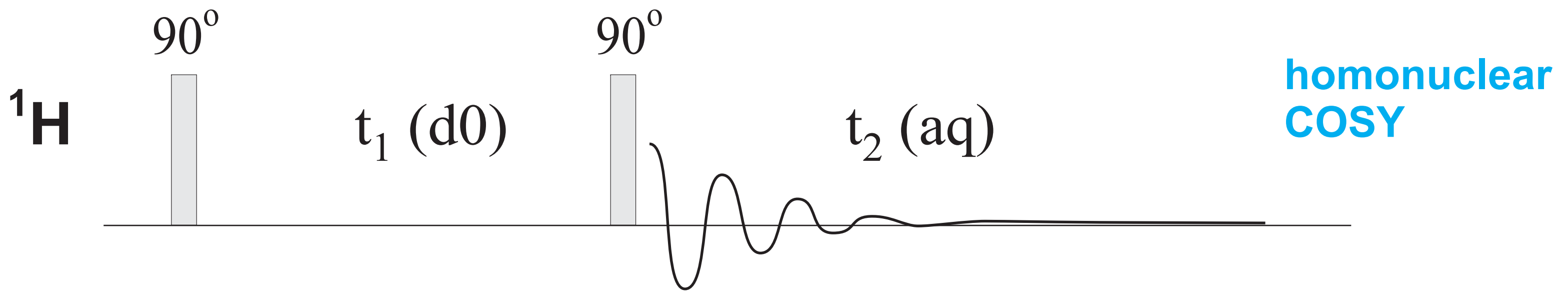
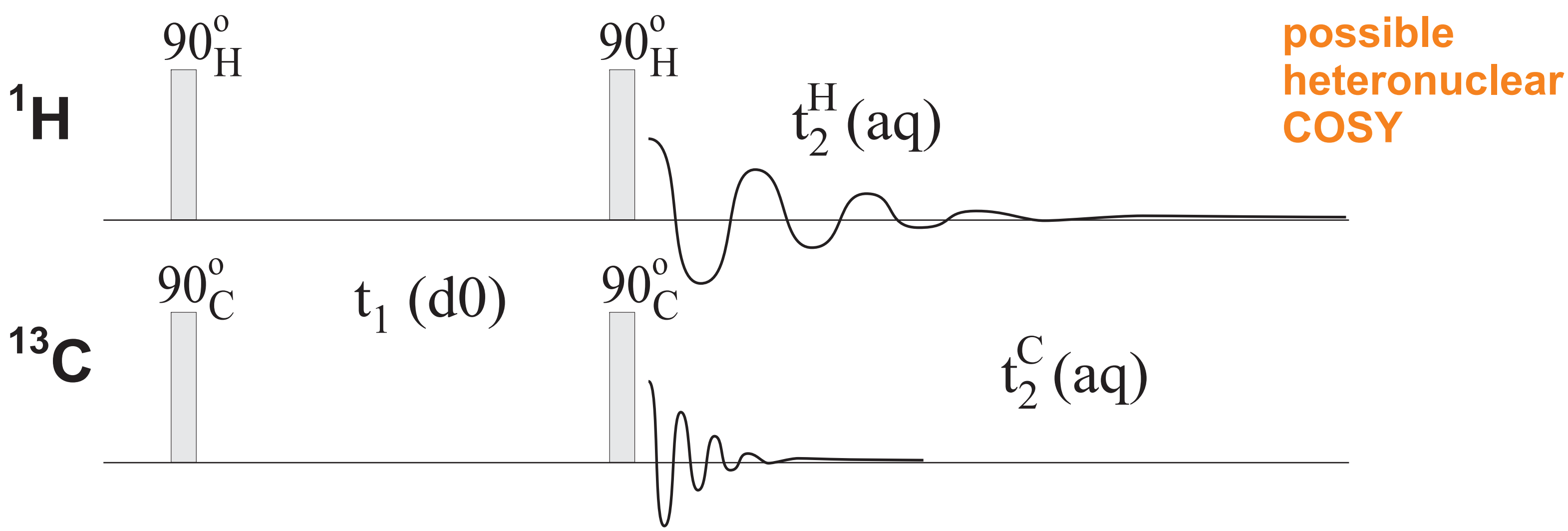
Schematic of the COSY Experiment



But what happens for a heteronuclear experiment?

The 90° pulses will not cover both sets of nuclei, and there would be issues with observation of both nuclei simultaneously.

These issues could (perhaps) be addressed by something like:



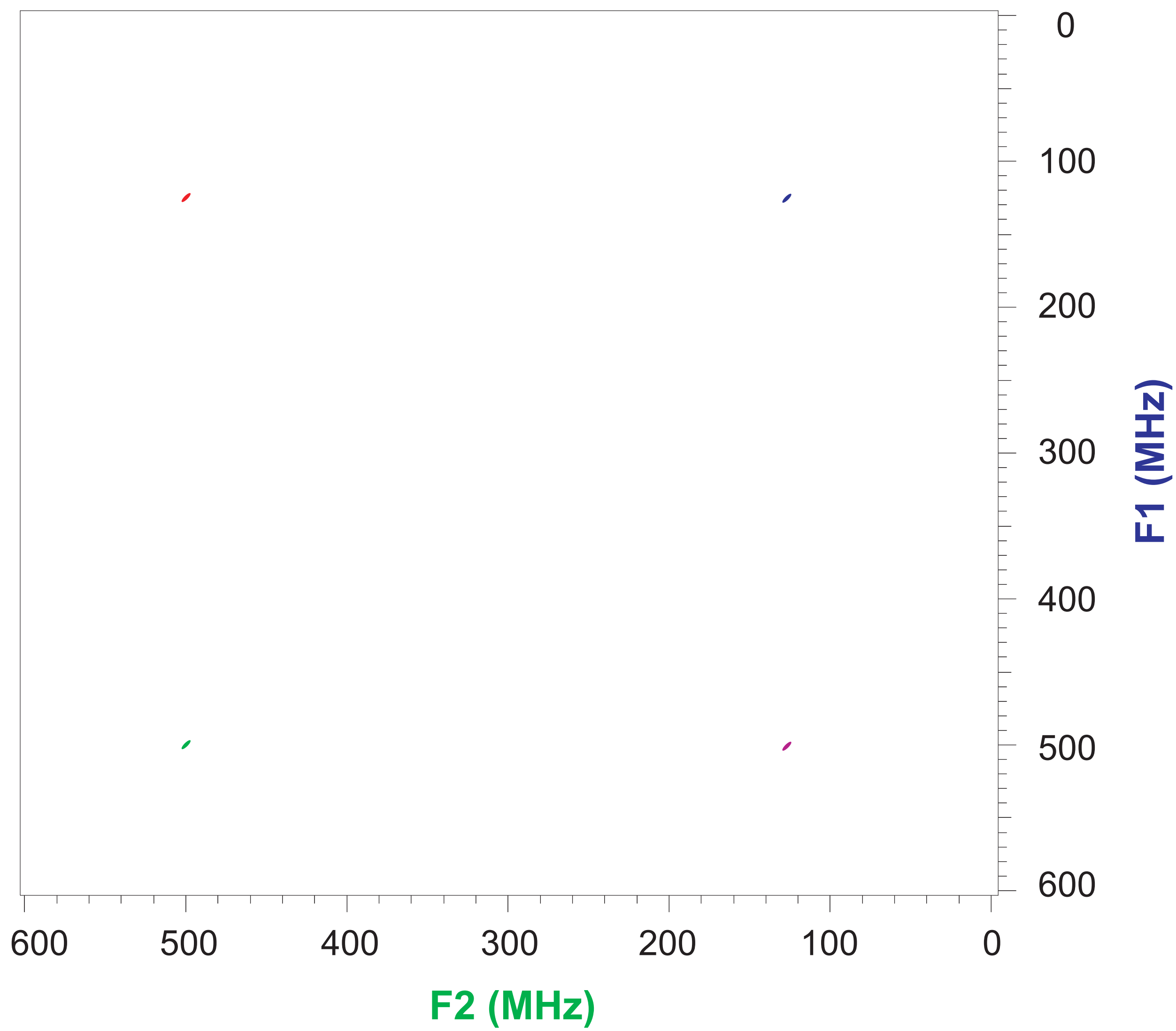
Cartoon of a Full Heteronuclear COSY

If we attempted this hetero-cosy exp, it would look something like the cartoon on the right,

