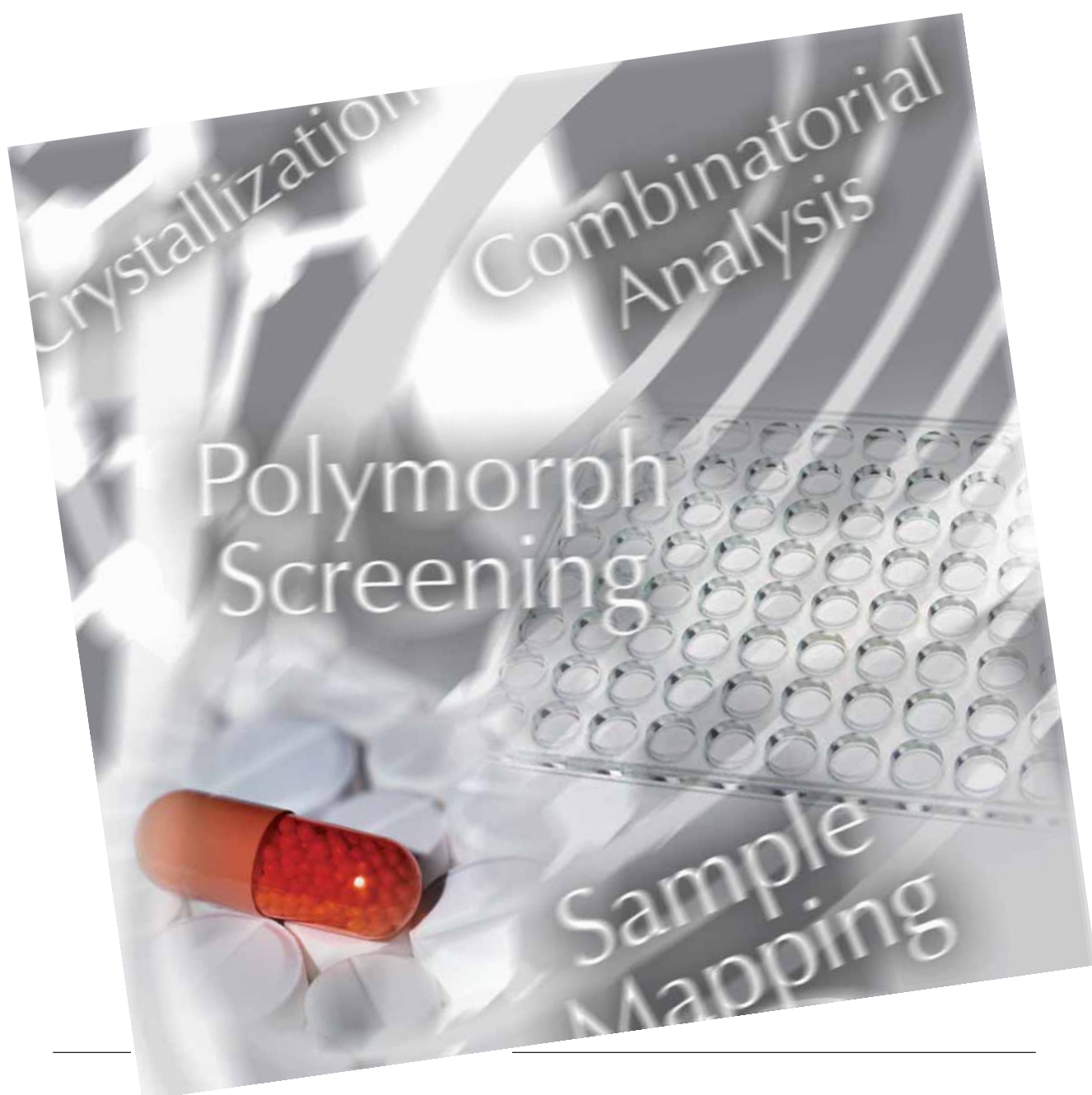


HIGH-THROUGHPUT SOLUTIONS
FOR PHARMA AND BIOTECHNOLOGY



High-Throughput X-Ray Diffraction for Discovery, Development and Production

- Combinatorial Analysis
- Crystallization Studies
- Polymorph Screening
- Quality Control

High-Throughput Screening

Parallel synthesis and screening of materials for useful properties reduce development times by up to orders of magnitudes, at a fraction of costs. In pharma and biotechnology high-throughput screening offers unprecedented capabilities for form discovery, characterisation and monitoring.

