Solid-state NMR advanced concepts I

Barth van Rossum, 08.06.2009

Overview

- dipolar interaction
  - Hamiltonian
  - recoupling
  - dipolar truncation

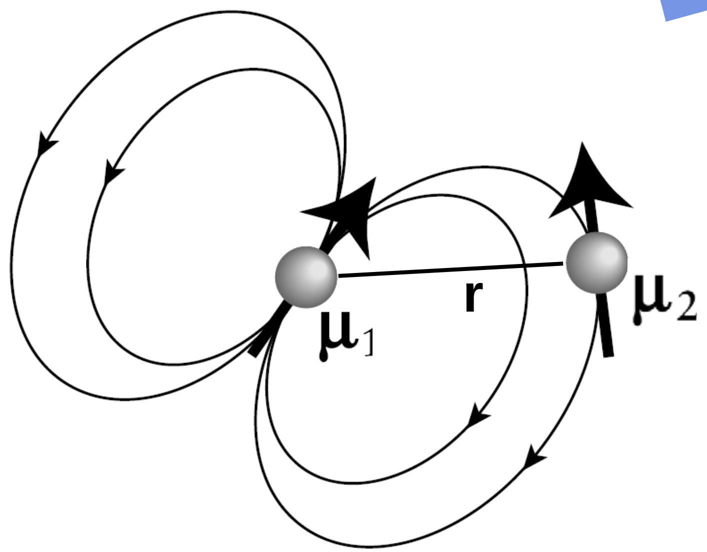
cross polarization (CP) - part II

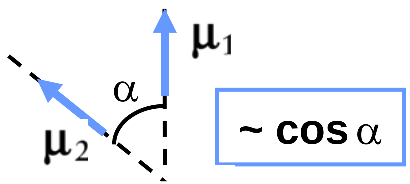
DNP (dynamic nuclear polarization)

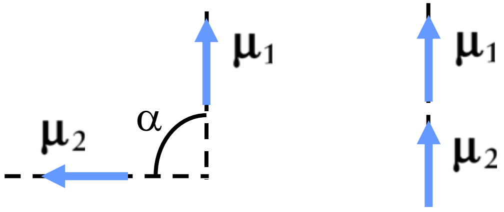
Dipolar interaction

the dipolar coupling is the interaction between two magnetic moments μ_1 and μ_2

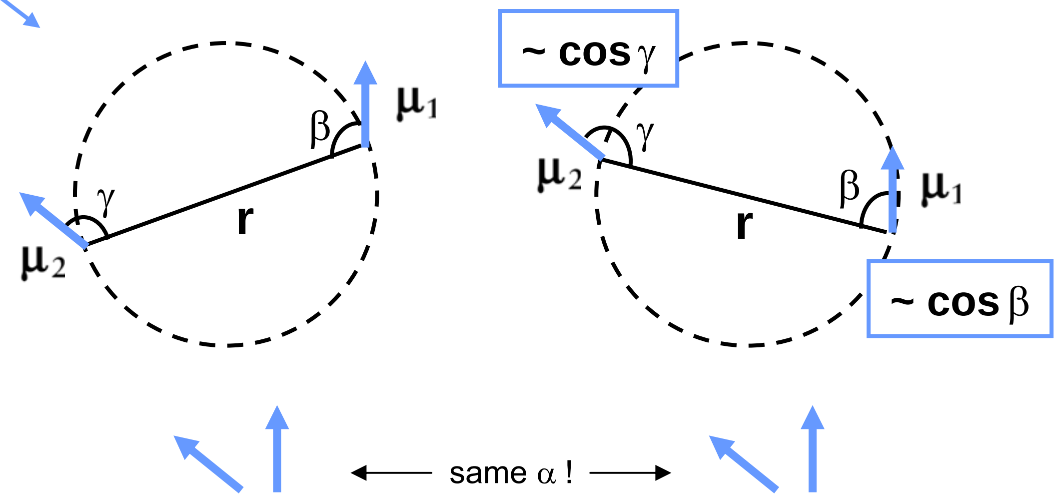
$$U = \left\{ \frac{\boldsymbol{\mu}_1 \cdot \boldsymbol{\mu}_2}{r^3} - 3\frac{(\boldsymbol{\mu}_1 \cdot \mathbf{r})(\boldsymbol{\mu}_2 \cdot \mathbf{r})}{r^5} \right\} \frac{\mu_0}{4\pi}$$





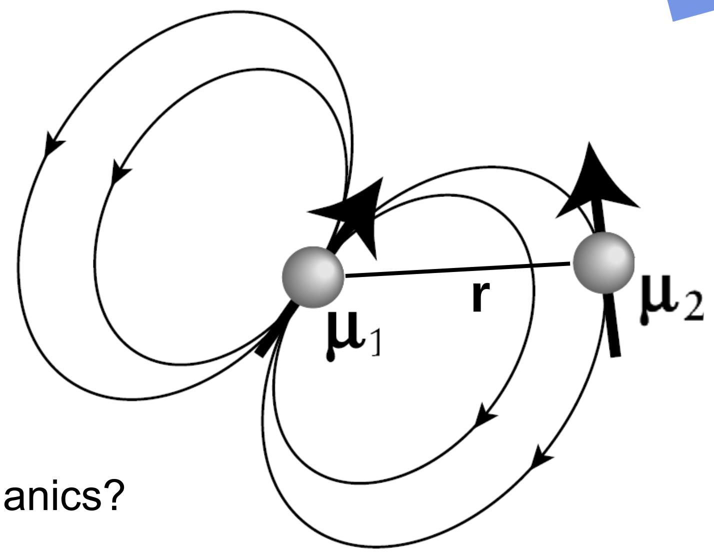


zero for α = 90°   max for α = 0°



Dipolar interaction

the dipolar coupling is the interaction between two magnetic moments μ_1 and μ_2



$$U = \left\{ \frac{\boldsymbol{\mu}_1 \cdot \boldsymbol{\mu}_2}{r^3} - 3\frac{(\boldsymbol{\mu}_1 \cdot \mathbf{r})(\boldsymbol{\mu}_2 \cdot \mathbf{r})}{r^5} \right\} \frac{\mu_0}{4\pi}$$

how does the dipolar coupling look in quantum mechanics?

$$\mu \rightarrow \hat{\mu} = \gamma \hbar \,\hat{\mathbf{I}}$$

(correspondence principle)

$$\hat{H}_{\mathrm{dd}} = -\left(\frac{\mu_0}{4\pi}\right)\gamma_I \gamma_S \hbar \left(\frac{\mathbf{I}\cdot\mathbf{S}}{r^3} - 3\frac{(\mathbf{I}\cdot\mathbf{r})(\mathbf{S}\cdot\mathbf{r})}{r^5}\right)$$

Dipolar interaction

$$\hat{H}_{\mathrm{dd}} = -\left(\frac{\mu_0}{4\pi}\right)\gamma_I \gamma_S \hbar \left(\frac{\mathbf{I}\cdot\mathbf{S}}{r^3} - 3\frac{(\mathbf{I}\cdot\mathbf{r})(\mathbf{S}\cdot\mathbf{r})}{r^5}\right)$$

$$\hat{H}_{\mathrm{dd}} = -\left(\frac{\mu_0}{4\pi}\right)\frac{\gamma_I \gamma_S \hbar}{r^3}[A + B + C + D + E + F]$$

“dipolar alphabet”

$$A = \hat{I}_z \hat{S}_z (3\cos^2\theta - 1)$$

$$B = -\frac{1}{2}(\hat{I}_x \hat{S}_x + \hat{I}_y \hat{S}_y)(3\cos^2\theta - 1)$$

$$C = -\frac{3}{2}[\hat{I}_z \hat{S}_+ + \hat{I}_+ \hat{S}_z]\sin\theta\cos\theta\, \mathrm{e}^{-i\phi}$$

$$D = -\frac{3}{2}[\hat{I}_z \hat{S}_- + \hat{I}_- \hat{S}_z]\sin\theta\cos\theta\, \mathrm{e}^{+i\phi}$$

$$E = -\frac{3}{4}[\hat{I}_+ \hat{S}_+]\sin^2\theta\, \mathrm{e}^{-2i\phi}$$

$$F = -\frac{3}{4}[\hat{I}_- \hat{S}_-]\sin^2\theta\, \mathrm{e}^{+2i\phi}$$

Dipolar interaction

Zeeman interaction (~500 MHz) >> dipolar interaction (~50 kHz)

Only terms that commute with Zeeman interaction (I_z) remain

A, *B* – terms:

commute with I_z (“secular terms”) → no time evolution under I_z

C, *D*, *E*, *F* – terms:

do not commute with I_z (“non-secular terms”) → time evolution under I_z

→ averaged to zero

→ ‘truncation’ or ‘quenching’

Dipolar interaction

truncated

$$\hat{H}_{\mathrm{dd}} = -\left(\frac{\mu_0}{4\pi}\right)\frac{\gamma_I \gamma_S \hbar}{r^3}\left[A + B + \cancel{C} + \cancel{D} + \cancel{E} + \cancel{F}\right]$$

$$\hat{H}_{\mathrm{dd}}^{\mathrm{homo}} = -\left(\frac{\mu_0}{4\pi}\right)\frac{\gamma_I \gamma_S \hbar}{r^3}\left(3\cos^2\theta - 1\right)\left[\hat{I}_z\hat{S}_z - \frac{1}{2}\left(\hat{I}_x\hat{S}_x + \hat{I}_y\hat{S}_y\right)\right]$$

B-term only relevant when $\omega_I \sim \omega_S$

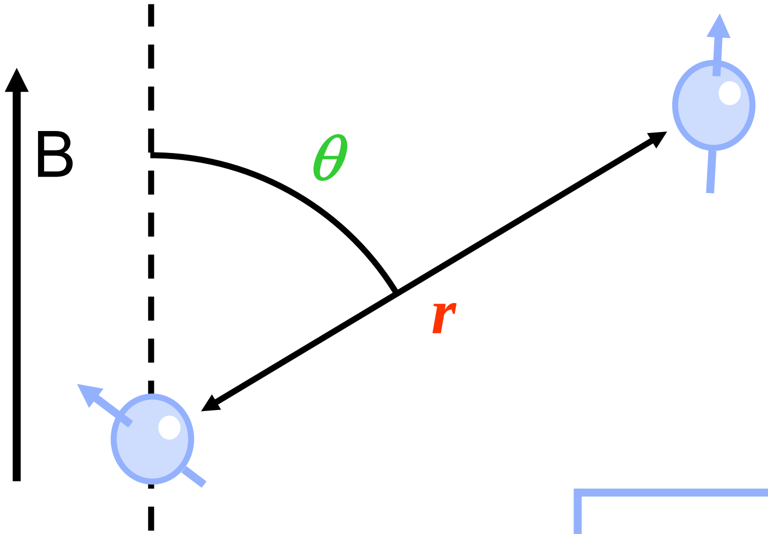
homonuclear case (e.g.^{1}H-^{1}H) → *B*-term

heteronuclear case (e.g. ^{1}H-^{13}C) → ~~*B*-term~~

r and θ : spatial parameters

$$\hat{H}_{\mathrm{dd}}^{\mathrm{hetero}} = -\left(\frac{\mu_0}{4\pi}\right)\frac{\gamma_I \gamma_S \hbar}{r^3}\left(3\cos^2\theta - 1\right)\hat{I}_z\hat{S}_z$$

Dipolar interaction



the dipolar coupling depends on :

- the distance between the spins (*r*)
- the angle θ between the magnetic field **B** and the vector connecting the spins

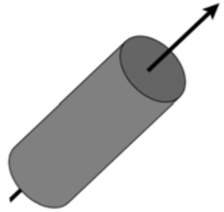
$$D \propto \frac{1}{r^3}\left(\underbrace{3\cos^2\theta - 1}\right)$$

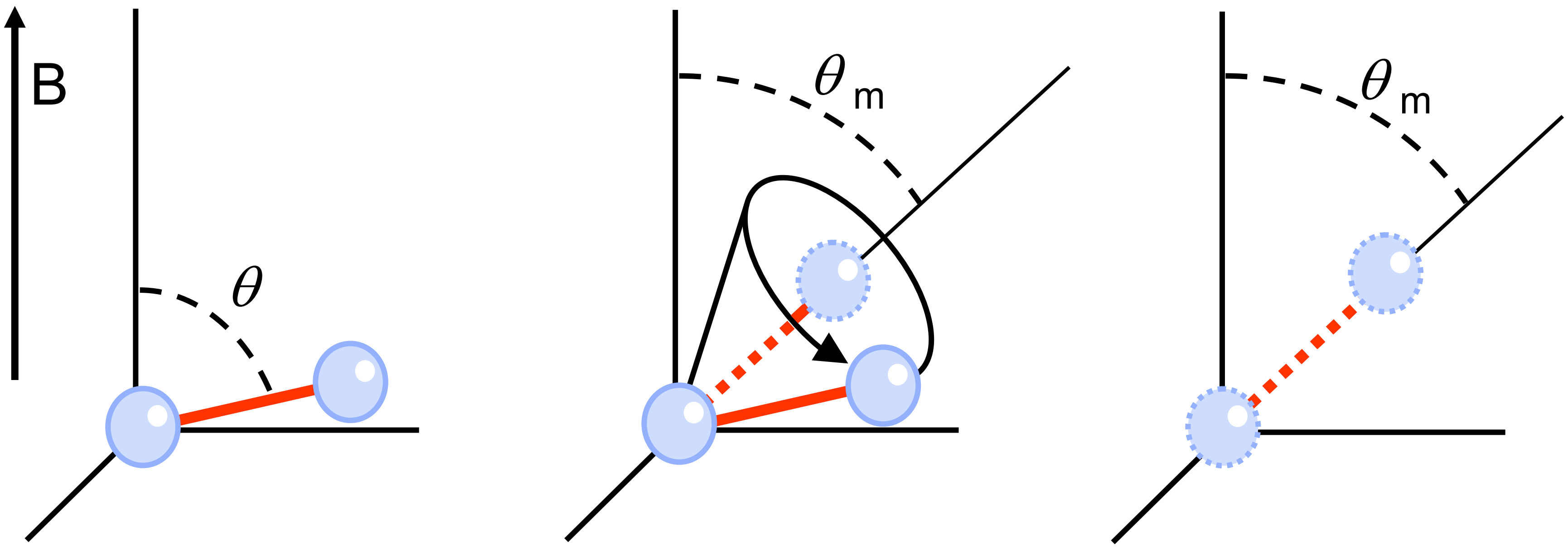
$$\langle 3\cos^2\theta - 1 \rangle \begin{cases} = 0 & \text{in isotropic liquids} \\ \neq 0 & \text{in solids or oriented media} \end{cases}$$