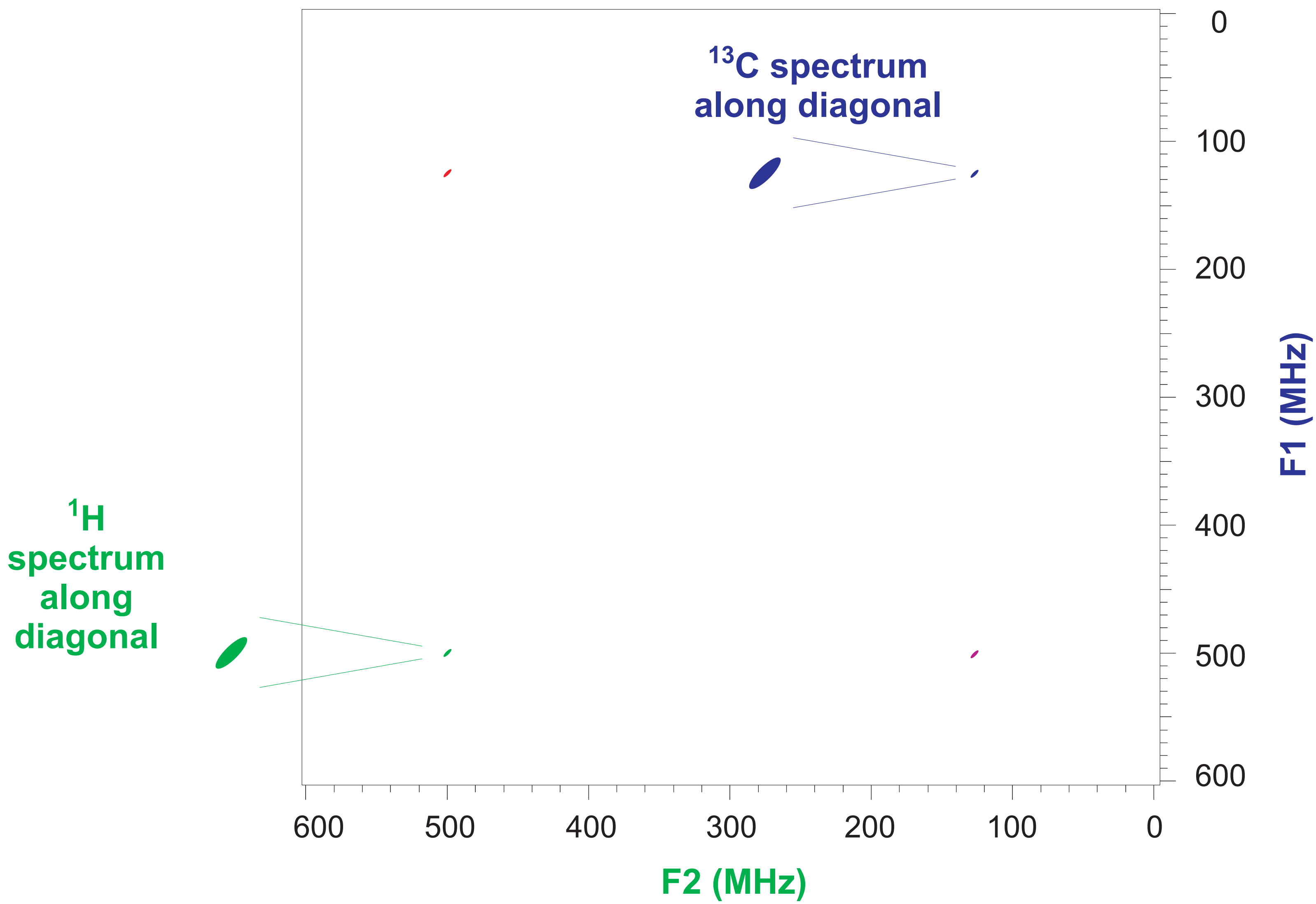
except that the shaded regions are hugely exaggerated:

the ^{1}H region would cover ~10ppm or 0.005 MHz,

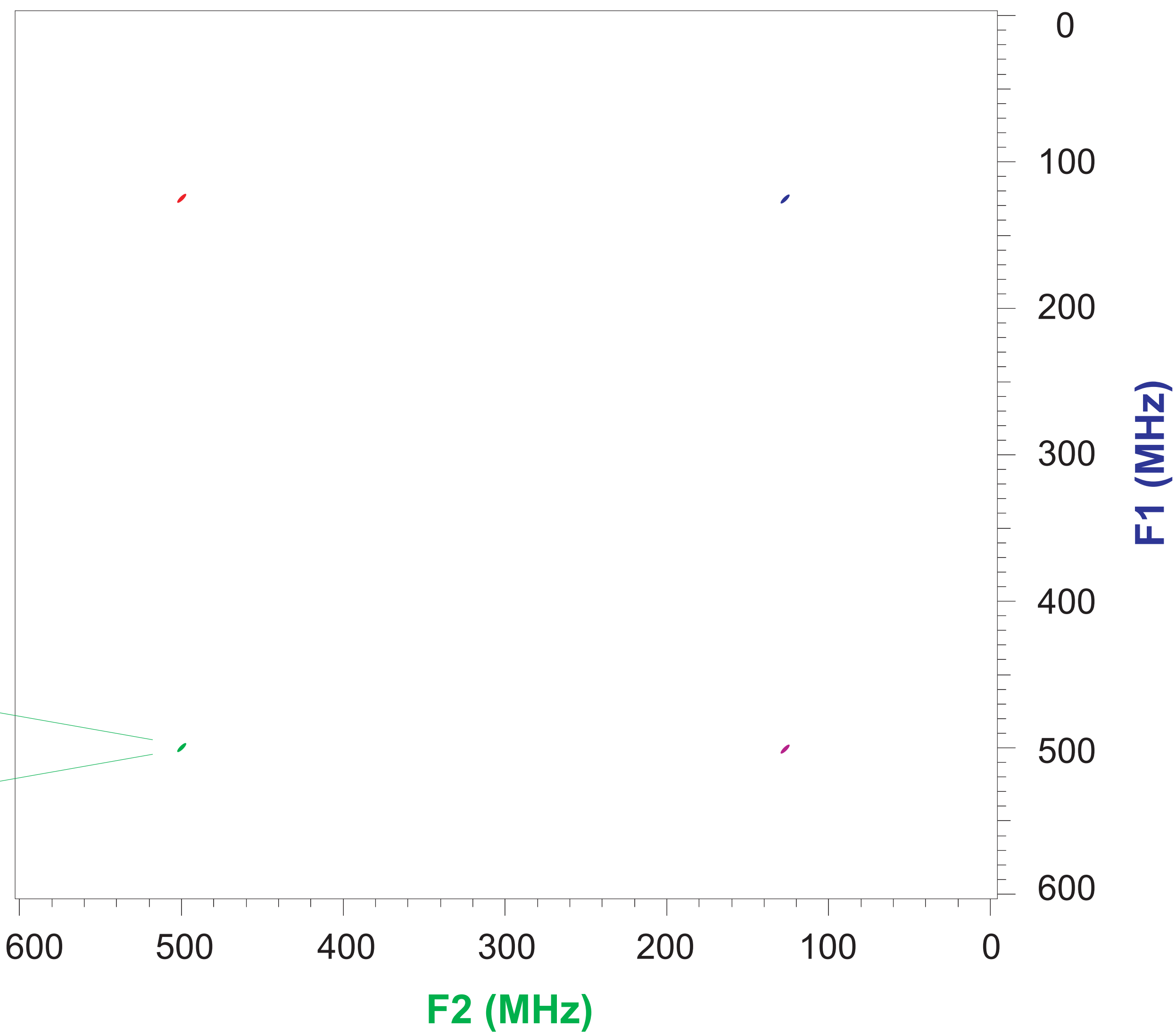
^{13}C regions would cover ~200ppm or 0.025 MHz.



