NMR: giving molecules the right spin

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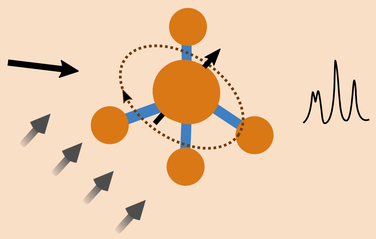
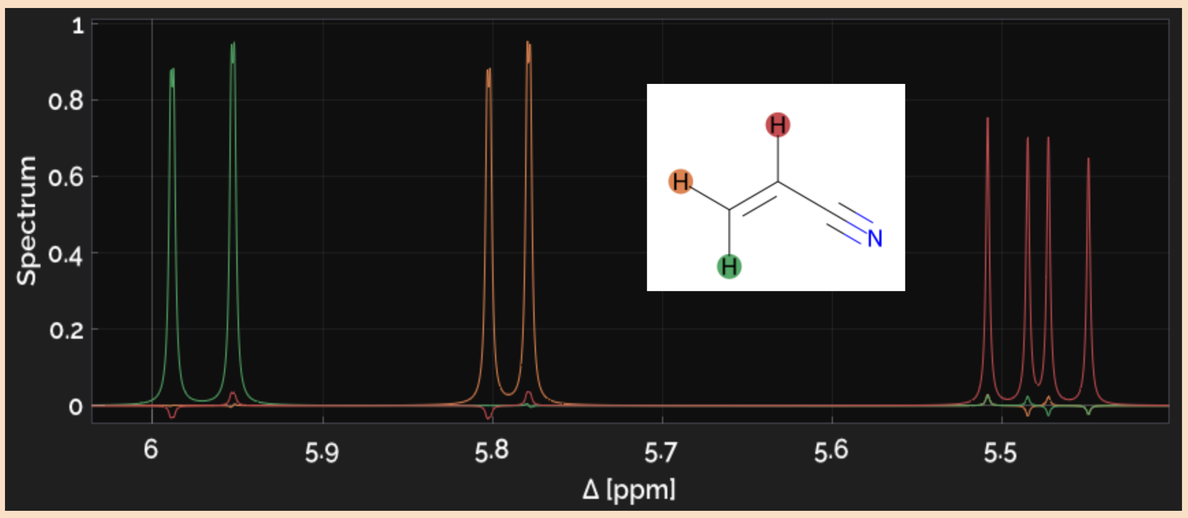
Nuclear magnetic resonance (NMR)

- **NMR spectroscopy** is one of the most important analytical techniques in chemistry and related fields[1]
  - Widely used to *identify molecules* or to obtain information about their structure, dynamics, and environment
- Nuclei in molecules are shielded by electrons against the magnetic field: $\hat{H}_Z = -\gamma(1+\delta)\mathbf{B}\cdot\mathbf{S}$



  - γ is the *gyromagnetic ratio*, δ the *chemical shift*
- At or near *resonance*, the system responds by producing an electromagnetic signal with a frequency characteristic of the field at the respective nucleus
- Peaks in an NMR spectrum are characterized by two parameters:
  - (isotropic) **chemical shift** δ_k relative to a reference compound
  - (indirect) **spin-spin coupling** J_{kl}, leading to a **multiplet** structure

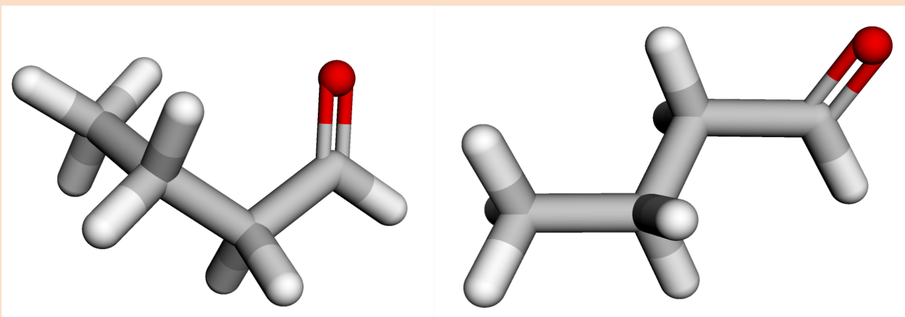


Quantum-chemical calculation of NMR parameters

- NMR **spin Hamiltonian** for molecules in the *liquid phase*:

$$\hat{H} = -\sum_k \gamma\,(1+\delta_k)\,\mathbf{S}_k\cdot\mathbf{B} + \frac{2\pi}{\hbar}\sum_{k<l} J_{kl}\,\mathbf{S}_k\cdot\mathbf{S}_l$$

- In **quantum chemistry**,[2] the NMR parameters are commonly calculated as *second derivatives* of the total energy E with respect to $\mathbf{B}$ and $\mathbf{S}_k$
- Complication: gauge-dependence of the vector potential
  - Commonly solved by employing *gauge-including atomic orbitals* (GIAOs), which make the resulting expressions gauge-independent
- For flexible molecules, a conformer/rotamer *sampling* is usually necessary[3]
  - "Average" spectrum obtained by weighting with *Boltzmann factors*
- **Advantages** and **disadvantages** of quantum-chemical approaches:
  - All shifts and J-couplings accessible at the same level of accuracy
  - Complex and expensive calculation, limitations of accuracy depending on level of theory



Empirical methods to obtain NMR parameters

Different estimations in the literature include:

- *Experimental data*: good for testing, requires assigned spectrum
- *Increments*: basic shift for atoms corrected by positive & negative terms for the substituents[4]
- *Cheminformatics*: HOSE and other substructure codes consider "spheres" of neighboring atoms, look up values in data set[5]
- *Machine learning*: learn a parameterized function to approximate NMR parameters; depends strongly on type and architecture of the network and the descriptors used

HQS Approach

- Start from structural formula representation and obtain 3D structures
- Conformer sampling and quantum-chemical parameter calculation to create data base for a pre-defined set of molecules
- Use data base for empirical approaches to obtain spin Hamiltonian for molecules not covered by the data base
- Implement solvers on classical and quantum computer (currently simulated)

HQS NMR Tool – Graphical User Interface (GUI)

Given a **molecule** or a **spin input** with corresponding parameters for δ_k and J_{kl}, the NMR-GUI can be used to simulate the NMR spectrum using several different solvers

- Direct approach (brute force)
- Factorization solver
- Lindblad/direct time solver
- Quantum computer solver

The following features are currently being implemented:

- Graphical web-browser interface
- Quantum-chemical parameter calculation
- Parameters from empirical approaches

[1] H. Günther, *NMR Spectroscopy: Basic Principles, Concepts, and Applications in Chemistry* (Wiley-VCH, 2013).
[2] T. Helgaker, M. Jaszuński, and K. Ruud, *Chem. Rev.* **99**, 293 (1999).
[3] S. Grimme, C. Bannwarth, S. Dohm, A. Hansen, J. Pisarek, P. Pracht, J. Seibert, and F. Neese, *Angew. Chem. Int. Ed.* **56**, 14763 (2017).
[4] E. Pretsch, T. Clerc, J. Seibl, and W. Simon, *Tables of Spectral D Compounds* (Springer Berlin/Heidelberg, 1989).
[5] W. Bremser, *Anal. Chim. Acta* **103**, 355 (1978).

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