The Many Walks of Magnetic Resonance

Past, Present and Beyond

Stanislav Sýkora

www.ebyte.it

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In essence, what *is* Magnetic Resonace

In *my* opinion,

Magnetic Resonance is a way to observe and manipulate particles with spin and magnetic moment and, in practical terms, one of the most important Physics developments of 20-*th* Century,

just after

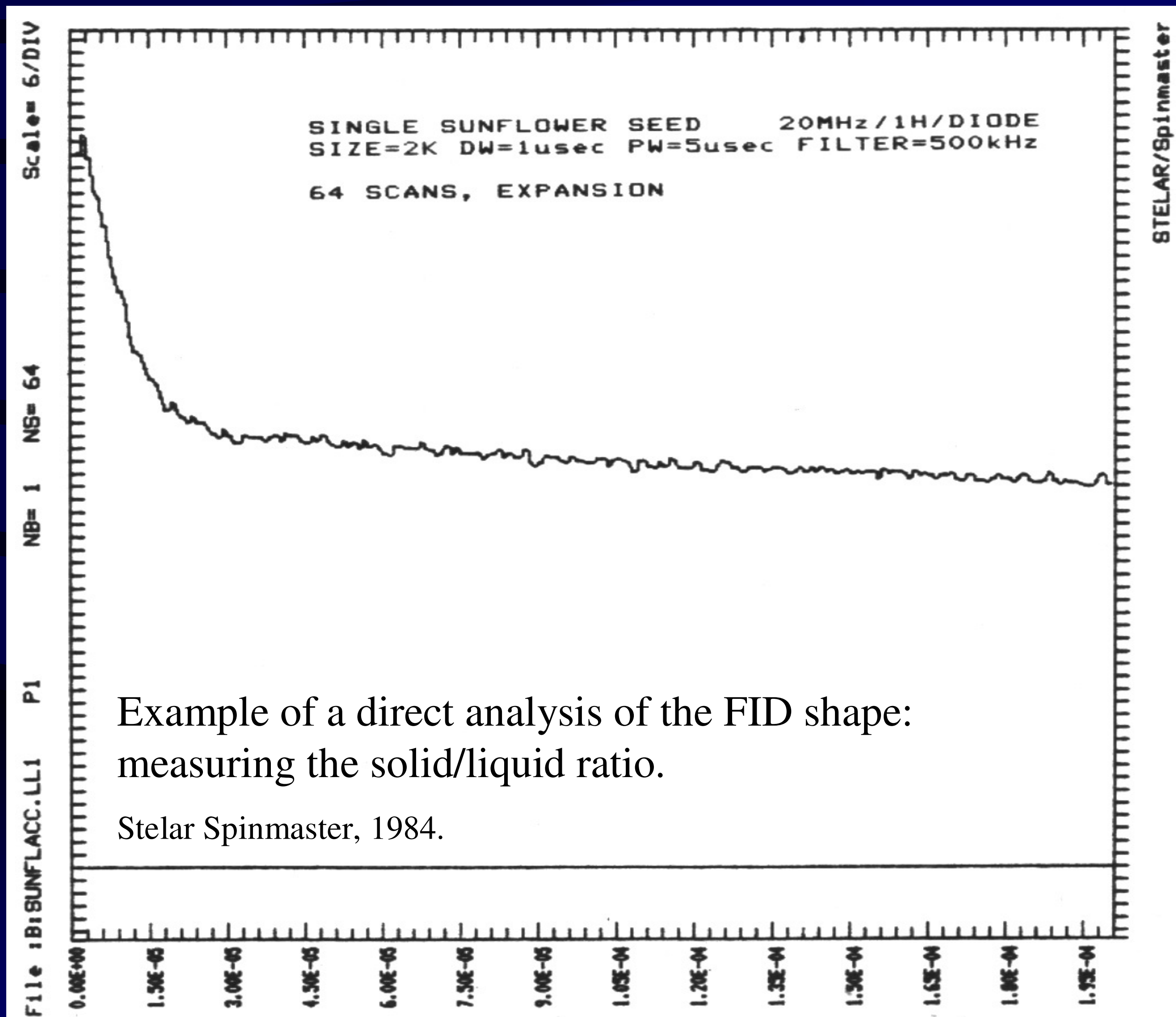
Quantum Physics itself

Without MR there would be
no modern Chemistry, Biochemistry and Farmaceutics,
and *only severely mutilated* Medical Diagnostics

Examples ?

Note: Originally, the following nine slides formed a sigle-slide, animated sequence

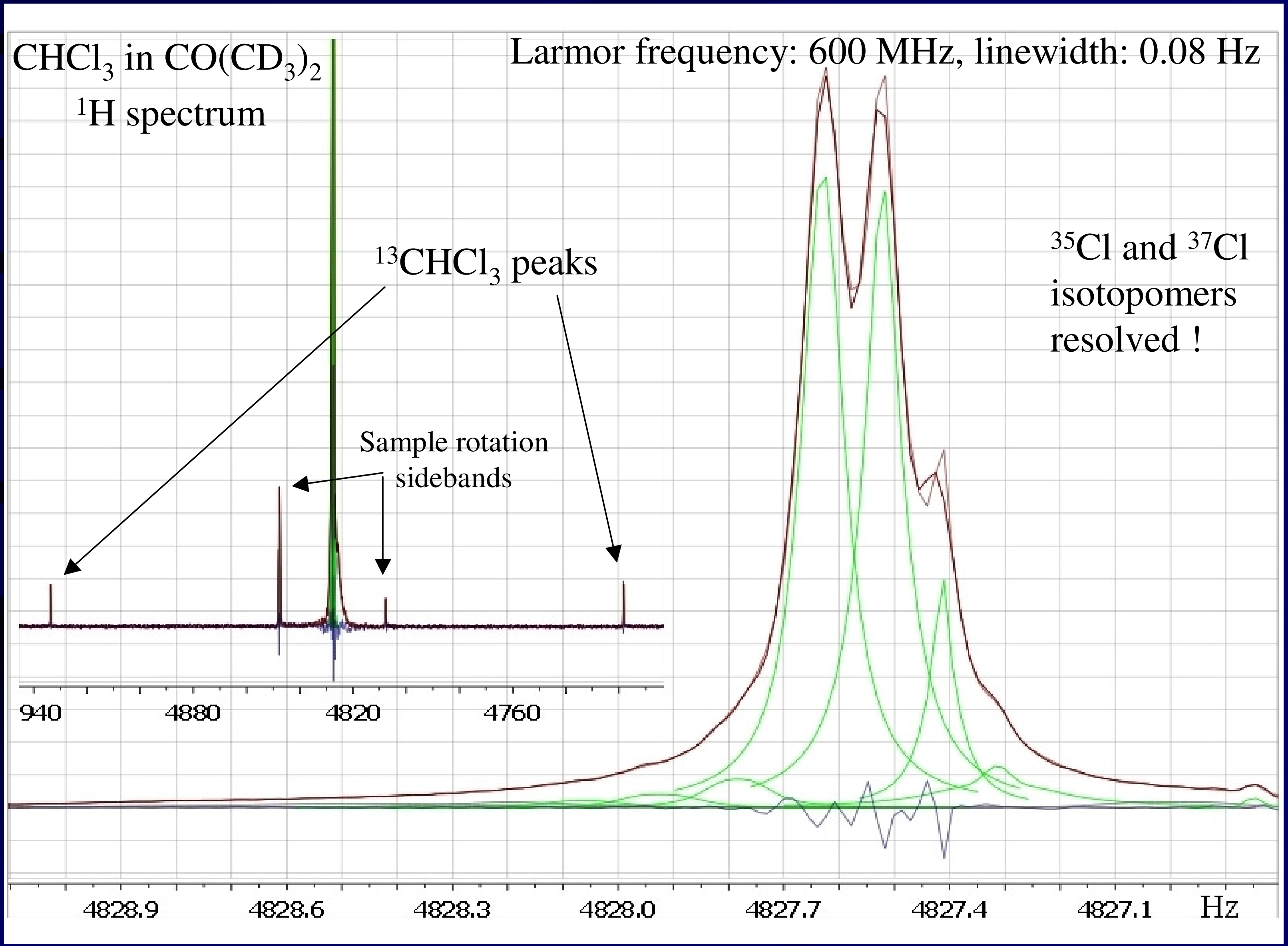
Time-domain NMR



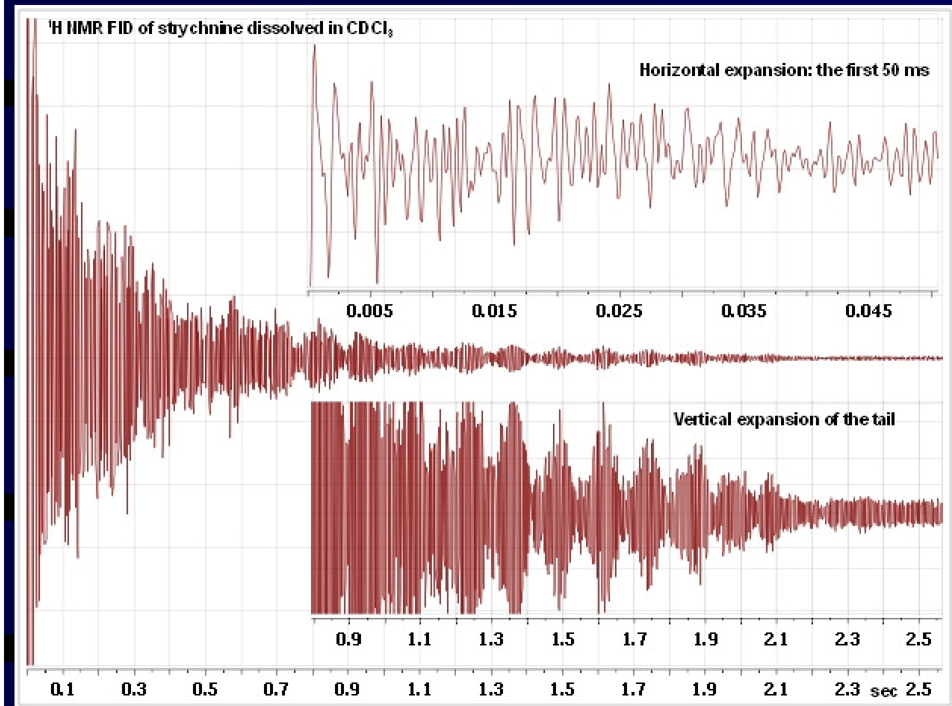
Example of a direct analysis of the FID shape: measuring the solid/liquid ratio.