The Diagonals of a Heteronuclear COSY



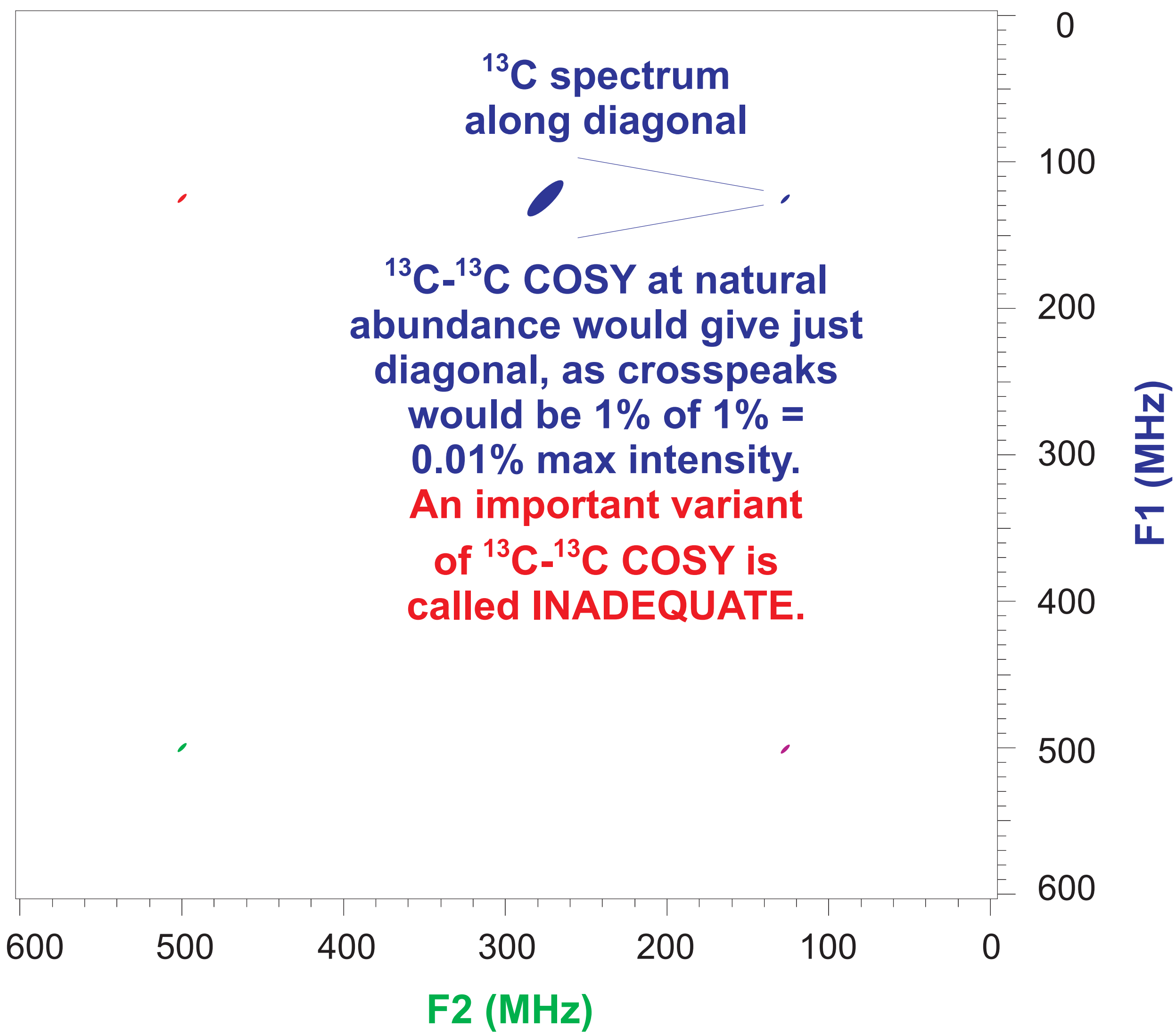
The Diagonals of a Heteronuclear COSY



^{1}H spectrum along diagonal

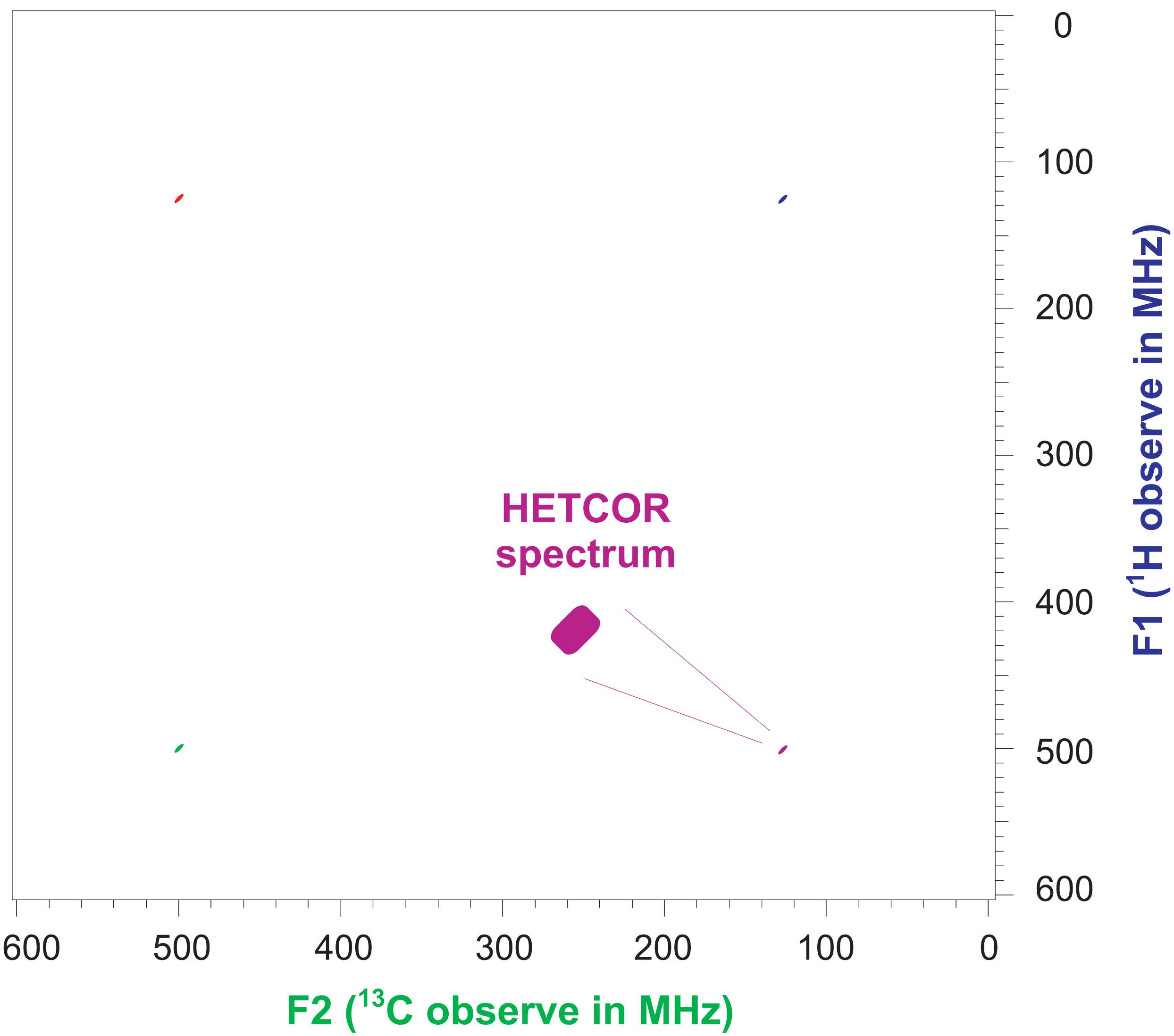
actually would see full ^{1}H-^{1}H COSY here

