Experiments, topics	Advantages	Problems
HSQC (Heteronuclear Single Quantum Correlation)		
Multiplicity edited HSQC		
HSQC and the proton-carbon single bond *J*-coupling		
Adiabatic carbon pulses in HSQC		
PFG (Pulse Field Gradient) selected/enhanced HSQC		
TANGO excitation with HSQC		
Sensitivity enhanced HSQC		
Carbon band-selective HSQC and aliasing/folding		
Non-decoupled HSQC		

Real-time pure shift BIRD HSQC		
HMQC (Heteronuclear Multiple Quantum Correlation)		
HMBC (Heteronuclear Multiple-Bond Correlation)		
HMBC and the proton-carbon multiple bond *J*-coupling		
H2BC (Heteronuclear Two-Bond Correlation)		
HSQC-TOCSY (Heteronuclear Single Quantum Correlation and Total COrrelation SpectroscopY)		
Fluorine observed experiments		
heteroCOSY (heteronuclear COrrelation SpectroscopY)		

The example sample: mixture of 26 mM cinchonidine, 33 mM quinidine, and 40 mM quinine in dmso-d_6. Note the overlap between quinine and quinidine resonances (use the CH next to the aromatic nitrogen, and the double bonded CH as easily identifiable parts of the spectrum).

HSQC: correlation between proton and carbon nuclei that are bonded to each other.

Sorting signals like the DEPT-135 with the multiplicity edited HSQC. The same trick (most of their problems are identical), but the HSQC experiment is more sensitive therefore normally faster and delivers much more than a DEPT spectrum.

Intensity of peaks in HSQC depends a lot on the value $^1J_{C13\text{-}H1}$.

Adiabatic HSQC improves sensitivity, and offers the possibility to reduce J-dependence of the HSQC assuming a linear relationship between carbon chemical shift and carbon-proton J-couplings.

PFG selection improves the quality of HSQC a lot compared to the old options, but it inherently reduces sensitivity, particularly when using low viscosity solvents like chloroform.

TANGO excitation is a method that can be used to replace the first proton pulse of any heteronuclear experiment. It will improve spectral quality by better suppression of not carbon-13 attached signals. It costs a bit of sensitivity.

Sensitivity enhanced HSQC is a version which can improve signal-to-noise ratio by 1.414, but theoretical gain is often not achieved due to extra relaxation losses. It works better with smaller molecules, and low viscosity solvents. It is also important when working with non-deuterated solvents (e.g. protein NMR).

Aliasing/folding is a method that can improve spectral resolution significantly in the carbon dimension, and also can reduce the experiment time of HSQC. Smart setup of the experiment is essential and extra effort for interpretation.

Heteronuclear decoupling is routinely applied in HSQC, which can cause sample heating, extra side-band signals. The spectral resolution is accordingly compromised in the proton dimension. A non-decoupled HSQC allows us to achieve the same resolution as in a normal 1D proton spectrum, at the cost of sensitivity. It is also useful to identify unwanted artefact signals (‘COSY-like’ and decoupling artefacts).

Advertisement: real-time pure shift HSQC offers simultaneous improvement in resolution and sensitivity. It has the ability to resolve quinine and quinidine signals (proton chemical shift difference is 0.004 ppm in one of the examples).

The HMQC spectrum is very similar to the HSQC, but there are significant differences which makes the HSQC to be the golden standard in almost all cases that are relevant in chemistry.

The HMBC experiment provides information about multiple bond proton-carbon correlations. Unfortunately, there are no general rules to distinguish between 2 and 3 bond correlations, which is the key to provide evidence for structural alternatives. It is perfect as part of a spectral characterization but real, unknown samples are very difficult to properly analyse. This is very different from HSQC, where the interpretation can be trusted much more. The lack of a correlation in an HMBC spectrum means very little.

H2BC aims to provide a solution to the problem with HMBC, but it usually does not replace HMBC. In desperate situations

one may try to use it to help assignment of HMBC spectrum. H2BS can only correlate protonated carbons.

HSQC-TOCSY is a very useful experiment when a series of repeating patterns are present in a complex mixture. The proper experiment setup requires understanding of the TOCSY experiment, but with experience this is more trustworthy than HMBC because the TOCSY transfer is easier to interpret correctly contrary to HMBC. The sensitivity of the HSQC is distributed among the coupled protons, and optimisation of the mixing time often requires multiple experiments. It costs time, but it delivers a lot of information.

Fluorine-carbon correlation experiments (or any other combination of NMR active nuclei with ½ spin) can be used in the same way. The experiment is identical regardless of the nuclei involved (assuming proper pulse programming), but we most often define different parameter sets for clarity. Fluorine specific problems are associated to the very large fluorine chemical shift range and often large *J*-couplings.

Heteronuclear COSY is an old experiment, which is rarely used. It is similar to the COSY, and as long as HSQC, HMBC, etc.. gives good results one would never want to run heteroCOSY. The main reason where it is useful is when there is a large range of unknown J-couplings which makes the other J-optimised methods very inefficient. Similarly to COSY, the heteroCOSY delivers all correlations that are coupled.