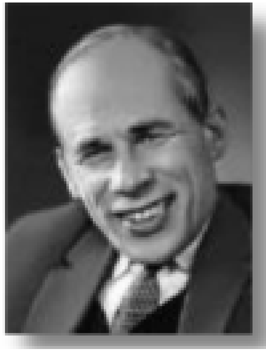
X International Voevodsky Conference "Physics and Chemistry of Elementary Chemical Processes" (VVV-2022)

Novosibirsk 05-09 Sep 2022



Adiabatic approach to polarize ^{15}N nuclei with SABRE at high magnetic fields

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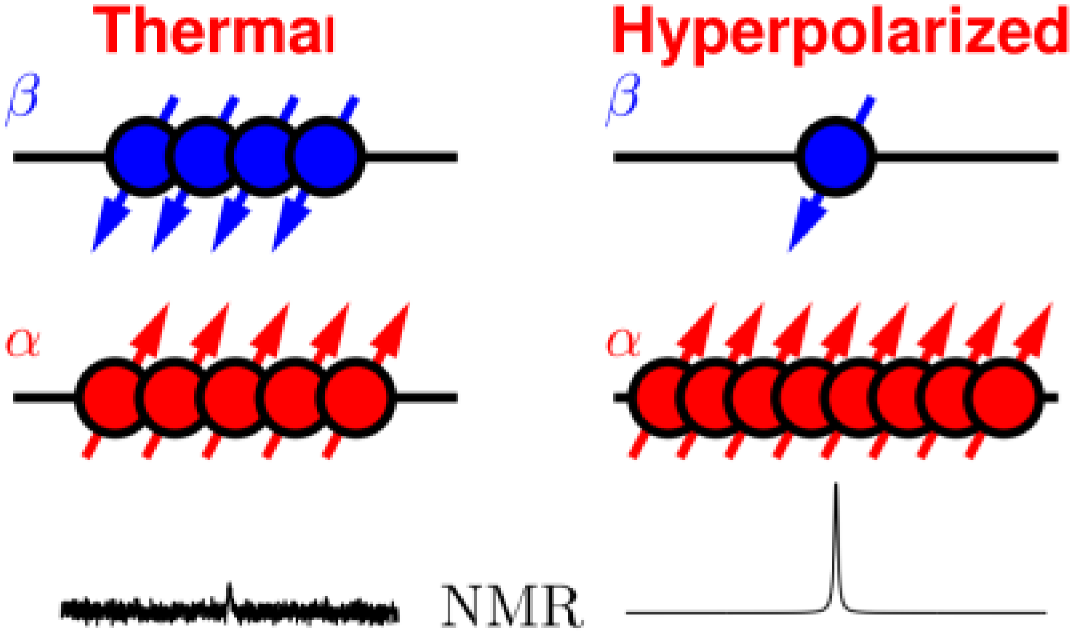
Hyperpolarization in NMR

Low sensitivity of NMR methods:

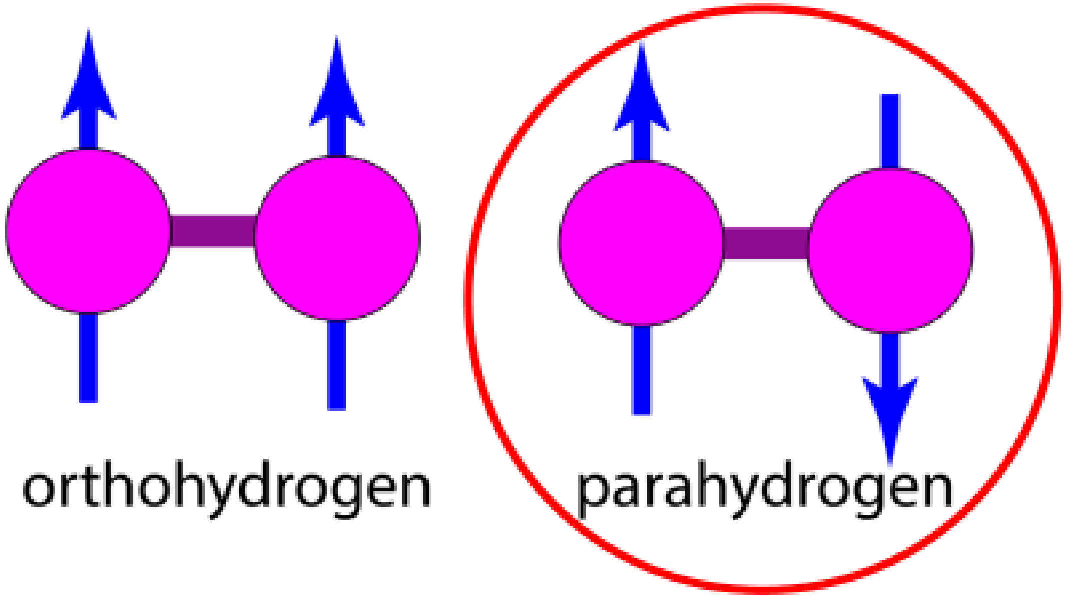
$$p_{eq} = \frac{p_\alpha - p_\beta}{p_\alpha + p_\beta} \approx \frac{\hbar\gamma_N B_0}{2k_B T} \ll 1$$

For protons at $B_0 = 15\ \mathrm{T}, T = 300\ K$

$p_{eq} \approx 5 \times 10^{-5}$



Para-hydrogen Induced Polarization (PHIP)



The source of hyperpolarization

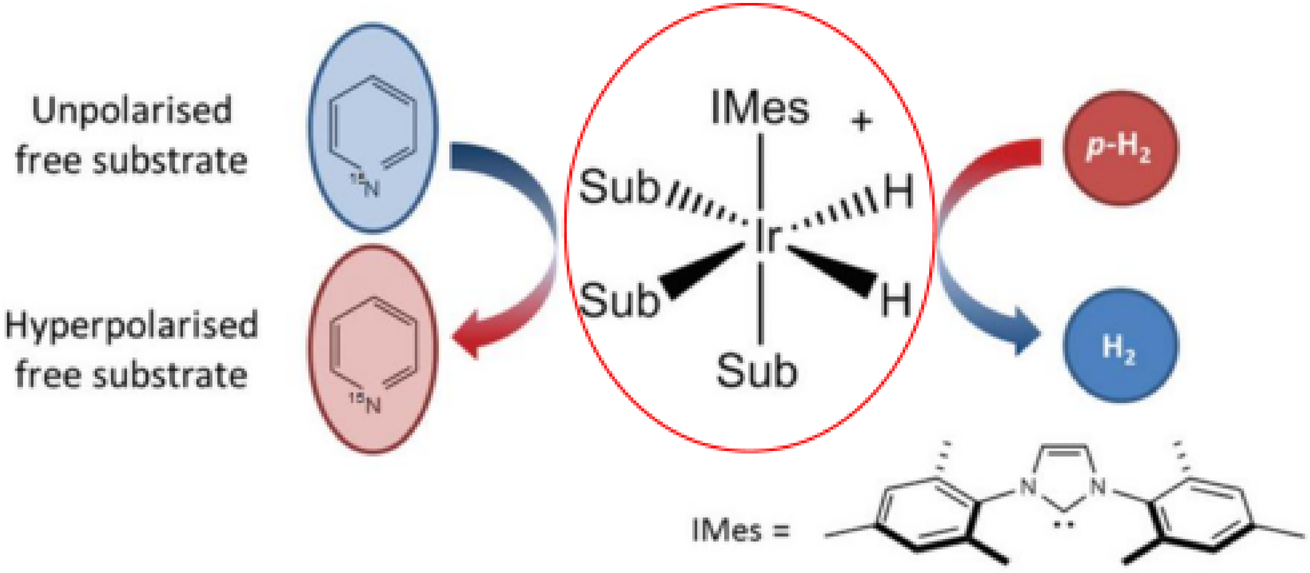
Konstantin L. Ivanov, Andrey N. Pravdivtsev et. al *The role of level anti-crossings in nuclear spin hyperpolarization*: Progress in Nuclear Magnetic Resonance Spectroscopy, 2014, **81**, 1-36

PHIP and SABRE

Para-hydrogen Induced Polarization (PHIP) → Hydrogenation of the substrate

Signal Amplification by Reversible Exchange (SABRE) → **No hydrogenation**

Polarization transfer complex



Strong coupling condition is fulfilled artificially in rotating reference frame (RF-pulses)

SABRE

($\delta\nu \cong J$ – strong coupling condition)

- ✓ For ^{15}N works at $B_0 \sim 10^{-6} - 10^{-7}$ T
- ✗ Special experimental setup is required

- ✓ High-field RF-SABRE
- ✓ No extra equipment
- ✗ Complicated experimental optimization

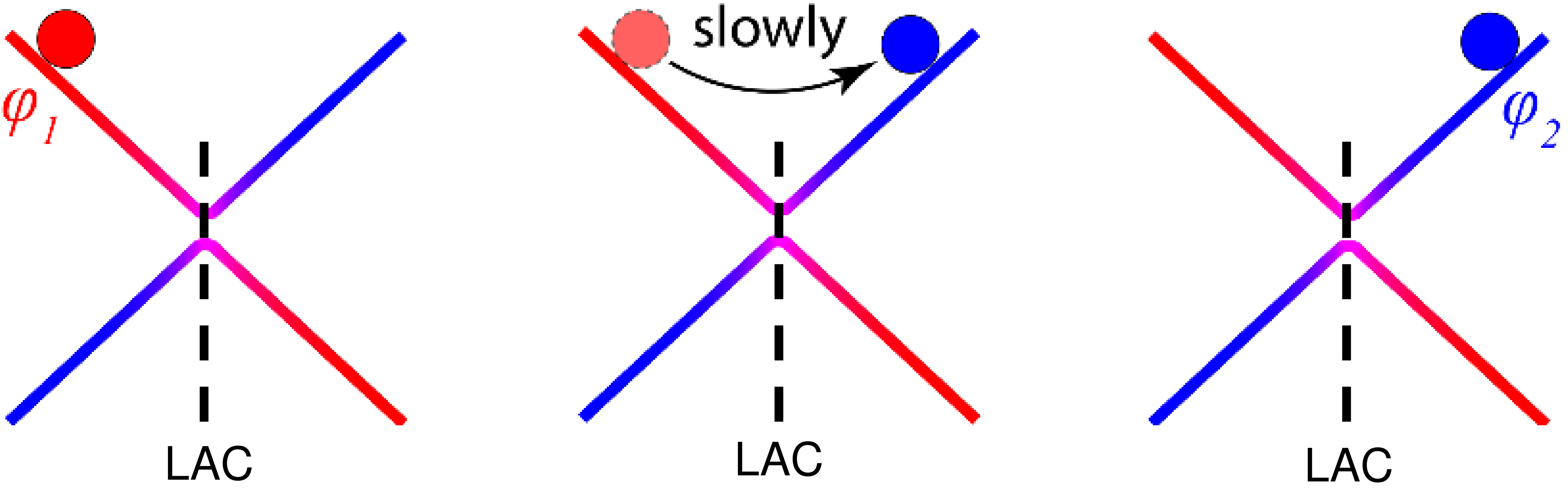
Peter M. Richardson, Andrew J. Parrot et al. SABRE hyperpolarization enables high-sensitivity 1H and 13C benchtop NMR spectroscopy: Analyst, 2018, ***143****, 3442*

