Hyperpolarization in Nuclear Magnetic Resonance

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Disclaimer:

This is not intended to be an exhaustive review on hyper-polarisation techniques in magnetic resonance.

The topic is too large to be covered here!

This presentation is directly reflecting the author’s own interest and is in no way a qualitative/quantitative comparisons between techniques.
Nuclear Magnetic Resonance

NMR can be used:

→ as a spectroscopy technique:

**Structural and dynamical information at the atomic scale!**

→ as a microscopy/imaging technique:

**Non-invasive technique, convenient for medical diagnostic!**

**Fields of application:** physics, material sciences, biology and medicine

• Main limitations of the technique: Sensitivity, sensitivity and sensitivity!*
Boltzmann Polarization in NMR

**NMR: Low energy transitions**

\[ M_s = -\frac{1}{2} \]

\[ \Delta E = \hbar \gamma B_0 = 3,3 \times 10^{-25} \text{ J} \quad @ \quad B_0 = 11,74 \text{ T} \]

\[ E_{\text{thermique}} (298 \text{ K}) = k_B T = 4,1 \times 10^{-21} \text{ J} \]

**Boltzmann distribution**

\[ P = \frac{n^+ - n^-}{n^+ + n^-} = \tanh \left( \frac{\gamma \hbar B_0}{2kT} \right) \quad \text{High Temperature Approximation} \]

\[ P \approx \frac{\alpha_0/2\pi}{\gamma B_0 \hbar} \cdot \frac{1}{2kT} \]

- **Nuclear polarization is typically of the order of tens of ppm!**
Signal to noise (S/N) in NMR

Mainly inductive detection… so far

\[ S \approx \frac{3 \gamma_e \gamma_d^2 B_0^2}{T_s} N_S \]

Broadly accepted expression…

Mainly thermal (Johnson) noise

\[ N \approx \sqrt{T_c} \sqrt{T_s} \sqrt{N_S} \]

- \( B_0 \): magnetic field;
- \( \gamma_e/\gamma_d \): gyromagnetic ratio of the excited/detected spin
- \( T_s \): Sample temperature;
- \( T_c \): Circuit temperature

• Goal: enhancement of the signal and reduction of the noise!
• FT NMR, High Field magnet, Cryo-probe, INEPT/CP, etc.
Current strategy: going to higher magnetic fields

- ~ x 10 polarization gain over the last 2 decades thanks to the development of high field magnets

Polarization as a function of $B_0$ and sample temperature:

$$P \approx \frac{\alpha j}{2\pi} \frac{\gamma B_0 \hbar}{2kT}$$

$0.007 \%$ $^1$H polarization @ 1 GHz / 300 K

- $\sim$ $5$ M +
- $\sim$ $200$ k
- $\sim$ $10$
Is this enough? – No!

We are still off by 4 to 5 orders of magnitude on the Polarization!
(compared to a fully polarized system)

**Solution-state NMR**

- 3D structure determination of biomolecules
- Small molecules studies:
  Metabolomics, molecular dynamics, etc.

**Solid-state NMR**

- 3D structure determination of insoluble/non crystalline biomolecules
- Materials studies (low gamma nuclei, etc), etc.

**Magnetic Resonance Imaging**

- anatomical imaging
- functional imaging
- molecular imaging, etc.

Further increase in sensibility is still high desirable...
What can we do?

Hyperpolarization techniques!

- Usually involve transfer from more ordered system (electron, pH\textsubscript{2}, photon)

- In the following we will concentrate on DNP experiments that are compatible with high field NMR detection!
Hyperpolarization techniques

Since the beginning of NMR, hyperpolarization techniques have always been around…

- Microwave Induced Dynamic Nuclear Polarization – (mw)-DNP

- Spin-Exchange Optical Pumping (SEOP) - Laser-polarized Xenon

- Para-hydrogen induced polarization – PHIP

- Optically Pumped Dynamic Nuclear Polarization – OPDNP, MI-ODNP

- Photo Chemically Induced Dynamic Nuclear Polarization – Photo-CIDNP

- Haupt effect

- etc.
Parahydrogen induced polarization

- PHIP principles
- Applications
- On-going challenges

H₂ molecules: made of two equivalent proton spins!
• **PHIP principles:**

- H2 molecules: ortho and para spin-isomers
- Production of p-H2
- Hydrogenation reaction creates the observable hyperpolarization step
- Pasadena versus Altadena experiments
- Transfer to an heteronuclei
Eigenfunctions for AX versus A₂ spin system