Dipolar interaction

under magic angle spinning, the average angle

between the connection vector and B is the magic angle θ_m



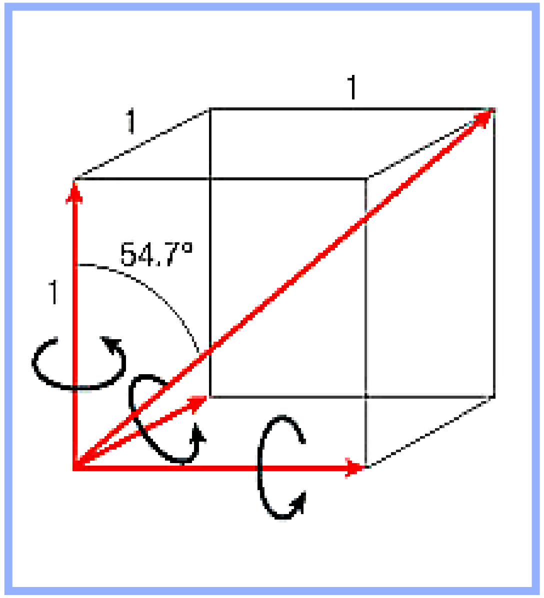


$$3\cos^2\theta - 1 \neq 0$$

$$3\cos^2\theta_m - 1 = 0$$

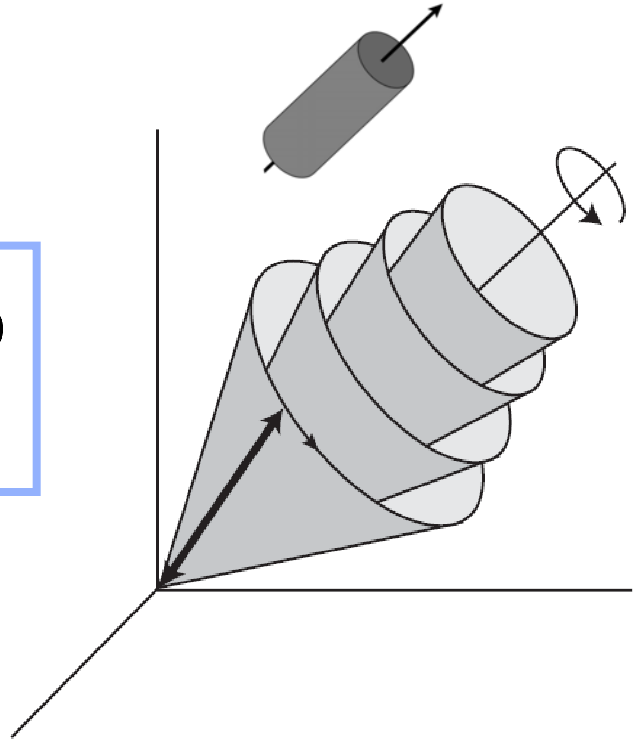
Dipolar interaction

The time average of every spin-pair has the connecting vector at the magic-angle → time average is zero for $\theta = 54.7°$



$$3\cos^2\theta_m - 1 = 0$$

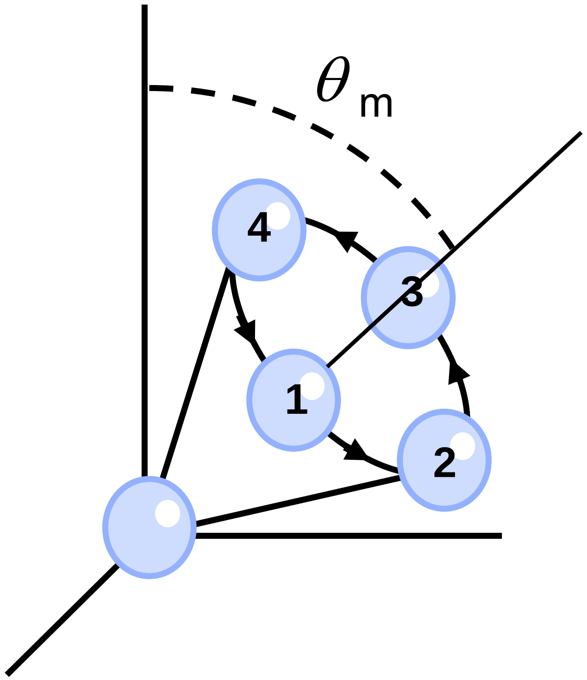
$$\theta = 54.7°$$

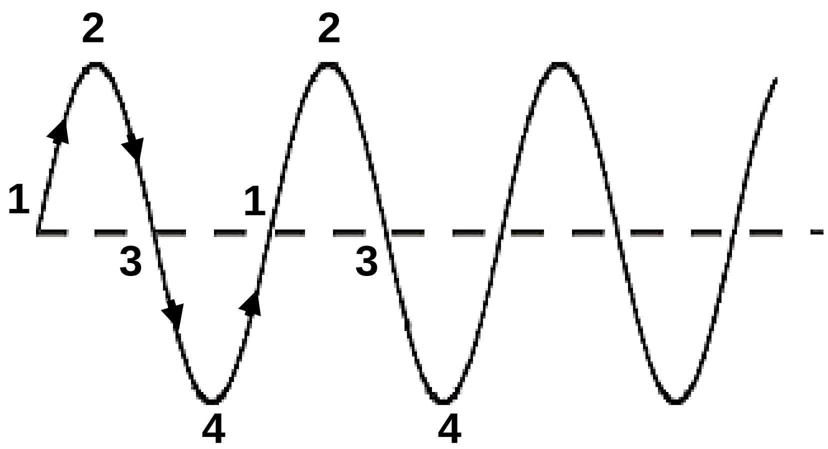


Dipolar interaction

Note: the time average is zero, **not** the dipolar coupling itself

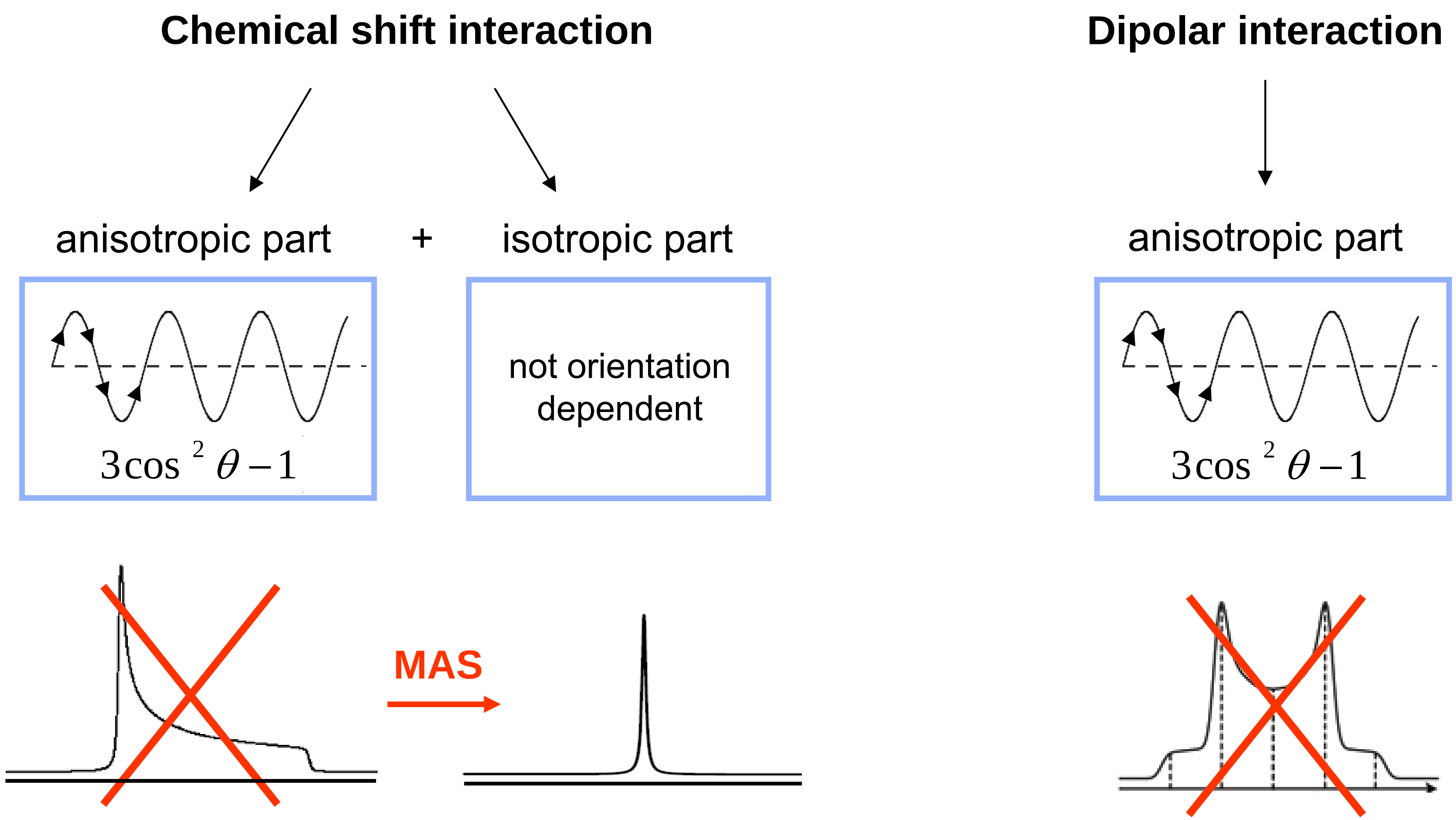
the dipolar interaction is time dependent and oscillates around 0





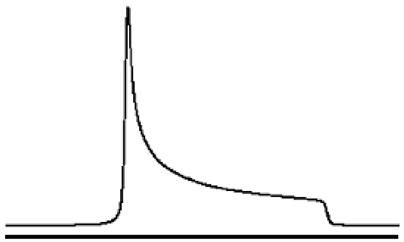
Interaction under MAS

Similar considerations can be made for any interaction that contains the $3\cos^2\theta - 1$ term, like the chemical shift interaction



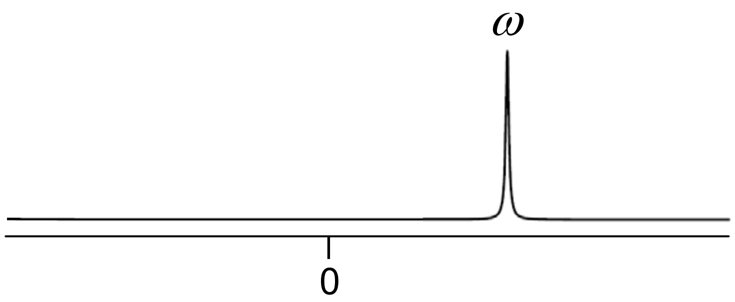
-intermezzo-

Chemical shift interaction

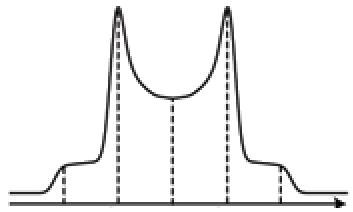


time evolution:

$$\propto e^{i\omega t}$$



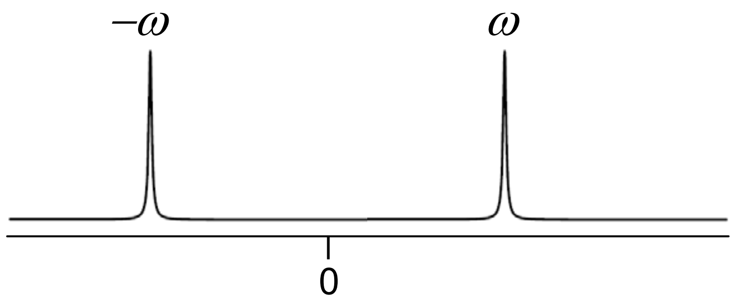
Dipolar interaction



time evolution:

$$\propto \cos \omega t$$

$$= \frac{e^{i\omega t} + e^{-i\omega t}}{2}$$



Interaction under MAS

MAS efficiently suppresses chemical shift anisotropy

→ high-resolution ^{13}C and ^{15}N spectra

concerning dipolar interactions, MAS generally does not give what you would like…

this is what you want…		… and this is what you get!		
✗	^{13}C - ^{1}H (resolution)	✔	^{13}C - ^{1}H	← **de**coupling
✗	^{1}H -^{1}H (resolution)	✔	^{1}H -^{1}H	← **de**coupling or ^{2}H
✔	^{13}C-^{13}C (correlations)	✗	^{13}C-^{13}C	← **re**coupling

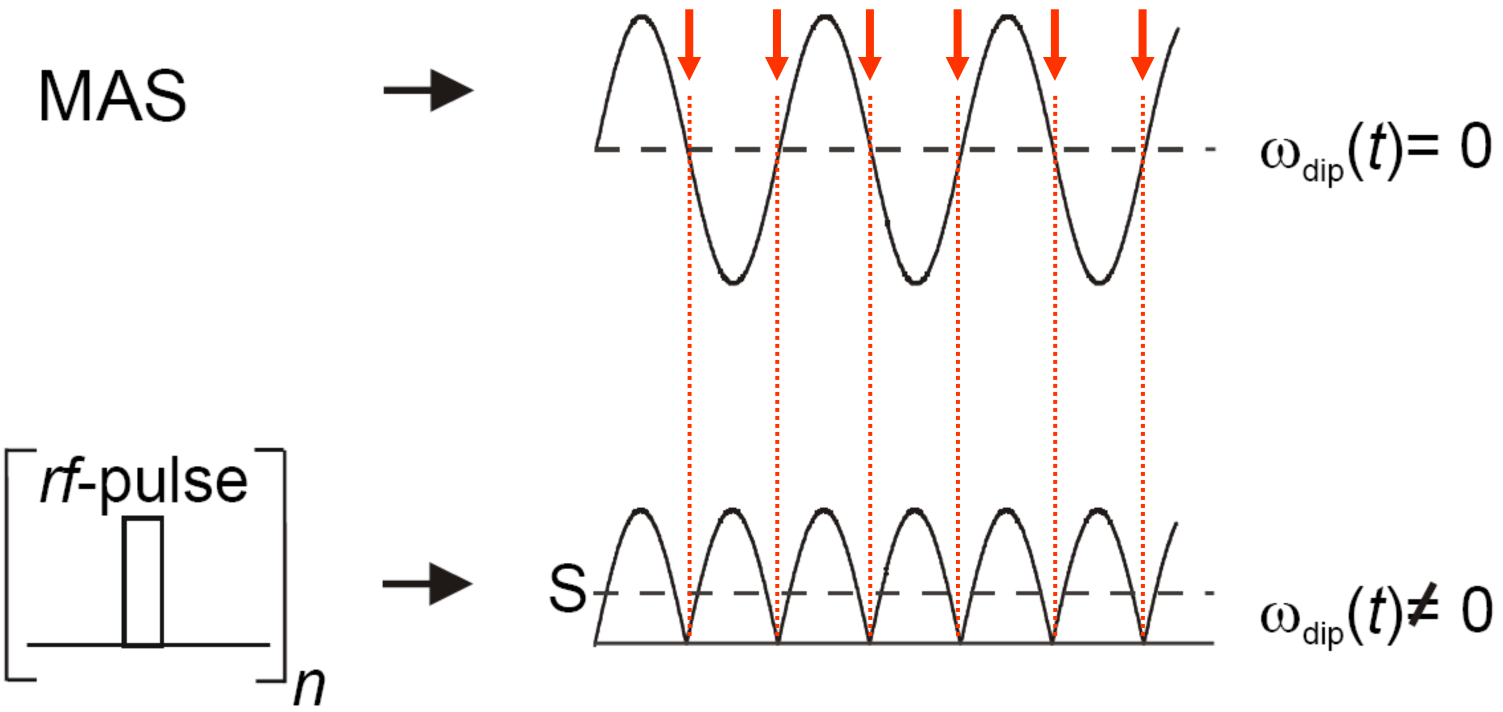
the invention of recoupling sequences formed an integral part of the solid-state NMR research (and snobbishness) during the last decade

… and each new one was better, and even more better. And even better than the one that was already better…no this one is really better than the others. No! this one is better, it is the best! bla bla etc...(Hey, heck, nobody is using this sequence called USEME!)

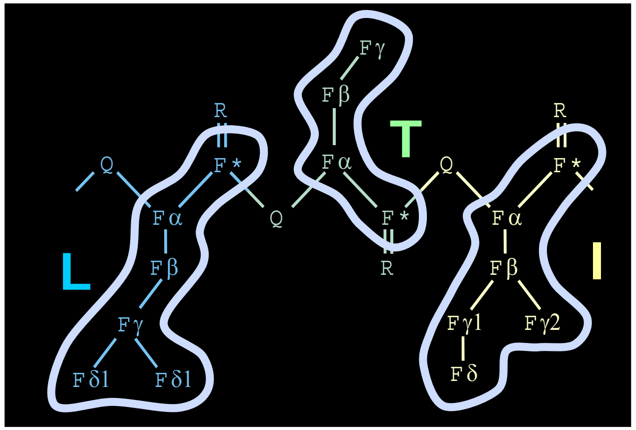
Recoupling

The time-average of the dipolar coupling is zero

but **not** the instantaneous coupling, it is oscillating around zero



Recoupling



recoupling techniques are useful for **short-range** transfer (e.g., for assignment of spin systems)

only for pair-wise isotope labelling, highly accurate distance information can be obtained

$$D \propto \frac{1}{r^3}\left(3\cos^2\theta - 1\right)$$

however, distance information is more difficult to obtain if more than two spins interact

in particular, for uniform isotope labelling, long range transfer is difficult due to **dipolar truncation** effects

