

Double-Resonance Experiments

The aim - to simplify complicated spectra by eliminating J -couplings.

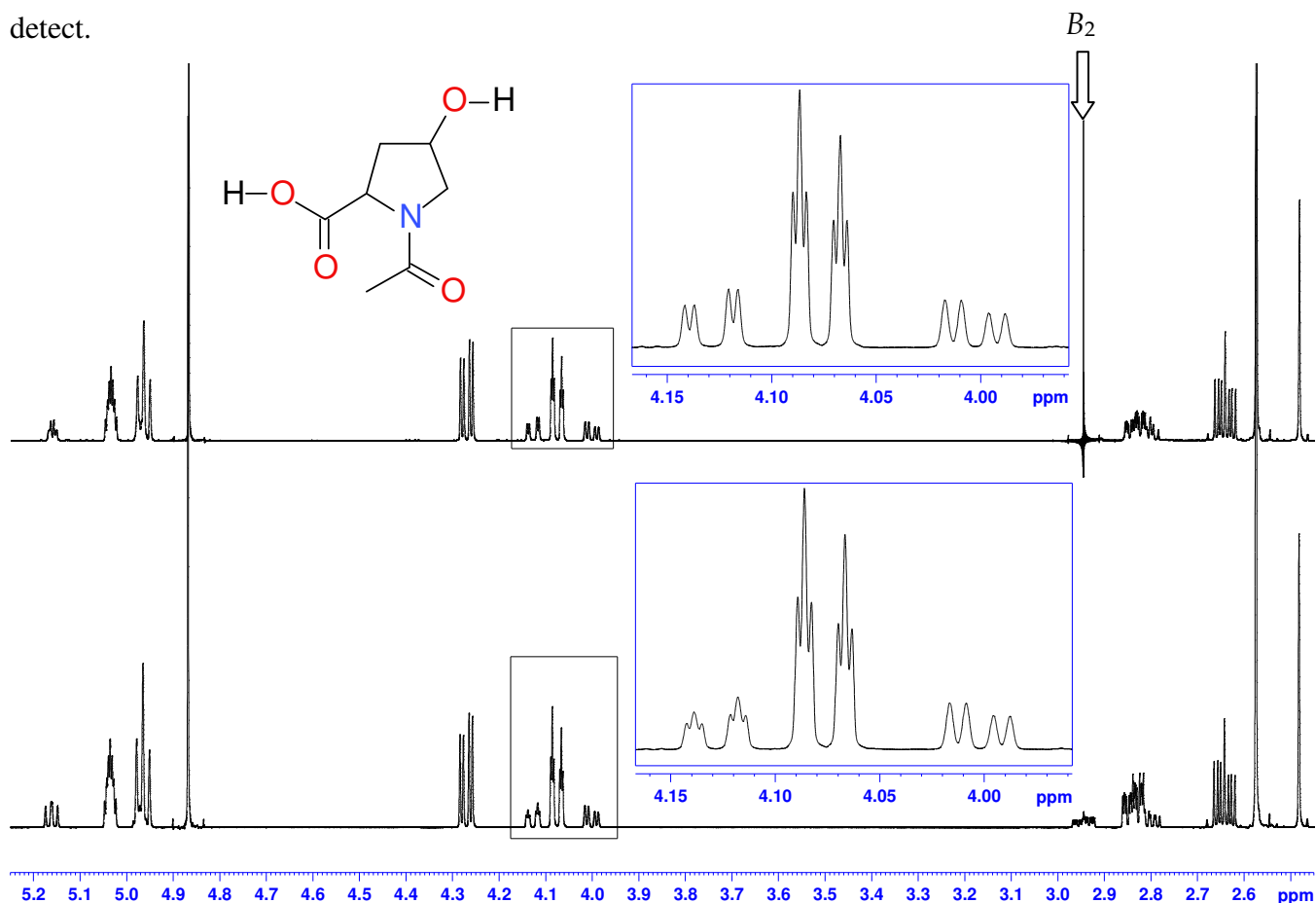
Homonuclear Decoupling

A double resonance experiment is carried out using a second rf source B_2 in addition to the rf transmitter B_1 used for the detection of the spectrum.

Homonuclear spin pair AX with a scalar $J_{AX} \neq 0$: if we observe the A nucleus while irradiating selectively the X nucleus, the scalar coupling J_{AX} vanishes. The necessary strength of the B_2 field: $\gamma B_2/2\pi > 2J_{AX}$.