AX - Two inequivalent spins ½

A₂ - For equivalent spins ½

Solution

Para or Singlet state

\[
\left( \frac{1}{\sqrt{2}} \right) (\alpha \beta - \beta \alpha)
\]

Ortho or Triplet state

\[
\left( \frac{1}{\sqrt{2}} \right) (\alpha \beta + \beta \alpha)
\]

• H₂ molecules are described by two spin isomers: o-H₂ and p-H₂

A₂ system: States should be symmetric or antisymmetric with respect to permutations (Fermi-Dirac statistics, etc.)
NMR for J-coupled AX versus A₂ spin system

Para or Singlet state

Ortho or Triplet state

AX - Two inequivalent spins

A₂ - For equivalent spins

NMR silent!
Parahydrogen conversion

- Energy of H\textsubscript{2} molecules (in absence of magnetic field) are given by their rotational states distribution:
  \[ E_J = \frac{J(J+1)\hbar^2}{2I} \]
  \[ g_J = 2J + 1 \]

- Ortho-hydrogen occupies only odd rotational states
- Para-hydrogen occupies only even rotational states

\[ \frac{E_{J=1} - E_{J=0}}{k_B} = 2\theta_{\text{rot}} = \frac{\hbar^2}{k_B I} = 174.98 \text{ K} \]

\[ E_{J=1} - E_{J=0} \sim 10^{12} \text{ Hz} \]

- Transitions between ortho and para hydrogen are symmetrically forbidden \(\rightarrow\) non-equilibrium mixtures are long lived
Parahydrogen conversion

- To induce the ortho to para conversion, one can use suitable catalyst at low temperatures (in order to break the symmetry)

\[
\frac{N_{\text{ortho}}}{N_{\text{para}}} = \frac{3 \sum_{\text{odd}} j(2J + 1)e^{-6(J(J+1)/T}}}{\sum_{\text{even}} j(2J + 1)e^{-6(J(J+1)/T}}
\]

The first synthesis of pure parahydrogen was achieved by Paul Harteck and Karl Friedrich Bonhoeffer in 1929.

- At 20K the conversion is almost completed
- By removing the catalyst, the ortho/para ratio is preserved!
Triplet state
\[ \frac{(\alpha\beta + \beta\alpha)}{\sqrt{2}} \]
Singlet state
\[ \frac{(\alpha\beta - \beta\alpha)}{\sqrt{2}} \]

The four states are equally populated

\[ @ B_0 = 0 \text{ and } T \approx 300 \text{ K} \]

\[ @ B_0 \approx 0 \text{ and } T \approx 20 \text{ K} \]

\[ \approx 10^{12} \text{ Hz} \]

Catalytic conversion
\[ o-H_2 \rightarrow p-H_2 \]

very slow reconversion!

- After the conversion process, only the singlet state is populated
- How can we use this? – a singlet state is NMR silent!
- The solution consists in breaking the symmetry using an hydrogenation reaction
- A2 becomes AX

In Pasadena experiments the hydrogenation reaction is carried out in the high field magnet

Whereas in the Altadena experiments the hydrogenation reaction is performed at earth magnetic field and the sample is then moved adiabatically to the high field magnet!
PHIP sensitivity gain

\[ \alpha \beta \rightarrow \beta \alpha \]

Longitudinal order

\[ \varepsilon \sim 10^5 \]

AB system – J-coupled

PHIP principles

Hydrogen isomers
H spins are equivalent

Ortho
Triplet state

(1/√2)(αβ + βα)

Para
Singlet state

(1/√2)(αβ - βα)

αα

ββ

−

Hydrogenation reaction

States mixing
States αβ and βα equally populated!

Almost complete conversion at \( T \sim 20 \, K \)

Ortho

Para

H spin are inequivalent

• Hydrogenation reaction induces an overpopulation of states αβ and βα
• Note: the para to ortho conversion is a very slow process even at room temperature!