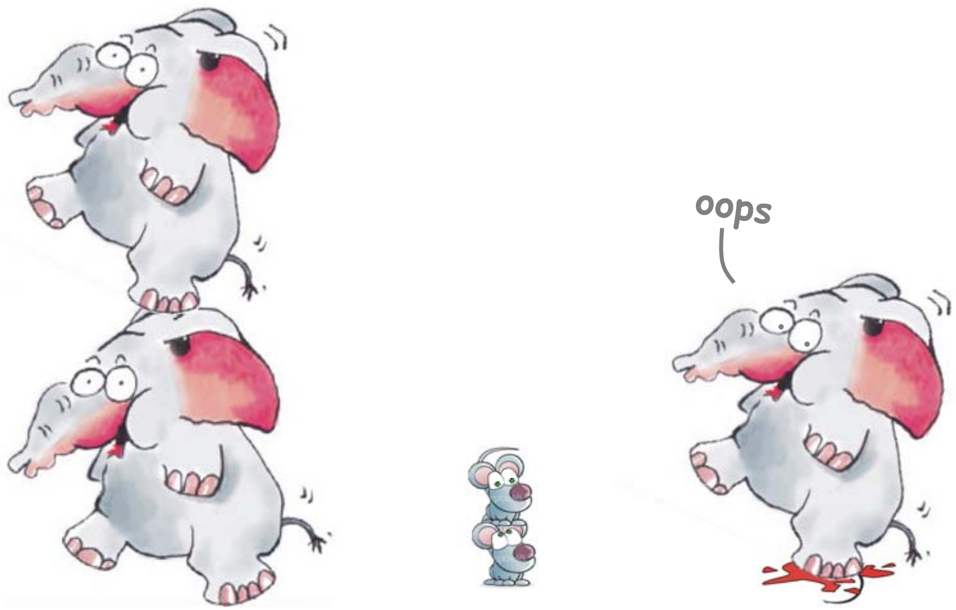
Dipolar truncation

the phenomenon that weak couplings are ‘quenched’ by the strong couplings

→ weak couplings contain the long-range distance information

$$D \propto \frac{1}{r^3}\left(3\cos^2\theta - 1\right)$$

The layman’s view on dipolar truncation



“strong coupling” **“weak coupling”**

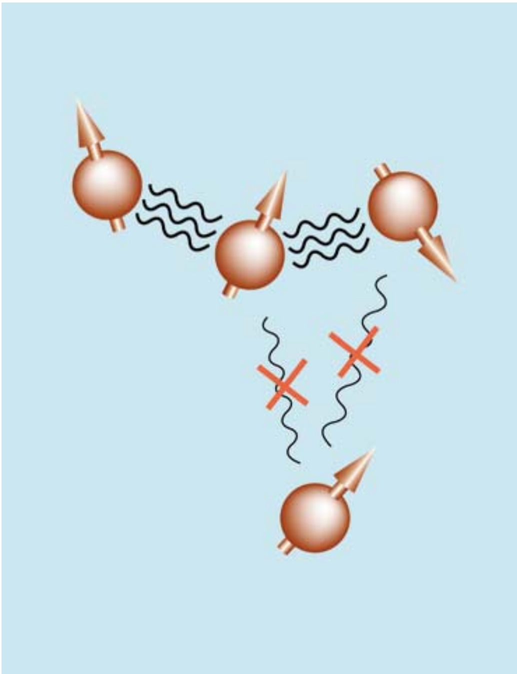
Dipolar truncation

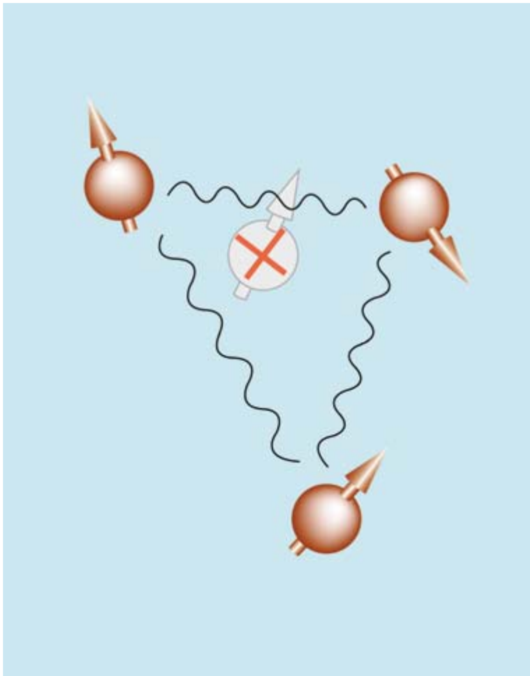
the phenomenon that weak couplings are 'quenched' by the strong couplings

→ weak couplings contain the long-range distance information

→ spin dilution

$$D \propto \frac{1}{r^3}\left(3\cos^2\theta - 1\right)$$





note: pair-wise labelling is maximal spin dilution

Dipolar truncation

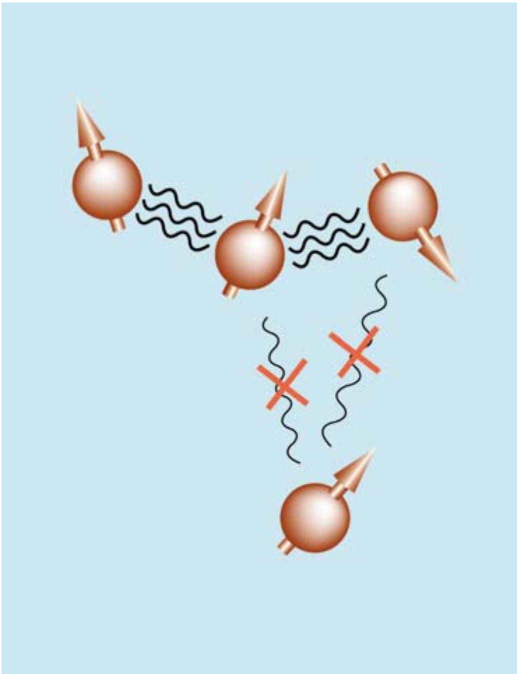
the phenomenon that weak couplings are 'quenched' by the strong couplings

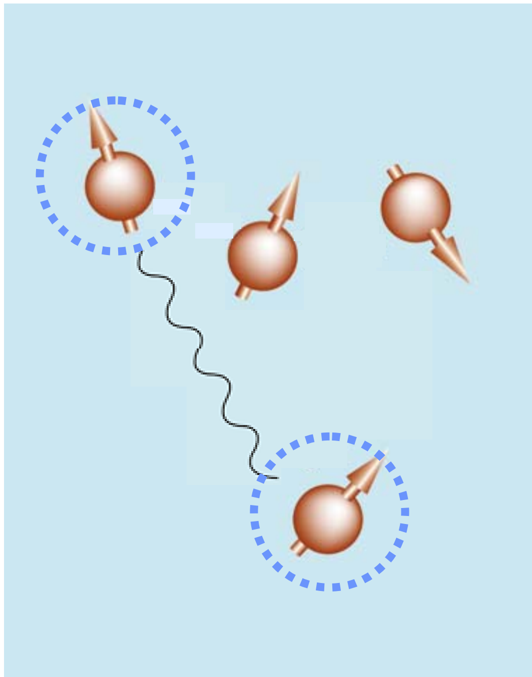
→ weak couplings contain the long-range distance information

→ spin dilution

→ selective recoupling

$$D \propto \frac{1}{r^3}\left(3\cos^2\theta - 1\right)$$



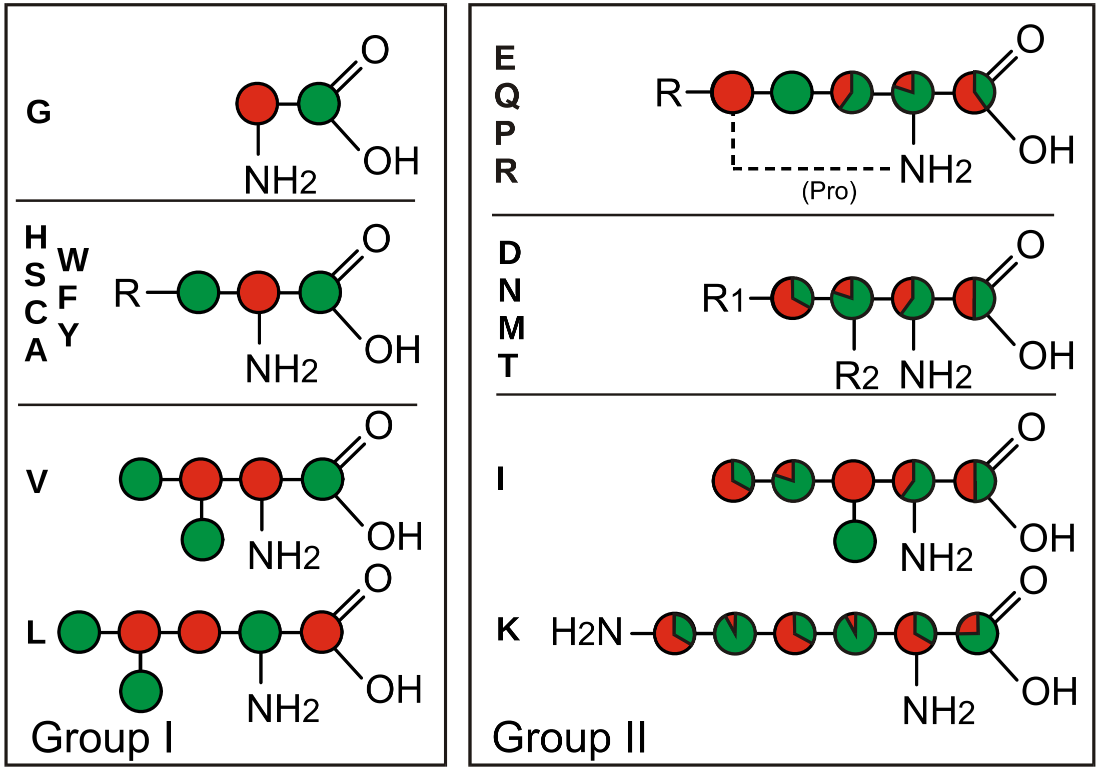


Extensive ^{13}C labelling to reduce dipolar truncation

amino-acid labelling bacteria grown on:

1,3-^{13}C glycerol (green)

or 2-^{13}C glycerol (red)



labelling mostly alternating

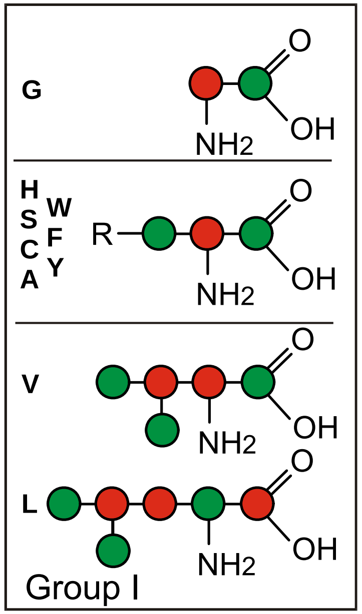
→ strong couplings removed

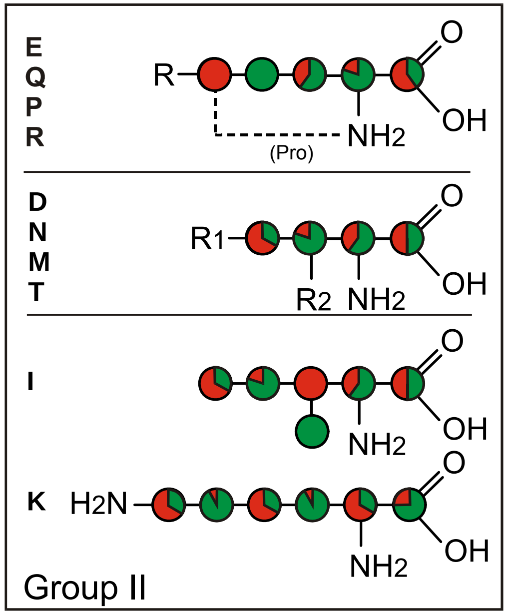
→ weak couplings not quenched

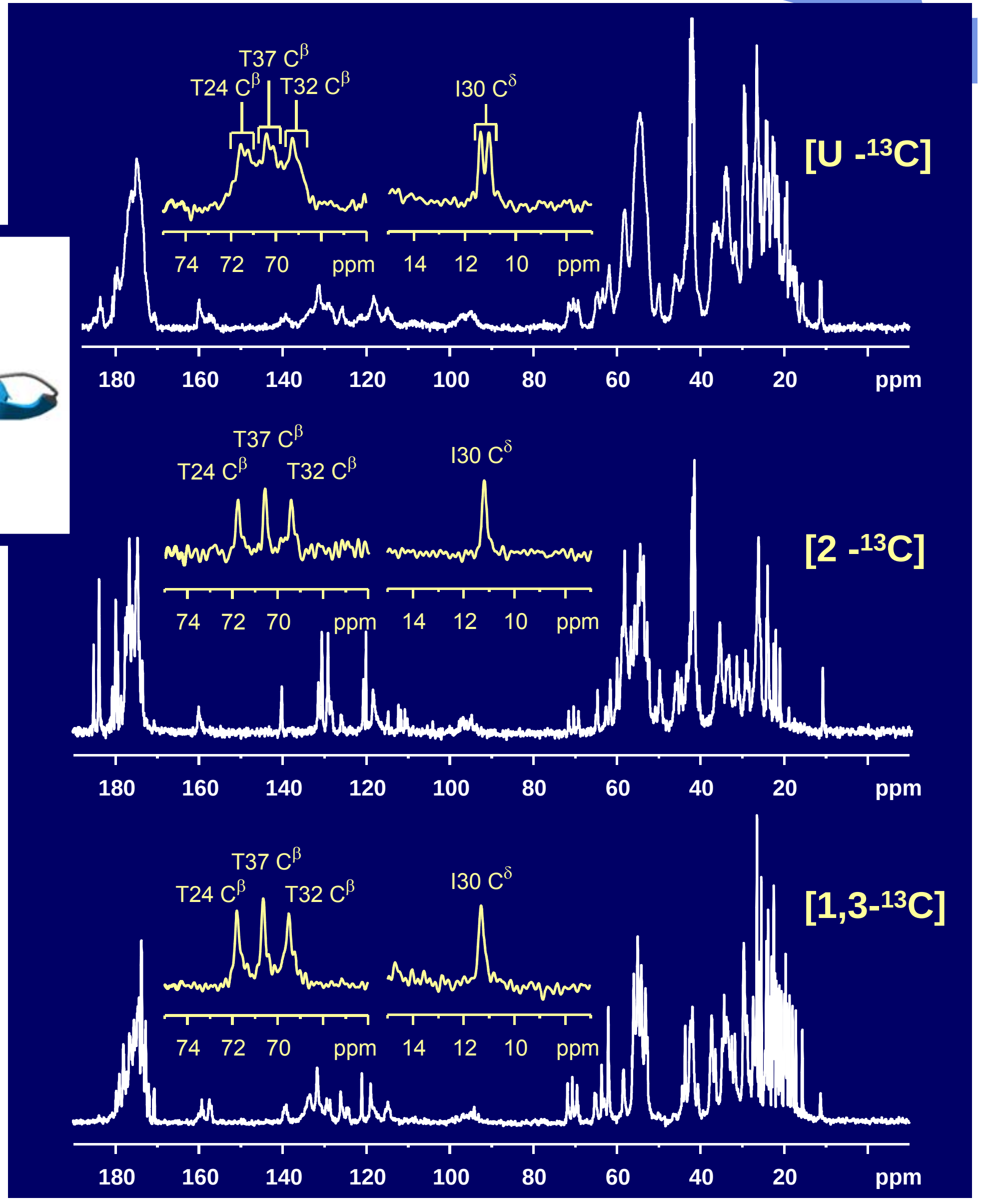
however, analytical treatment will still be extremely difficult

Extensive ^{13}C labelling to reduce dipolar truncation

- → less signals in the spectra
- → partial suppression of *J*-couplings
- → less assignment options







Overview

dipolar interaction

- Hamiltonian
- recoupling
- dipolar truncation

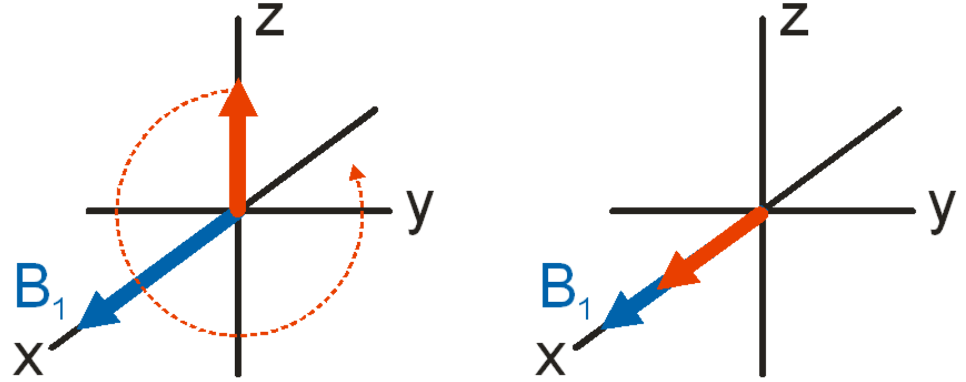
cross polarization (CP) - part II

DNP (dynamic nuclear polarization)

Cross polarization (CP) – part II

first to refresh your memory:

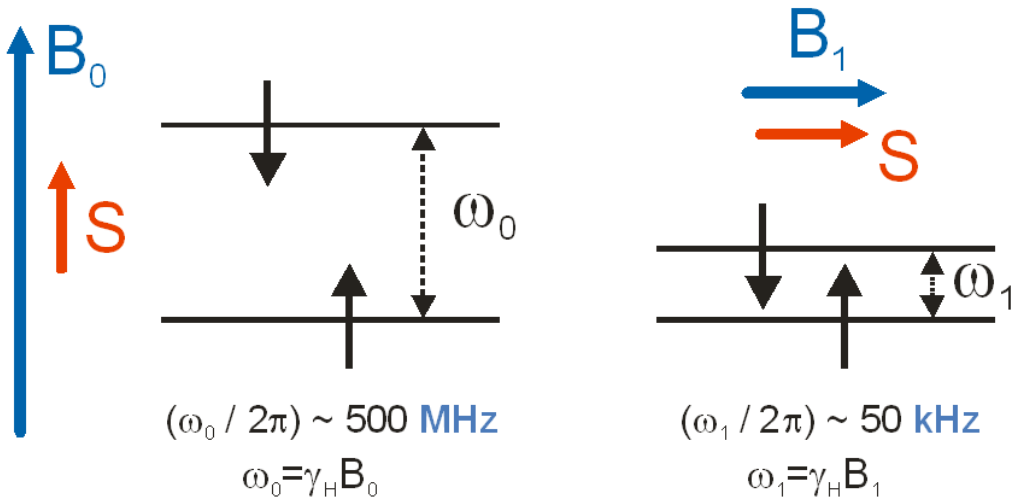
during CP, both spin-types (^{1}H and ^{13}C) are ‘**spin-locked**’