X-Ray Powder Diffraction (XRPD)

The ability to unequivocally differentiate one crystallographic phase from another has proven to be the greatest asset in the pharmaceutical field: XRPD patterns of each crystalline form contain characteristic sets of peaks unique to that form, allowing the patterns to be used as fingerprints. Among the different analytical tools for detecting polymorphs, like IR- and Raman-spectroscopy or a variety of thermal methods XRPD offers potentially the most unambiguous way for the identification and structural characterisation of any solid form.

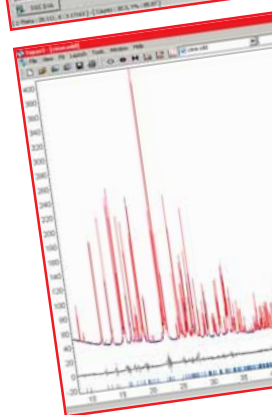
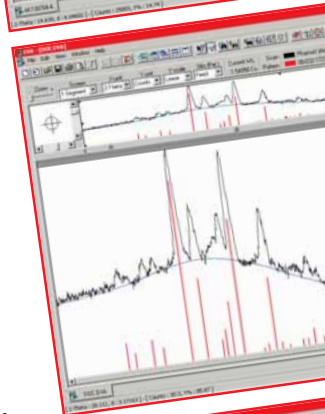
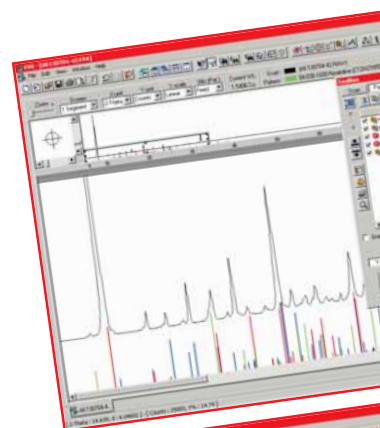
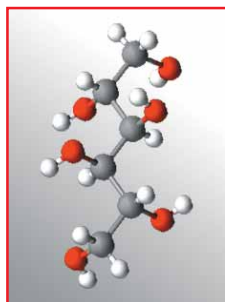
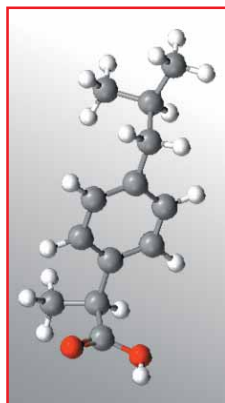
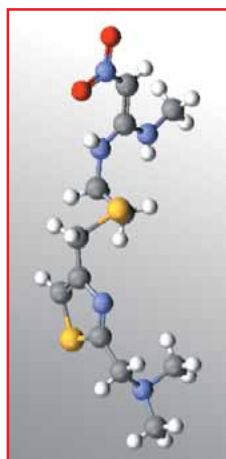
XRPD applications range across the entire pharmaceutical value chain, including

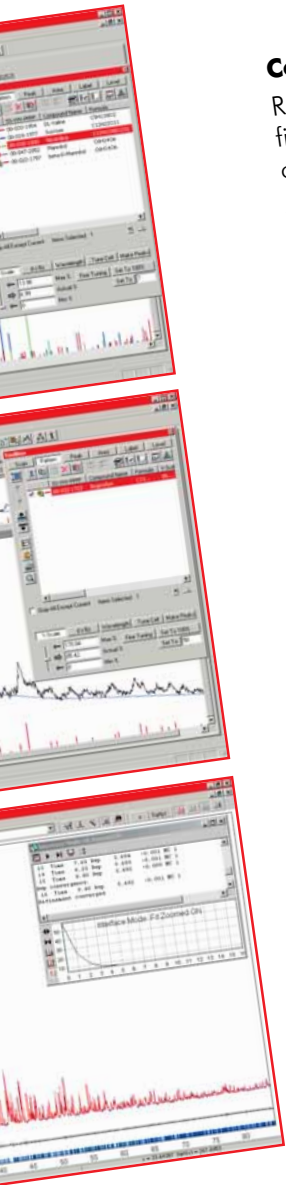
- Drug discovery: Identification of new leads
- Drug and process development: Lead optimization and development
- Production: Monitoring of solid state properties of the active ingredients and excipients

APIs can exist in a variety of distinct solid forms, including polymorphs, solvates, hydrates, salts, co-crystals and amorphous solids. X-ray powder diffraction is an ideal probe for API characterisation because it is non-destructive and allows simultaneous analysis of important parameters such as phase compositions and ratios including amorphous and crystalline contents.