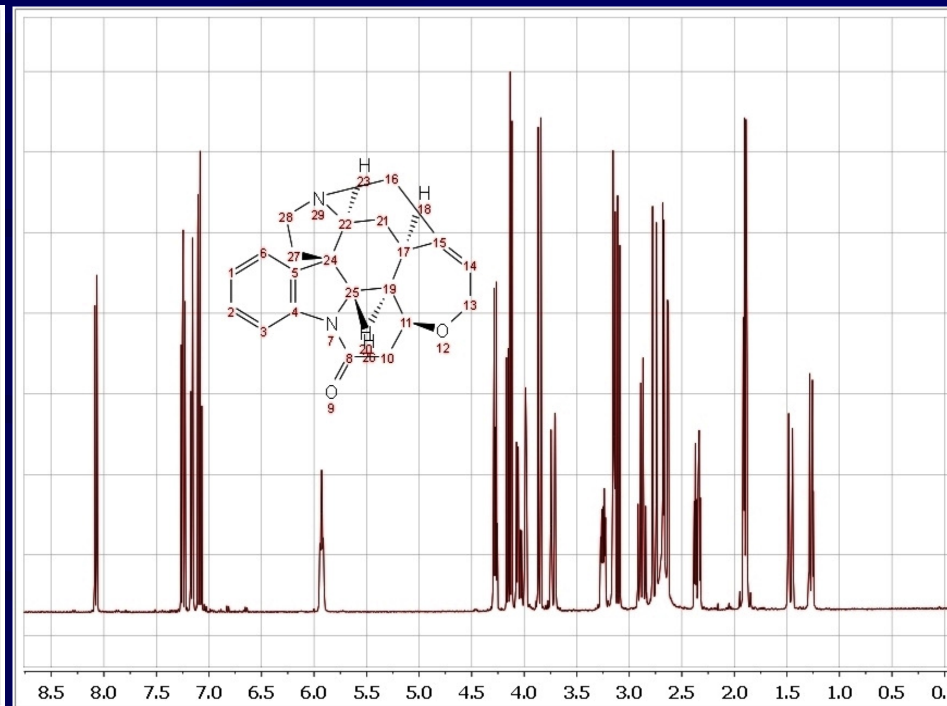
Stelar Spinmaster, 1984.

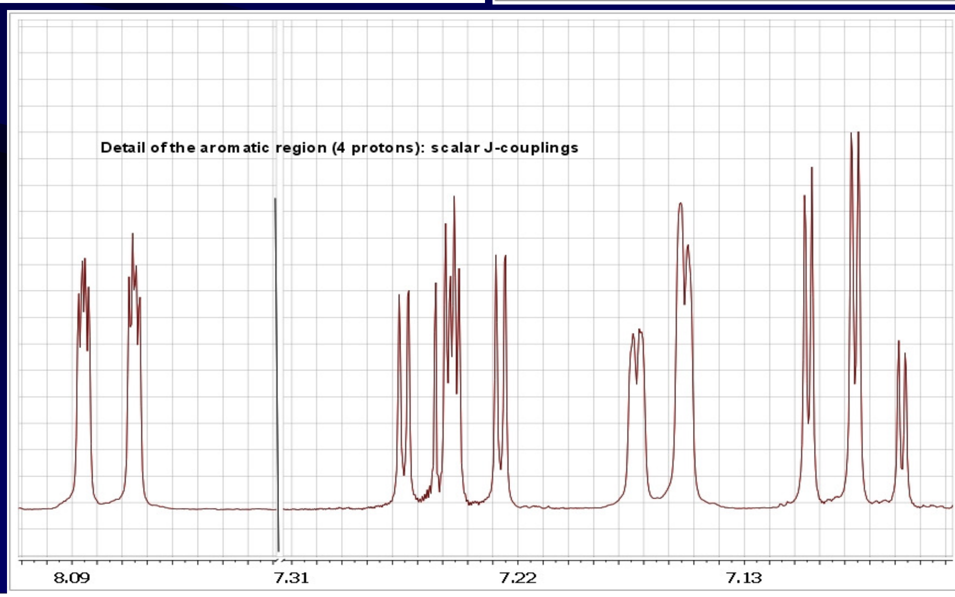
Spectroscopy with its amazing resolution



