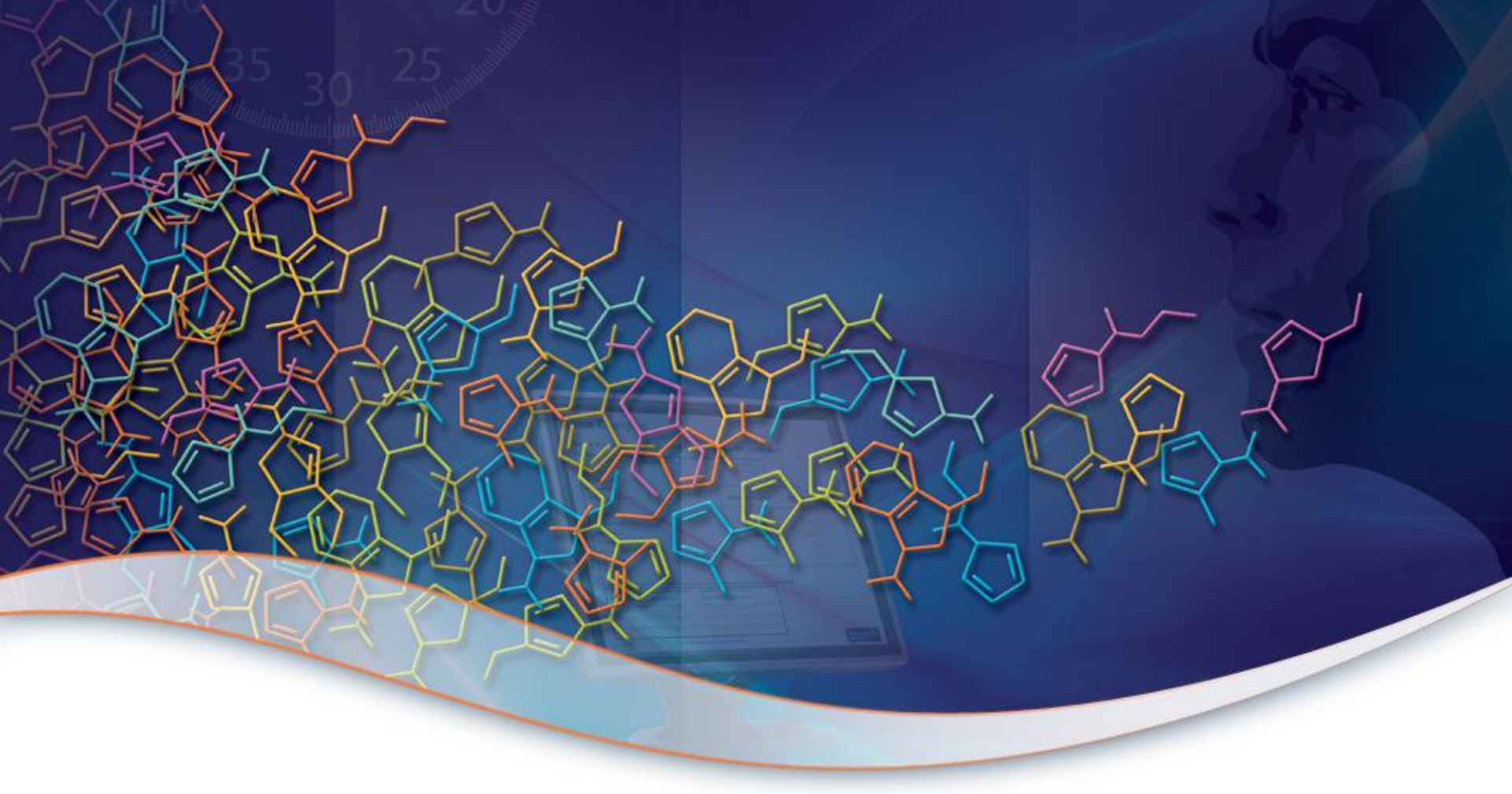


The Tripos Chemistry Extensions

Dr. Fabian Bös, Senior Application Scientist

CERTARA
Translational Science Solutions

About Certara

Scientific and technical breadth with expertise from discovery through clinical drug development

