

PANACEA/NIH Maglab workshop



Introduction to the theory of Dynamic Nuclear Polarization
Frédéric Mentink-Vigier



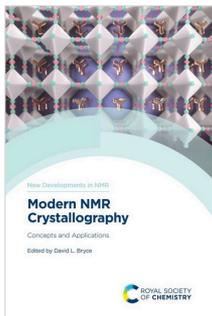
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BOOK CHAPTER

Chapter 10: Dynamic Nuclear Polarization for Solid-state NMR Spectroscopy

By Daniel Lee ; Frederic Mentink-Vigier

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Dynamic nuclear polarization (DNP) is a transformative technique in the field of solid-state nuclear magnetic resonance (NMR) spectroscopy that improves the detection sensitivity of nuclear spin signals by orders of magnitude. By capitalizing on the large electron spin polarization, DNP has opened new avenues for the NMR detection of species with low concentration, nuclei with low isotopic abundance, and traditionally challenging isotopes. This has pushed the boundaries of NMR crystallography by facilitating studies of complex biological systems, catalytic systems, and a wide range of materials. Herein, both the theory and methodology behind the current application of DNP for solid-state NMR spectroscopy are detailed.

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Aim at providing an
accessible introduction to
DNP and its applications

Overview

- 2009, 1st commercial MAS-DNP instrument
- 2012 → no general theoretical model explaining DNP under MAS
- How I contributed?
 - 2012 – First theoretical model for MAS-DNP
 - 2014 – Simulating Overhauser mechanism with BPDA
 - 2015 – New insight on the DNP process {e.g. depolarization process, Helium spinning}
 - 2017 – Large scale simulations, understanding of “heterobiradicals”
 - 2018 – ab initio design of biradicals
 - 2019 and subsequent: multiple demonstration of quantitative simulations
 - 2023 – Proof of spin diffusion around radicals
 - 2024 – mw absorption at high freq, and DNP at high temp

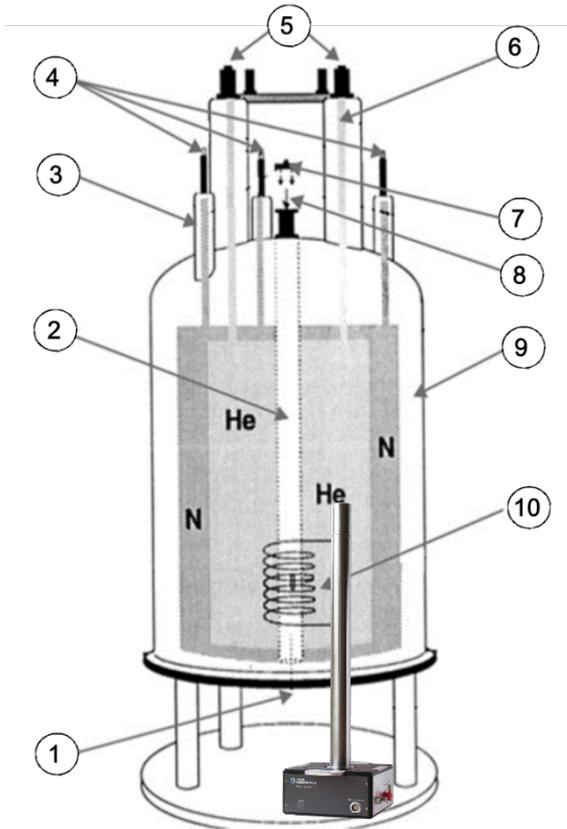
Note: most of this has not been published and is here as a pedagogical tool



Today's aim

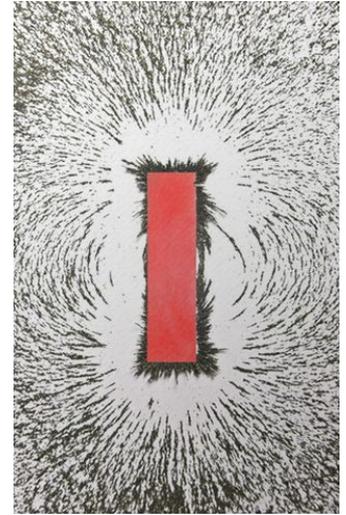
- The Overhauser – Effect
 - The example of BDPA
 - The example of solitons
- The Solid – Effect + its properties
 - What happens, rotor-events involved?
 - How does it behave under MAS?
- The Cross – Effect + its properties
 - How does rotor-events works?
 - MAS properties?
 - Unexpected effect: The importance of depolarization
- How does spin diffusion works?
 - What defines Build-up
 - How do we control it?
 - Effect of paramagnetic species?

NMR in a nutshell

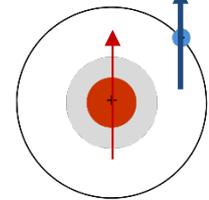


Big coil: creates the magnetic field

B_0



Hydrogen Atom

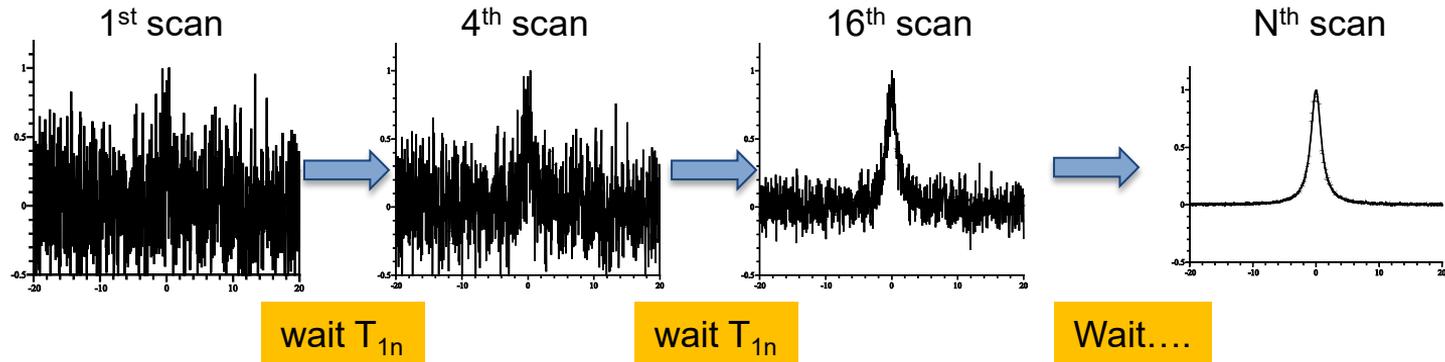
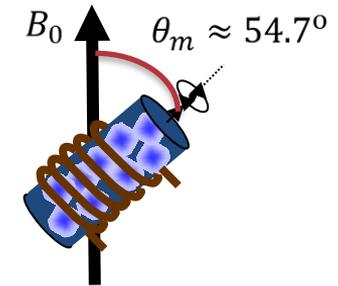


Proton spin = weak magnet

Probe: contains the sample and the detection setup

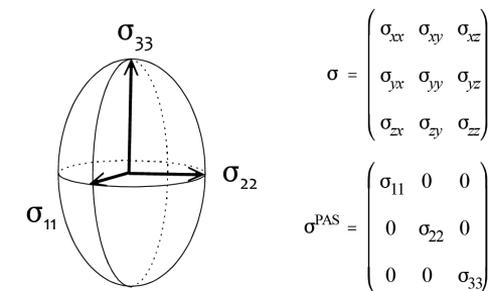
Nuclear Magnetic Resonance issues

- Nuclear magnetic resonance
 - High resolution even in solid state: Magic Angle Spinning (MAS)
 - structural information: material application
 - One chemical site = one resonance
 - Easy to manipulate spins
 - Low signal to noise:
 - Scan averaging for better signal/noise ratio
 - Complex study impossible at low natural abundance or surface
 - DNP Development



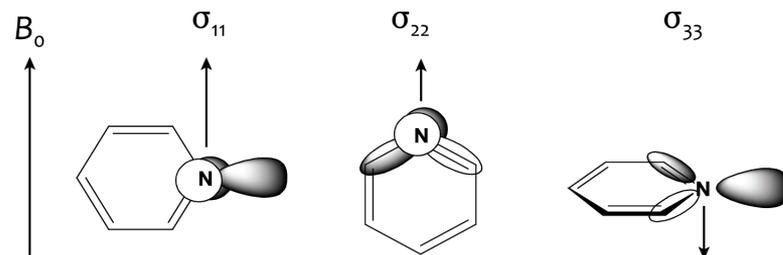
Chemical shift anisotropy

- CSA

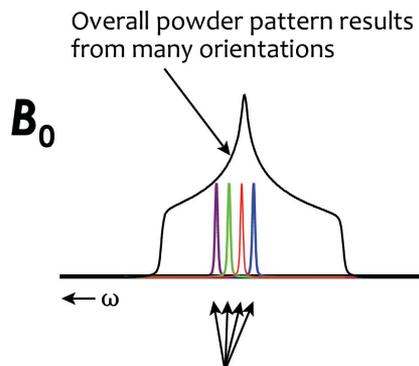
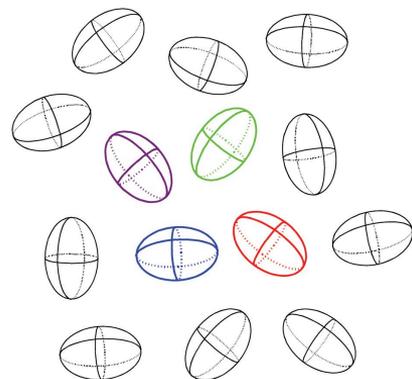


CS tensor in the molecular frame

CS tensor in its own **principal axis system (PAS)**



- Case of a powder

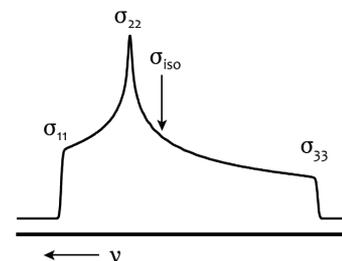


Overall powder pattern results from many orientations

Individual crystallites have the tensors oriented in one position w.r.t. B_0 , and give rise to a discrete frequency

σ_{33} : Direction of highest shielding

σ_{11} : Direction of lowest shielding

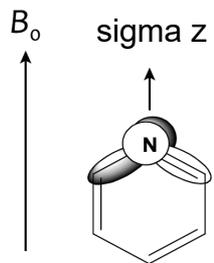


These orientations, and the many possible others, give rise to the solid-state NMR powder pattern

Rotation under MAS

- For a crystal aligned along the z -axis

sigma z

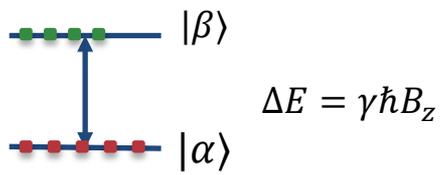


sigma x

sigma y

Nuclear and Electron Magnetic Resonance

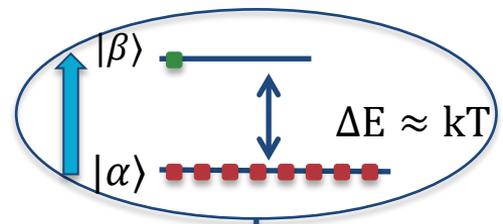
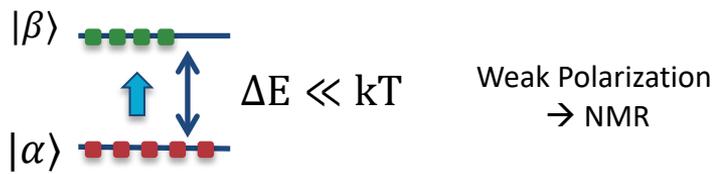
- Spins under magnetic field



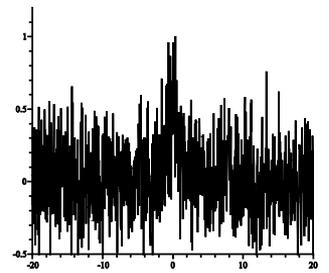
At thermal equilibrium, $k_B T \sim 6.25$ THz at RT

$$\hat{\rho} = e^{-\frac{\hat{H}_z}{k_B T}}, \quad \text{and} \quad P = \frac{N_{|\alpha\rangle} - N_{|\beta\rangle}}{N_{|\alpha\rangle} + N_{|\beta\rangle}} = \frac{e^{\frac{\Delta E}{2k_B T}} - e^{-\frac{\Delta E}{2k_B T}}}{e^{\frac{\Delta E}{2k_B T}} + e^{-\frac{\Delta E}{2k_B T}}}$$

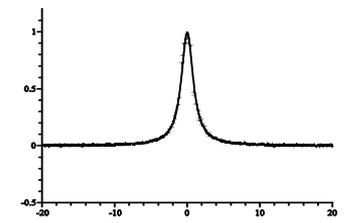
- Assembly of spins: polarization and relaxation



Majority of NMR experiments \rightarrow low NMR signal + slow relaxation towards equilibrium (T_{1n})



Routine condition in high field EPR at low temperature Fast relaxation toward equilibrium (T_{1e})



Dynamic Nuclear Polarization: combining EPR sensitivity with NMR exceptional resolution

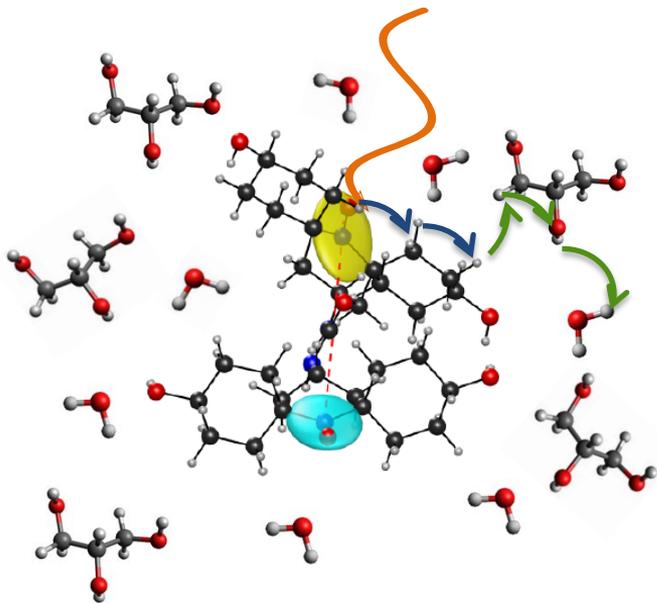
How does DNP “works*”