Speed

Requiring sample amounts not more than several μg , XRPD measurement times are of the order of seconds up to a few minutes, allowing even more than 1000 measurements per day. The fully automatic data evaluation allows the cost effective handling of the enormous amount of information obtained and to concentrate on significant analysis results only.





Combinatorial Synthesis

Rapid screening accelerates the process of finding new materials as well as suitable crystal forms of a compound.

X-ray powder diffraction adds value due to

- decreased cost per sample
- faster time to market
- fully automated operation

Polymorph Screening

Full characterisation of the polymorphic behaviour of drug systems is a requirement from scientific, technical, legal and regulatory perspectives. The unexpected appearance of novel crystalline forms as well as „disappearing polymorphs“ can be a commercial disaster.

X-ray powder diffraction offers manifold benefits manifested in:

- identification and characterisation of new polymorphs
- minimised delays in chemical development
- better and safer products
- improved intellectual property position

Regulation and Intellectual Property

The importance of X-ray diffraction as an analytical tool for characterisation, quality assurance and control of pharmaceuticals is recognized by regulatory authorities and for patenting purposes.

X-ray powder diffraction provides for

- strengthened offensive and defensive intellectual property position
- better and longer patent protection
- easier regulatory compliance

New drug submissions as well as patent applications invariably contain XRPD patterns of the various phases that can be isolated of the active drug.

Quality Control

Monitoring of solid state properties of the active ingredients and excipients are fundamental elements of the pharmaceutical development.

X-ray powder diffraction helps to

- reveal batch to batch inconsistencies
- improve manufacturing of the pharmaceutical dosage form
- control the quality of the formulation, the bioavailability and drug stability

Enhanced Competitive Advantage: Increase of Innovation – Decrease of Risks

- Higher number of new materials
- Better products and processes
- More effective and longer patent protection
- Easier compliance with regulatory demands

D8 DISCOVER with GADDS

The World`s Fastest Lab X-ray Diffractometer

- Laser/Video system for automatic sample alignment and monitoring
- High-brilliant X-ray source for minimized measurement times
- 2-dimensional HI-STAR detector for collection of large areas of diffraction data with high speed, high sensitivity, low noise, and in real time
- Horizontal XYZ sample stage for easy loading of samples including loose powders and liquids
- Motorized retractable knife edge for elimination of cross-contamination



The **D8 DISCOVER with GADDS** is the ultimate system for high throughput X-ray powder diffraction for form discovery, characterisation, and monitoring.

Perfectly addressing the analytical requirements of high-throughput screening, the D8 DISCOVER with GADDS can be configured for reflection or transmission geometry (CS or CST).



D8 DISCOVER with GADDS CST

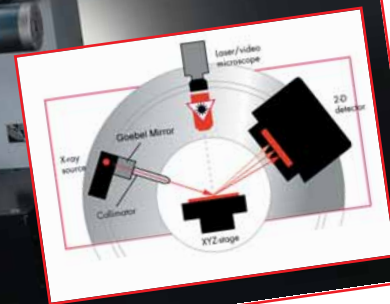


The **Combination of high-brilliant X-ray source** and the unique **2-D HI-STAR detector** allows non-destructive XRPD with unbeatable speed, sensitivity, and accuracy. Sophisticated measurement strategies make use of innovative diffraction techniques for simultaneous screening of a wide variety of material properties such as

- crystalline phase identification
- sample composition and phase ratios
- amorphous and crystalline contents
- crystallite sizes and orientations

The **D8 DISCOVER with GADDS** operates with a high-level of automation. Placed on the motorized XYZ-stage the sample library is automatically aligned in respect to the X-ray beam making use of the unique Laser/Video system.