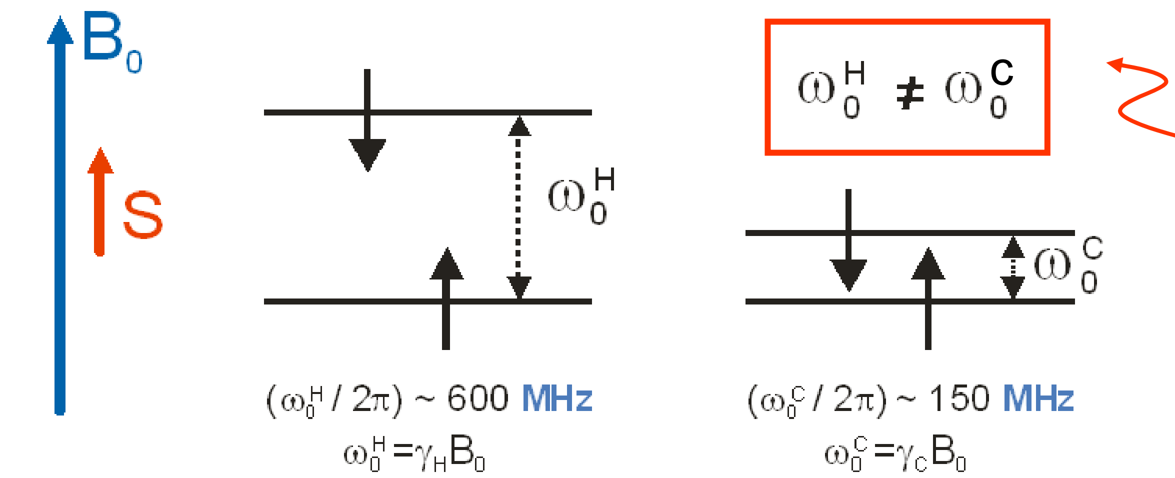
pulse :
spins rotate

spin-lock pulse:
spins are trapped

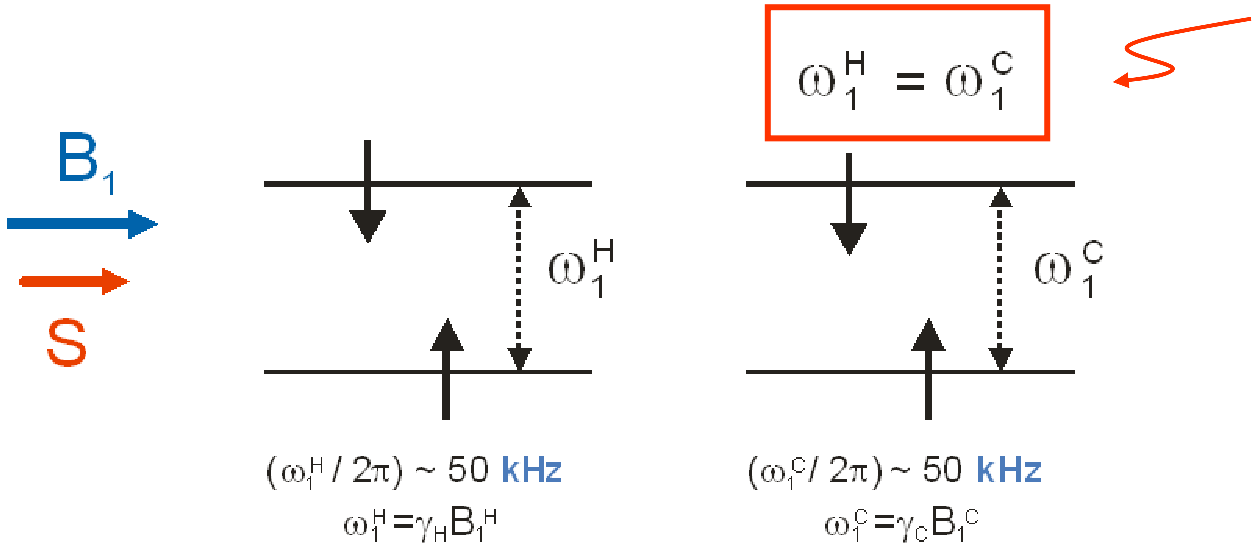
like the Zeeman interaction, the spin-lock pulse gives rise to a **splitting** (spin up, spin down)



Cross polarization (CP) – part II



since B_0, γ_H and γ_C are all fixed, the Zeeman splitting is different for ^1H and ^{13}C …



… however, the spin-lock fields B_1^H and B_1^C can be **chosen** so that the splitting for ^1H and ^{13}C becomes equal

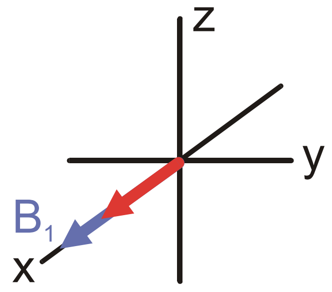
Hartmann-Hahn Matching

Cross polarization (CP) – part II

the heteronuclear dipolar interaction between ^{1}H (*I*-spins) and ^{13}C (*S*-spins) drives the polarization transfer:

$$H \sim b \cdot I_z \cdot S_z$$

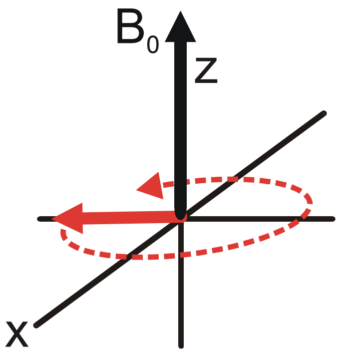
during CP, the spin lock pulses are along x-axis…



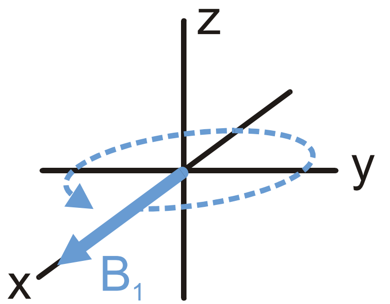
…transform to a frame that rotates around the x-axis

-intermezzo- rotating frames

in NMR, everything is rotating…



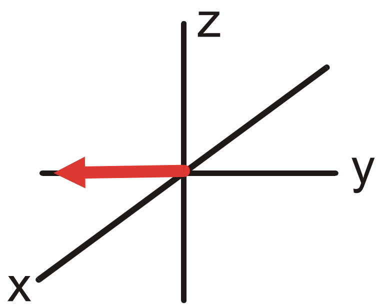
spins rotate with the Larmor frequency…

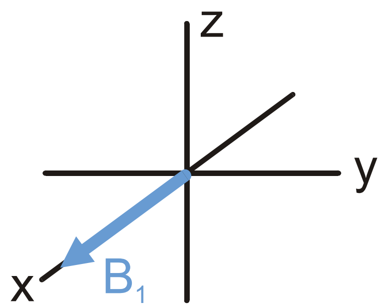


RF pulses are rotating with the Larmor frequency…

observation from a frame that rotates itself, makes everything appear static

it is as if the Zeeman interaction has ‘gone’…..



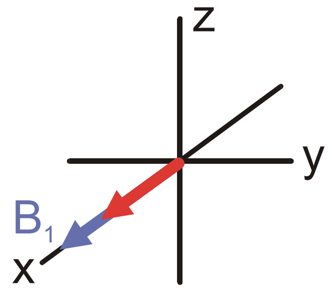


these kind of transformations are quite common in NMR (rotating frame, interaction frame…)

Cross polarization (CP) – part II

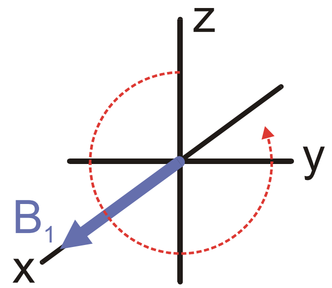
the heteronuclear dipolar interaction between ^{1}H (I-spins) and ^{13}C (S-spins) drives the polarization transfer:

$$H \sim b \cdot I_z \cdot S_z$$



during CP, the spin lock pulses are along x-axis…

…transform to a frame that rotates around the x-axis with ω_1^H (for the I spins) and ω_1^C (for the S spins)



$$H' \sim b' \cdot (I_z \cdot S_z + I_y \cdot S_y) \cos(\omega_1^H - \omega_1^C)t =$$

$$= b' \cdot (I_z \cdot S_z + I_y \cdot S_y) \qquad [\text{ for } \omega_1^H = \omega_1^C]$$

Hartmann-Hahn matching !

Cross polarization (CP) – part II

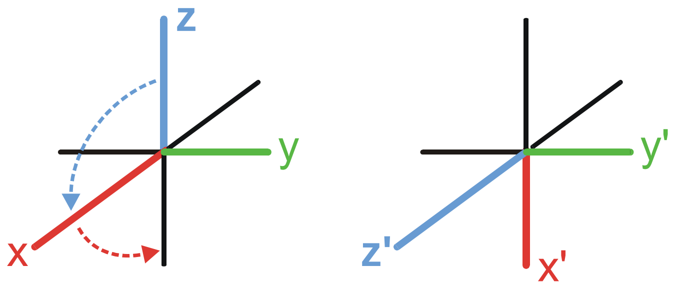
$$H' \sim b' \cdot (I_z \cdot S_z + I_y \cdot S_y)$$

the magnetization is along x-axis

→ transform to a frame with the new z' axis along the old x-axis

replace x,y,z as follows:

$$\begin{cases} x \rightarrow z' \\ y \rightarrow y' \\ z \rightarrow -x' \end{cases} \quad \text{or} \quad \begin{cases} I_x \rightarrow I_z \\ I_y \rightarrow I_y \\ I_z \rightarrow -I_x \end{cases}$$



$$H'' \sim b' \cdot (I_x \cdot S_x + I_y \cdot S_y)$$

rewrite, using raising and lowering operators:

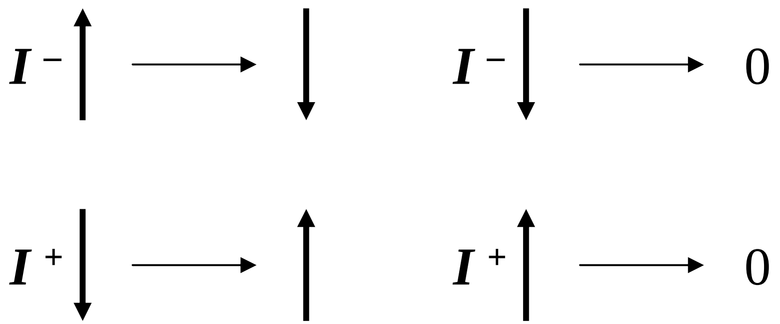
$$\begin{cases} I_x = \tfrac{1}{2} (I^+ + I^-) \\ I_y = -\tfrac{1}{2} \cdot i (I^+ - I^-) \end{cases}$$

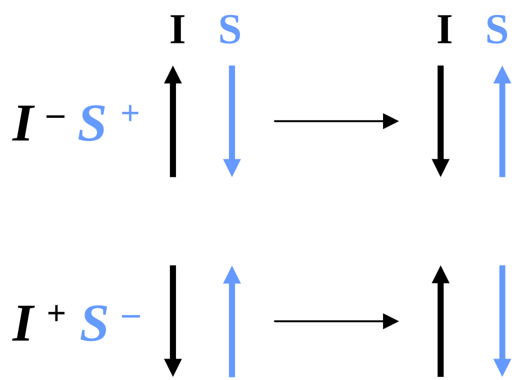
Cross polarization (CP) – part II

$$H'' = b' \cdot (I_x \cdot S_x + I_y \cdot S_y)$$

$$H'' = b' \left[\tfrac{1}{2} (I^+ + I^-) \cdot \tfrac{1}{2} (S^+ + S^-) + (-\tfrac{1}{2} \cdot i) (I^+ - I^-) \cdot (-\tfrac{1}{2} \cdot i) (S^+ - S^-) \right]$$

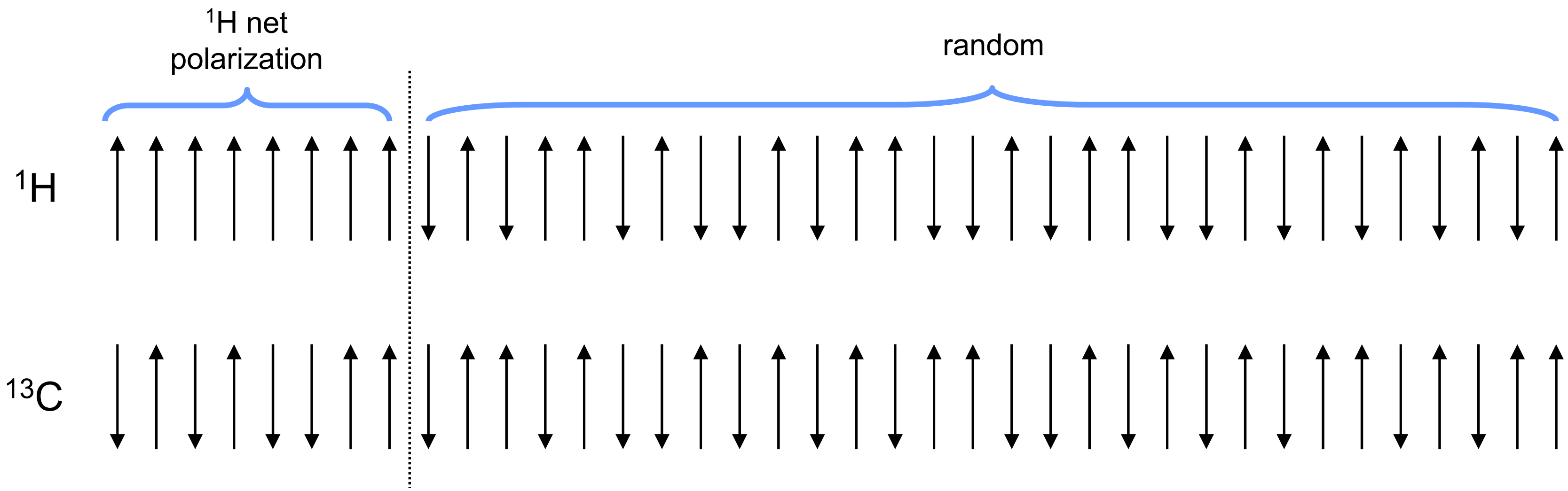
$$H'' = \tfrac{1}{2} \cdot b' (I^+ \cdot S^- + I^- \cdot S^+)$$

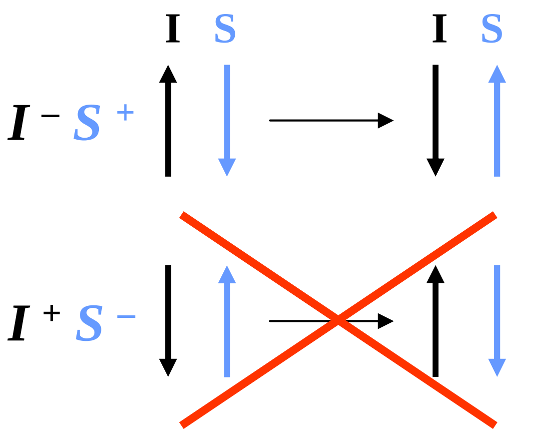




all other combinations give zero

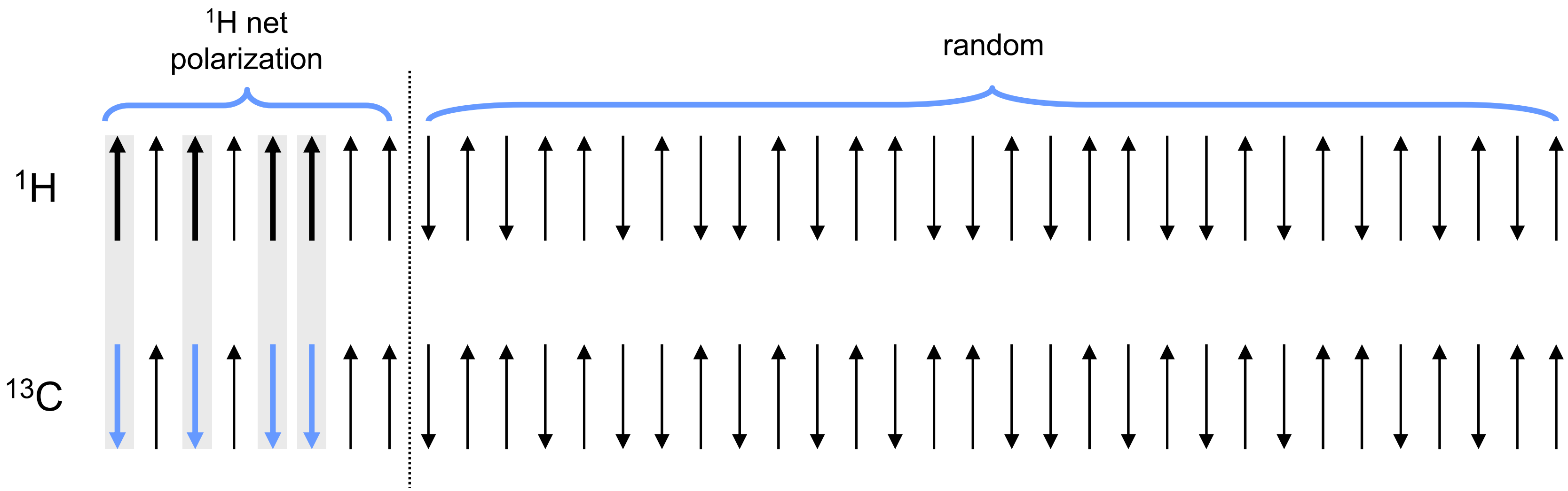
Cross polarization (CP) – part II

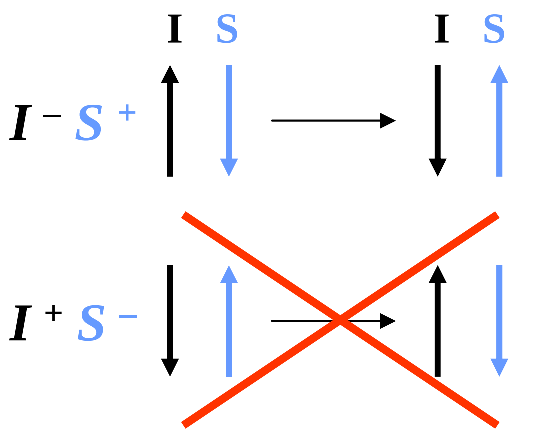




net magnetization is 'spin-up' for ^{1}H (*I*-spins)