- * I will only focus on [^1H]

Microwave perturbs the radical polarization

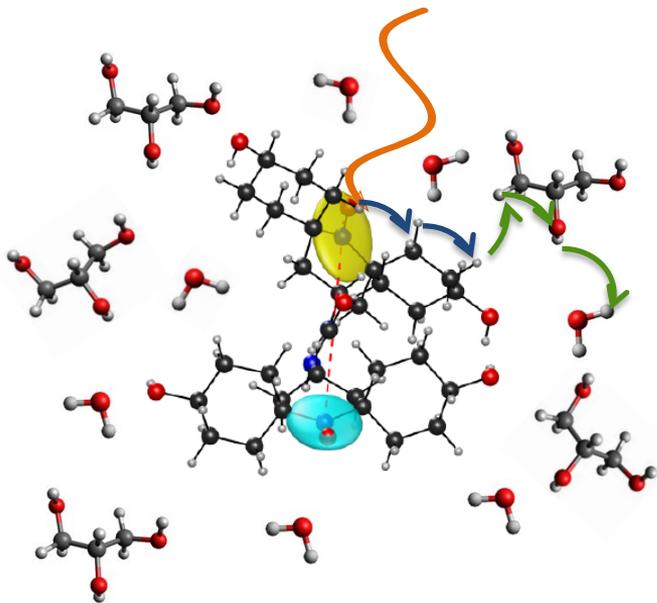
Nuclear hyperpolarization is generated on local [^1H] and transferred to the surroundings

Then transferred to the surroundings



How does DNP “works*”

- * I will only focus on [^1H]



$$\frac{dP_n(\vec{r}, t)}{dt} = -R_{1,n}(\vec{r})(P_n(t, \vec{r}) - P_n^B) - R_{\text{DNP}}(\vec{r})(P_n(t, \vec{r}) - P_{\text{DNP}}) + D(\vec{r})\nabla^2 P_n(t, \vec{r})$$

A simple model

- Diffusion equation of nuclear polarization P_n (like Fick equation)

$$\frac{dP_n(\vec{r}, t)}{dt} = -R_{1,n}(\vec{r})(P_n(t, \vec{r}) - P_n^B) - R_{\text{DNP}}(\vec{r})(P_n(t, \vec{r}) - P_{\text{DNP}}) + D(\vec{r})\nabla^2 P_n(t, \vec{r})$$

Thermal equilibrium \rightarrow goes back to P_n^B

Hyperpolarization \rightarrow source is P_{DNP}

Diffusion in between nuclei

- Spin diffusion is fast (case of ^1H) \rightarrow take average over \vec{r}

$$\frac{d\langle P_n(t) \rangle}{dt} = -\langle R_{1,n} \rangle (\langle P_n(t) \rangle - P_n^B) - \langle R_{\text{DNP}} \rangle (\langle P_n(t) \rangle - P_{\text{DNP}})$$

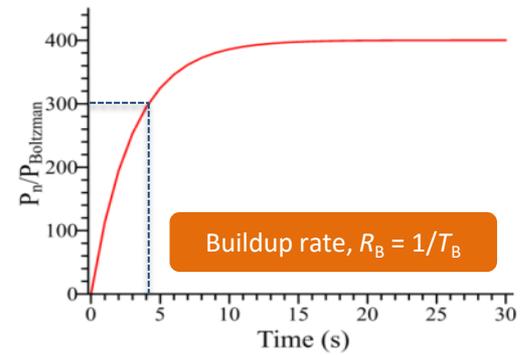
$$\langle R_{\text{DNP}} \rangle \propto \frac{N_{\text{DNP}}}{N_{\text{Total}}}, N_{\text{DNP}} \text{ number of protons undergoing DNP}$$

- Solving (no brackets for simplicity)

$$P_n(t) = \frac{R_{\text{DNP}}P_{\text{DNP}} + R_{1,n}P_n^B}{R_{\text{DNP}} + R_{1,n}} (1 - e^{-(R_{\text{DNP}} + R_{1,n})t})$$

hyperpolarization

Buildup rate, $R_B = 1/T_B$



$$\frac{R_{\text{DNP}}P_{\text{DNP}} + R_{1,n}P_n^B}{R_{\text{CE}} + R_{1,n}}$$

hyperpolarization

A simple model (analysis)

$$P_n(t) = \frac{R_{\text{DNP}}P_{\text{DNP}} + R_{1,n}P_n^B}{R_{\text{DNP}} + R_{1,n}} (1 - e^{-(R_{\text{DNP}}+R_{1,n})t})$$

Buildup rate

Hyperpolarization

Case #1

If $R_{\text{DNP}} \ll R_{1,n}$
(fast 1H relaxation/slow DNP)

$$\frac{1}{T_B} = R_B = R_{\text{DNP}} + R_{1,n} \approx R_{1,n} = \frac{1}{T_{1,n}}$$

T_B dominated by [^1H] relaxation

$$P_n(\infty) = \frac{R_{\text{DNP}}P_{\text{DNP}} + R_{1,n}P_n^B}{R_{\text{DNP}} + R_{1,n}} \approx P_n^B + \frac{R_{\text{DNP}}}{R_{1,n}} P_{\text{DNP}}$$

No or weak DNP

Case #2

If $R_{\text{DNP}} \gg R_{1,n}$
(slow 1H relaxation/fast DNP)

$$\frac{1}{T_B} = R_{\text{DNP}} + R_{1,n} \approx R_{\text{DNP}}$$

T_B dominated by DNP

$$P_n(\infty) = \frac{R_{\text{DNP}}P_{\text{DNP}} + R_{1,n}P_n^B}{R_{\text{DNP}} + R_{1,n}} \approx P_{\text{DNP}}$$

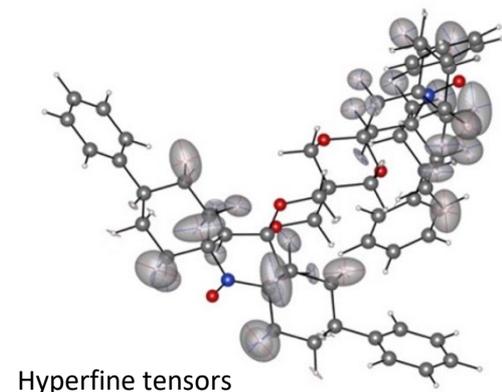
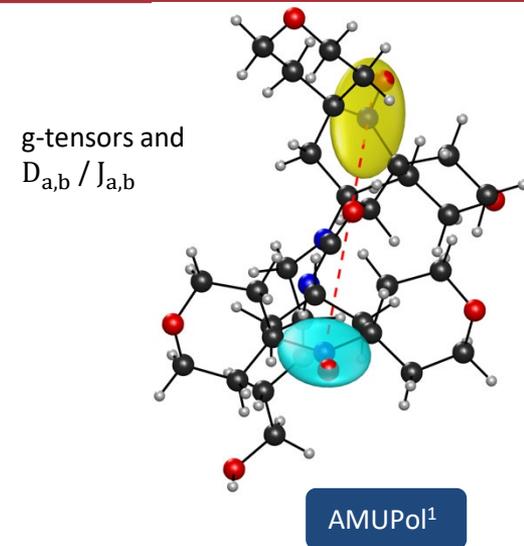
Hyperpolarization limited by P_{DNP}
(electron spin dynamics)

An introduction to EPR

Magnetic interactions: N. Wili, JMRO, 2023, 16–17, 100108.

- **g -tensor** \leftrightarrow chemical shift (isotropic-anisotropic)
 - Anisotropy arise from orbital angular momentum
 - Nitroxides [2.01-2.002] (~ 1 GHz at 9.4 T)
 - BDPA [2.0027-2.0025] (~ 80 MHz at 9.4 T)
 - $\hat{H}_{\text{Zeeman}} = \beta \vec{B}_0 \hat{g} \vec{S} = \beta g \hat{S}_z B_0$
- Dipolar and exchange interaction (homonuclear dipolar/J coupling)
 - **spin-spin coupling** through space + some orbital angular momentum ($D_{a,b} \sim 10$ s MHz range)
 - interaction through nascent bonds ($|J_{a,b}| \sim 0-100$ MHz)
 - $\hat{H}_{D/J} = D_{a,b}(2S_{z,a}S_{z,b} - \frac{1}{2}(S_{+,a}S_{-,b} + S_{-,a}S_{+,b})) - 2J_{a,b}(S_{z,a}S_{z,b} + \frac{1}{2}(S_{+,a}S_{-,b} + S_{-,a}S_{+,b}))$
- Hyperfine coupling (hetero-nuclear dipolar coupling)
 - spin-spin coupling through space + some orbital angular momentum ($\sim 1-10$ s MHz range)
 - $\hat{H}_{e,n} = A_{\text{iso}}(S_{z,a}I_z + \frac{1}{2}(S_{+,a}I_- + S_{-,a}I_+)) + A_{\text{aniso}}(2S_{z,a}I_z - \frac{1}{2}(S_{+,a}I_- + S_{-,a}I_+)) + A_{a,n}^+ S_{z,a}I_+ + A_{a,n}^- S_{z,a}I_-$

Ensure “contact” between e and n \rightarrow hyperpolarization



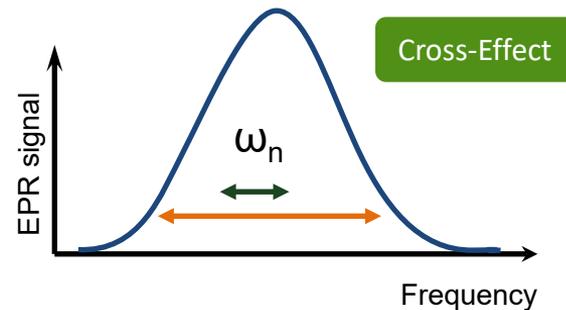
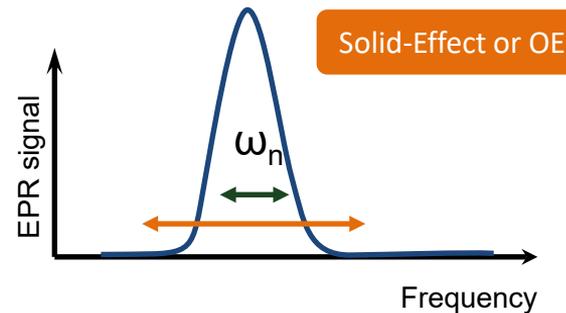
Some DNP background

- Under static conditions: 4 mechanisms
 - Overhauser
 - Solid Effect
 - Cross Effect (low radical concentration) → Thermal Mixing (high concentration)
- Rule of thumb
 - If EPR linewidth < Larmor frequency of nucleus
→ Solid Effect = monoradicals with narrow lines
 - If electron spin = conductive electrons or if fast fluctuations of hyperfine couplings
→ Overhauser
 - If EPR linewidth > Larmor of nucleus
→ Cross-Effect/Thermal Mixing

Active research area, with good convergence

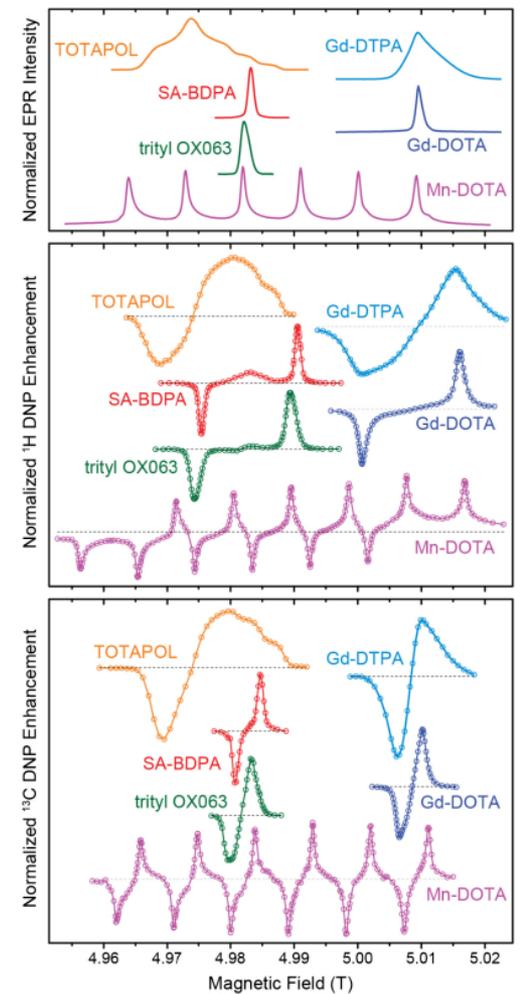
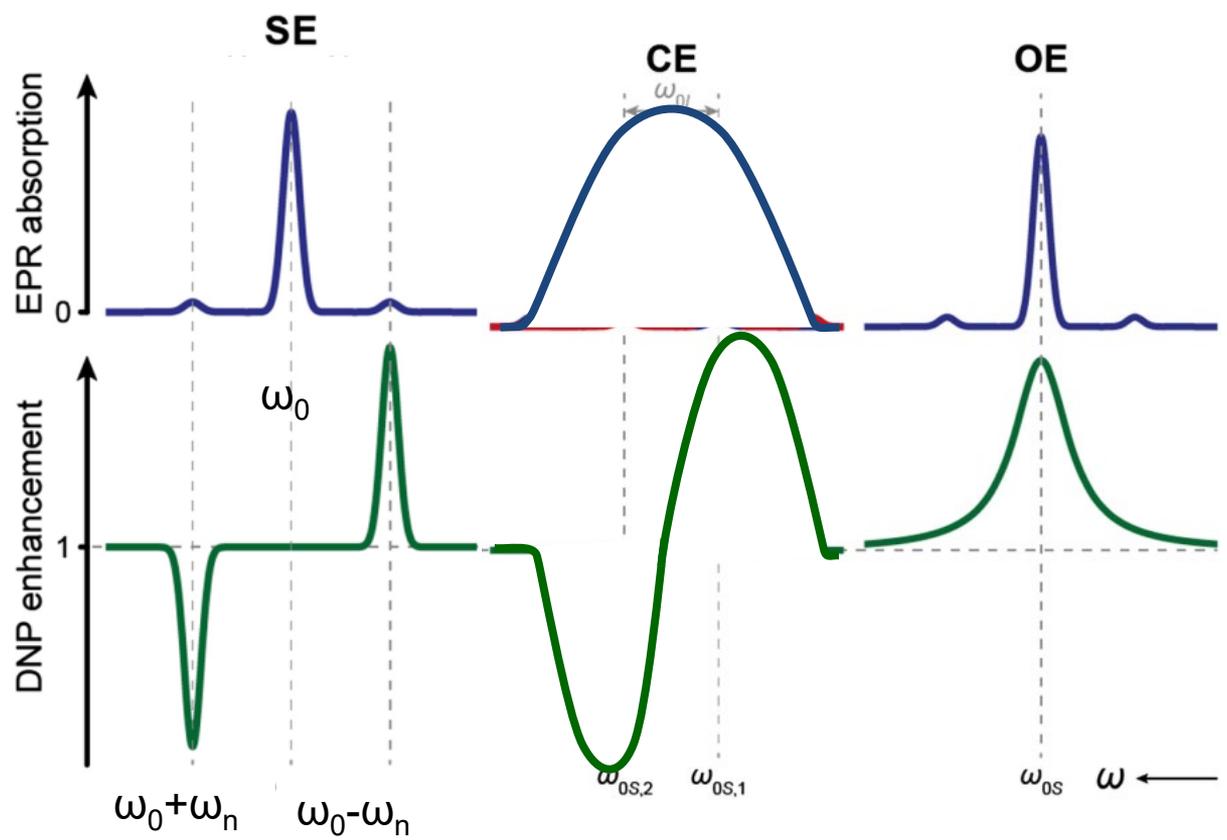
- Yesterday Abagam/Goldman, Borghini, Hwang, Wenckbach...
- Modern: Vega's, Griffin's, Kockenberger's, Rosso's, Bodenhausen's group, Wenckebach...