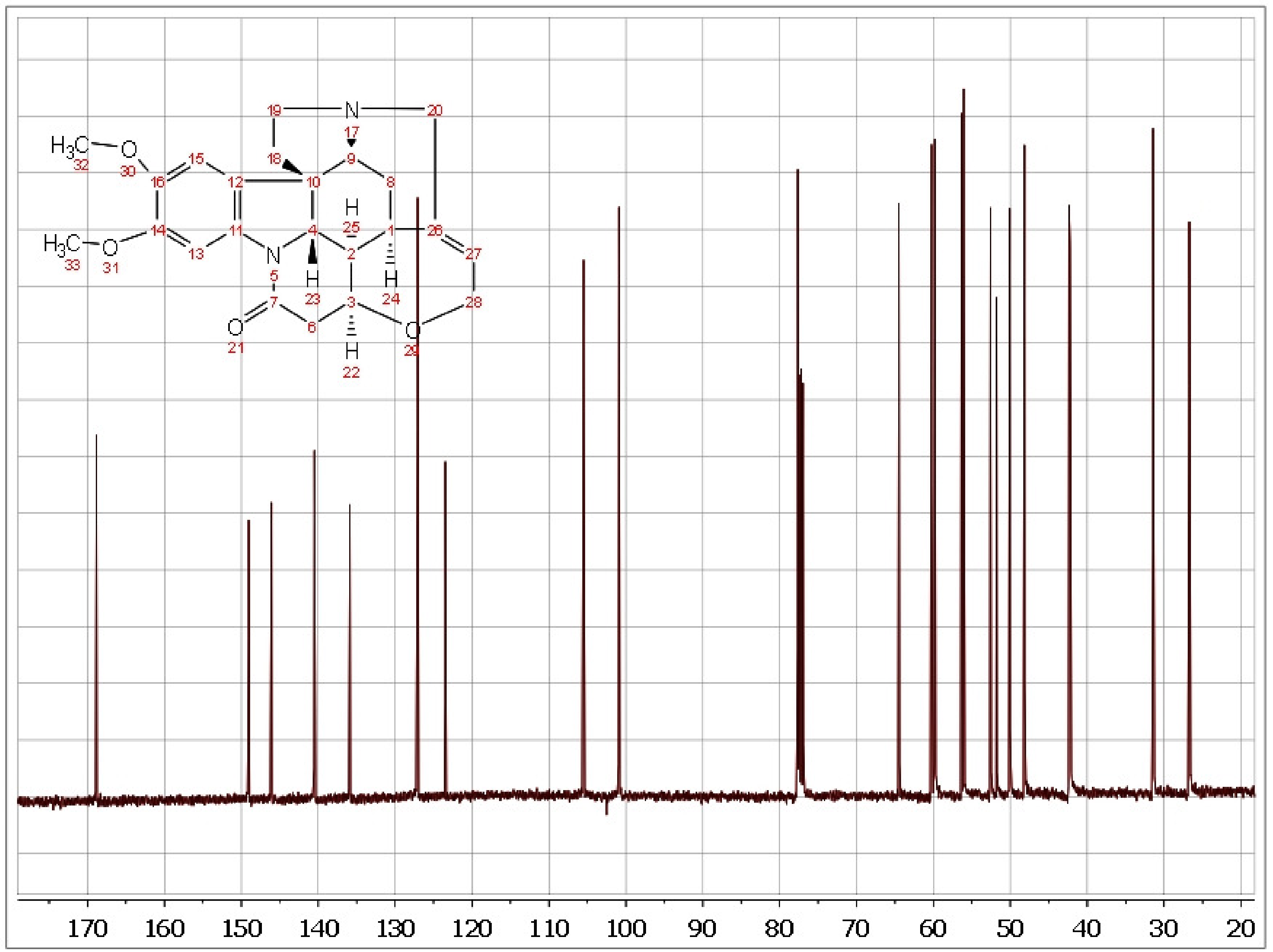
1D FT Spectroscopy in Chemistry



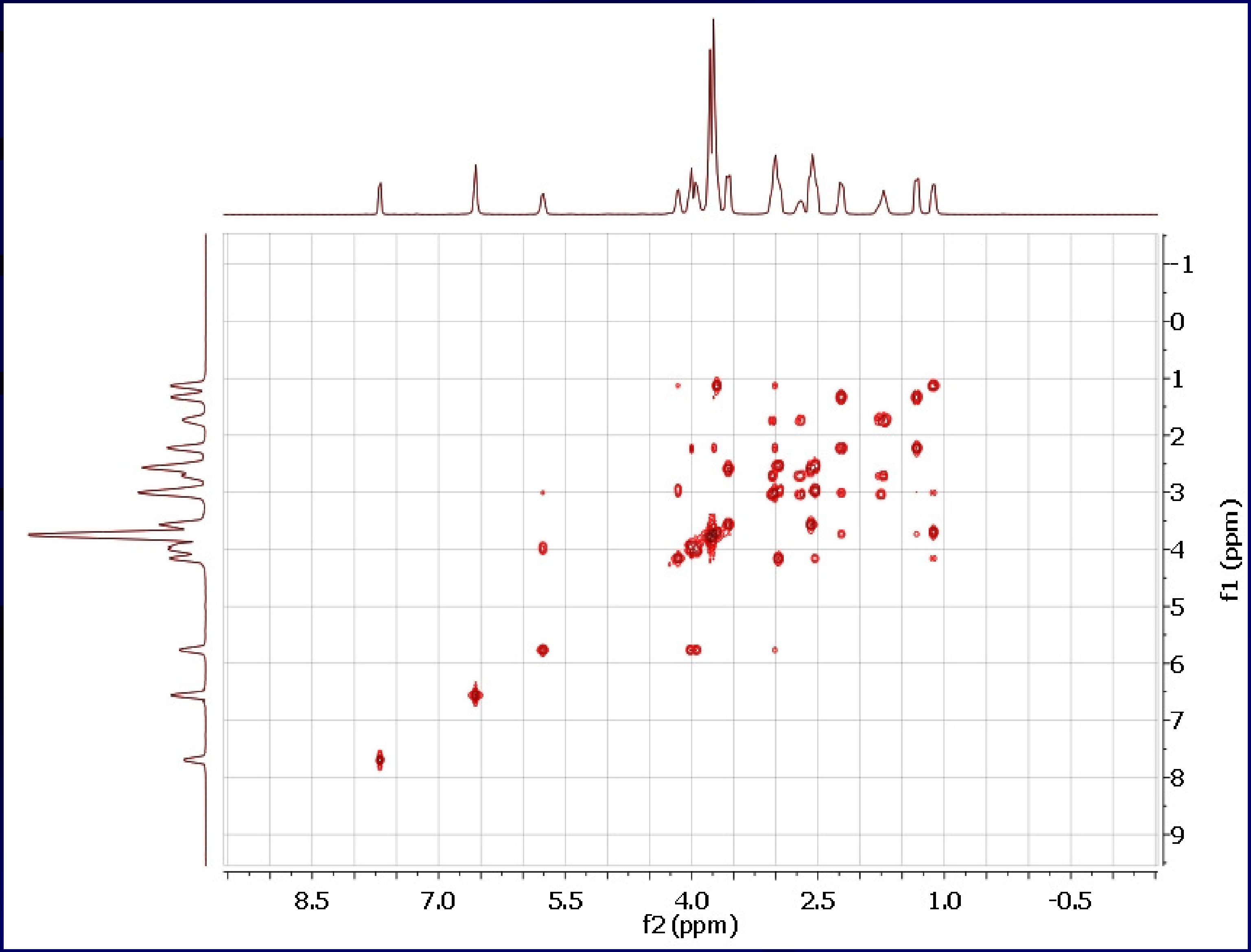




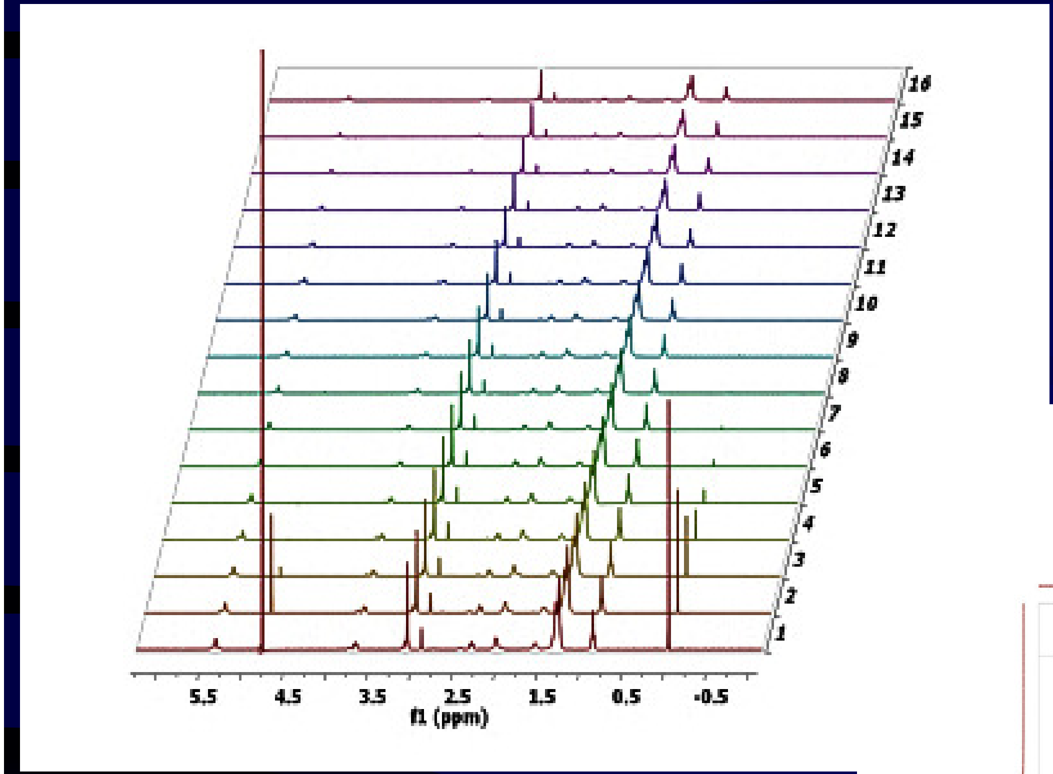
Spectroscopy of ^{13}C (and other nuclides)

