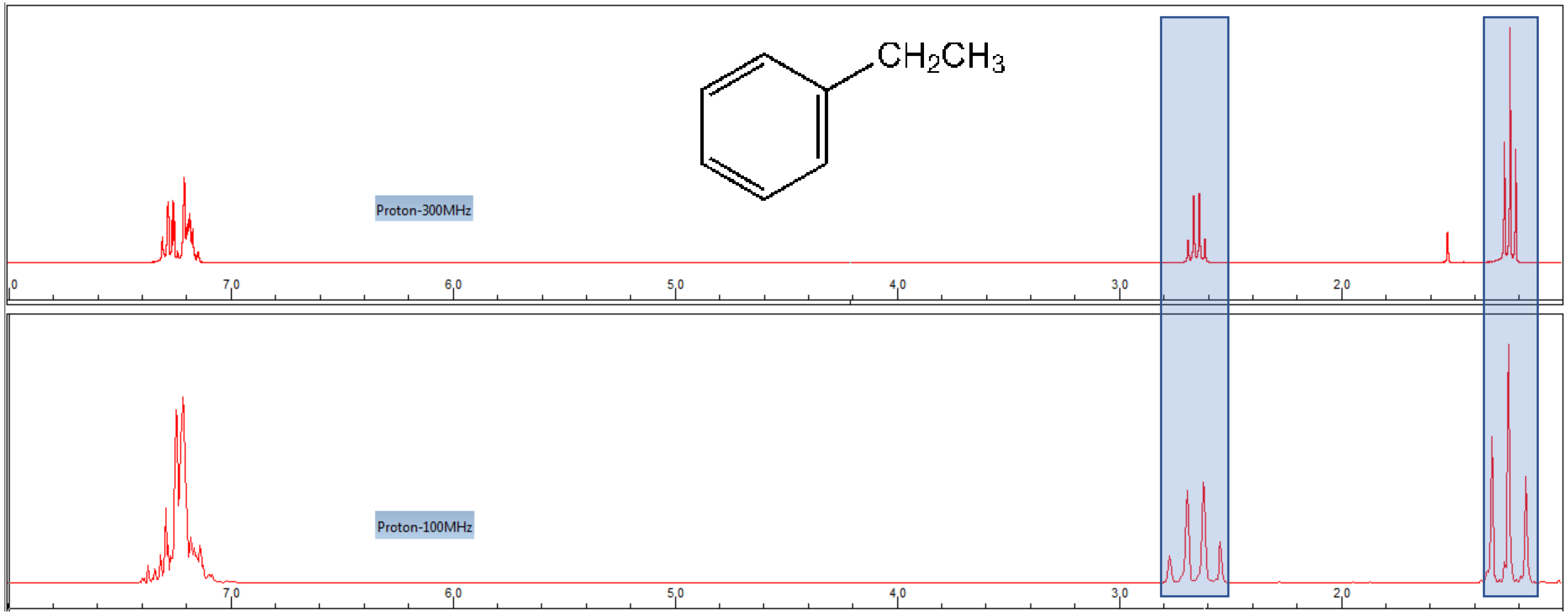
$$\delta(X) = 10^6 \, [60{,}000{,}120 - 60{,}000{,}000] \, / \, 60{,}000{,}000 = 2 \text{ (ppm)}$$

Chemical shifts are field independent and are reported in ppm units with typical ranges of 15 ppm for ^1H and 250 ppm for ^{13}C.

Chemical shifts increase from right to left.

NMR Parameters - Chemical Shift

- Example: ^{1}H spectrum of Ethylbenzene at 7.05 T and 2.35 T



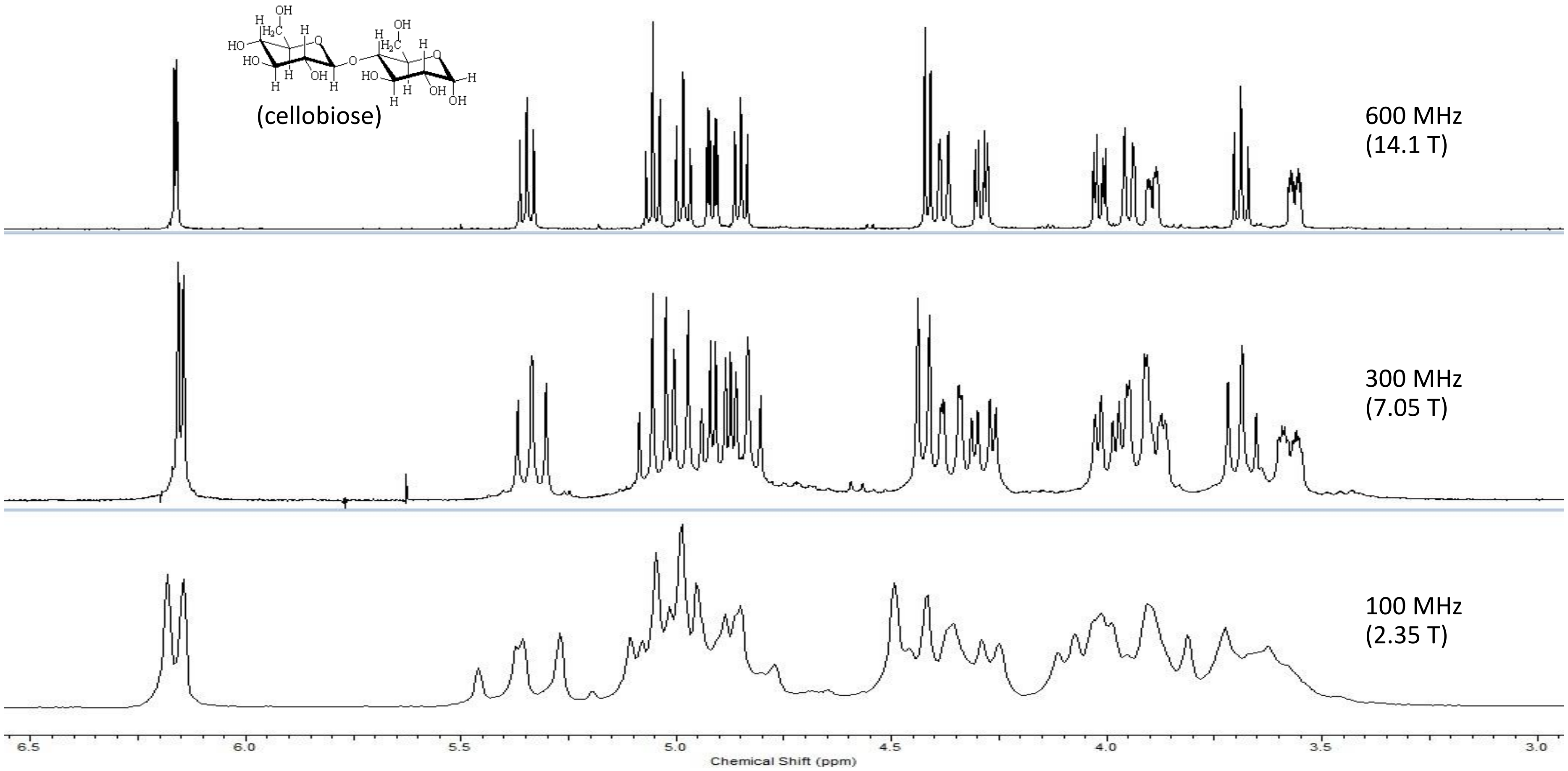
- Chemical shifts (measured in ppm) are identical at different magnetic fields.

- Couplings (Signal splittings, measured in Hertz) are also identical at different fields, but take up less space at higher fields/frequencies.

➡ **Better chemical shift dispersion at higher fields.**

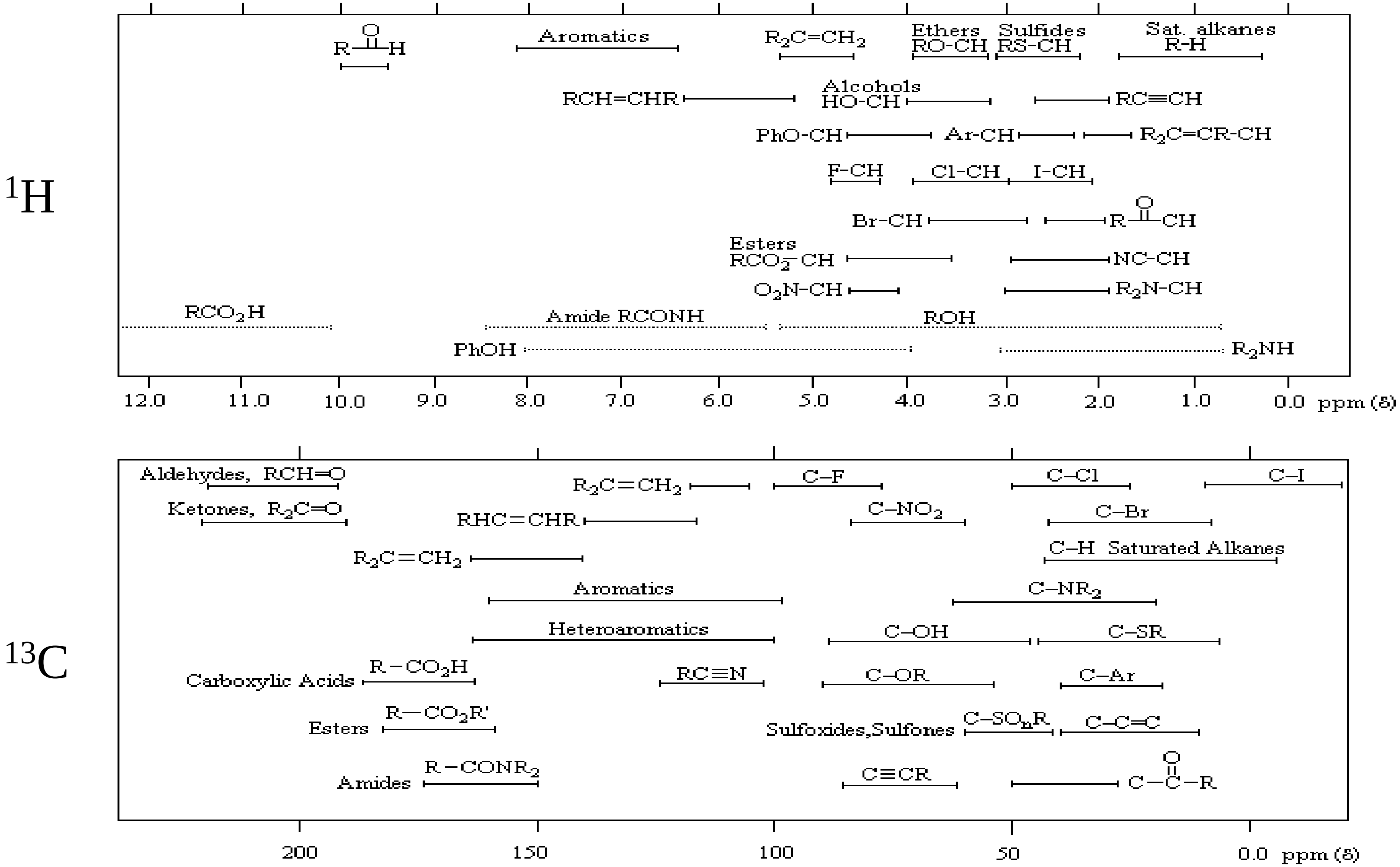
NMR Parameters - Chemical Shift

- Example: ^1H spectrum of Cellobiose Octaacetate at 14.1 T, 7.05 T, and 2.35 T



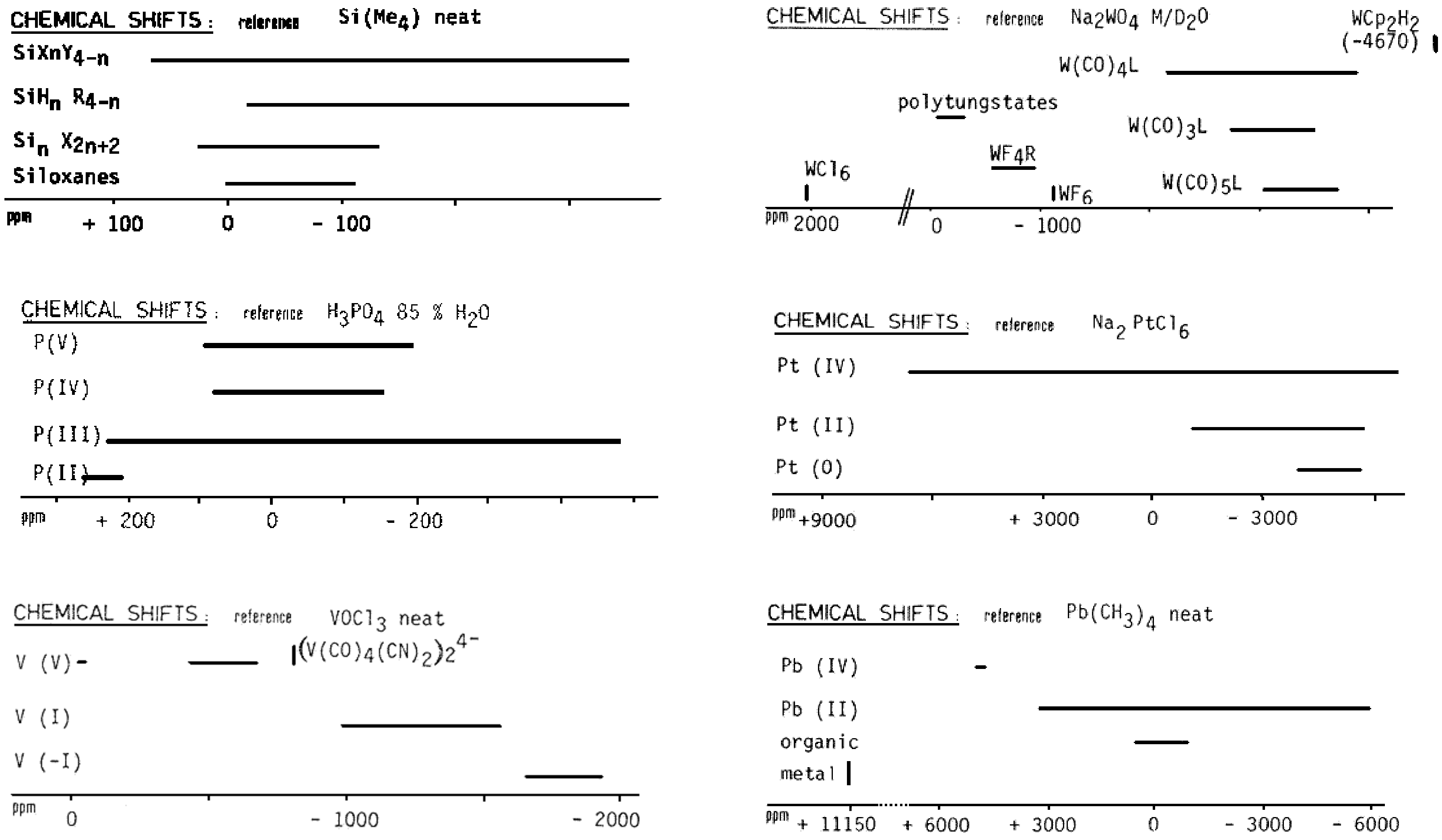
Large molecules will benefit most from a higher magnetic field strength.

NMR Parameters - Chemical Shift



Chemical shifts of ^1H and ^{13}C relative to TMS (0 ppm)

NMR Parameters - Chemical Shift

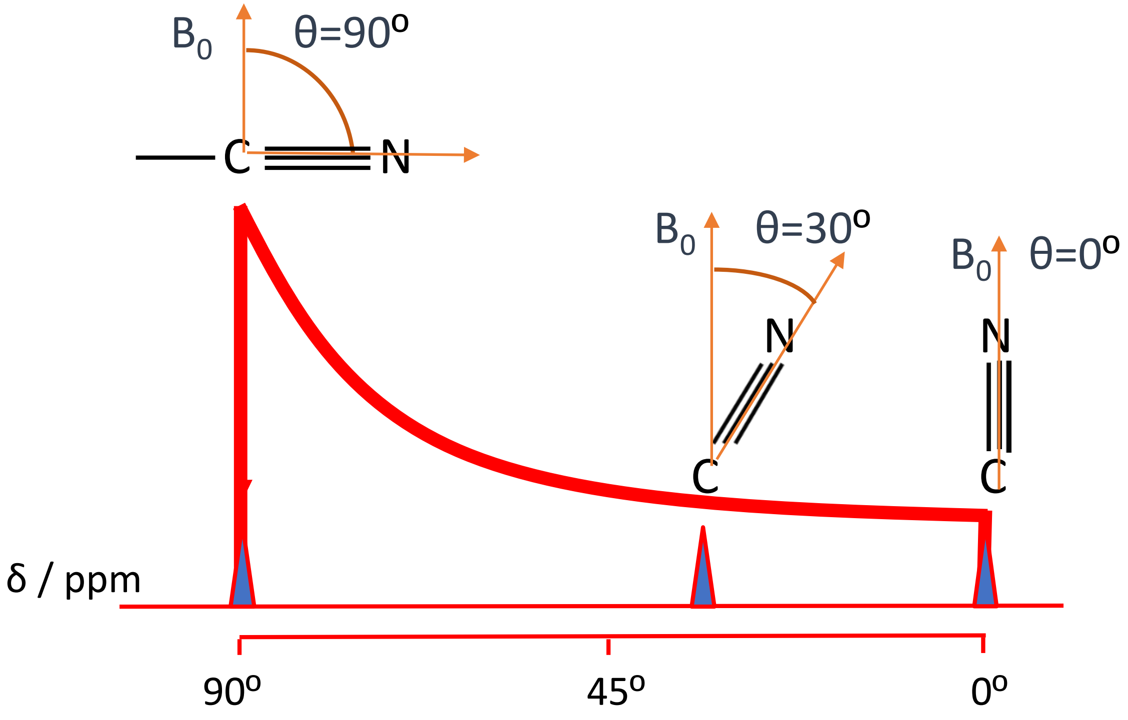


Chemical shift ranges for common inorganic nuclei.

