Chemical annotation in the Crystallography Open Database

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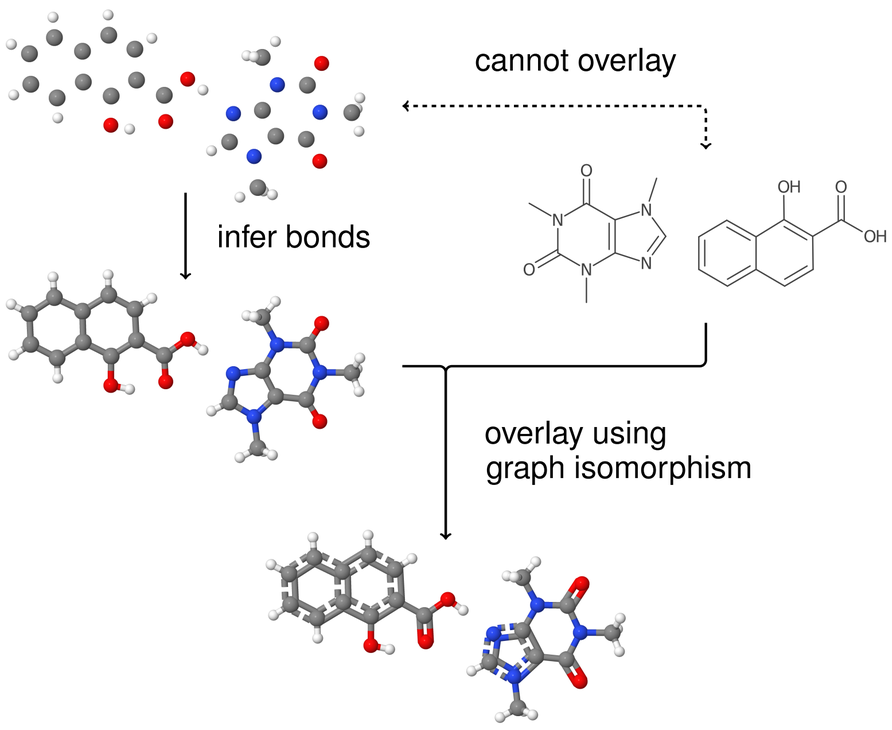
Abstract

Reliable knowledge about structure and properties of chemical compounds is essential for many branches of science. The most accurate data about the structure of molecules are obtained from X-ray crystallographic (XRC) analyses. These data are not immediately usable by chemists, as XRC does not detect atomic charges, bond types or the presence of lone electrons in radicals. All such information needs to be inferred from the crystallographic data, either manually [1], or using heuristics, implemented as computer programs [2, 3]. The existing programs rarely consider information other than the coordinates and their heuristics are usually specifically tailored for organic molecules. Thus the derivation of chemical annotations by these programs is not always reliable, especially for metal-organic complexes. Atomic coordinates in crystal structure reports are usually accompanied by additional chemical information, such as systematic chemical names and connectivity details, albeit mostly in forms not suitable for automated overlaying on the coordinate data. All this information could be employed to annotate crystallographic data with chemical details provided the mapping between different representations is known. The largest open access crystallographic database, the Crystallography Open Database (COD, [4]), contains computer readable chemical descriptions for nearly half of its entries [1]. Currently, these descriptions are not linked to particular atoms in crystals, thus studies that require the combined crystallographic and chemical information have to infer the correspondence on their own. Graph-based algorithms could be used to supplement the COD with the information about such missing links. Open-access nature of the COD allows dissemination of this information under FAIR (Findability, Accesibility, Interoperability and Reusability [5]) principles on the Web, immediately enabling numerous computational searches and research by pharmaceutical companies and academic groups.