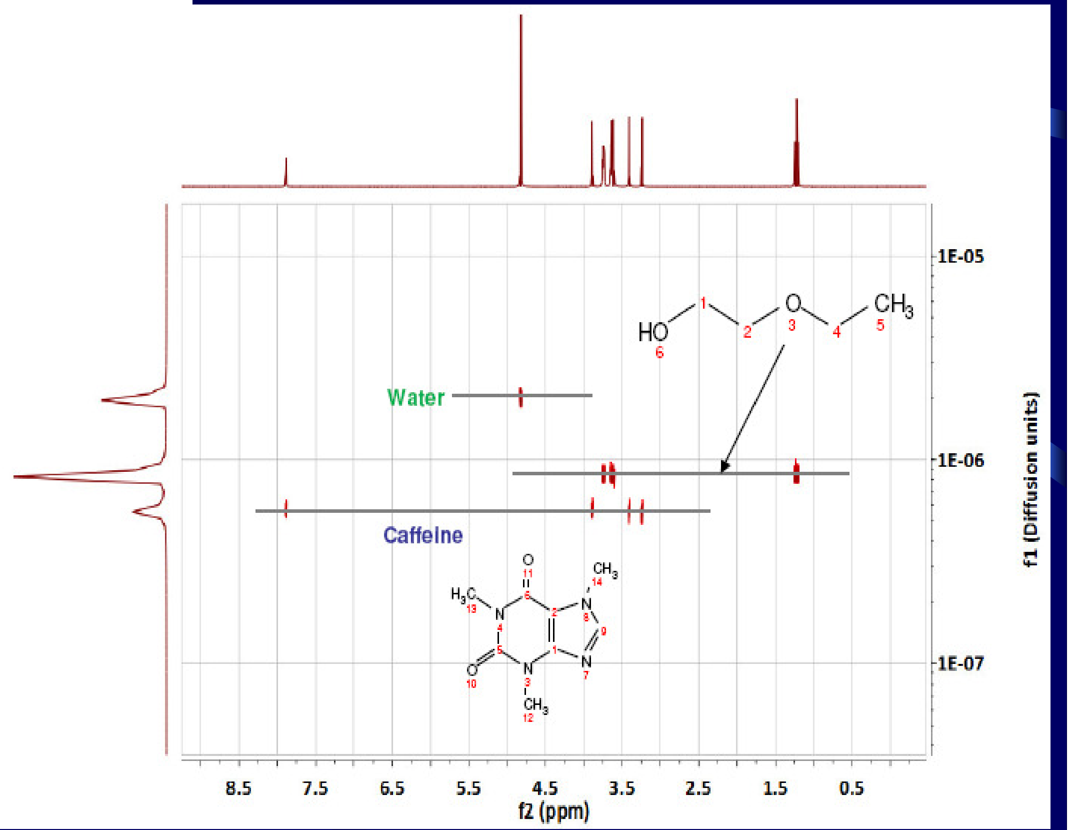


Multi-dimensional FT Spectroscopy methods

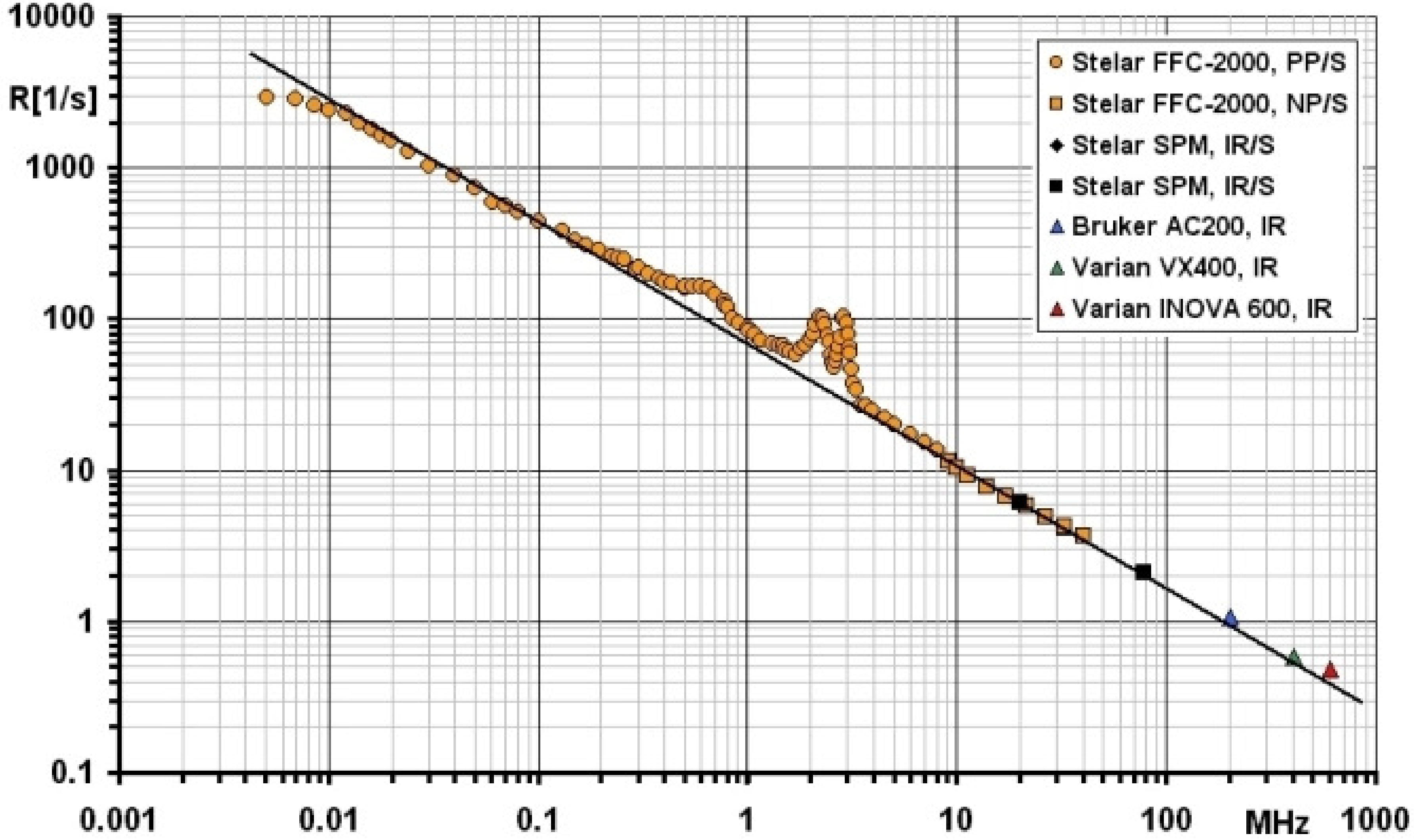


Dynamic NMR (kinetics and diffusion)





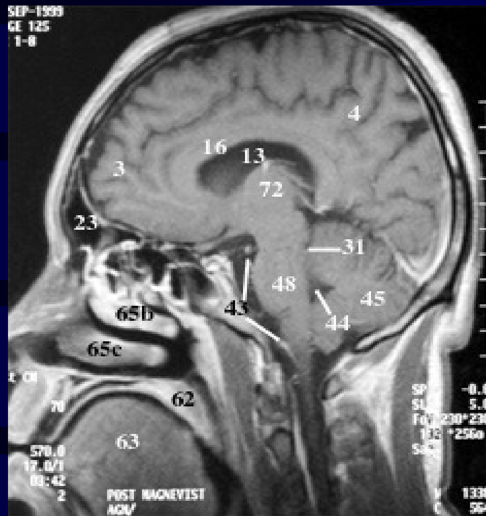
NMR Relaxometry: a ^{1}H NMRD profile



^{1}H longitudinal relaxation rate $R = 1/T_1$ of solid, anhydrous Bovine Serum Albumine (BSA) as a function of magnetic field strength (measured in terms of Larmor frequency).
See www.ebyte.it/stan/Poster_NmrdOfSolidBsa.html

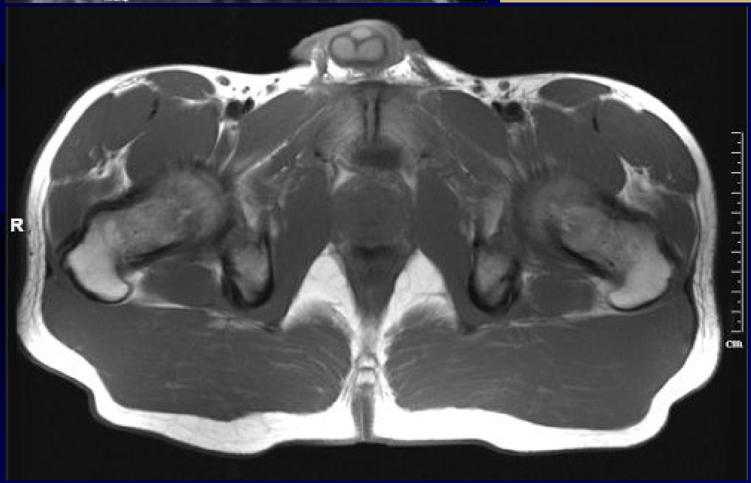
MR Imaging (MRI)

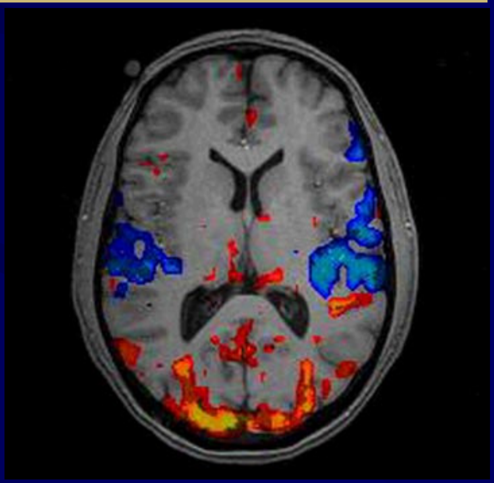
MRI atlas



MR angiography

Male pelvis





Functional MRI

Examples taken at random from various websites

Can all this have a simple common basis

(Yes: *Spin* and *Magnetic moment*)

The many kinds of Magnetic Resonance …

NMR	Nuclear Magnetic Resonance (^{1}H, ^{2}D, ^{13}C, ^{31}P, ^{19}F, …)
EMR	Electron Magnetic Resonance (alias EPR or ESR)
μMR	Muon Magnetic Resonance
NQR	Nuclear Quadrupole Resonance
FMR	Ferro (anti-ferro) Magnetic Resonance
MRI	Magnetic Resonance Imaging
MRFM	Magnetic Resonance Force Microscopy
etc.	often including double- and triple-combinations

Notice that the classification criteria are incoherent:

sometimes it is the **subatomic particle**, but other times it may be the **macroscopic system**, the **hardware**, or the **application area**

… all branching (NMR)

nuclide(s):	^{1}H, ^{13}C, ^{2}D, ^{31}P, ^{23}Na, ^{15}N, ^{14}N, ^{19}F, ^{29}Si, … + combis
excitation:	CW, Pulsed, Hadamard, Noise excited, DNP, …
detection:	Induction, Direct/Indirect, Optical, Force, …
field type:	High/Low value, High/Low resolution, Ex-situ, …
signal type:	Time/Frequency domain
methodology:	Spectroscopy (1D, 2D, …, DOSY, …)
	Relaxometry (at fixed or variable field) …
	Logging (such as well-logging), …
object:	Chemical compounds, Proteins, Tissues, Materials, …
context:	In-vitro / In-vivo, Large scale (geophysical), …

… and branching again (MRI)

Sample size:	Microscopy, Small scale (arts, animals), Whole body, …
Field value:	Low (< 2T) or High (> 2T)
Weighted by:	Density, T1, T2, Flow, Diffusion, Susceptibility, …
Contrast agent:	None, Generic, targeted for Organ/Function/Pathology, …
Context:	Medical (Diagnostic/Interventional), Archeological, …
Methodology:	Standard scan, MR Angiography, functional NMR, …
Organ:	Brain, Heart, Knee, Pelvis, …
etc	

… etc (EMR, NQR, …)

The history behind the complexity

Naturally, the present state of MR is the result of its historic evolution.

Starting from its discovery in bulk matter in
1944 (ESR, E.Zavoisky) and 1945 (NMR, F.Bloch and E.Purcell),
Magnetic Resonance always kept evolving at an amazing rate

The historic aspect, including its weird twists, adds another dimension to the labyrinth of present-day techniques. But we need the history, since *otherwise it is impossible to tell where the future of MR might be pointing* (it is almost impossible anyway).

Magnetic Resonance and Quantum Physics

The roots of Magnetic Resonance penetrate the

treacherous terrain of Quantum Physics.