Further reading: Pasadena versus Altadena

In Pasadena experiments the hydrogenation reaction is carried out in the high field magnet.

Whereas in the altadena experiments the hydrogenation reaction is performed at earth magnetic field and the sample is then moved adiabatically to the high field magnet!
Advantages and drawbacks of the PHIP approach

• PHIP is particularly interesting for **low field NMR** (but not only)

• PHIP was used to study **hydrogenation reactions**

• **Transfer to other nuclei** is difficult but possible! – this implies the design of hydrogenated molecules with long relaxation time to allow polarization transfer to occur.

• **Application to MRI** was demonstrated in 2001 – Recent PHIP experiments involve the use of $^{13}$C labeled (metabolically relevant) unsaturated precursors

• **Long time storage of para-hydrogen** (liquid or gas phase) requires very low paramagnetic impurities.

• **Design adequate pulse sequences** to improve the anti-phase detection (caused by the initial longitudinal order)

• etc.


Key authors: Bowers, Weitekamp, Golman, Canet, and others
Reversible Interactions with para-Hydrogen Enhance NMR Sensitivity by polarization transfer

“We show here that a metal complex can facilitate the reversible interaction of para-hydrogen with a suitable organic substrate such that up to an 800-fold increase in proton, carbon, and nitrogen signal strengths are seen for the substrate without its hydrogenation.”
On-going research – PHIP and Zero-Field NMR

Parahydrogen-enhanced zero-field nuclear magnetic resonance

Zero-Field NMR Enhanced by Parahydrogen in Reversible Exchange

“Here we demonstrate direct detection of zero-field NMR signals generated through parahydrogen-induced polarization, enabling high-resolution NMR without the use of any magnets. The sensitivity is sufficient to observe spectra exhibiting $^{13}$C–$^1$H scalar nuclear spin–spin couplings (known as J couplings) in compounds with $^{13}$C in natural abundance, without the need for signal averaging. The resulting spectra show distinct features that aid chemical fingerprinting.”
Laser-polarized Xenon
Laser-polarized Xenon

- Laser
- Optical Pumping
- \( \sigma^+ \)
- Collision: spin-exchange
- Rb
- Xe
- \( N_2 \)
- \( B_0 \)
- Photon angular momentum
- Electron spin of metal atom (Rb)
- Noble gas
- Nuclear spin
• The metal ion is polarized by OP. This circularly polarized laser beam allows the selective depopulation of one of the two magnetic ground states of Rubidium atoms.

• The induced electronic polarization is transferred by cross-relaxation to xenon nuclear spins (or other noble gas).

Key authors: Pines et al., Desvaux, Berthault, etc.

G. Navon, A. Pines and co-workers (Science, 271, 1996, 1848)
Preparation of laser-polarized Xenon

Experimental apparatus @ CEA-IRAMIS

Left: the lasers and the optics.

Center: the pumping cell and the coils for creating the magnetic field

Right: the electronics and the pumping group

Typical sensitivity gain @ 10 T, \( \varepsilon \approx 45,000 \) !

• Typical production: 1ml in 5 min at 1 atm
Hyperpolarized Xenon – main applications

- He/Xe MRI → enhanced anatomical imaging (gas phase)
- Xenon NMR → bio-sensing using laser polarized xenon
- Polarization transfer from Xenon to other nuclei: SPINOE/CP experiment
  → Enhancement of $^1$H NMR for the cage molecule (Saclay, 1999)
  → Surface-enhanced NMR (Xe adsorption and NOE transfer)
  → Exploration of protein hydrophobic cavities, etc.

Key authors: Pines et al., Desvaux, Berthault, etc.
Hyperpolarized Xenon – challenges & perspectives

For Solution NMR:

• Xenon can easily be dissolved in solution but polarization transfer from the highly polarized Xenon to surrounding nuclei is still an unsolved problem: very weak interaction between xenon and other molecules!