The Diagonals of a Heteronuclear COSY



Heteronuclear COSY – HETCOR

Direct observation of ^{13}C, with indirect evolution of ^{1}H (in t_1/F1), was the first widely used heteronuclear COSY experiment. It is compatible with older hard-ware (e.g., the ACs), but suffers from the relatively poor sensitivity of directly-observed ^{13}C.

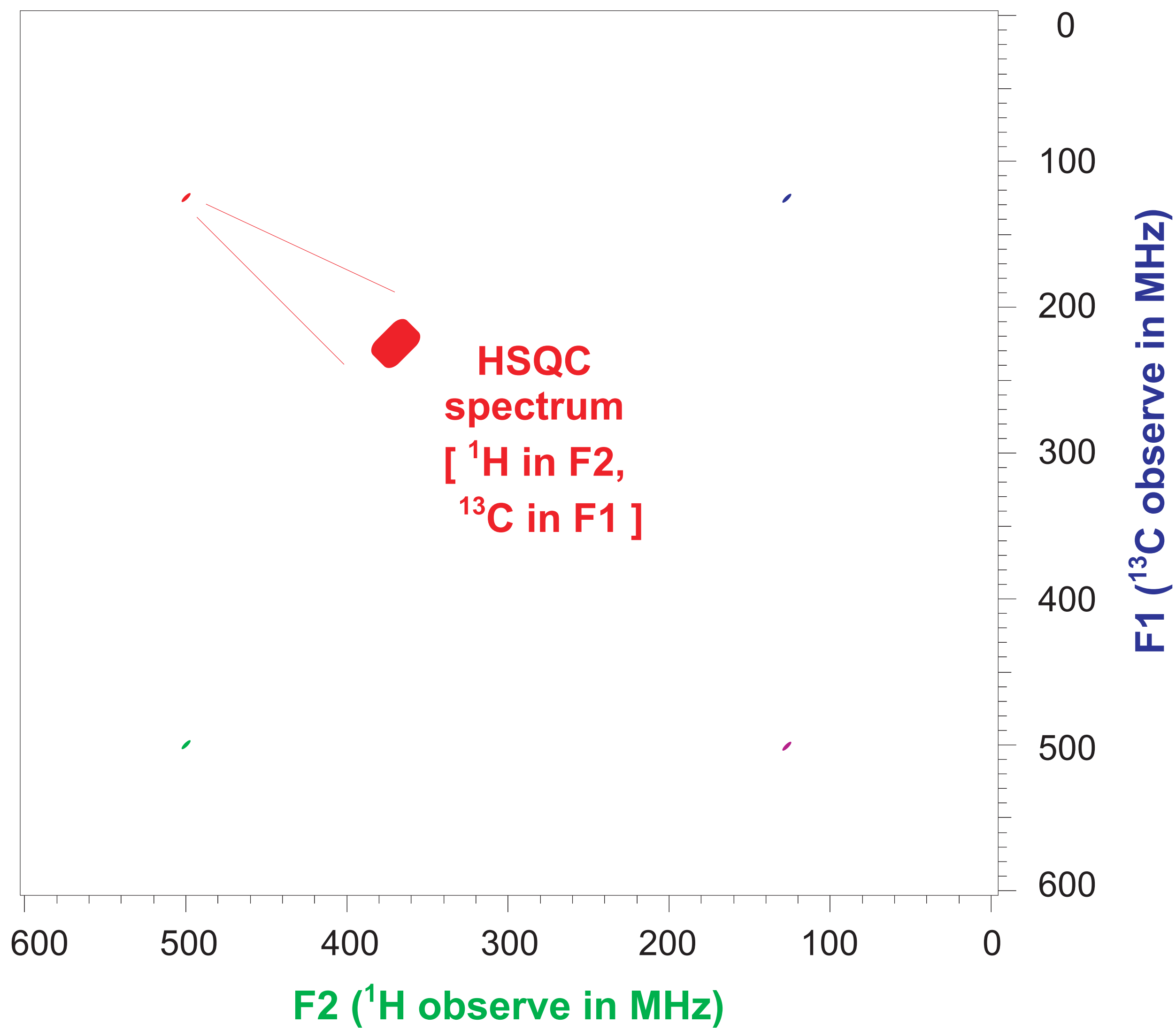


Regions of Heteronuclear COSY

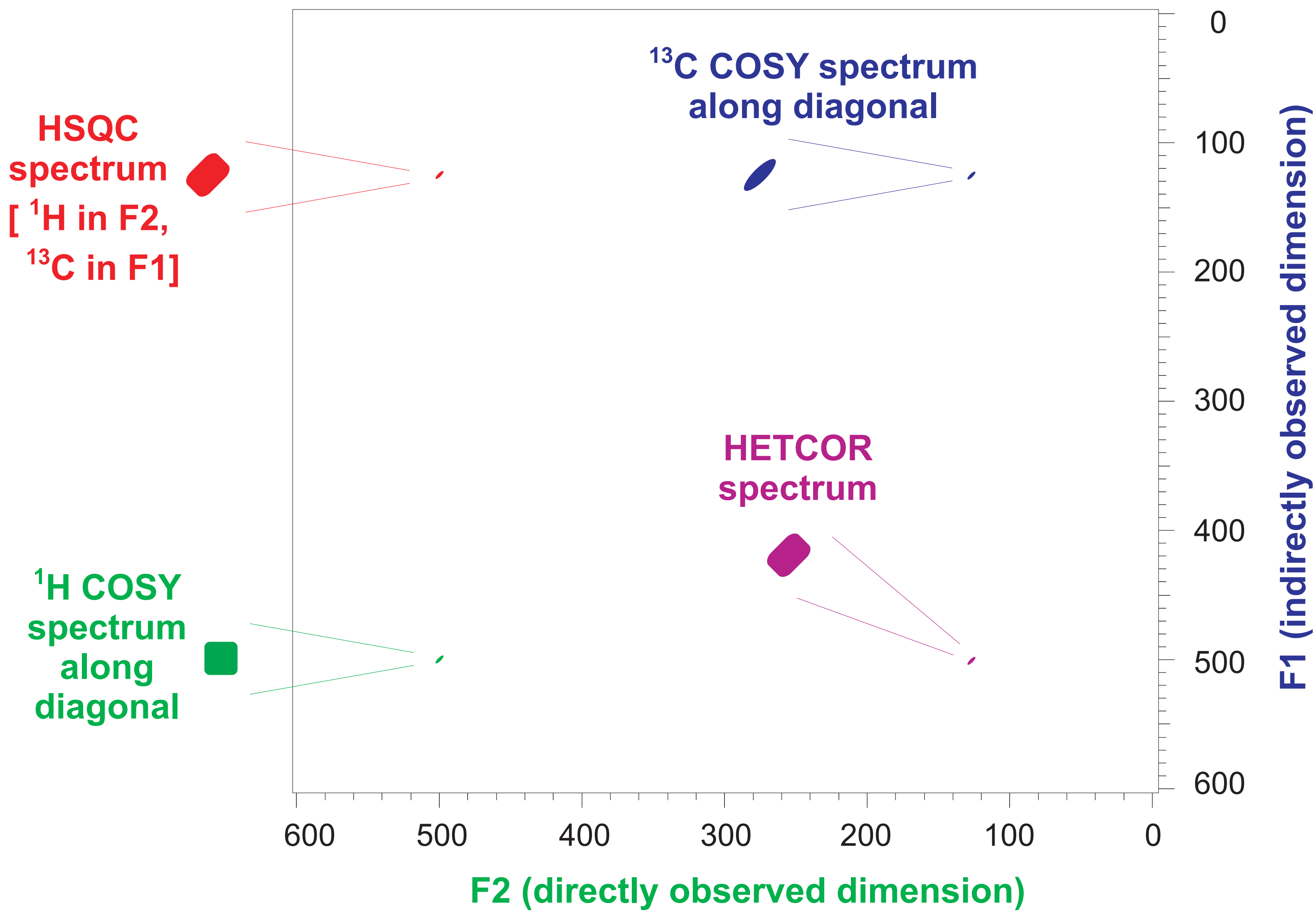
Direct observation of ^1H, with indirect evolution of ^{13}C (in t_1/F1), offers 8× the sensitivity of the HETCOR exp.,