Level anti-crossing (LAC)

$$\hat{H} = \hat{H}_0 + \hat{V}$$

$$\langle \varphi_1 | \hat{V} | \varphi_2 \rangle \neq 0$$

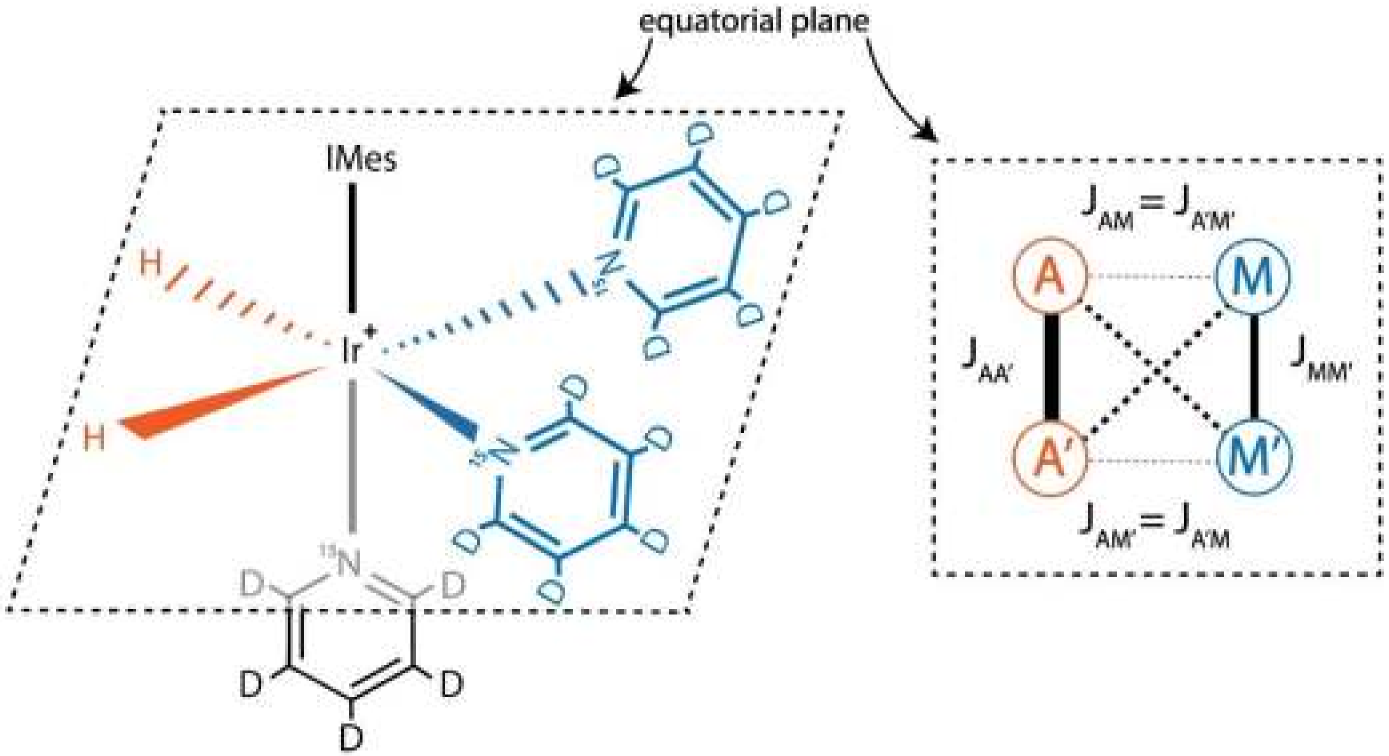
Quantum states $|\varphi_1\rangle, |\varphi_2\rangle$ tend to cross, but due to the perturbation $\hat{V}$ the degeneracy is lifted and the crossing is avoided (LAC)



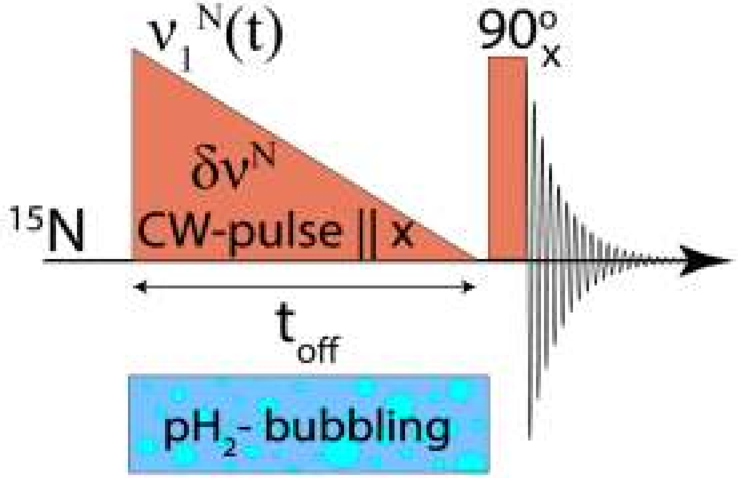
Adiabatic passage through level anti-crossing (Landau-Zener problem)

Populations exchange between the states $|\varphi_1\rangle, |\varphi_2\rangle$

High-field RF-SABRE



The simplest variant of the high-field SABRE using adiabatic RF-switching



$\nu_1^N(t)$ - adiabatic RF-pulse amplitude

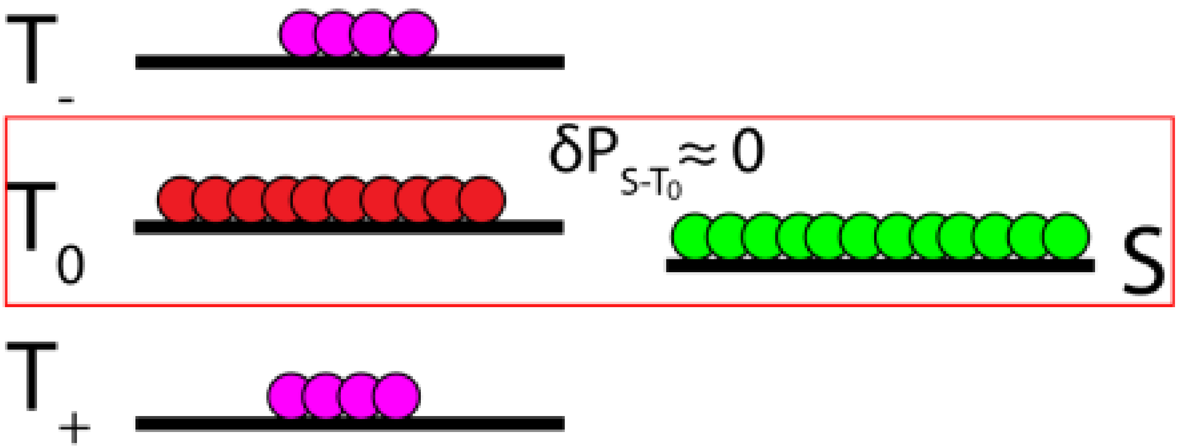
$\delta\nu^N = \nu^N - \nu_{rf}^N$ - resonance offset

δP_{S-T_0} in molecular hydrogen is converted into ^{15}N nuclei magnetization along the effective field in the rotating reference frame

Amplitude modulation of the CW-pulse provides adiabatic LAC passage

High-field RF-SABRE

✗ In a real SABRE-system, effective $S - T_0$ mixing takes place in molecular hydrogen

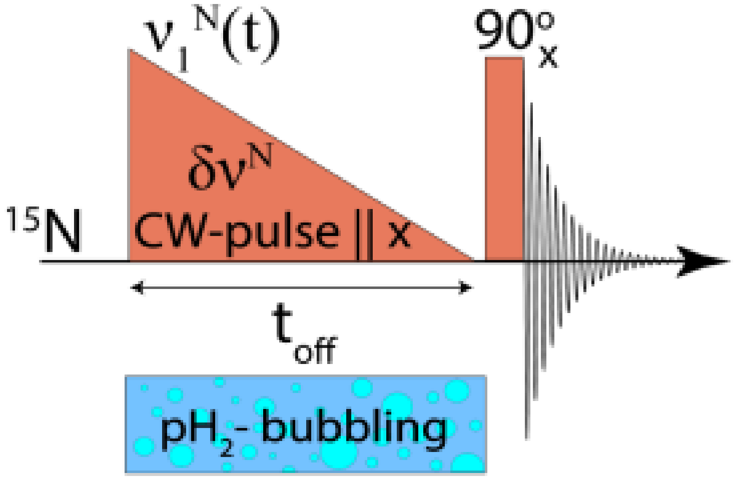


$$\hat{\rho}_S = \frac{1}{4}\hat{E} - (\hat{\boldsymbol{I}}_1\hat{\boldsymbol{I}}_2)$$

Conversion In H_2

$$\boxed{\hat{\rho}_{ZZ} = \frac{1}{4}\hat{E} - \hat{I}_{1_z}\hat{I}_{2_z}}$$

✗ There is no generation of SABRE-polarization at high field, because $\delta P_{S-T_0} \approx 0$



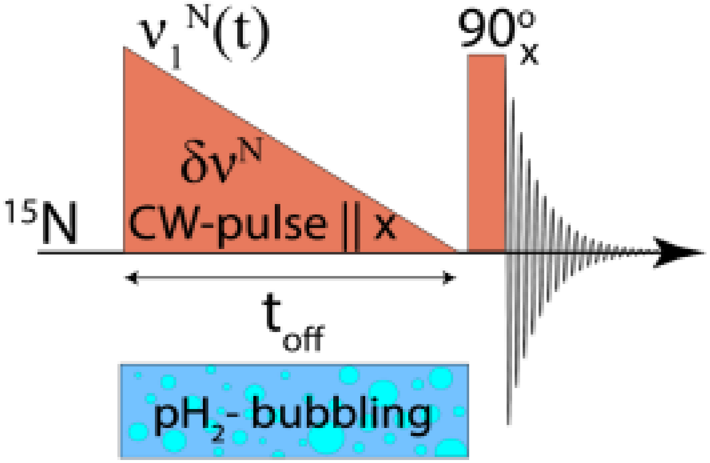
Single-frequency pulse sequence becomes completely ineffective

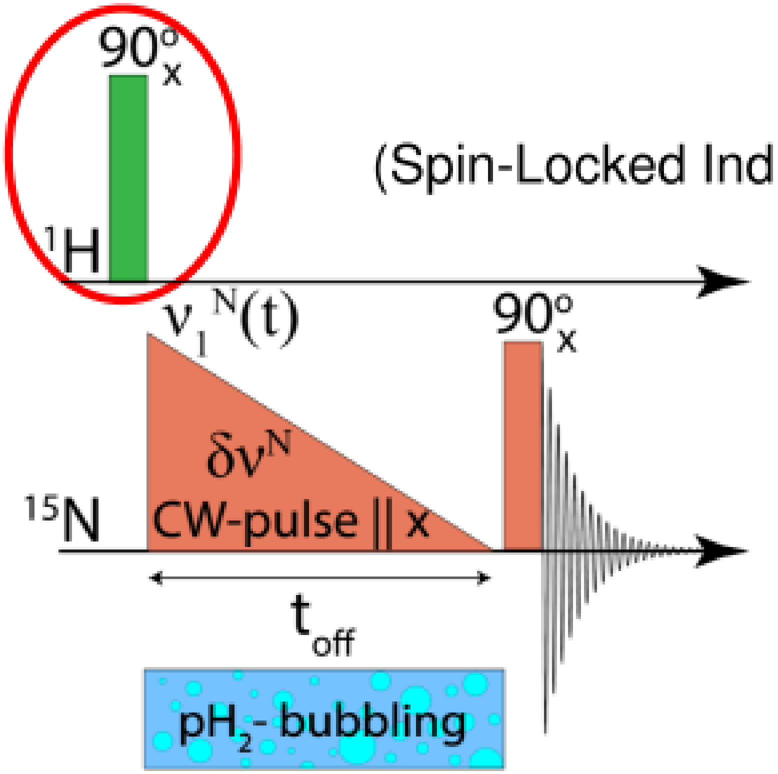
Danil A. Markelov, Vitaly P. Kozinenko et al. Singlet to triplet conversion in molecular hydrogen and its role in parahydrogen induced polarization // Phys. Chem. Chem. Phys., 2021, **23**, 20936-20944.

