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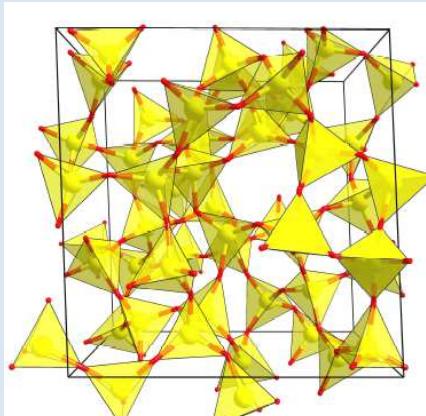
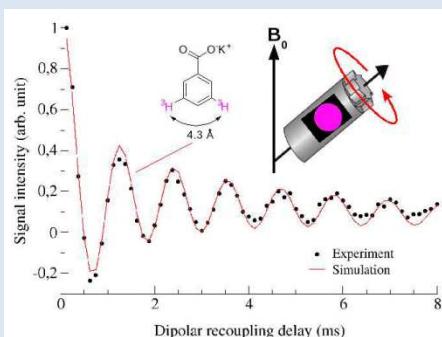
Experiment and Modelling in Structural NMR

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France

Basic principles of
NMR and MRI

[01001]



SiO₂ structure from NMR studies



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Basic principles of NMR and MRI

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Abstract. This introduction presentation addresses in a general way the historical invention of Nuclear Magnetic Resonance and its general aspects and characteristics: sensitivity and its consequences, nature of the interactions, observation methods, sophistications, longitudinal and transverse relaxation, and principle of Magnetic Resonance Imaging.

The aim of this presentation is to describe the basic principles underlying Nuclear Magnetic Resonance in a general way, without formulas but with an emphasis on the physical ideas. It is therefore epistemological in nature.

Nuclear Magnetic Resonance, or NMR, was invented in 1945, simultaneously but independently by two groups, using totally different conceptual approaches which eventually proved to refer to the same basic phenomenon. This possibility came about as an offspring of the progress made by electronics during World War II. Although a natural extension of optical spectroscopy, NMR witnessed the introduction and development of highly new and unusual features, initially unsuspected. The domain of NMR proper always combined fundamental physical research and highly valuable practical applications in an astonishing number of diverse domains: condensed-matter physics, nuclear and particle physics, solid-state and liquid-state chemistry, structural biology, physiology and medicine.

After general considerations on the reason for the intrinsically low sensitivity of NMR, which limits in practice its observation to condensed matter only, a “limitation” that makes it a privileged tool for the study of the latter, we consider in turn several central topics in the form of brief reviews.

- the various types of spin-spin and spin-lattice interactions: magnetic dipolar, electric quadrupolar, magnetic electron-nuclear in conducting media and in diamagnetic insulators are considered in turn and schematically described. Special emphasis is put on the fundamental interactions of use for structural investigation of covalently bonded molecules: chemical shift and indirect interactions.

- the main observation methods are sketched in their simplest form, CW, the historical one, and the pulse methods, which had to wait for the

development of computers to supersede almost completely the former one.

- a short list of “sophistications” is presented, elaborations of NMR or major applications, many of which constitute a subject in itself, whose description could justify a whole Winter or Summer school. Even a short account of any of them is too much for this introduction.

- spin-lattice relaxation, limited to the evolution of magnetization through the coupling of the spins to the surrounding medium (le lattice), mostly via the model of time-dependent interactions. The cases of transverse relaxation (often referred to in the literature as spin-spin relaxation) and longitudinal relaxation are discussed in turn.

- the principle and implementation of Magnetic Resonance Imaging is then treated in slightly more detail, with a few illustrations.

- last but not least, the Nobel Prizes awarded for NMR are listed, all six of them. A dozen more might have been added, for scientists who did important work in magnetic resonance or around it but got the Prize for work on different subjects, such as Rabi, Ramsey, Bloembergen, Townes, Schawlow, de Gennes, Müller, Dehmelt, Kastler, Cohen-Tannoudji; Mössbauer.

Basic Principles of NMR and MRI

Maurice Goldman
Membre de l'Académie des sciences

Nuclear Magnetic Resonance (NMR)

It is a physical discipline of Hertzian spectroscopy,
extension of optical spectroscopy in the
radiofrequency domain.

Invented independently in 1945 by two American
teams, using different conceptual approaches.

Practiced on the spins of atomic nuclei subjected
as a rule to a magnetic field.