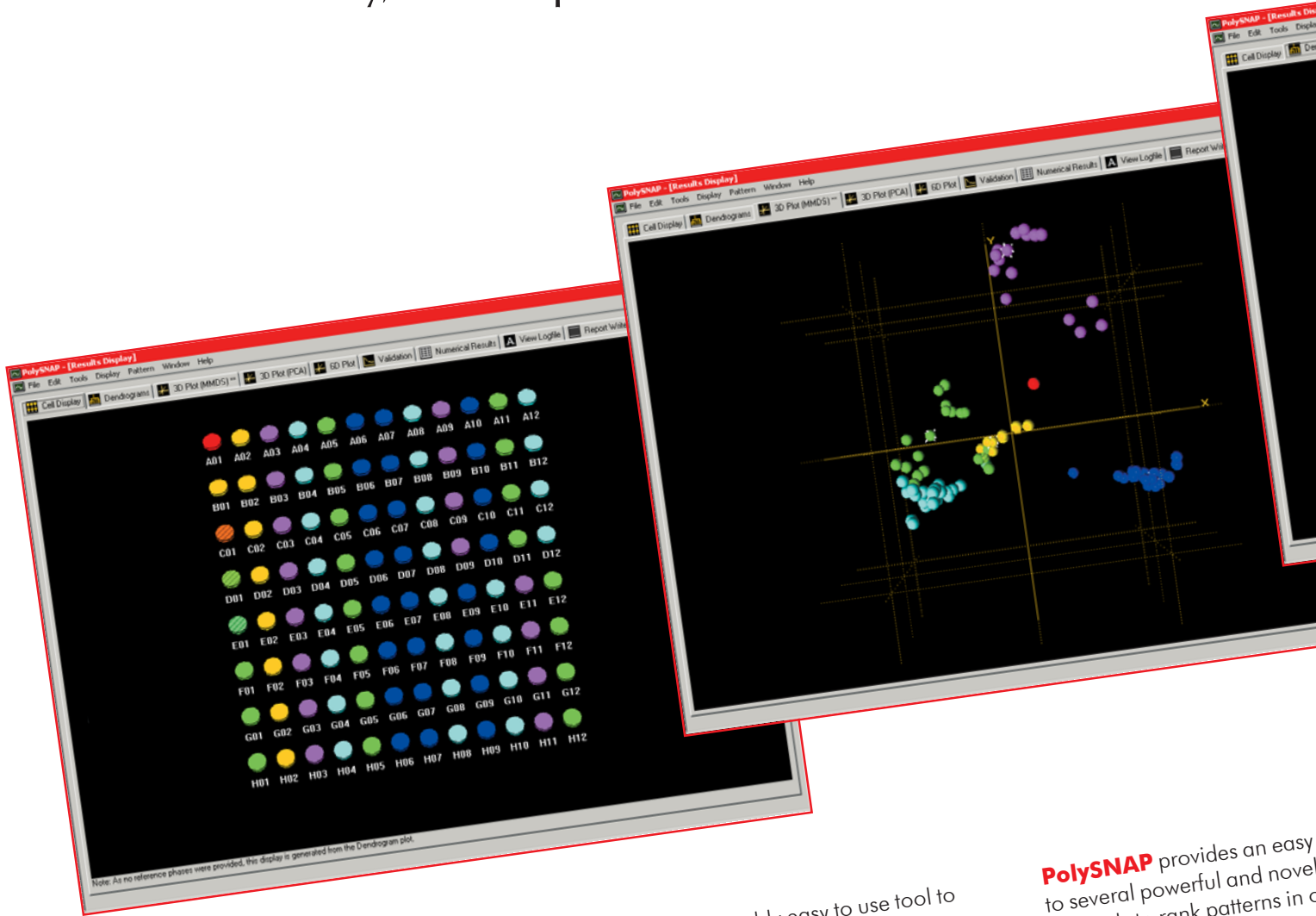
Data collection and evaluation is performed without user intervention. Dedicated sample movements (translation and rotation) can be applied to improve particle statistics and to minimize preferred orientation effects.



D8 DISCOVER with GADDS CS

PolySNAP

High-Throughput XRD Data Analysis for Discovery, Development and Production Control