High-field RF-SABRE

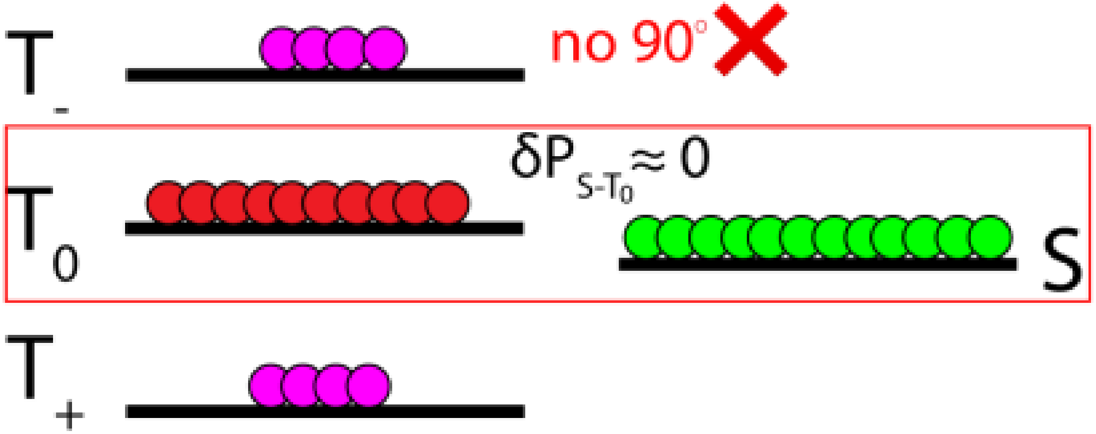
How to make the pulse sequence effective once again?

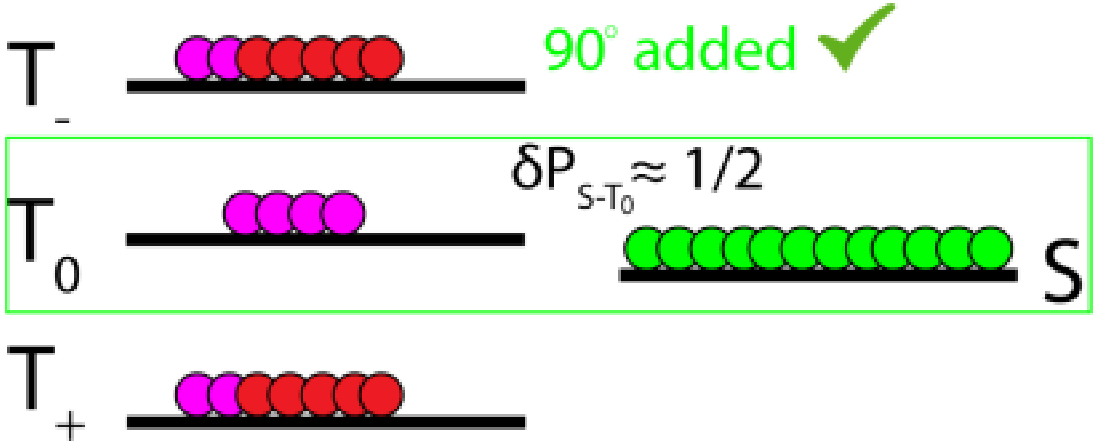
1) The first variant





SLIC-SABRE
(Spin-Locked Induced Crossing)

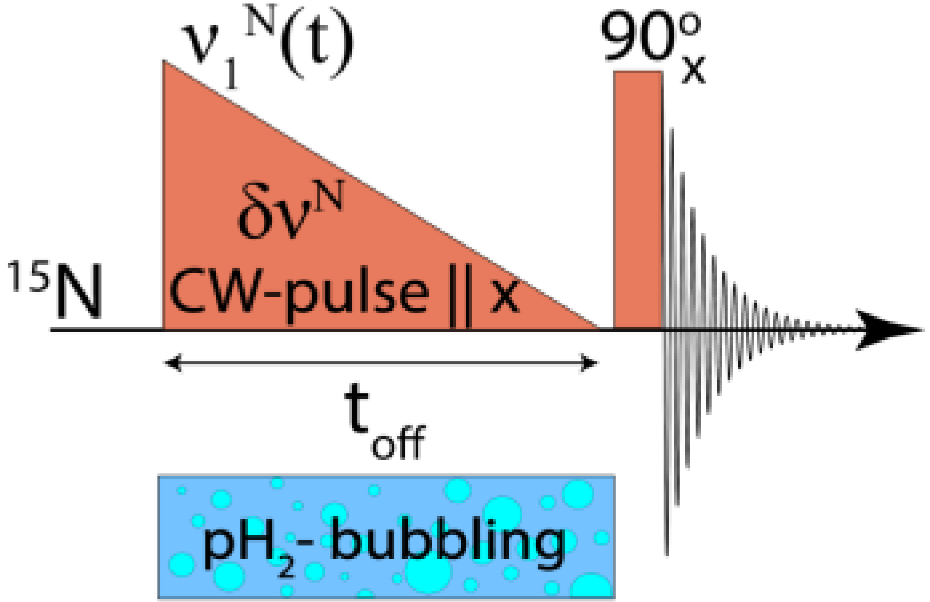




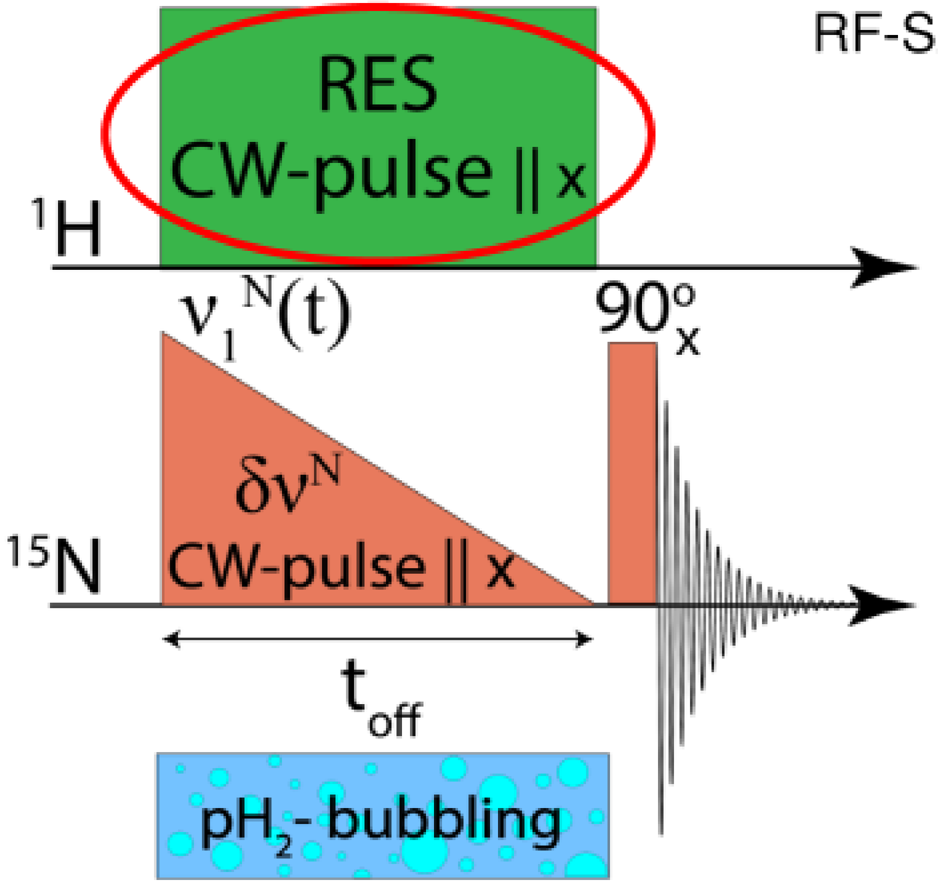
High-field RF-SABRE

How to make the pulse sequence effective once again?