but this inverse exp. (HSQC is only one of many variants) must, to high precision, remove ^1H bonded to ^{12}C (99%) during F2, requiring newer/ better hardware.

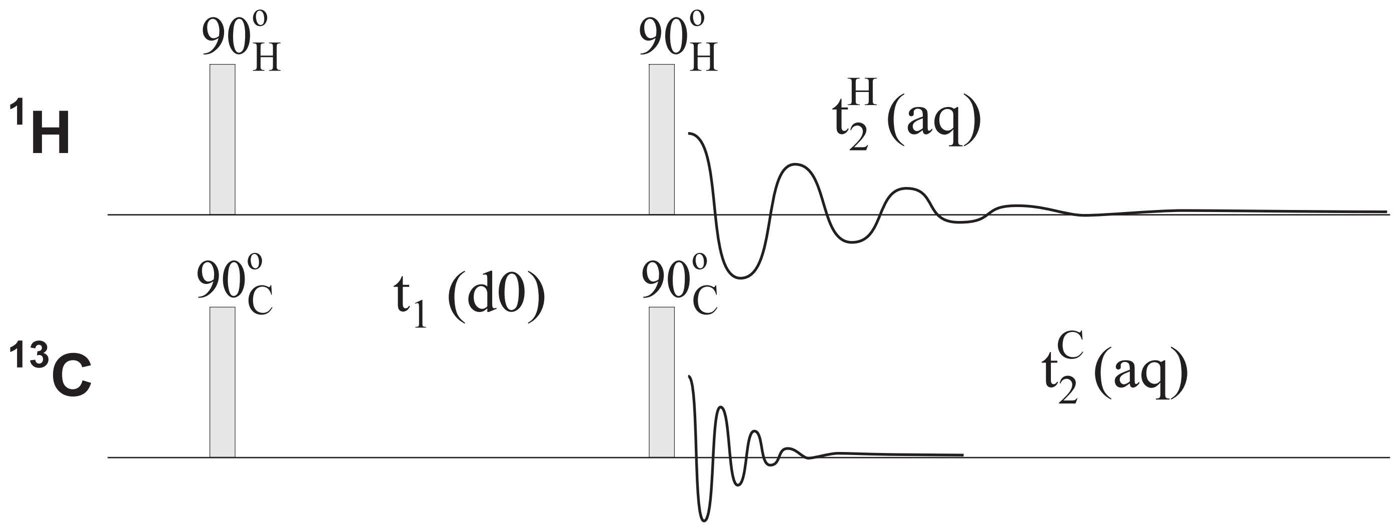
This inverse exp. is now common-place in NMR labs.



Regions of Heteronuclear COSY



Schematic of the HSQC Experiment

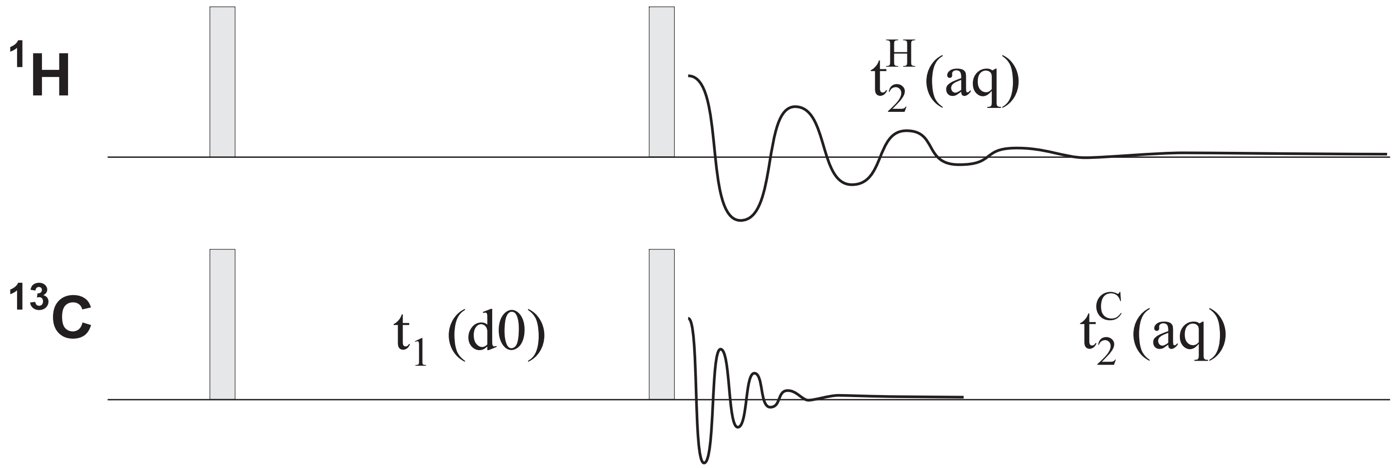


Impracticalities of performing the full experiment as shown on the previous pages, and it's superior sensitivity, makes HSQC the heteronuclear experiment to perform.

HSQC: ^{1}H directly observed/evolving in t_2/F2
^{13}C indirectly observed/evolving in t_1/F1.

Schematic of the HSQC Experiment

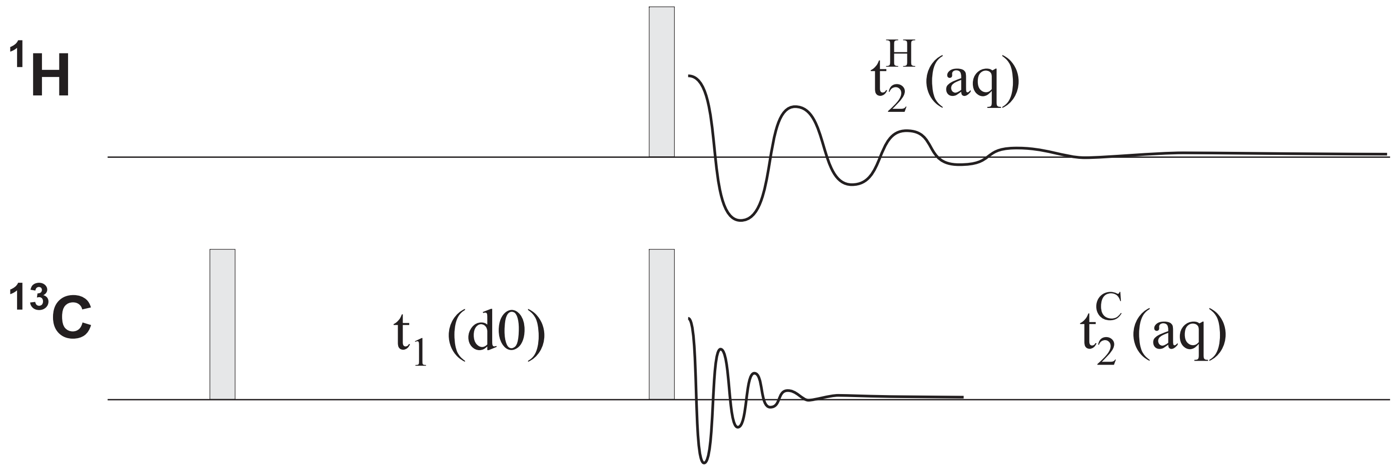
HSQC spectrum [^1H in F2, ^{13}C in F1]



Don't need 1st proton pulse for ^{13}C evolution in t_1.