They draw nutrients from it but also help to stabilize it

(a role which might become more prominent in coming years)

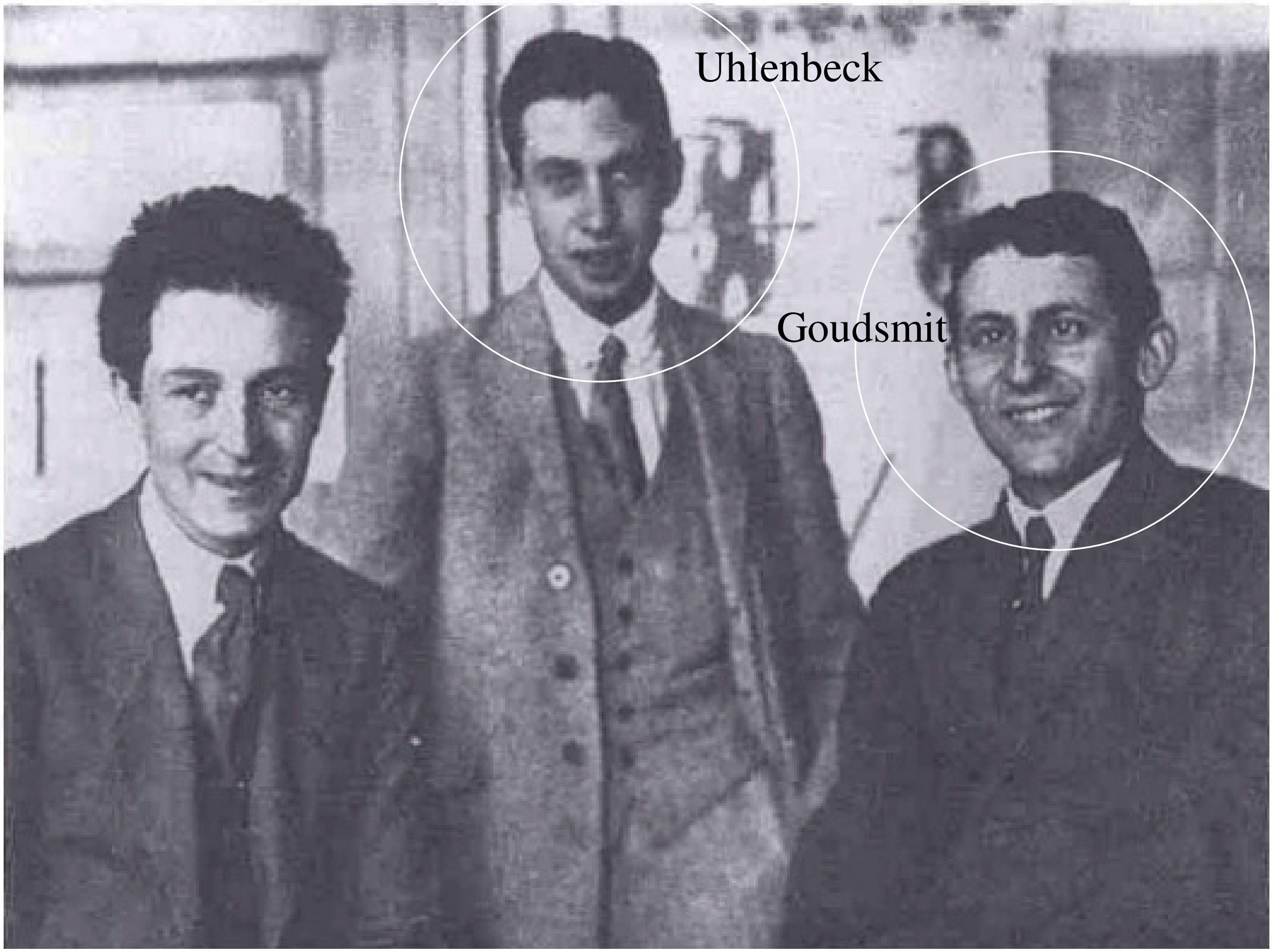
But how did the MR start-up platform arise ?

A mini-chronicle of electron spin

- 1897: Pieter Zeeman finds that magnetic field broadens spectral lines
- 1921: Arthur H.Compton advocates axial electrons to explain magnetism
- Atoms have nearly twice the expected number of spectral lines
- In the Wilson cloud chamber, electron trajectories have strange "kinks"
- 1925: Ralph Kronig suggests that electron has an angular momentum (spin)
- Wolfgang Pauli tells him it is a foolish idea and poor Ralph desists !
- Later in 1925: George E.Uhlenbeck & Samuel A.Goudsmit submit a paper to *Naturwissenshaften*, also claiming that electron has a spin
- They show it to the great Hendrik A.Lorentz who deems it impossible !
- They urge the Editor to *please* withdraw the paper, but it is too late !
- Fortunately, further investigations by many physicists prove them correct. The paper becomes a cornerstore of modern physics !
- 1927: a converted Wolfgang Pauli builds the best formal model of spin
- Later: Paul A.M.Dirac, the theoretician, says that *"... a particle with a spin of half a quantum is really simpler than a particle with no spin at all ..."*
- In other words: ***what's all the fuss about, isn't it trivial to start with ?***

Note: Names in red indicate Nobel Prize winners

The pioneers (electron spin)



1926: Oscar Klein, George E.Uhlenbeck, and Samuel A.Goudsmit.
Courtesy of AIP Emilio Segré Visual Archives

The dawn of nuclear spins & magnetic moments

- In 1922, the experiment of Otto Stern and Walter Gerlach confirms the quantization of the *directions* of an angular momentum (*spin is unknown*!)
- In 1927, David M.Dennison studies the thermodynamics of the hydrogen molecule and notes that proton should have spin ½ to explain the results
- Still in 1927, T.E.Phipps and J.B.Taylor reproduce the Stern-Gerlach experiment with protons (instead of the more complex silver atoms)
- The idea that nuclei may possess a spin is generally accepted in 1927-28. So is the realization that proton has spin ½
- In 1937 Isidor Isaac Rabi adds the RF (gyrating magnetic field) to the Stern-Gerlach setup and the molecular rays method is born
- In 1938 the group of Isidor I.Rabi exploits resonance to *precisely* measure nuclear magnetic moments (*converting field strength to frequency*!)

Magnetic Resonance is born,

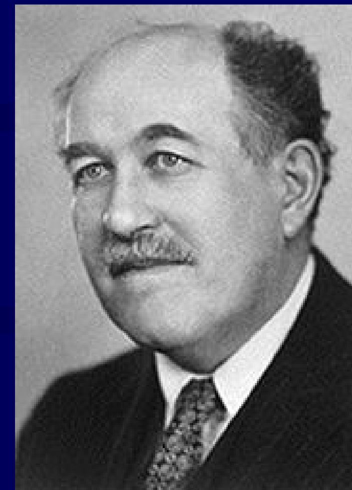
albeit not in bulk matter.

By 1945, many nuclear moments are quite precisely known, including that of neutron (L.W.Alvarez, F.Bloch, 1940)

More pioneers (nuclear spin)

Dennison, ^{1}H spin   Kronig, e-spin, really

1925 From left; Yoshio Nishina (1890–1951), David M. Dennison (1900–1976), Werner Kuhn (1899–1963), Ralph de Laer Kronig (1904–1995), Bidu Bhusan (B.B.) Ray in Copenhagen,



Otto Stern

Walter Gerlach

Isidor Isaac Rabi - he named

Magnetic Resonance

In 1938 it was known *for sure** that:

There are particles of many kinds

and *<u>all</u>* the particles of *<u>each kind</u>* are *<u>exactly</u>* alike,

and *<u>some kinds</u>* have a *<u>permanent</u>*

half-integer spin

and thus an *<u>immutable</u>*

angular momentum,

always associated with a

magnetic moment,

and all these quantities are vectors.

$\mathbf{M} = \hbar \mathbf{S}$ $\boldsymbol{\mu} = \gamma \mathbf{M}$ $\hbar$ ... Planck constant, γ ... gyromagnetic ratio

Plus, all particles obey the exclusion principle!

* Well, at least that is what we still believe, and it <u>still</u> takes an awful lot of Faith.
It covers about half of Quantum Physics

The quest for MR in condensed phases

- 1936: The idea is already around. W.Heitler & E.Teller estimate nuclear spin-lattice relaxation rates which might pre-condition its viability!
- 1936: C.J.Görter describes a resonant apparatus for NMR in bulk matter
- 1936: C.J.Görter reports a failure ! They used to do *that* then …
- 1937: B.G.Lasarew & L.W.Schubnikow detect nuclear contribution to the susceptibility of liquid H_2. This is an early non-resonant measurement!
- 1940: F.Bloch & A.Siegert publish a theoretical study of an MR effect which will be confirmed experimentally only many years later.
- 1941: W.E.Lamb estimates internal diamagnetic fields induced by electron shells: theoretical introduction of *chemical shifts* and their *predictions*!
- 1941: Evgenij Zavoisky reportedly sees NMR signals in bulk matter but, since they are badly reproducible, dismisses the finding!
- 1942: C.J.Görter & L.J.F.Broer report another failure! The guys are plain unlucky: without knowing it, they pick up only samples with extremely long relaxation times like LiF, LiCl, KF (looking for ^{19}F and ^{7}Li).

Had they used whisky, or even *just* water, the Nobel was their's!