- Building a family of companies aimed at providing life science organizations with computational solutions that span from discovery through Phase III clinical trials
- History of anticipating trends and introducing innovative products and services to assist in drug discovery and development
  - Tripos: software enabling life science researchers to accelerate the identification and optimization of new compounds in the drug, chemical, research, food, flavoring and fragrance markets
  - Pharsight: software and services to improve the value and availability of preclinical and clinical program data for PK/PD modeling, analysis, data management, and reporting

Introduction: TCE

Tripos Chemistry Extensions (TCE) for KNIME

- Integrates our chemoinformatic capabilities into KNIME
  - read & write and process chemical structures
  - perform basic and advanced chemoinformatic tasks
  - integrates with other Tripos desktop software
- No additional software required to be installed
- Basic nodes can be used at no cost
  - Available at http://www.tripos.com/knime

- Tripos Workshop, Friday, 13:30-15.00, Room „C“, 2nd floor
- Webinar recording available at www.tripos.com

The Tripos node repository

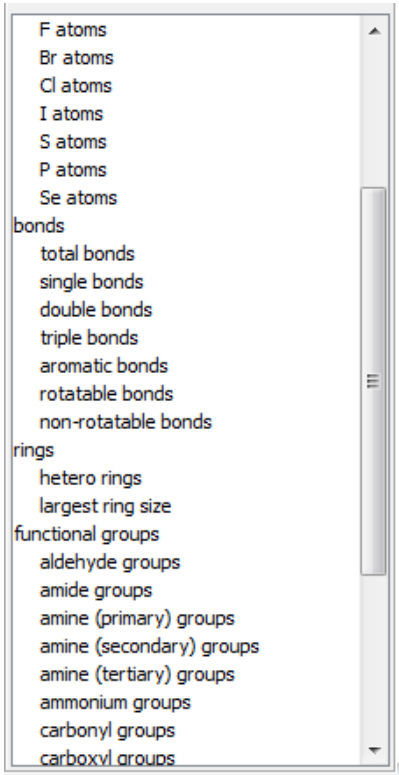
The nodes can be grouped into

- Reading/writing chemical structures and databases
- Molecular property calculation
- Similarity comparison (fingerprints, shape comparison)
- Automated QSAR
- UNITY nodes for substructure, similarity, pharmacophore 3D and Flex searches
- Tools for format conversion, parsing, scoring

The Tripos node repository

Molecular property calculation

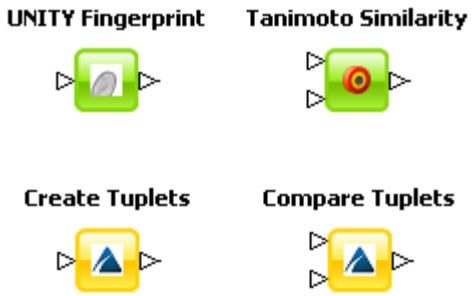
- 2D properties
  - MW, hydrogen bond acceptors/donors etc.
- Substructural properties
  - Counting atoms, bonds, rings, functional groups
- ADME/Tox properties
  - TPSA, Lipinski violations, AlogP

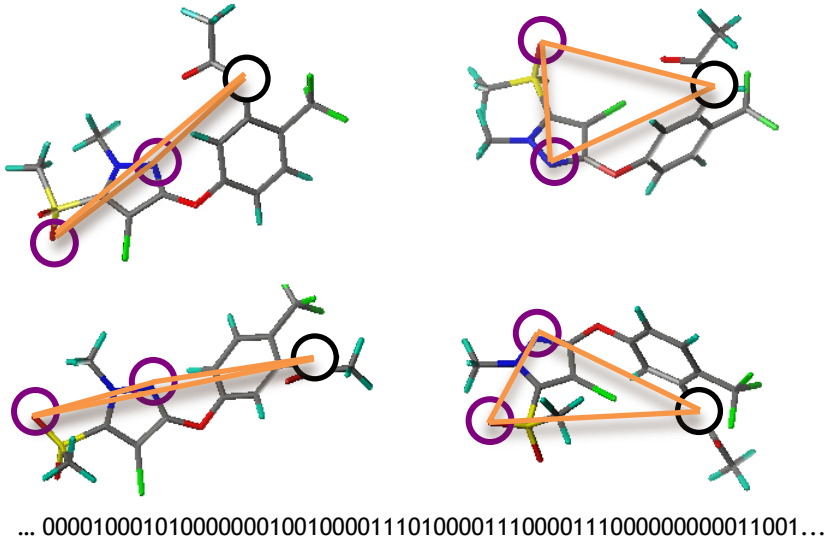


The Tripos node repository

Similarity comparison of molecules

- UNITY fingerprints
- Tuplets
  - Bitmaps encoding pharmacophoric features of molecules
  - Created from multiple conformers of one molecule
  - Allow fast fingerprint-like searching





