IMPRS on Multiscale Biosystems

Title: Juggling with flexible biomolecules
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Project description: Apart from the large number of rigidly folded proteins, many biomolecules retain an inherent flexibility that is important for their biological functions. The time scale on which this internal conformational change takes place is usually not directly accessible to conventional experimental techniques. Nuclear Magnetic Resonance (NMR) spectroscopy experiments in solution provide a broad variety of indirect means to uncover the hidden dynamics: position and intensity of the resonance peaks of various spins sensitively depend on the tumbling, flipping or wagging of a molecule. But, these experimental data do not deliver information to distinguish between the (interesting) internal switching, and the (rather uninteresting) overall tumbling. In Figure 1, a rather ingenious trick is sketched of how to make significant progress in this direction: the resonances are influenced by a molecular probe that is directly attached to the molecule of interest.

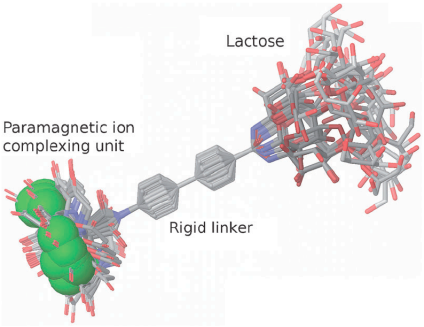

Figure 1. "Juggling" lactose: the conformational space of this disaccharide is made visible by overlaying conformations at different times (computer simulation, the overall rotation has been removed). A paramagnetic unit has been added to the molecule via a long rigid linker that trims the overall tumbling, and probes evenly all resonances within the saccharide by dipole interactions through space. Picture taken from Griesinger *et al*, *Chem. Eur. J.* **2011**, 17, 9368 – 9376.

The goal of this project is to investigate the conformational variation of recently synthesized carbohydrate molecules that are similar in structure, but induce a strongly varying immune response when used as immunogens specifically recognized by antibodies. The prospective student will learn how to jointly use chemical synthesis, basic experimental NMR approaches and computer simulations with atomistic models as a valuable complementary tool needed to interpret experimental results. At a later stage, he or she will use state-of-the-art techniques to refine the initial investigations. Following this strategy we will foster our understanding of how small chemical modifications of carbohydrates can enforce a dynamical behavior that suits a particular biological function.

Required background: The prospective student should have a good background in chemistry, physical chemistry or physics. Interest in numerical/theoretical methods is advantageous.
Paper to read before the interview: Mate Erdelyi, E. d'Auvergne, A. Navarro-Vazquez, A. Leonov and C. Griesinger. Dynamics of the Glycosidic Bond: Conformational Space of Lactose. *Chem. Eur. J.* (**2011**) DOI: 10.1002/chem.201100854

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