Conditions for Dissolution DNP and/or static sample



Some background

- Under static conditions: Observations

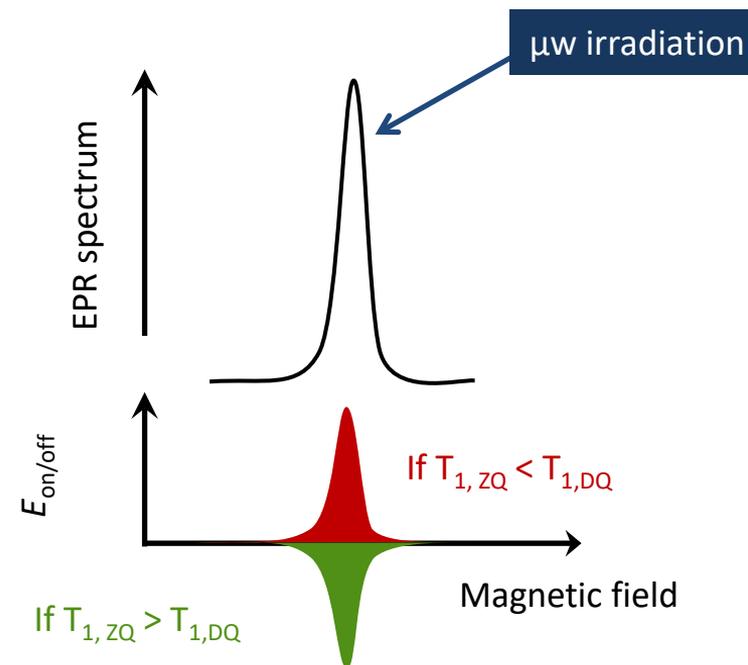
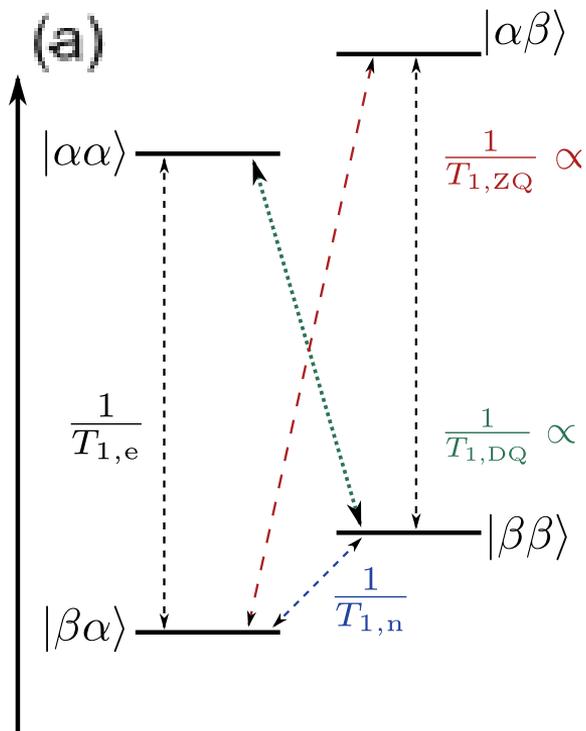


The Overhauser effect under MAS

- Generalities:

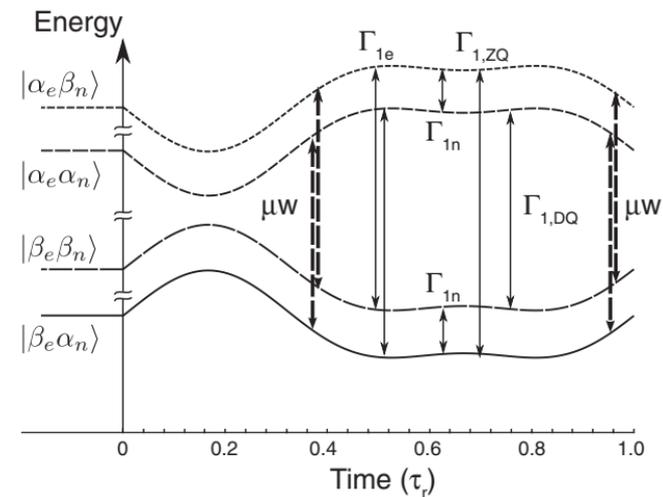
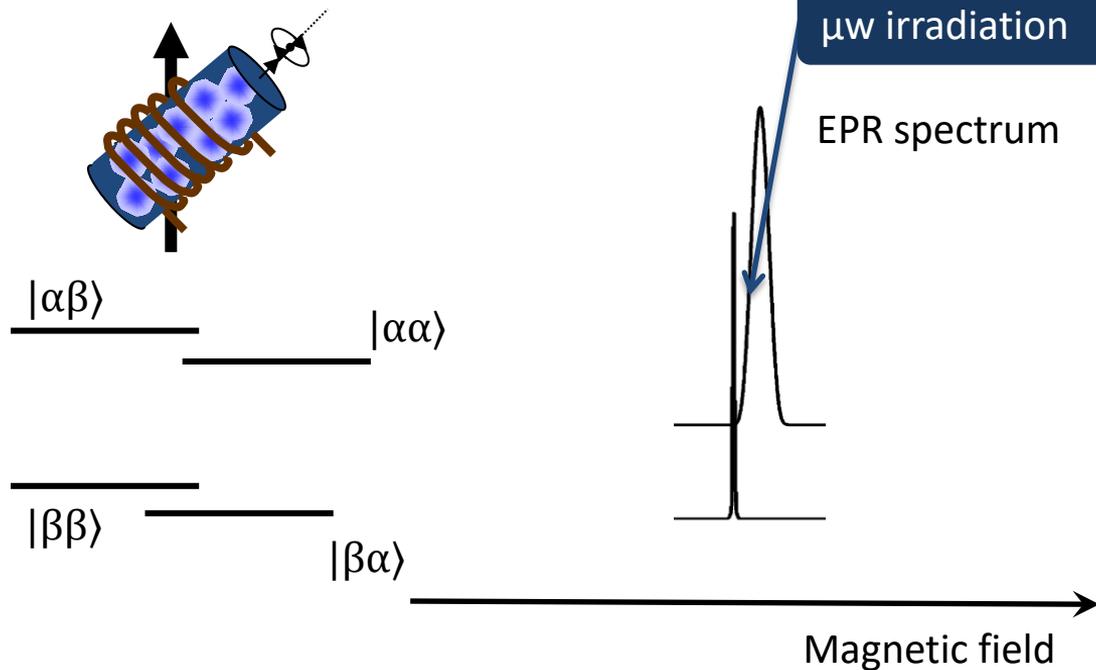
- 2 spins system = electron + nucleus
- Based on irradiation the allowed EPR transitions
Electron/Nuclear Cross relaxation

$$\hat{H}_{e,n} = A_{iso}(S_{z,a}I_z + \frac{1}{2}(S_{+,a}I_- + S_{-,a}I_+)) + A_{aniso}(S_{z,a}I_z - \frac{1}{2}(S_{+,a}I_- + S_{-,a}I_+)) + A_{a,n}^+ S_{z,a}I_+ + A_{a,n}^- S_{z,a}I_-$$



Overhauser Effect rotor-events

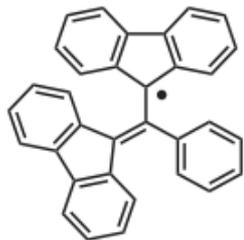
- Overhauser effect + MAS



Irradiation effect is not continuous \rightarrow step process
But essentially the same as static

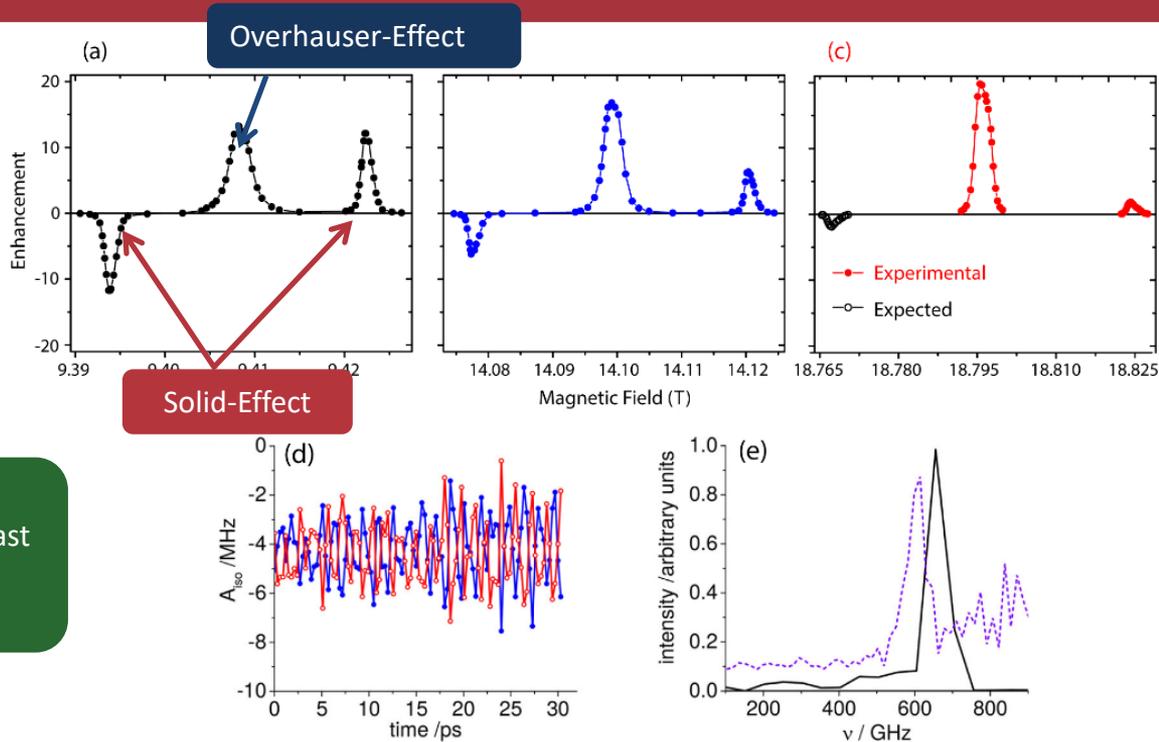
Examples

- 2% BDPA in Poly-Styrene: insulating solids



Origin of the Overhauser effect:

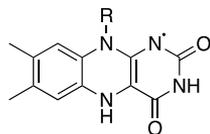
- (1) BDPA has large isotropic hyperfine couplings + fast motion
- (2) fast motion proven with MD then CCSD(T)



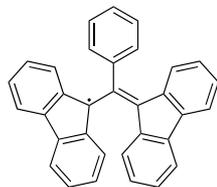
- (1) Can, T. V.; Caporini, M. A.; **Mentink-Vigier, F.**; Corzilius, B.; Walish, J. J.; Rosay, M.; Maas, W. E.; Baldus, M.; Vega, S.; Swager, T. M.; Griffin, R. G. *J. Chem. Phys.* 2014, 141, 64202.
- (2) Pylaeva, S.; Ivanov, K. L.; Baldus, M.; Sebastiani, D.; Elgabarty, H. J. *Phys. Chem. Lett.* 2017, 8, 2137.
- (3) S. Pylaeva, P. Marx, G. Singh, T. D. Kühne, M. Roemelt and H. Elgabarty, *J. Phys. Chem. A*, 2021, 125, 867–874.