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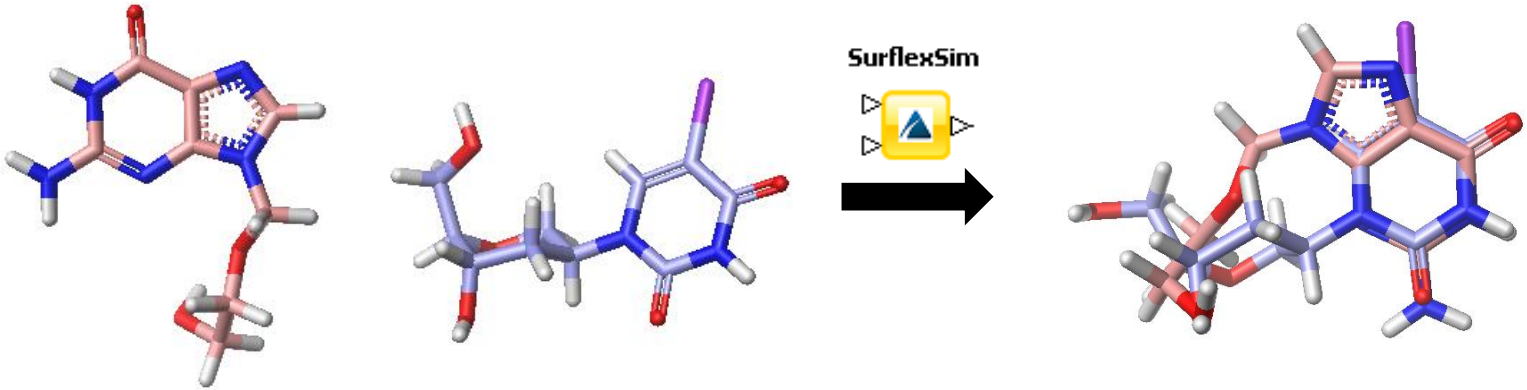
The Tripos node repository

Similarity comparison of molecules

- Surflex-Sim (A. Jain, UCSF)
  - Uses molecular shape, hydrogen bonding and electrostatic properties to compare molecules
  - Automated flexible alignment of structures to a given reference conformation
  - Successfully used in LBVS, alignment tasks and off target prediction



The Tripos node repository

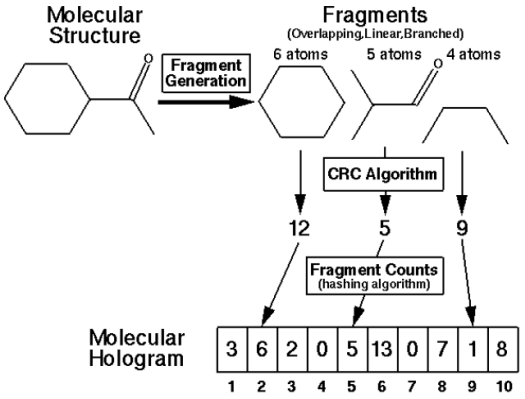
Topomer Similarity

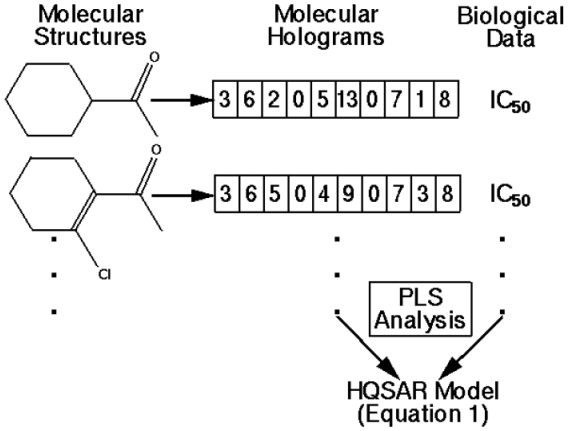
- Originates from shape similarity searching in very large libraries
- A Topomer is a “Characteristic Pose” of a fragment
  - Generated by rules, thus automated and fast
  - Topomers emphasize consistency over reproducing experimental or low energy conformations
  - Similar structures yield similar poses (shapes)
- Topomers shown to exhibit neighborhood behavior
  - Ligands assembled from shape similar fragment sets tend to share biological activities
- Very fast ligand based virtual screening tool
  - Used for lead hopping, r-group or scaffold replacement
  - No pregenerated 3D conformation needed