Spin and magnetic moment

$$\mu = \gamma I$$

γ = gyromagnetic ratio

Larmor Theorem:

μ precesses around the magnetic field \mathbf{B} at a frequency proportional to it:

$$\omega = -\gamma B$$

(Algebraic equation)

East coast (Purcell, Torrey, Pound)

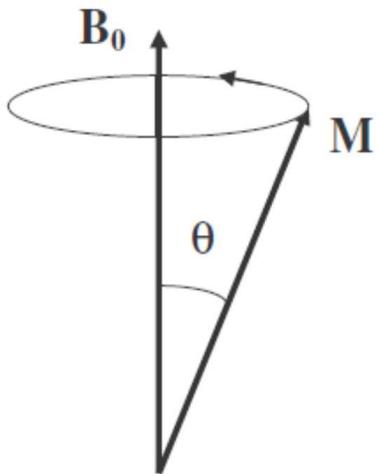


Zeeman Effect

- Quantized Zeeman levels,
- Resonant transitions according to Fermi Golden Rule,
- Selection rules,
- Absorption if level populations are at thermal equilibrium with the environment (the lattice)

Approach inspired from optical atomic spectroscopy

West coast (Bloch, Hansen, Packard)



Larmor Precession

- Macroscopic electromagnetic approach,
- A small field normal to the main, static field and rotating at the Larmor frequency produces a small transverse magnetization of same frequency,
- This magnetization induces in a coil a e.m.f. which is detected.

Which is the good one?

- Apparently different, these two approaches describe the same phenomenon. The difference with traditional optics originates from the coherence of the excitation: rf field of non-vanishing amplitude.
- It will disappear with the development of lasers.
- One uses either one, whichever is the most convenient in the case under study.

NMR is fundamentally of low sensitivity

Reason 1: The energy of the photons is low

$$h\nu_{\text{rf}} \ll h\nu_{\text{opt}}$$

Example: (recall: $\lambda = c/\nu$)

Protons at 60 MHz (MRI): $\lambda = 5 \text{ m}$

Green light for optical spectroscopy: $\lambda = 0.5 \mu\text{m}$

Reason 2: The energy of the photons is low

At thermal equilibrium, the populations of the various levels are very close: the polarization is low.

Consequence

- One must observe many spins in a restricted space,
- They are therefore close to each other, i.e. in condensed matter,
- They are therefore subjected to interactions, between spin pairs or with the surrounding medium (lattice), which perturb the resonance.

Inconvenience or advantage?

It is an advantage!

- It is these perturbations that one studies, from which one deduces the properties of the lattice.
- Due to the weakness of the spin-lattice coupling, NMR is a non-perturbing probe of the surrounding medium.
- NMR gives access to much slower dynamics than any other physical probe.

The interactions

1- Magnetic dipolar interactions

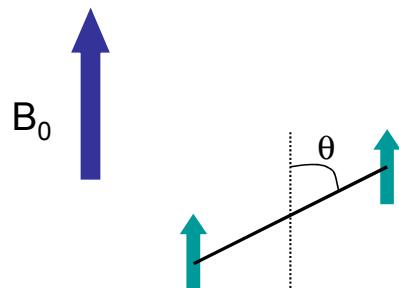
Between nuclear spins, or with electron paramagnetic spins.

In high external field, they must be truncated.

Depend on the angle θ

Solids, θ fixed : dominant
large anisotropic resonance line

Liquids, θ varies : vanishing average



2- Electric quadrupole interactions

Spins larger than $\frac{1}{2}$, subjected to an electric field gradient of crystalline origin in an anisotropic environment.

Large: can be observed in zero external magnetic field (but with a magnetic rf field) : pure quadrupole resonance.

Small: observed as normal NMR, with an applied static field. Produces a broadening of the resonance.

3- Magnetic electron-nucleus interactions

Conducting solids: metals and semi-conductors

The contact interactions give rise:

- to a resonance frequency shift (Knight shift)
- to spin-lattice relaxation (Korringa law)
- to a huge increase of the nuclear polarization when the conduction electron spins are saturated (Overhauser effect)

(When this prediction was presented, all authorities thought it violated the Second Law, and was necessarily wrong)

Non-conducting diamagnetic substances

Two effects for covalent bonds, of fundamental importance to chemistry, were discovered serendipitously, both simultaneously by two independent groups.

Chemical shift

The magnetization, by the external field, of the electronic shells surrounding a nuclear spin produces a resonance shift of the latter, which depends on the nature of the chemical bond, and serves to characterize it.

