Optimization of NMR 2D experiments for molecular characterization of nanoparticles.

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Nanoparticles are molecules with a nanometric metallic core on which surface simple ligands are immobilized. They are very promising systems because their potential applications as multivalent biomedical tool therefore it is essential to characterize then at a molecular level.

2D NMR experiments are a very useful and common tool to characterize molecules based on organic structures. Then NMR allows extract data on individual atoms reflecting their structural properties (i.e. chemical shift environments). Unfortunately, routine 2D standard experiments of nanoparticles, tend to fail because magnetization decays too fast to observe the expected cross-peaks due to their very short transversal relaxation times. We have explored the behaviour of Glyconanoparticules (nanoparticles with sugars immobilized on the core by flexible linkers of variable length) towards different homonuclear 2D experiments. As Glyconanoparticules have a large metallic core with flexible carbohydrate moieties attached, the overall correlation time is large, but the organic parts still have relatively short internal correlation times. This is reflected in a short T_2 with broad signals while T_1 is more favourable.

First, we have compared dipolar coupling based experiments with antigen Lewis-X gold-nanoparticles finding that while ROESY peaks disappear very fast, NOESY experiments yield strong and readily observable cross-peaks. This observation reflects the effect on the different mixing schemes of the respective relaxation times (T_1 and T_2).

We also have explored the performance of several TOCSY mixing schemes using glyconanoparticles of different sizes and metallic cores (gold or silver). Here we present the evaluation of several TOCSY sequences, based on:

1.- Clean or relaxation compensated isotropic mixing times, that prevent the cancellation of positive TOCSY correlations by negative ROESY-type cross-peaks, that are very strong due to the favourable T_2.: clean MLEV17, rc-dipsi2.

2.- Relaxation optimized sequences that optimize the time spend by the magnetization during the mixing period in the plane x-y or in the z axis**:** MOCCA, Adiabatic-TOCSY.