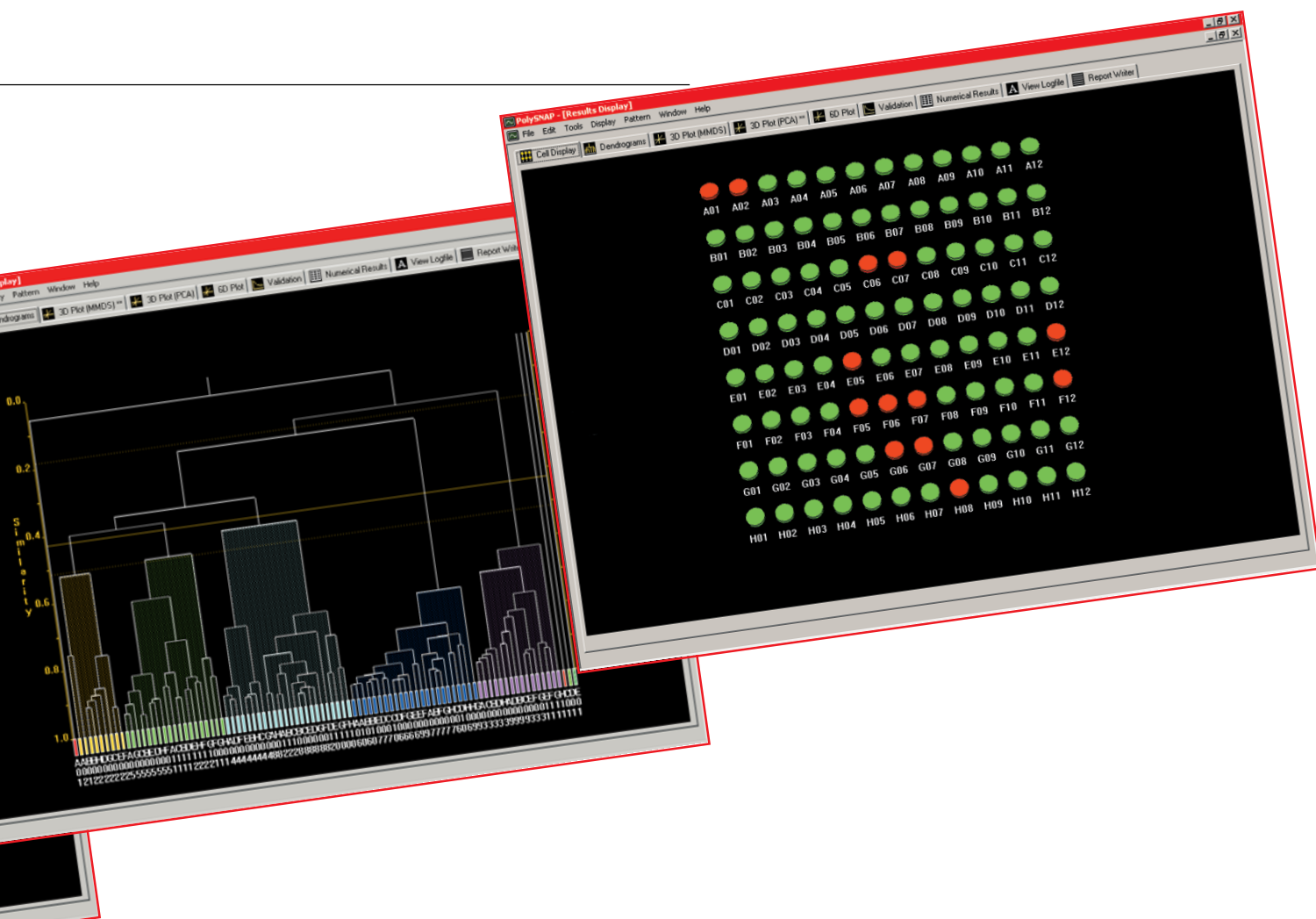
Fully unattended data evaluation is a self-evident requirement, but modern software offers more than automation of existing procedures:

- drastic reduction of analysis efforts and time despite increased sample throughput
- shifting the focus of the laboratory's staff from redundant to effective work by allowing to concentrate on significant analysis results only: **PolySNAP**

PolySNAP is a notably easy to use tool to get reliable and accurate results in no time - no matter what the data amounts are. This includes

- phase identification
- pass / fail analysis
- similarity analysis
- automatic mixture detection
- automatic amorphous phase detection
- quantitative analysis of mixtures

PolySNAP provides an easy access to several powerful and novel methods to rank patterns in order of similarity to any selected sample, known as well as unknown patterns identified. In quantitative mode, given a reference pattern and potential pure phase patterns, it can identify which patterns are present and quantify their proportions easily.



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Seamless integration with all Bruker AXS diffraction systems ranging from the D4 ENDEAVOR to the D8 DISCOVER with GADDS.