NMR Parameters - CSA

Chemical Shift Anisotropy:

The chemical shift depends on the relative orientation of a molecule or a crystal to the B_0 field.



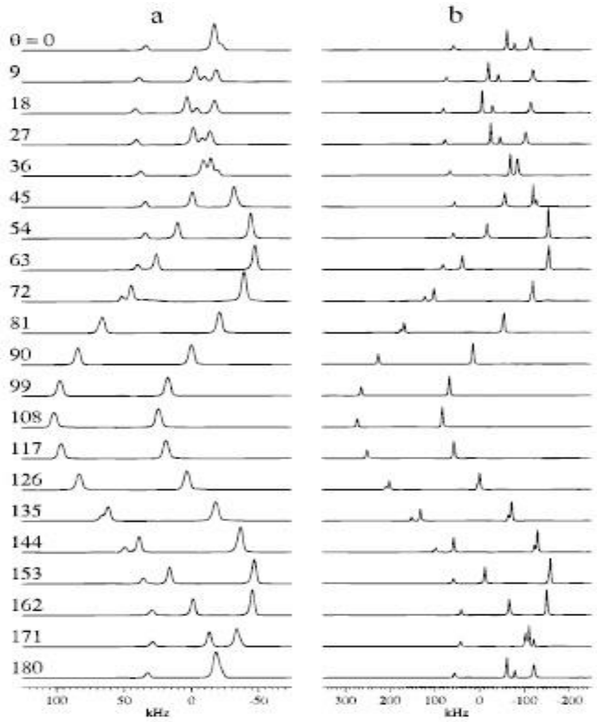


Figure 1. ^{71}Ga (a) and ^{69}Ga (b) single-crystal NMR spectra showing the region of the central transitions for the twin β-Ga_2O_3 crystal. Both sets of spectra are recorded for rotation about the $-x^T$ axis.

A single crystal will have a sharp NMR signal at a chemical shift that depends on the angle θ between B_0 and the principal axis of the crystal:

$$\nu \approx (3 \cos^2 \theta - 1)$$

A powder sample consists of a large number of microscopic crystals at random orientations.
A powder spectrum represents a superimposition of all individual crystal orientations in the sample.

NMR Parameters - CSA

Chemical Shift Anisotropy:

A powder sample consists of a large number of microscopic crystals at random orientations.
This leads to a superimposition of the signals of all individual crystals, resulting in a powder pattern spectrum.

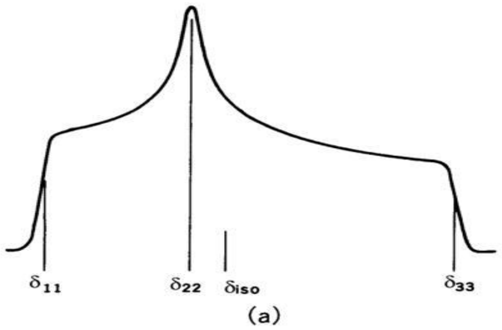
$\nu \approx (3 \cos^2 \theta - 1)$

The lineshape is determined by the axial asymmetry of the electronic and molecular surrounding.

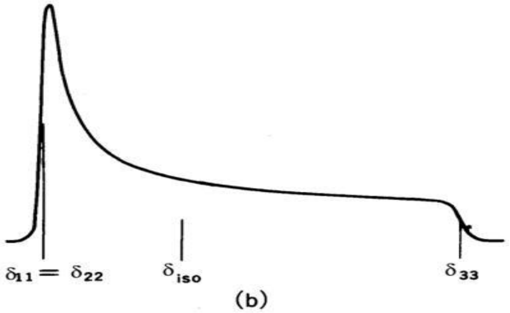
In **solution** the Brownian motion will average all orientations, leading to a single sharp signal. In **solid** samples we need to simulate rapid re-orientation of the molecules:
Spinning a powder sample around the “magic angle” (54.7º) will sharpen the signal around the isotropic chemical shift.

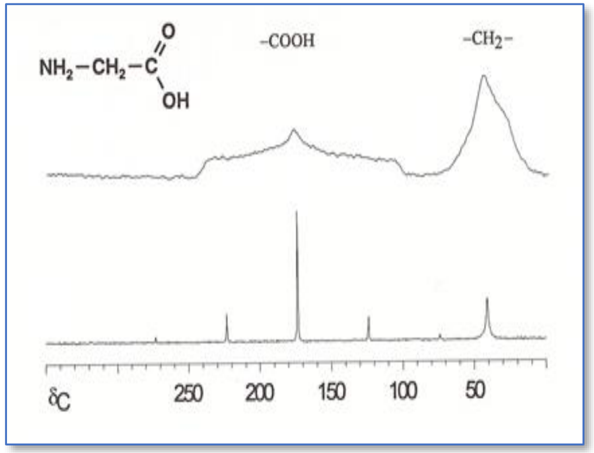
$(3 \cos^2 \theta - 1) = 0 \quad \text{for } \theta = 54.7^{o}$

axially asymmetric



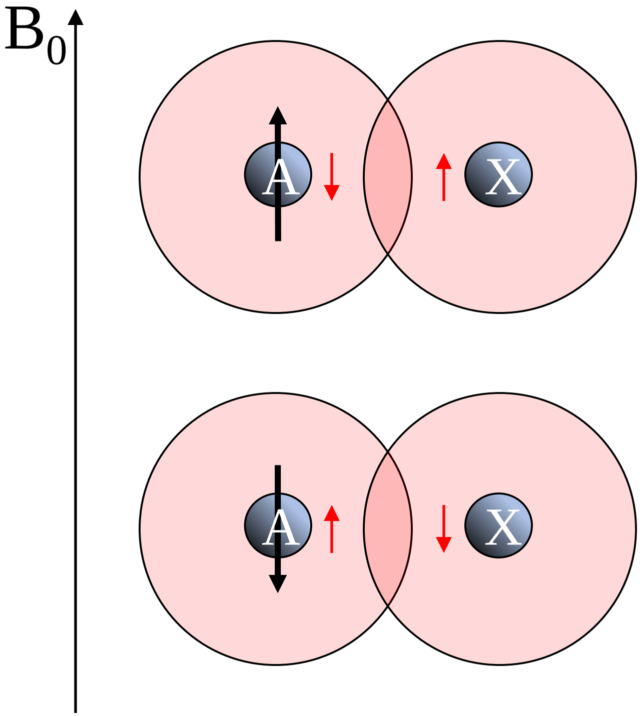
axially symmetric

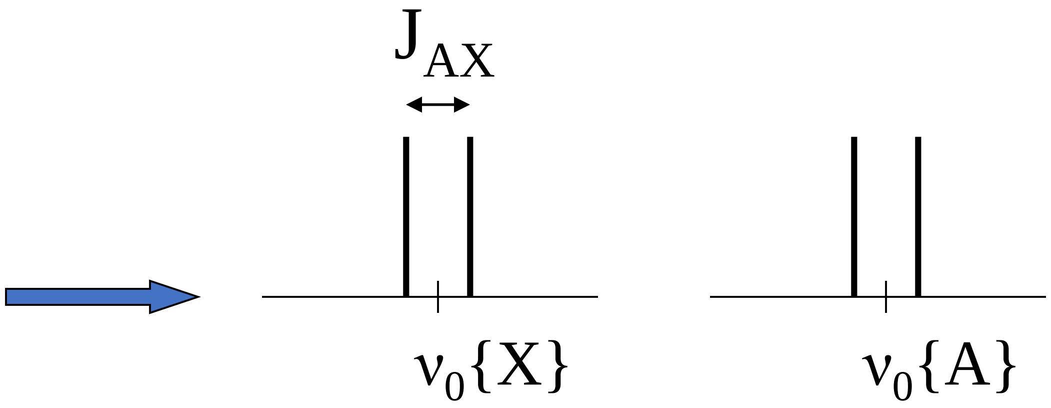




NMR Parameters - Couplings

- Spin, Spin Coupling (scalar coupling, J-coupling)
  Interaction between spins through valence electrons.





$$\Delta E = J_{AX} \cdot I(A) \cdot I(X)$$

The magnetic field at nucleus X will be enhanced or attenuated depending on the orientation of spin A.

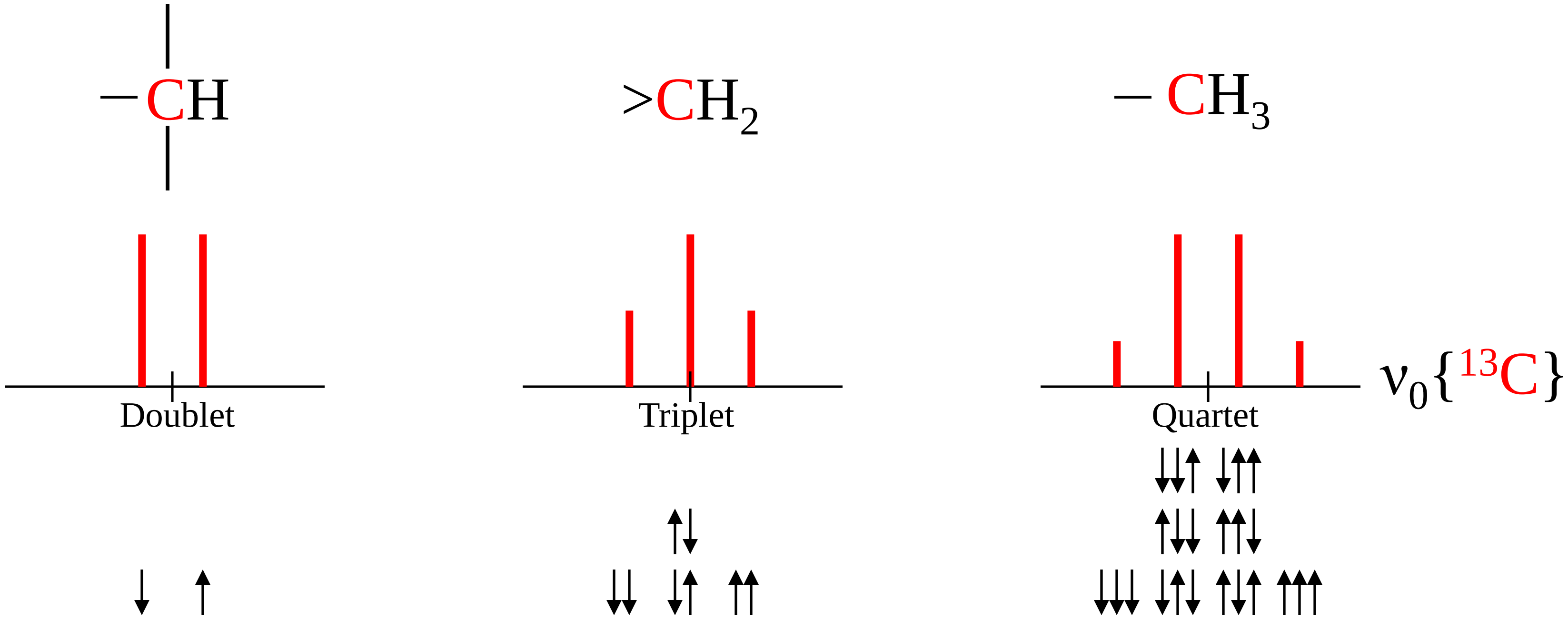
NMR Parameters - Couplings

- Doublets, Triplets, … Multiplets

Couplings to more than one nucleus increase multiplicity.

Multiplicity: **n + 1**
for n protons
(spin-1/2).

Use: **2·I·n + 1**
for other spins **I**.

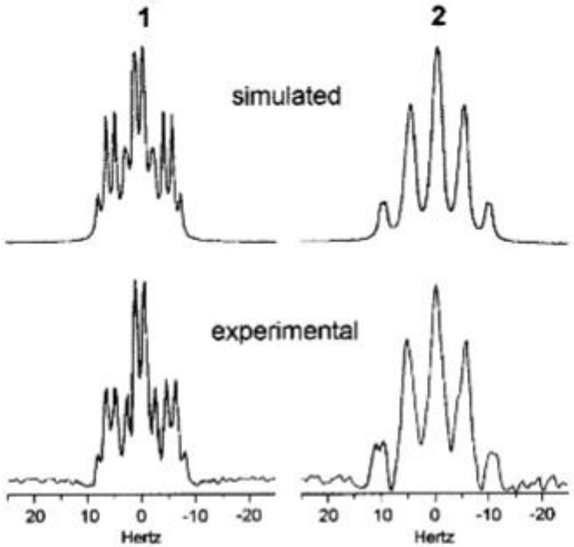


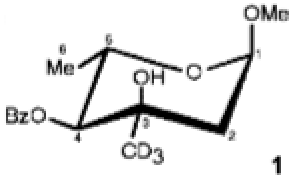
Couplings to chemically and magnetically different spins can lead to complex multiplicity patterns (dd, ddd, dt, ... , m)

NMR Parameters - Couplings

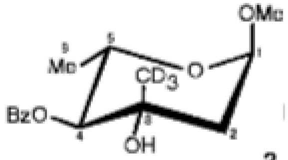
- Doublets, Triplets, … Multiplets

Simulate spectra with measured or calculated couplings to determine multiplicity.

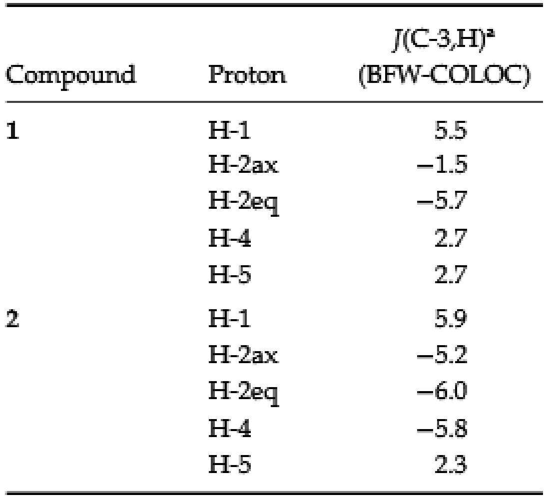




1



2



Compound	Proton	J(C-3,H)[a] (BFW-COLOC)
1	H-1	5.5
	H-2ax	−1.5
	H-2eq	−5.7
	H-4	2.7
	H-5	2.7
2	H-1	5.9
	H-2ax	−5.2
	H-2eq	−6.0
	H-4	−5.8
	H-5	2.3

•J. Schulte, J. Lauterwein, M. Klessinger, and J. Thiem, *Magnetic Resonance in Chemistry* **41**, 123-130 (2003), "Configurational Assignment in Alkyl-Branched Sugars via the Geminal C,H Coupling Constants."

Couplings to chemically and magnetically different spins can lead to complex multiplicity patterns (dd, ddd, dt, ... , m)

NMR Parameters - Couplings

- single-bond vs. multi-bond coupling constants

C-H	$^1J_{CH}$:	100 to 200 Hz
C-C-H	$^2J_{CH}$:	-10 to +10 Hz
C-C-C-H	$^3J_{CH}$:	0 to +10 Hz

H-C-H	$^2J_{CH}$:	-5 to -15 Hz
H-C-C-H	$^3J_{CH}$:	0 to +10 Hz

Couplings are always quoted in Hertz units (also: cps)

Couplings are independent of the magnetic field.

