Robust cross-validated models for accurate assessment of chemical toxicity

Discovery Studio

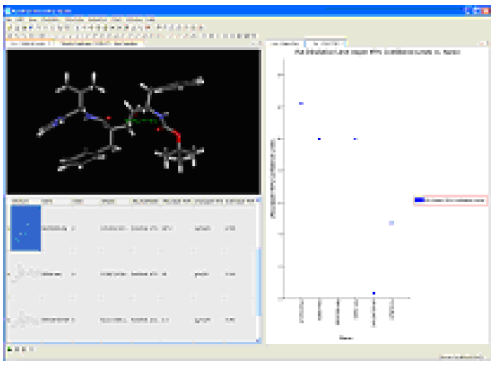
Predictive Toxicology in Discovery Studio

A structure-activity relationship (SAR) is a computer-based statistical technique that allows chemical testing based solely on a chemical's molecular structure. It is one component of the more comprehensive Quantitative Structure Activity Relationship (QSAR), which is capable of quantifying the type of relationship identified. While there are numerous QSAR-based software programs commercially available, none offers the depth, scope, and validation tools of Accelrys' Discovery Studio (DS) TOPKAT®.

Many regulatory agencies use SAR. The US Environmental Protection Agency (EPA) has indicated its support for the use of alternative testing technologies. In particular, the Agency acknowledged that it "... actively encourages companies to consider alternatives such as SAR ... (because) SAR approaches can be used both to help define categories and to help assess individual chemicals."

DS TOPKAT: A Step Beyond SAR

DS TOPKAT has been used for toxicity testing by universities, private companies and government agencies including the Amgen, Pfizer, US CDC, US NIH, and Health and Welfare Canada. The QSAR-based system generates and validates accurate, rapid assessments of chemical toxicity solely from a chemical's molecular structure. Unique among SAR-based technologies, DS TOPKAT uses robust, cross-validated models based on experimental data of highly consistent protocol. The models are subjected to extensive diagnostics for accuracy and validity. And only DS TOPKAT uses patented Optimum Prediction Space (OPS) technology to assure that the compounds under investigation are well represented in the models. Included within DS TOPKAT are tools that allow you to easily build molecules or queries from available fragment libraries. DS TOPKAT can be used for tests including physical/chemical, environmental fate, ecotoxicity, toxicity, mutagenicity, and subchronic reproductive/developmental. DS TOPKAT is fast, cost-effective, and proven.



DS TOPKAT prediction of known HIV inhibitors for Rat Inhalation

DS TOPKAT in the Discovery Studio Research Environment

DS TOPKAT is an integrated application module in Discovery Studio, which includes a comprehensive suite of modeling and simulation solutions for life science researchers. Built on SciTegic Pipeline Pilot, Accelrys' scientific operating platform, Discovery Studio provides a flexible research environment, which allows DS TOPKAT to read multiple file formats and integrate data with many other premium application modules, which provide functionality for such tasks as molecular docking and pharmacophore modeling.

Users can access DS TOPKAT technology through multiple interfaces. In addition to being accessible through DS Visualizer Pro Enterprise, which serves as the user interface for Discovery Studio, DS TOPKAT is also available as a component for use with SciTegic Pipeline Pilot, a high-throughput data analysis and mining solution that allows you to streamline your workflows. DS TOPKAT is also available as a stand-alone command line executable for high throughput calculation and/or for integration with in-house workflows.

Various tasks, such as accessing a user specified sub-model, outputting result tables for reporting feature similarities and descriptor contribution to toxicity, can be enabled from the command line as well.

Defensible, Dependable Results

Accelrys also offers DS TOPKAT technology as part of its toxicity assessment service and under licensing agreements; both arrangements offer distinct benefits. Accelrys' Contract Research Toxicity Assessment Service removes all testing and management burdens from you. Once a chemical and endpoint have been submitted for computational assessment, Accelrys' team of toxicological experts undertakes the required test and prepares an in-depth report. Many companies prefer to use the computational toxicological assessment service, even though they may require multiple tests. For example, one major chemical company requested toxicological assessments for multiple endpoints for more than 70 chemicals. The resulting reports were completed within one month and at substantial time and cost savings when compared to conventional experimental testing. Alternatively, DS TOPKAT's modules are available under licensing agreement, either individually or collectively. Once licensed, the software can be employed for multiple chemical assessments, slashing the cost of per-chemical testing. Using DS TOPKAT as opposed to traditional testing methods can achieve significant cost savings. Plus, while those traditional methods can take months to complete, a full chemical assessment using DS TOPKAT typically takes only a few days.

Available DS TOPKAT modules:

- Rodent Carcinogenicity
- Ames Mutagenicity
- Rat Oral LD50
- Rat Chronic LOAEL
- Developmental Toxicity Potential
- Skin Sensitization
- Fathead Minnow LC50
- Daphnia Magna EC50
- Weight of Evidence Rodent Carcinogenicity
- Rat Maximum Tolerated Dose
- Aerobic Biodegradability
- Eye Irritancy
- Log P
- Rabbit Skin Irritancy
- Rat Inhalation Toxicity LC50
- Rat Maximum Tolerated Dose

A partial list of DS TOPKAT Clients:

- Amgen
- Buckman Labs International
- US Centers for Disease Control and Prevention (CDC)
- Heath and Welfare Canada
- US National Cancer Institute (NCI)
- US National Institute for Occupational Safety
- Pfizer
- National Institute for Public Health and Environment, Netherlands.
- US Environmental Protection Agency (EPA)
- Vertex Pharmaceuticals
- Walter Reed Army Institute of Research
- Wyeth Pharmaceuticals.

Platform requirements:

- Windows 2000
- Windows XP
- Red Hat Linux WS3.0
- Red Hat Linux WS4.0

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