The Tripos node repository

HQSAR – Hologram QSAR

- rapidly and easily generate QSAR models of high statistical quality and predictive value
- uses an extended form of fingerprint, known as a Molecular Hologram for PLS analysis
- Molecular Hologram contains counts of all possible molecular fragments within a molecule, including overlapping fragments





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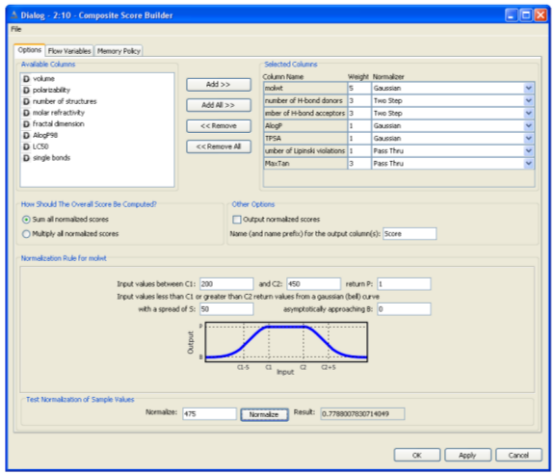
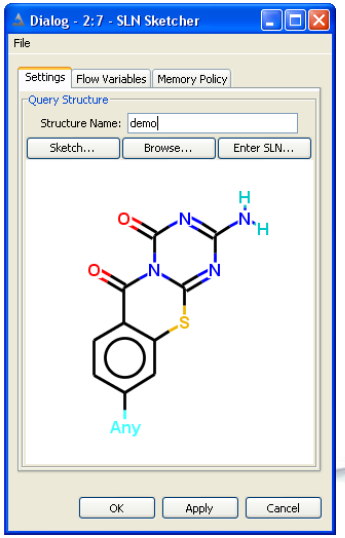
The Tripos node repository

Tools for format conversion, parsing, scoring

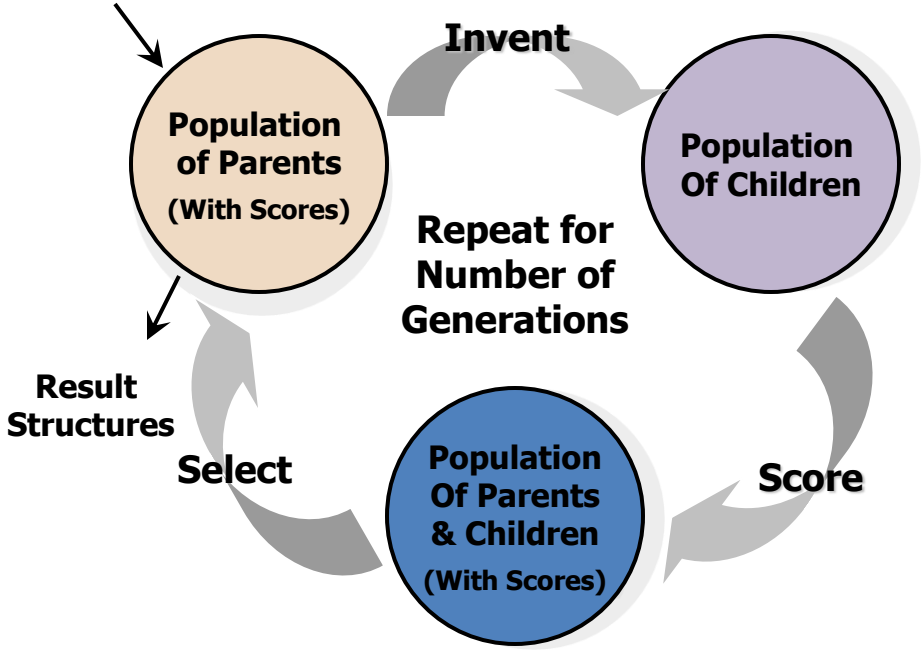
- Format conversion and more
- Quick 3D coordinate generation
- Generate multiple conformations
- Molecular parser and validator
- SLN sketcher for input of structures
- Composite scoring
- External tool node
- Integration to Tripos desktop software