For Magnetic Resonance Imaging:

• towards molecular imaging!

i.e. combination of hyperpolarized Xe MRI and biosensing approach*

Frequency-selective laser-polarized 129Xe MRI images: proof of principles

* More detail: see NMR group @ IRAMIS

Key authors: Pines et al., Desvaux, Berthault et al., etc.
Microwave induced DNP
Microwave induced Dynamic Nuclear Polarization

The mechanism of dynamic polarisation whereby a large polarisation is ‘artificially’ transferred to the nuclear spins is closely related to the mechanism of nuclear relaxation by paramagnetic electronic impurities through which the nuclei ‘feel’ the temperature of the lattice and acquire their ‘natural’ polarisation of thermal equilibrium.

Abragam, Goldman, 1978

Key authors: Overhauser, Carver, Slichter, Abragam, Goldman, Jeffries, Hill, etc.
Microwave induced Dynamic Nuclear Polarization

DNP mechanisms:
- Overhauser effect – Metal and liquids
- Solid Effect – solids
- Cross Effect / Thermal Mixing – solids

Two types of interactions:
- Fermi contact (isotropic)
- Dipolar interaction (anisotropic)

Key authors: Overhauser, Carver, Slichter, Abragam, Goldman, Jeffries, Hill, etc.
Overhauser effect in Metals

Polarization of Nuclear Spins in Metals*

T. R. CARVER† AND C. P. SLICHTER
Department of Physics, University of Illinois, Urbana, Illinois
(Received August 6, 1953)

• $^7\text{Li}$ NMR @ $\omega_0/2\pi = 50$ kHz
  (30.3 Gauss ~ 3 mT)

• EPR @ $\omega_0/2\pi = 84$ MHz

A. Overhauser, Phys. Rev. (1953)
Carver and Slichter, Phys. Rev. 92 (1953)
Phys. Rev. 102 (1956)

• Initial prediction of the effect in 53’ by Overhauser
• First demonstration of the Overhauser effect in metals in 53’
• Extension of the effect for liquids!
Dynamic Nuclear Polarization: History

- **1950’** Overhauser experiments in metals
  Overhauser, Carver, Slichter (1953-1956)

- **1960-80** Liquids and Solids DNP
  Abragam, Goldman, Protovorov *et al.*
  Hauser, Mueller-Warmuth, Richards *et al.*

- **1980’** MAS-DNP (polymers, diamond)
  Wind, Yannoni, Schaefer *et al.*

- **1990-now** High Field MAS-DNP (amyloid, membrane proteins)
  Griffin *et al.*

- DNP principle is far from being new but its application to high magnetic fields is very challenging!
Effect of saturating the EPR transitions in a liquid

Let us consider a two spin system composed of one nuclei and one electron spin

Irradiation at the EPR transitions

Thermal equilibrium for a two spin system (n - e)

No DNP effect!!

• What have we missed?

Hyperfine coupling between n (I spin) and e (S spin):

\[
\left\langle H(t) = \frac{\gamma_e \gamma_n \hbar^2}{r^3} (A + B + C + D + E) \right\rangle = 0
\]

\[
E = \frac{-3}{4} S^+ I^+ \sin^2(\theta) \exp(-2i\phi) \quad F = \frac{-3}{4} S^- I^- \sin^2(\theta) \exp(2i\phi)
\]

\[
A = S_z I_z \left(1 - 3 \cos^2(\theta)\right)
\]

\[
B = \frac{-1}{4} \left(S^+ I^- + S^- I^+\right) \left(1 - 3 \cos^2(\theta)\right)
\]

\[
C = \frac{-3}{4} \left(S^+ I^- + S^- I^+\right) \sin(2\theta) \exp(-i\phi)
\]

\[
D = \frac{-3}{4} \left(S^- I_z + S_z I^-\right) \sin(2\theta) \exp(i\phi)
\]
Solution-state DNP: Overhauser effect

\[ W_0 = \frac{1}{20} \frac{\gamma_e}{r^6} J(\omega_e, \tau_e) \]
\[ W_1 = \frac{6}{20} \frac{\gamma_e}{r^6} J(\omega_e, \tau_e) \]
\[ W_2 = \frac{3}{20} \frac{\gamma_e}{r^6} J(\omega_e, \tau_e) \]

- Motional averaging can induce additional (efficient) relaxation pathways: \( W_0, W_1, W_2 \)
- By saturating the EPR lines, we induce a competition between two processes: saturation (W) and dipolar relaxation towards thermal equilibrium \((W_0, W_1, W_2)\)
Effect of saturating the EPR transitions

• Competition between relaxation towards Boltzmann equilibrium and saturation of the EPR lines!