Cross polarization (CP) – part II





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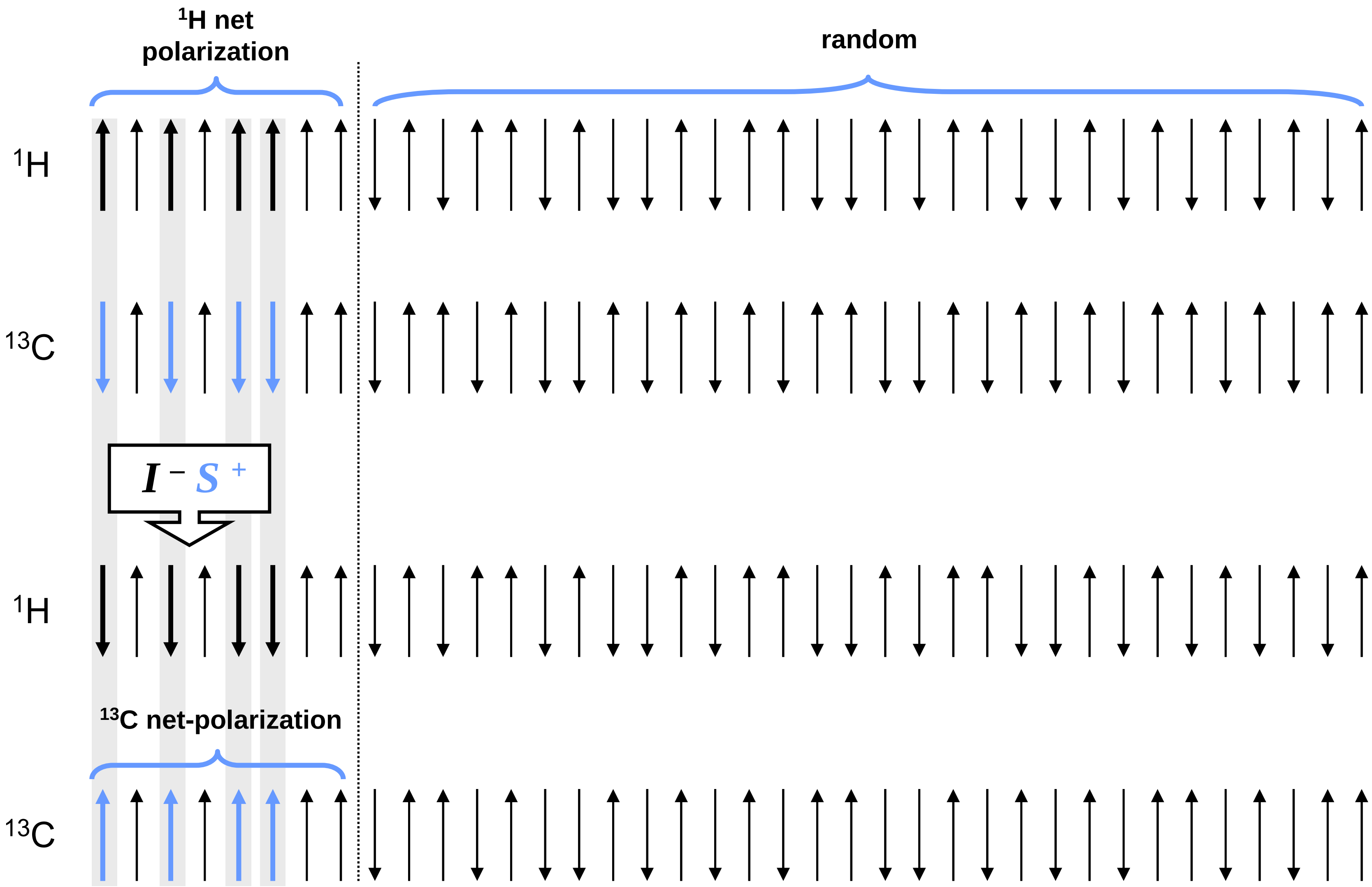


Overview

dipolar interaction

- Hamiltonian
- recoupling
- dipolar truncation

cross polarization (CP) - part II

DNP (dynamic nuclear polarization)

DNP (dynamic nuclear polarization)

Why DNP?

low sensitivity is one of the biggest bottlenecks in solid state NMR

(^{13}C detection, relatively low resolution, small amount of sample)

→ DNP is a relatively new technique to enhance the sensitivity of NMR signals

DNP (dynamic nuclear polarization)

standard cross-polarization (CP): use protons to enhance carbon signal

protons have a gamma (gyromagnetic ratio) γ_{1H} that is four times higher than γ_{13C}

CP enhancement: ~ γ_{1H} / γ_{13C} ~ 4

→ reduces time for signal averaging by factor 4^2 = 16 !

DNP: use electrons to enhance proton signal

electrons have a gamma γ_{1e} that is 660 times higher than γ_{1H}

DNP enhancement: ~ γ_{1e} / γ_{1H} ~ 660

→ reduces time for signal averaging by factor 660^2 = …

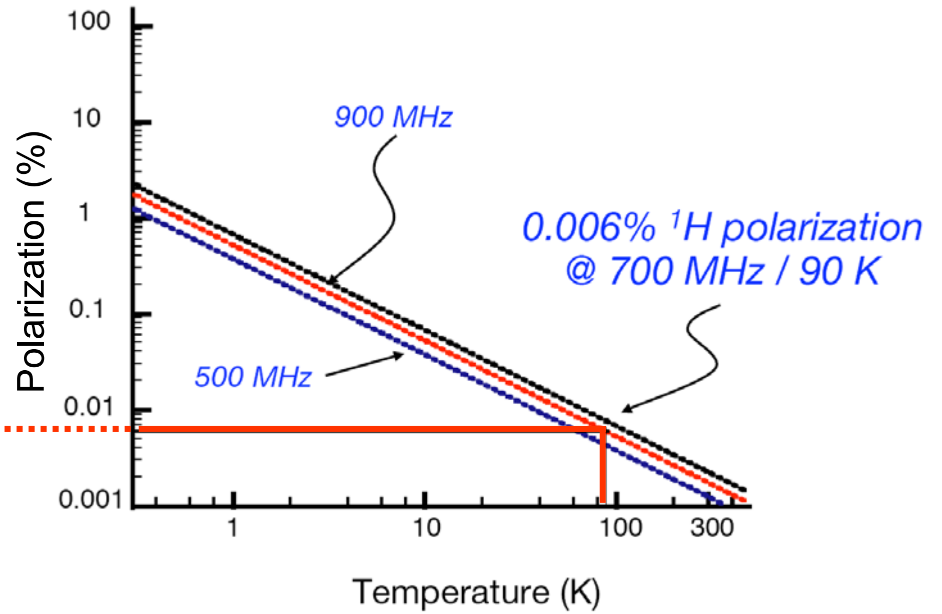
DNP (dynamic nuclear polarization)

at 300K: ~0.002% of the protons are polarized (one ^{1}H out of 50,000)

at 90K: ~0.006% of the protons are polarized (one ^{1}H out of 17,000)

experiments performed at low temperature → higher Boltzmann population
→ higher sensitivity

at 90 K → increase of factor 3 due to Boltzmann population



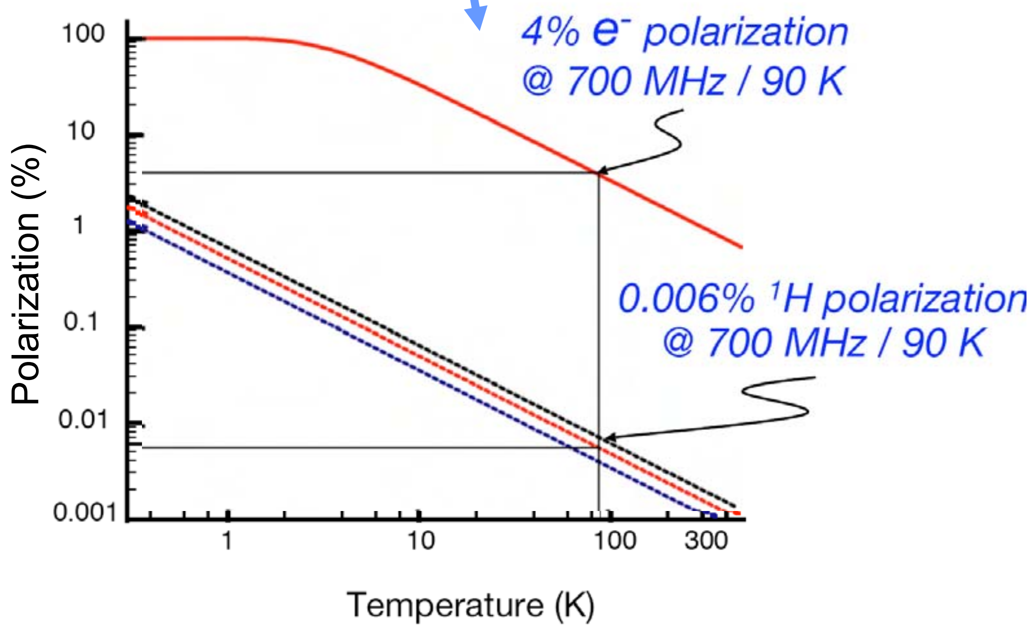
DNP (dynamic nuclear polarization)

Electrons have a much higher γ_e → higher Boltzmann population

at 90K: ~0.006% of the protons are polarized (one ^1H out of 17,000)

~4% of the electrons are polarized (one e^- out of 25)

DNP = transfer of e^- polarization into nuclear (^1H) polarization

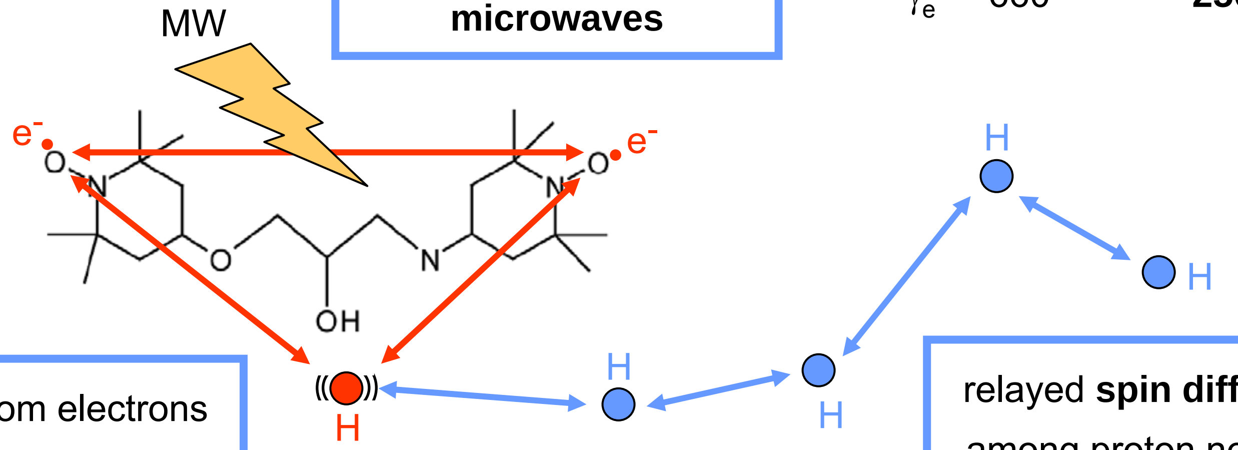


DNP (dynamic nuclear polarization)

irradiation with **microwaves**

$\gamma_{1H} = 1.00 \xrightarrow{9.5T}$ 400 MHz

$\gamma_e = 660 \longrightarrow$ **250 GHz**



transfer from electrons to nearby protons (the "**cross effect**")

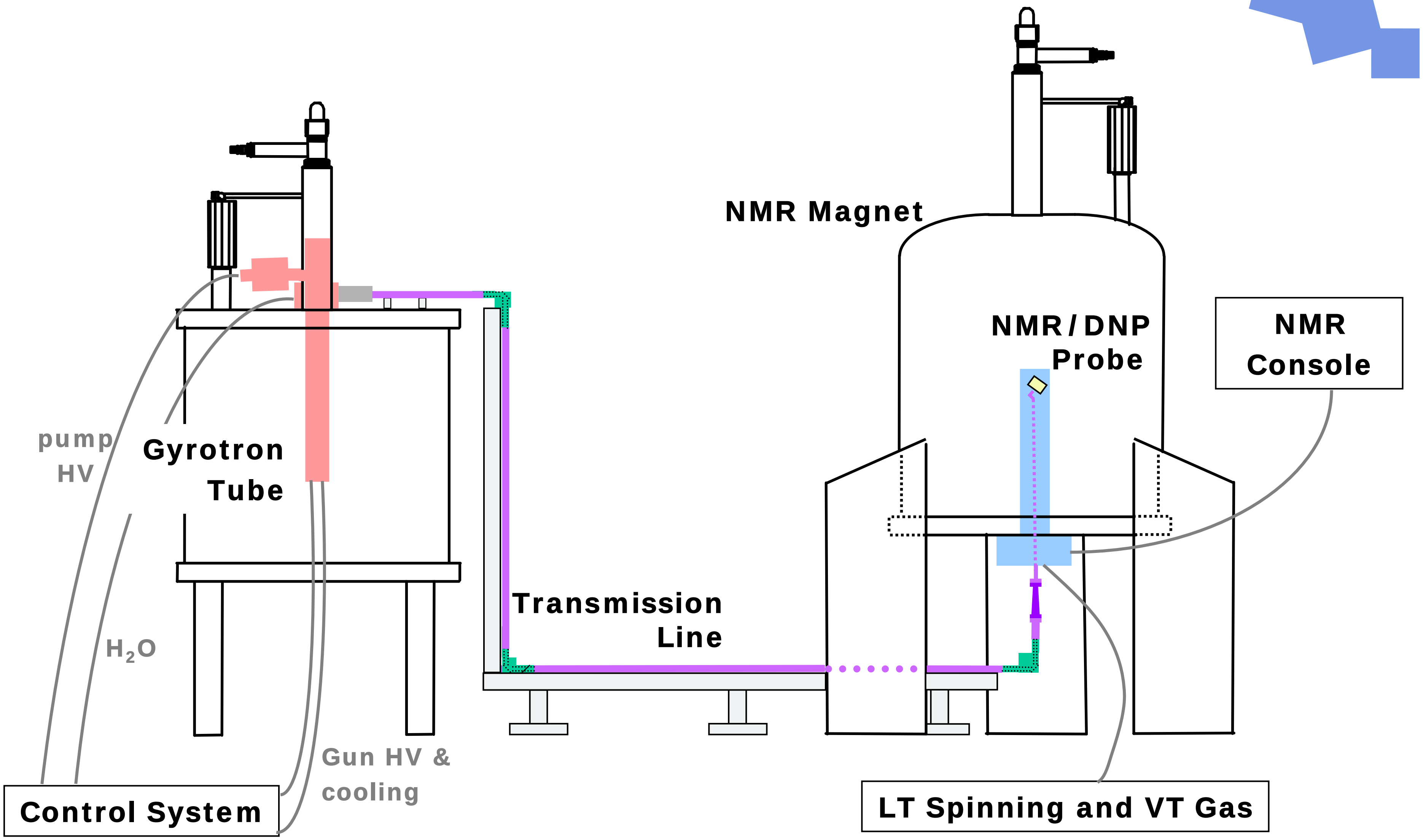
relayed **spin diffusion** among proton network

mixture of deuterated glycerol, D_2O, H_2O, biradical → provides glass forming matrix

non-glass-forming matrix → crystals formed upon freezing
→ much lower DNP enhancement