Longer range couplings are only visible, if all nuclei in the coupling pathway are in the same plane.
(W configuration – zig-zag arrangement)

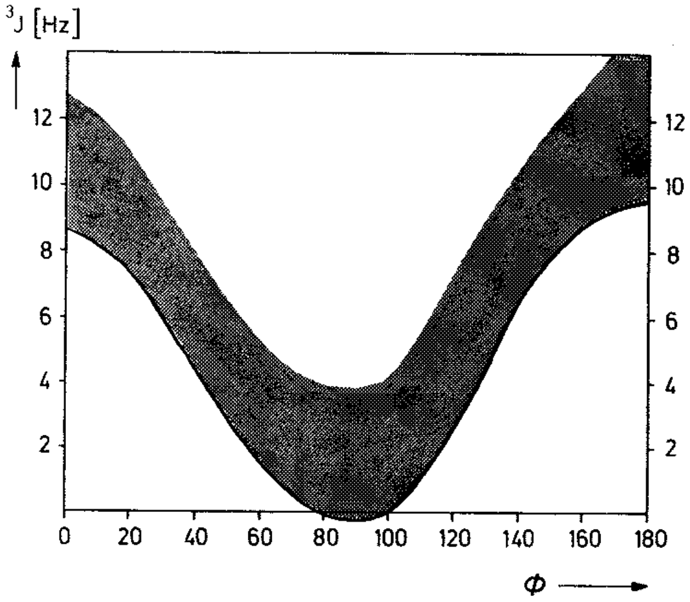
NMR Parameters - Couplings

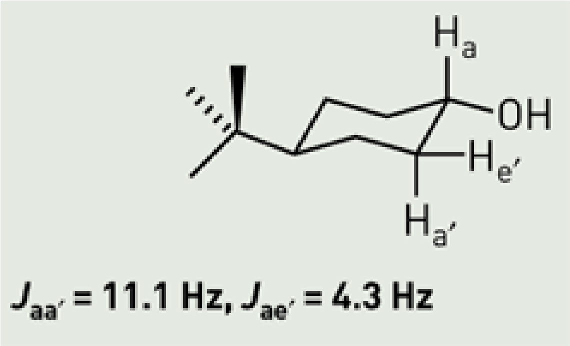
- Structural dependence of vicinal J couplings

Karplus Equation for
H-C-C-H, C-C-C-H and C-O-C-H
dihedral angles:

$$^{3}J(\Phi) = A + B\cos\Phi + C\cos^{2}\Phi$$

(A, B and C can be tuned to fit different classes of compounds)



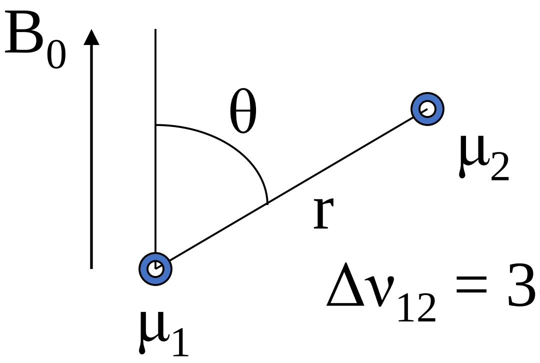


$J_{aa'}$ = 11.1 Hz, $J_{ae'}$ = 4.3 Hz

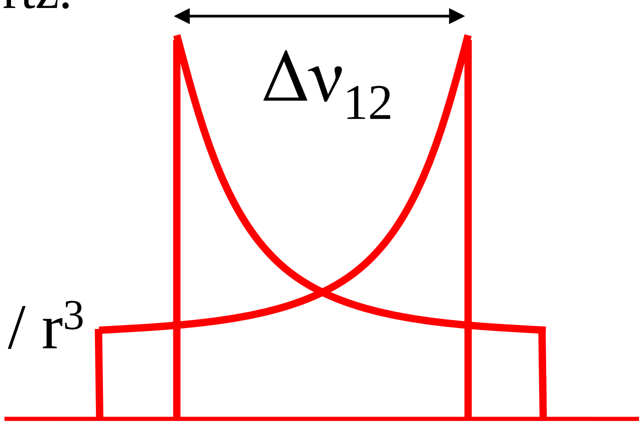
NMR Parameters - Couplings

- Dipolar Coupling (d)

Interaction between spins through space. No bonds are necessary.
Dipolar couplings can span thousands of hertz.

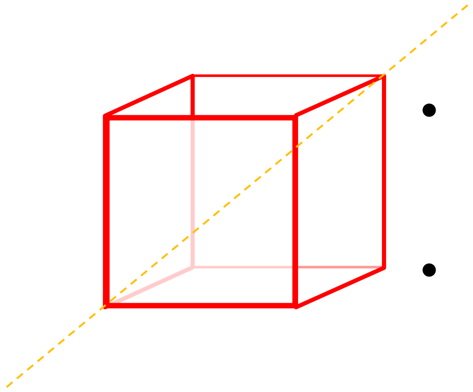


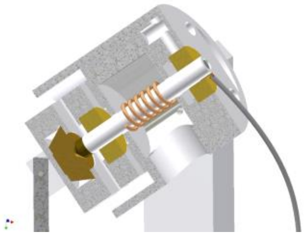
$$\Delta\nu_{12} = 3d_{12}/2\ (3\cos^2\theta - 1) / r^3$$



- In liquids the Brownian motion averages all orientations. $(3\cos^2\theta - 1) = 0$, no dipolar splitting.
- Solids and molecules dissolved in liquid crystals are aligned. $(3\cos^2\theta - 1) \neq 0$, dipolar splitting / broadening.
- Sample spinning around $\theta = 54.7°$ can remove broadening.

Magic Angle Spinning (MAS)





NMR Parameters - Relaxation

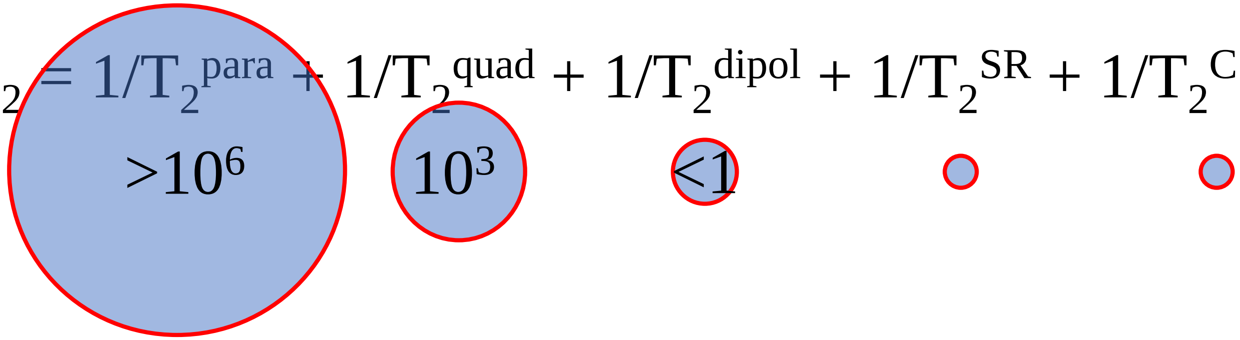
- What is relaxation?
  - Loss of magnetization through interaction of a spin with other spins or with the sample ("lattice") will allow the spins to return to a thermal equilibrium.

- Some mechanisms for relaxation:

•Paramagnetic relaxation	(proximity of free electrons: paramagnetic metals, radicals)
•Quadrupolar relaxation	(nuclei with I > 1/2)
•Dipolar relaxation	(proximity of other spins, typ. ^{1}H)
•Spin rotation relaxation	(i.e. rotating methyl groups)
•Chemical shift anisotropy (CSA) relaxation	

- Relaxation <u>rates</u> are additive:

$$R_2 = 1/T_2 = 1/T_2^{para} + 1/T_2^{quad} + 1/T_2^{dipol} + 1/T_2^{SR} + 1/T_2^{CSA} + \ldots$$

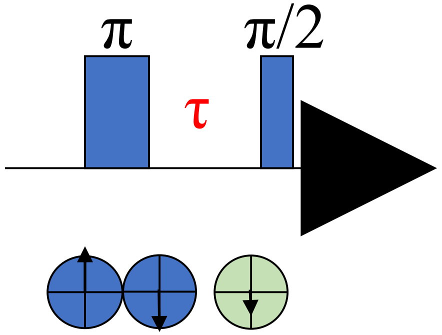


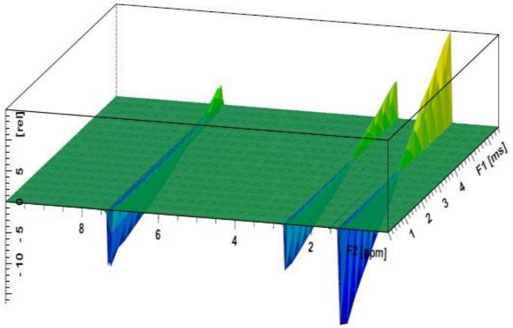
NMR Parameters - Relaxation

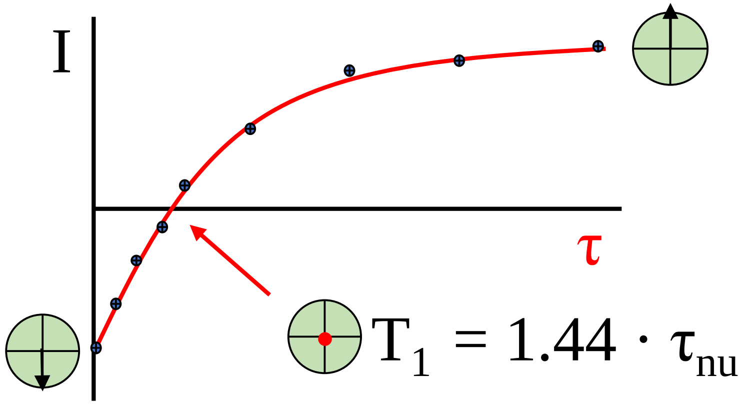
- **T_1 relaxation** (spin-lattice relaxation, longitudinal relaxation)

  Heat is released to the lattice (sample) when the spin reverts to the lower energy level.

T_1 Measurement by “Inversion Recovery” technique:







$T_1 = 1.44 \cdot \tau_{null}$

Measure Intensities for various τ values and fit with: $I = 2I_0 \cdot \exp(-\tau / T_1)$

Typical T_1’s: - seconds to minutes for Spin-½ nuclei (i.e. ^1H: 2 sec., ^{13}C: 20 sec., ^{15}N: 200 sec)

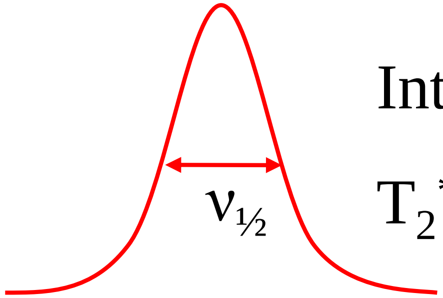
- milliseconds for quadrupolar nuclei (i.e. ^{17}O: 20 ms for H_2O, <1 ms for organic molecules)
- microseconds for paramagnetic nuclei, signal decays too fast to be observed.

NMR Parameters - Relaxation

- **T_2 relaxation** (spin-spin relaxation, transverse relaxation)
  Energy dissipation by interactions between spins.

T_2 is always shorter than T_1 (because of field inhomogeneity).

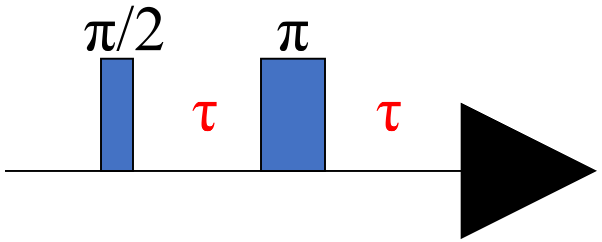
T_2 can be estimated from the width of the signal at half height:

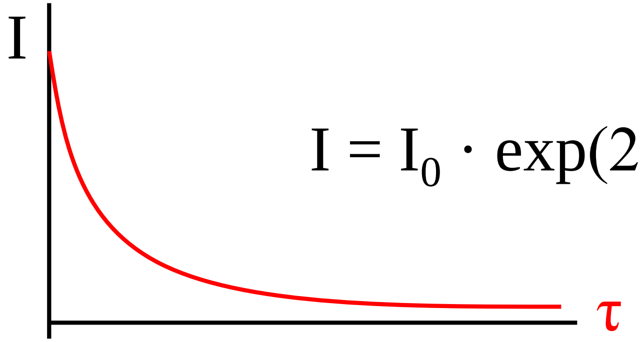


Intrinsic T_2 relaxation:

$T_2^* = 1/\pi\cdot\nu_{½}$ with $1/T_2^* = 1/T_2 + 1/T_2^{inh.}$

T_2 can be measured more accurately by the "Spin-Echo" technique:





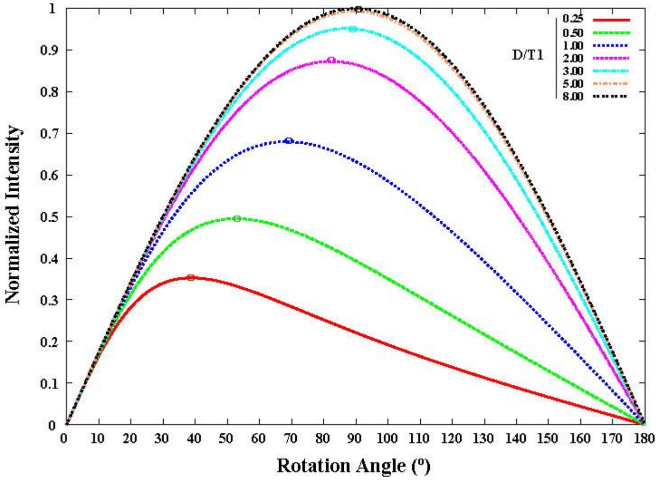
$I = I_0 \cdot \exp(2\ \tau / T_2)$

NMR Parameters - Relaxation

- **Recap:**
  - T_2 determines the linewidth of the NMR signal.
    “Short T_2 lead to broader signals.”
  - T_1 determines the repetition rate of the NMR experiments.
    “Most of the experimental time is spent waiting for the magnetization to recover between scans.”
  - After a 90 degree pulse:
    Wait $5 \cdot T_1$ for 99% magnetization recovery.
    Wait $2 \cdot T_1$ for 88% magnetization recovery.
  - Better: Use a smaller pulse angle, i.e. 60°:

$$\cos\theta = \exp(-t_r/T_1)$$

(θ: pulse angle, t_r: repetition time)



Examples: ^{1}H

90°, T_1 = 2 s → $5 \cdot T_1$ = 10 s → 100 s for 10 scans @ 100% signal: Int.=3.1
60°, T_1 = 2 s → $1 \cdot T_1$ = 2 s → 100 s for 50 scans @ 60% signal: Int.=4.2

^{13}C

90°, T_1 = 10 s → $5 \cdot T_1$ = 50 s → 100 s for 2 scans @ 100% signal: Int.=1.4
30°, T_1 = 10 s → $\mathbf{t_r}$ = 2 s → 100 s for 50 scans @ 50% signal: Int.=3.5
30°, T_1 = 60 s → $\mathbf{t_r}$ = 2 s → 100 s for 50 scans @ 10% signal: Int.=0.7

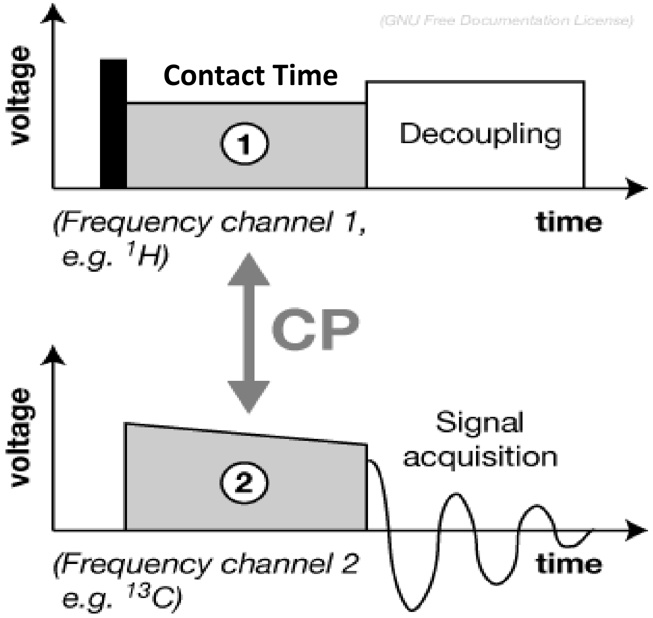
Key Techniques for Solid State NMR:

1. Cross Polarization (CP)

- CP is achieved by simultaneously irradiating two nuclei for a duration called "contact time". Magnetization is being transferred from the abundant spin (^1H) to the rare spin (^{13}C).
- CP is most efficient at the "Hartmann-Hahn-match":

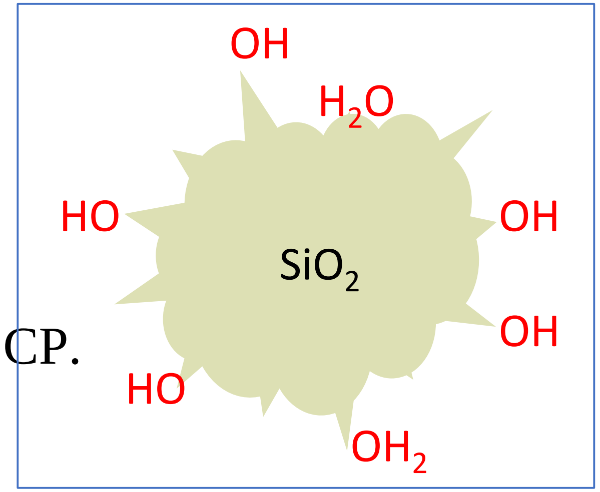
$$\gamma_H B_H = \gamma_C B_C$$

(B refers to the B_1 field of the RF pulse, not the magnet's B_0.)