In terms of the vector model: the frequency $\nu_2 = \gamma B_2/2\pi$ coincides with the Larmor frequency of the X nucleus $B_{eff} = B_2$, i.e., the vector μ_X precesses around B_2 and thus around x axis. The nuclear spin vectors I_A and I_X are then quantized along the z - and the x -axis respectively. They are orthogonal and their scalar product ($E = J_{AX} I_A I_X$) is therefore zero (the scalar spin-spin coupling vanishes).

For simple spectra, the results are straightforward: record two spectra, one with and another without selective decoupling and check which multiplets change. For more crowded spectra, it is common to take the difference between the two spectra in order to observe changes that would otherwise be difficult to detect.



Main problems:

(i) suffers from difficulties associated with selective irradiation of only those spins which are desired;

(ii) Bloch-Siegert shift: $\nu'_A \approx \nu_A + \frac{\gamma B_2^2}{8\pi^2(\nu_A - \nu_X)}$

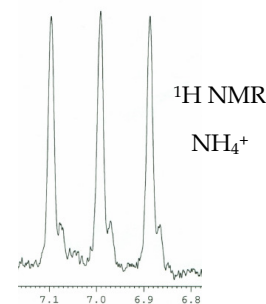
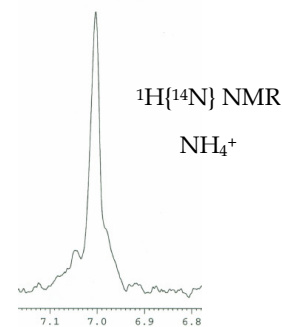
If several spin-decoupling experiments are desired, it is generally more time-efficient to perform a two-dimensional COSY experiment in order to establish connectivities.

Heteronuclear Decoupling

The frequency difference $\nu_2 - \nu_1$ lies in the MHz range. The second field B_2 is produced by a separate transmitter.

A curly bracket is used to indicate which nucleus is being decoupled during the experiment, e.g. $^{13}\text{C}\{^1\text{H}\}$ indicates a ^{13}C spectrum acquired with ^1H decoupling.

Can be used for simplifying spectra complicated by heteronuclear J -couplings (e.g., J_{HF} or J_{HP}) or for removing line broadening caused by quadrupolar nuclei (e.g., ^{14}N).



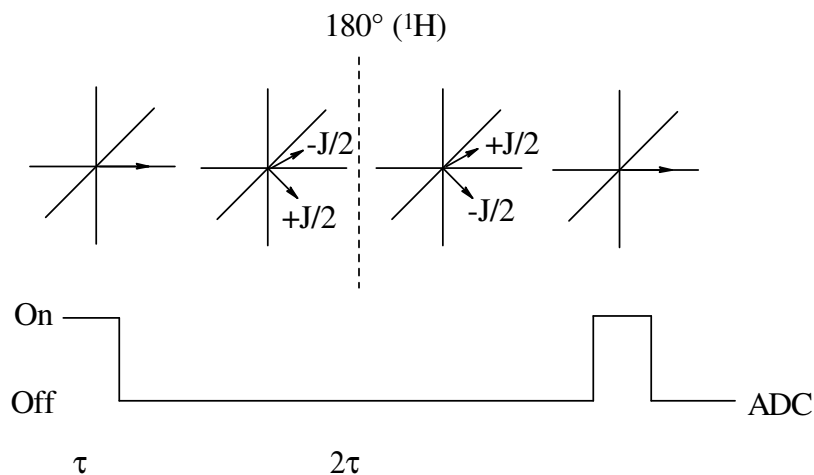
Broadband decoupling

Broadband decoupling is used in order to eliminate the coupling between two nuclei completely. For example, broadband ^1H decoupling while acquiring ^{13}C spectrum leads to singlets for each ^{13}C environment and a substantial increase in the sensitivity of the experiment.

Previously broadband decoupling techniques were based on the combined use of high-power decoupling and frequency modulation of the B_2 frequency with a randomly varying waveform (proton “noise” decoupling). Generally, this results in an inefficient broadband decoupling and leads to loss of both sensitivity and resolution.

