NMR Spectroscopy: Combining computation and experiment

Nuclear Magnetic Resonance (NMR) has historically been a fundamental technique to explore the molecular structure of new substances. Today, modern powerful ab-initio simulations allow to predict NMR results with unprecedented accuracy, making this technique able for the first time to give even deeper insights into crystalline order in both organic and inorganic compounds. This new potential, however, can be somehow stifled by the practical problems posed by the usage barrier between experimental NMR scientists and the running and interpretation of computational simulations.

The CCP for NMR Crystallography, or CCP-NC, aims at abating this barrier by releasing software tools designed to make it easier and more intuitive to interpret ab-initio NMR results and compare them with experiment, as well as automate as much as possible of the process. Its first product, MagresView, has now been fully released as a live web application and provides the experimental community with the possibility to visualise and post-process NMR data in the "magres" file format. This format is now being pushed as a new standard for the field, and MagresView is contributing to its diffusion by providing a standard tool that employs it.

Since its inception, Nuclear Magnetic Resonance has been a very precious tool in unraveling the details of chemical structure in many substances, compensating for the weaknesses of other techniques such as X-Ray Diffraction. Fundamentally, NMR is a technique that allows us to measure the magnetic field experienced by specific atomic nuclei inside a sample. This magnetic field is strongly influenced by the arrangement of the electronic cloud surrounding the atom itself, and thus can be a precious insight in what kinds of bonds the atom itself is forming and with which species. In addition, since the signal has such a short ranged origin (a few Angstroms at best), NMR does not require fully grown single crystals like some other spectroscopic techniques and works well with powders or even liquids

However, the relationship between chemical structure and local magnetic fields is all but trivial. Historically, empirical observation and basic theoretical considerations allowed for interpretation of the strongest contributions to the signal, but the smaller details would be too hard to predict, and the information they conveyed lost. Recently, though, new advancements in both algorithms and sheer computational power have made it possible to obtain far more accurate predictions of NMR parameters starting with chemical structure using ab-initio simulations. This paved the road to proper NMR crystallography, a previously unthinkable enterprise, extending the amount of information that we can extract from the same data about the overall molecular and crystalline structure of a substance. Such a technique has great potential in those fields, like pharmaceutical research, that work with organic molecular compounds that organise in many subtly different crystalline forms but can be hard to investigate with diffraction techniques due to the predominance of light atoms or the difficulty to grow large single crystals.

One of the bigger obstacles to this approach being adopted by the community at large lies in the difficulties of connecting properly the computational and the experimental sides in terms of skills, know-how, conventions and language. As it is often the case, these two different fields have developed different ways of describing the same things, and it does not help that the measured quantities in NMR experiments are often pretty far removed from the most natural physical descriptions of the parameters as an ab-initio simulation can derive them. For example, a typical product of an ab-initio NMR calculation could be the "shielding tensor" at a given site, a matrix returning the magnetic response of the electronic wavefunction to an external field; however, chemical NMR most often deals with "chemical shift", namely the trace of that tensor referenced to the same value in some standard chemical compount (since absolute values are easily calculated but fundamentally nigh impossible to measure in an experiment). The vast amount of data processing required just to parse the results of an ab-initio calculation in a form that is easily digestible and comparable to experiment can in itself be a huge barrier to usage of this novel approach. For that reason CCP-NC has funded the creation of MagresView, a software tool dedicated exactly to solving this problem in a user-friendly way.

MagresVies is a web application relying on JMol, a commonly used open source molecular visualisation software developed by Robert Hanson. JMol works also as a web applet (both Java and Javascript), and through a close collaboration with its creator in the last years it has implemented both the ability to parse magres files, the CCP-NC format of choice for storing NMR data, and process basic NMR quantities. In addition to that, the magres file format has been adopted as output both by the CASTEP and the Quantum Espresso ab-initio software packages, making it a possible candidate for a future general standard. What MagresView adds on top

of the basic JMol capabilities is a Javascript powered user interface that allows to execute all the most common visualisation and post-processing operations in a simple, intuitive manner.

For example, tensorial quantities like the shieldings and the electric field gradients are visualised in MagresView in ellipsoid form. This provides an easy way to convey the information contained in the tensors' eigenvalues and eigenvectors, which is far more meaningful than their explicit form. In addition, it provides text and color scale labeling based on all the most commonly defined ways of expressing them: chemical shift, anisotropy and asymmetry, but also span and skew, used by different conventions. Similarly, visual links are employed to display atom-atom coupling effects, limiting the number of links visualised at a time by user selection to avoid overcrowding the plot.

In addition to these capabilities, MagresView also provides some basic computational ones. Not only are tensors diagonalised, but the relative rotation of their principal frames can be expressed in the form of Euler angles (a commonly used quantity in quadrupolar NMR), dipolar couplings can be calculated from scratch, quadrupolar shifts include up to second-order corrections, and quantities that are affected by the choice of isotope or magnetic field properly account for them. All this can be saved into textual output that can

then serve as input for other software. An important target of MagresView in fact is to ease the use of spin dynamics software like SIMPSON, which are necessary to predict the results of the most sophisticated NMR experiments, even given the basic parameters. MagresView provides formatted output that can be directly copy-pasted into a SIMPSON input file, thus reducing the distance from ab-initio simulation to NMR experiment simulation to one simple step.

MagresView has been available to the public for more than a year now at http://www.ccpnc.ac.uk/magresview as a live web version and on CCPForge as stand-alone source code. The success of the software across the NMR community, especially the UK one, is very satisfying, with Google Analytics reporting often more than 100 page hits per week. We hope that it will be the first stepping stone to build a better bridge between the computational and experimental communities in this sector and prelude to a vaster collaboration leading to systematic understanding and classification of chemical structures by their computed NMR parameters, which would all-around greatly benefit future crystallography efforts.

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