Benefits:

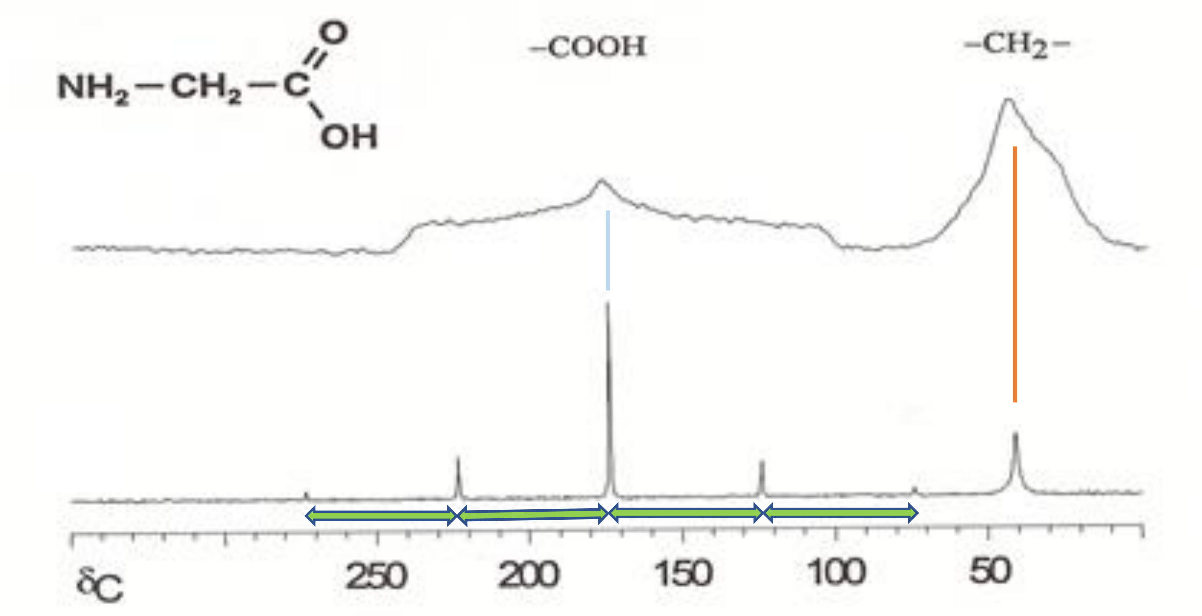
- Max. signal enhancement: $\gamma_H/\gamma_{X,}$ i.e. H/C = 4, H/N = 9
- $T_1(^1H) << T_1(X)$ → faster scanning
- CP is usually combined with MAS → "CP/MAS"
- Surface Analysis:
  Surfaces often carry protons (-OH, -NH, water) and are favorable for CP.
  Nuclei in the interior of a particle will not benefit from CP.
  Comparison of CP with non-CP spectra can identify location.



Key Techniques for Solid State NMR:

2. Magic Angle Spinning (MAS)

- MAS will remove dipolar and CSA broadening and collapse the broad powder patterns into sharp peaks.

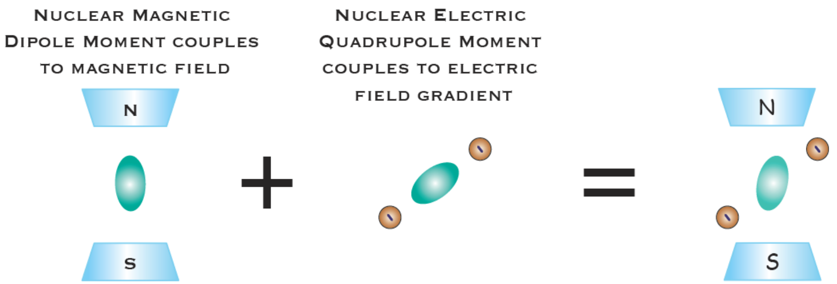


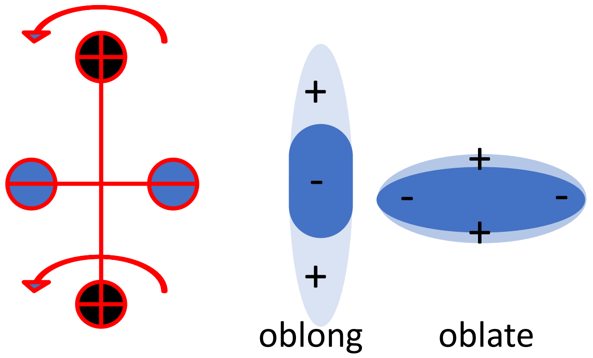
- The isotropic ^{13}C signals in the MAS spectrum for glycine are: 40 ppm for the methylene carbon and 173 ppm for the carbonyl carbon. A solution NMR spectrum would show signals at the same chemical shifts.
- The additional peaks are MAS sidebands, spaced at the MAS speed intervals (here: 5 kHz).

Key Techniques for Solid State NMR:

3. Double Angle Spinning (DAS, DOR)

Quadrupole nuclei (I > ½)

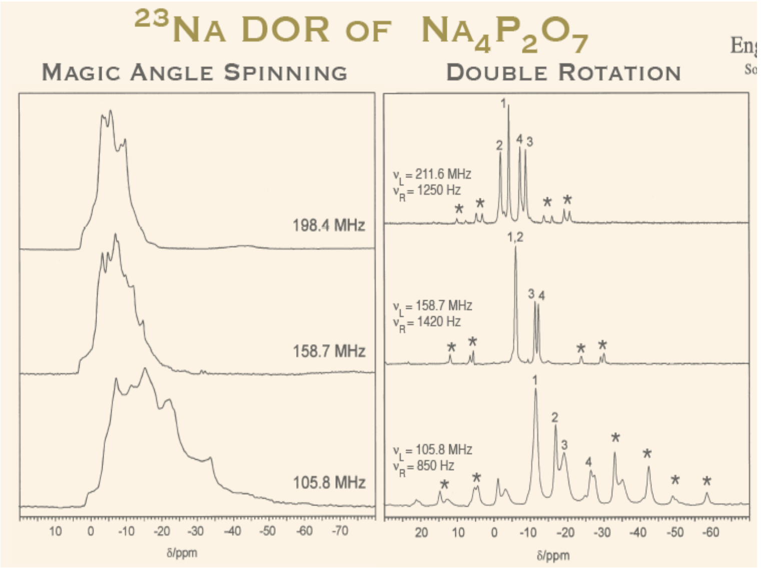




The electrical quadrupole (eQ) of a nucleus couples with the molecule’s electric field (eq):

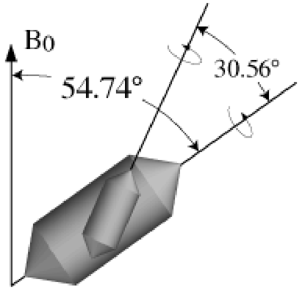
The Quadrupole Coupling Constant $\chi = (eq_{zz}eQ)/\hbar$ can broaden signals by several MHz, which cannot be removed with MAS alone.

- Removing higher order effects requires spinning around a second axis.
  DAS: switches the rotor angle during the experiment.
  DOR: spins a rotor within a rotating capsule.



DAS

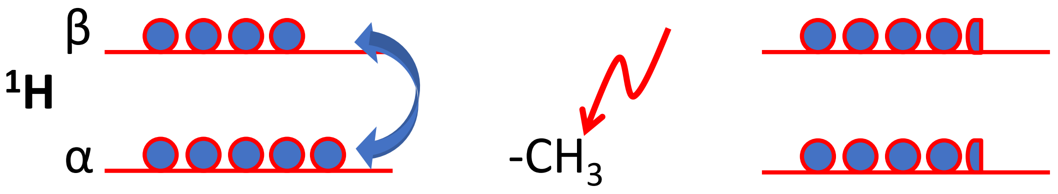
DOR



Key Techniques for Solid State NMR:

4. Decoupling

Irradiating a nucleus (typically ^{1}H) will lead to an equal distribution of its α and β populations. ^{1}H will become "invisible" to other nuclei. ➔ multiplets collapse into single peaks.



<u>Decoupling Techniques:</u>

CW decoupling (single frequency)

BB decoupling (random 10 ppm frequency modulation)

CPD decoupling (composite pulses for a more uniform decoupling)

<u>Side effect:</u>

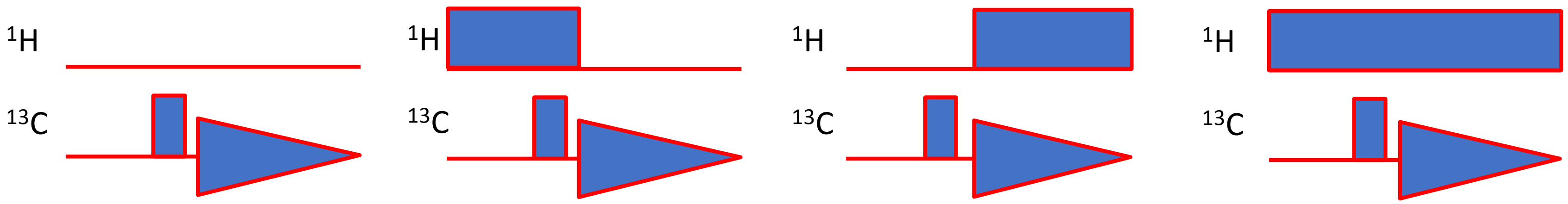
Magnetization is simultaneously being transferred to other nuclei (i.e. ^{13}C), changing their signal intensity through the *Nuclear Overhauser Effect* (NOE).

The NOE is beneficial for ^{13}C: Proton decoupling provides up to 50% enhancement.
^{15}N, ^{29}Si experience a negative NOE, which may lead to signal loss.
require special decoupling technique:

Key Techniques for Solid State NMR:

4. Decoupling

Frequently used Proton Decoupling Experiments:



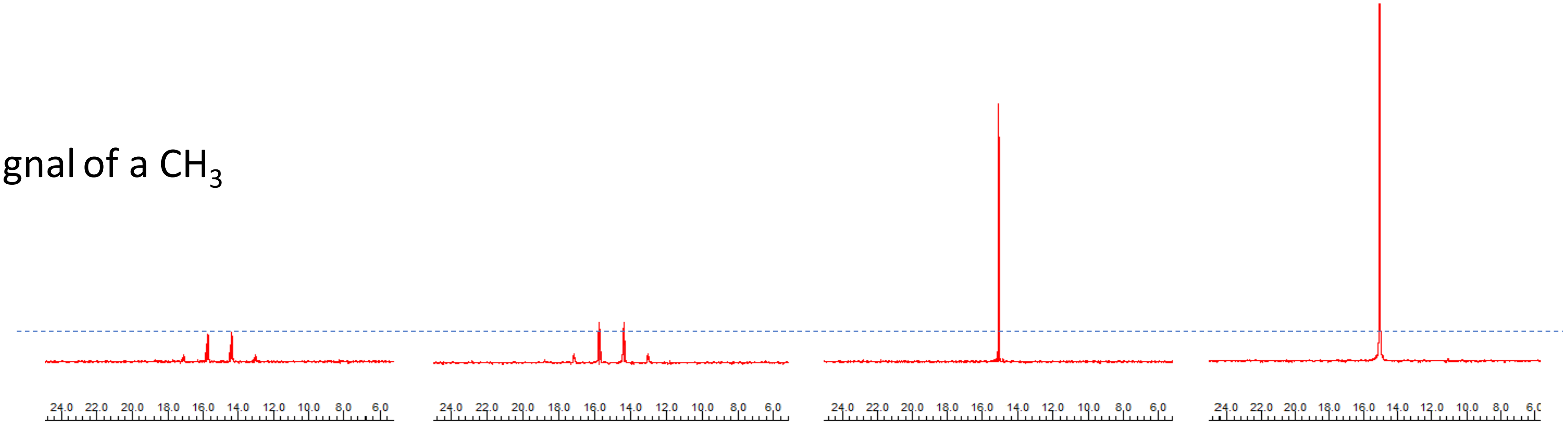
No Decoupling:
(no NOE, no simplification)

Gated Decoupling:
(NOE, no simplification)

Inverse Gated Decoupling:
(simplification, no NOE)

Broadband Decoupling:
(NOE + simplification)

^{13}C NMR signal of a CH_3



Technique for:

measurement
of couplings

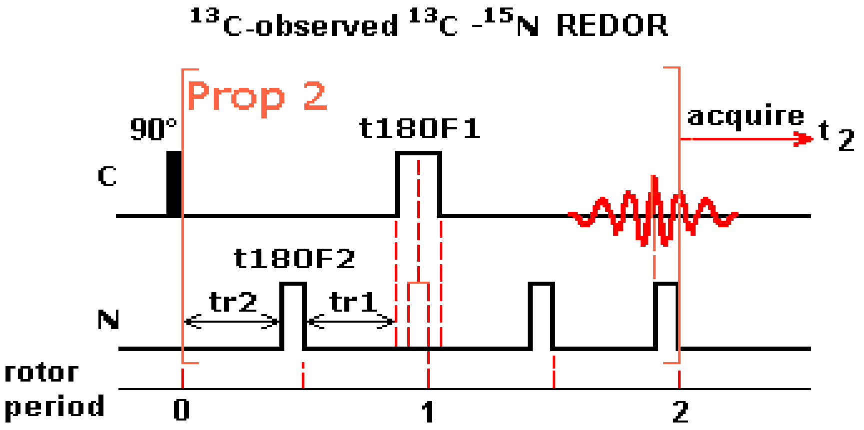
quantitative NMR,
default for Solids

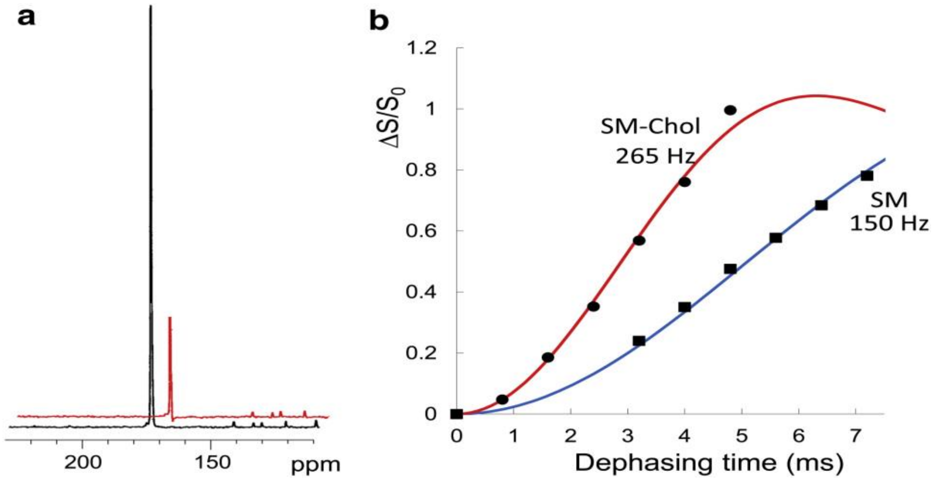
best sensitivity for ^{13}C,
avoid for ^{15}N, ^{29}Si

Key Techniques for Solid State NMR:

5. Recoupling

- While most couplings are removed by decoupling and MAS, dipolar couplings can be useful, as their size depends on the distance between nuclei.
- Recoupling experiments, i.e. REDOR, selectively re-introduce dipolar couplings between individual nuclei by synchronizing refocusing pulses with the MAS rotor speed.





- The size of the coupling constant determines the speed by which a magnetization of a nucleus is dephased.

Strong coupling → close proximity between nuclei.

Topics:

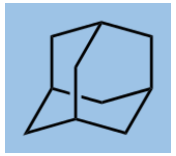
- Part I – Introduction
  - History of NMR
  - NMR Hardware
- Part II – NMR Theory
  - Nuclei – Spin – Magnetic Moments
  - Shielding – Chemical Shifts
  - Coupling – Molecular Structure
  - Relaxation – Linewidth
- **Part III – NMR Experiments**
  - **Sample preparation**
  - **Solution vs. Solid State NMR**
  - **Techniques for optimizing Solid State NMR**
  - **Research Examples**

Sample preparation:

- Obviously, no solvents must be used.
- We don’t need single crystals. Grind samples into a fine powder, or...
- Films can be cut into strips or punched into disks for bundling or stacking.
- Load and compact the rotors tightly and uniformly. Inspect rotors for cracks or damage.
  (imperfections are dangerous at spinning speeds of 10 kHz = 600,000 RPM !)

- Watch MAS Sample Preparation Video
  https://www.youtube.com/watch?v=bNFJj2g0UjI

Solid State NMR Experiments - Flowchart



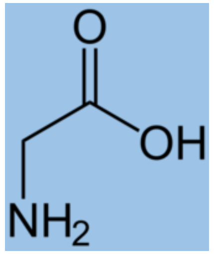
Adamantane Sample (^{13}C) **– Shimming (improve Magnet Homogeneity)**

↓↑

KBr Sample (^{79}Br) **– MAS Angle Adjustment**

These steps need only be performed occasionally.