2) The second variant



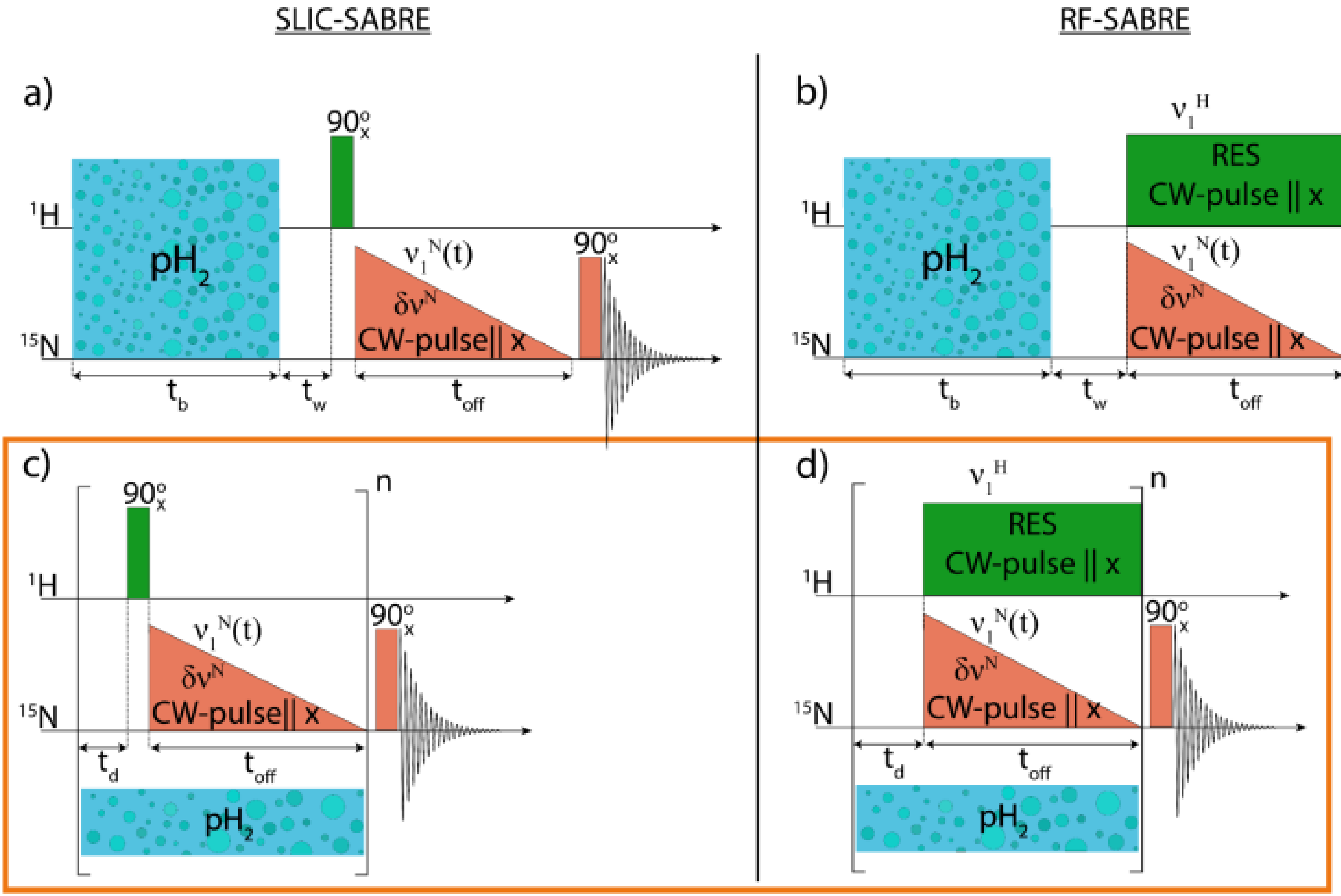
RF-SABRE



✗ Single-frequency pulse sequence is ineffective

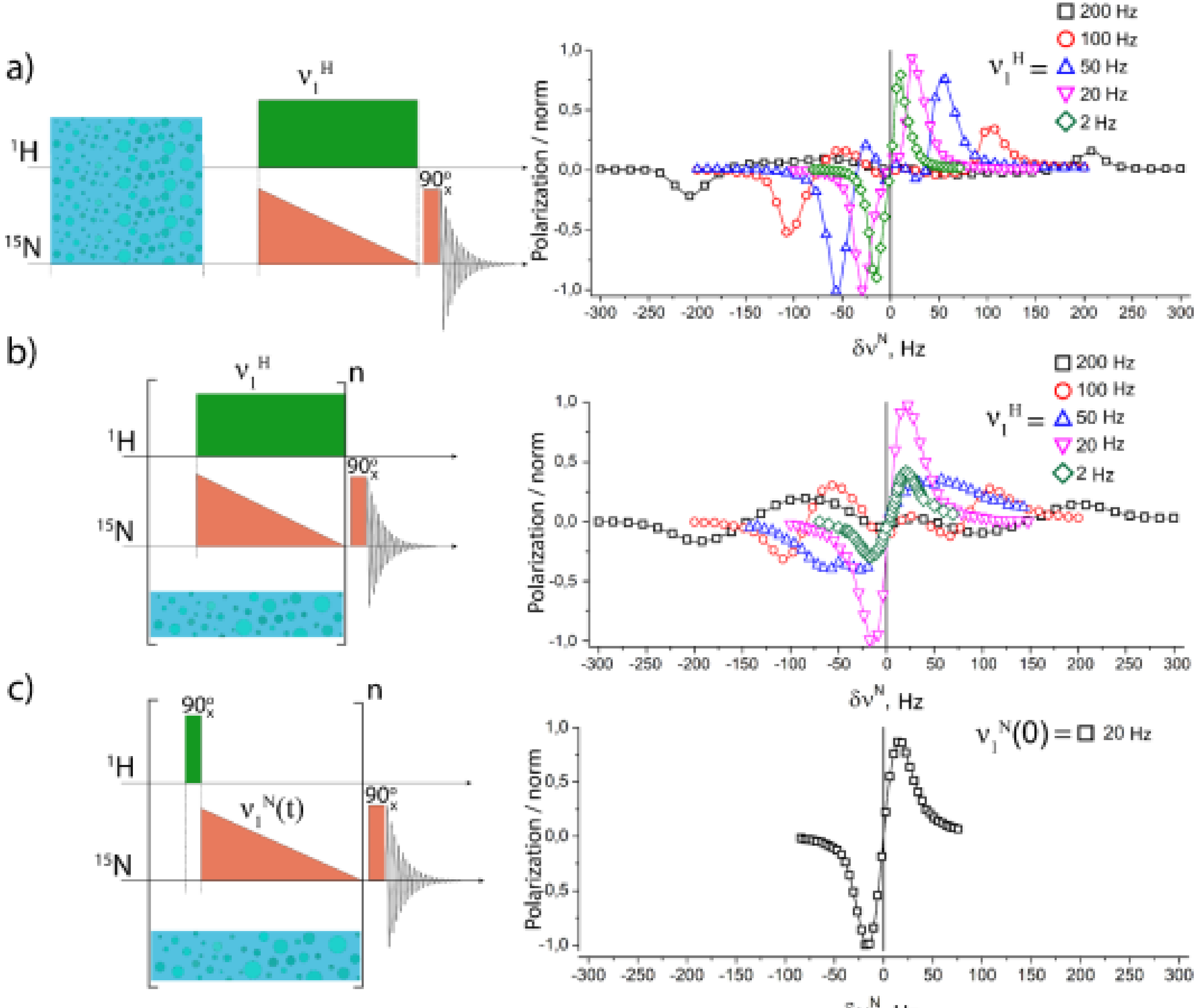
✓ $\delta P_{S-T_\pm}$ in molecular hydrogen is converted into magnetization
LAC condition: $\nu_1^N(t) \approx \nu_1^H$

High-field SABRE pulse sequences



Accumulation of heteronuclear polarization due to their long T_1 - relaxation time

RF-SABRE and SLIC-SABRE with linear RF-amplitude switching profile



$\nu_1^H = 20\ Hz$ – optimal value for RF-SABRE

[Catalyst] = 2 mM,
[Substrate] = 70 mM.
Other parameters:
a) $t_{off} = 1\ s$,
$t_b = 20\ s$, $t_w = 0.5\ s$
b), c) $t_{off} = 50\ ms$,
$t_d = 500\ ms$, $n = 50$;

RF-amplitude switching profile calculation

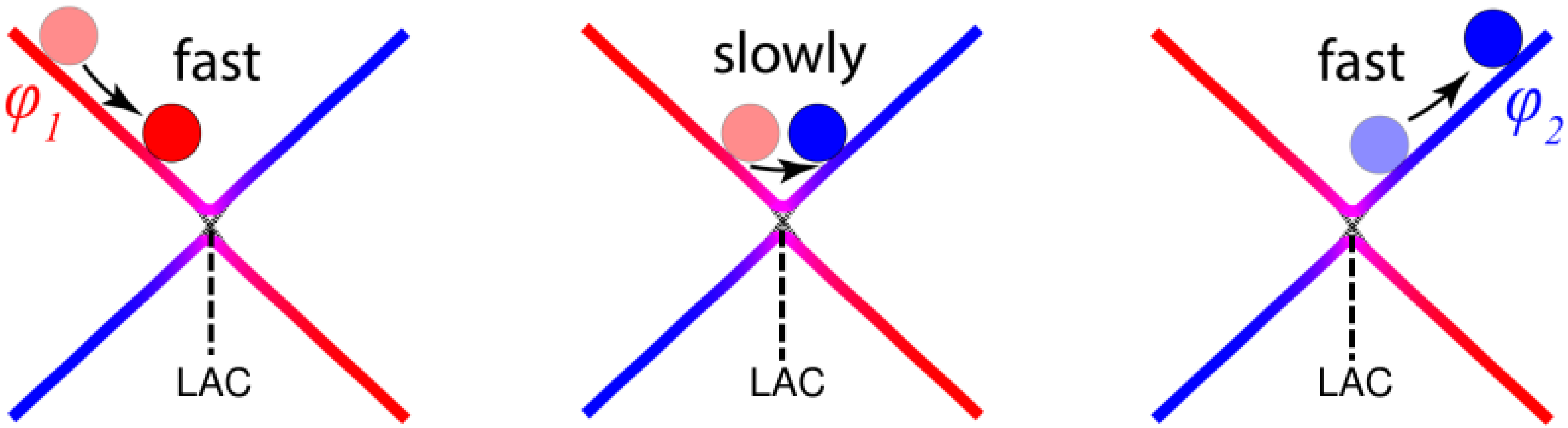
Linear RF-amplitude switch profile is not always optimal for effective generation of nuclear polarization

↓

RF-amplitude switch profile calculation

↓

The main idea – slow RF-amplitude switch near the LAC region, and fast switch outside the LAC-region



1) Spin dynamics in a «static» SABRE-complex

RF-amplitude switching profile calculation

1) The first way – Constant Adiabaticity Profiles (CAP) calculation

✗ In this approach we don't take into account SABRE chemical dynamics

$$\xi_{ij} = \left| \frac{\left\langle i \middle| \frac{d}{dt} \middle| j \right\rangle}{(E_i - E_j)} \right| = \left| \frac{\left\langle i \middle| \frac{d}{dt}\hat{H} \middle| j \right\rangle}{(E_i - E_j)^2} \right|$$

$$\sqrt{\sum_{i\neq j} \xi_{ij}^2} = \xi_0 \ll 1 = const$$

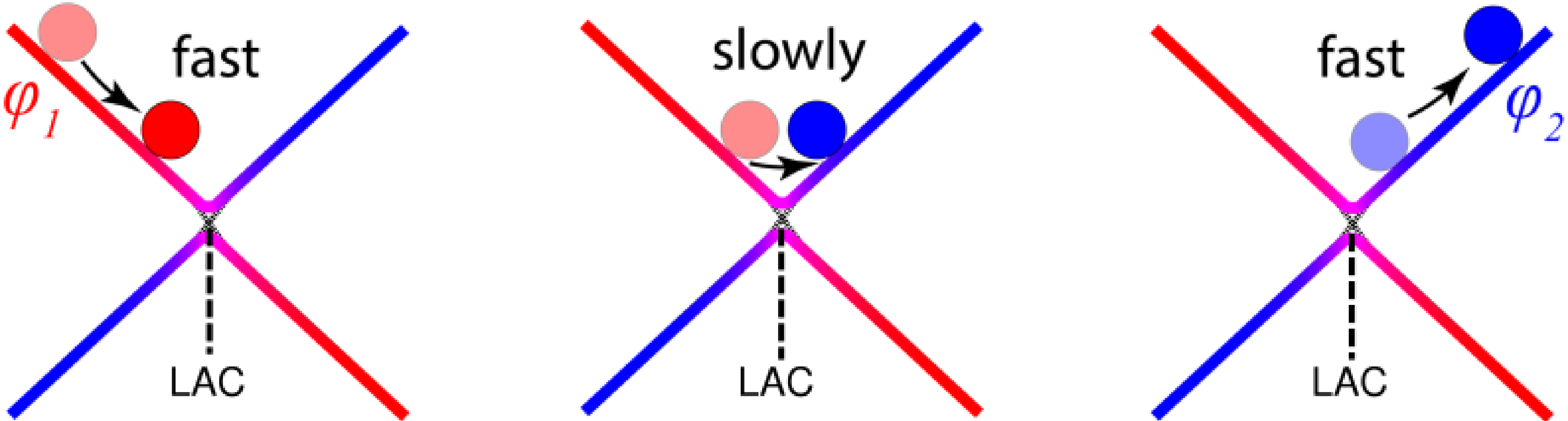
→

$$\frac{d}{dt}\nu_1^N(t) = -\xi_0 \left\{ \sum_{i\neq j} \frac{|\langle i|(\hat{I}_{Nx} + \hat{I}_{N'x})|j\rangle|^2}{(E_i - E_j)^4} \right\}^{-\frac{1}{2}},$$

with initial condition (RF-SABRE):

$$\nu_1^N(0) = \nu_1^H + 10\ Hz$$

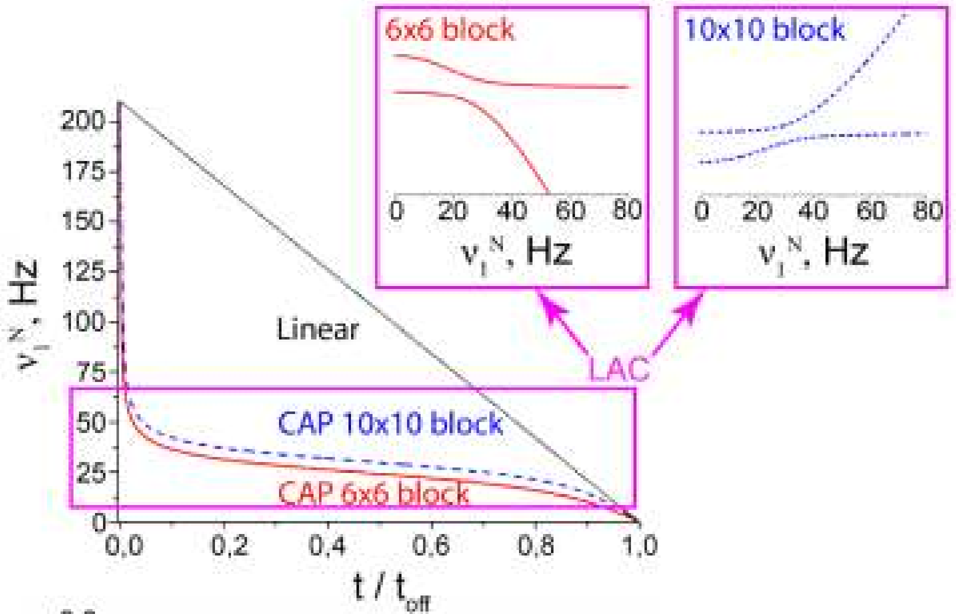
→ Solve the equation in the AA'XX' symmetry group basis (to avoid Level-Crossing)

