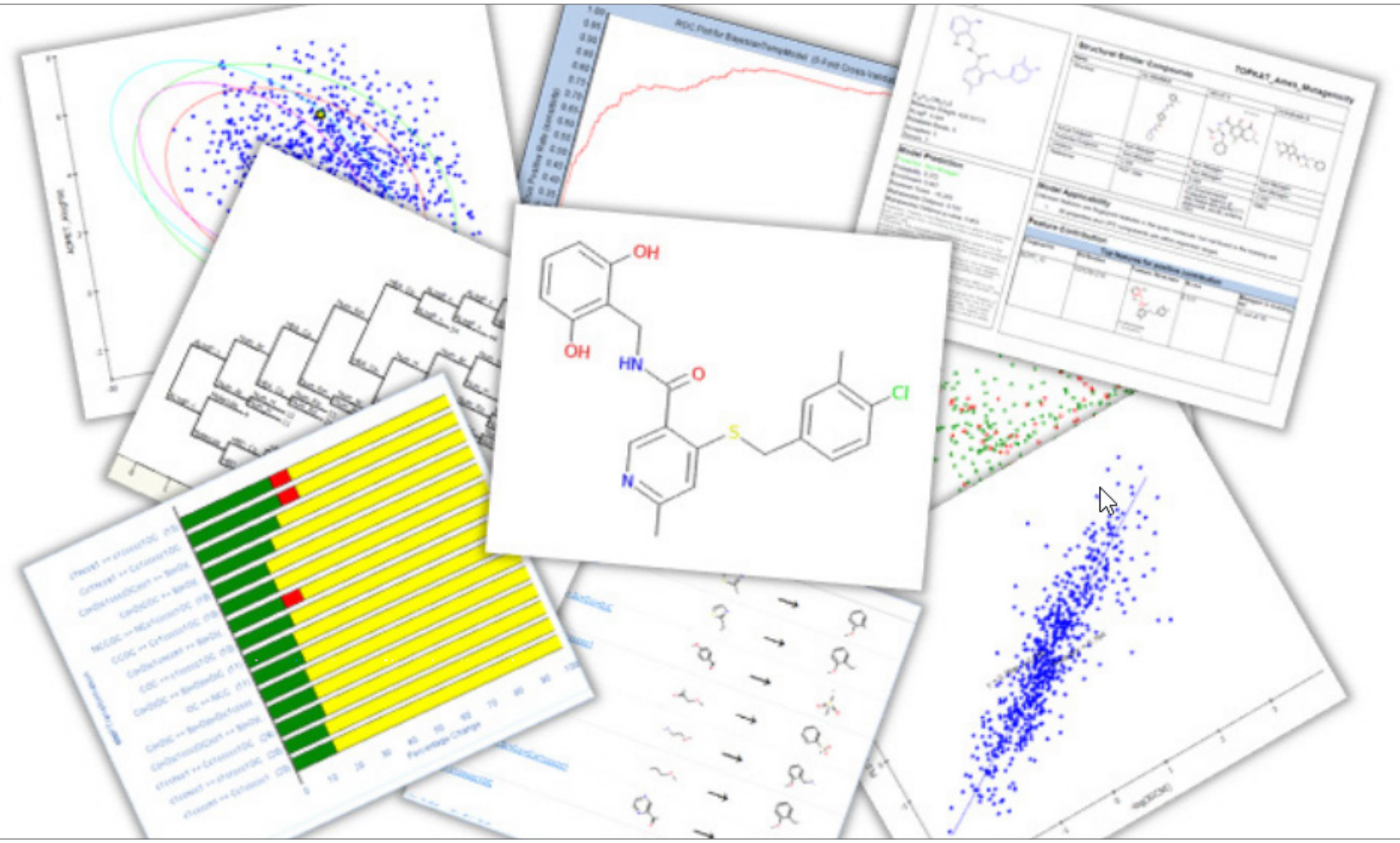
DASSAULT SYSTEMES

BIOVIA

QSAR, ADMET AND PREDICTIVE TOXICOLOGY WITH BIOVIA DISCOVERY STUDIO

DATASHEET



PREDICTING DEVELOPMENT RISKS

Understanding and quantifying structure-activity relationships can significantly impact lead optimization and drug development by minimizing tedious and costly experimentation. BIOVIA Discovery Studio QSAR/QSPR models allow for the calculation of physicochemical properties and the prediction of biological activity as well as the evaluation of absorption, distribution, metabolism, excretion and toxicity (BIOVIA Pipeline Pilot ADME-Tox). BIOVIA Discovery Studio® offers a comprehensive suite of tools to develop your own BIOVIA Discovery Studio models, including pre-built and validated BIOVIA Pipeline Pilot ADME-Tox models, to better identify lead compounds.

LIGAND AND DATASET PREPARATION

- Generate training and test datasets with diverse splitting methods
- Prepare response property (scaling and binning)
- Calculate numerous physicochemical, topological, electronic, geometric and fingerprint properties
- Calculate semiempirical (**BIOVIA Discovery Studio VAMP®**) and DFT (**BIOVIA Discovery Studio DMoL³®**) descriptors

GENERATE SAR MODELS

- Classification SAR
  - Bayesian Model
  - Recursive Partitioning (Single Trees and Forest)
- Regression SAR
  - Partial Least Squares(PLS)
  - Genetic Functional Analysis
  - Multiple Linear Regression
  - 3D Molecular Field Analysis
  - Free-Wilson Analysis
- Analyze and validate models
  - Model applicability domains
  - Automatic test set validation
  - Cross validation and statistical metrics
  - Fingerprint feature contribution

STUDY SAR

- Identify Matched Molecular Pairs (MMPs) transformations and study activity cliffs
- Analyze structural trends for significance
- Study activity cliff chemical transformations for lead optimization

BIOVIA PIPELINE PILOT ADME-TOX DESCRIPTORS

