BIOVIA® MATERIALS STUDIO® POLYMORPH PREDICTOR™

DATASHEET

BIOVIA Materials Studio Polymorph Predictor allows you to predict potential polymorphs of a given compound directly from the molecular structure. Polymorphism is the ability for a compound to crystallize in more than one chemically identical but crystallographically distinct form. Crystalline materials are prevalent in many industries, including pharmaceuticals, agrochemicals, pigments, dyes, explosives, and specialty chemicals. Polymorphs may differ in key properties such as shelf-life, bioavailability, solubility, morphology, vapor pressure, density, color, and shock sensitivity. It is therefore important to know how many polymorphs are possible as well as how their properties might differ when working in the solid state.

THE CHALLENGES FACED

Once a particular solid form of a material is chosen for its desired properties, researchers need to control the crystallization and formulation conditions so that unwanted polymorphs do not appear. In order to do so, they need to fully understand the structural aspects of each polymorph. This knowledge is also important for patenting and registration purposes.

The most common method for determining a crystal structure is to grow quality crystals for single crystal X-ray diffraction. Growing single crystals of appropriate size, however, is often difficult or even impossible. Furthermore, one can not be certain that all possible polymorphs have been discovered experimentally. Thus, methods that help predict potential stable and metastable crystal packing arrangements from the knowledge of just the contents of the asymmetric unit, would be extremely valuable.

WHAT DOES BIOVIA MATERIALS STUDIO POLYMORPH PREDICTOR DO?

BIOVIA Materials Studio Polymorph Predictor explores and ranks polymorphs of fairly rigid, non-ionic or ionic molecules (1, 2, 3). The approach is based on the generation of possible packing arrangements in all reasonable space groups to search for the lowlying minima in lattice energy.

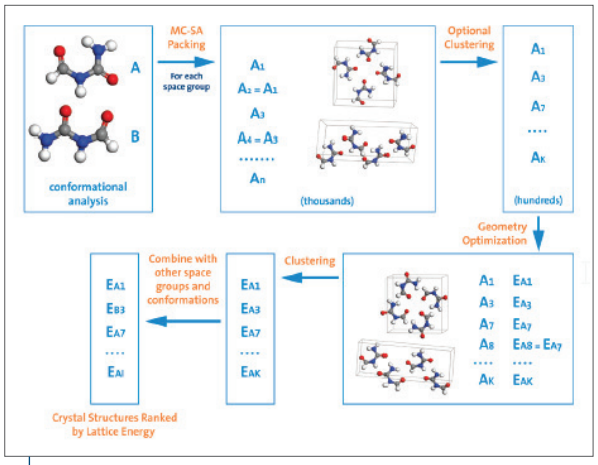
BIOVIA Materials Studio Polymorph Predictor employs the following procedure:

- A fast and reliable Monte Carlo simulated annealing process (MC-SA) searches the lattice energy hypersurface for probable crystal packing alternatives, typically generating thousands of possible structures
- Optionally, these potential structures are clustered into unique groups based on packing similarity
- The geometry of each unique structure is optimized with respect to all degrees of freedom or with rigid body constraints where the relative distance between a group of atoms are fixed
- The optimized structures are clustered again to remove duplicates
- The final structures are ranked according to lattice energy
- The resulting low-energy crystal structures are potential polymorphs. Powder patterns simulated for these structures can be compared to experimental powder data for verification using BIOVIA Materials Studio Reflex. Rietveld refinement can be performed to optimize the agreement with the experimental powder data. Additionally, polymorphs can be scored based on a statistical analysis of their hydrogen bond topology with respect to known crystal structures using MS Motif.

THE BIOVIA MATERIALS STUDIO ADVANTAGE

BIOVIA Materials Studio Polymorph Predictor is operated within the BIOVIA Materials Studio® modeling and simulation suite. BIOVIA Materials Studio's integrated model building and editing tools enable you to construct, visualize, and manipulate molecular structures in an asymmetric unit or structures of crystalline solids (e.g. drugs, pigments, metal oxides, and zeolites).

Potential crystalline structures suggested by the BIOVIA Materials Studio Polymorph Predictor can be analyzed using BIOVIA Materials Studio's spreadsheetlike table (called a study table) environment. The study table combines an easy association of structures and crystalline properties (e.g. space group, cell parameters, density, and energy for each structure) with powerful sorting and plotting functionality. It also provides a flexible and convenient way to evaluate additional structural properties for developing quantitative structure-property relationship models.



BIOVIA Materials Studio Polymorph Predictor workflow

The potential crystalline structures can further be optimized using molecular mechanics tools (BIOVIA Materials Studio Forcite and BIOVIA Materials Studio Compass), or quantum mechanics tools (BIOVIA Materials Studio DMol^3 or BIOVIA Materials Studio CASTEP).

HOW DOES BIOVIA MATERIALS STUDIO POLYMORPH PREDICTOR WORK?