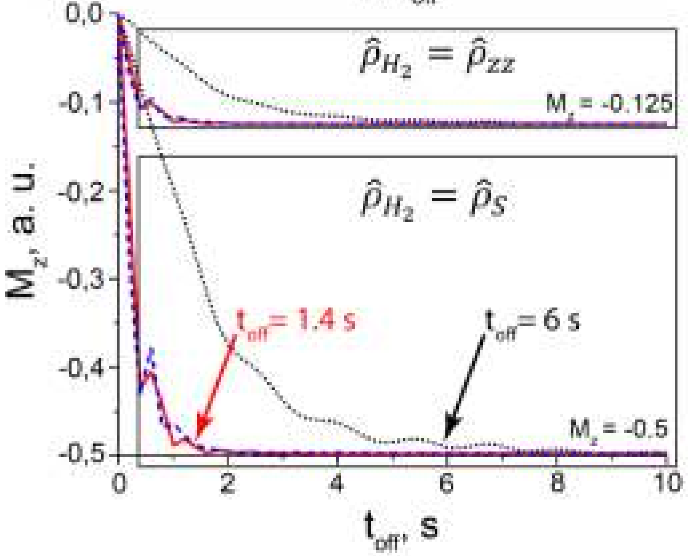


1) Spin dynamics in a «static» SABRE-complex

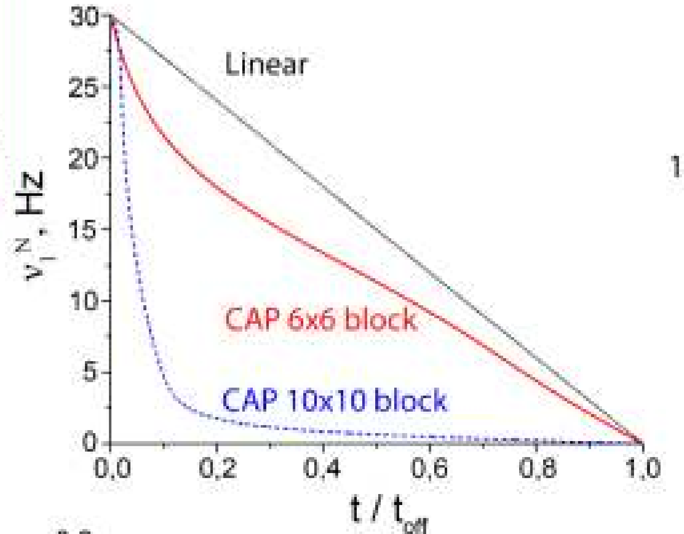
CAP calculation

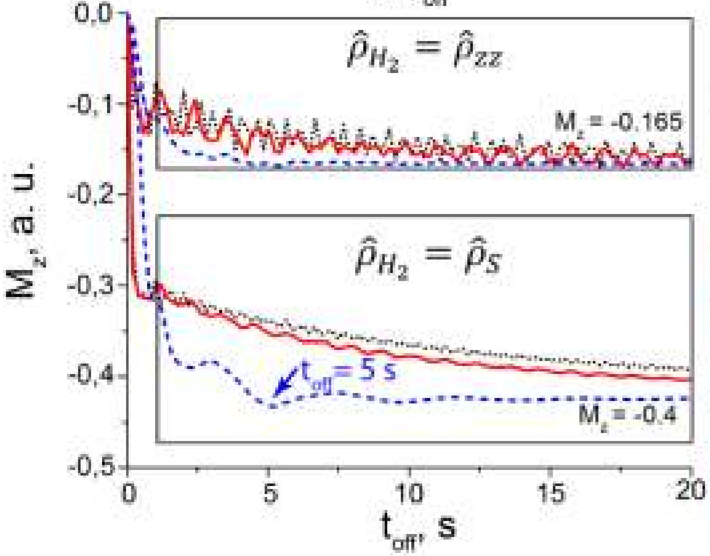
$\nu_1^H = 200$ Hz

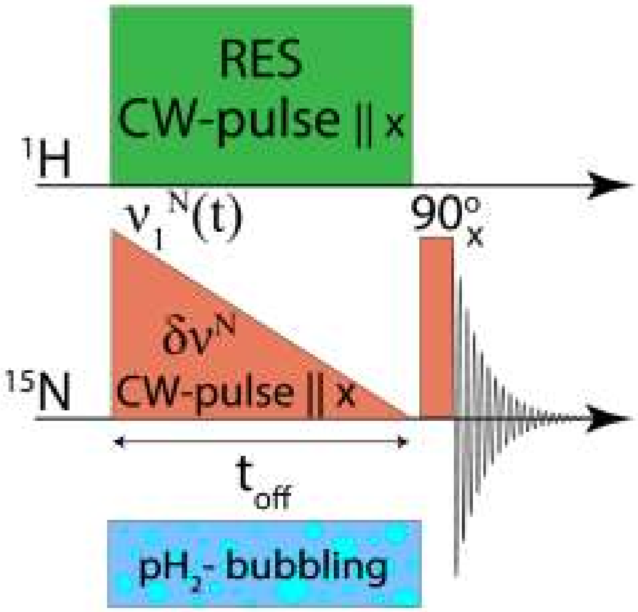




$\nu_1^H = 20$ Hz







$$\hat{\rho}_S = \frac{1}{4}\hat{E} - (\hat{\boldsymbol{I}}_1\hat{\boldsymbol{I}}_2)$$

$$\hat{\rho}_{ZZ} = \frac{1}{4}\hat{E} - \hat{I}_{1z}\hat{I}_{2z}$$

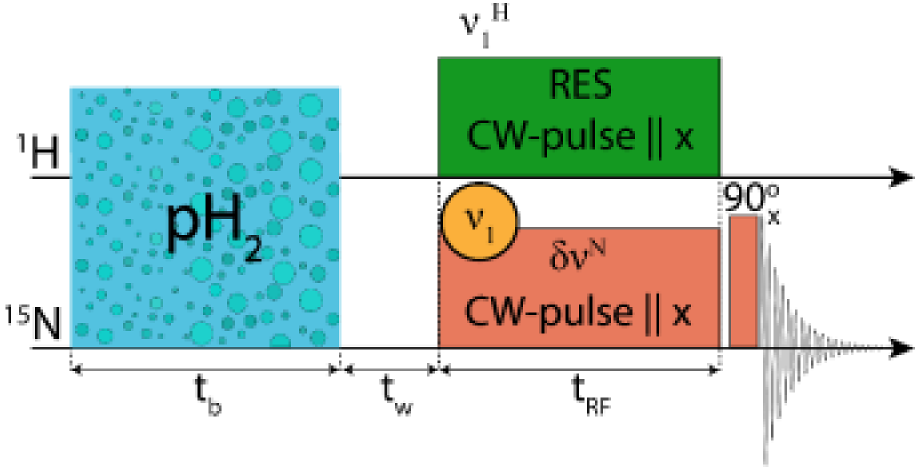
In experiment we are limited by the lifetime of the SABRE complex and T_1-relaxation time

Stationary value of magnetization for CAP's is reached at $t_{off} \le T_1$

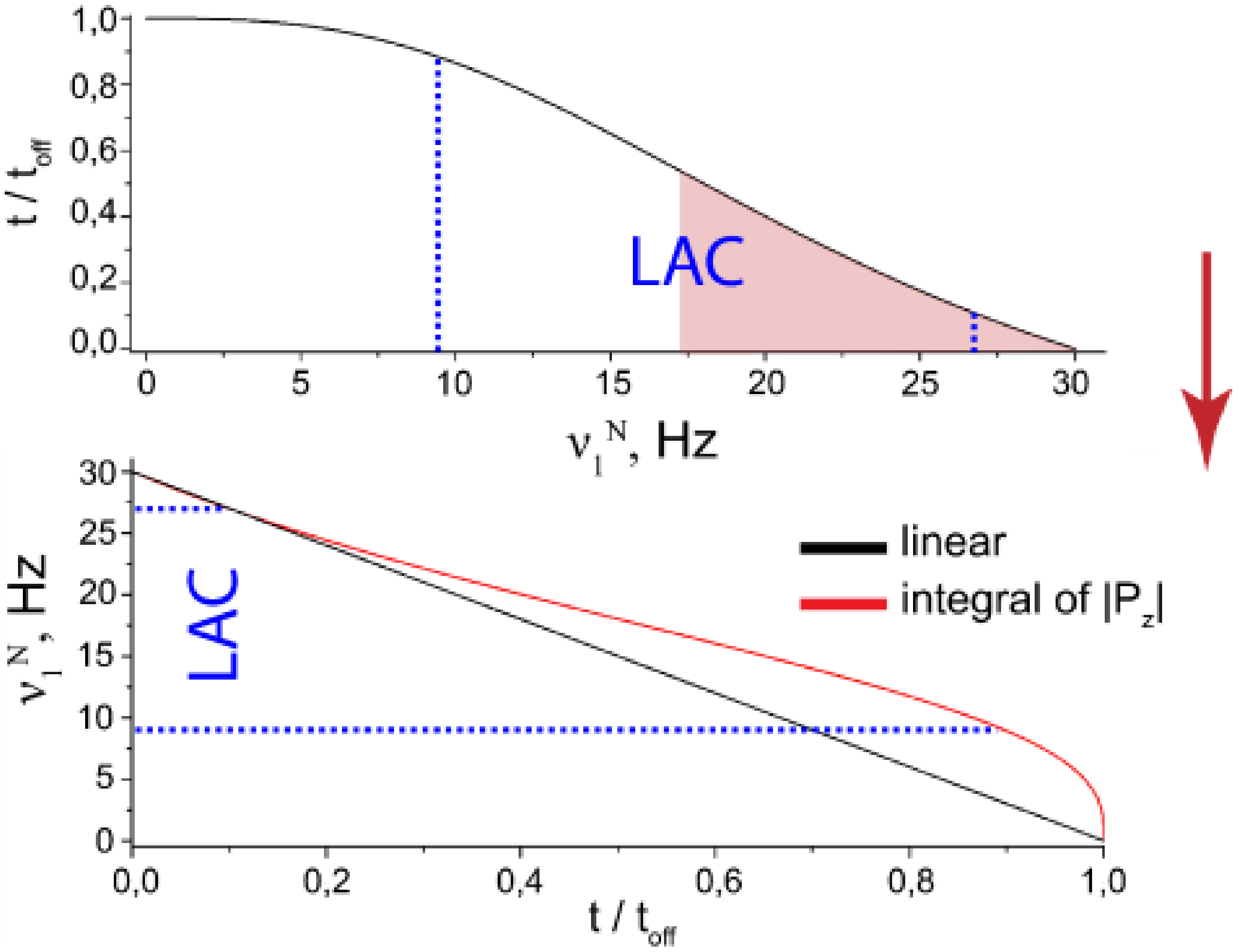
2) Spin dynamics taking into account chemical exchange

RF-amplitude switch profile calculation

2) The second way – extract RF-amplitude switch profile from experimental data and calculations which take into account chemical dynamics



Here we use RF-pulses with <u>constant amplitude</u> (scanning)



Assumption:

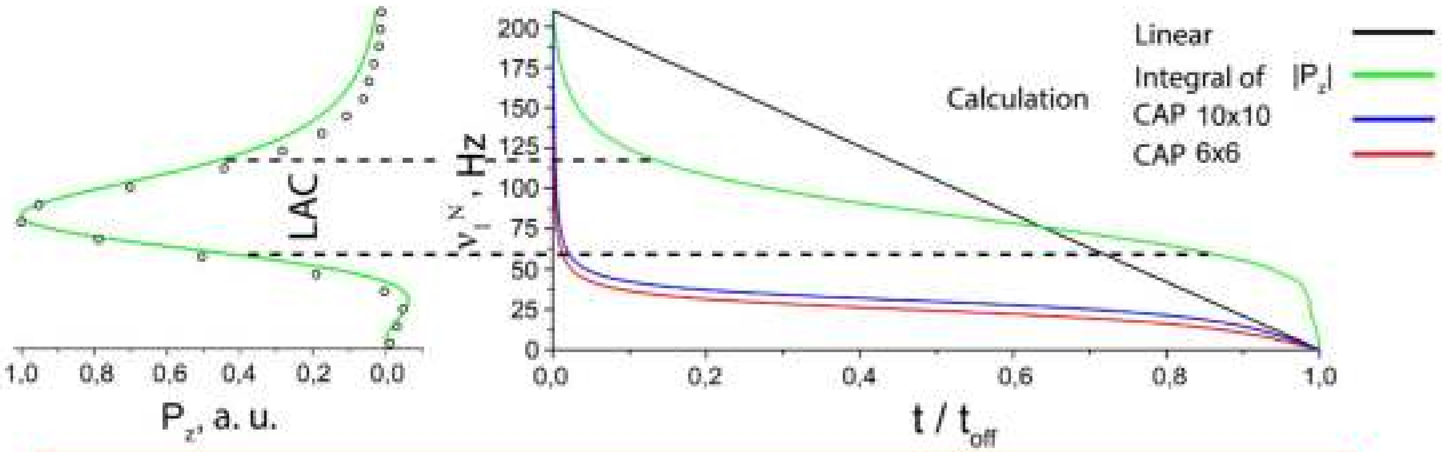
$$\frac{t}{t_{off}}(\nu_1^N) = A\int_{\nu_1^N}^{\nu_1^N(0)} |P_z(\nu_1)|\,d\nu_1$$

