Solving structures from powders using intermolecular distances

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This work presents a methodology that integrates additional structural information derived from solid-state NMR (ssNMR) experiments in the form of intermolecular distances, which are used as constraints during global optimization in direct-space methods [1]. Direct-space methods for crystal structure determination from powder diffraction (PD) data are powerful tools, especially when only a laboratory diffractometer is available. These methods rely on global optimization algorithms and, simply said, operate by trial-and-error testing whether proposed structural models match the measured data.

For simple, well-diffracting compounds, the probability of finding the correct solution using these methods is high. However, as the number of variables increases, the success rate drops significantly. For example, solving a very simple and well-diffracting compound with only six degrees of freedom (DOF) may take just a few seconds. Compounds with around 20 DOF may require several minutes, while more complex ones with 30 DOF can take several hours. Compounds with around 40 or more degrees of freedom are often unsolvable from PD data alone, although there are some exceptions [2]. The challenge becomes even greater for poorly crystalline compounds that exhibit substantial peak broadening. In such cases, the limited resolution of the diffraction data may eventually become insensitive to the structural model. As a result, the correct solution becomes indistinguishable from random alternatives due to the high number of variables and the low number of meaningful observations.

Adding observations obtained from other analytical methods can help overcome this limitation. We collected intermolecular distances using specific ssNMR experiments and incorporated them into the structure determination process as additional constraints. The FOX [3] software was extended to include a new term in the cost function, accounting for experimentally determined distances between selected atoms of different molecules. These distances, defined with precision based on NMR data, were used as restraints during structure solution. The methodology was tested on relatively simple isothiouronium salts, where low-quality diffraction data were simulated by artificially broadening the peaks. The results showed that incorporating ssNMR-derived restraints improved the success rate of obtaining correct structures.

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