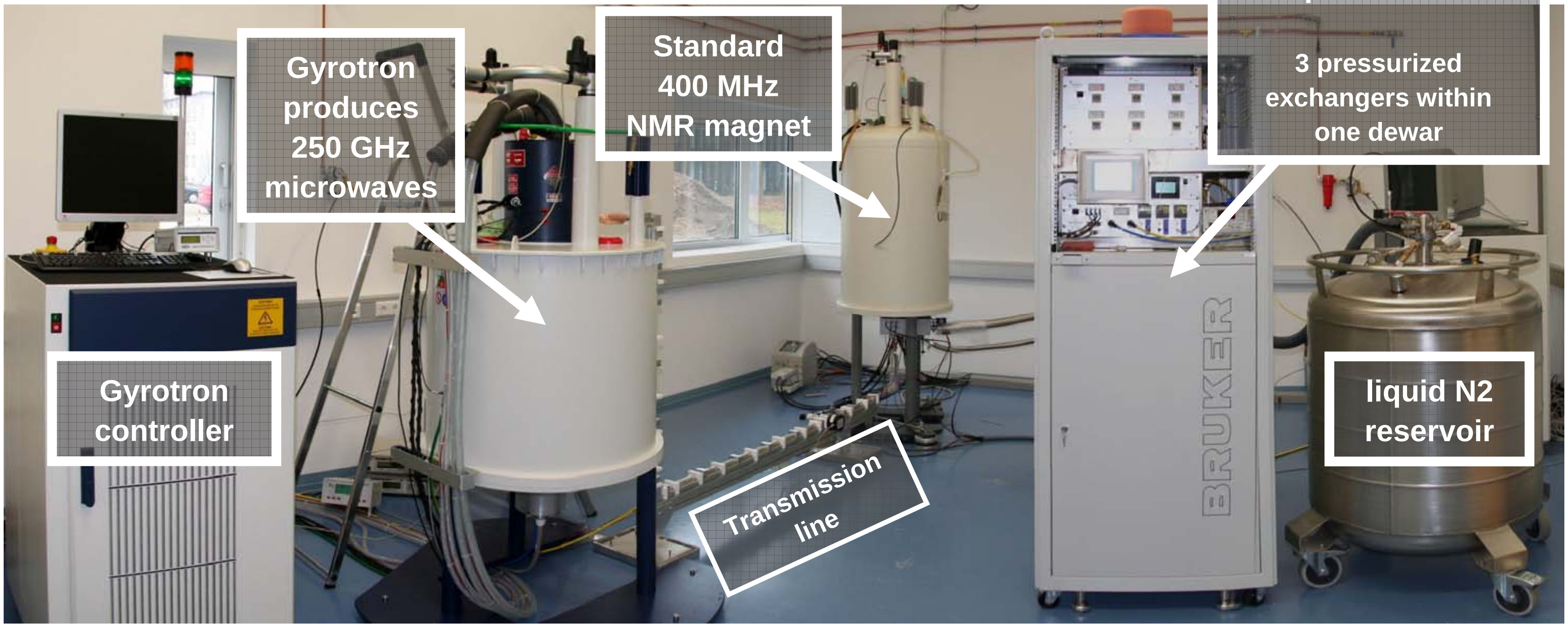
(partially) deuterated matrix → more complete polarization of smaller proton reservoir

DNP (dynamic nuclear polarization)



DNP (dynamic nuclear polarization)

DNP set up



DNP (dynamic nuclear polarization)

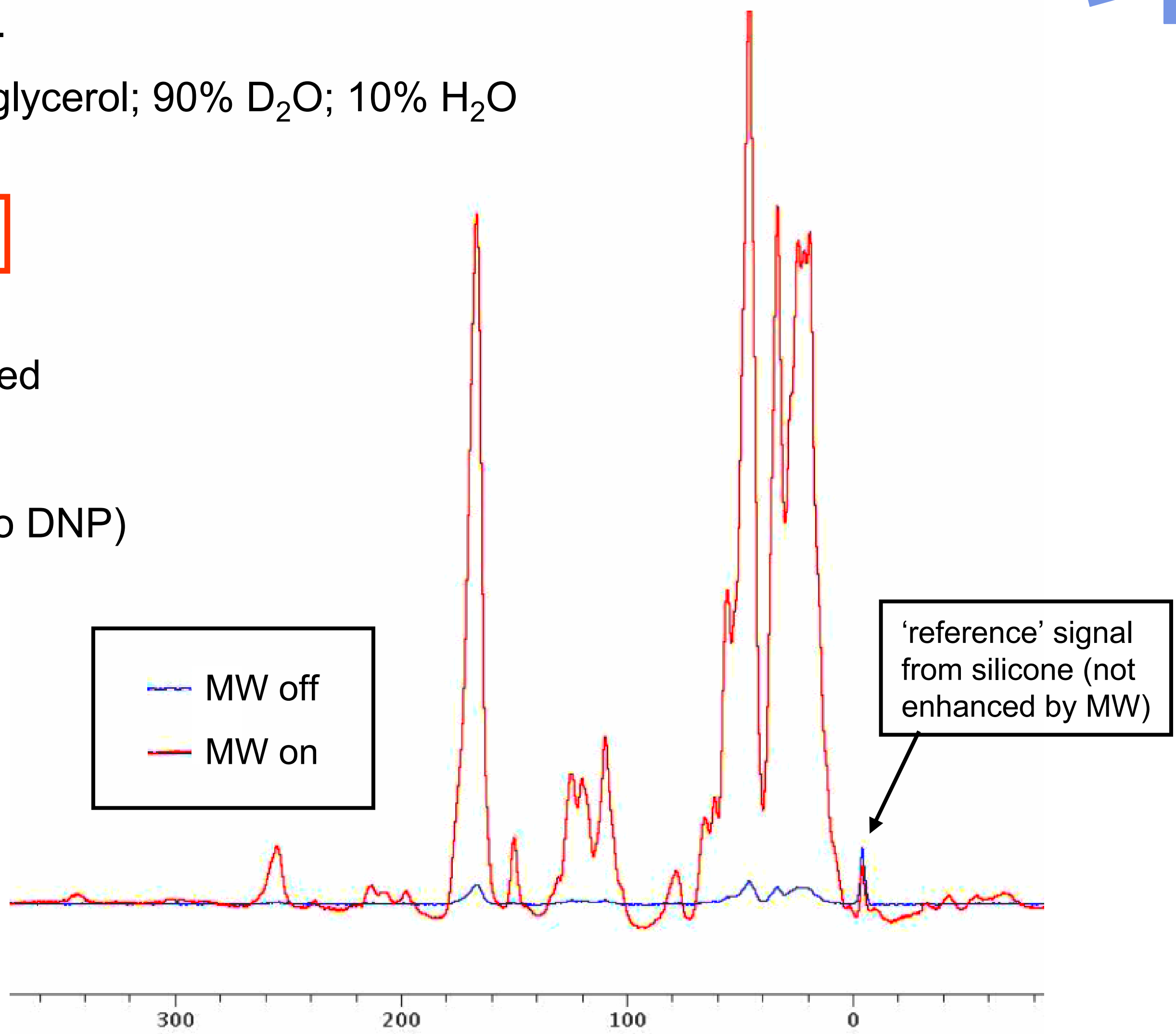
Test on an ‘old’ SH3 sample.

Added 20mM Totapol in D_6-glycerol; 90% D_2O; 10% H_2O

signal enhancement is ~40

the same S/N can be achieved
in 40^2 = 1,600 less time!!

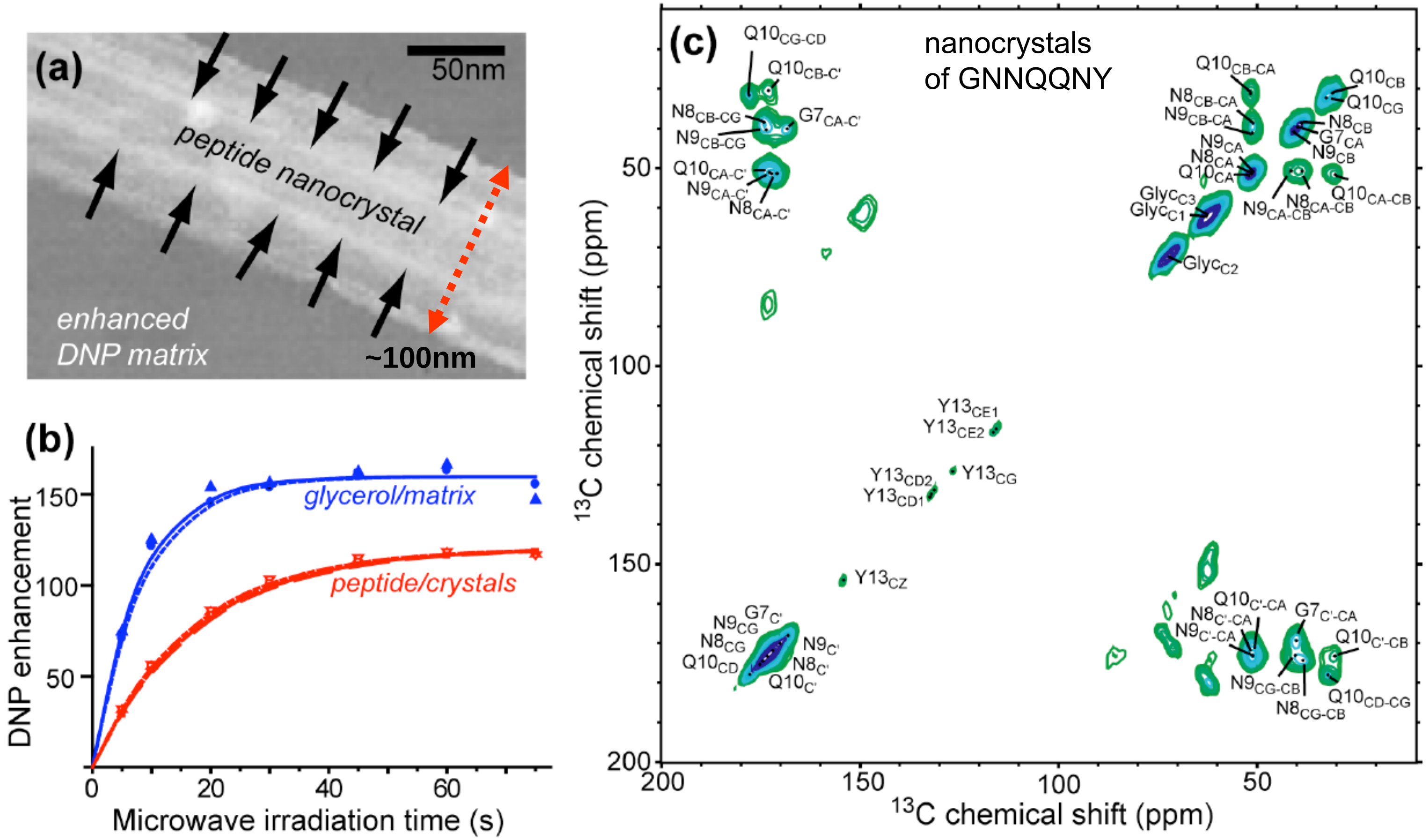
1 hour (DNP) vs. 66 days (no DNP)



DNP (dynamic nuclear polarization)

radicals not in direct contact with bulk nuclei → minimal line broadening by radicals

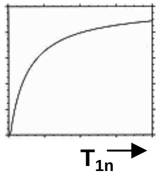
polarized ^1H magnetization can penetrate into non-radical doped domains by spin diffusion



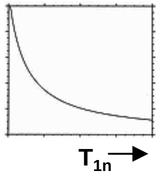
DNP (dynamic nuclear polarization)

spin-lattice relaxation time (T_{1n})

T_{1n} = long: sufficient time for transfer from electrons and 1H spin diffusion



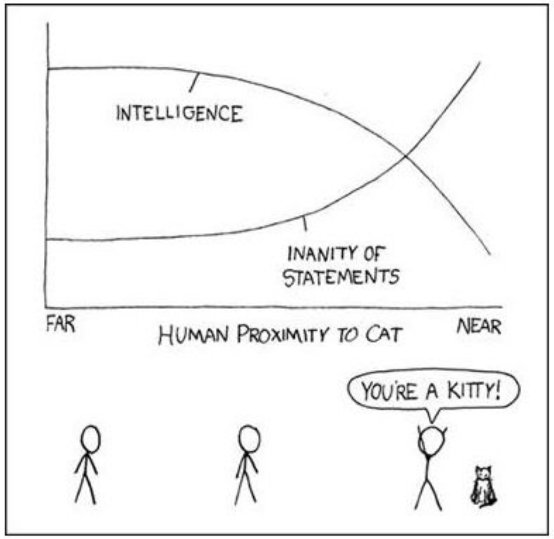
T_{1n} = short: increased data collection rate



T_{1n} lengthened by low temperature

T_{1n} shortened by radicals, act as relaxation agents

T_{1n} ~0.5 – 1.0s



DNP (dynamic nuclear polarization)

two mechanism: solid effect (SE) and cross effect (CE)

SE: possible when EPR linewidth (δ) < ω_n

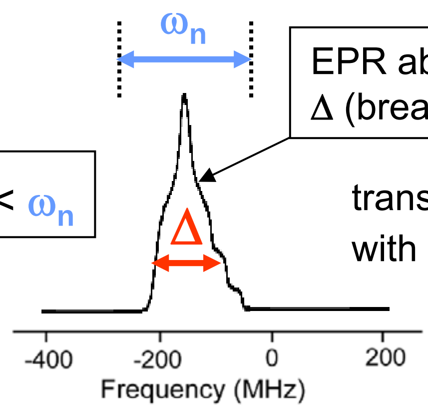
$1\ e^- \leftrightarrow 1\ n$

'forbidden transitions'

(second-order perturbation theory)

transition probability always low

$\delta < \omega_n$



EPR absorption line shape
Δ (breadth of spectrum) ~ δ

transition probability scales with $1/(\omega_n)^2 = 1/(B_0)^2$

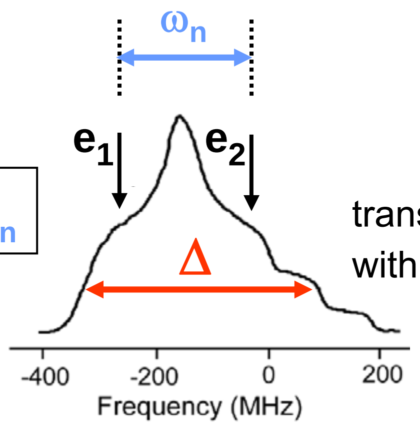
CE: possible when EPR linewidth (δ) > ω_n

$2\ e^- \leftrightarrow 1\ n$

two paired electrons, EPR frequencies separated by Larmor frequency

transition probability can be high at match → energy-conserved flip-flop process

$\delta > \omega_n$

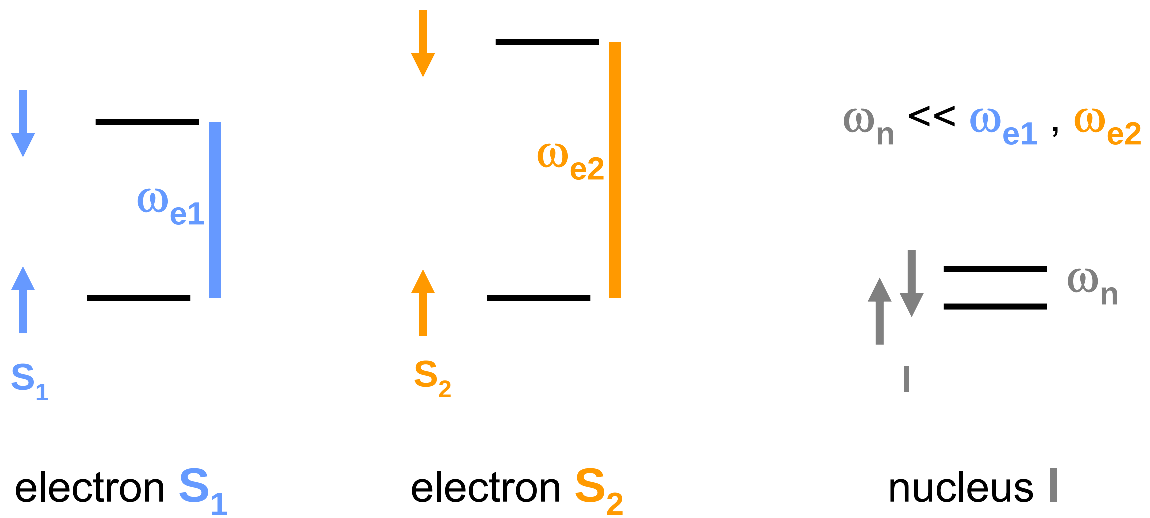


transition probability scales with $1/(\omega_n) = 1/(B_0)$

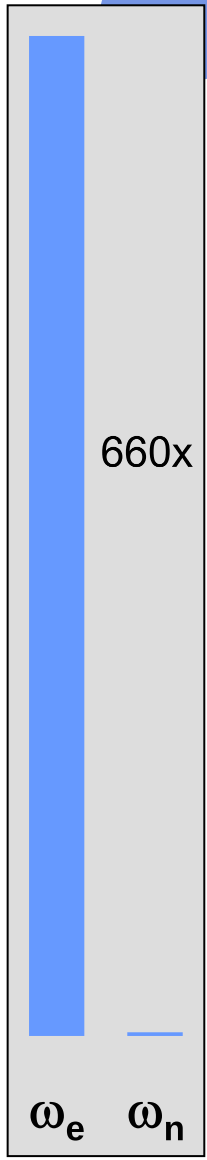
DNP (dynamic nuclear polarization)