Thermal equilibrium

Efficient relaxation pathways

Hypothesis:
\[ W_0 \] dominates
\[ \frac{p_{\alpha\beta}}{p_{\beta\alpha}} = \frac{p_{0\alpha\beta}}{p_{0\beta\alpha}} \]

Efficient pathways

Irradiation at the EPR transitions

Hypothesis:
\[ W >> W_e \]

DNP equilibrium

DNP effect!

• Complete derivation is possible!

Scalar relaxation:
\[ e \sim - \gamma_e / \gamma_n \]

Dipolar relaxation:
\[ e \sim \frac{1}{2} \gamma_e / \gamma_n \]
**High magnetic field regime**

*Complete derivation is possible...*

Coupling parameter

$$\rho(\omega_0, \tau_c) = \frac{W_2 - W_0}{W_0 + 2W_1 + W_2}$$

$$\mathcal{E} = 1 - \rho f s \frac{\gamma_s}{\gamma_I}$$

**Leakage factor**

$$f = \frac{W_0 + 2W_1 + W_2}{W_0 + 2W_1 + W_2 + W_n}$$

**Saturation Factor**

$$s = \frac{\langle S_0 \rangle - \langle S_2 \rangle}{\langle S_0 \rangle} = \frac{W}{W + W_r}$$

- High Field Overhauser should not be very efficient!

Loening et al.
Solid-state DNP: the Solid Effect

Hyperfine coupling between e (S spin) and n (I spin):

\[
H = \frac{\gamma_e \gamma_n \hbar^2}{r^3} (A + B + C + D + E)
\]

\[
A = S_z I_z (1 - 3 \cos^2 (\theta))
\]

\[
B = -\frac{1}{4} (S_z I_z + S_z I_z^-) (1 - 3 \cos^2 (\theta))
\]

\[
C = -\frac{3}{4} (S_z I_z + S_z I_z^-) \sin (2\theta) e^{-i\phi}
\]

\[
D = -\frac{3}{4} (S_z I_z + S_z I_z^-) \sin (2\theta) e^{i\phi}
\]

\[
E = -\frac{3}{4} S_z I_z^- \sin^2 (\theta) \exp (-2i\phi)
\]

\[
F = -\frac{3}{4} S_z I_z^- \sin^2 (\theta) \exp (2i\phi)
\]

Key authors: Abragam
Solid-state DNP: the Solid Effect

Secular approximation for electron Zeeman interaction:

\[ H = \omega_n I_z + A S_z I_z + B S_z I_x \]

- No efficient relaxation exist for the zero- or double-quantum transitions, saturation of the EPR transitions is probably not a good idea!

- What will happen if we perform an EPR irradiation along the so called “forbidden transitions” \(\omega_0\) or \(\omega_2\)? – nothing if B is neglected!

Key authors: Abragam
Solid-state DNP: the Solid Effect

Secular approximation for electron Zeeman interaction:

$$H = \omega_0 S_z + \omega_{\alpha n} I_z + A S_z I_z + \mu B S_z I_x$$

- No efficient relaxation exist for the zero- or double-quantum transitions, saturation of the EPR transitions is probably not a good idea!

- What happen if we perform an EPR irradiation along the so called “forbidden transitions” $\omega_0$ or $\omega_2$? – nothing if B is neglected!

- If B is large enough, it can mix state $\alpha\beta$ and $\beta\beta$ as well as $\alpha\alpha$ and $\beta\alpha$. Then the transitions are not so forbidden anymore…

Key authors: Abragam
The Solid Effect: irradiating the forbidden transitions

\[ \varepsilon \approx \left( \frac{\gamma_e}{\gamma_n} \right) \left( \frac{B_{1mw}}{B_0} \right)^2 \]

**SE DNP enhancement**

- Note: $1/B_0^2$ dependency!!

\[ \omega_{mw} = \omega_e - \omega_n \]

\[ \omega_{mw} = \omega_e + \omega_n \]
The well-resolved solid Effect

\[ \omega_{n0} > \text{EPR linewidth} \quad \text{and} \quad \omega_{n0} \approx \text{EPR linewidth} \]

- SE efficiency is inversely proportional to the \( B_0^2 \)
- SE is applicable when the EPR FWHH is smaller than the \( \omega_{n0} \)
- But this is not generally the case at high magnetic field…
Three spin mechanism DNP: two electrons and one nuclei

Fortunately other mechanisms are possible...which involve more than one electron spin...

