Licensable Technologies

Powder Diffraction X-Ray Crystallography

Applications:

- Screening potential pharmaceutical materials for binding to proteins or macromolecules
- Optimizing ligand binding and identifying binding modes
- Determining whether a material is suitable as a drug

Benefits:

- More robust than traditional dye-replacement or single-crystal structure determination; experimental conditions can be broader.
- Fracturing is irrelevant to the results of powder diffraction experiments.
- Adaptable to high throughput experiments

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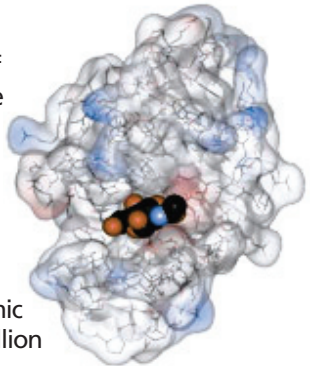
Summary:



The emergence of proteomics as an important component of the drug discovery process has generated excitement because the rewards are expected to exceed those achieved by genomics—particularly in the development of commercial products and personalized therapeutics. The importance of proteomics lies in the fact that proteins are the molecules that carry out virtually all biological processes. Most drugs work by correcting the protein abnormalities that cause disease. Collectively, the current value of markets for proteomic technologies is about $2 billion, expected to increase to $6 billion by the year 2005, and $10 billion by the year 2010.

The drug discovery process would benefit from methods capable of screening a specific protein to identify lead compounds—substances believed to have the potential to treat disease. Methods that provide structural information on the binding modes of the drug target would also be very useful. This requires verification of the details of protein-ligand interactions under a wide variety of conditions. Current techniques require the growth of protein-ligand single crystals of sufficient quality for X-ray diffraction analysis or the interpretation of nuclear magnetic resonance (NMR) spectra. Growing single crystals of proteins is an arduous process, and NMR is limited by spectrometer resolution.

Powder diffraction offers a distinct advantage over single-crystal techniques in its complete immunity to crystal fracture and to any phase change that may accompany complex formation. Current diffraction techniques are not very robust. A high-intensity X-ray source, usually a synchrotron, is required and high-resolution data collection remains a challenge. The measurements are time-consuming and the crystals must remain stable long enough in the beam to ensure required quality of the diffraction.

LANL researchers have developed a suite of powder diffraction X-ray crystallography techniques that enable relatively low-cost, simple experiments to identify and optimize the binding of ligands to biomolecules. Using a patent pending, high-throughput technique a number of different ligands can be screened simultaneously. The resulting data show the optimal binding ligand for the sample target. Data from these experiments have been used to develop statistical computational models to predict molecular binding. The Powder Diffraction portfolio represents a combination of methods for determining the position and orientation of ligand molecules on a target biomolecule and optimizing ligand binding to macromolecules. These methods have been modified to work with existing high-throughput screening techniques.

Development Stage:

Inventions have been demonstrated in the lab.

Patent Status:

Patent Application: High Throughput Screening of Ligand Binding to Macromolecules Using High Resolution Powder Diffraction

Patent Application (CIP): High Throughput Screening of Ligand Binding to Macromolecules Using High Resolution Powder Diffraction

Patent Application: Analysis of Macromolecules, Ligands and Macromolecule-Ligand Complexes

Licensing Status:

Available for exclusive and non-exclusive licensing.

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