How does the cross effect work?

coupled system of two electrons (e1 and e2) and and nucleus (n)



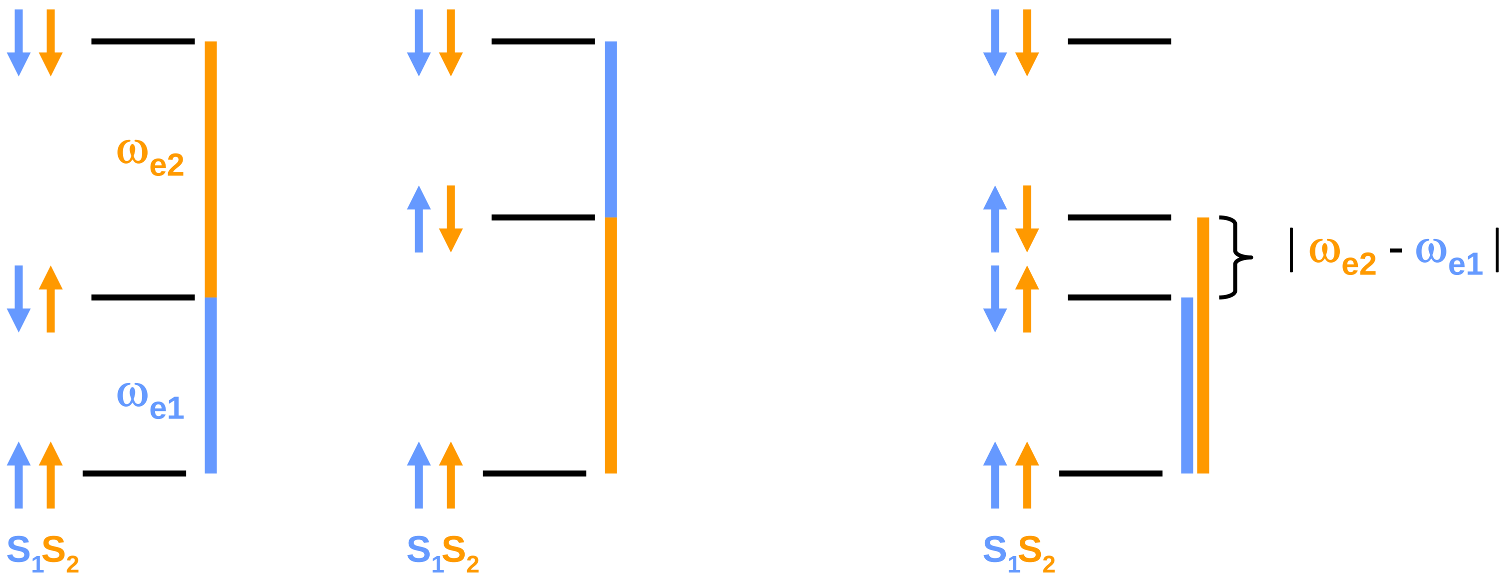
note: Zeeman splittings ω_{e1} and ω_{e2} about 660 times larger than ω_n !!



DNP (dynamic nuclear polarization)

cross effect

two coupled electron spins give rise to four energy levels

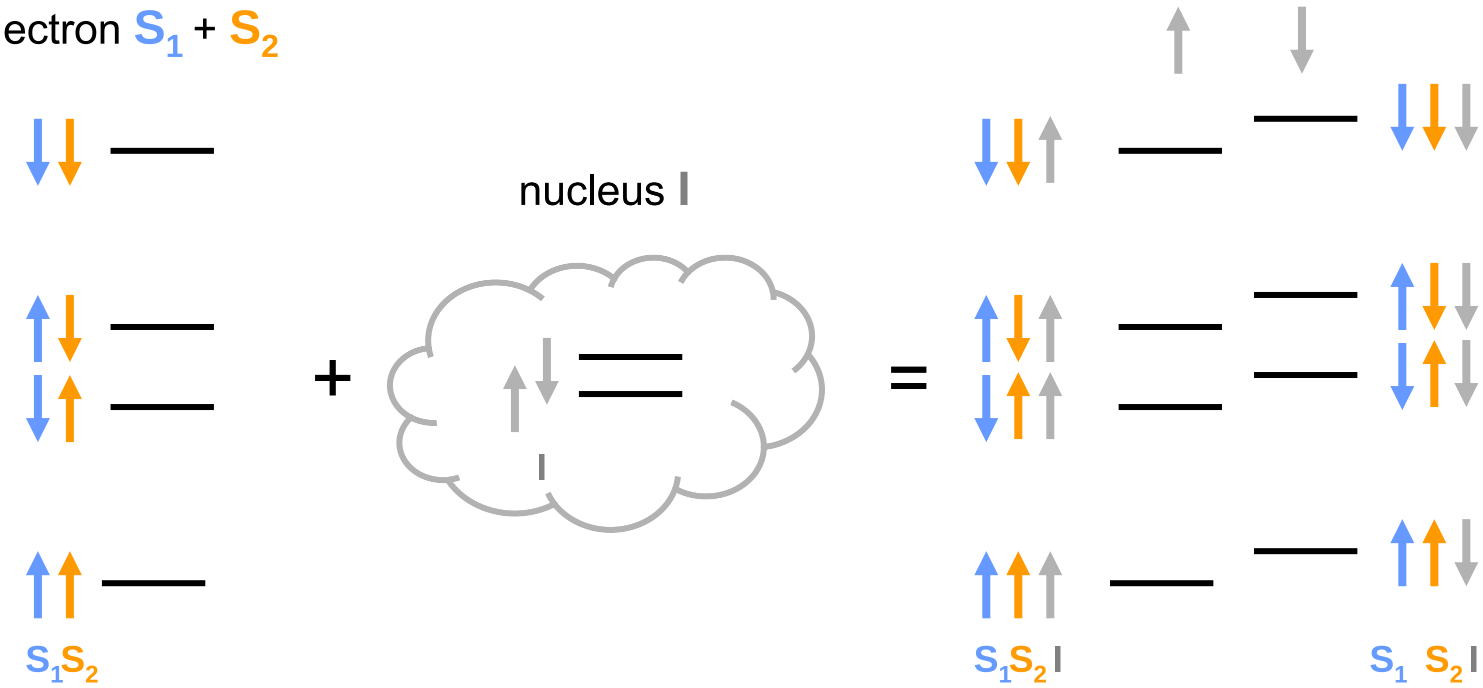


electron S_1 + S_2

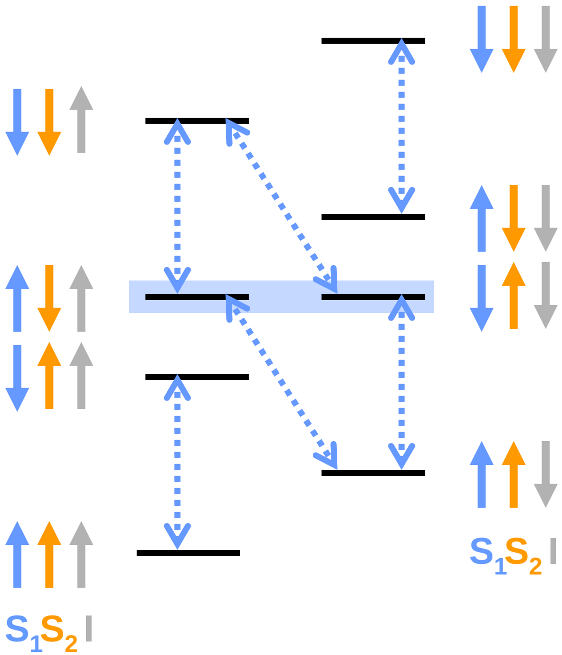
DNP (dynamic nuclear polarization)

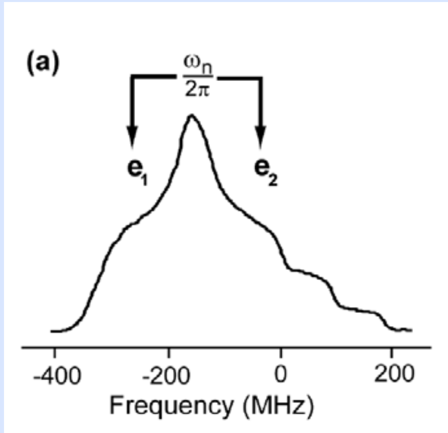
now also add the nuclear spin…

electron S_1 + S_2



DNP (dynamic nuclear polarization)





when the matching condition

$$|\omega_{e2} - \omega_{e1}| = \omega_n$$

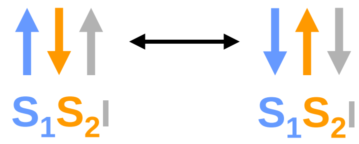
is fulfilled, the levels ↑↓↑ and ↓↑↓ are degenerate

Irradiating with MW at frequency ω_{e1} will not only saturate S_1 (↑ and ↓)

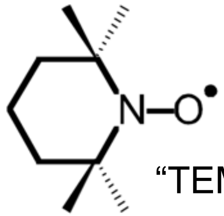
but also the pair S_2I (↑↓ and ↓↑), if matching condition is fulfilled

DNP (dynamic nuclear polarization)

irradiation at resonance frequency ω_{e1} of **e1** will produce simultaneous spin flip of both **e2** and the nucleus **n**

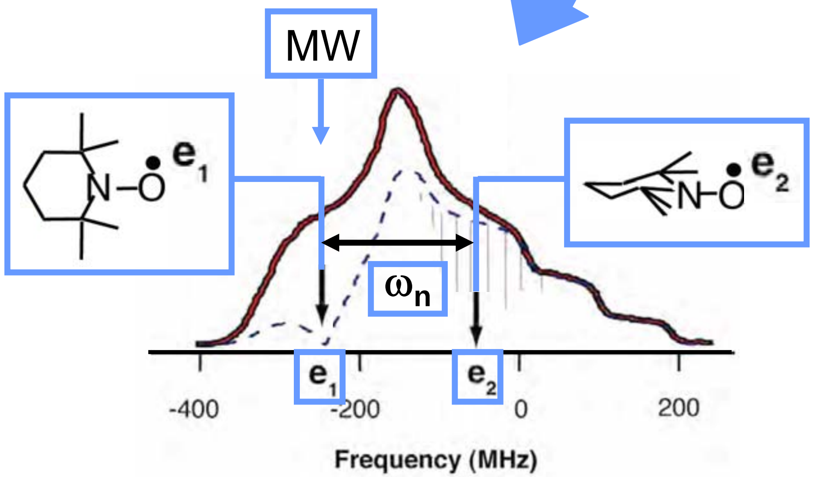


using a single-radical polarization agent (e.g., TEMPO)



"TEMPO"

two TEMPO molecules must have:
- correct distance
- correct relative orientation



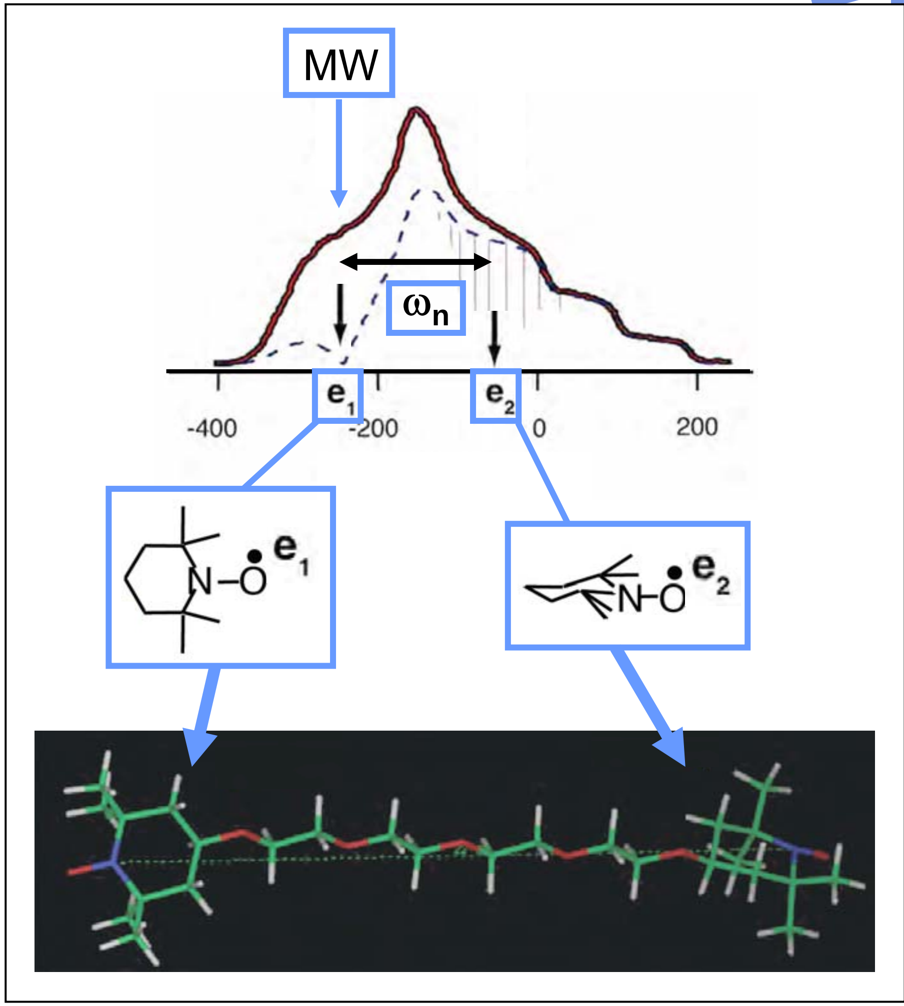
use of mono-radicals is inherently inefficient:
only a fraction of the spins in a powder have correct distance and relative orientations to contribute to DNP

DNP (dynamic nuclear polarization)

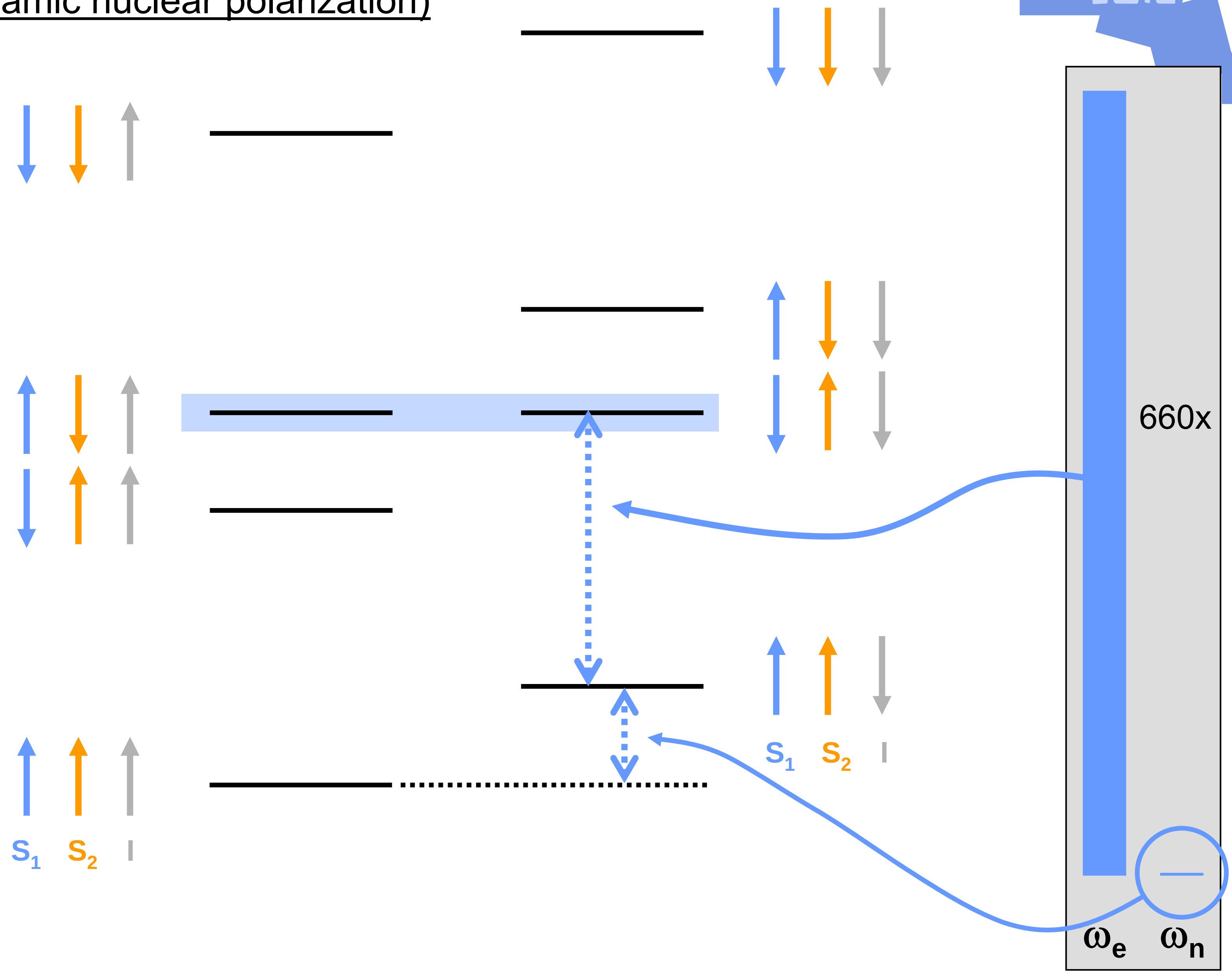
the trick:
use biradicals instead of mono-radicals

the 'perfect' biradical:
both distance *and* angle of the two radicals provide the correct frequency difference between the two electrons