Overhauser Effect Example

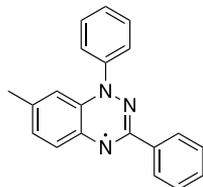
• Other molecules



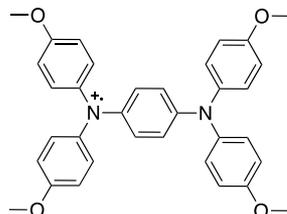
FD-Semiquinone



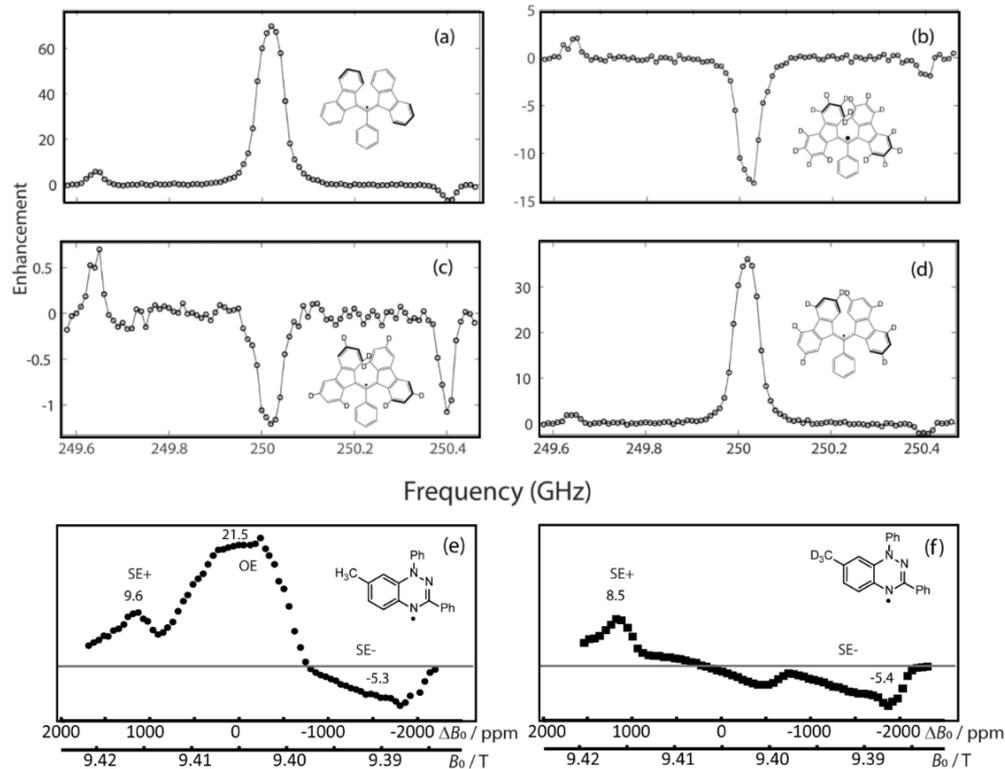
BPDA



Blatter radical



N^1,N^1,N^4,N^4 -tetrakis(4methoxyphenyl)-benzene-1,4-diamine



- (1) T. Maly, D. Cui, R. G. Griffin and A.-F. Miller, *J. Phys. Chem. B*, 2012, 116, 7055–7065.
- (2) O. Haze, B. Corzilius, A. A. Smith, R. G. Griffin and T. M. Swager, *Water-Soluble Narrow-Line Radicals for Dynamic Nuclear Polarization*, *J. Am. Chem. Soc.*, 2012, 134, 14287–14290.
- (3) A. Gurinov, B. Sieland, A. Kuzhelev, H. Elgabarty, T. D. Kühne, T. Prisner, J. Paradies, M. Baldus, K. L. Ivanov and S. Pylaeva, *Angew. Chem. Int. Ed.*, 60, 2021.
- (4) F. A. Perras, D. F. Flesariu, S. A. Southern, C. Nicolaides, J. D. Bazak, N. M. Washton, T. Trypiotis, C. P. Constantinides and P. A. Koutentis, *J. Phys. Chem. Lett.*, 2022, 13, 4000–4006.

Deuteration

→ affects the OE

→ protons on the radical are key

Overhauser Effect Example

- Polymers/Conduction electrons

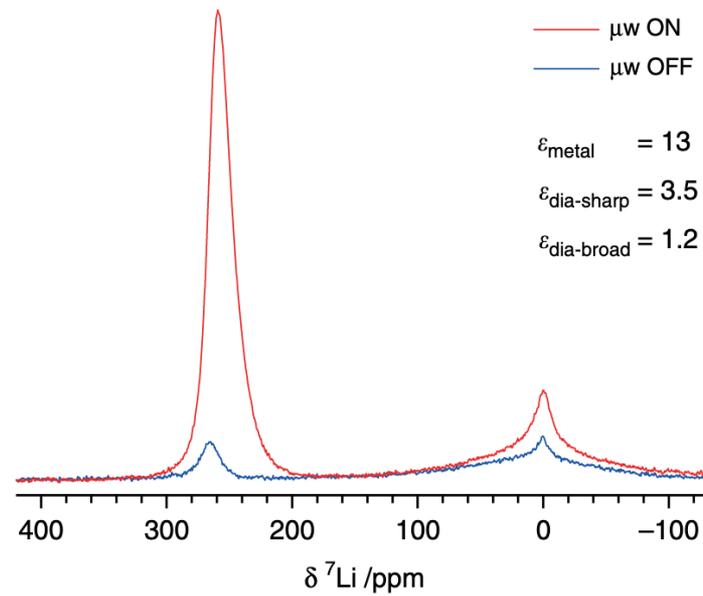
Linear and cyclic Polyacetylene

- Z. Miao, F. J. Scott, J. van Tol, C. R. Bowers, A. S. Veige and F. Mentink-Vigier, *J. Phys. Chem. Lett.*, 2024, 3369–3375.

Non-¹H DNP (Lithium)

- M. A. Hope, B. L. D. Rinkel, A. B. Gunnarsdóttir, K. Märker, S. Menkin, S. Paul, I. V. Sergeev and C. P. Grey, *Selective NMR observation of the SEI–metal interface by dynamic nuclear polarisation from lithium metal*, *Nat Commun*, 2020, 11, 2224.

Polymers defects



Properties of Overhauser

- Low microwave power needed
 - Irradiate **allowed transition** → **weak ω_1 works** (e.g. solid-state source)
- Often slow build up times...
 - $T_B = 30\text{-}60\text{ s} \sim T_{1,n}$ (equivalent as undoped matrix)
 - Sensitivity is low = $\frac{S}{\sqrt{T_B}} \approx \frac{R_{\text{DNP}}}{R_{1,n}^{1/2}} P_{\text{DNP}}$ (rough approximation)
 - e.g. N. J. Brownbill, D. Gajan, A. Lesage, L. Emsley and F. Blanc, *Chem. Commun.*, 2017, **53**, 2563–2566.

$$\frac{1}{T_B} = R_B = R_{\text{DNP}} + R_{1,n} \approx R_{1,n} = \frac{1}{T_{1,n}}$$
$$P_n(\infty) = \frac{R_{\text{DNP}} P_{\text{DNP}} + R_{1,n} P_n^B}{R_{\text{DNP}} + R_{1,n}} \approx P_n^B + \frac{R_{\text{DNP}}}{R_{1,n}} P_{\text{DNP}}$$
$$S \approx \frac{R_{\text{DNP}}}{\sqrt{R_{1,n}}} P_{\text{DNP}}$$

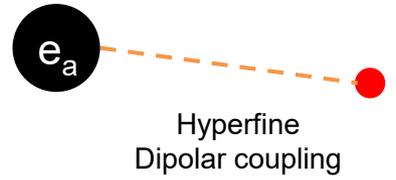
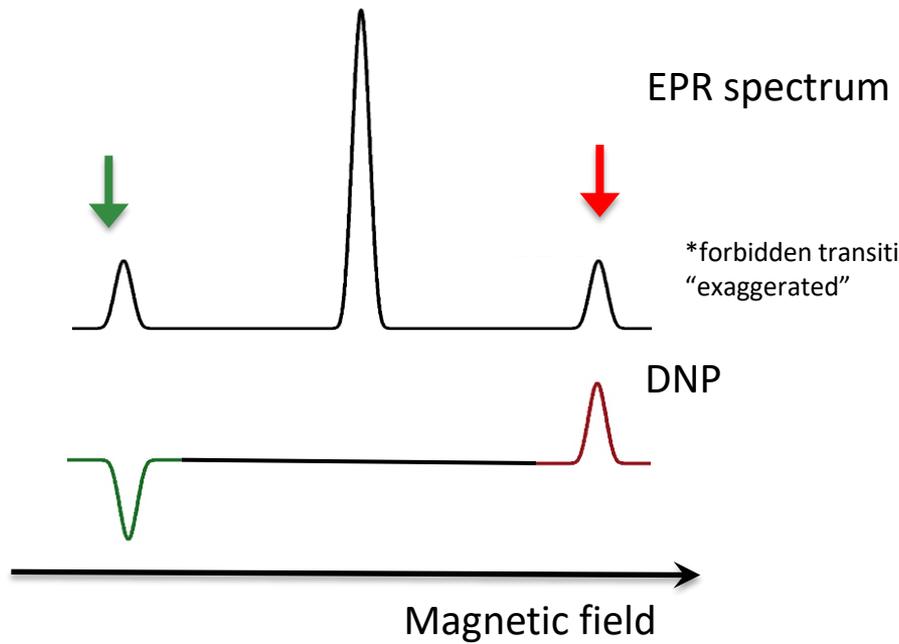
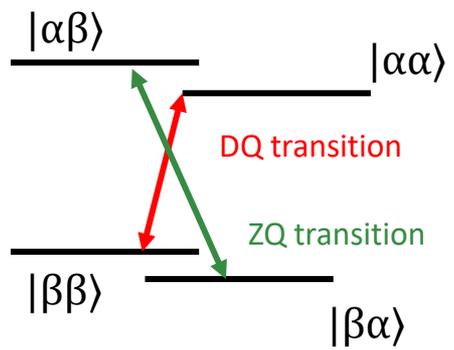
Potentially interesting but under specific conditions as T_B is slow and DNP is limited by $T_{1,n}$

- Note for BDPA
 - Effect is stronger at higher magnetic field
 - Polarization should be constant with MAS frequency but... Polarization increases (bulk effect, S. R. Chaudhari, et al, *J. Am. Chem. Soc.*, 2017, 139, 10609–10612.
 - **There exists a controversy, could be multi-electron effect, [Songi Han's group]¹**

Solid-Effect background

- Generalities:
 - 2 spins system = electron + nucleus
 - Based on irradiation of “forbidden” transitions → Zero and Double Quantum

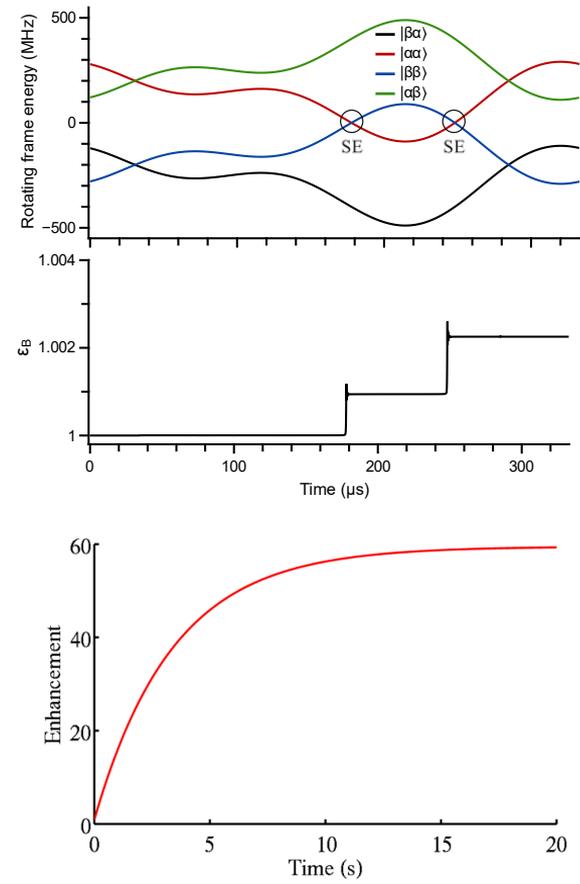
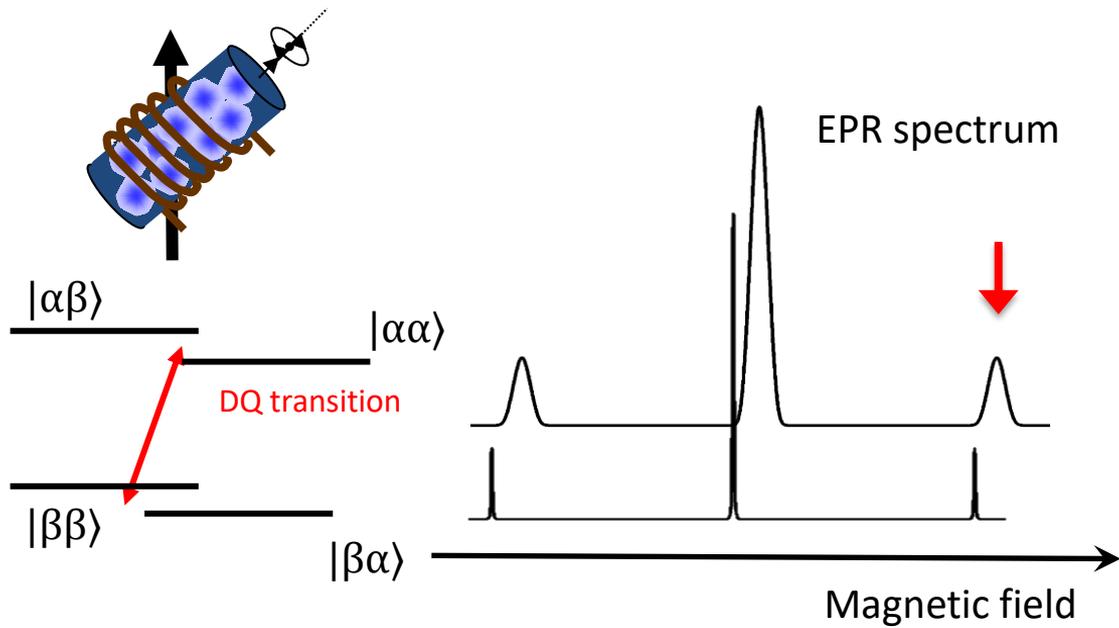
- Static DNP



$$\hat{H}_{en} = A_{Iso}(S_{z,a}I_z + \frac{1}{2}(S_{+,a}I_- + S_{-,a}I_+)) + A_{z,aniso} S_{z,a}I_z + \boxed{A_{a,n}^- S_{z,a}I_- + A_{a,n}^+ S_{z,a}I_+}$$

Solid-Effect Rotor-Events

- Solid-Effect + MAS



Hyperpolarization is result of fast energy levels crossings (rotor events)

$$\hat{H}_{12}(t) = \frac{1}{2} \begin{pmatrix} \Delta\omega_{12}(t) & \xi_{12}(t) \\ \xi_{12}^*(t) & -\Delta\omega_{12}(t) \end{pmatrix}$$

Rotor events involve 2 levels \rightarrow fictitious spin $\frac{1}{2}$

Solid-Effect properties

- Relies on irradiation of forbidden transitions (ZQ/DQ)
 - Requires high mw power (large ω_1)
 - Rate of DNP, RDNP, depends on hyperfine coupling and Larmor frequency : (rough approximation)

$$R_{\text{DNP}} \propto \frac{[\text{radical}]}{[\text{proton}]} \left(\frac{\omega_1 A_{a,n}^{\pm}}{\omega_n} \right)^2 \times \frac{1}{\Delta\omega_{\text{EPR}}} \longrightarrow \text{EPR linewidth}$$

- Becomes weaker at high magnetic field ($\omega_n \nearrow$)

- Longer $T_{1,n} \rightarrow$ better DNP

$$\frac{1}{T_B} = R_B = R_{\text{DNP}} + R_{1,n} \approx R_{1,n} = \frac{1}{T_{1,n}}$$

$$P_n(\infty) = \frac{R_{\text{DNP}} P_{\text{DNP}} + R_{1,n} P_n^B}{R_{\text{DNP}} + R_{1,n}} \approx P_n^B + \frac{R_{\text{DNP}}}{R_{1,n}} P_{\text{DNP}}$$

- Often slow build up times...