Schematic of the HSQC Experiment

HSQC spectrum [^{1}H in F2, ^{13}C in F1]



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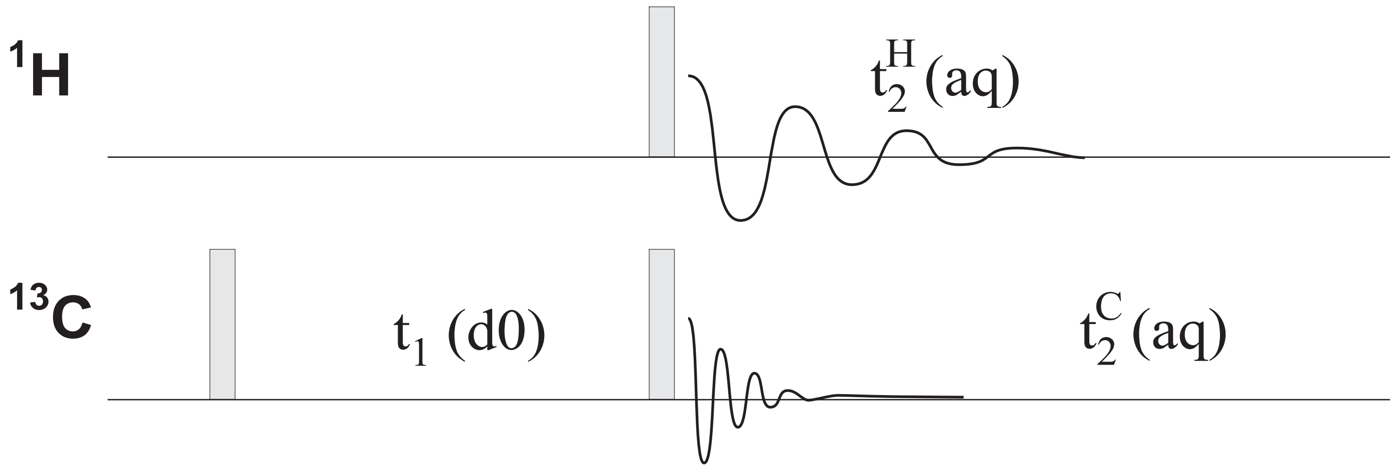
Schematic of the HSQC Experiment

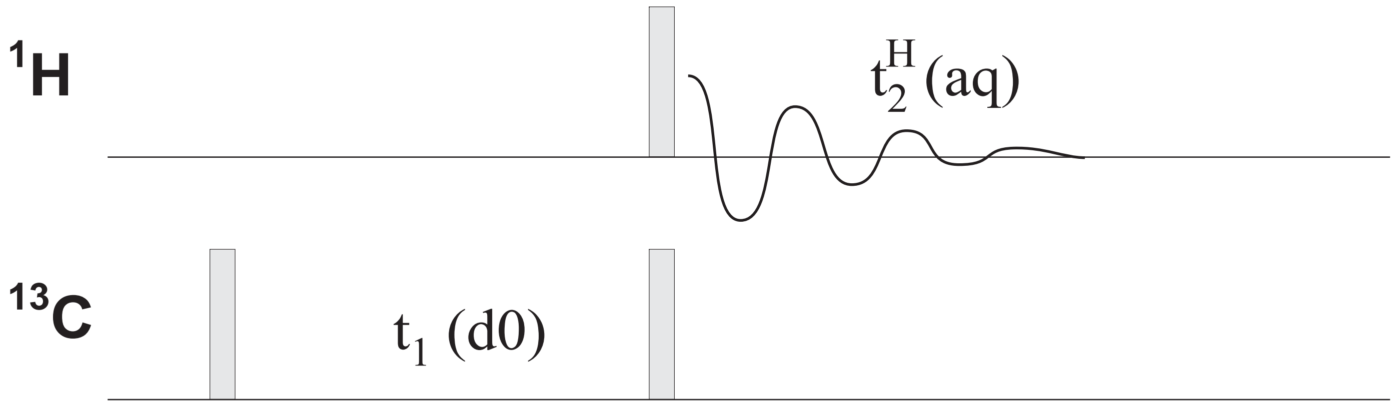
HSQC spectrum [^{1}H in F2, ^{13}C in F1]



Don't need ^{13}C detection during t_2 (^{13}C observed indirectly).

Schematic of the HSQC Experiment

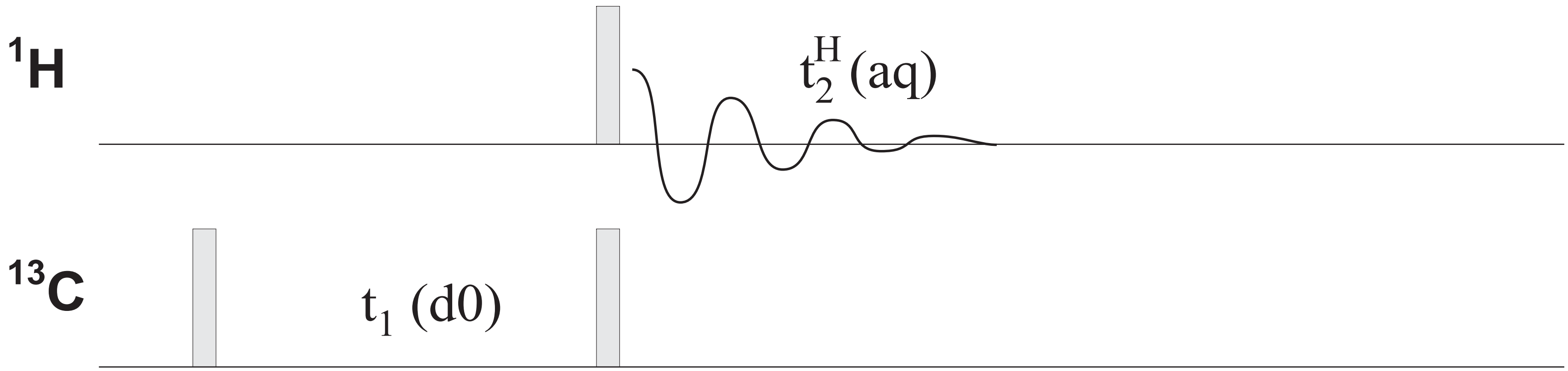
HSQC spectrum [^{1}H in F2, ^{13}C in F1]



Don't need ^{13}C detection during t_2 (^{13}C observed indirectly).