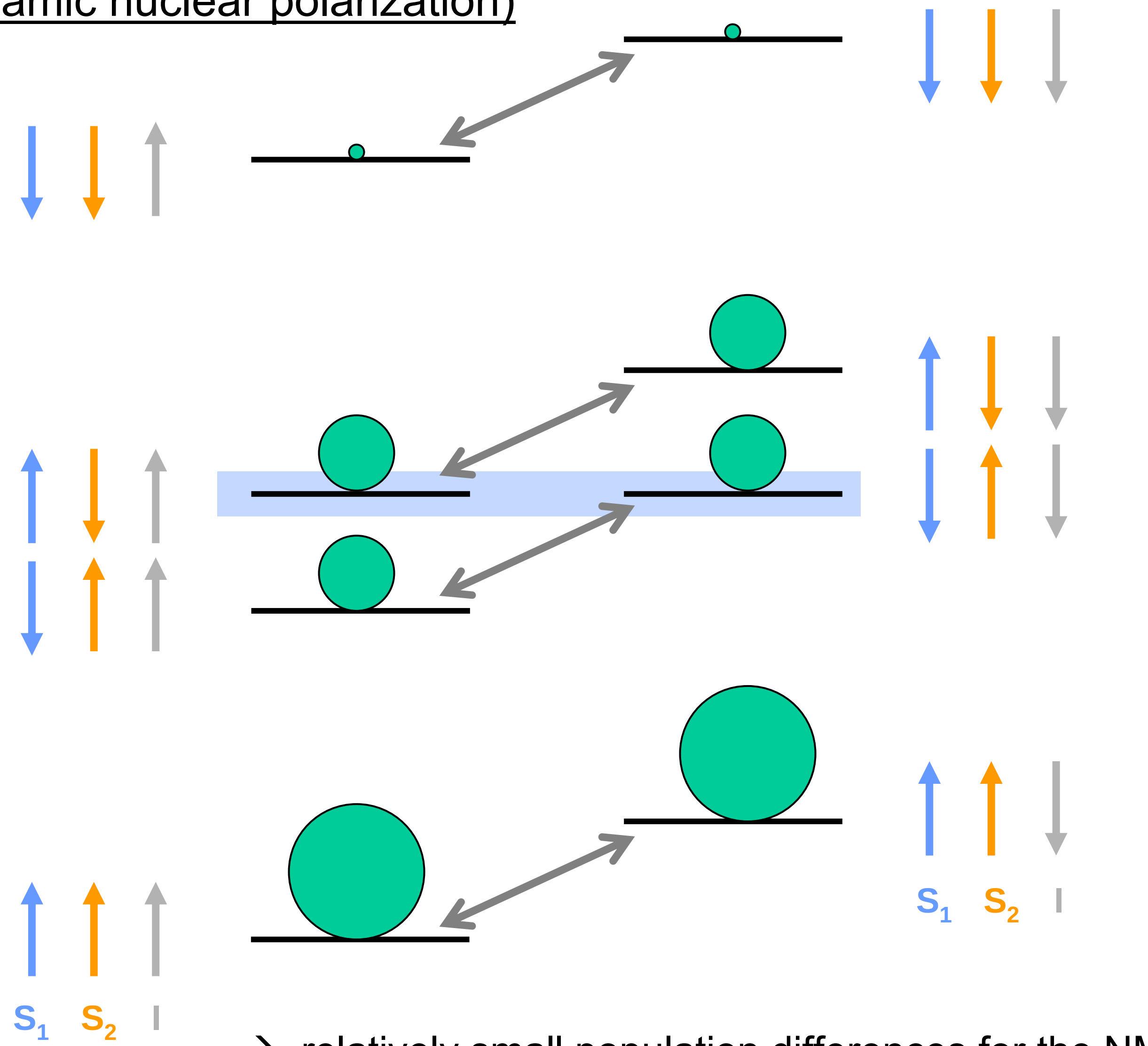
more efficient than mono-radicals
→ concentration of radical centres can be much lower

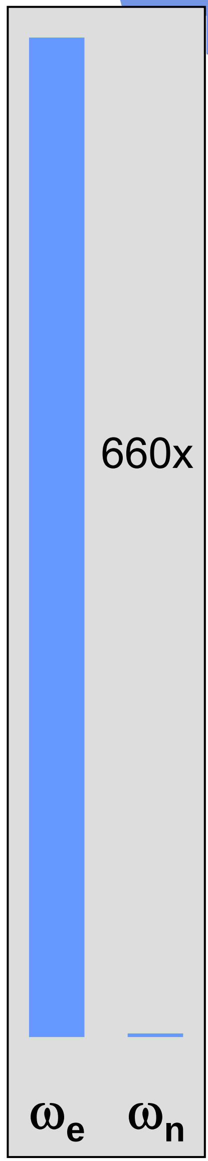


DNP (dynamic nuclear polarization)



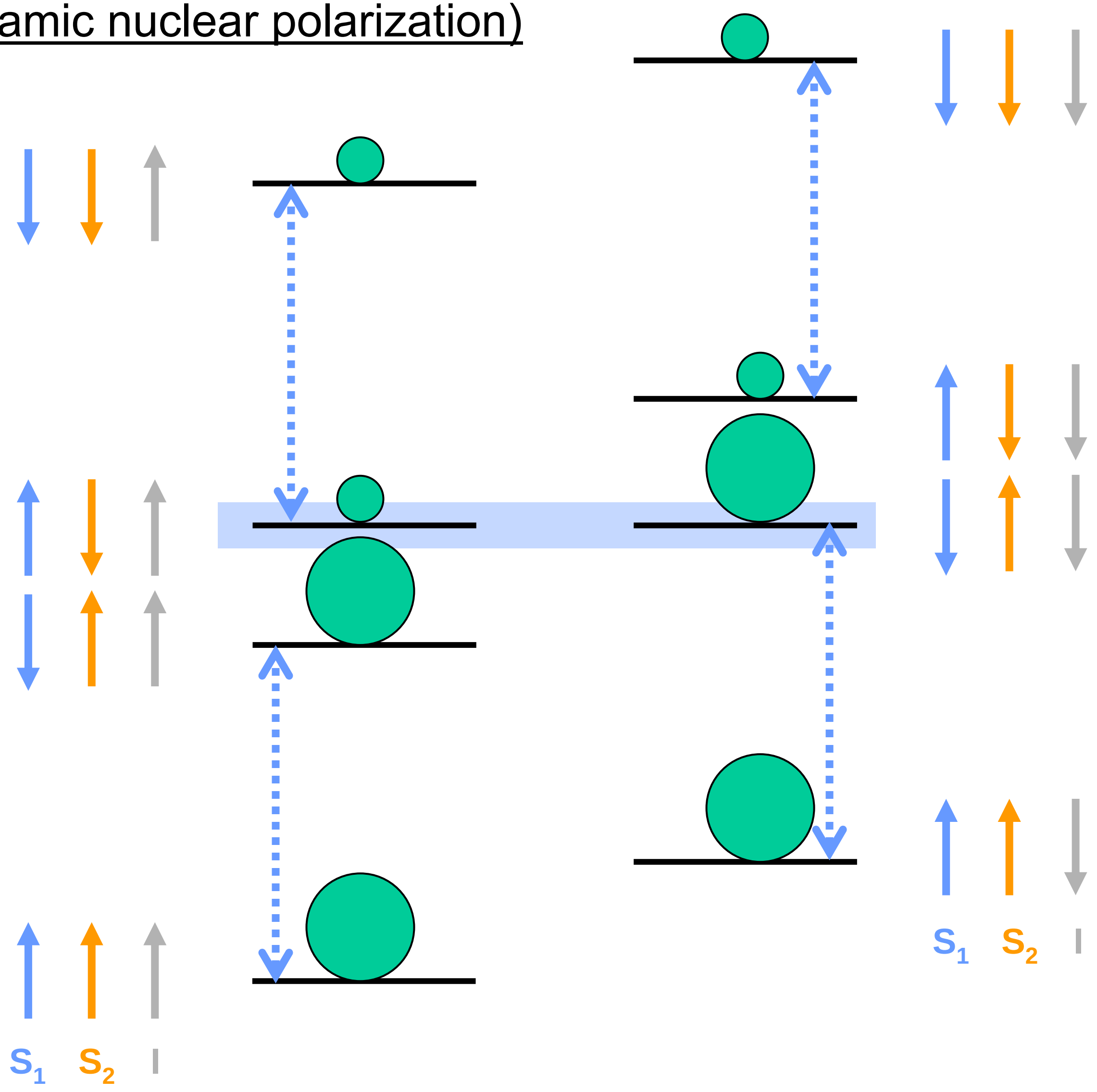
DNP (dynamic nuclear polarization)





→ relatively small population differences for the NMR transitions (i.e. the 'normal' NMR population difference)

DNP (dynamic nuclear polarization)



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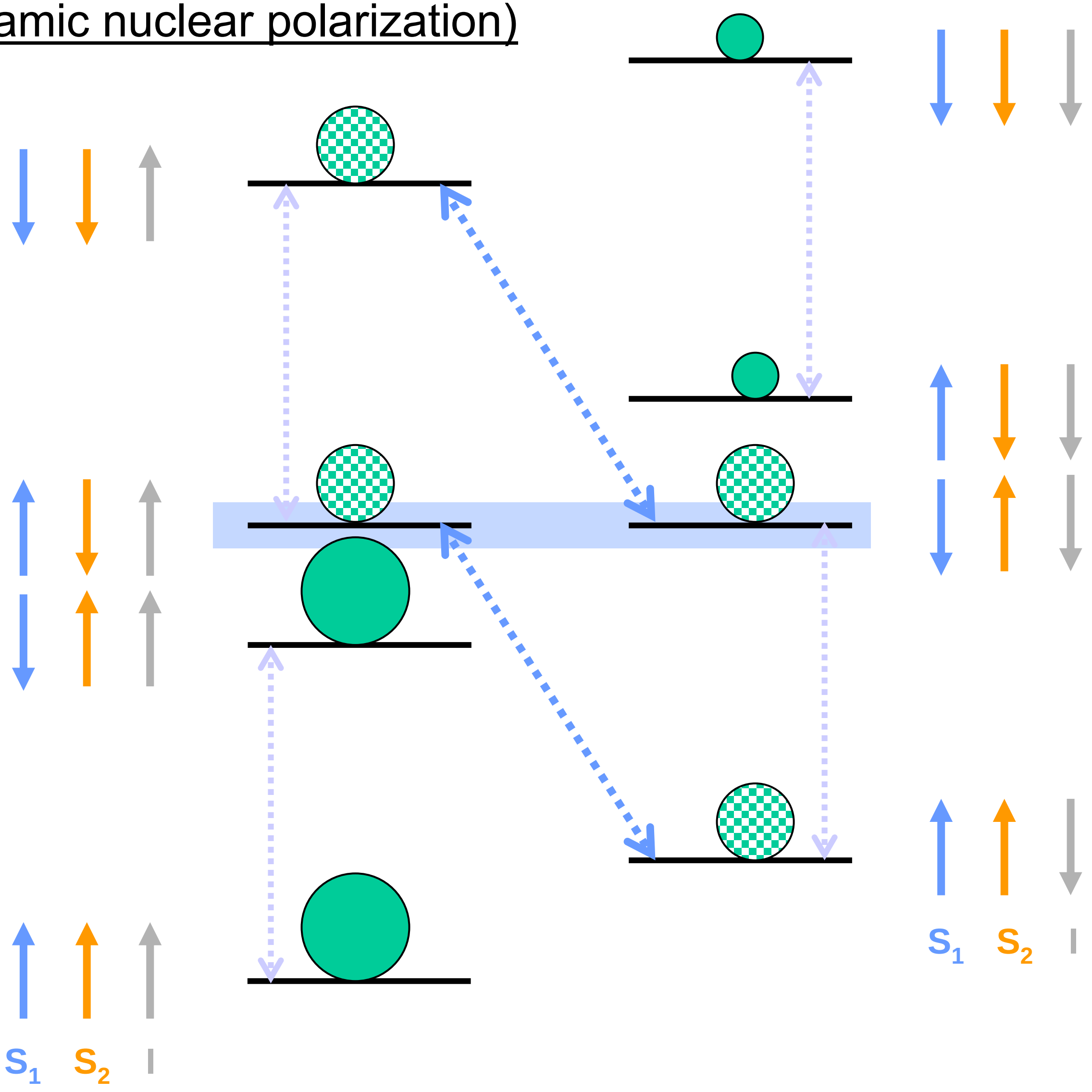
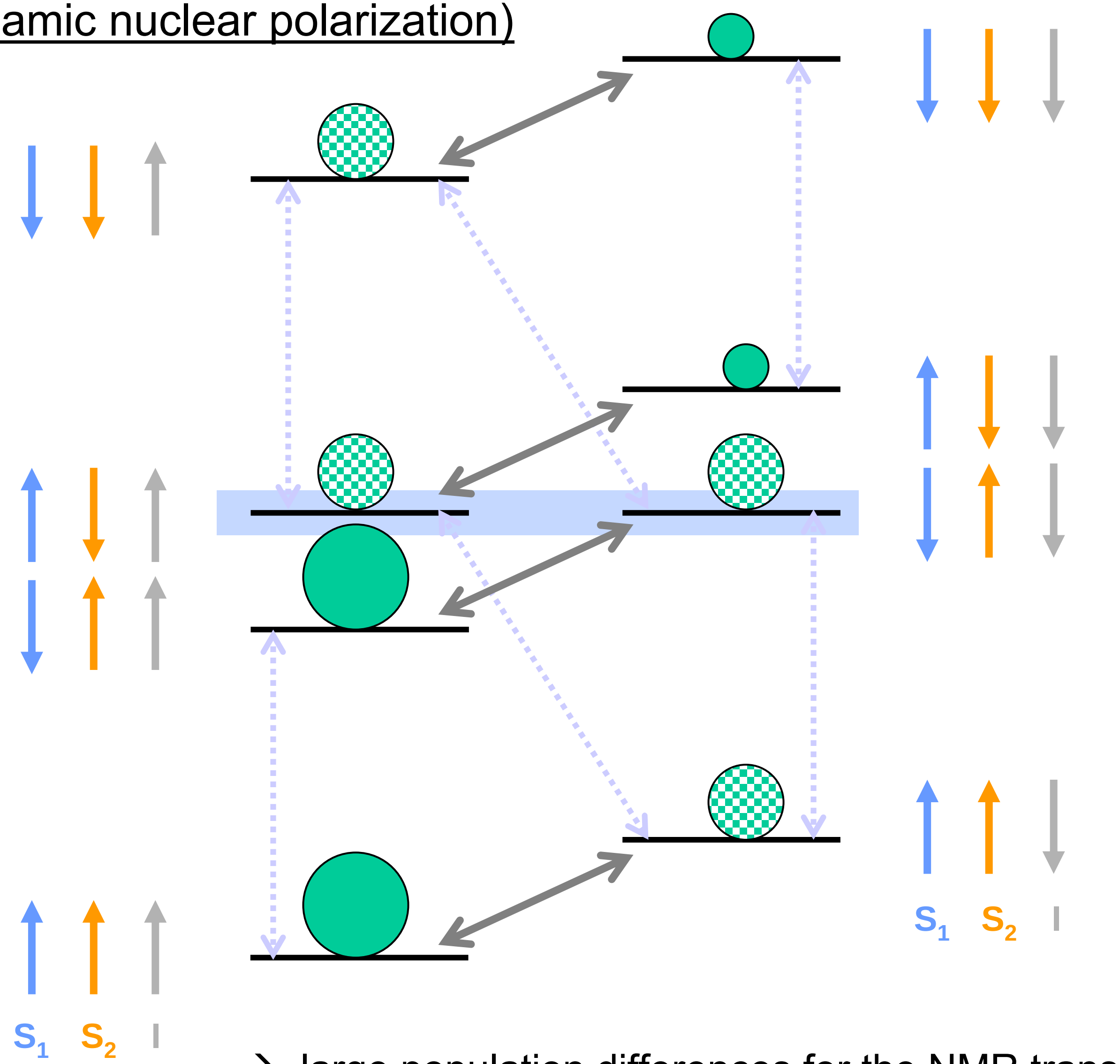


DNP (dynamic nuclear polarization)



→ large population differences for the NMR transitions


THANK
YOU