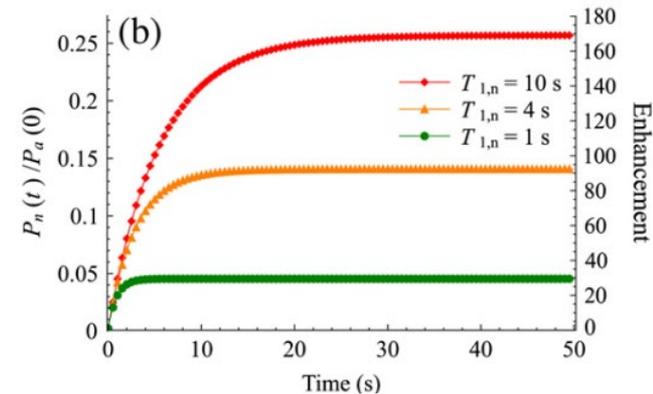
- $T_B = 30\text{-}60 \text{ s} \sim T_{1,n}$ (equivalent as undoped matrix)

- Sensitivity is low = $\frac{S}{\sqrt{T_B}} \approx \frac{R_{\text{DNP}}}{R_{1,n}^{1/2}} P_{\text{DNP}}$

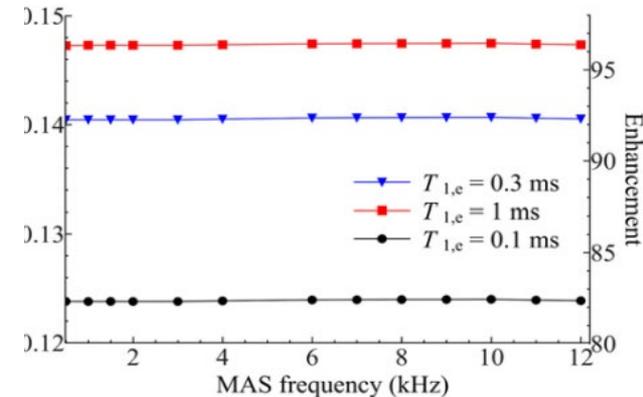
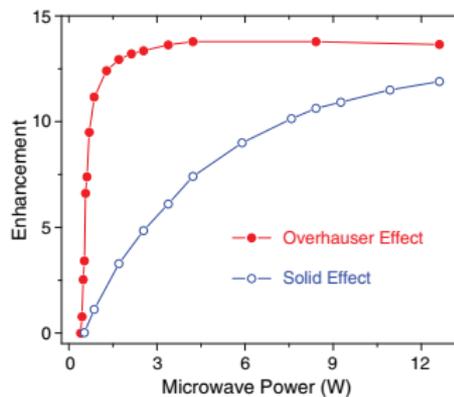
(rough approximation)

- Compensated with high μw nutation frequency (ω_1)
- No MAS dependence (à priori)

Mentink-Vigier, F.; Akbey, U.; Hovav, Y.; Vega, S.; Oshkinat, H.; Feintuch, A. J. Magn. Reson. 2012, 224, 13.



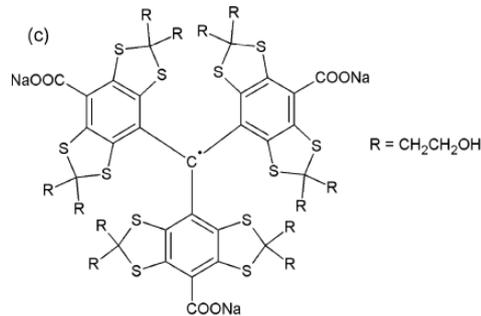
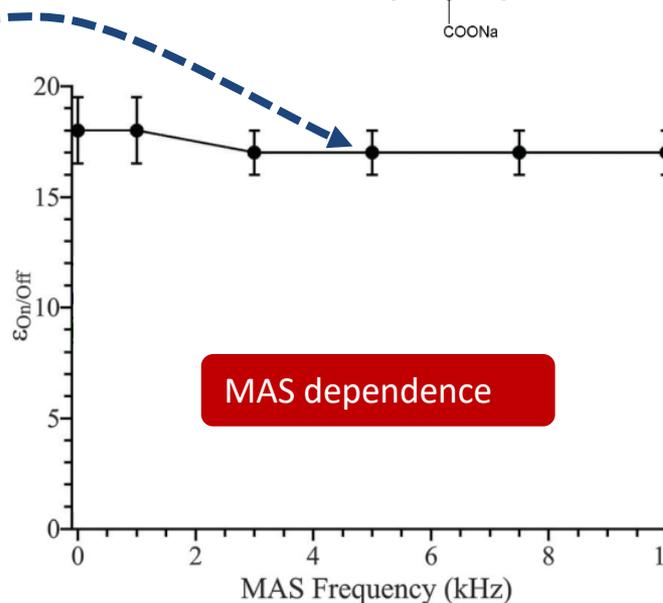
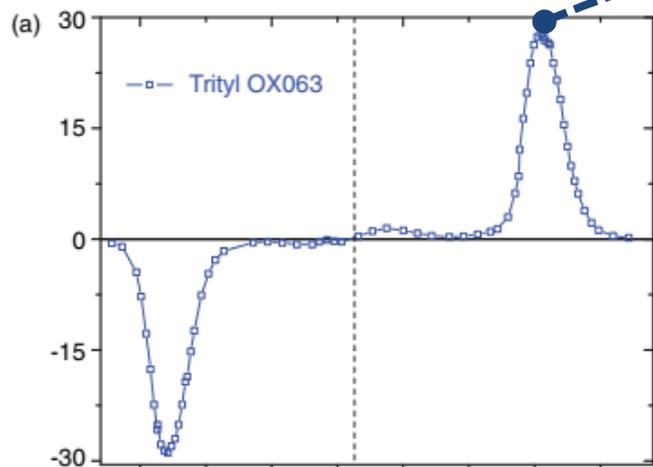
Can, T. V. et al. J. Chem. Phys. 2014, 141



Experimental example

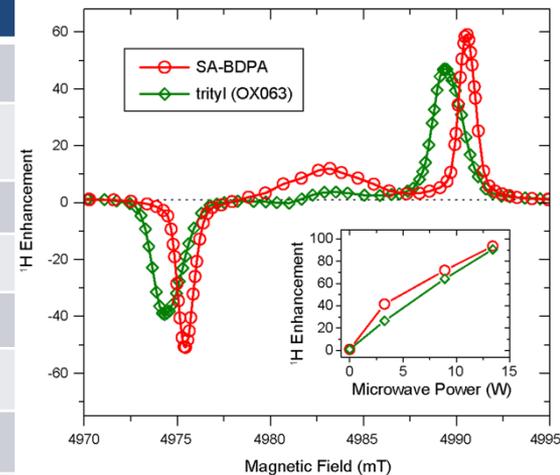
- 40 mM Trityl in d8-Glycerol/D₂O/H₂O
 - At 9.4 T and 100 K
 - Build up times $T_B = 60$ s
 - (For reference, $T_{1,n} = 65$ s, so $R_{DNP} \sim 10^{-3} \text{ s}^{-1}$)

($\epsilon_{\text{on/off}} \sim 15$ at 14.1 T, value expected from simple model ~ 10)



Summary

Mechanism	Overhauser	Solid-Effect
Model	1e + 1n	1e + 1n
Transition involved	Allowed single quantum	Forbidden (Zero or Double Quantum)
Characteristic	Within EPR line, constant sign	Outside EPR line, opposite sign
Power requirement	Low	High
Field dependence	None a priori or small increase	Decrease significantly with field
MAS dependence	None a priori (except bulk effect)	None A priori (except bulk effect)
Build-up times	Long ($\sim T_{1,n}$)	Long ($\sim T_{1,n}$)
Sensitivity?	Low in general	Low in general
Examples	BDPA in PS/OTP, Mixed Valence compounds, Blatter radicals, conductive materials	Trityl in Glycerol/Water BDPA in PS/OTP



$$\frac{1}{T_B} = R_B = R_{\text{DNP}} + R_{1,n} \approx \frac{1}{T_{1,n}}$$

$$P_n(\infty) \approx P_n^B + \frac{R_{\text{DNP}}}{R_{1,n}} P_{\text{DNP}}$$

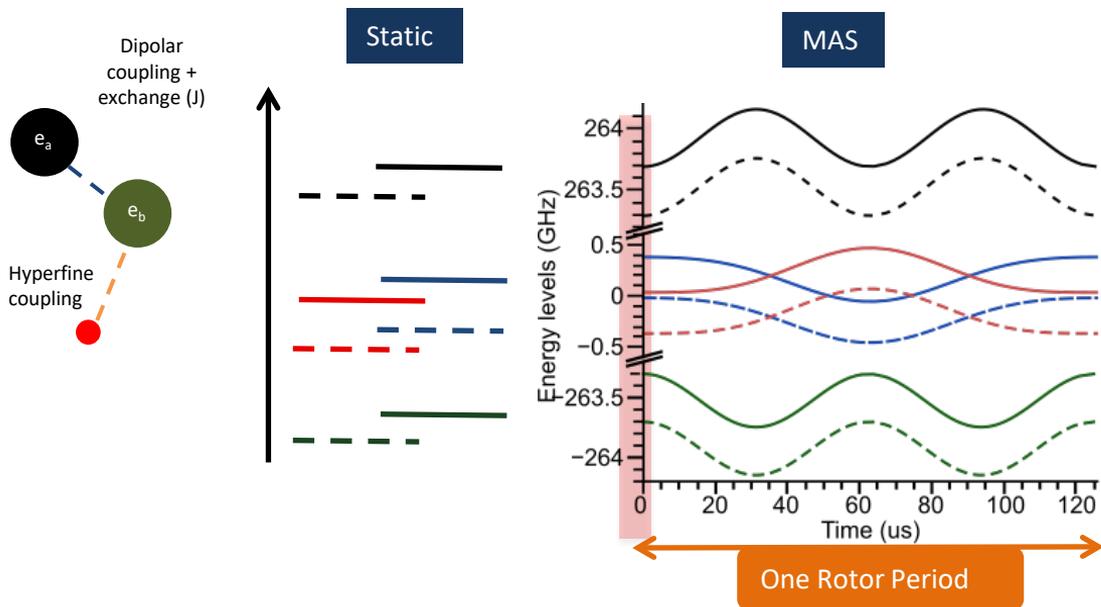
$$S \approx \frac{R_{\text{DNP}}}{R_{1,n}^{1/2}} P_{\text{DNP}}$$

Potentially interesting but under specific conditions as T_B is slow and DNP is limited by $T_{1,n}$

What about Cross-Effect under MAS?
Most used mechanism...

Cross-Effect Rotor-Events

- Bi-radical model : 2 electrons + 1 nucleus = 8 energy levels



Energy levels now time dependent

- Static analysis does not hold (like for SE)
- DNP results from fast energy levels crossings [1-4]

[1] Thurber, K. R.; Tycko, R. J. Chem. Phys. 2012, 137, 084508.

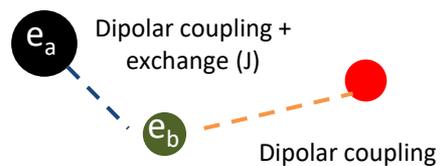
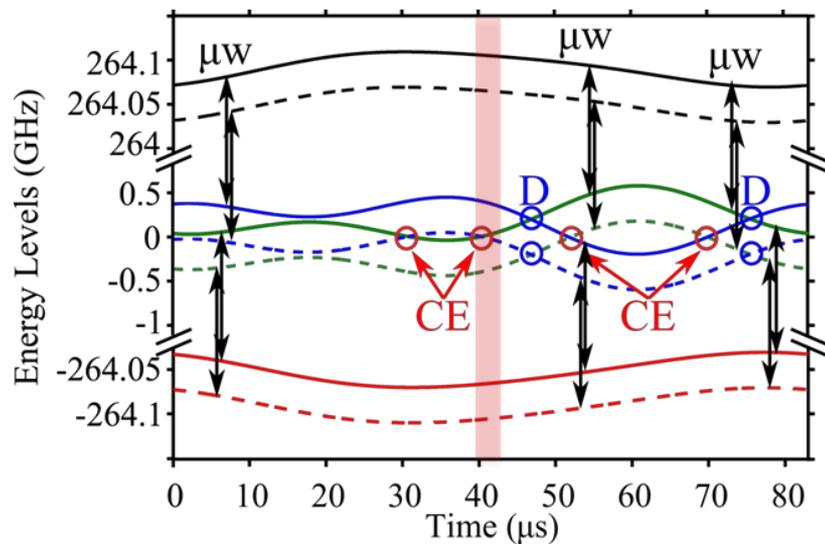
[2] Mentink-Vigier, F.; Akbey, U.; Hovav, Y. et al. J. Magn. Reson. 2012, 224, 13–21.

[3] Mentink-Vigier, F. et al. J. Magn. Reson. 2015, 258, 112-120.

[4] Mance, D., P. Gast, M. Huber, et al., J. Chem. Phys. 142, 234201 (2015).