Proportional to the field, it is expressed in ppm

Anisotropic in solids, but only its isotropic average show up in liquids.

Indirect interactions

The electronic shells, magnetized by interaction with a nuclear spin, interacts with another nearby nuclear spin. The result is a bilinear interaction between the two nuclear spins, which splits their resonances. As a rule, it is limited to nearest or next-nearest nuclear neighbors in covalently bonded molecules.

Independent of the field, it is expressed in Hz.

Anisotropic in solids and isotropic in liquids.

Serves to characterize the proximity within the molecule.

Observation methods

The CW method (mostly historical)

- Apply a small rf field of frequency close to the Larmor frequency,
- Slowly sweep either the field or the frequency,
- Detect the absorption signal : rotating transverse magnetization in quadrature with the rf field (lagging behind).

The pulse method (much better than CW)

- Apply a strong rf field during a short time (a pulse) near the Larmor frequency,
- Observe and sample the following transient signal (the transverse magnetization). It oscillates and decays as a function of time: it is the Free Induction Decay, or F.I.D.,
- Compute its Fourier transform: it is the resonance spectrum.

Why? By virtue of the **Linear Response Theorem**

Linear Response Theorem

When the response of a system to an excitation is both:
causal (response at a given time depends only on the past excitation) and
linear (response proportional to excitation),
Then: the responses to infinitely sharp pulse and infinitely small sinewave excitations are the Fourier transforms of each other.

Often valid outside these two infinities: finite pulse length and angle, but one must be careful.

Sophistications

- Spin echoes,
- Stimulated spin echoes,
- Multi-dimensional NMR,
- Multiple quantum transitions,
- High-Resolution in solids by multi-pulses,
- Magic angle spinning (MAS),
- MQMAS,
- Magic Sandwich,
- Spin temperature, Dynamic Nuclear Polarization,
- Etc.

Spin-lattice Relaxation

In the presence of motion (ex: liquids), the interactions depend on time, which has a double consequence:

- 1- The resonance lines narrow, whence the free precession signal decreases more slowly : it is transverse relaxation (Time T2),
- 2- The time necessary for achieving a thermal equilibrium polarization is modified by large extent : it is longitudinal relaxation (Time T1).

Are strongly dependent on the motion rates, and open the way to characterize and measure them.

Transverse relaxation

For isotropic motions, many interactions (among them the dipolar ones) average to zero.

However, the resonance line does not become infinitely narrow. To second order, these interactions have a residual effect on linewidth, that depends on the rate at which these interactions vary.

Similar behavior for all anisotropic interactions: anisotropic chemical shift or indirect interactions, quadrupole interactions, etc.

Longitudinal relaxation

The most noteworthy features

1- Cross-relaxation

Between spins of different resonance frequencies under the time-variation of the inter-spin interactions. Provides information on the spatial proximity. Makes it also possible to measure the pair correlation times, from which one deduces the local mobility in a molecule.

Constitutes a generalization to nuclear spins, to dipolar interactions and to dynamics of the Overhauser Effect.

2- Limit of evolution

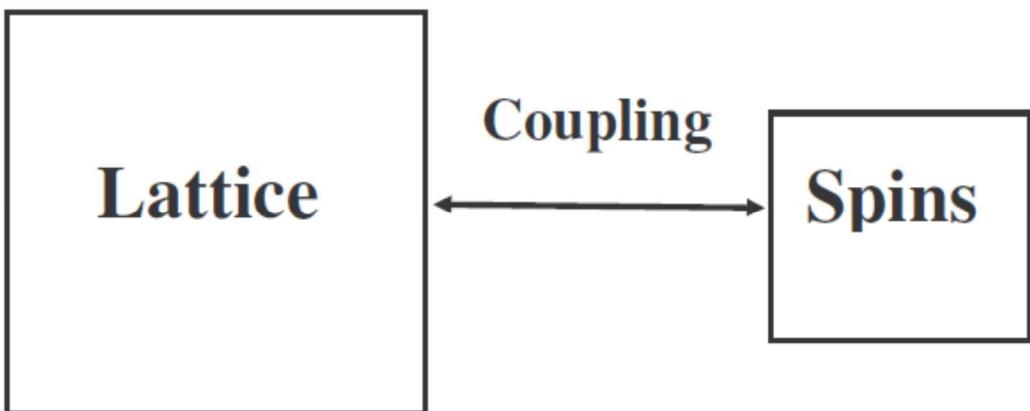
In the classical model of thermal motion, the latter is random (Ex: Brownian motion) and so is the modulation of the interactions experienced by the spins.