First clear signals from bulk matter

1944, in Kazan (ex Soviet Union, now Tatarstan):

Evgenij K.Zavoisky discovers ESR (same as EPR and EMR)

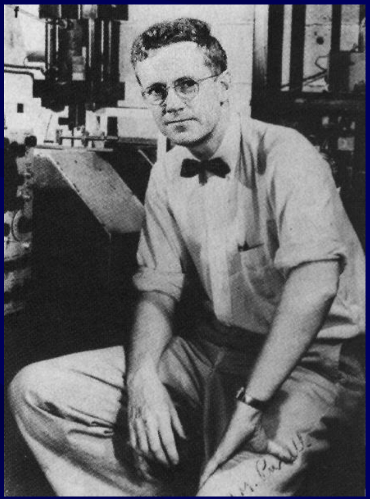
1945, December 15, at Harvard University, Massachusetts:

Edward M.Purcell, H.C.Torrey and Robert V.Pound detect NMR

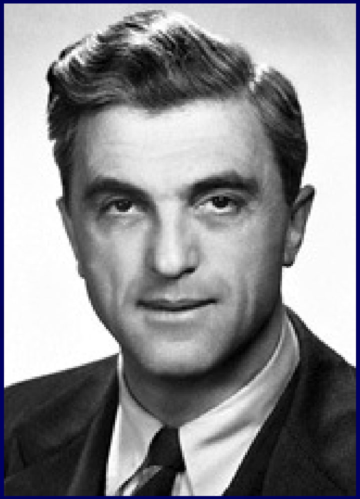
1945, December 23, at Stanford University, California:

Felix Bloch, W.W.Hansen, Martin E.Packard detect NMR

Evgenij Zavoijsky

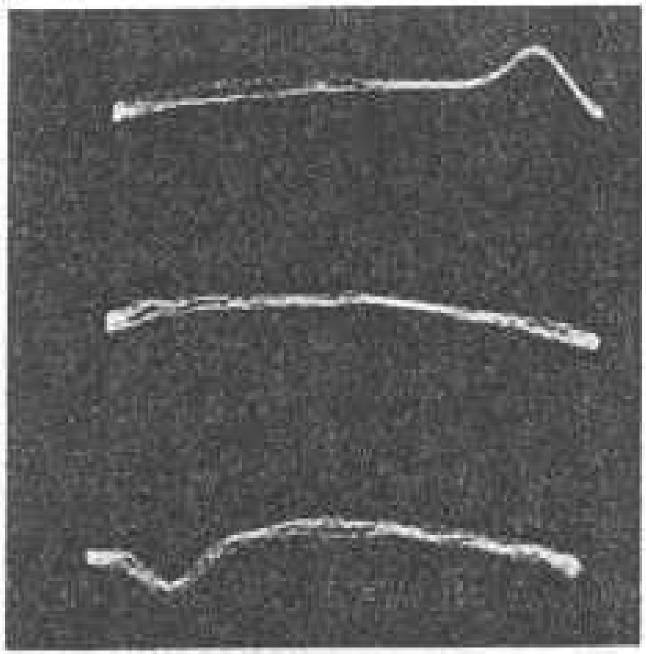


Edward Purcell



Felix Bloch

How did the first signals look?

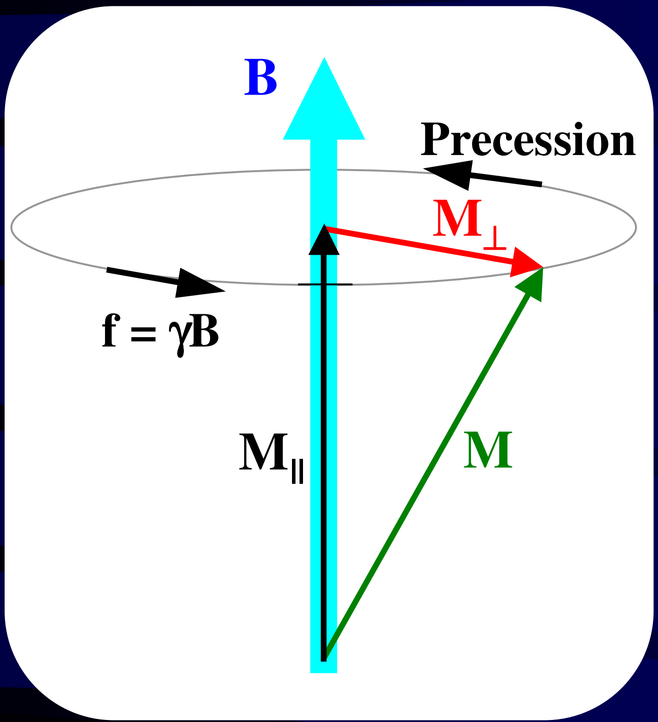


A photographic record of the first NMR signal (doped water protons)

The three traces differ by the RF phase difference between the transmitter and the receiver (0^o, 90^o, and 180^o)

From: Felix Bloch, Nuclear Induction, Phys.Rev. 69, 127 (1946)

The master principle: Larmor precession



Particles (nuclei) have magnetic moments **μ**

The moments interact with the external magnetic field **B** according to the classical formula

$$E = -\,\boldsymbol{\mu}.\mathbf{B} \text{ (Zeeman interaction)}$$

This gives rise to a torque – a couple of forces trying to align the moment with the field

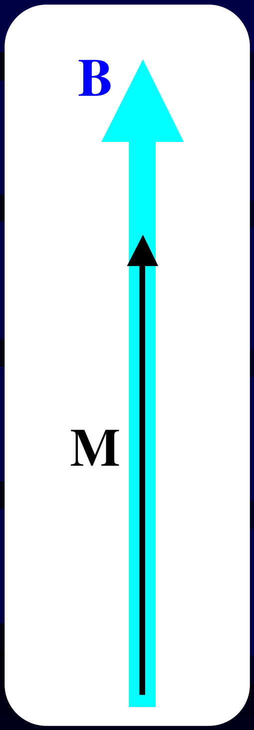
But particles have <u>*also*</u> an angular momentum **M** and **μ = γM**. They resemble gyroscopes that never wind down and behave like them!

Like with all gyroscopes and spinning top toys, the result is a precession.

In this case, the spins precess about the magnetic field **B** with a frequency f = γ**B**.

This is called Larmor precession and its angular rate is the Larmor frequency

The equilibrium state



In general, the total sample magnetization has two components: one transversal to the field, and one parallel to it.

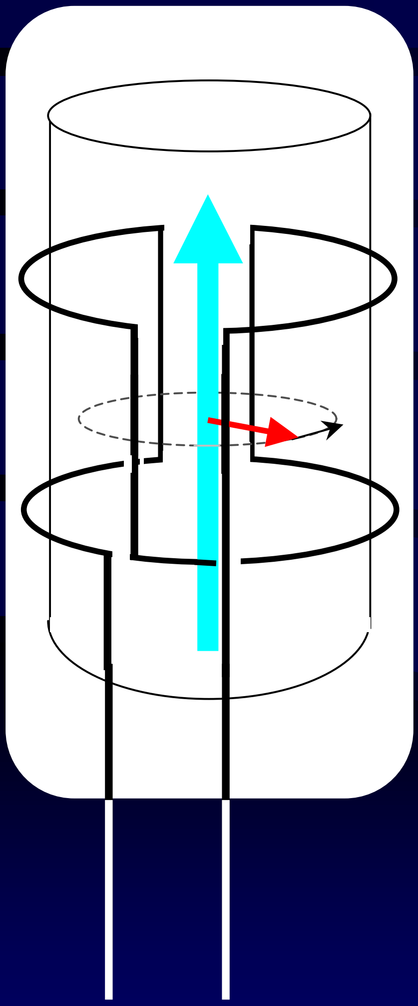
Both tend to return to an equilibrium state in which **M** is oriented along **B** so that there is only the longitudinal component, while the perpendicular one is zero.

Once the equilibrium state is reached, there is no precession.

The amount of magnetization in the equilibrium state is given by the Boltzman statistics and decreases with temperature. It's value is normally very, very low - about 0.0001 % of the theoretical maximum. This ratio is called polarization.

Anticipation: the higher the polarization, the larger is the detected signal and the better is the sensitivity, measured by the signal to noise ratio S/N

What do we detect ?



Usually we use an induction coil to detect the signal.

Consequently, only the precessing transversal component of nuclear magnetization generates any signal in the coil.

The longitudinal component is invisible to the reciver.

In the equilibrium state, there is no detected signal.

All signals are transient. To see something, the system must be brought out of equilibrium – a process called excitation.

Once there is a transversal component, the detected signal oscillates at Larmor frequency (RF) and relatively slowly decays to zero.

How is the excitation done ?

As always in spectroscopy, there are two ways:

- Continuous irradiation (CW – continuous wave) or
- Sharp, strong radiation pulses of radiofrequency

In both cases we need an RF transmitter.