Broadband decoupling techniques based upon the spin flip experiment (MLEV, Malcolm Levitt):

^1H $\pi - \tau - \pi - \tau - \pi - \tau - \pi - \tau - \pi - \tau - \dots$
 ^{13}C $\pi/2$ Acquire \dots



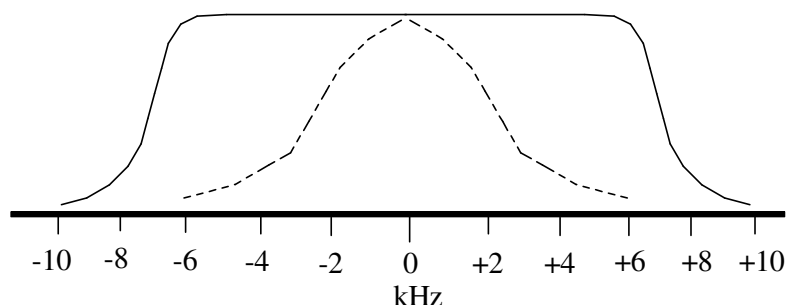
A train of π pulses will be susceptible to the errors due to pulse length inaccuracy, since they will accumulate. The non-ideal π pulse can be replaced with a *composite pulse*.

Composite π_y pulse: $\left(\frac{\pi}{2}\right)_x \pi_y \left(\frac{\pi}{2}\right)_x$

Examples of composite pulse decoupling techniques: WALTZ-16 and GARP

The linewidth achievable in WALTZ-16 ^{13}C NMR spectra is $\sim 0.1 - 0.3$ Hz (suitable for detecting small effects such as $^{35/37}\text{Cl}$ isotope effects of a few ppb).

---- conventional modulation technique; — composite pulse decoupling



Broadband decoupling of nuclei with large chemical shift ranges (^{19}F , ^{31}P) with ^1H observation becomes much more feasible on using such decoupling techniques as GARP.

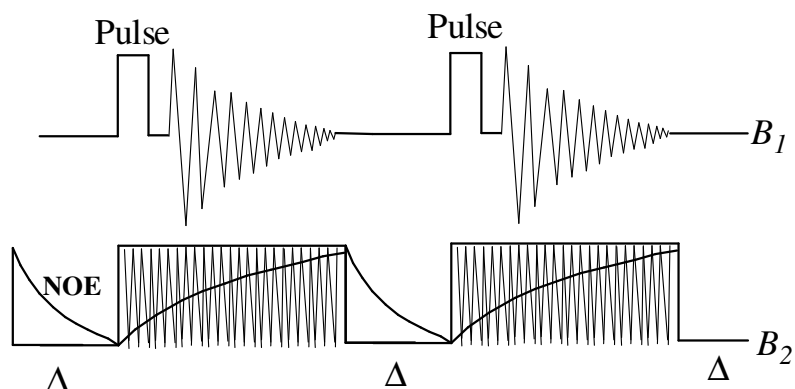
The effective decoupling bandwidth: WALTZ-16 $2B_2$ ($B_2 \approx 5$ kHz)

GARP-1 $5B_2$ (slightly greater residual broadening of the lines)

Gated decoupling

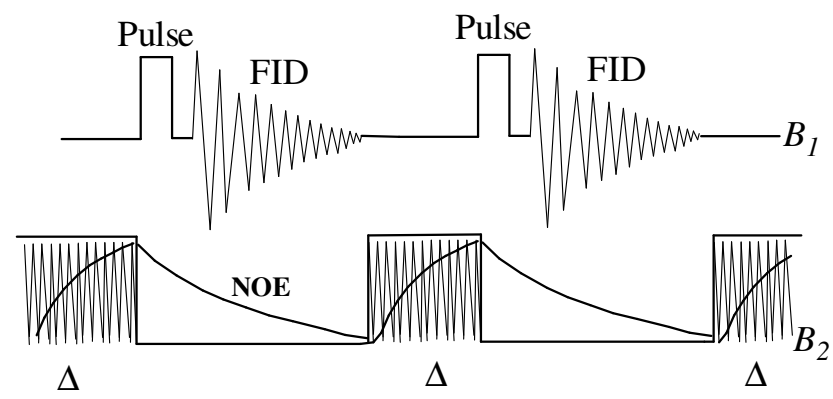
Disadvantages of $^{13}\text{C}\{^1\text{H}\}$ spectra: (i) the nuclear Overhauser effect (NOE) leads to intensity distortions and the integration of these spectra becomes questionable; (ii) the elimination of line splittings prevents the measurement of $^{13}\text{C}, ^1\text{H}$ coupling constants.