- DIFFRAC^{plus} EVA and SEARCH for highly sophisticated phase analysis and search in conjunction with user defined databases or ICDDs PDF2 and PDF4
- GADDS^{plus} PILOT for simultaneous display of measurement frames and sample pictures e.g. taken with the video/laser system or any other imaging system

PolySNAP applications

- Automatic phase ID of knowns
 - identical colors denote identical samples
 - different colors denote different samples
- Automatic detection of unknown or unexpected phases or patterns
- Automatic detection of amorphous phases
- Automatic detection and quantification of mixtures

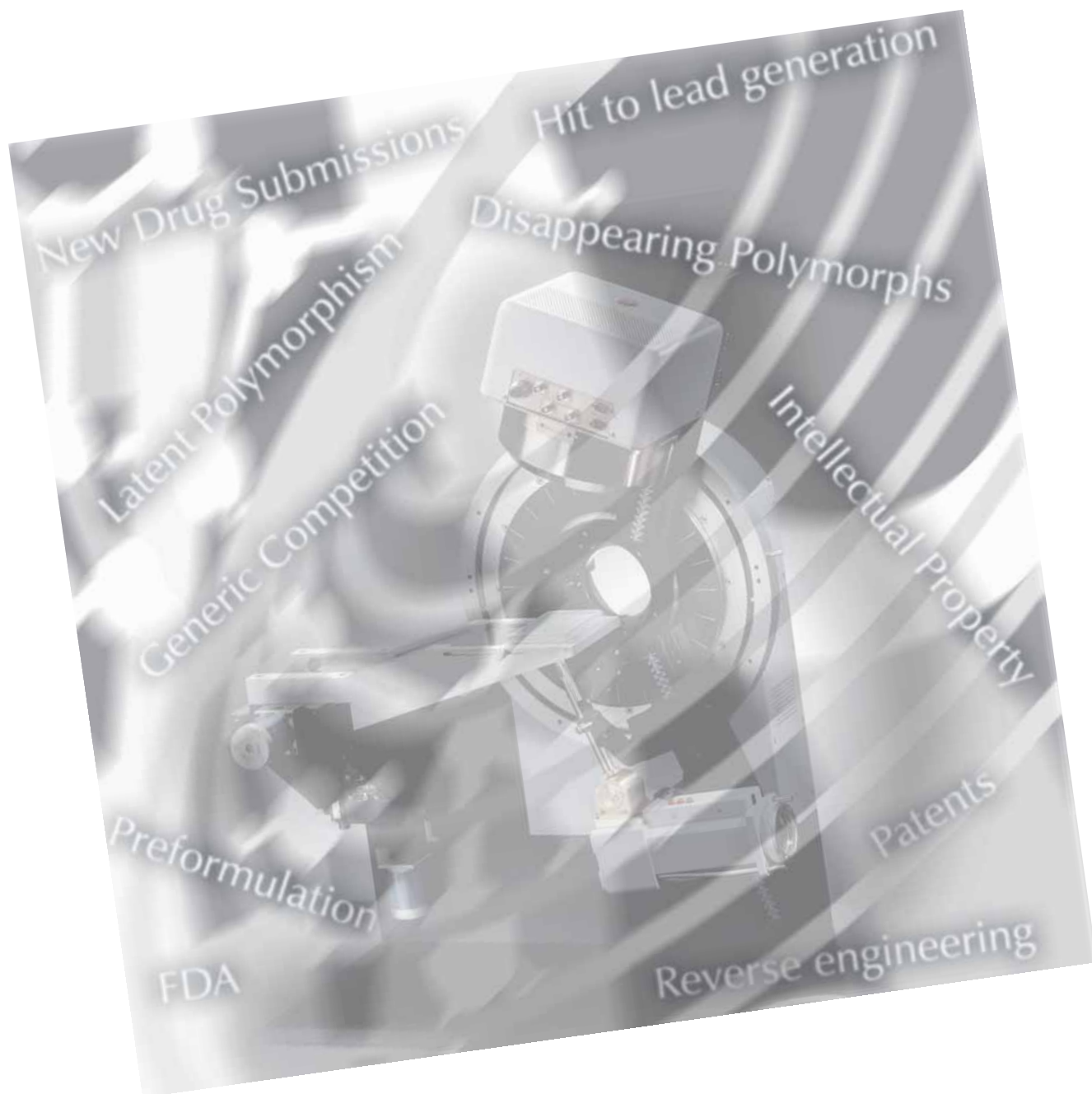


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PolySNAP is developed
at the University of Glasgow

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