The most useful 2D NMR spectra for the analysis of small organic molecules

$^{13}$C-HSQC (“heteronuclear single-quantum correlation”) Correlates $^{13}$C with $^1$H via $^1J_{CH}$ couplings, i.e. no quaternary carbons

$^{13}$C-HMQC (“heteronuclear multiple-quantum correlation”) Same as $^{13}$C-HSQC, but worse lineshape in the $^{13}$C-dimension

$^{13}$C-HMBC (“heteronuclear multiple-bond correlation”) Correlates $^{13}$C with $^1$H via $^nJ_{CH}$ couplings. Useful for the detection of quaternary carbons

DQF-COSY (“double-quantum filtered COSY”) Correlates $^1$H with $^1$H via $J_{HH}$ couplings

TOCSY (“total correlation spectroscopy”) Correlates $^1$H with $^1$H via $J_{HH}$ couplings and transmits the magnetization via multiple relay steps

NOESY (“NOE spectroscopy”) Correlates $^1$H with $^1$H via NOEs (i.e. spatial proximity)

ROESY (“rotating frame NOE spectroscopy”) Same as NOESY, except that transverse magnetization rather than longitudinal magnetization is transferred

$^{13}$C-INADEQUATE Double-quantum spectrum between $^{13}$C spins at natural isotopic abundance. Very insensitive experiment, but independent of $^1$H spins.
The spectrum was recorded in $d_6$-DMSO. Negative cross-peaks are expected for compounds of low molecular weight. This spectrum is of a carbohydrate containing hydroxyl protons in the range between 3.5 and 6 ppm. Explain the origin of the positive cross-peaks!
Whereas NOESY is designed to let longitudinal magnetization migrate between different spins, ROESY is designed for exchange of transverse magnetization. For small molecules, NOESY and ROESY spectra should look the same. For large molecules, NOESY cross-peaks are positive (i.e. the same sign as the diagonal), whereas ROESY cross-peaks remain negative. ROESY thus is the experiment of choice for in-between molecular weights, where the NOE is zero.

In practice, the ROESY spin-lock generates artifacts. In (a), the positive cross-peaks arise from TOCSY transfers as a side-effect of the ROESY spin-lock. This problem is solved in the Tr-ROESY version in (b), but other problems remain (sample heating by the spinlock pulse, decreased cross-peak intensities due to off-resonance effects).
This spectrum was recorded with multiplicity editing that inverts the signals from CH$_2$, but not from CH and CH$_3$ groups. Multiplicity editing introduces only a very small penalty in sensitivity.
A COSY has big diagonal peaks with dispersive lineshapes that destroy much of the spectrum. They are suppressed in a double-quantum-filtered (DQF) COSY. Always record a DQF-COSY! Although it takes 4-times longer to record for the same signal-to-noise ratio, the cleaner diagonal is worth it.
Usually, the digital resolution in the indirect ($F_1$) dimension will be worse than in the directly detected dimension (why?). If the resolution were the same, the spectrum would be perfectly symmetric about the diagonal.

Even in a DQF-COSY, the diagonal peaks are not purely absorptive. Therefore, only use cross-peaks for phase correction.

The multiplet components observed in 1D NMR spectra are also present in COSY cross-peaks. The picture above shows the cross-peak of an A₂X spin-system. The X-spin appears in the 1D spectrum as a quartet. In the COSY cross-peak, all four multiplet components have the same intensity.

Pascal’s triangle can be used to predict the relative peak intensities (left panel for 1D spectra, right panel for COSY multiplicities):

\[
\begin{array}{ccccccc}
1 & & & & & & \\
1 & 1 & & & & & \\
1 & 2 & 1 & & & & \\
1 & 3 & 3 & 1 & & & \\
1 & 4 & 6 & 4 & 1 & & \\
\end{array}
\]

\[
\begin{array}{ccccccc}
1 & & & & & & \\
1 & -1 & & & & & \\
1 & 0 & -1 & & & & \\
1 & 1 & -1 & -1 & & & \\
1 & 2 & 0 & -2 & -1 & & \\
\end{array}
\]