If \( \omega_{e2} - \omega_{e1} \sim \omega_n \)

\( \Delta \omega_e = \omega_n \)

Equilibrium

Positive Enhancement

Negative Enhancement

Key authors: Kessenikh, Manenkov, Hill, Goldman, Abragam, etc
Cross Effect and Thermal Mixing DNP

- Three and more spin process have proven very useful, especially at high $B_0$
- Detailed mechanisms are complicated!

- EPR inhomogeneous breath: $\Delta - g$ anisotropy
- EPR homogeneous linewidth: $\delta - ee$ dipolar couplings
- NMR Larmor Frequency: $\omega_{0n}$

Crude (but simple) classification of the various DNP mechanisms...

- if $\omega_{0n} >> \Delta$: Two spin process (Solid Effect)
  $\epsilon \sim 1/B_0^2$

- if $\delta < \omega_{0n} < \Delta$: Three spin process (Cross Effect)
  Very efficient when $\omega_{e1} - \omega_{e2} \sim \omega_{0n}$
  $\epsilon \sim 1/B_0$

- if $\omega_{0n} < \delta$: Multiple electron spin process
  Thermal Mixing
Challenges of High Field DNP

• All DNP mechanisms presented here appear less favorable at high magnetic fields!

• Combining DNP with high field NMR also imposes several additional constraints:

→ MW heating is a concern (especially for liquids)
→ High power high frequency microwave sources are limited
→ Difficult to design resonant structure for the microwave irradiation that are compatible with MAS spinning, etc.

Current on-going research areas:

- **High Field MAS solid-state DNP** (*in situ*, LT, 5-15 T, high power source)
- **Dissolution DNP** (*ex situ* DNP at 4K and 3 Tesla, dissolution, NMR/MRI)
- **Shuttling DNP for liquids** (Low Field Overhauser – High Field NMR)
- **High Field Overhauser for liquids** (with E-free mw resonator!)
Dissolution DNP
Dissolution DNP – ex situ DNP

Principle:

- DNP at moderate field and 1.2 K during ~1h
- dissolution step
- transfer to high field

Solid material doped with unpaired electrons

$P_e = 94\%$ and $P_C = 0.086\%$


3.35 T and 1.2K
The DNP $^{13}$C polarizer

**Challenges and limitations:**

- Preserving the nuclear magnetization during the dissolution step
- Dilution factor
- Keep the magnetization during the transfer to high field magnet (design of two centers magnet, etc.)
- One shot experiment

**Main applications:**

- $^{13}$C hyperpolarization: small molecules structure determination, metabonomics, …
- $^{13}$C hyperpolarization for MRI: U-13C pyruvate etc…

$^{13}$C Urea (n.a.) at 9.4 Tesla

- Single Shot
  - Acq= 1s, P=20%

$^{13}$C Urea at RT

- Acq= 65h, P=7.5 ppm

$\varepsilon \sim 30000$
High Field MAS solid-state DNP
High Field Dynamic Nuclear Polarization

\[ P \approx \frac{\gamma \hbar B_0}{2kT} \]

- DNP results from transferring spin polarizations to surrounding nuclei

\[ \varepsilon_{DNP} \approx \frac{\gamma_e}{\gamma_{1H}} \approx 660 \]

\( \approx 10\% e \) polarization @ 10 T / 90 K

\( \approx 0.01\% 1H \) polarization @ 10 T / 90 K
High Field Solid-state MAS DNP – the Griffin approach

High Field Dynamic Nuclear Polarization

\[ P \approx \frac{\gamma_e \hbar B_0}{2kT} \]

- DNP is produced by applying at the sample an irradiation with a frequency close to the electron spin transition

\[ \varepsilon_{DNP} \approx \frac{\gamma_e}{\gamma_{1H}} \approx 660 \]

\[ \sim 10\% \text{ e polarization at } 10\,\text{T} / 90\,\text{K} \]

\[ \sim 0.01\% \text{ } 1\text{H polarization at } 10\,\text{T} / 90\,\text{K} \]
High Field Dynamic Nuclear Polarization

\[ P \approx \frac{\gamma \hbar B_0}{2kT} \]

