Multivalency in Carbohydrate-Carbohydrate Interactions. A 3D View by Using NMR

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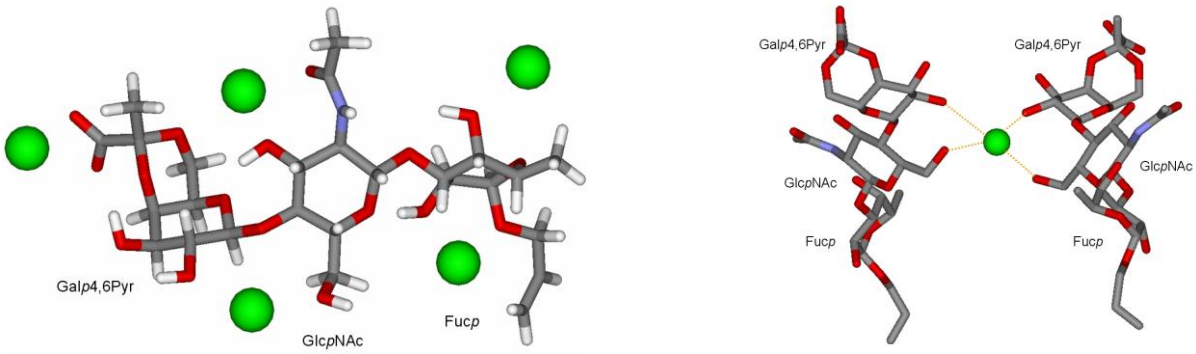
Molecular recognition events are at the heart of live processes. Depending on the chemical nature of the interacting moieties, different ranges of affinities are accessible, with distinct associated features. In the last decades, it has been shown that glycoconjugates are involved in many signalling processes, especially when interacting with protein receptors. Nevertheless, it has also been shown that interactions among carbohydrates are also involved in adhesion and fertilization processes. These sugar-sugar contacts, at the single molecule level, are extremely weak in nature and thus, the existence of multivalency is essential to enhance the interaction. We now have addressed the experimental demonstration of the existence of carbohydrate-carbohydrate interactions in solution by using a combined NMR/modeling approach, as a complement to other biophysical methods that rely on surface coating. Thus, a gold glyconanoparticle, coated with the marine-sponge trisaccharide has been used as "receptor" molecule, while the same trisaccharide entity has been chosen as the "ligand".

In a first step, the conformational study of the trisaccharide has been carried out by using a combination of NMR experiments assisted by MD calculations with the MM3* force field. The computed conformational populations have been used to quantitatively calculate the expected Nuclear Overhauser Effects, using a full matrix relaxation approach. The expected NOE data have been compared with those experimentally measured. Then, the sugar-sugar interaction has been explored using a variety of NMR methods, including DOSY, STD, and TR-NOE experiments. The experimental results unequivocally show the existence of specific interactions between the gold glyconanoparticle and the isolated trisaccharide, mediated by Ca^{2+} ions.



Finally, to propose a geometrical perspective of the carbohydrate-carbohydrate recognition process, MD simulations on a multivalent trisaccharide-Ca^{2+} system using explicit water molecules by means of the AMBER force field have been carried out. The obtained trisaccharide-Ca^{2+}-trisaccharide 3D models are in agreement with the observed NMR data.

The CIB group thanks MEC/MCINN for financial support (CTQ2006-10874-C02). S. M.-S. thanks MEC for a Ramón y Cajal contract.