The application of a method known as gated decoupling experiment successfully handles spin-spin coupling and intensity distortions. In the first case, the decoupler is switched on during acquisition, but switched off during the remaining time before the next pulse. The ^{13}C - ^1H coupling is thus eliminated without producing NOE, as the integrals depend mainly on the intensities of the initial points of the time domain function.



Alternatively, relaxation reagents (e.g., chromium acetylacetonate) can be used to eliminate unwanted NOEs. Because of their paramagnetic moment, relaxation reagents provide an efficient mechanism for ^{13}C spin-lattice relaxation that suppresses dipolar relaxation, which is the main phenomenon leading to NOEs.

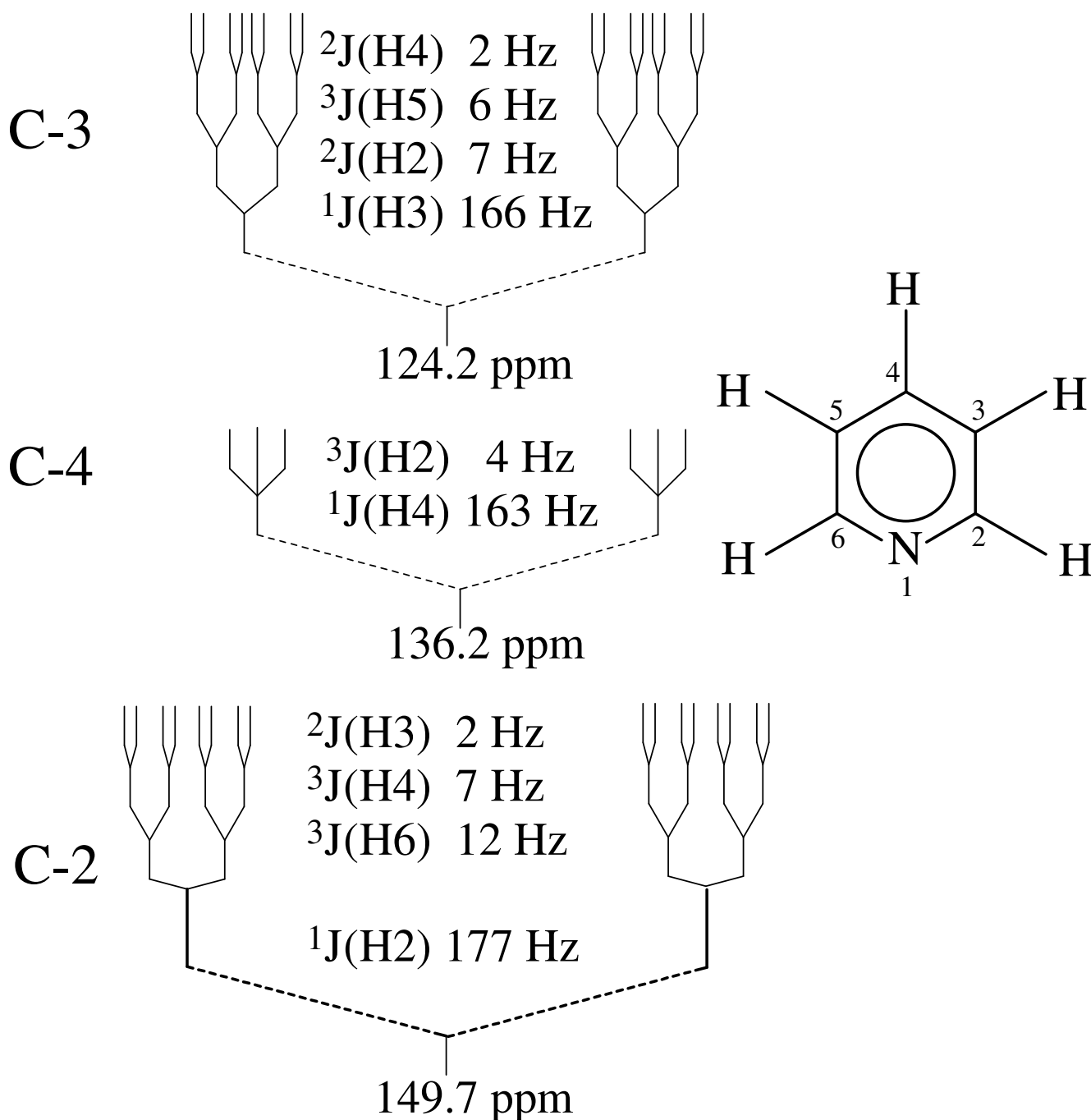
In the second case, the decoupler is gated: it is on during the delay time between different pulses and switched off during acquisition.