Schematic of the HSQC Experiment

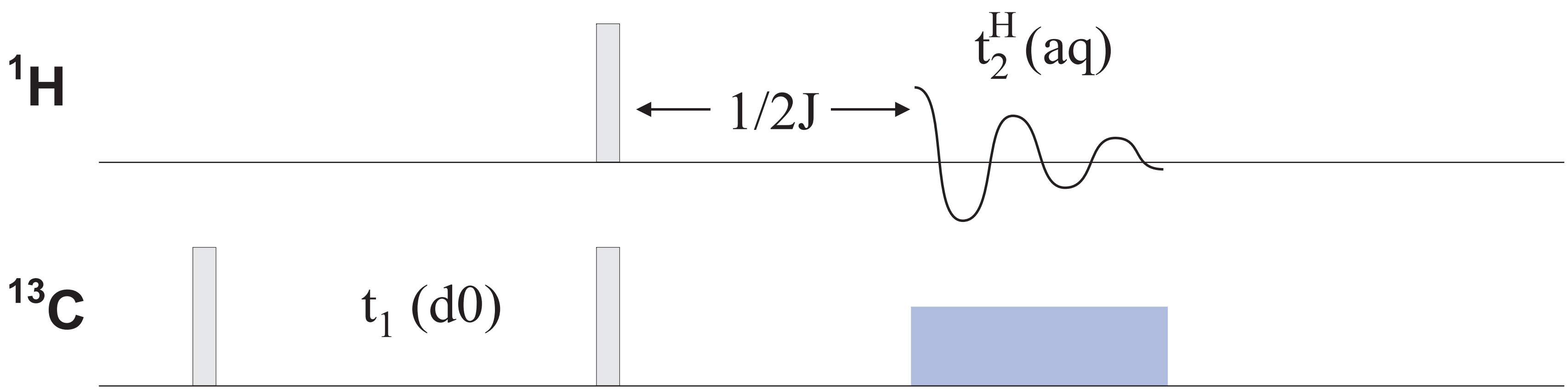
HSQC spectrum [^{1}H in F2, ^{13}C in F1]



Can improve sensitivity by allowing $I_xS_z \rightarrow I_y$ before detection, and include decoupling (removing heteronuclear coupling in t_2).

Schematic of the HSQC Experiment

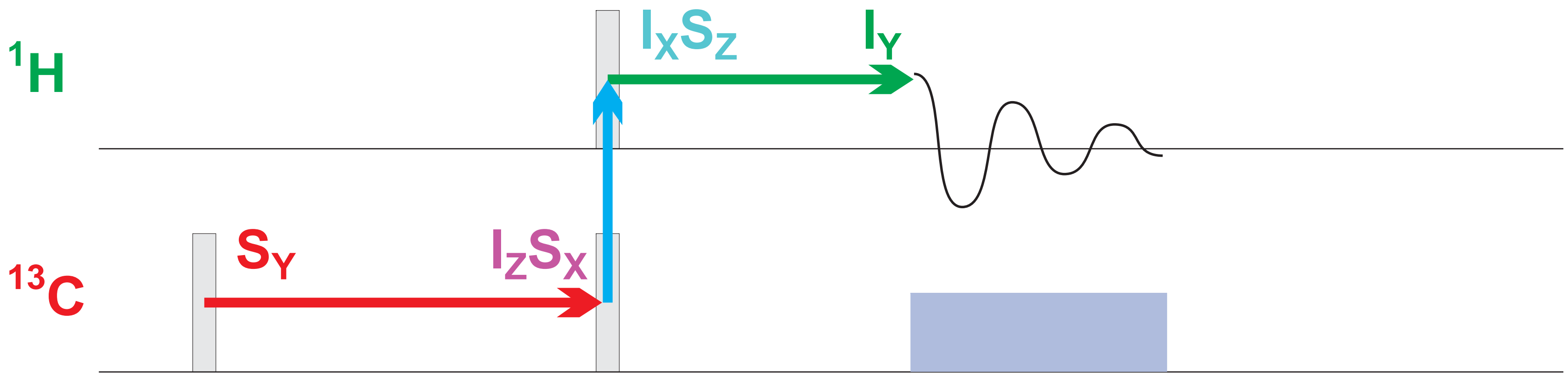
HSQC spectrum [^{1}H in F2, ^{13}C in F1]



Can improve sensitivity by allowing $I_xS_z \rightarrow I_y$ before detection, and include decoupling (removing heteronuclear coupling in t_2).

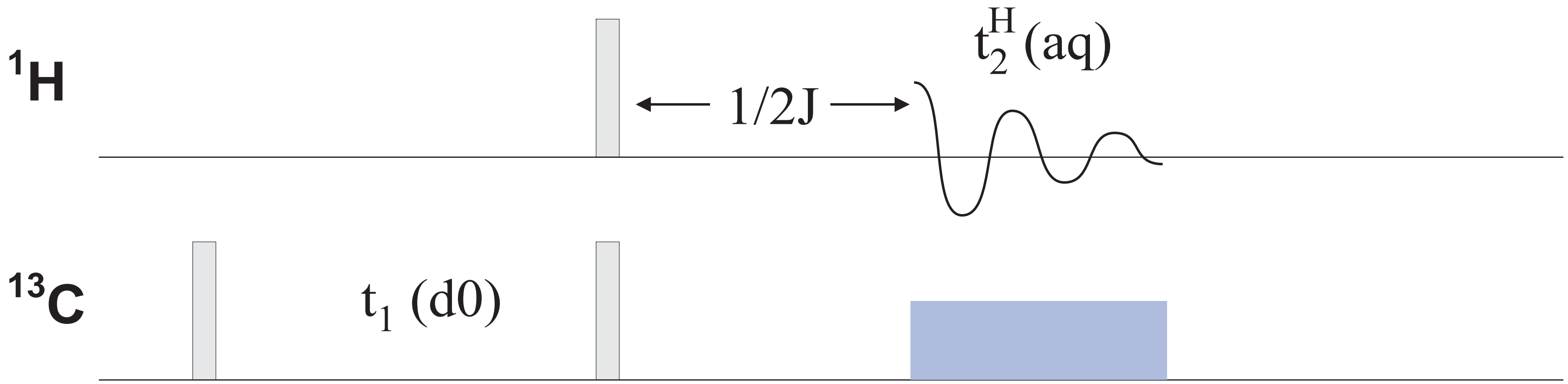
Schematic of the HSQC Experiment

HSQC spectrum [^1H in F2, ^{13}C in F1]



Schematic of the HSQC Experiment

HSQC spectrum [^{1}H in F2, ^{13}C in F1]

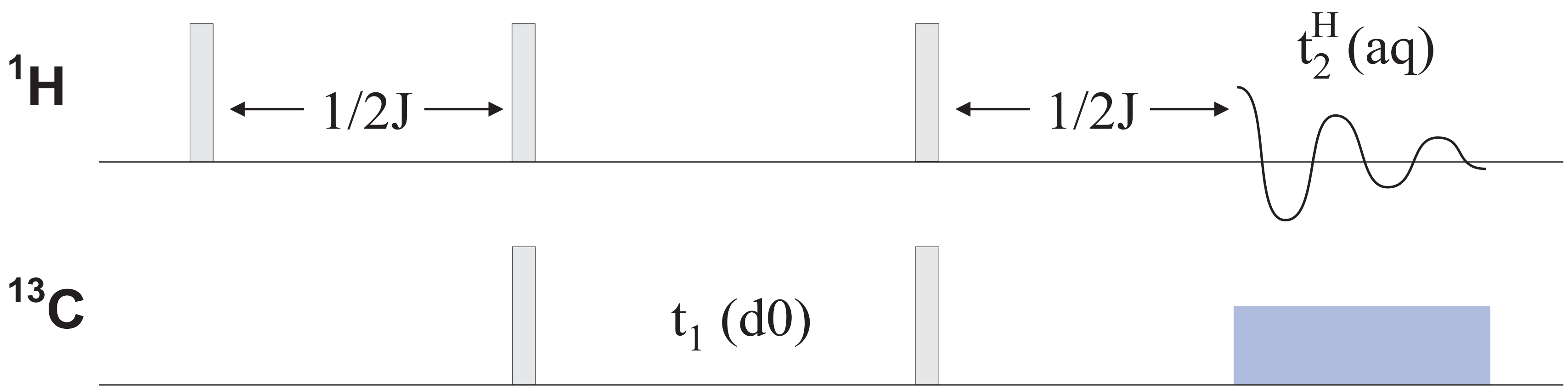


^{1}H detection is $(\gamma_H/\gamma_C)^{3/2}$ more sensitive than ^{13}C detection.