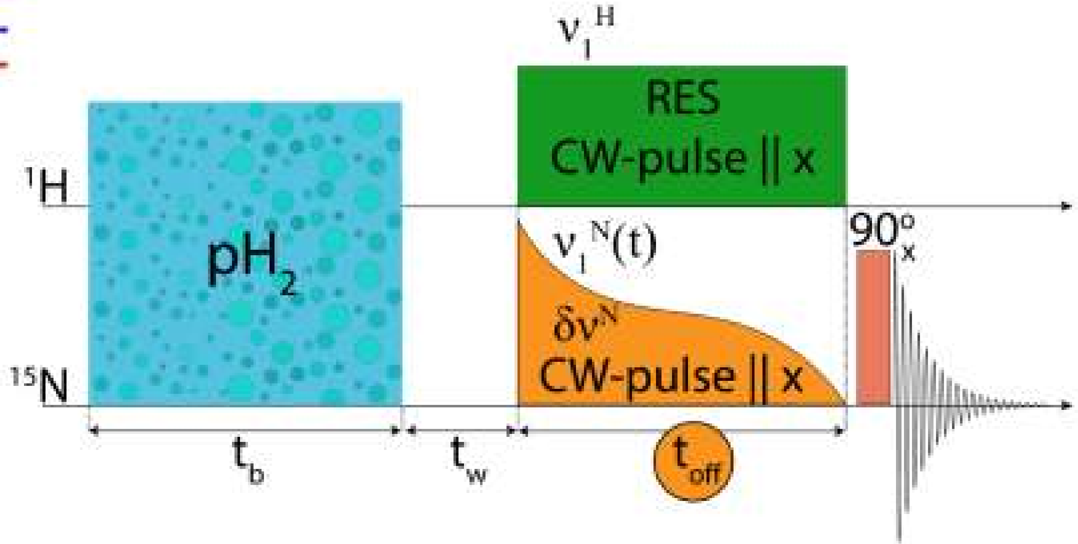
Normalization constant

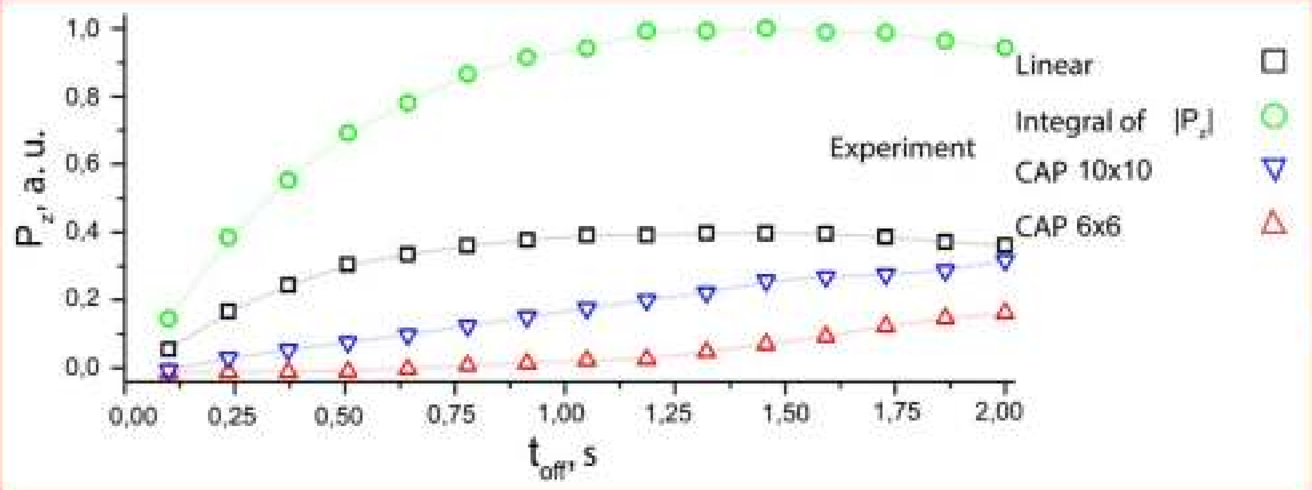
2) Spin dynamics taking into account chemical exchange

RF-SABRE experiments with different switching profiles

$\nu_1^H = 200$ Hz





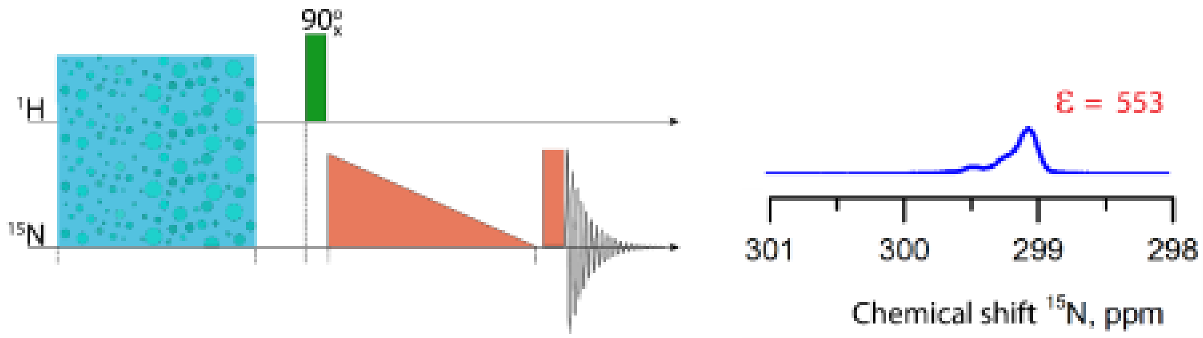


Our profile works 3 times more efficient in comparison with linear profile

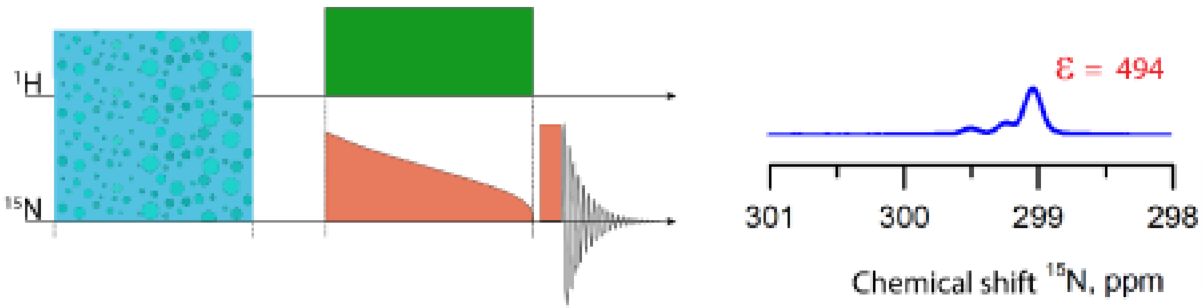
$$\delta\nu^N = -207.7 \text{ Hz}$$

Comparison of the pulse sequences

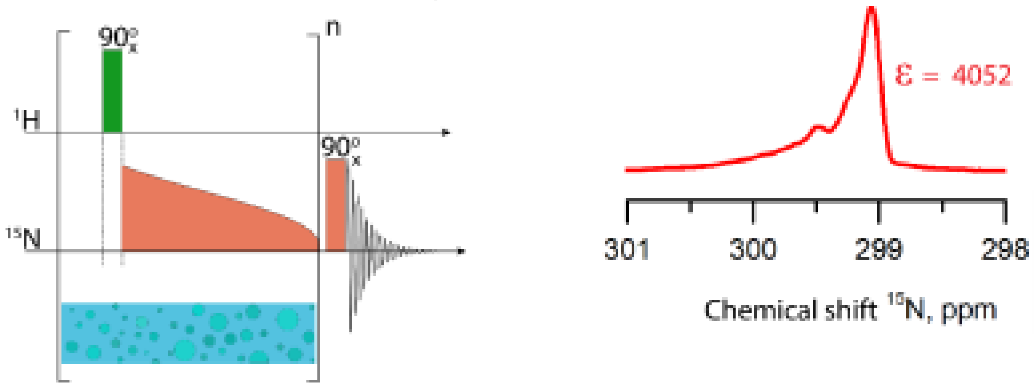
a)



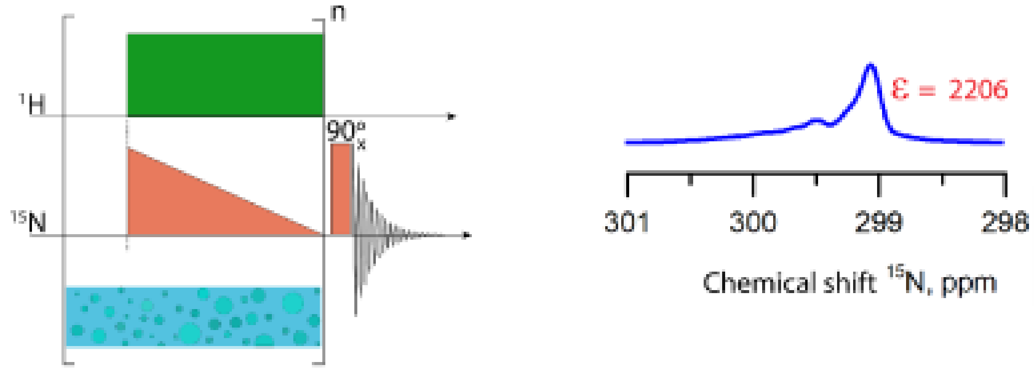
b)



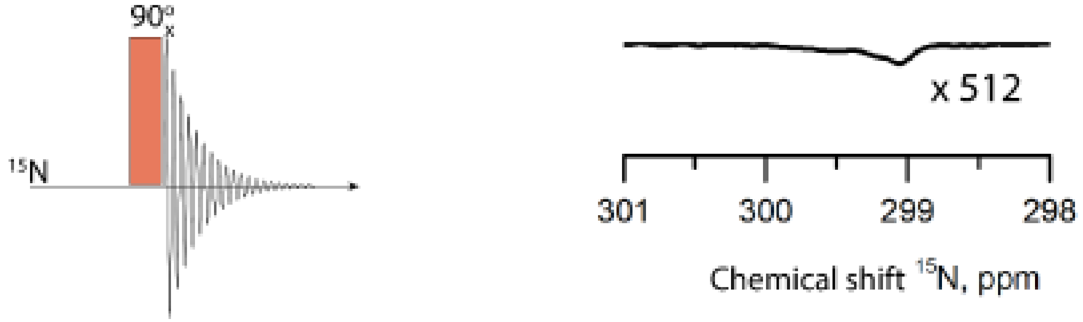
c)



d)



e)



Thermal ^{15}N signal at strong magnetic field (9.4 T, 25 °C)

Conclusions

1. The analysis of SABRE pulse sequences in a strong magnetic field based on adiabatic RF-amplitude modulation has been carried out. Various RF-switching profiles have been calculated and tested experimentally. It has been shown that SABRE chemical exchange essentially changes LAC's positions, and an approach to calculating switching-profiles based on LvN equation solution and experimental data has been proposed. For RF-SABRE with $\nu_1^H = 200$ Hz our profile works 3 times more efficient in comparison with linear profile
2. It has been shown that after experimental optimization, the biggest signal enhancement was achieved for SABRE with polarization cycles. Maximal enhancement equals 4000 has been achieved for SLIC-SABRE. Such enhancement factors are comparable with one obtained with ULF for our catalyst and substrate concentrations