Cross-Effect Rotor-Events

- Rotor period analysis

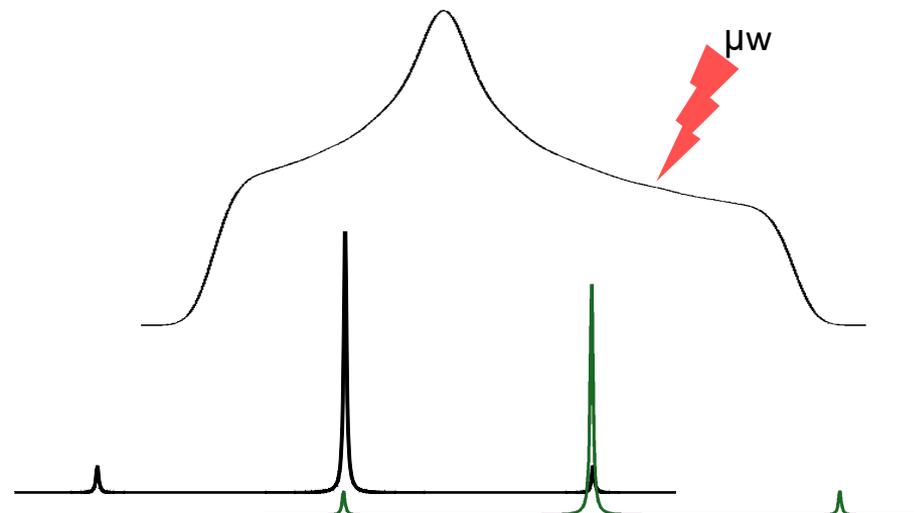


Change in one electron polarization

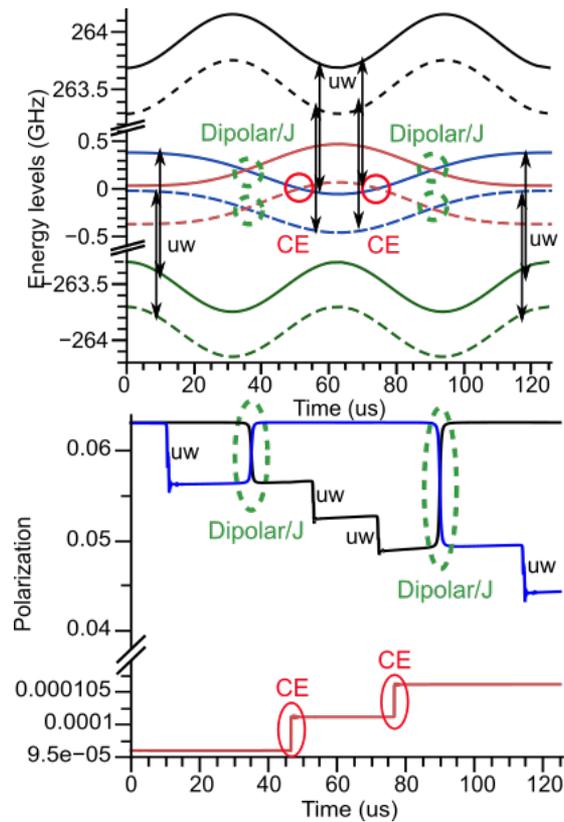
Transfer to nucleus

Electron polarization exchange

“Bis nitroxide-like”
EPR spectrum

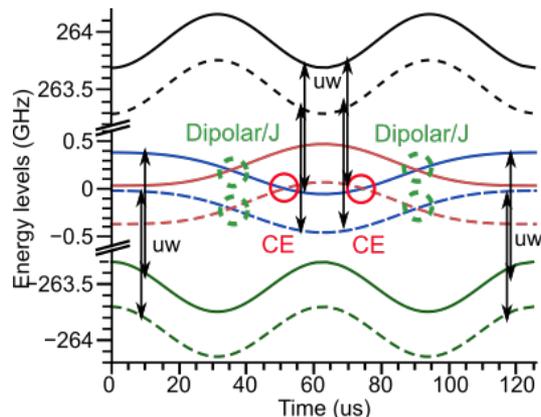


Cross-Effect Rotor-Events



- Spin dynamics = series of "fast" rotor-events

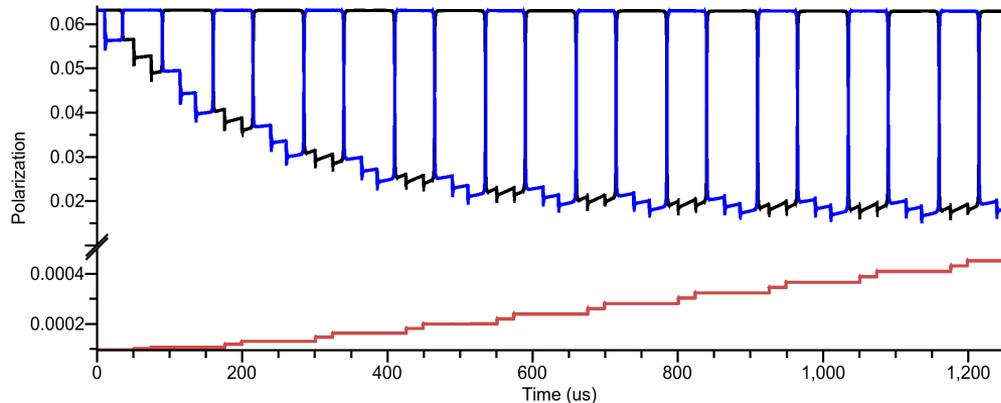
Cross-Effect Rotor-Events



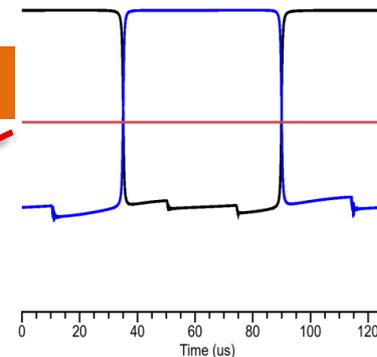
Spin dynamics = series of "fast" rotor-events

- Electrons quickly reach a "quasi-periodic steady state"

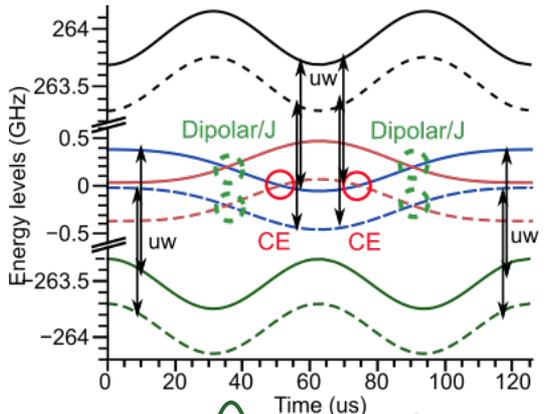
- Nuclear polarization increase \rightarrow slowly towards steady state



+30 s



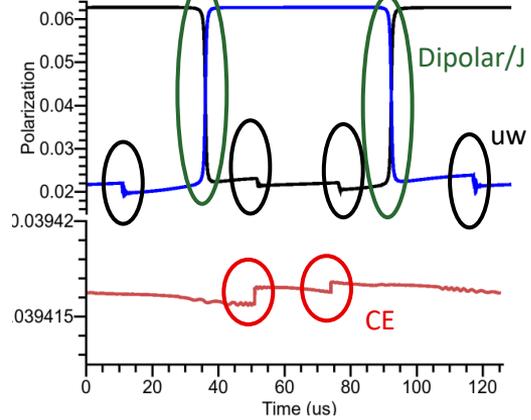
Cross-Effect Rotor-Events



Spin dynamics = series of “fast” rotor-events

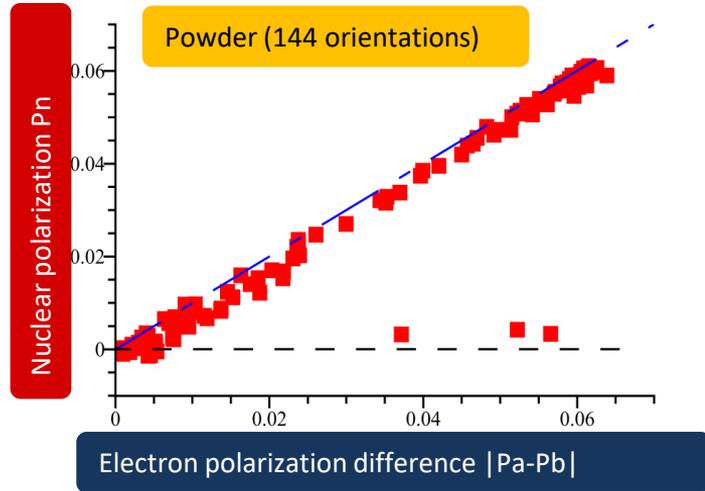
- Electrons quickly reach a “quasi-periodic steady state”

- Nuclear polarization increase \rightarrow slowly towards steady state
- $|P_n| = P_a - P_b$

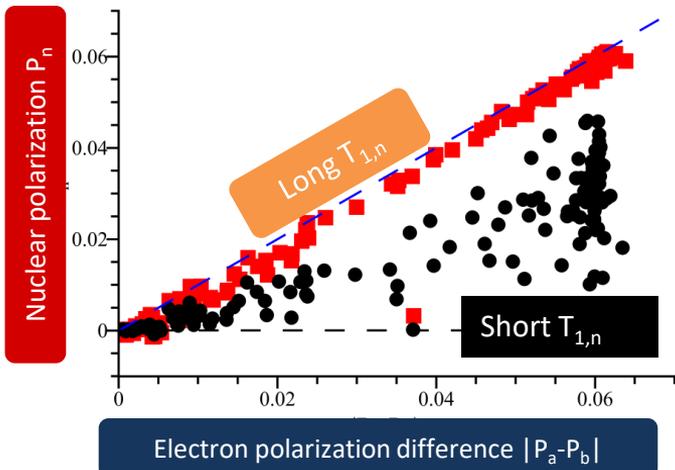
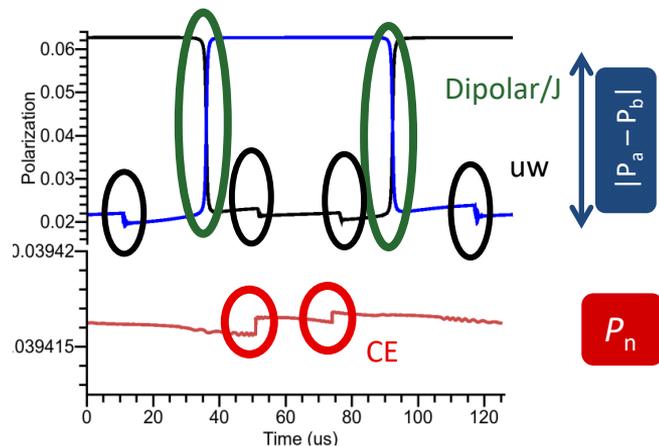


$|P_a - P_b|$

P_n



Cross-Effect Rotor-Events



$$P_n(t) = \frac{R_{\text{DNP}}P_{\text{DNP}} + R_{1,n}P_n^B}{R_{\text{DNP}} + R_{1,n}} (1 - e^{-(R_{\text{DNP}}+R_{1,n})t})$$

$$= \frac{R_{\text{CE}}\Delta P_e + R_{1,n}P_n^B}{R_{\text{CE}} + R_{1,n}} (1 - e^{-(R_{\text{CE}}+R_{1,n})t})$$

With $P_{\text{DNP}} = \Delta P_e = \langle |P_a - P_b| \rangle$

$$R_{\text{CE}} \propto \frac{[\text{biradicals}]}{[^1\text{H}]} \frac{\langle n/\chi \rangle \pi}{2(\Delta\omega_a + \Delta\omega_b)} \left(\frac{\langle (D_{a,b} + 2J_{a,b})^2 \rangle \langle (A_{a,n}^\pm - A_{b,n}^\pm)^2 \rangle}{\omega_n^2} \right) [1]$$

Sensitivity?

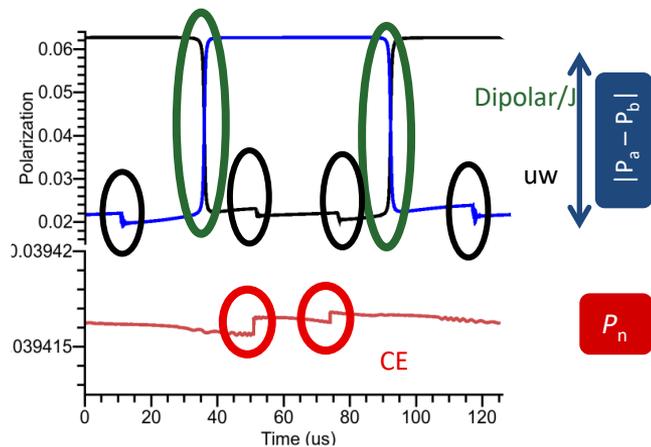
$S \approx R_{\text{CE}}^{1/2} \Delta P_e$ (rough approximation) much higher!

What determines ΔP_e ?

- Microwave nutation \rightarrow large uw [2,3,4]
- Large $D_{a,b} + 2J_{a,b}$ to maintain ΔP_e [4,5]
- T_{1e} decreases $|P_a - P_b| \rightarrow$ Long T_{1e} (how long? [3,4,6])
- Relative orientation between radicals (g-tensor distance) [7,8]

- [1] S. Chatterjee, A. Venkatesh, S. Th. Sigurdsson and F. Mentink-Vigier, J. Phys. Chem. Lett., 2024, 15
- [2] K. R. Thurber and R. Tycko, J. Chem. Phys., 2012, 137
- [3] F. Mentink-Vigier, Ü. Akbey, Y. Hovav, S. Vega, H. Oschkinat and A. Feintuch, J. Mag. Res., 2012, 224
- [4] F. Mentink-Vigier, Ü. Akbey, H. Oschkinat, S. Vega and A. Feintuch, J. Mag. Res., 2015, 258
- [5] F. Mentink-Vigier, et al. Phys. Chem. Chem. Phys., 2015, 17
- [6] C. Sauvée, et al. Chem. Eur. J., 2016, 22, 5598–5606.
- [7] F. Mentink-Vigier, Phys. Chem. Chem. Phys., 2020, 22
- [8] F. Mentink-Vigier, T. Dubroca, J. Van Tol and S. Th. Sigurdsson, J. Mag. Res., 2021, 329

Cross-Effect Rotor-Events



Rotor events involve 2 levels → fictitious spin $\frac{1}{2}$

$$H_{1,2}(t) = \begin{pmatrix} \omega & x \\ x & -\omega \end{pmatrix}$$

Probability of change depend on $\frac{d\omega}{dt}$

$$P = 1 - \exp\left(-\frac{\pi x^2}{d\omega/dt}\right)$$

$$\frac{d\omega}{dt} \propto \omega_r \Delta\omega_{\text{EPR}} \text{ [first approximation]}$$