↓



Glycine sample
(^{13}C) **– Probe RF Tuning / Impedance Matching**
(^{13}C) **– P_{90} Adjustment**
(^{13}C) **– CP Hartman-Hahn Match**
(^{13}C) **– Calibration**

↓

Research sample
(^{13}C) **– Probe RF Tuning/Matching**
(^{13}C) **– P_{90} Adjustment**
(^{13}C) **– Run desired experiment**

These steps need to be performed for any nucleus or sample to be investigated.

↓

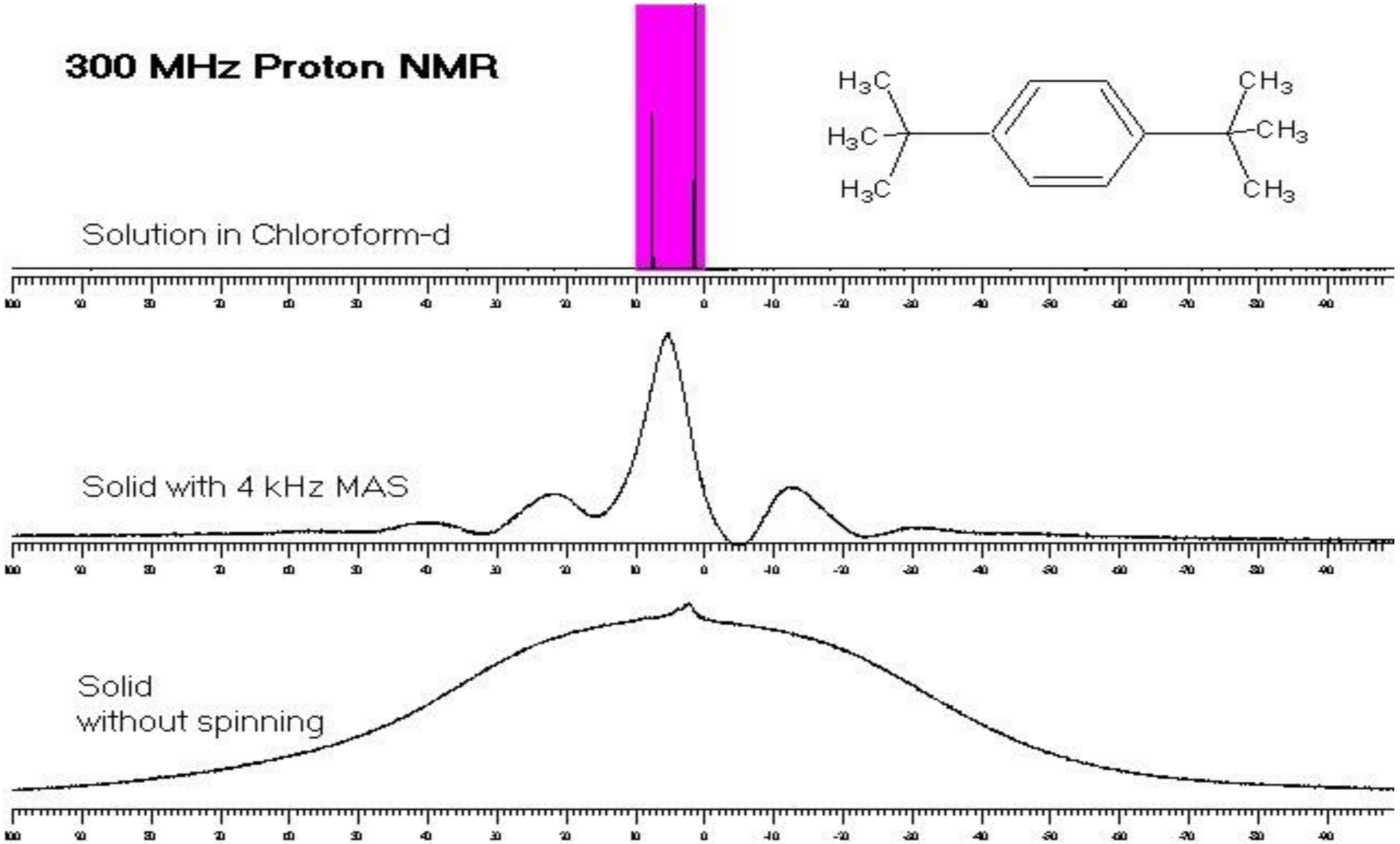
Final Spectrum

Solid State NMR

Which nuclear properties affect Solid State NMR experiments:

Problem	Symptom	Solutions
Nucleus with Low Natural Abundance	Weak Signals	Cross-Polarization Isotopic labeling, uniform or specific (expensive options: stronger magnets, cryoprobes, DNP, ultrafast MAS probes)
Chemical Shift Anisotropy	Broad Signals (Hz - kHz)	MAS
Dipolar Coupling (homonuclear)	Broad Signals (kHz)	MAS
Dipolar Coupling (heteronuclear)	Broad Signals (kHz)	Decoupling, usually ^{1}H or ^{19}F
Quadrupole Nucleus	Broad Signals (MHz) Satellite Transitions	MAS, DOR MQ-MAS
Paramagnetic Nucleus	Extremely Broad Signals (MHz+)	Record spectrum in segments and add the segments together. Relaxation may be faster than electronics.

Solution vs. Solid State NMR



Slow MAS speeds lead to spinning sidebands occurring at periodic intervals.
Ideally, MAS speeds should be faster than the width of the non-spinning signal. (unrealistic)
Special probes allow MAS speeds above 100 kHz, but 10 kHz is more common.

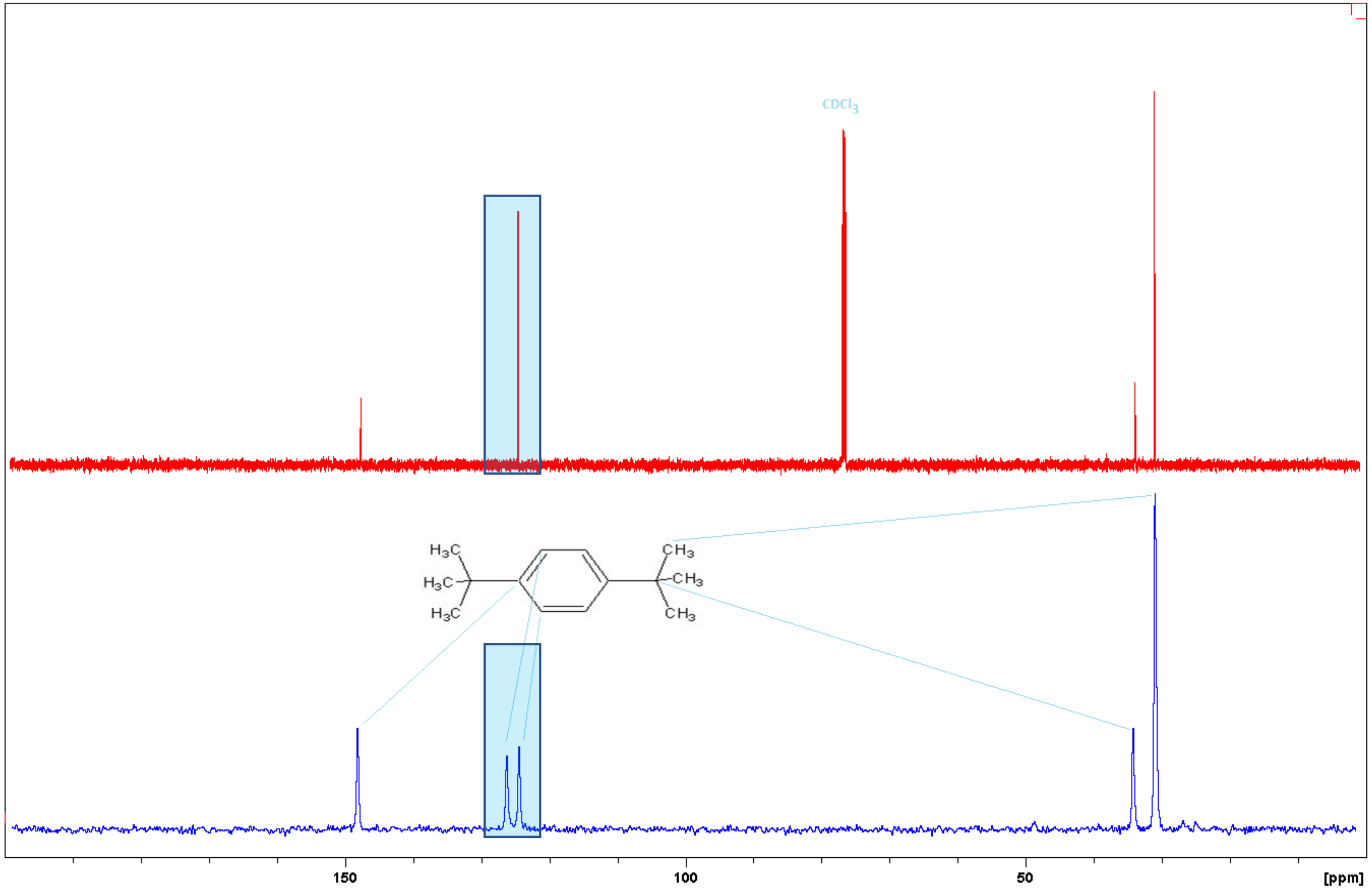
^{1}H

Solution NMR:
The well-resolved spectrum shows individual signals for aromatic and methyl protons.

Solid State NMR:
Severe broadening due to CSA and dipolar couplings can be partially alleviated by “Magic Angle” Spinning.

^{1}H observation only has limited usefulness for Solid State NMR

Solution vs. Solid State NMR



^{13}C is “spin-dilute” (1.1% natural abundance). → negligible dipolar broadening from other ^{13}C.
Dipolar interactions with protons are removed through “proton decoupling”.
CSA broadening is removed through Magic Angle Spinning (MAS).

^{13}C

Solution NMR:
The well-resolved spectrum shows individual signals for aromatic and aliphatic carbons.

Solid State NMR:
Crystalline samples give sharper signals than amorphous samples.

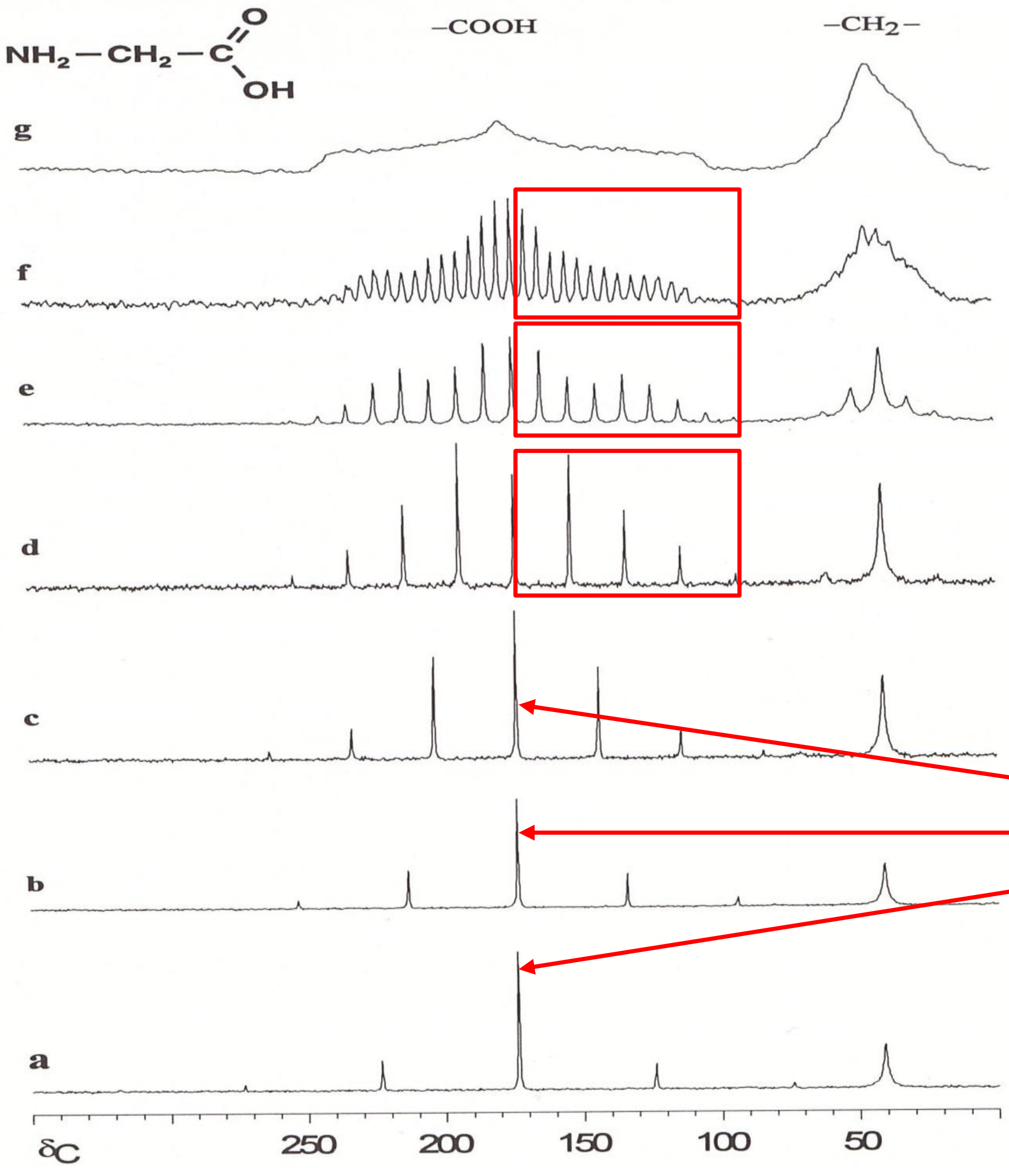
Restricted molecular motion can lead to separate ^{13}C signals for chemically equivalent C atoms.

High Resolution ^{13}C Solid State NMR is achievable.

Optimizing the MAS Speed

^{13}C

Carbon-13 - Glycine



Static powder pattern, no MAS

MAS = 500 Hz

MAS = 1 kHz

MAS = 2 kHz

MAS = 3 kHz

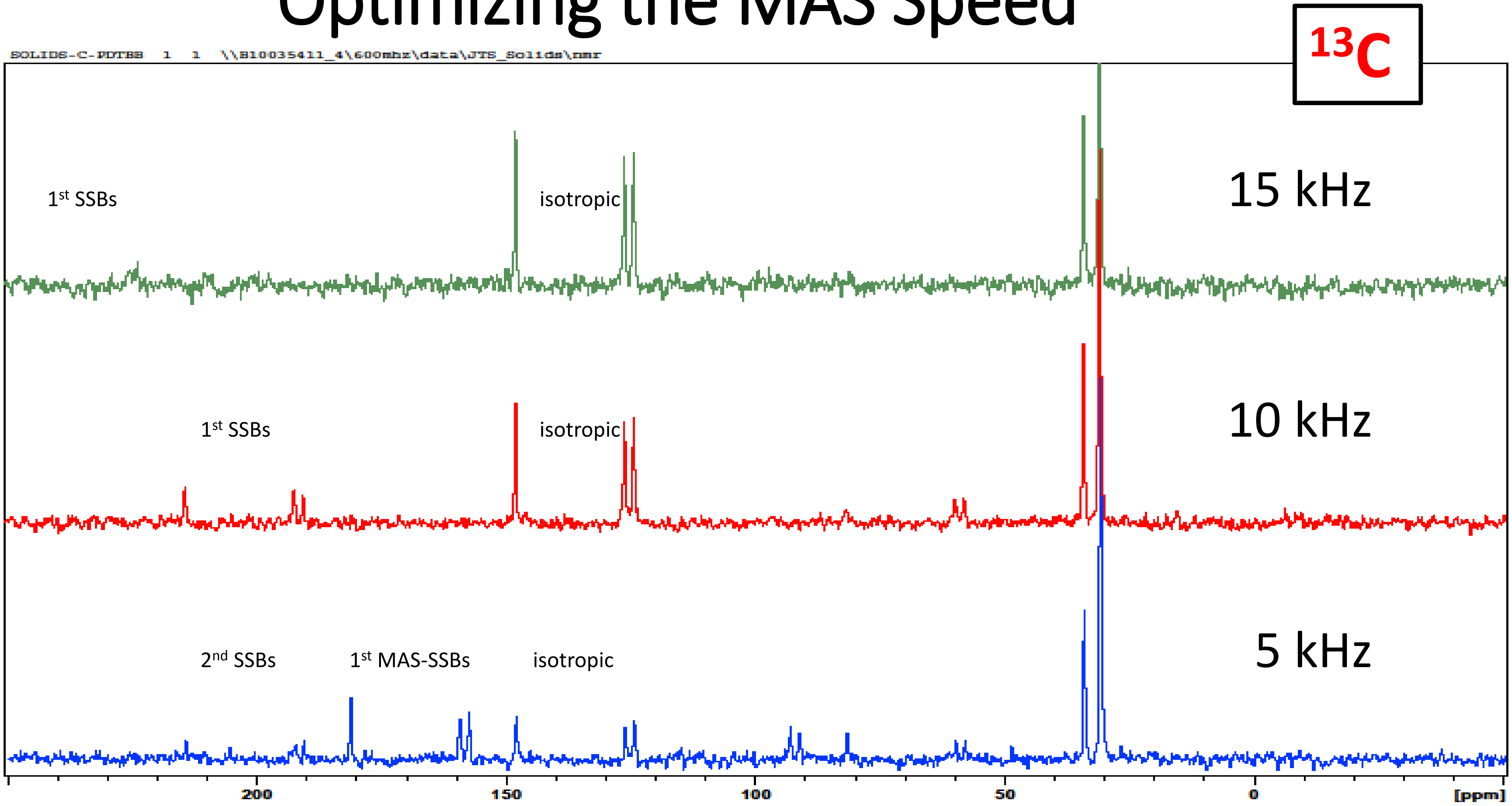
MAS = 4 kHz

MAS = 5 kHz

MAS generates patterns with individual sidebands separated by the MAS speed.