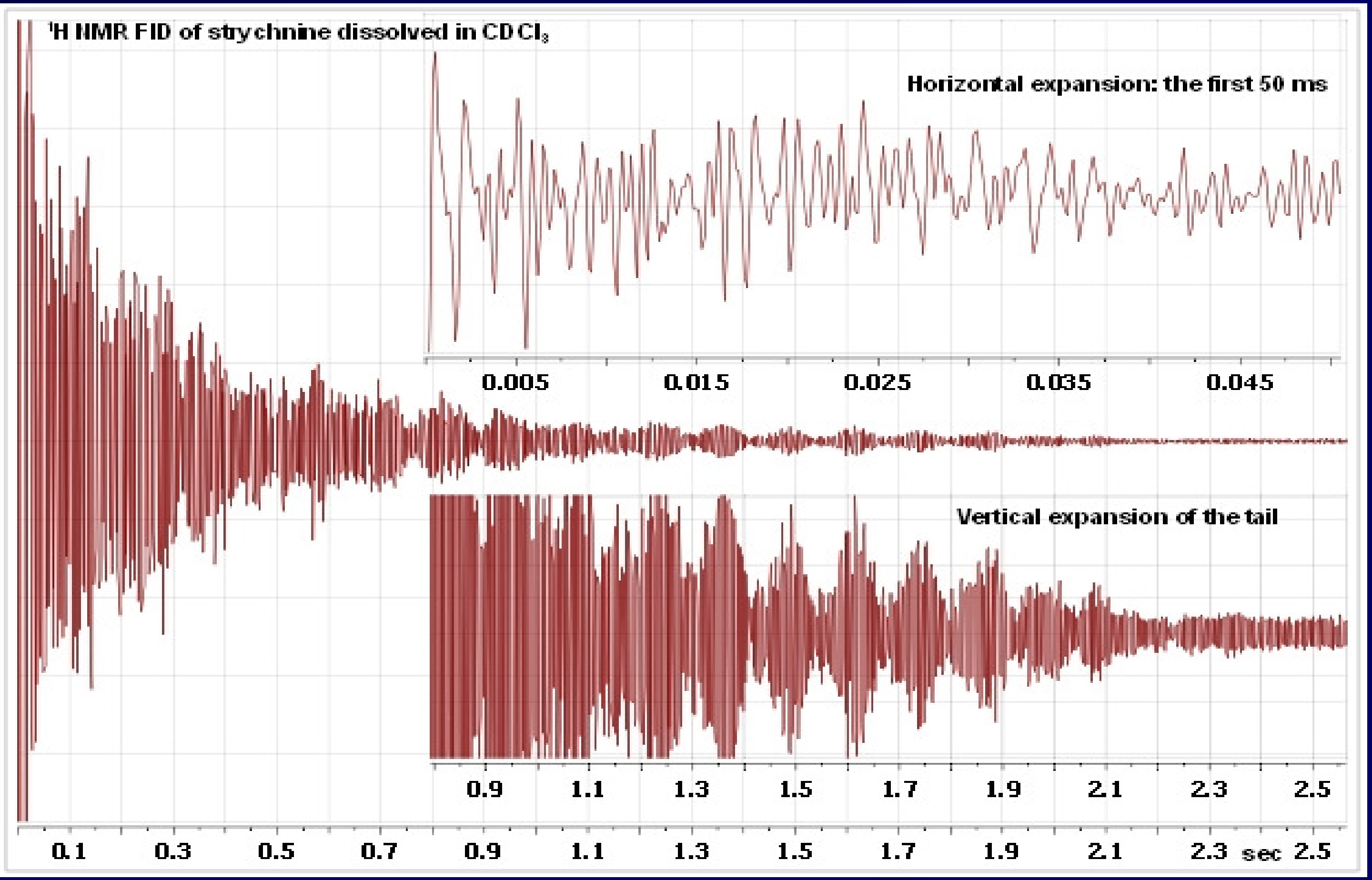
And in both cases the spins interact with the magnetic component of the irradiation via the usual Zeeman interaction. It can be easily shown that a macroscopic effect can be obtained only when the “carrier” frequency is close to the Larmor frequency (the resonance condition).

The pulsed method is today definitely preferred, because it is much more sensitive, requires less hardware and permits an infinity of tricks with so called pulse sequences consisting of a series of accurately distanced pulses. It requires the use of Fourier Transform but with computers, that is trivial.

The era of CW ended around 1970 due to the work of Richard Ernst and to the advent of mini-computers

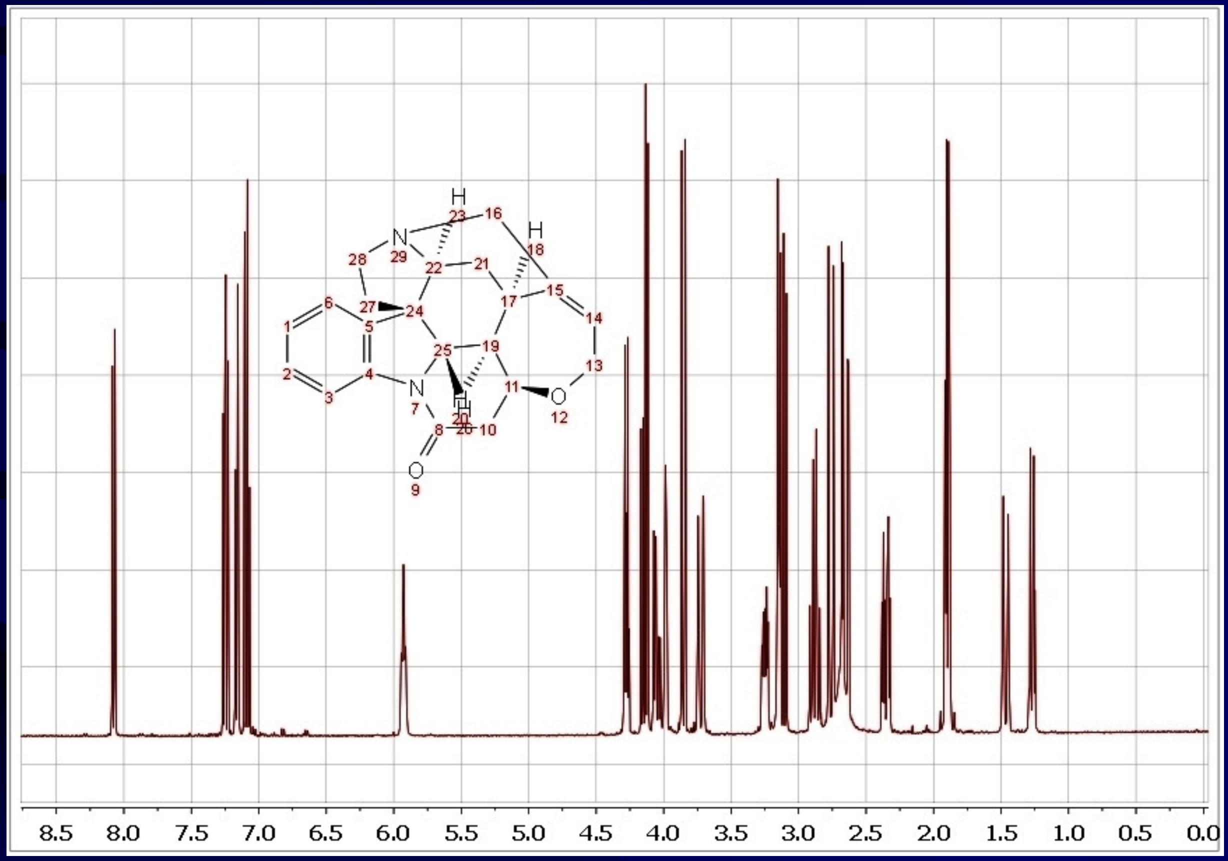
A spectroscopic example: the FID

A strong (over 100 W) RF pulse is applied to the coil for a brief period (in this case 10 μs). Thereafter, a weak transient signal (called free induction decay or FID) corresponding to the transversal magnetization component is detected. Depending upon the sample and upon the homogeneity of the field, this can last anywhere from tens of microseconds (solids) to many minutes (liquids). In this strychnine solution it took 2.5 seconds.



A spectroscopic example: the spectrum

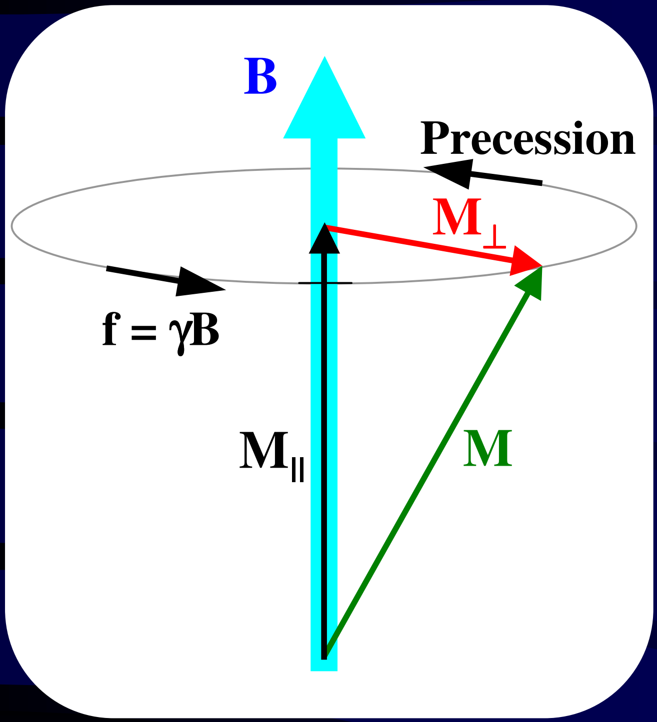
Applying the Fourier Transform to the FID data, we separate the individual component signals with different Larmor frequencies and thus obtain the spectrum.



Anticipation: why are there different spectral components? Because each proton in the molecule is subject to a slightly different screening by the binding electrons (chemical shifts). But be careful: the scale is in ppm of the carrier frequency!

A spectroscopic example: the instruments

The three evolutions



The most prominent motion is the Larmor precession (for example 500 MHz) because the interactions of the magnetic moments with the external magnetic field are the strongest ones.