Acknowledgements

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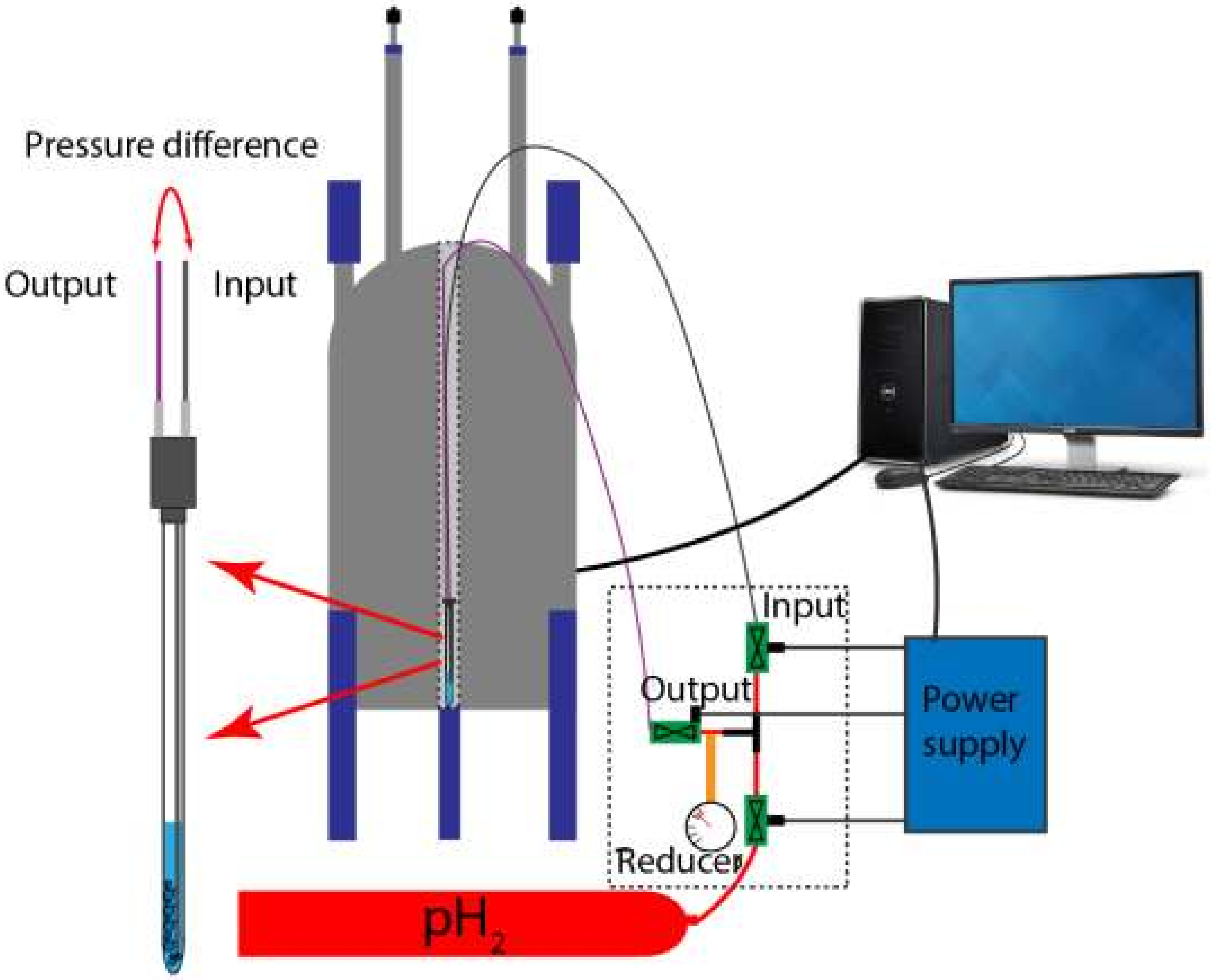
Thanks for your attention!

Extra Slides

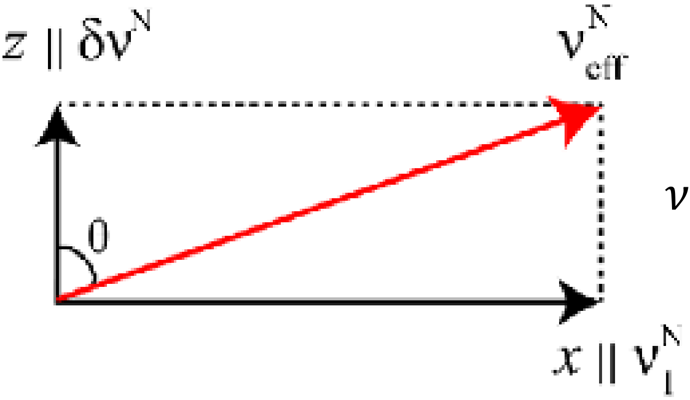
Extra slides
Experimental setup



Extra slides

SLIC-SABRE and RF-SABRE LAC's

SLIC-SABRE



$$\nu^N_{eff} = \sqrt{\left(\nu^N_1\right)^2 + \left(\delta\nu^N\right)^2}$$

LAC $|SS\rangle$ and $|T_0T_-\rangle$: $\nu^N_{eff} = -J_{HH'} - J_{NN'}$

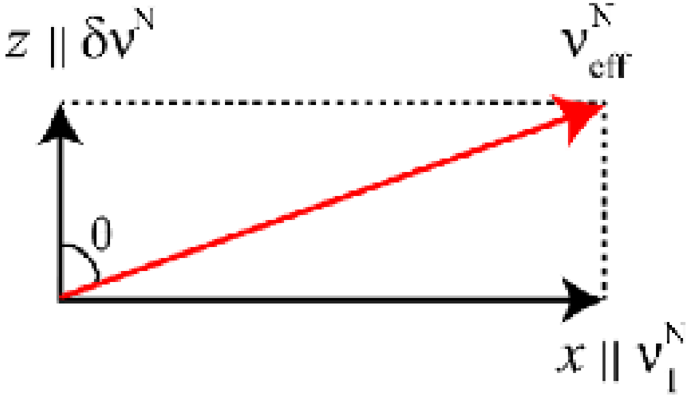
LAC $|ST_+\rangle$ and $|T_0S\rangle$: $\nu^N_{eff} = -J_{HH'} + J_{NN'}$

$$|SS\rangle, |ST_+\rangle, |ST_0\rangle, |ST_-\rangle \xrightarrow[\text{LAC exchange}]{} |T_0T_-\rangle, |T_0S\rangle, |ST_0\rangle, |ST_-\rangle$$

Polarization = 0

Polarization = -0.5

RF-SABRE



LAC $|ST_+\rangle$ and $|T_+S\rangle$: $\nu^N_{eff} = \nu^H_1 - J_{HH'} + J_{NN'}$

LAC $|ST_-\rangle$ and $|T_-S\rangle$: $\nu^N_{eff} = \nu^H_1 + J_{HH'} - J_{NN'}$

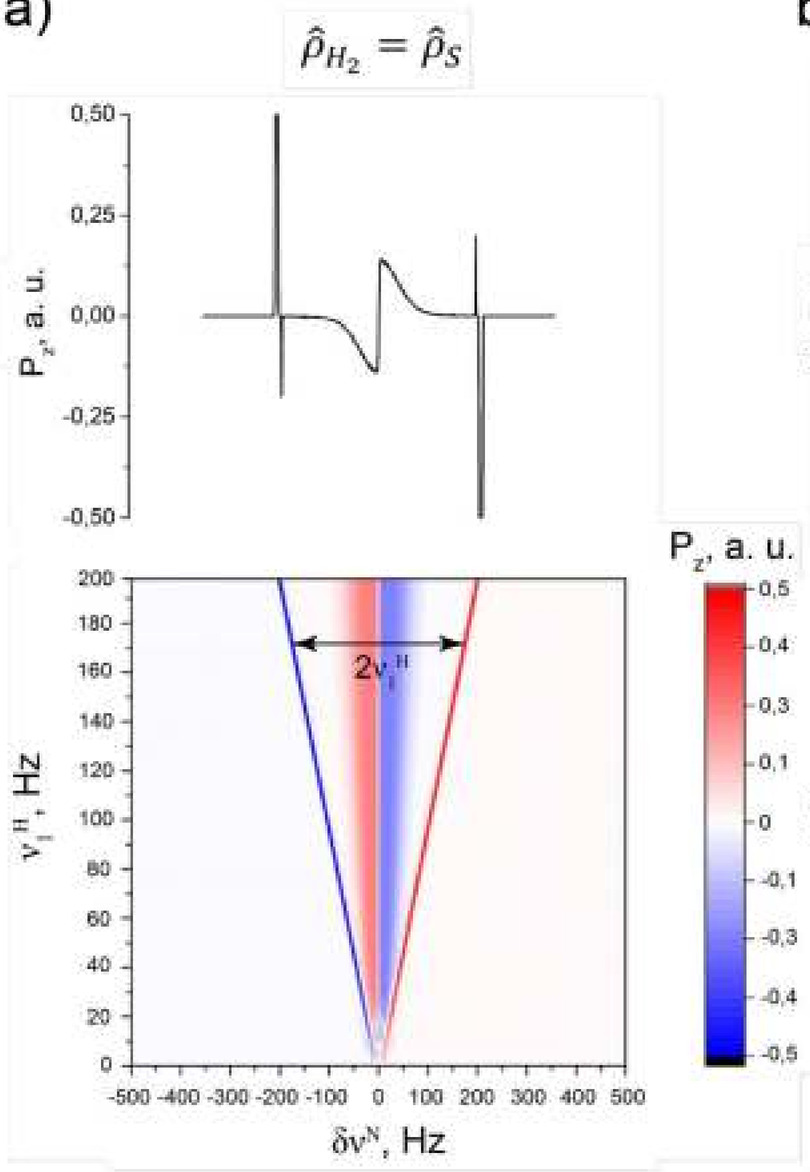
LAC $|SS\rangle$ and $|T_+T_-\rangle$: $\nu^N_{eff} = \nu^H_1 - J_{HH'} - J_{NN'}$

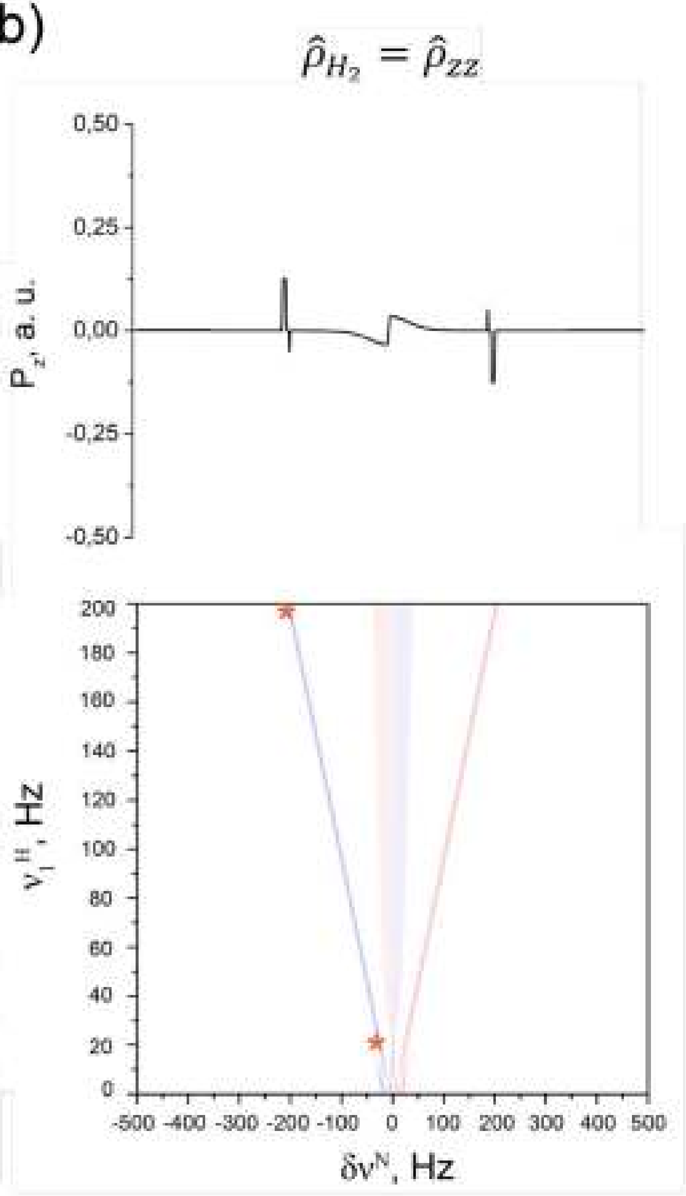
LAC $|SS\rangle$ and $|T_-T_+\rangle$: $\nu^N_{eff} = \nu^H_1 + J_{HH'} + J_{NN'}$