The position of the isotropic peak remains unaffected by the MAS speed. (Isotropic chemical shift)

Optimizing the MAS Speed

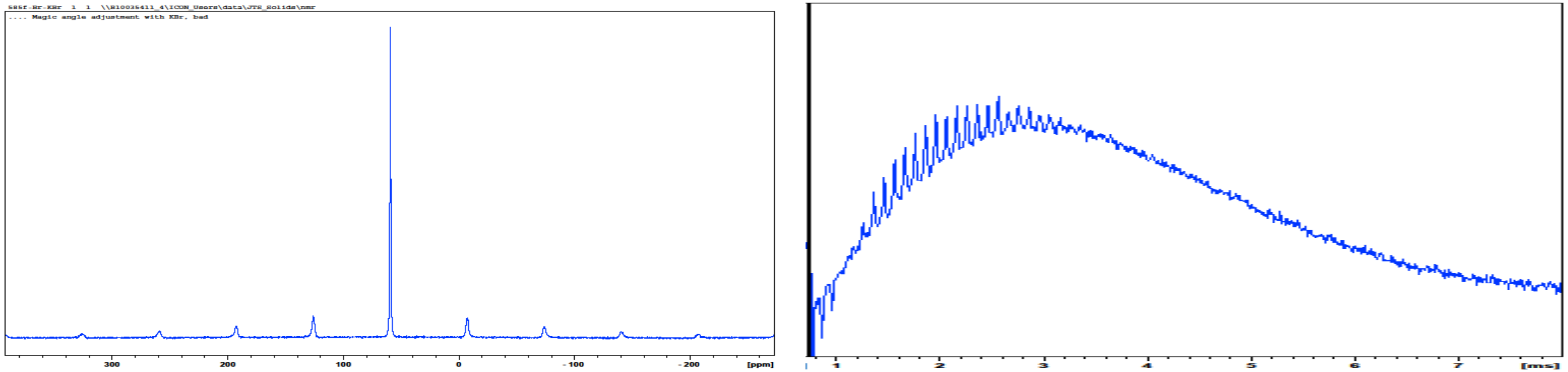


Optimizing the MAS Angle

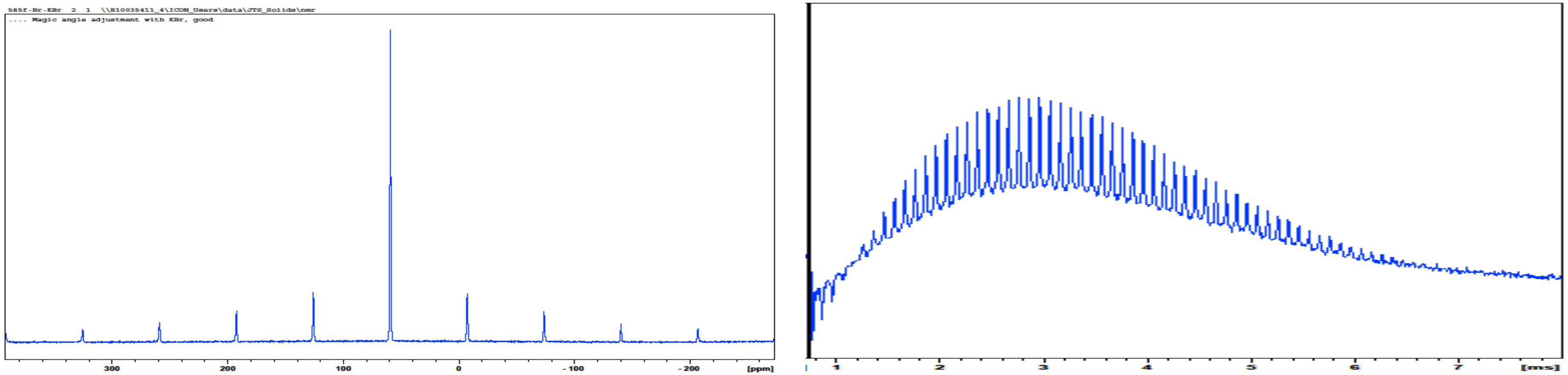
^{79}Br

Br-79 NMR (quadrupole nucleus), Sample: KBr, MAS=10 kHz

54.0°



54.7°

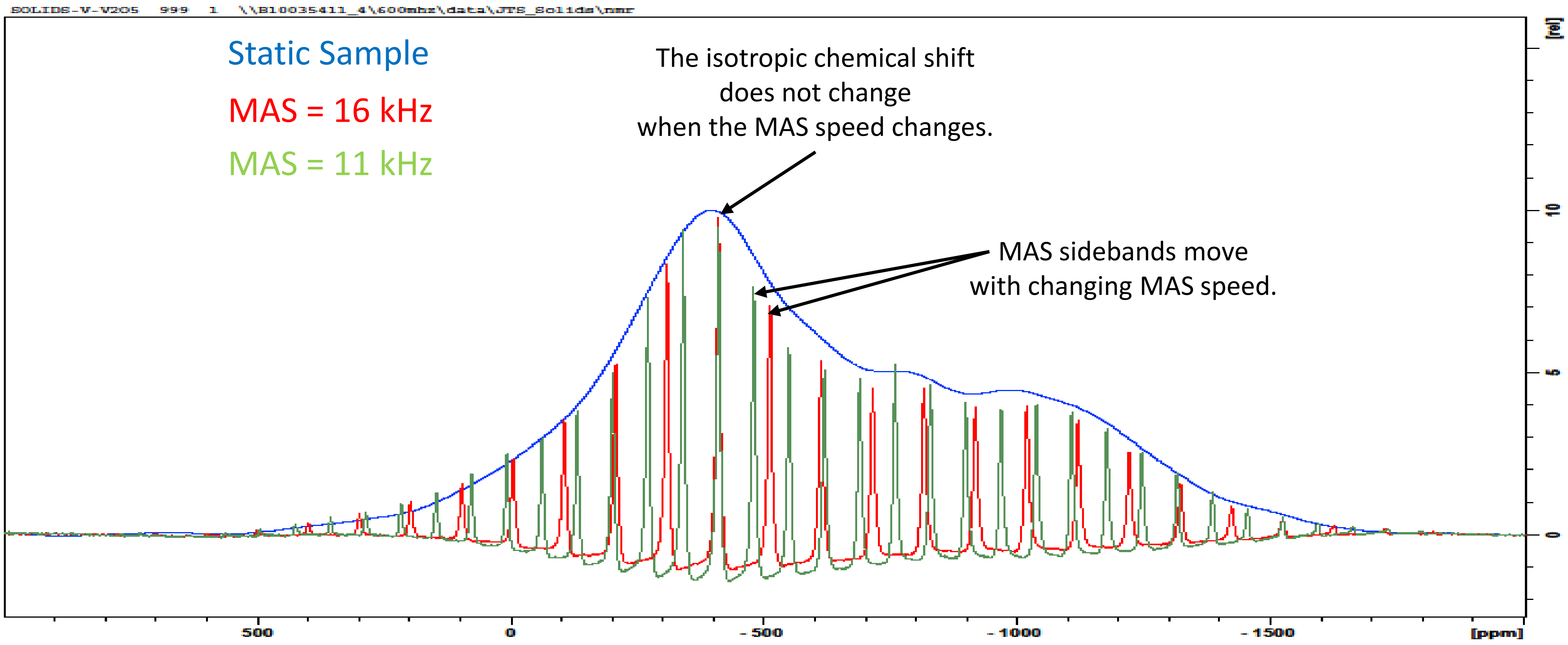


The correct MAS angle will give the sharpest peaks in the spectrum and the longest FID echo.

Quadrupole Nuclei (I > 1/2)

V-51 (I=7/2), 99.7 % nat. abundance – example: V_2O_5

^{51}V



The isotropic chemical shift does not change when the MAS speed changes.

MAS sidebands move with changing MAS speed.

- This is just the central -1/2 ➔ 1/2 transition …

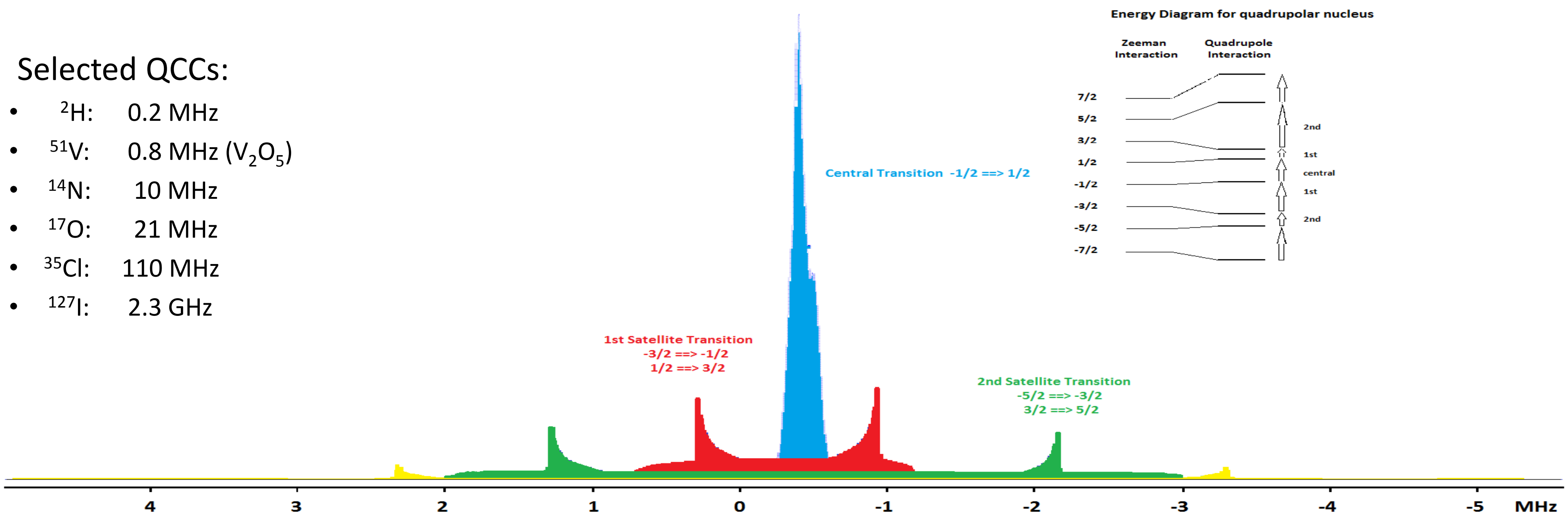
Quadrupole Nuclei (I > 1/2)

V-51 (I=7/2), 99.7 % nat. abundance – example: V_2O_5

^{51}V

- Transitions between higher spin states can span several Megahertz.
  Higher-order transitions are much weaker in intensity and can only be detected in segments.
  Due to bandwidth limitations of most NMR probes often only the central transition is studied.
- The central transition is often significantly broadened by CSA, as well as quadrupolar and dipolar couplings.

- Selected QCCs:
  - ^{2}H: 0.2 MHz
  - ^{51}V: 0.8 MHz (V_2O_5)
  - ^{14}N: 10 MHz
  - ^{17}O: 21 MHz
  - ^{35}Cl: 110 MHz
  - ^{127}I: 2.3 GHz



Quadrupole Nuclei (I > 1/2)

V-51 (I=7/2), 99.7 % nat. abundance:

^{51}V

- The CSA shape of the central transition reveals structural details about the VO coordination in vanadium-based heterogenous catalysts:

- A more symmetrical environment results in sharper signals due to smaller CSA values.

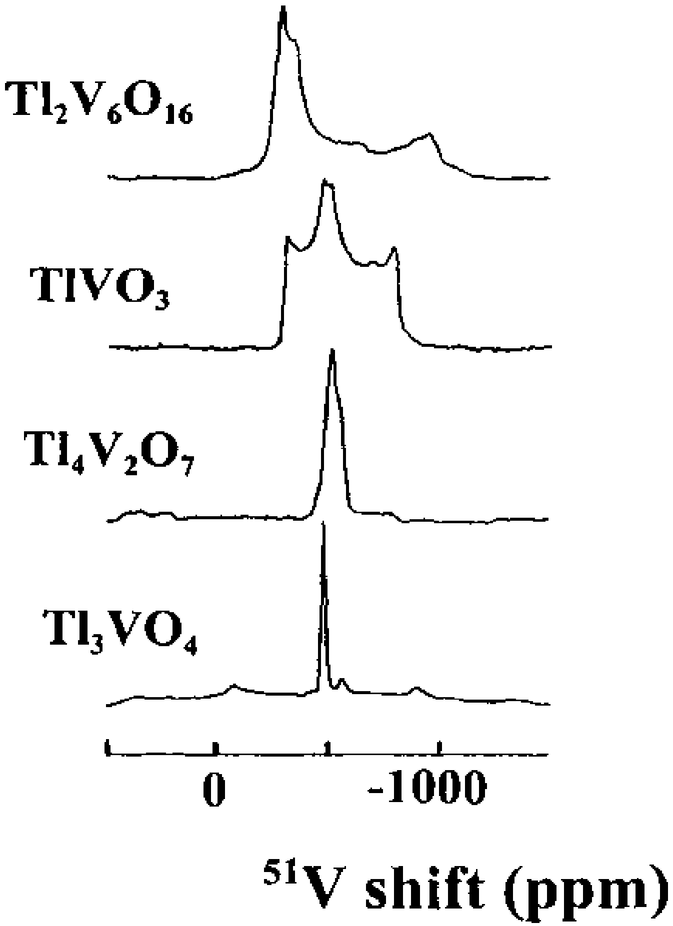
- A tetrahedral coordination with oxygen atoms leads to the highest symmetry for the vanadium nucleus.

distorted octahedron:

octahedron:

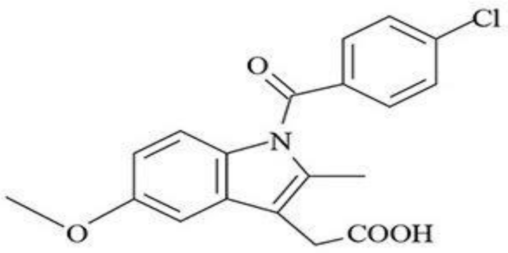
distorted tetrahedron:
(one “O” is shared by 2 “V”)

VO_4 tetrahedron:

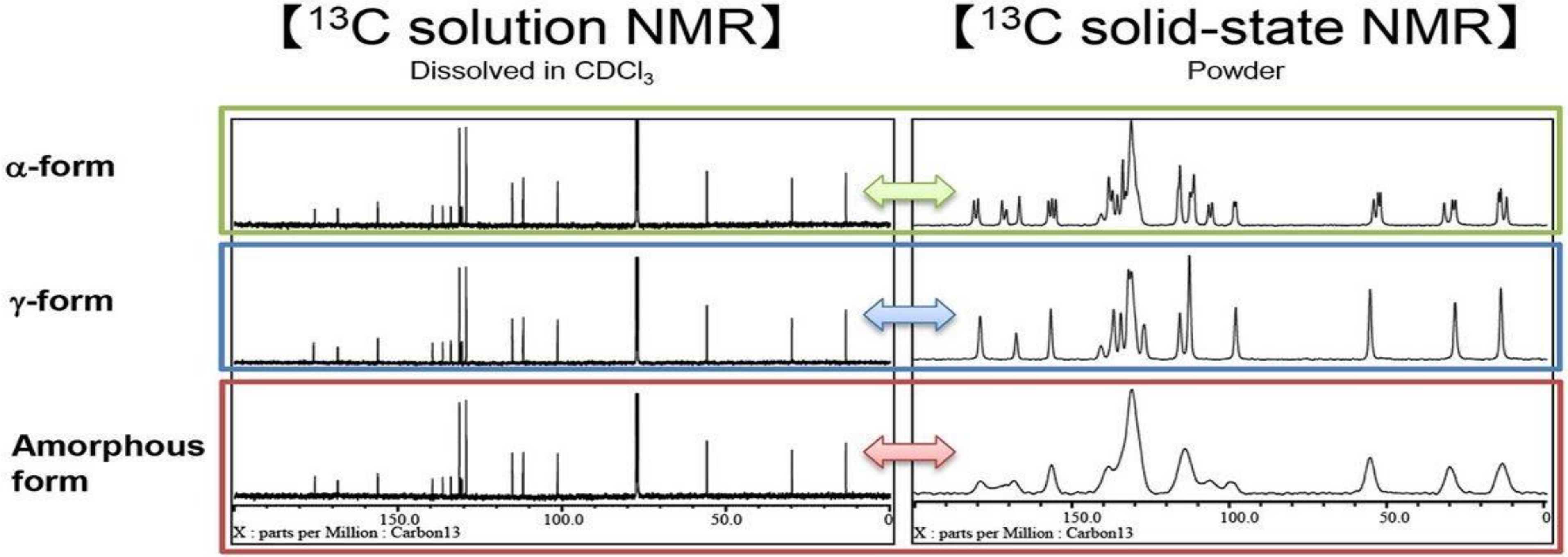


Identification of Polymorphs

^{13}C



Indometacin



https://www.jeol.co.jp/en/applications/detail/1149.html

Instrument: JNM-ECZ500R, ROYALPROBE™ and 3.2mm CPMAS probe

Silicon-29 NMR

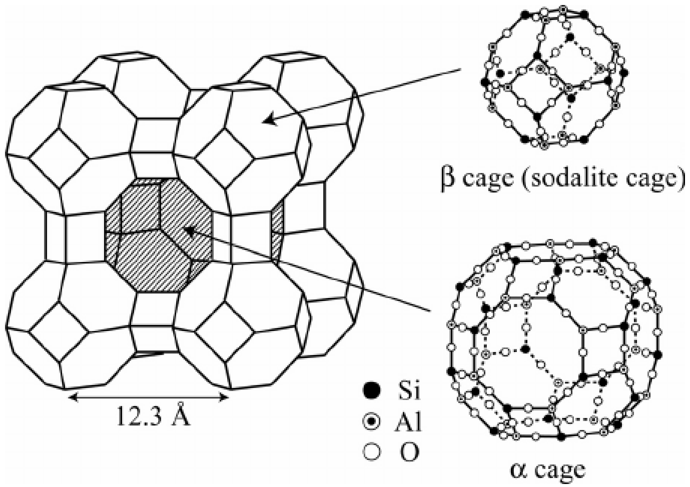
^{29}Si

Zeolites:

Five Silicon environments – five peaks:

Si4Al … Si3Al ... Si2Al … Si1Al ... Si0Al

Al	Al	Al	Al	Si
O	O	O	O	O
Al O Si O Al	Al O Si O Si	Al O Si O Si	Si O Si O Si	Si O Si O Si
O	O	O	O	O
Al	Al	Si	Si	Si



Zeolite NaX

Determination of Si/Al ratio in Zeolites:

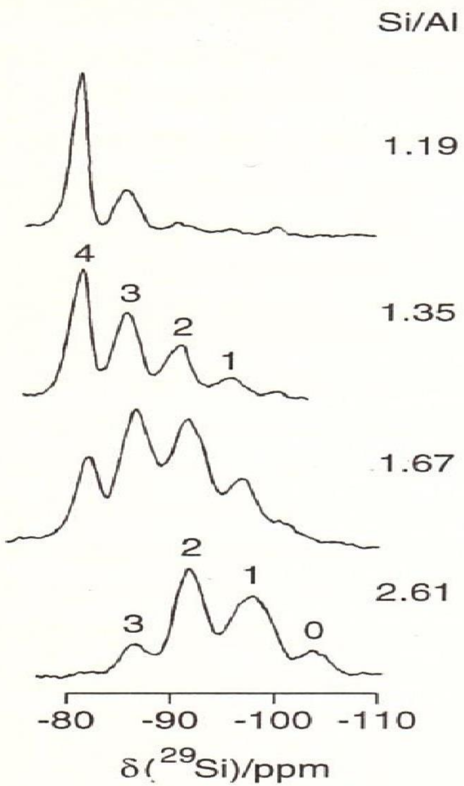


Fig. ^{29}Si NMR spectra of synthetic zeolites recorded with magic angle spinning. The resonances of Si atoms linked to *n* AlO_4 and (4 – *n*) SiO_4 tetrahedra are labelled *n* = 0, 1, 2, 3, 4. The Si/Al ratios are as indicated. (Adapted from J. Klinowski, S. Ramdas, J. M. Thomas, C. A. Fyfe, and J. S. Hartman, *J. Chem. Soc., Faraday Trans. II*, 1982, **78**, 1025.)

Silicon-29 NMR

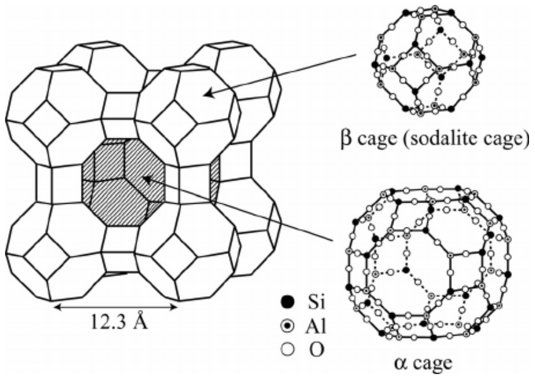
^{29}Si

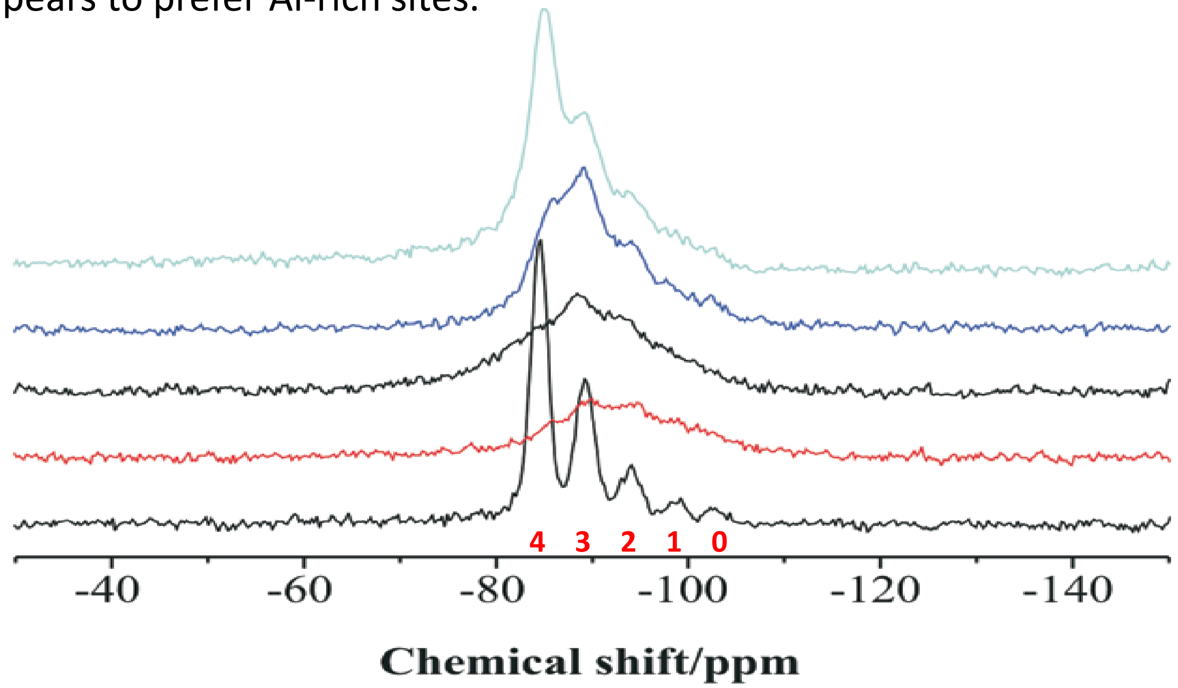
Zeolite: NaX

Differentiation of the strength of binding sites:

- Addition of paramagnetic Cu^{2+} cations uniformly broadens all silicon signals.
- Addition of ammonia forms a stable $[Cu(NH_3)_4]^{2+}$ complex which does not bind to the zeolite and can be flushed out of the cages.

Signal “4” recovers only after adding the maximum amount of NH_3.
→Cu^{2+} appears to prefer Al-rich sites.





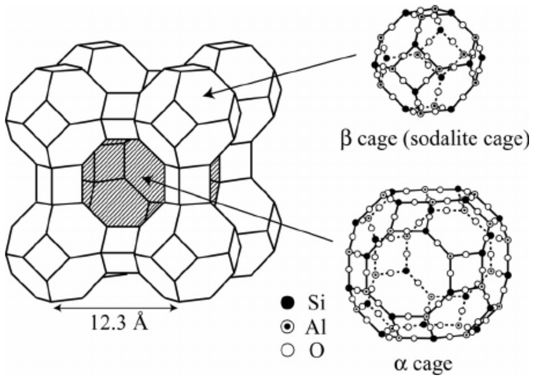
C. C. Kowenje, D. Doetschman, J. Schulte, C. Kanyi, J. DeCoste, S. Yang, B. Jones, *South African Journal of Chemistry* **63**, 6-11 (2010), "Effects of Copper Exchange Levels on Complexation of Ammonia in Cu(II)-exchanged X Zeolite."

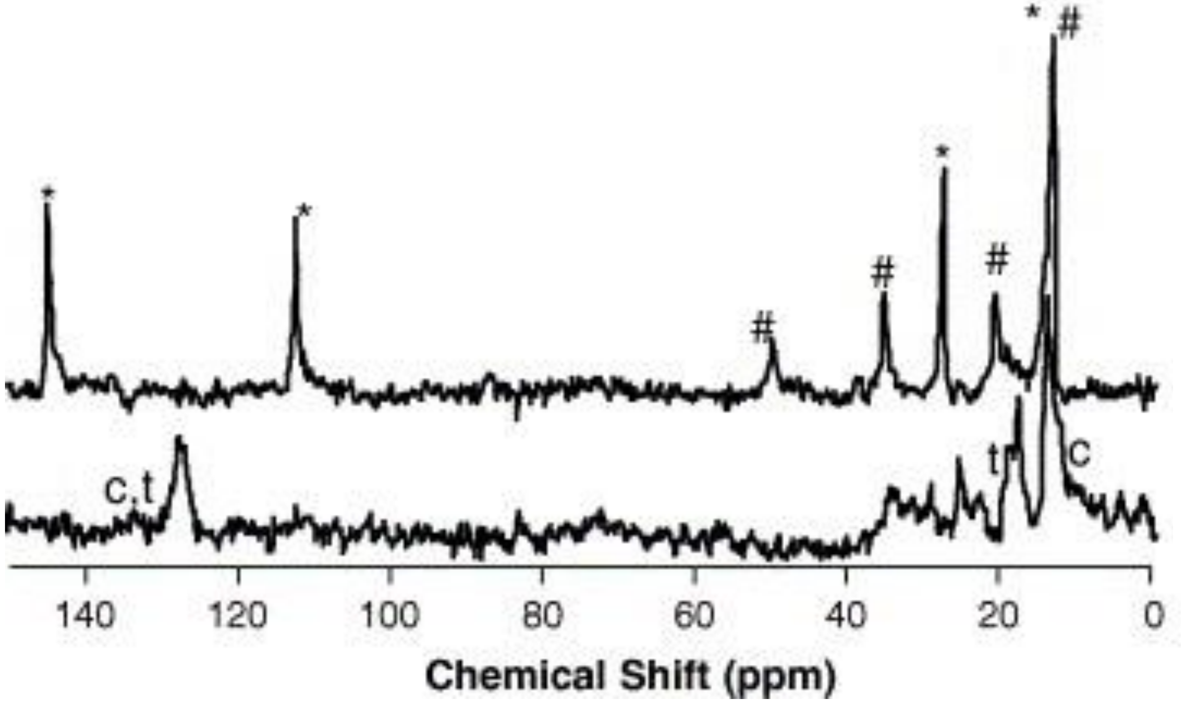
Carbon-13 NMR

^{13}C

Reactions in Zeolites:

Zeolites have a high affinity to volatile functionalized organic molecules.
They are used in gas masks to capture and neutralize poisonous gases.





Reaction of 1-chlorobutane:

in NaX → 1-butene

in Na^0/NaX → cis / trans 2-butene

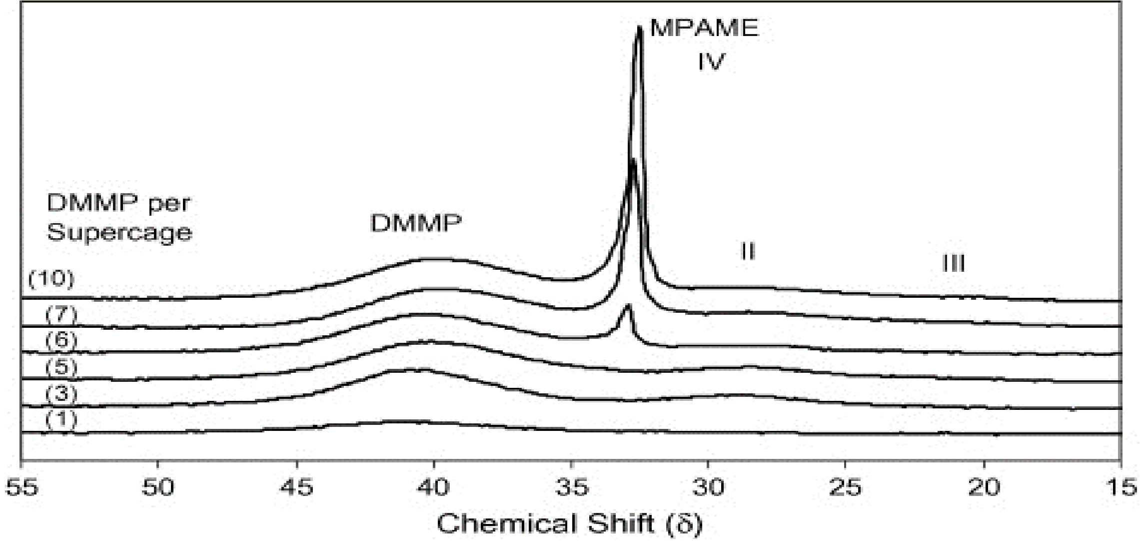
C. Kanyi, D. Doetschman, J. Schulte, K. Yan, R. Wilson, B. Jones, C. Kowenje and S. Yang, *Microporous and Mesoporous Materials* **92**, 292-299 (2006), "Linear, primary monohaloalkane chemistry in NaX and NaY faujasite zeolites with and without Na0-treatment: Zeolites as nucleophilic reagents II."

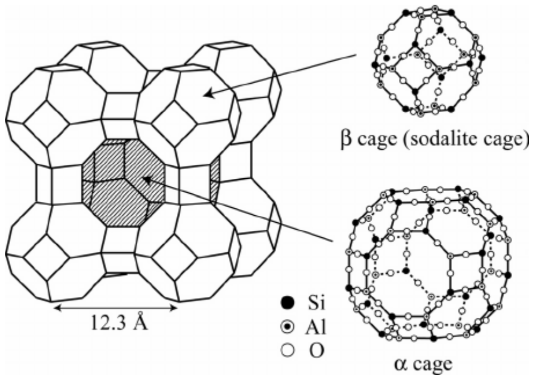
Phosphorus-31 NMR

^{31}P

Reactions in Zeolites:

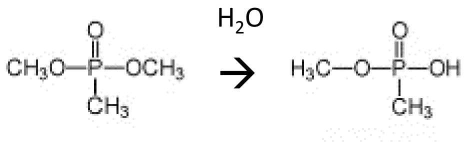
Hydrolysis of Dimethyl Methylphosphonate (DMMP)





The zeolite surface was activated with H_2O.

DMMP undergoes hydrolysis in NaX.



$$\mathrm{CH_3O{-}\underset{CH_3}{\overset{O}{P}}{-}OCH_3} \xrightarrow{H_2O} \mathrm{H_3C{-}O{-}\underset{CH_3}{\overset{O}{P}}{-}OH}$$

(DMMP)

MPAME (V)

DMMP is used as a precursor in the production of chemical warfare agents Sarin and Soman.

Here DMMP was used as a safe alternative to nerve agents to study the zeolite's ability to neutralize harmful substances.