Theory, classical or quantum, then predicts that the spin magnetization should evolve towards zero.

In order that the longitudinal magnetization evolves towards its thermal equilibrium value, it is imperative to treat formally the lattice, and its motions, as a quantum system coupled to the spins system.

As a rule, the heat capacity of the lattice is practically infinite, and its temperature remains constant.

Thermal reservoirs



Equalization of temperatures

Magnetic Resonance Imaging (MRI)

General idea:

Since the resonance frequency is proportional to the applied field, it suffices to make it vary within the sample (by a field gradient) to code position by frequency.

By sampling the precession signal observed after a rf pulse, one does not directly obtain the position, but its Fourier transform.

Rationale of imaging

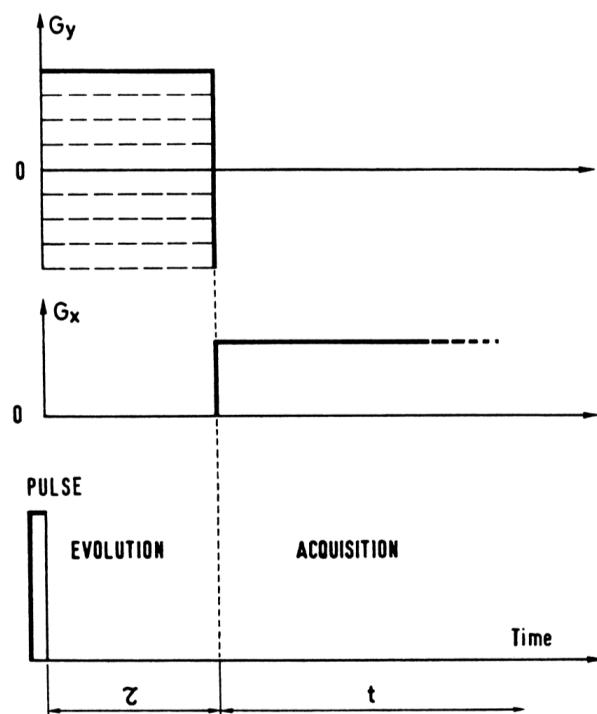
$$\begin{array}{ccc} F(t) & = & G(k) \\ \downarrow & & \uparrow \\ \boxed{\text{Fourier transform}} & & \\ \downarrow & & \uparrow \\ S(\omega) & = & g(x) \end{array}$$

Simplest implementation

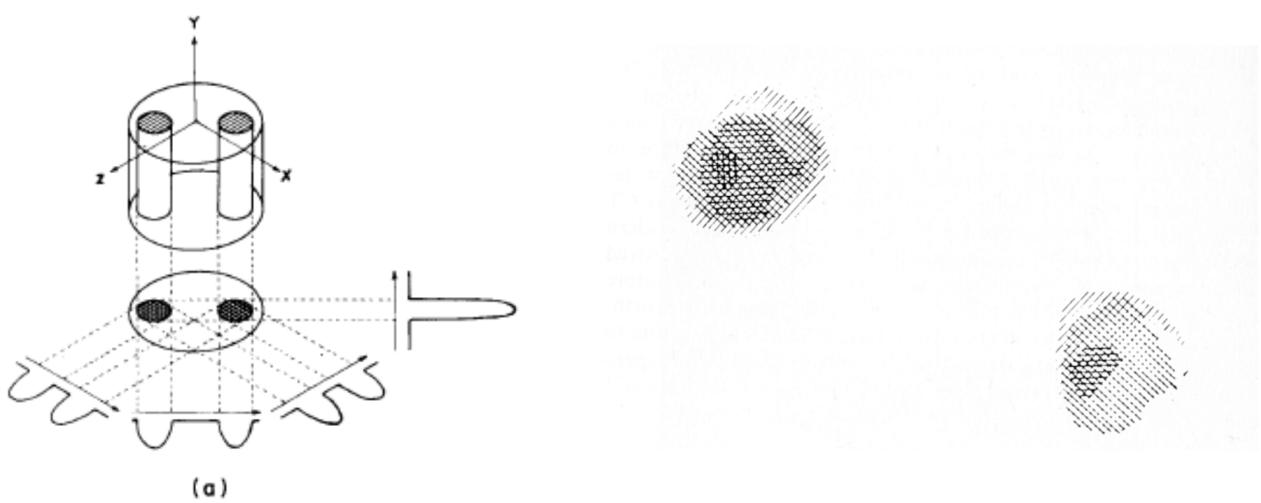
- 1- Excite a slice by a rf pulse in the presence of a gradient G_z ,
- 2-Apply a gradient G_y of duration τ , realizing a (blind) phase encoding in this direction,
- 3-Apply a gradient G_x and sample the signal in the course of time t ,
- 4-Start again with a different gradient G_y .