We can improve the experiment by another factor of γ_H/γ_C by providing ^{1}H excitation (now utilizing polarization transfer in the other direction: $I_y \rightarrow I_xS_z \rightarrow I_zS_x \rightarrow S_y$).

Schematic of the HSQC Experiment

HSQC spectrum [^{1}H in F2, ^{13}C in F1]



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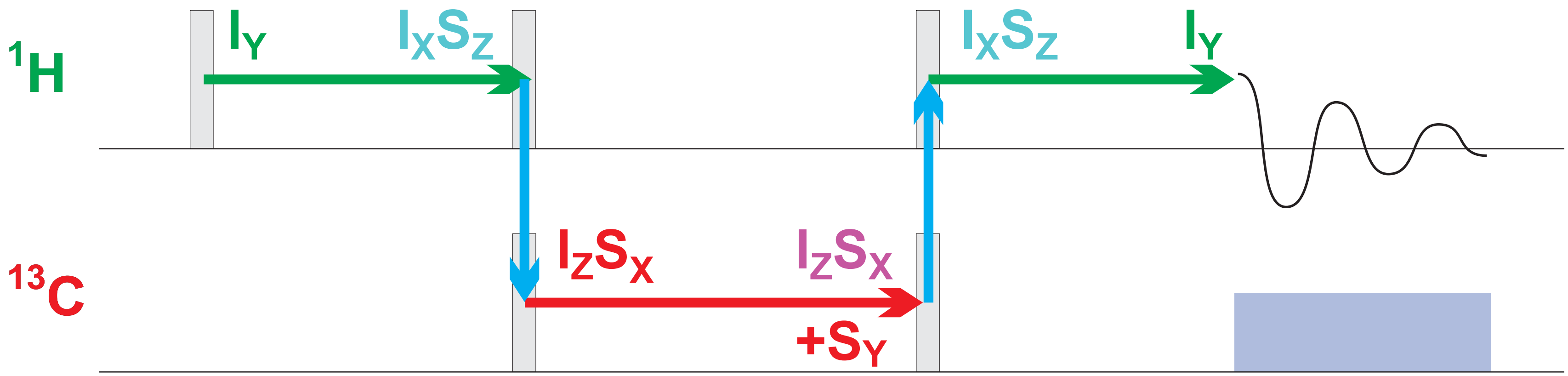
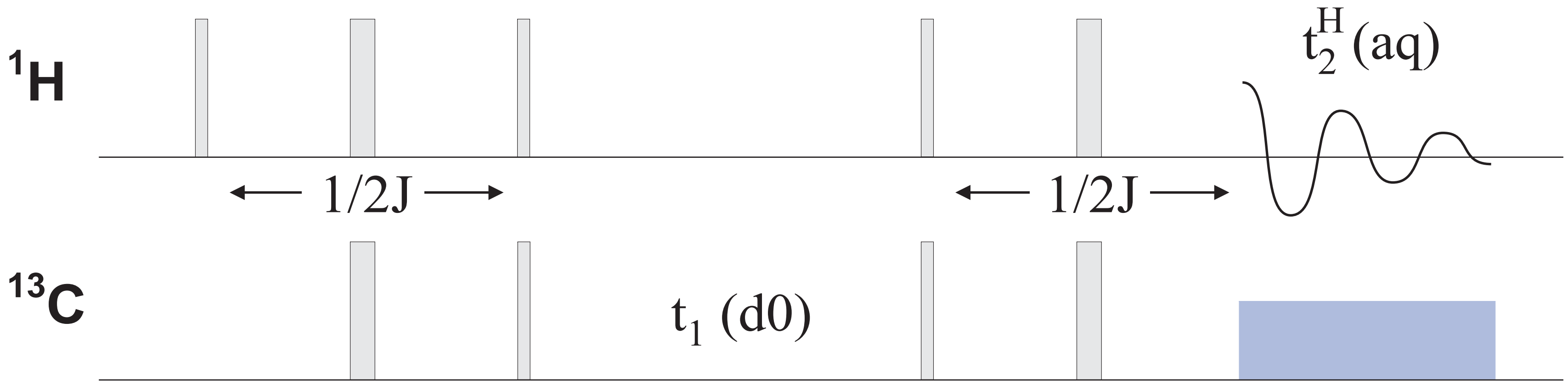
Schematic of the HSQC Experiment

HSQC spectrum [^{1}H in F2, ^{13}C in F1]



Schematic of the HSQC Experiment

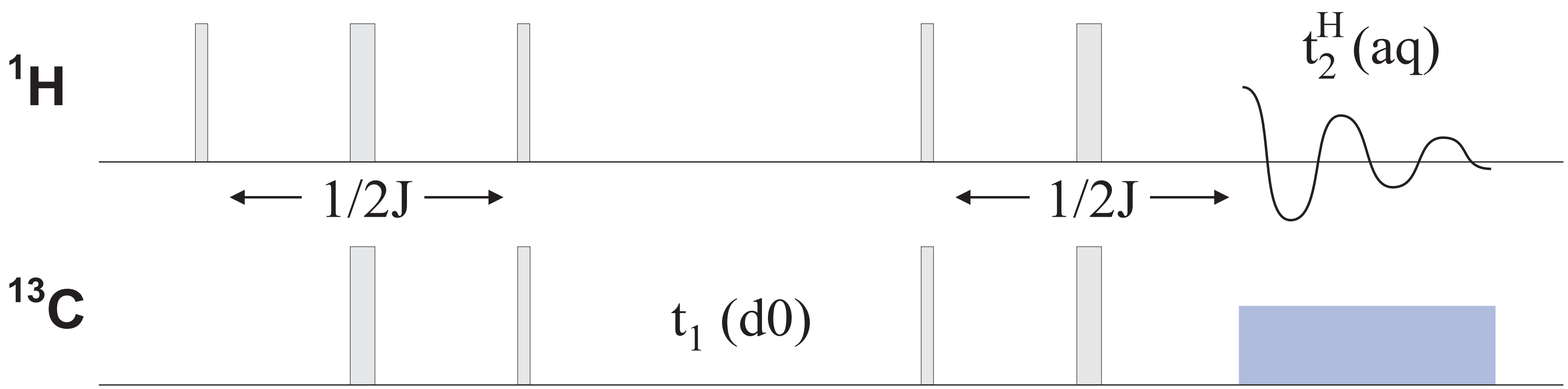
HSQC spectrum [^{1}H in F2, ^{13}C in F1]



180° pulses remove chemical shift during the J-evolution (polarization transfer) sections of the experiment.

Other components of a usable experiment, involving novel spin gymnastics (e.g., the BIRD sequence), and/or phase cycling, and/or pulsed-field gradients, are required to remove the 99% of protons bonded to ^{12}C.

Schematic of the HSQC Experiment



Theoretically (fairly close to empirical observations),

HSQC is $4^{5/2}$ ~ 32× better than ^{13}C direct (but 3 for NOE, so ~ 10× more sensitive, ~100× better in time).

$10^{5/2}$ ~ 320× better than ^{15}N direct (10^5× in time).