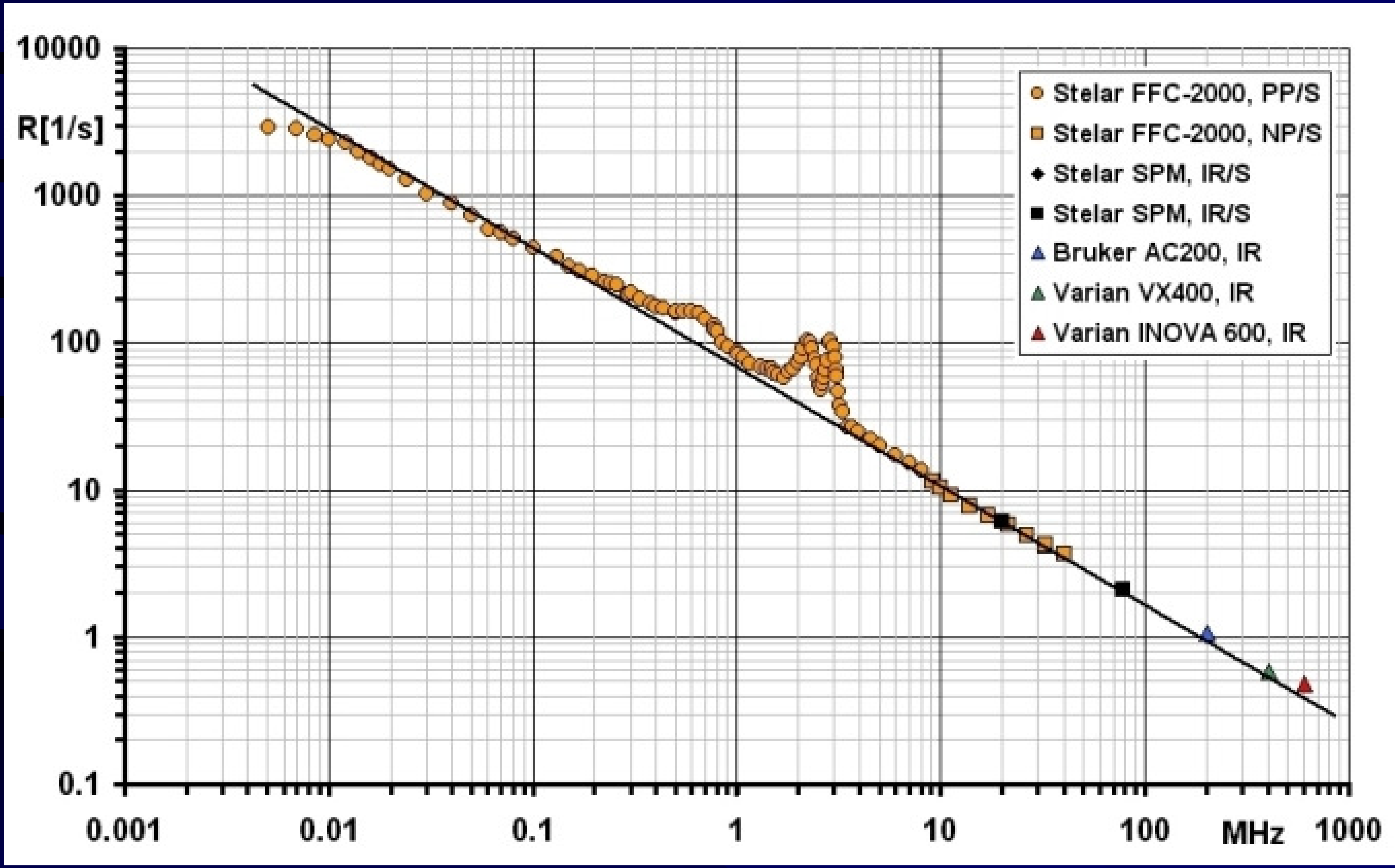
The return(s) to equilibrium (relaxations) are due to stochastic interactions between the nuclei themselves which are much smaller. Consequently, relaxation processes are much slower (typically 10^{-3} to 10^{+3} s)

The study of the dynamics of the return(s) to equilibrium is called MR Relaxometry.

NMR relaxometry is the principal method of investigating molecular dynamics.

Note: Transversal magnetization never decays to zero faster than the rate at which longitudinal magnetization returns to its equilibrium value. Apart from that, the two relaxation processes (transversal and longitudinal) are *independent*.

NMR relaxometry: example of a study



Longitudinal relaxation rate of dry Bovine Serum Albumine (BSA) as a function of Larmor frequency from 5 kHz to 600 MHz (six decades !)

But wait – let us return to the FT!

You should now ask me:

* If the Larmor frequency corresponds linearly to the effective field perceived by each nucleus, and

* if we can so easily separate the various Larmor frequencies by means of a simple Fourier transform,

can't we play all kind of games with the nuclides and make them dance to our own tunes ?!? …

For example, could we apply external field gradients so that nuclides positioned at different locations would be *forced* to precess at different Larmor frequencies ???

MRI: Making the nuclides dance to our tune

… In which case I would have to exclaim:

Great, you have just invented **Magnetic Resonance Imaging**!

It really is that simple! Sure, you need to find out how many different gradient settings you need (directions and values), build the coils to generate them, and find a mathematical way to recover the complete map of where the nuclides are.

But those are mere technical details,
the idea is sound and, being simple,
works beautifully!

Want details? Read this: www.ebyte.it/library/educards/mri/K-SpaceMRI.html

Historic shame on us Physicists!

The basic principle of **MRI** is in fact so simple
that when it came about in late 70's,
nobody was surprized by it !

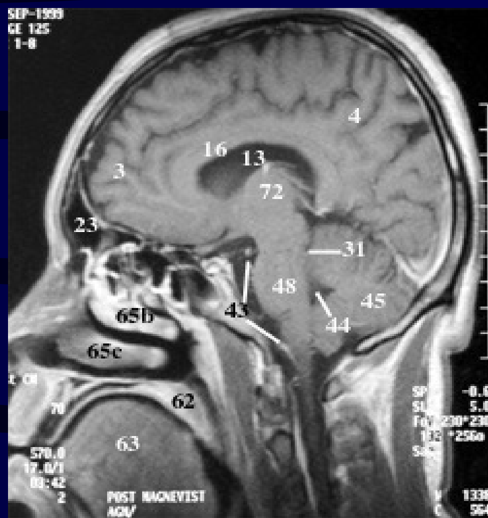
I have a very clear recollection of those days:
All we were amazed by was the idea of a magnet large enough to accomodate a human body. It sounded so monstrous and unnatural!

But not the theory – that was immediately quite clear.

Had we been mentally more flexible about technical details,
MRI could have reached clinics a decade earlier.

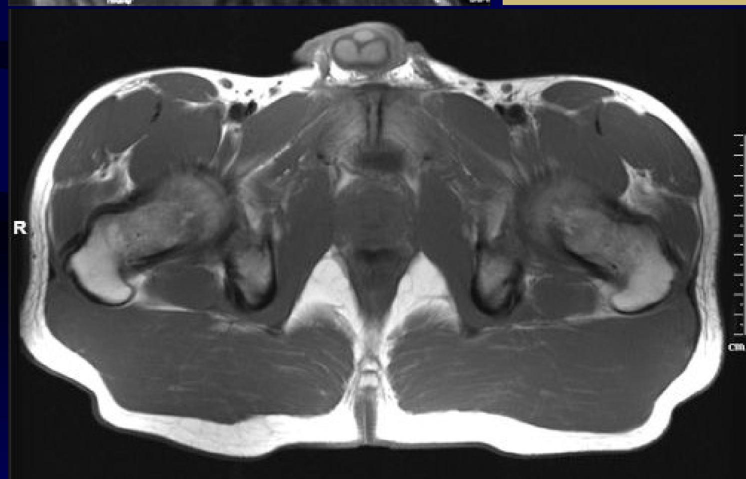
A few examples of MR imaging

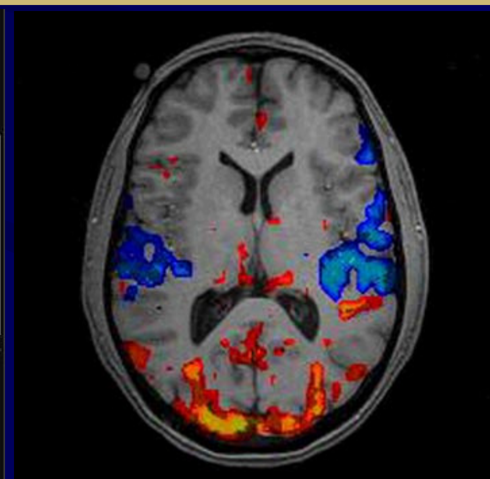
MRI atlas



MR angiography

Male pelvis





Functional MRI

Examples taken at random from various websites

Modifications of the local magnetic field:
a key to organizing the subject of MR ?

Modify the *effective local magnetic field* to which a nucleus is subject
and it will change its Larmor frequency.
And *that* is very easy to detect!

Much of the history of MR is related either to discoveries of the natural sources of such local magnetic field modifications (chemical *shifts*, direct and indirect *couplings* between nuclei) or to imposing them by artificial means (additional magnetic gradients or RF fields). Other modifications of the spin-system Hamiltonian (decoupling, sample rotation) can be also cast into this frame. *Only relaxometry does not quite fit this picture.*

I would certainly love to try out such a classification,
but my time is running out and I still have two things to say

Why is NMR so succesfull ?

I think that it is due to a very lucky balance of the following factors:

- The γ-ratios put nuclear Larmor frequencies in the *RF range* where
- interactions with matter are *weak enough* to let the radiation penetrate deep into the sample but, at the same time, also
- *strong enough* to make detection possible and relatively easy.
- *Noninvasive* manipulation of nuclides by means of remotely generated magnetic fields is possible and
- it affects their Larmor *frequencies* which, as all frequencies, can be measured with extreme precision.
- In addition, there are several abundant nuclides which are constituents of exactly those 'systems' which interest us most: organic molecules, materials, and biological tissues.

What is behind the corner ?

This is difficult to say. I can offer just some personally biased ideas:

- Several new magnet technologies (such as cryogen-free supercons)
- New electronics (FPGA's) should slash prices by a large factor
- A drop in prices (and a boost in production capacities) - a *must* if we want to bring MRI into the reach of everybody on this planet
- New ways of boosting the inherent sensitivity and/or polarization
- Remote MR detection (or is this still a science-fiction?)

What I did NOT tell you ?

This was a primer for physicists, so I have stressed the historic roots of the physical principles of MR instead of its applications. I also wanted to:

- cover the history of MR after its discovery but that would take three more hours,
- talk about the instruments but that would also take several more hours,
- talk about MR software but, again, it would require much more time,
- and so would a coherent treatment of MR relaxation theory.

For all these things I wanted to tell you but did not,

I apologize

Thank you for your patience

Any questions ?

Please, visit my NMR blog at www.ebyte.it/stan/blog.html

(or just look for "Stan NMR" on Google)