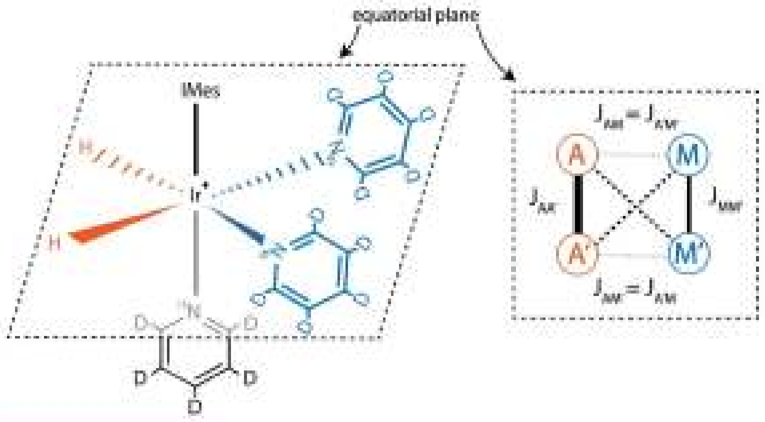
Polarization = ±0.5

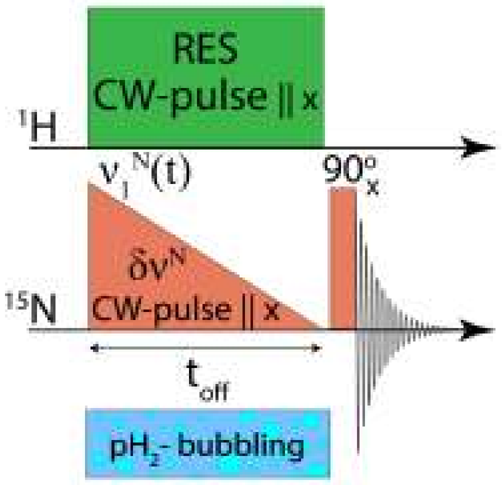
Extra slides

RF-SABRE magnetization calculation









RF-SABRE is still effective in the presence of singlet-triplet conversion in molecular hydrogen

Extra slides

CAP calculation

$$\frac{d}{dt}\nu_1^N(t) = -\xi_0\{\sum_{i\neq j}\frac{|\langle i|(\hat{I}_{Nx}+\hat{I}_{N'x})|j\rangle|^2}{(E_i-E_j)^4}\}^{-\frac{1}{2}},$$

with initial condition: $\nu_1^N(0) = \nu_1^H + 10$ Hz

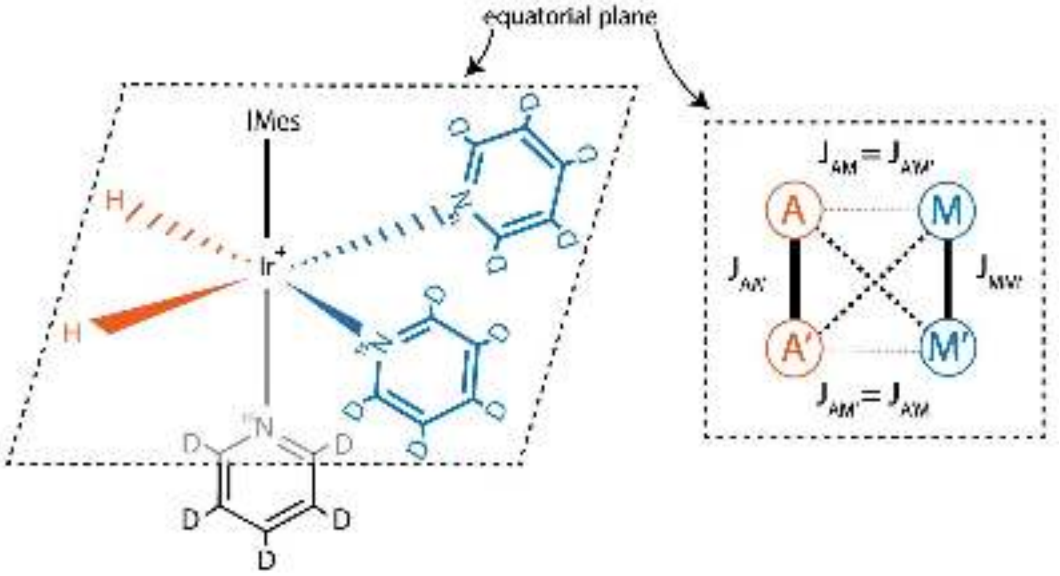
We have to avoid LC’s in order to calculate CAP correctly (calculation in AA’XX’ symmetry group basis)

$G_{AA'XX'}$	()	(12)(34)
A	1	1
B	1	-1
Spin representation = 10A+6B	16	4

A - $\{T_+T_+, T_+T_0, T_+T_-, T_0T_+, T_0T_0, T_0T_-, T_-T_+, T_-T_0, T_-T_-, SS\}$,

B - $\{T_+S, T_0S, T_-S, ST_+, ST_0, ST_-\}$.

Avoid LC’s between different irreps



Extra slides

LvN equations with chemical exchange

$$\begin{cases} \frac{d\hat{\rho}_S}{dt} = \hat{\hat{L}}_S\hat{\rho}_S - W_a\hat{\rho}_S + k_d Tr_{H_2}\{\hat{\rho}_C\} \\ \frac{d\hat{\rho}_C}{dt} = \hat{\hat{L}}_C\hat{\rho}_C - k_d\hat{\rho}_C + W_a\left(\hat{\rho}_S \otimes \hat{\rho}^{Ir}_{H_2}\right) \end{cases}.$$

→ Integral Encounter Theory equations

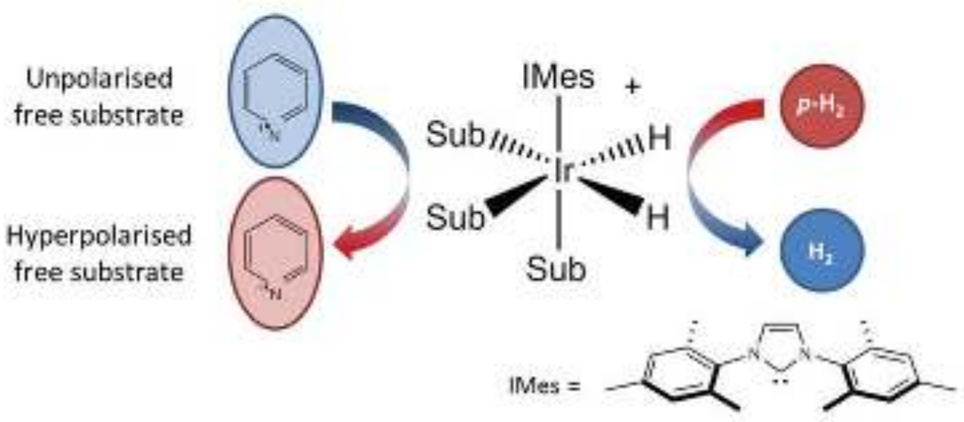
$$W_a = k_d\frac{[C]}{[S]} \qquad \hat{\hat{L}}_{C,S} = -i\hat{\hat{H}}_{C,S} + \hat{\hat{R}}_{C,S}$$

$$\hat{\hat{H}}_{C,S}\hat{\rho}_{C,S} = [\hat{H}_{C,S}, \hat{\rho}_{C,S}]$$

$$R_{ij,mn} = \frac{1}{2}\left(2J_{im,jn} - \delta_{jn}\sum_l J_{lm,li} - \delta_{im}\sum_l J_{lj,ln}\right)$$

↓

Relaxation superoperator
(extreme narrowing regime)



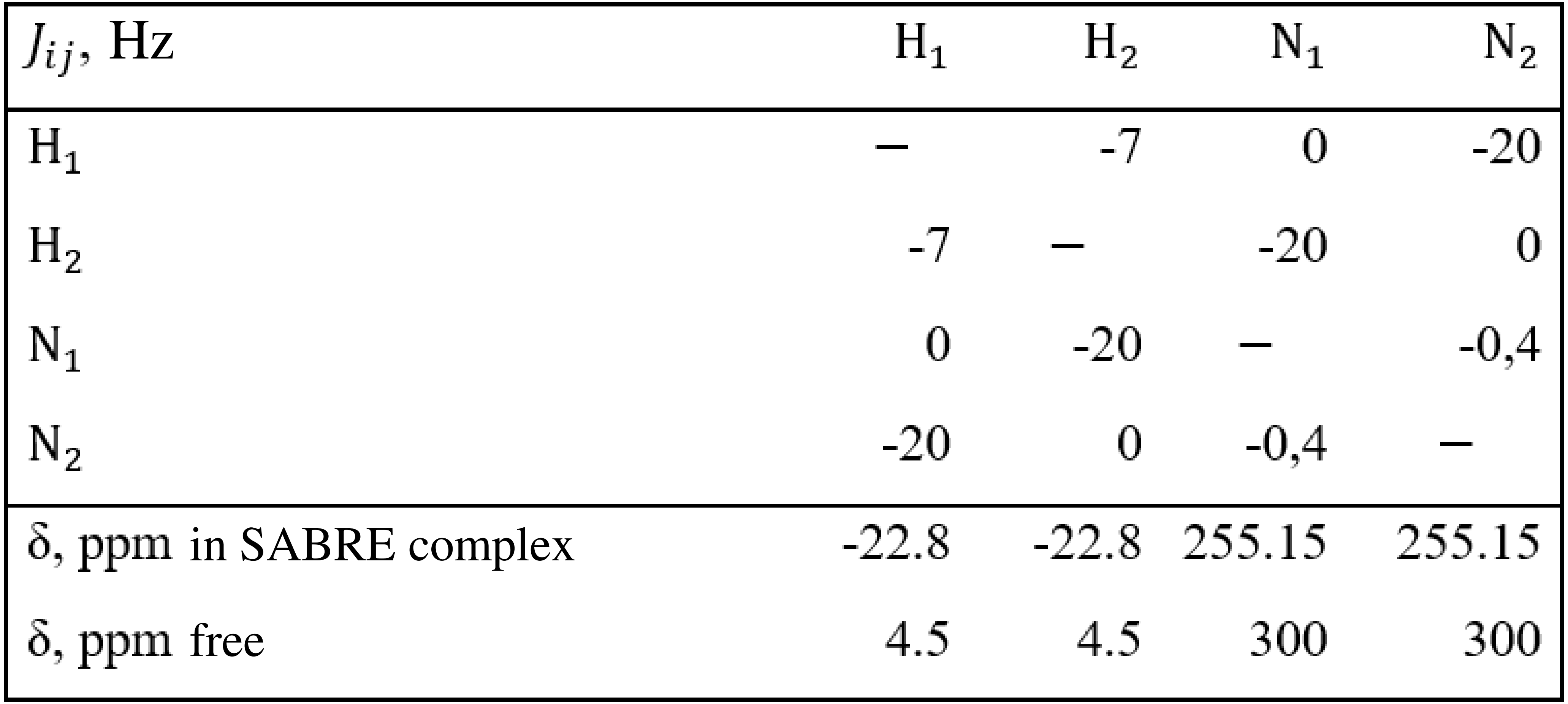
$$J_{ij,mn} = \sum_{k=1}^{n}\sum_{q=x,y,z}\frac{1}{T_{1,k}}\langle i|\hat{I}_{kq}|j\rangle\langle n|\hat{I}_{kq}|m\rangle$$ → Spectral density

$$Tr\{\hat{\rho}_C\} = \frac{[C]}{[C]+[S]}, \; Tr\{\hat{\rho}_S\} = \frac{[S]}{[C]+[S]}$$ → Density matrix normalization

$$T_1^{IrH} = 1 \text{ s}, T_1^{bS} = 3 \text{ s}, T_1^{fS} = 30 \text{ s}$$

Extra slides

Spin-coupling constants



J_{ij}, Hz	H_1	H_2	N_1	N_2
H_1	–	-7	0	-20
H_2	-7	–	-20	0
N_1	0	-20	–	-0,4
N_2	-20	0	-0,4	–
δ, ppm in SABRE complex	-22.8	-22.8	255.15	255.15
δ, ppm free	4.5	4.5	300	300