The goal of BIOVIA Materials Studio Polymorph Predictor is to search for lowlying minima of a high-dimensional potential energy surfaces representing all possible packing arrangements of molecules in a crystalline environment as a function of space groups, lattice parameters, and contents of an asymmetric unit.

HOW DOES BIOVIA MATERIALS STUDIO POLYMORPH PREDICTOR BENEFIT YOU?

Polymorphism has been recognized as a phenomenon that many industries are increasingly trying to control and exploit. The appearance of an undesirable polymorph late in product development can lead to costly delays. In order to control polymorphism, researchers need to understand how the crystal structures of each polymorph differ. Knowledge of polymorphic forms is also important for patenting and registration purposes. BIOVIA Materials Studio Polymorph Predictor searches for all possible packing arrangements of crystalline materials from their molecular structures. Once the different crystal structures are known, additional analyses can be performed to help explain other characteristics unique to each polymorph, including analysis of surface chemistry for different facets.

Researchers can define parameters for each step with an easy-touse graphical user interface. The required input is the molecular structures of the contents of an asymmetric unit. The starting conformations of these molecules can be imported from an existing crystal structure or created using 3D Sketcher tools in Materials Visualizer and conformational analysis.

BIOVIA Materials Studio Polymorph Predictor can be utilized in two ways:

1. When experimental powder data is available, it may be used to aid the identification of the correct crystal structure from the list of generated trial structures using the Powder Comparison feature and to refine the structural parameters using the Rietveld method in BIOVIA Materials Studio Reflex.
2. Ab initio prediction of polymorphs when experimental powder data is not available.

BIOVIA Materials Studio Polymorph Predictor can be used alone or as the first step in a sophisticated structural analysis with other modules in BIOVIA Materials Studio. BIOVIA Materials Studio Visualizer can be used to examine the packing accelrys.com/materials-studio arrangement and hydrogen bonding for each structure. In order to control crystal shape and growth, the surface chemistry can also be analyzed. Furthermore, if medium- to high quality experimental powder data is available, BIOVIA Materials Studio Reflex Plus, better suited to analyze salts, solvates, and more flexible compounds, can be used to determine the structure directly from the powder data.

KEY FEATURES

- Crystals with more than one molecule in the asymmetric unit can be considered.
- Geometry Optimizations can be run in parallel
- Simulation results for each space group are stored in trajectory files for further analysis.
- Analysis is carried in study tables, displaying various properties such as space group, energy and cell parameters.
- The Powder Comparison analysis feature allows for the automated quantitative comparison of experimental powder data to simulated powder patterns for each generated structure.
- The Crystal Similarity Measure analysis feature allows for the automated quantitative comparison of experimentally determined crystal structure to each generated structure.
- The Polymorph Clustering analysis feature allows for automated quantitative comparison of each generated structure to all the other structures generated in the same or different space group, and same or different simulation runs.
- A variety of property calculations, including
- Powder Comparison and Crystal Similarity measures, can be carried out on all or a subset of the crystal structures in a study table.
- You can access Polymorph functionality through the MaterialsScript API. Scripting allows you to automate repetitive task and customize workflows.

RUNNING JOBS

- All BIOVIA Materials Studio Polymorph Predictor jobs are run in the background freeing up the BIOVIA Materials Studio client for other research.
- All BIOVIA Materials Studio Polymorph Predictor jobs can be submitted to remote computer servers.

RESULTS

Simulation results for each space group are stored in trajectory files for further analysis.

ANALYSIS

- Analysis is carried out with the help of spreadsheet-like tables, called study tables.
- Multiple trajectories files (e.g. corresponding to different space groups) can be imported into a study table to be analyzed simultaneously.
- When each trajectory file is loaded, various properties such as space group, energy and cell parameters, are automatically entered into the study table as well.
- Each crystal structure is embedded in the study table, which can be viewed independently and displayed along with various properties.
- The Powder Comparison analysis feature allows for the automated quantitative comparison of experimental powder data to simulated powder patterns for each generated structure.
- The Crystal Similarity Measure analysis feature allows for the automated quantitative comparison of experimentally determined crystal structure to each generated structure.
- The Polymorph Clustering analysis feature allows for automated quantitative comparison of each generated structure to all the other structures generated in the same or different space group, and same or different simulation runs.
- A variety of property calculations, including Powder Comparison and Crystal Similarity measures, can be carried out on all or a subset of the crystal structures in a study table.

To learn more about BIOVIA Materials Studio, go to **accelrys.com/materials-studio**

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Dassault Systèmes Corporate
Dassault Systèmes
175 Wyman Street
Waltham, Massachusetts
02451-1223
USA

BIOVIA Corporate Americas
BIOVIA
5005 Wateridge Vista Drive,
San Diego, CA
92121
USA

BIOVIA Corporate Europe
BIOVIA
334 Cambridge Science Park,
Cambridge CB4 0WN
England