As a result, the spectra are not decoupled and most of the NOE is preserved. This provides higher sensitivity for measurements of $J(^{13}\text{C}, ^1\text{H})$ couplings.

Example of signal multiplicities in a proton-coupled ^{13}C NMR spectrum

^{13}C , ^1H coupling constants in pyridine



Polarization Transfer

The aim - to increase sensitivity by transferring favourable NMR properties of the proton to another nucleus.

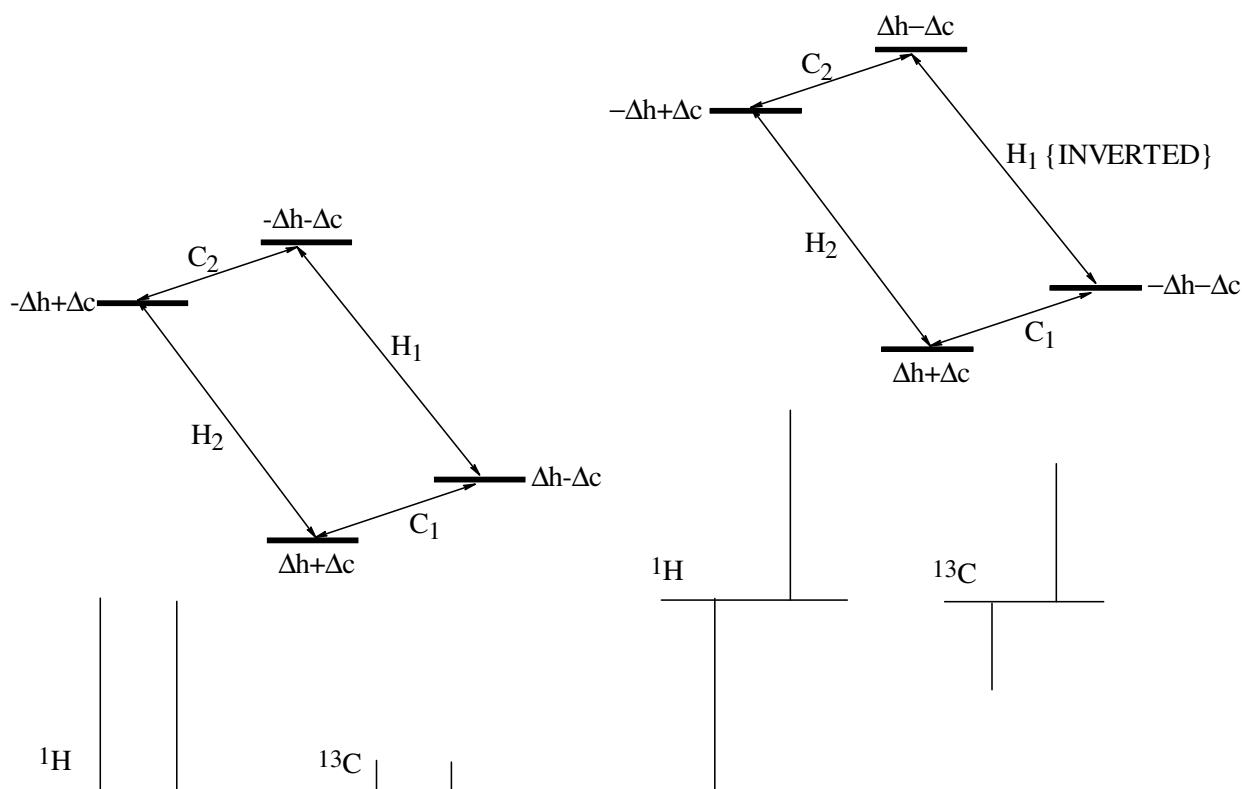
$$N_{\beta}/N_{\alpha} = \exp(-\Delta E/kT) \approx 1 - \Delta E/kT = 1 - \gamma\hbar B_0/kT$$