~10% e polarization @ 10 T / 90 K

~0.01% 1H polarization @ 10 T / 90 K

\[ \epsilon_{DNP} \approx \frac{\gamma_e}{\gamma^{1H}} \approx 660 \]

\[ \epsilon_{\text{max}} = \frac{P_{\text{blue}}}{P_{\text{red}}} = 2000 \]

But recycling is possible (5-10 s) which could translate in 4 \(10^6\) time savings!!
DNP with gyrotrons

Dynamic Nuclear Polarization with a Cyclotron Resonance Maser at 5 T

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(Received 26 July 1993)

DNP (dynamic nuclear polarization) experiments at 5 T are reported, in which a cyclotron resonance maser (gyrotron) is utilized as a 20 W, 140 GHz microwave source to perform the polarization. MAS (magic angle spinning) NMR spectroscopy with DNP has been performed on samples of polystyrene doped with the free radical BDPA (α,γ-bisdi phenylene-β-phenylallyl) at room temperature. Maximal DNP enhancements of ~10 for 1H and ~40 for 13C are observed and are considerably larger than expected. The DNP and spin relaxation mechanisms that lead to these enhancements at 5 T are discussed.

1.5 % efficient

\[ \varepsilon \sim 10 \]

\[ \varepsilon \sim 40 \]

\[ (\gamma_e/\gamma_n) \sim 660 \]
• High Frequency Dynamic Nuclear Polarization has been pioneered in the Griffin group @ MIT over the last two decades…

T= 90 K
\{\gamma\} = 8 kHz

DNP Enhanced $^{13}\text{C}$ MAS Spectra – $^{13}\text{C}$ Urea
High Field DNP experiments @ MIT

DNP components

- Probe
- Gyrotron
- Transmission Line
- Polarizing Agents

Polarizing agents that are widely applicable and stable:
- TEMPO (nitroxides), Biradicals, metal ions

Typically (1H, 13C, 15N and electrons) -- performing Magic Angle Spinning at 90 K

Millimeter wave microwave sources
- 10-100 watts in the 100-600 GHz regime
- Gyrotrons (cyclotron resonance masers)

Direction des Sciences de la Matière

INSTITUT NANO SCIENCES ET CYROGÉNIE
CEA
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CNRS
Experimental setup for high field DNP

- Gyrotron
- NMR magnet
- 90K DNP probe
- 90 K power supply

Griffin group @ MIT
DNP up to 10 Tesla
ε ~300 @ 90 K
Solid-state DNP: qualitative picture and challenges

• To increase $T_{1n}$, $T_s \sim 10-100$ K are often required

• Use of cryoprotectant to obtain glassy matrix
  - avoid ice crystal formation
  - ensure uniform distribution of electrons

• DNP mechanism = e-H polarization transfer and relayed HH spin diffusion
Griffin’s biradical

- EPR spectrum is 600 MHz wide @ 5 Tesla
- Inhomogeneous broadening i.e. $\Delta \gg \omega_{0n}$
- Hole burning experiment on Tempo radicals
  $\rightarrow$ e-e couplings between the spin packets

- For CE: we need $\omega_{e1} - \omega_{e2} \sim \omega_n$

- Design of biradical in order to maximize the CE efficiency!

- For Totapol radical:
  - e-e coupling is 25 MHz
  - Electron concentration $\sim$ 10 mM
Polarization transfer to various systems

- Enhancement ~50 to 300 are routinely observed at 5 to 10 T and 90 K
- Development of optimized polarizing agents (e.g. TOTAPOL, BT2K)
- This approach has proven efficient in polarizing 100 nm size particles in 5 to 10 s
DNP in Amyloid Nanocrystals

Distribution of Polarization via $^1$H Spin Diffusion

- When the dimensions of the system are large a polarization gradient develops!

\[ \varepsilon = 160 \]
\[ \varepsilon = 80 \]

\( \text{Courtesy, Griffin et al.} \)
Thank you for your attention