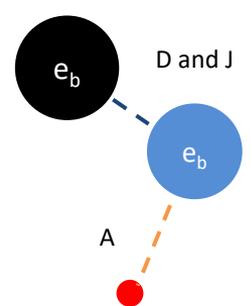
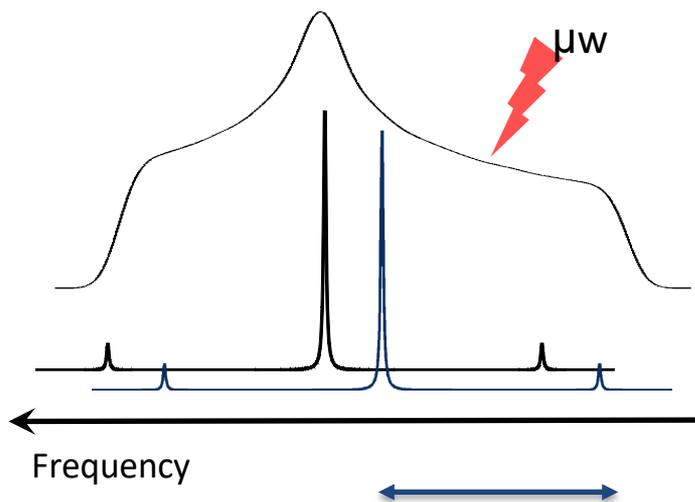
Efficiency of rotor events affected by:

- Interaction strength
- Duration: faster rotor-events with
 - Higher MAS frequency
 - Higher magnetic field

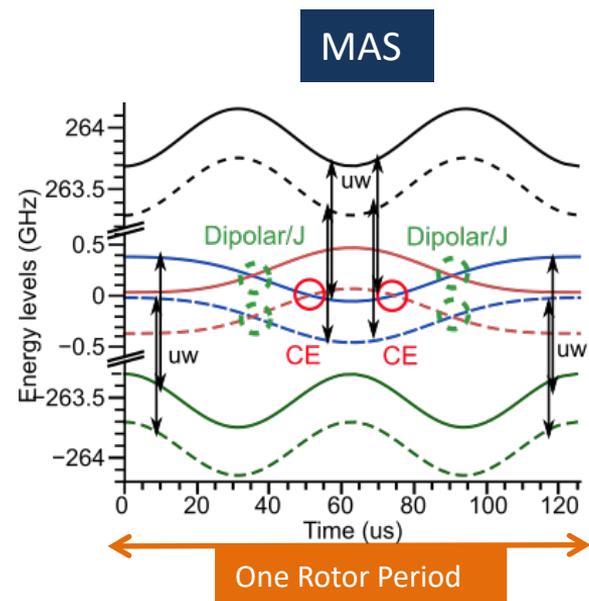
Temperature → impacts relaxation times!

Cross – Effect model introduction under MAS

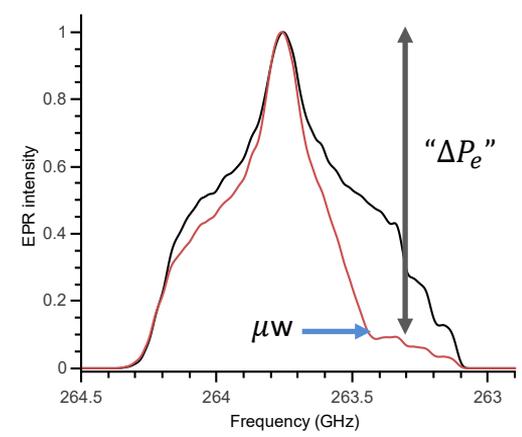
- Biradical model : 2 electrons + 1 nucleus = 8 energy levels



“Bis nitroxide-like”
EPR spectrum



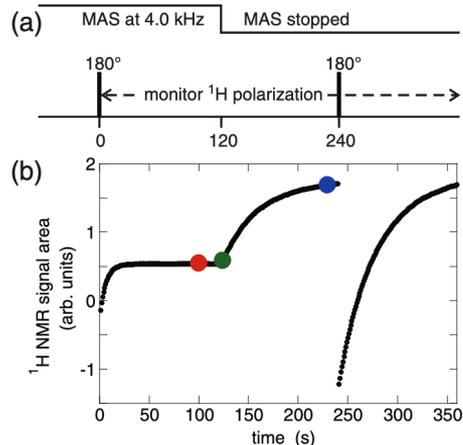
Time dependent
→ complex interplay



Electron polarization
difference, ΔP_e
→ source of hyperpolarization

Cross-Effect, the ugly side → depolarization

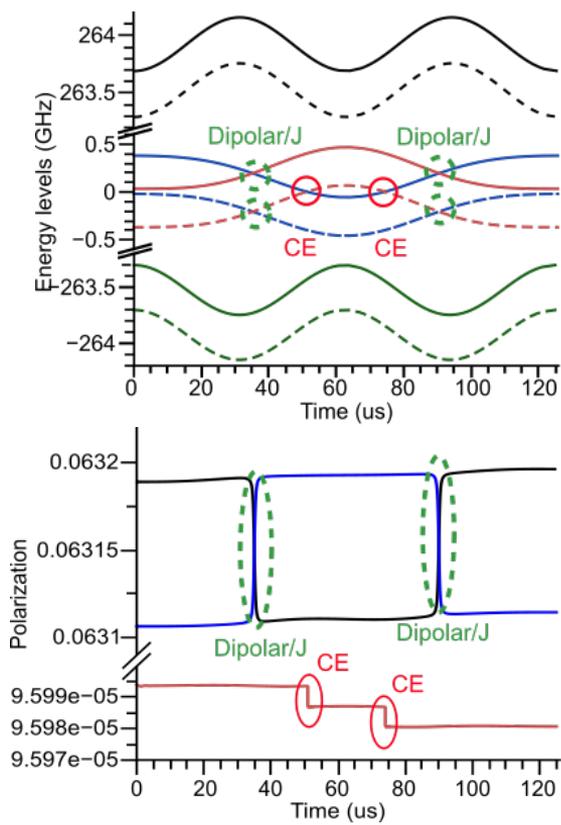
- Back in 2013, suddenly enhancement become very large (e.g see Sauvee et al, 2013)
- Enhancement getting closer to theoretical limit...
- 2013:
 - Me: code debugging, an unexpected effect... error? nope
 - In parallel, Tycko stumbles upon an experimental effect at low T.



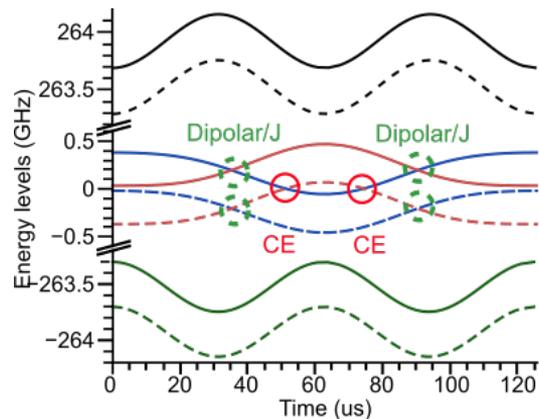
No microwave (so no “DNP”)
Nuclear polarization different under static vs spinning! Odd

Electron’s spin dynamic still present!
Electrons and nucleus still in “contact”

Unexpected effect! → P_n decreases!

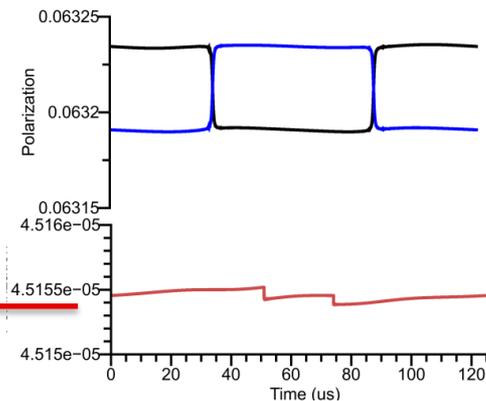
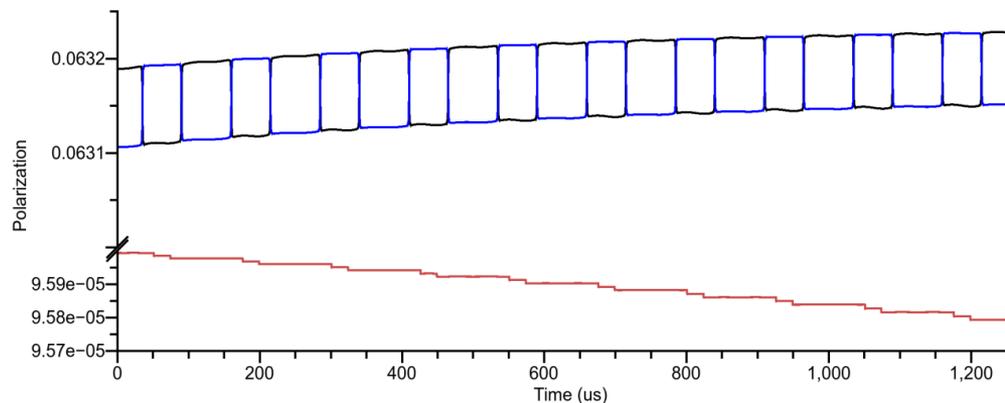


Cross-effect under MAS \rightarrow depolarization

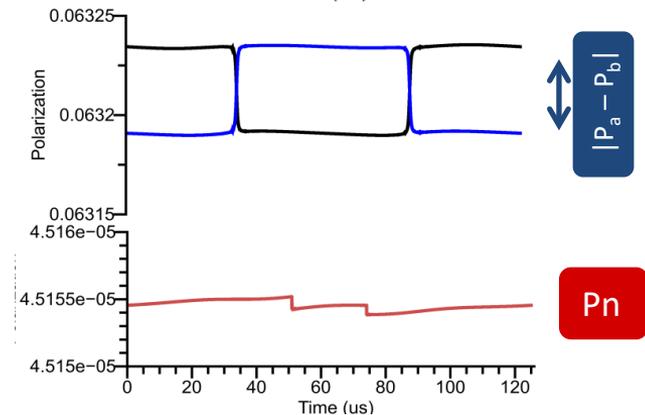
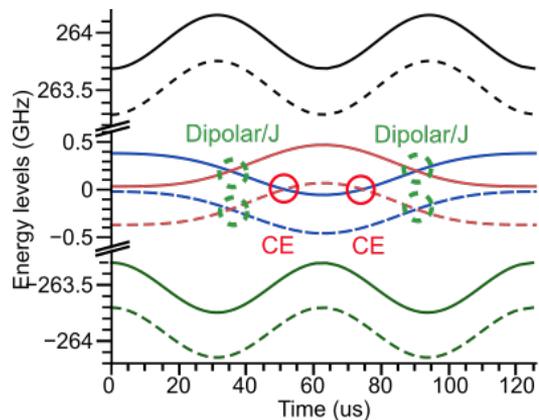


Electron's spin dynamic still present!
Electrons and nucleus still in "contact"

Unexpected effect! $\rightarrow P_n$ decreases!



Cross-effect under MAS \rightarrow depolarization

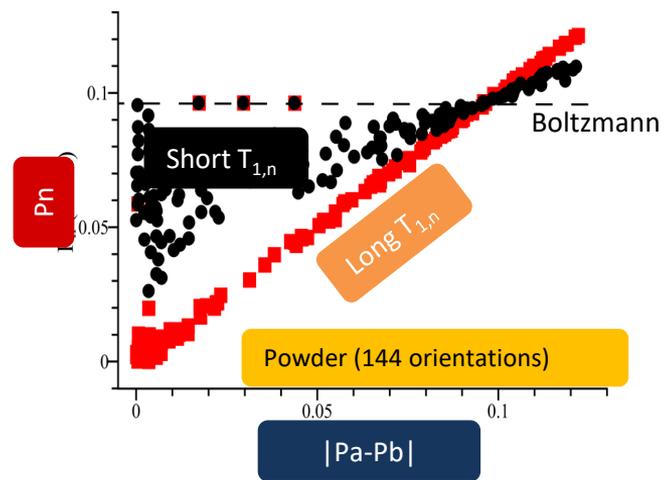


Electron's spin dynamic still present!
Electrons and nucleus still in "contact"

Unexpected effect! $\rightarrow P_n$ decreases!

$|P_a - P_b|$ essential again with major impact:

- T_{1e} and Dipolar/J,
- spinning speed, magnetic field...

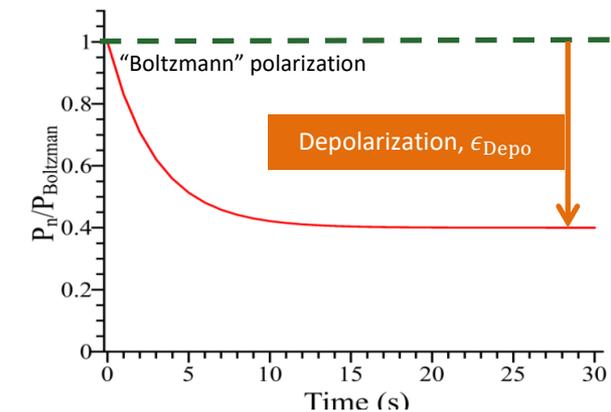
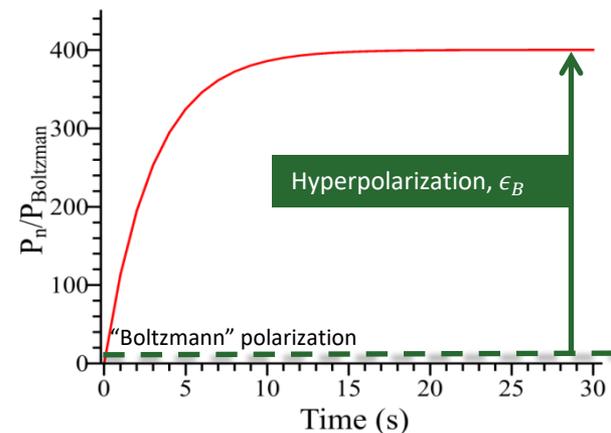
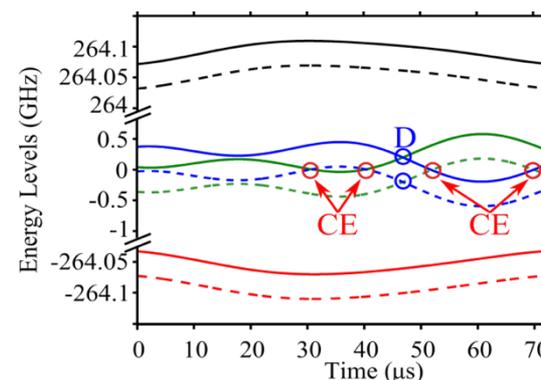
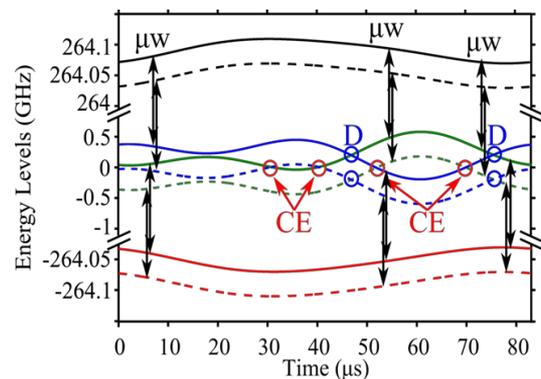