Problem

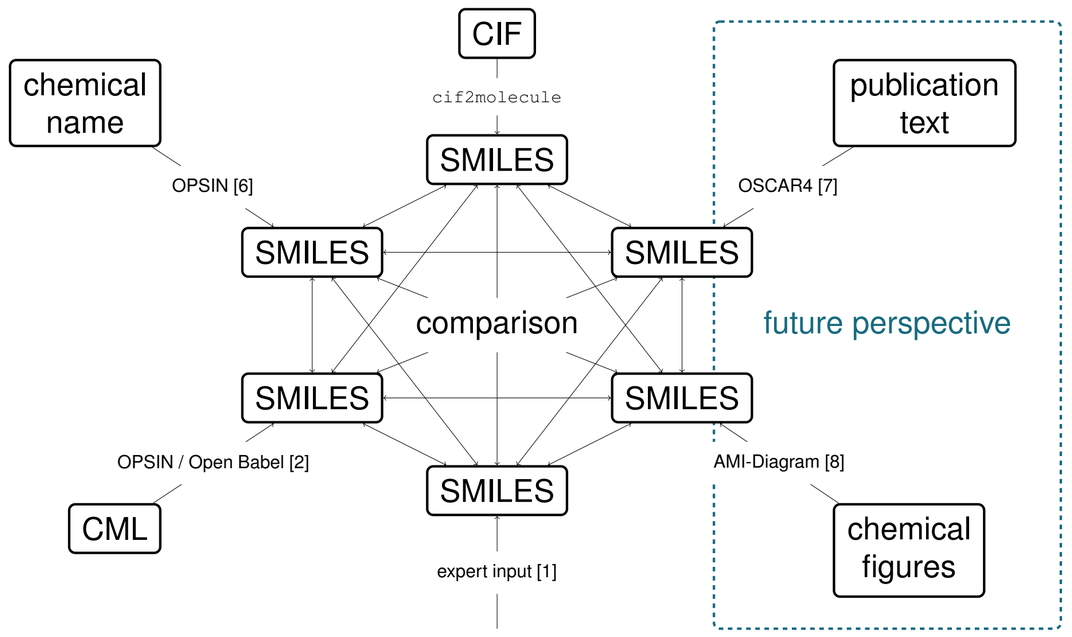
- Papers contain crystallographic and chemical descriptions of compounds;
- Information is scattered in items of different formats:
  - coordinates in CIF;
  - systematic chemical name in CIF;
  - systematic chemical name in publication title;
  - Chemical Markup Language (CML) files;
  - SMILES;
  - figures with chemical structures;
  - ...
- No automated methods exist to interrelate these descriptions.

Overlaying crystallographic and chemical annotations

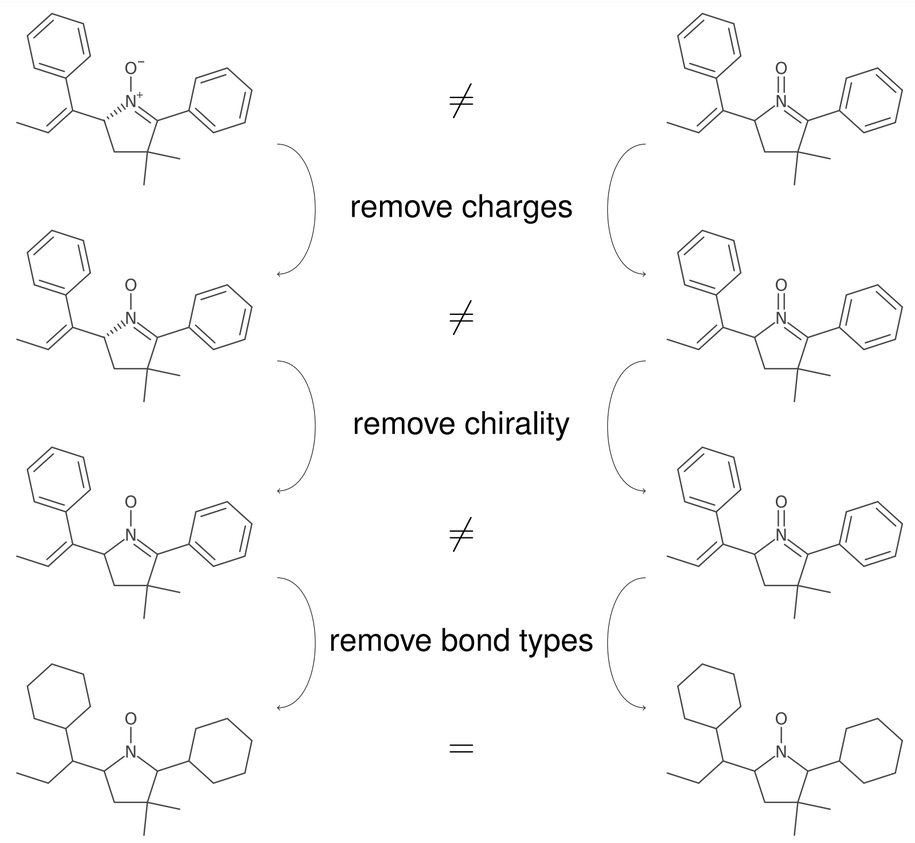


1. Connectivity is inferred from the coordinates;
2. Crystal contents are broken down into moieties;
3. Moieties of compared crystals are matched;
4. Corresponding moieties are overlayed.

Workflow



Comparison



- Stripping chemical attributes until match is found;
- Marking nonmatching structures for further review.

Results

Source #1	Source #2	No. of pairs	Matches
Coordinate-derived	Chemical names	38 640	88%
Coordinate-derived	CML	1551	89%
Coordinate-derived	Expert-curated [1]	187 935	57%

- Analysis of a couple dozens of mismatches identified incomplete or incorrect published chemical annotations.

Challenges to address

- Polymer molecules are difficult to process;
- More interesting traits are dominated by differences in notation:
  - aromatic form vs. Kekulé form;
  - marked vs. unmarked metal coordination [9].

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On-line version of the poster:
https://j.mp/3fWZHDS

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