COURSE: RESIDUAL DIPOLAR COUPLINGS (RDCS) AND RESIDUAL CHEMICAL SHIFT ANISOTROPY (RCSAS)
ESSE CURSO SERÁ MINISTRADO EM INGLÊS!!!!

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RECOMMENDED PREREQUISITE READING reading: High-Resolution NMR Techniques in Organic Chemistry, Tim Claridge.

REQUISITES: The student should bring their own laptops where the necessary software (MSpin, MNova, StereoFitter) will be installed. Students are encouraged to bring stereochemical problems of their own.

TOPICS OF THE COURSE: The 2D structure of most small molecules can be straightforwardly determined by manual or automatic analysis of 1D and 2D NMR experiments providing trough-bond connectivity (COSY, TOCSY, HSQC, HMBC and ADEQUATE/INADEQUATE based experiments), Once the 2D structure is available, the determination of relative configuration and preferred conformation is a more challenging task commonly addressed by using NOE and ^{3}J coupling constants analysis, and more recently by application of DFT predicton of ^{13}C chemical shifts. However, it is difficult to assess how many samples are sitting on the laboratory's refrigerators waiting for an independent methodology that could lift some of the ambiguities generated by the use of conventional NMR methods. The development of the application of Residual Dipolar Couplings (RDCs) has matured enough in the recent years to perform this task is an almost straightforward way, without even the need of using NOE and ^{3}J coupling analysis, as it will be presented here for the analysis of rigid and semi-rigid small molecules.

Residual Chemical Shift Anisotropy (RCSA) is another highly valuable anisotropic NMR parameter for the structural analysis of small organic molecules. Due to the presence of unwanted isotropic chemical shifts, the accurate measurement of RCSAs is not as straightforward as measuring Residual Dipolar Couplings (RDCs), While RDCs encode information about the relative orientation of internuclear vectors (E.g, C-H bonds), RCSAs encode information about the relative orientation of chemical shift tensors. Hence, RCSAs are a valuable complement to RDCs in highly proton-deficient molecules specially those containing sp^2 carbons (aromatic rings, double bonds, carbonyl groups, etc.).

Outline of the course

1. The theory behind the alignment of small molecules. *The alignment tensor. Least-squares fitting. Conformational analysis, the single tensor approximation*.

Here the students will learn the basics about molecular alignment and the least-squares fitting of aligment tensors to molecular structures including systems with molecular flexibility and free rotors.

2. Alignment media for small molecules. *Polymer gels. Lyotropic phases. Preparation and practical recommendations.*

In this section of the course the student will learn about the currently available alignment media and practical tricks for optimal preparation and sample loading as well as analysis of the physical homogeneity of the media.

3. Experimental Measurement of RDC and RCSAs. *RDC measurement: HSQC-type experiments. The strong coupling problem. Measurement of RCSAs in polymer gels*.

In this section we will discuss the current state of the art for acquisition of RDC data using different types of HSQC experiments. Best procedure for extraction of data will be presented using the MNova software. The problem of strong-coupling will be discussed. Finally the use of ^{13}C experiment for RCSA data extraction using polymer gels will be discussed.

4. Solving structural problems with RDCs and RCSAs. Molecular modeling and conformational analysis. Fitting RDC and RCSA data to trial structures and conformational ensembles.

The student will learn about the molecular modeling protocols best suited for analysis of RDC and RCSA data. Different scenarios, will be illustrated with the use of the MSpin and StereoFitter programs.