Muse: Software for multi-criteria molecular design

34 structure-modifying operators
May preserve substructure(s)
May tailor evolutionary process
May add custom fragment library
May exclude undesirable chemistry

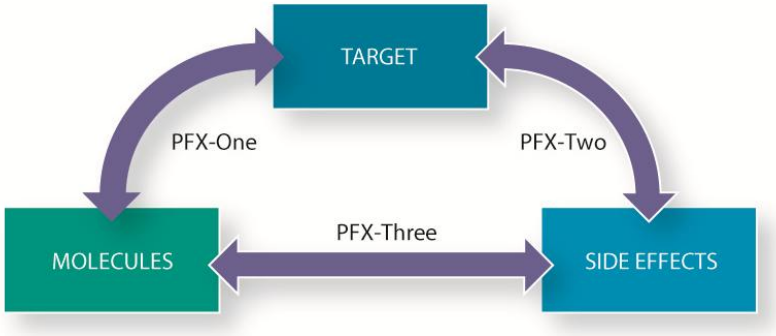


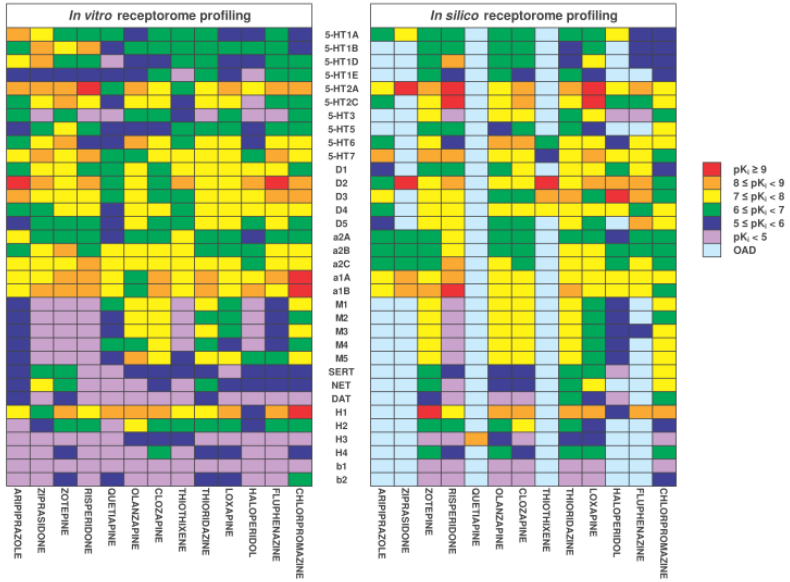
Tripos Score using KNIME workflow in the background

PredictFX: Polypharmacology prediction

Using PredictFX (J. Mestres/Chemotargets), users can:

- Predict a wide spectrum of off target biological activities
- Easily incorporate in-house chemistry and biological data to improve the predictions for their company's proprietary chemistry
- Integrate PredictFX into in-house IT/IS systems so that any scientist can make PredictFX predictions





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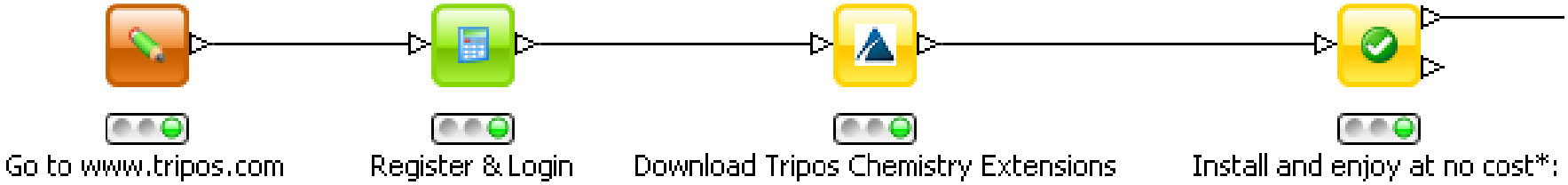

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Questions? Comments?

fabian.boes@certara.com