NMR chemical shifts in crystalline compounds

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Crystal structure

**X-ray single crystal diffraction**
- Provides accurate structural model
- Single-crystals of good size and quality cannot be grown

**X-ray powder diffraction (XRPD)**
- Very accurate in detecting long range ordering and crystal symmetries

**ss-NMR spectroscopy**
- Very sensitive at local structural details

Specialized software
NMR chemical shifts

Most of NMR crystallography applications relied on $^{13}\text{C}$ ($^{15}\text{N}$) Cross-Polarization Magic Angle Spinning (CP-MAS) spectra recorded on natural abundance samples

- number of molecules in the asymmetric unit
- presence of impurities
- different solid forms
- presence of structural and/or dynamical disorder in the lattice
- can validate the proposed structure solution (RMSD = 1.9 ppm)

NMR chemical shifts computations

**Software:**

- Quantum ESPRESSO: integrated suite of Open Source computer codes
- CASTEP / NMR CASTEP: modules of Materials Studio environment from Accelrys Company
  - a tool for predicting NMR chemical shift for many types of material
  - very good parallel efficiency

**Hardware:**

- **Past:** 2xOpteron dual-core 2224E, 16GB RAM 333 MHz
- **Present:** Hewlett Packard Blade C7000 with 16 Proliant BL280c G6 (2 Intel Quad-core Xeon x5570 @ 2.93 GHz, 16 GB RAM, 500 Gb HDD)
- **Future:** IBM System x iDataPlex DX360 M4, Two Head Node Server: 6-core, with 2.93 GHz, and 12 MB L3 cache, 28 Nodes: Two Intel Xeon Sandy Bridge E5-2665 8-Core 2.4 GHz, 20 MB L3 cache, DDR3 64 GB 1600 MHz ECC (448 cores) (2 of this nodes have also NVIDIA Tesla M2090 GPU); Network Connection: FDR Infinite band with 56 GB band width
NMR chemical shifts dependencies on C-H and N-H bonds length

✓ The isotropic chemical shifts for each carbon and proton site were computed on a set of molecular structures obtained by varying the C-H and N-H bond length in the range 1.03 – 1.13 Å

✓ The maximum variations were obtained for nuclear spins belonging to directly bonded C-H and N-H, namely 6-6.5 ppm per each C-H bond within a CHn moiety in the case of 13C, and 2-3.5 ppm for 1H, respectively.
Application: ethoxzolamide structure

Application: quercetin structure

NMR assisted crystallography protocol is successfully used to determine the molecular architecture in powders. This protocol, which combines X-ray powder diffraction (XRPD) with complementary techniques such as solid-state NMR (SS-NMR) and molecular modeling (MM), is able to facilitate the validation and selection of the accurate structure solution.
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Projects:
Modern high-throughput methodologies for obtaining and characterizing new solid forms of pharmaceutical compounds / HT-PHARMA (Dr. Mihaela Pop)
  - Sectorial Operational Programme “Increase of economic competitiveness”
  - Priority Axis 2 – Research, Technological Development and Innovation for Competitiveness

Modern approaches for solid form screening of active pharmaceutical ingredients and structural characterization on powders (Dr. Carmen Tripon)
  - PNII – Human Resources - Postdoctoral research project

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Cluster configuration:

Structural Analysis in Solids

NMR spectroscopy
X-Ray diffraction
Solid forms screening

Datacenter