Introduction: the Cross-Effect with three spins

- Simple model but information rich
 - Prediction of nuclear depolarization!^{1,2}

$$\epsilon_{\text{on/off}} = \frac{\epsilon_B}{\epsilon_{\text{Depo}}}$$

$\epsilon_{\text{on/off}} > 658$ is possible (and absurd)!³
 ϵ_{Depo} and ϵ_B depends on biradical^{2,4}

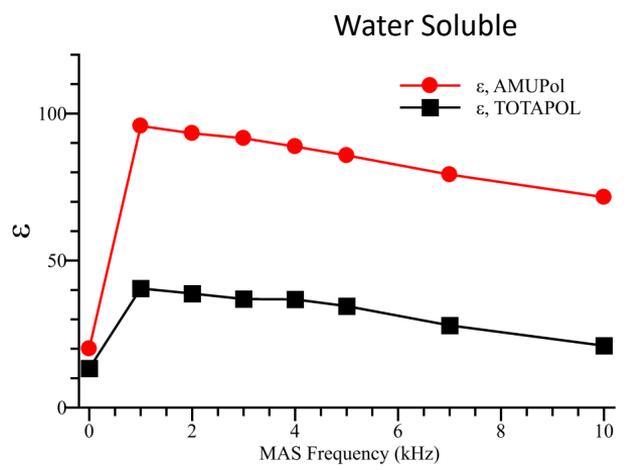


1. K. R. Thurber, K. R. and R. Tycko, J. Chem. Phys. 2014
2. F. Mentink-Vigier, et al., Phys. Chem. Chem. Phys 2015
3. E. Bouleau, et al. Chemical Sci. 2015
4. F. Mentink-Vigier, Phys. Chem. Chem. Phys 2020

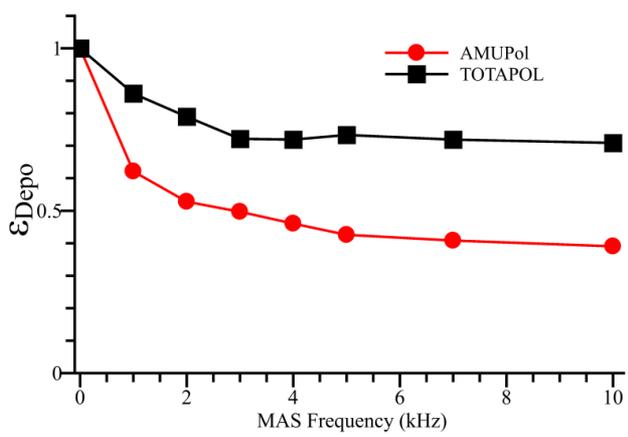
Is it a true effect?

- Experimental results

On + MAS



Off + MAS



2015:
AMUPol → will never be improved!
CE has reached its limits

$\epsilon_{on/off}$ → not reliable at 100 K!
Real gain AMUPol ~~240~~ → 80-90...
we reconsidered the possibility of better biradicals...

Major signal loss in absence of μw !
AMUPol real gain $\epsilon = 100!$ Not $\epsilon_{on/off} = 240!$
Off = 60 % losses

Mentink-Vigier et al, PCCP, 2015

Summary

Mechanism	Overhauser	Solid-Effect	Cross-Effect
Model	1e + 1n	1e + 1n	2e + 1n
Transition involved	Allowed single quantum	Forbidden (Zero or Double Quantum)	Allowed (Single Quantum)
Characteristic	Within EPR line, constant sign	Outside EPR line, opposite sign	Inside EPR line, opposite sign
Power requirement	Low	High	Moderate
Field dependence	None a priori or small increase	Decrease significantly with field	Decrease with field
MAS dependence	None a priori (except bulk effect)	None a priori (except bulk effect)	Present, goes down with spinning speed
Build-up times	Long ($\sim T_{1,n}$)	Long ($\sim T_{1,n}$)	Short
Sensitivity?	Low in general, $\frac{R_{\text{DNP}}}{R_{1,n}^{1/2}} P_{\text{DNP}}$	Low in general, $\frac{R_{\text{DNP}}}{R_{1,n}^{1/2}} P_{\text{DNP}}$	Very high in general ($S \approx R_{\text{CE}}^{1/2} \Delta P_e$)
Examples	BDPA in PS/OTP, Mixed Valence compounds, Blatter radicals, conductive materials	Trityl in Glycerol/Water BDPA in PS/OTP	TOTAPOL or AMUPOL in Glycerol/Water, TEKPol in OTP, TCE $\epsilon_{\text{on/off}}$ is not gain w.r.t thermal equilibrium

$$\frac{1}{T_B} = R_B = R_{\text{DNP}} + R_{1,n} \approx \frac{1}{T_{1,n}}$$

$$P_n(\infty) = \frac{R_{\text{DNP}} P_{\text{DNP}} + R_{1,n} P_n^B}{R_{\text{DNP}} + R_{1,n}} \approx P_n^B + \frac{R_{\text{DNP}}}{R_{1,n}} P_{\text{DNP}}$$

$$\frac{1}{T_B} = R_B \approx R_{\text{DNP}}$$

$$P_n(\infty) = \frac{R_{\text{DNP}} P_{\text{DNP}} + R_{1,n} P_n^B}{R_{\text{DNP}} + R_{1,n}} \approx P_{\text{DNP}}$$

Summary

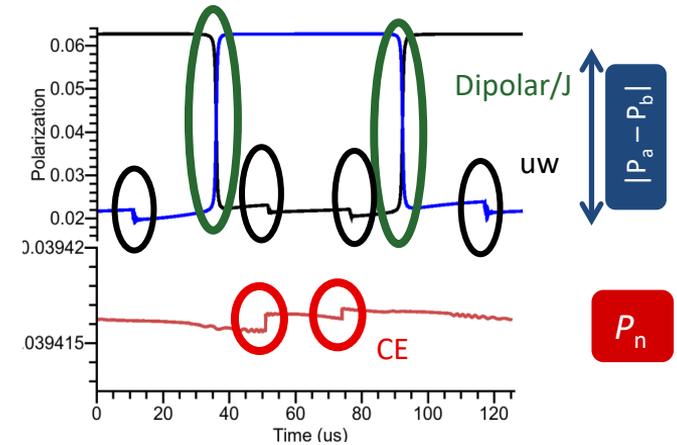
- Mechanisms
 - Anisotropy+MAS \rightarrow OE, SE, CE work by “steps”
 - MAS has little impact on OE and SE
 - MAS has big impact on CE! \rightarrow design of biradicals

- Practical aspects

$$P_n(t) = \frac{R_{\text{DNP}} P_{\text{DNP}} + R_{1,n} P_n^B}{R_{\text{DNP}} + R_{1,n}} (1 - e^{-(R_{\text{DNP}} + R_{1,n})t})$$

hyperpolarization
Buildup rate, R_B

- OE and SE \rightarrow low R_{DNP} making it sensitive to bulk relaxation $R_{1,n}$
 - Sample degassing and deuteration of the solvent needed
- CE \rightarrow high R_{DNP} (R_{CE})
 - Depend on the biradical
 - Deuteration and degassing less critical (for some radicals, e.g. the AsymPols)



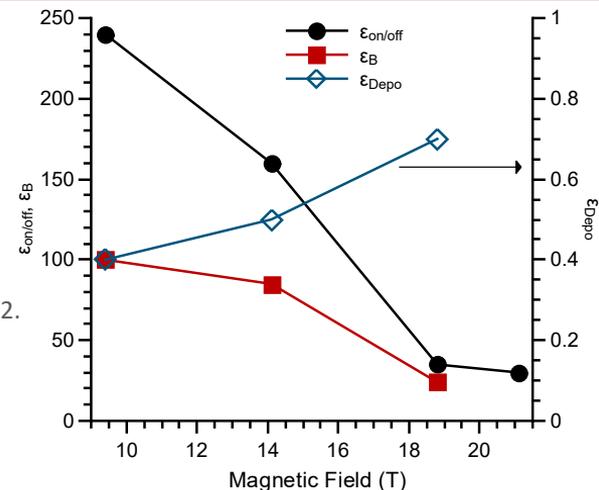
What I did not discuss

• High field MAS-DNP

- Theory: modest field dependence for bis-nitroxides
- Experiment:
 - difficult in 3.2 mm rotors, better in 1.3 or 0.7 mm³
 - high field DNP require larger $x = \omega_1$
- Sample absorption appears to be critical
 1. F. J. Scott, T. Dubroca, R. W. Schurko, S. Hill, J. R. Long and F. Mentink-Vigier, *J. Mag. Res.*, 2024, 365, 107742.

• Intrinsic defects for DNP

- Metal ions Refer to M. Leskes, L. Emsley, F. Blanc, F. Perras, B. Corzilius
 1. D. Jardón-Álvarez and M. Leskes, *Progress in Nuclear Magnetic Resonance Spectroscopy*, 2023, 138–139, 70–104.
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 3. A. L. Paterson, F. A. Perras, M. F. Besser and M. Pruski, *J. Phys. Chem. C*, 2020, 124, 23126–23133.
 4. D. J. Cheney, P. C. Vioglio, A. Brookfield and F. Blanc, *Phys. Chem. Chem. Phys.*, 2024, 26, 24395–24406.
 5. S. L. Carnahan, K. Riemersma, et al., *J. Phys. Chem. A*, 2024, 128, 3635–3645.
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 7. B. A. DeHaven, J. T. Tokarski, A. A. Korous, F. Mentink-Vigier, T. M. Makris, A. M. Brugh, M. D. E. Forbes, J. van Tol, C. R. Bowers and L. S. Shimizu, *Chem. Eur. J.*, 2017, 23, 8315–8319.



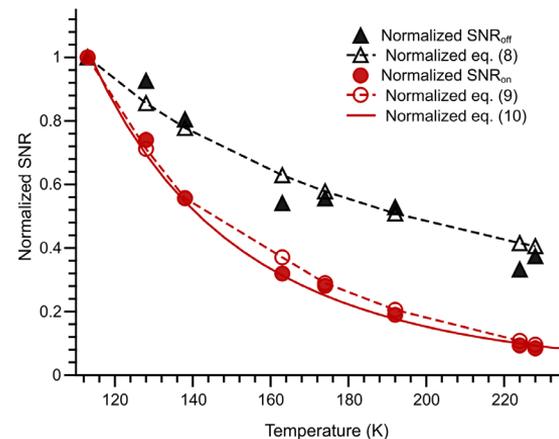
What I did not discuss

- DNP at higher temperature

- Use of special matrices for viable DNP application > 200 K
 - Ortho-Terphenyl
 - M. Lelli et al. *J. Am. Chem. Soc.*, 2015, 137, 14558–14561.
 - G. Menzildjian, at al. *J. Phys. Chem. B*, 2021, 125, 13329–13338.
 - Trehalose
 - M. Kaushik, et al., *Phys. Chem. Chem. Phys.*, 2022, 24, 12167–12175.
 - Sorbitol
 - F. J. Scott, et al., *J. Phys. Chem. Lett.*, 2024, 8743–8751.

- DNP at helium temperature ❤️ ❤️ ❤️ ❤️

- Y. Matsuki and T. Fujiwara, in *eMagRes*, John Wiley & Sons, Ltd, 2018, pp. 9–24.
- K. Thurber and R. Tycko, *J. Mag. Res.*, 2016, 264, 99–106.
- S. Paul, E. Bouleau, et al., *J. Mag. Res.*, 2023, **356**, 107561.



DNP at higher temperature (for biological samples)

- Predicting the SNR with temperature^{1?}

- electron polarization difference ΔP_e

- $$\Delta P_e \propto \left(1 - \frac{\left(1 - \exp\left(-\frac{\tau_r}{2T_{1,e}}\right) \right)}{\left(1 - \left(1 - 2 \frac{\pi^2 \omega_1^2 \tau_r}{\Delta\omega_a + \Delta\omega_b}(\tau_r) \right) \exp\left(-\frac{\tau_r}{2T_{1,e}}\right) \right)} \right)$$

- Depends on $T_{1,e} \propto 1/T^2$ (Raman process)
- Noise from coil $\text{Noise} \propto \sqrt{T + T_p}$

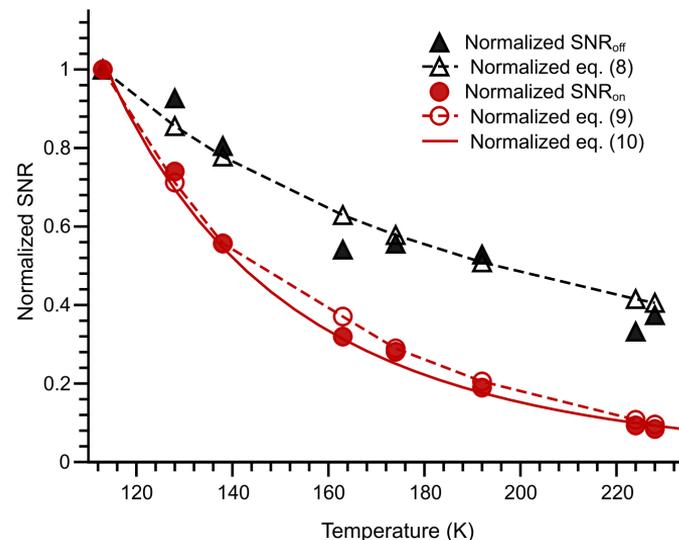
- DNP at high temperature

- Challenging
- Lower uw power required (sample melting, had to use sapphire shards)

- Microwave penetration is important for DNP

- Lack of measurements of dielectric constant in the literature at DNP frequencies
- No characterization of matrices
- Critical for hardware development
- Critical for high field DNP → why small rotors better for > 18.8 T DNP?

$$\frac{\text{SNR}_{\text{on}}(T)}{\text{SNR}_{\text{on}}(T_{\text{ref}})} = \frac{T_{\text{ref}} \Delta P_e(T)}{T \Delta P_e(T_{\text{ref}})} \left(\frac{T_{\text{ref}} + T_p}{T + T_p} \right)^{0.5}$$



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