$$\Delta n = N_{\alpha} - N_{\beta}$$

$$\Delta n \propto \gamma\hbar B_0/kT$$

Selective population inversion

A two-spin system $^1\text{H}-^{13}\text{C}$ (e.g., in CHCl_3)



$$\gamma_{\text{H}} \approx 4 \gamma_{\text{C}}$$

$$\Delta h \approx 4 \Delta c$$

^{13}C

+1 : +1

-3 : +5

Relative intensities for the X multiplet of an AX_n group:

at Boltzmann distribution

after selective population inversion

					n					
					0					
					1					
					2					
					3					
					4					
1	4	6	4	1	4	-15	-28	6	36	17

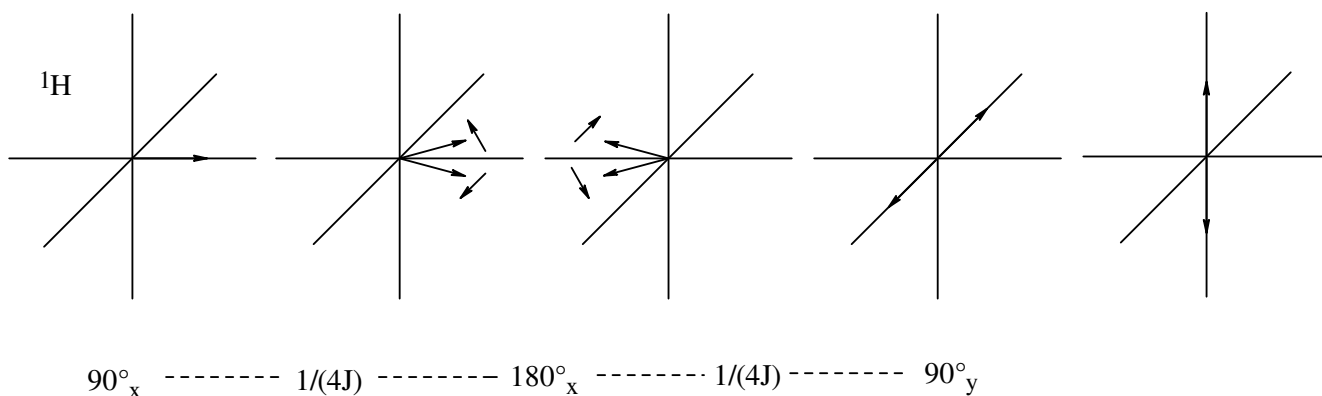
INEPT (Insensitive Nuclei Enhanced by Polarization Transfer)

$${}^1\text{H}: \left(\frac{\pi}{2}\right)_x - \tau - \pi_x - \tau - \left(\frac{\pi}{2}\right)_y$$

$${}^{13}\text{C}: \quad \pi_x \quad \left(\frac{\pi}{2}\right)_x \quad \text{Acquire}$$

$$\tau = 1 / (4 J_{CH})$$

Non-selective pulses are used to put pairs of proton transitions into antiphase.



The proton magnetisation vectors are prepared in antiphase: the α vector along $+z$ and the β vector along $-z$ (as in SPI). This corresponds to inverted ${}^1\text{H}$ spin populations with the excess population in the upper level. A ${}^1\text{H} \rightarrow {}^{13}\text{C}$ polarization transfer occurs and a fourfold ($\gamma_{\text{H}}/\gamma_{\text{C}}$) enhancement in ${}^{13}\text{C}$ signal-to-noise ratio is achieved. As relaxation times $T_1({}^1\text{H})$ are shorter than $T_1({}^{13}\text{C})$, there is a further gain in the rate at which signals can be accumulated.

DEPT (Distortionless Enhancement by Polarization Transfer)

$${}^1\text{H}: \left(\frac{\pi}{2}\right)_x - \frac{1}{2J} - \pi_x - \frac{1}{2J} - \theta_{\pm y} - \frac{1}{2J} - (\text{Decouple})$$

$${}^{13}\text{C}: \quad \left(\frac{\pi}{2}\right)_x \quad \pi_x \quad \text{Acquire}(\pm x)$$

$\theta_{\pm y}$ – a pulse of variable length. To separate CH, CH₂ and CH₃ subspectra, experiments with $\theta = \pi/4, \pi/2$ and $3\pi/4$ are performed.