The image of the slice is obtained by a double Fourier transform with respect to $G_y\tau$ and $G_x t$ (computed by FFT during the acquisition).

Schematic sequence

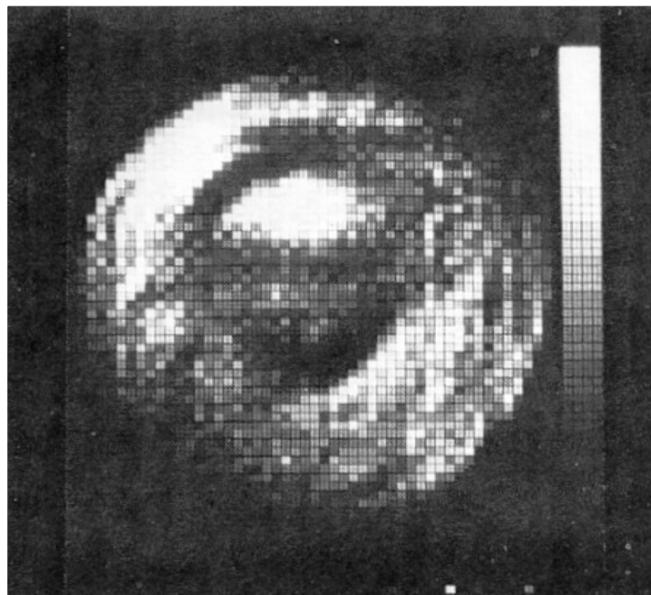


Lauterbur (1973)
two capillaries of water



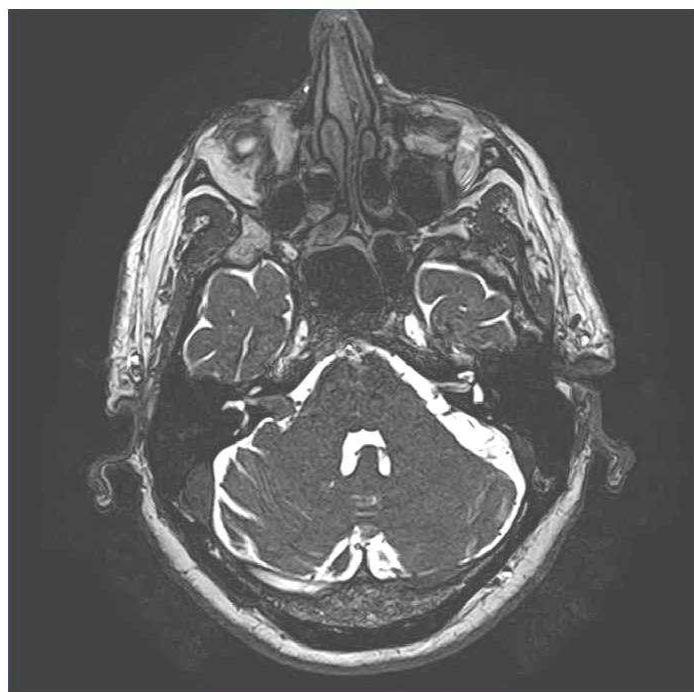
Uses back projection

Mansfield, Maudsley (1977) cross section of finger



Use Fourier Transform

My radiologist (2008)
head and brain (slice thickness sub mm)



Nobel Prizes for NMR

Physics

- 1952 : F. Bloch and E.M. Purcell, discovery of NMR.
- 1997 : D.M. Lee, D.D. Osheroff and R.C. Richardson, experimental discovery by NMR of superfluidity of Helium 3.
- 2003 : Sir A.J. Leggett, theory of NMR in superfluid He 3.

Chemistry

- 1991 : R.R. Ernst, methodology of high-resolution NMR.
- 2002 : K.Wüthrich, 3D structures of biological macromolecules in solution.

Physiology or Medicine

- 2003 : P.C. Lauterbur and Sir P. Mansfield, discovery of Magnetic Resonance Imaging.