A General Method for The Structure Determination of Amorphous Drugs By NMR

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NMR crystallography is a powerful method to determine the structure of molecular solids. However, structure determination of amorphous materials remains challenging, owing to the disorder inherent to these materials. In particular, disorder prevents the unambiguous identification of a modelled periodic structure as representative of the whole material through density functional theory chemical shift computations. Here, we determine the structure of an amorphous drug by combining solid-state NMR experiments with molecular dynamics simulations and machine-learned chemical shifts. By considering the combined shifts of several atomic sites in the molecule, we determine the structure of the amorphous drug AZD4625 by identifying an ensemble of local molecular environments that are in agreement with experiment and extract preferred conformations and intermolecular interactions in the amorphous sample.