- Filter poor candidates with undesirable chemical groups based on published SMARTS, Lipinski and Veber rules
- Available BIOVIA Pipeline Pilot ADME-Tox models:
  - **BIOVIA Pipeline Pilot ADME-Tox Absorption**: Predicts Human Intestinal Absorption (HIA) after oral administration
  - **BIOVIA Pipeline Pilot ADME-Tox Aqueous Solubility:** Predicts the solubility of each compound in water at 25°C
  - **BIOVIA Pipeline Pilot ADME-Tox Blood Brain Barrier:** Predicts the ratio of concentrations of compound on both sides of the blood brain membrane after oral administration
  - **BIOVIA Pipeline Pilot ADME-Tox Plasma Protein Binding:** Predicts whether or not a compound is likely to be highly bound to carrier proteins in the blood
  - **BIOVIA Pipeline Pilot ADME-Tox CYP2D6 Binding:** Predicts cytochrome P450 2D6 enzyme inhibition
  - **BIOVIA Pipeline Pilot ADME-Tox Hepatotoxicity:** Predicts dose-dependent human hepatoxicity of compounds

PREDICTIVE TOXICOLOGY

- Based on **TOPKAT®** (Toxicity Prediction by Komputer Assisted Technology) with updated training sets and advanced modeling techniques from **BIOVIA Enterprise Platform®**
- Legacy **TOPKAT®** models also available
- Model applicability, feature contribution and similar compounds reported to assist in interpreting results
- Extend models and improve coverage of chemistry space by adding new training data
- Available toxicological endpoints:
  - Ames mutagenicity
  - Rodent carcinogenicity (NTP and FDA data)
  - Weight of evidence carcinogenicity
  - Carcinogenic potency TD50
  - Developmental toxicity potential
  - Rat oral LD50
  - Rat maximum tolerated dose
  - Rat inhalation toxicity LC50
  - Rat chronic LOAEL
  - Skin irritancy and sensitization
  - Eye irritancy
  - Aerobic biodegradability
  - Fathead minnow LC50
  - Daphnia magna EC50
  - Log P

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