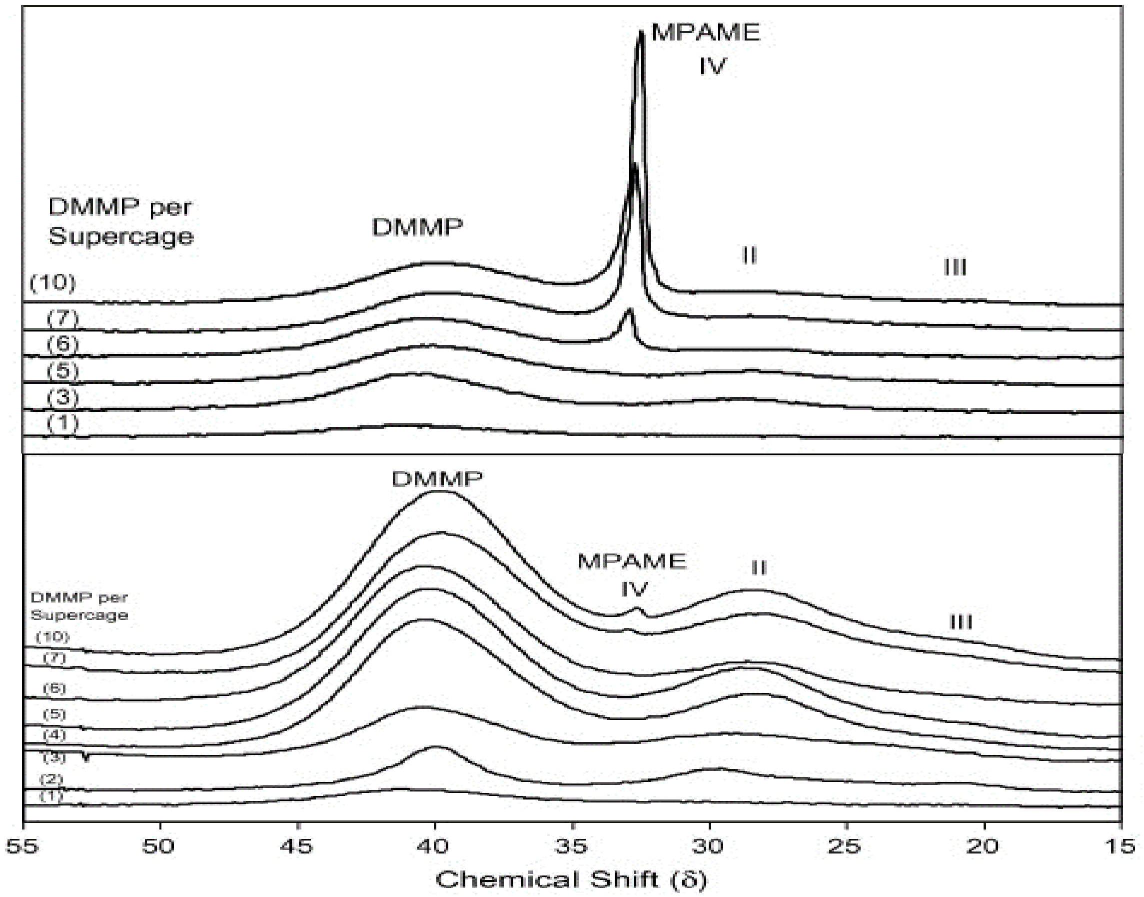
J. Sambur, D. Doetschman, S. Yang, J. Schulte, B. Jones, J. DeCoste, *Microporous and Mesoporous Materials* **112**, 116-124 (2008), "Multiple effects of the presence of water on the nucleophilic substitution reactions of NaX Faujasite zeolite with dimethyl methylphosphonate (DMMP)."

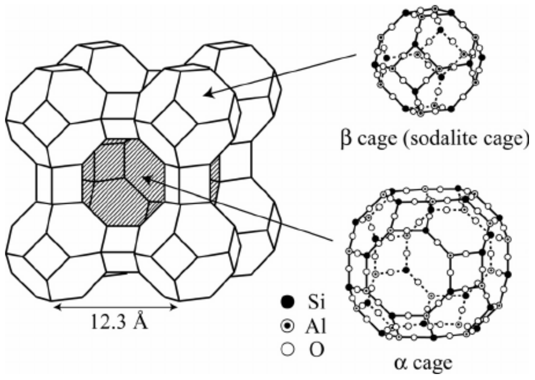
Phosphorus-31 NMR

^{31}P

Surface Analysis: CP vs. non-CP spectra

(Molecules have to be immobilized at a hydrogen-rich surface to benefit from CP.)





Top: without CP

Bottom: with CP

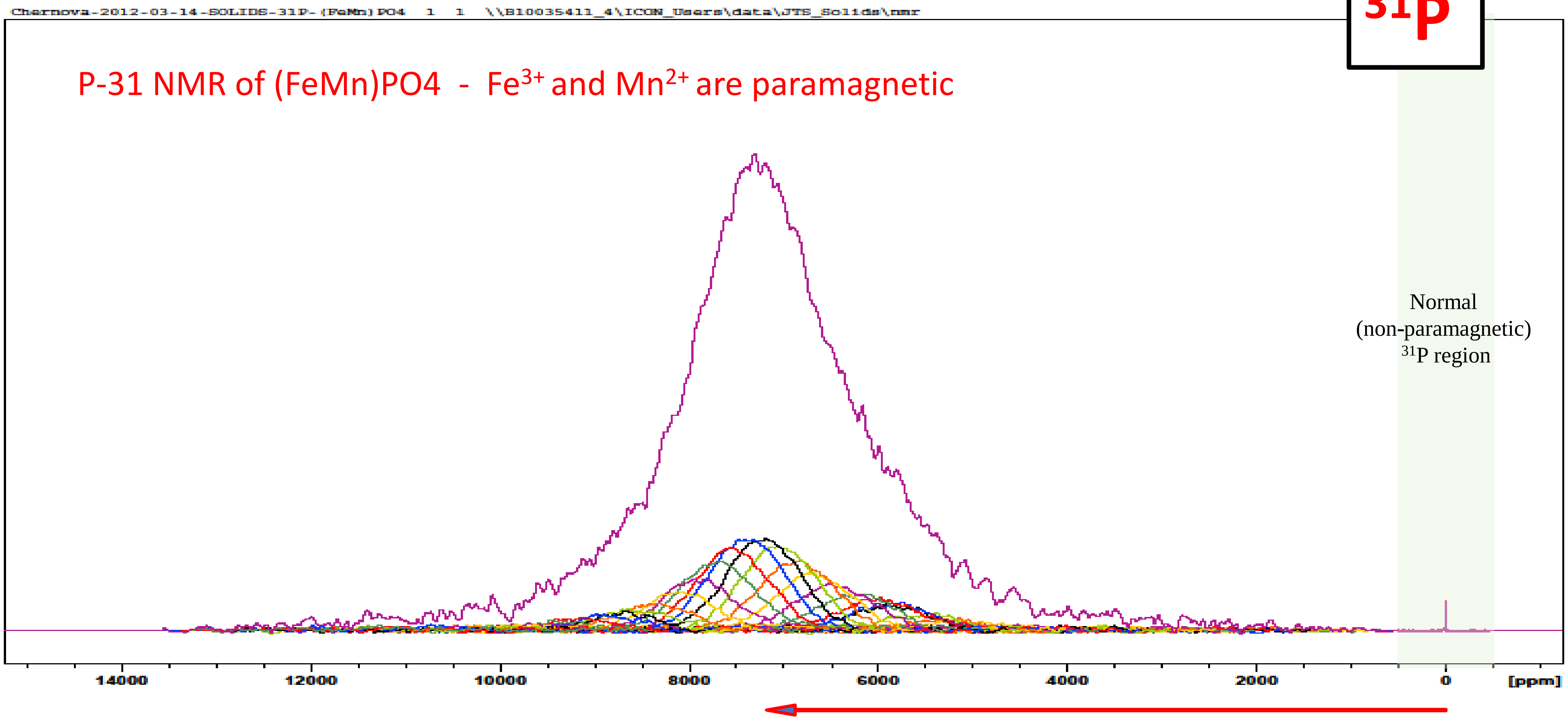
The zeolite surface was activated with H_2O.

DMMP is bound to the surface (strong CP signal).

Hydrolysis product MPAME is mobile (weak CP signal).

J. Sambur, D. Doetschman, S. Yang, J. Schulte, B. Jones, J. DeCoste, *Microporous and Mesoporous Materials* **112**, 116-124 (2008),
"Multiple effects of the presence of water on the nucleophilic substitution reactions of NaX Faujasite zeolite with dimethyl methylphosphonate (DMMP)."

Paramagnetic compounds



^{31}P

P-31 NMR of (FeMn)PO4 - Fe^{3+} and Mn^{2+} are paramagnetic

Normal
(non-paramagnetic)
^{31}P region

- Unpaired electrons can shift the NMR signal by several 1000 ppm from the expected region.
- Signals can be too broad to record in a single experiment.
  ➔ Combine multiple spectra recorded with shifted frequency offsets to cover the entire spectrum.

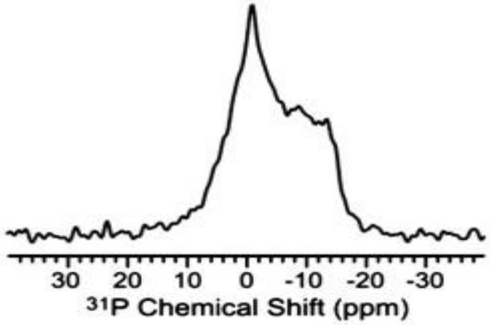
Biomolecules

^{31}P

Some DNAs, RNAs, peptides, and proteins are insoluble.
Others may be soluble, but we want to study their interactions with insoluble constructs, i.e. cell membranes.

External addition of peptide to lipid bilayer:

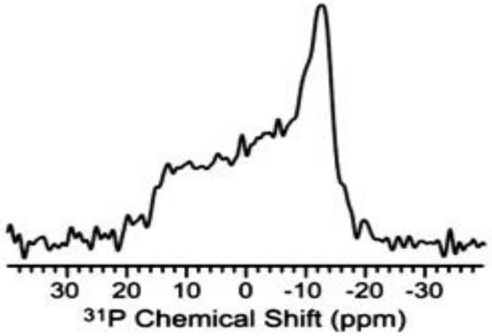
Narrow CSA pattern



Insertion of peptide in lipid bilayer:

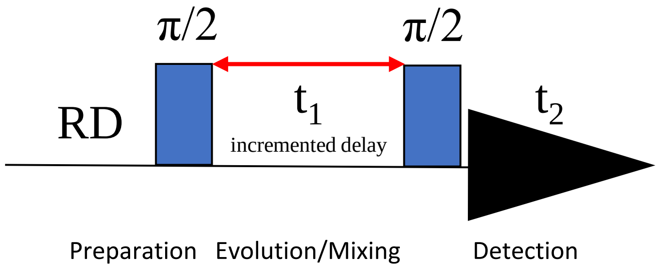
Broad CSA pattern

→ disruption of lipid membranes

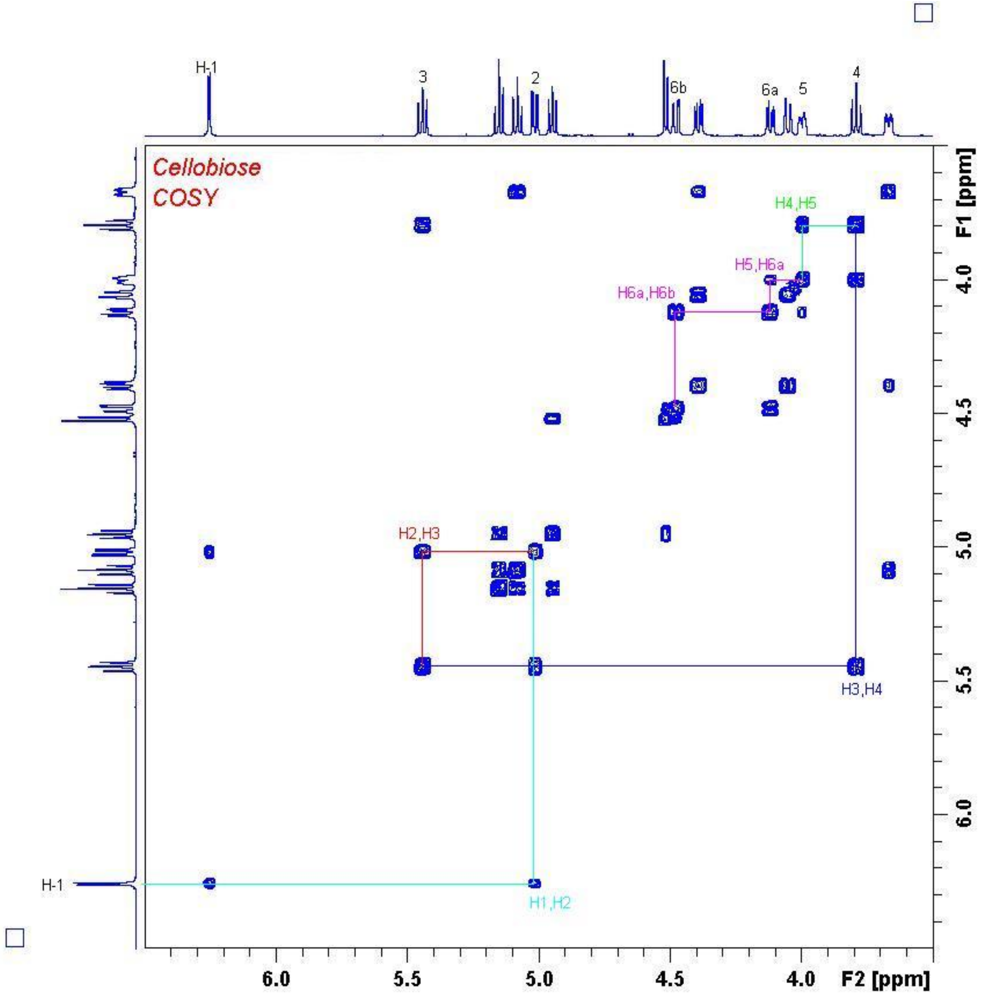


W. Qiang, W. Yau, J. Schulte, *Biochemica et Biophysica Acta - Biomembranes* **1848**, 266-276 (2014),
"Fibrillation of beta-amyloid peptides in the presence of phospholipid bilayers and the consequent membrane disruption."

2-Dimensional Experiments



COSY



Concept of 2D experiments:

One delay in the pulse sequence is systematically incremented to create a second time dependence, t_1. Fourier Transform in two dimensions creates two frequency axes.

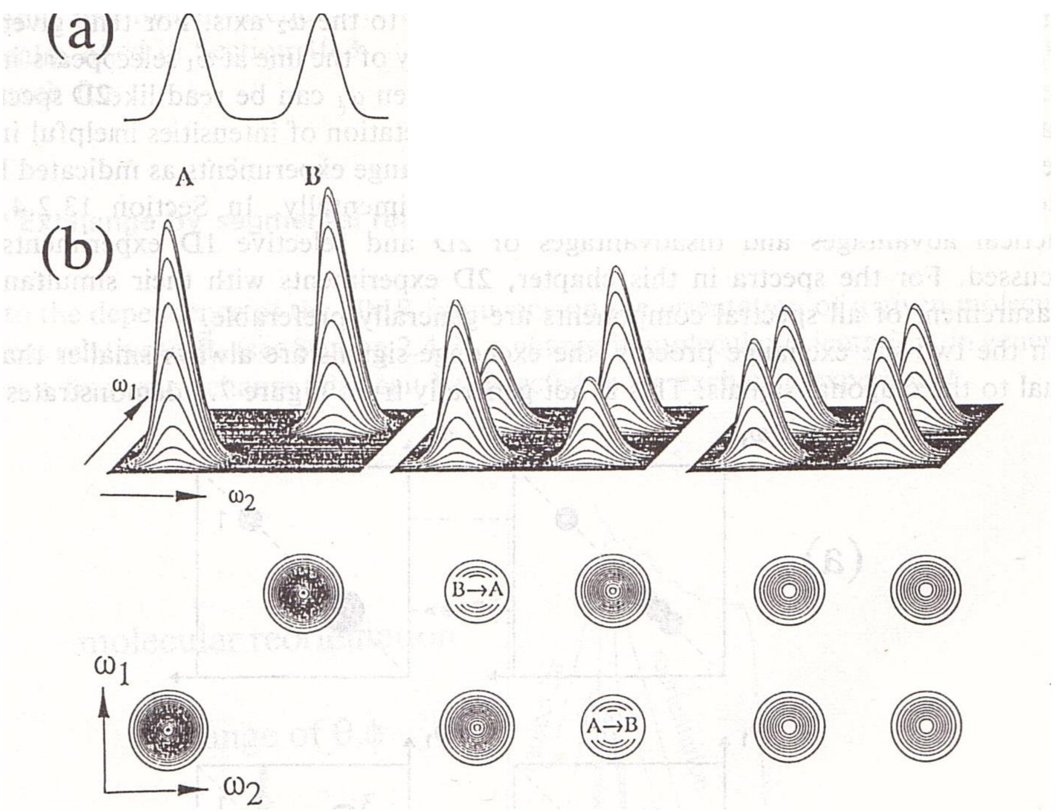
Additional pulses and/or delays during the evolution period can be used to probe specific structural properties and interactions.

The resulting 2D spectrum shows correlations between different atoms based on one or more structural parameters, i.e.:

- Couplings
- Proximity
- Exchange
- Diffusion

Polymer Dynamics

Molecule “X” can exist in two orientations, giving two signals A and B.
Is there a dynamic exchange between forms A and B?



no exchange slow exchange fast exchange

2D Exchange Spectroscopy allows distinction between:

-motion of the molecule

-internal motion of a fragment

-no motion