Enabling decision support for chemical liability assessment

*Integrating Bioclipse and OpenTox*

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Bioclipse – an open source workbench for the life sciences


Component-based architecture
Bioclipse Scripting Language

(a) biows.queryEMBL("X56734")
   biows.queryRefseq("NM_000410")
   biows.queryUniProtKB("INSR_HUMAN")

(b) mol=cdk.f
    seqs = biows.queryEMBL("X56734,X56735");
    aln = kalignws.alignDNA(seqs);
    biojava.sequencesToFASTAfile(aln, "save here");

(c)
Eclipse: Proven technology
Example: Dutch railways
Bioclipse and OpenTox: Shared goals – predictive toxicology

- OpenTox
  - Defines an API, ontology, and services for predictive toxicology

- Bioclipse
  - Rich GUI, built for taking advantage of networked services
  - Local predictions

→ A good match!
From data to predictions

Preprocess data
- Download, edit, visualize, preprocess structures and metadata

Create and assess models
- Statistical modeling and validation

Deploy models
- Package and deliver model to users in a flexible, secure format

Consume models
- Enable user-friendly consumption of services
Bioclipse-QSAR: Reproducible QSAR datasets

Bioclipse-QSAR with OpenTox
From data to predictions

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Bioclipse Decision Support for assessing chemical liabilities

- Original plan: Use Bioclipse workbench and provisioning system to:
  - Run models locally
    - fast execution, no need for network connection
  - Deliver a customizes prediction workbench
    - Just install the plugins you desire

- Evolution: Also take advantage of networked services (e.g. SOAP, XMPP, OpenTox)
Bioclipse Decision Support for assessing chemical liabilities

• Integrate various predictive technologies
  – Similarity searches (InChi, signatures, fingerprints)
  – Structural alerts (SMARTS + Signature alerts)
  – QSAR models (signatures, SVM)

• Safety endpoints based on open data:
  – Mutagenicity (AMES)
  – Carcinogenicity (CPDB)
  – AHR inhibition (PubChem BioAssay 2796)

Bioclipse Decision Support

Chemical Liability Assessment

Report date: 2010/08/28

Query structure:

Properties
- Mol: 146.143
- H dones: 1
- H: 1
- alogP: 1.031

Compound: cyanarin

SMILES: O=C(O)(O)C=C=CC=C1C=C1

InChI: i/c120h116/c1-16/c38h60o2w26/h19-0-6-1-7-3-1-2-4-0(7)11-30-11h

Endpoint: AHR

- Model: AHR exact matches
  - Consensus: NEGATIVE
- Model: AHR nearest neighbour
  - Consensus: NEGATIVE
- Model: AHR Signature Alerts
  - Consensus: NEGATIVE
- Model: AHR Signature Significance
  - Consensus: NEGATIVE

Classification: NEGATIVE

Consensus: NEGATIVE
Bioclipse Decision Support

Bioclipse

Core bio- and chem-informatics

Data-independent implementations

Data and models

Mutagenicity

Carcinogenicity

AHR

predictions

Model discovery

<additions>

<additions>

OpenTox
Rich GUI for predictions
OpenTox in Bioclipse
OpenTox in Bioclipse (2)
From data to predictions

- **Proprocess data**: Download, edit, visualize, preprocess structures and metadata
- **Create and assess models**: Statistical modeling and validation
- **Deploy models**: Package and deliver model to users in a flexible, secure format
- **Consume models**: Enable user-friendly consumption of services

Remote

Local
Next steps…

• Improve UI
  – Better indication of A&A, encryption, status
  – Selection of local and remote services
  – Highlight substructure results
  – More wizards and editors for OpenTox functionality

• Report accuracy from OpenTox predictions

• Include MetaPrint2D site-of-metabolism predictions, other open models…

• Consensus modeling
Future prospects

• Deploy Bioclipse models in OpenTox
  – Implement a bridge from OSGi services to OpenTox

• Run local server for offline OpenTox predictions

• Include OpenTox modeling in wizards (e.g. ToxCreatr)
Experiences from the Bioclipse-OpenTox integration

• Open standards and ontology/API greatly simplify integration
• Open and collaborative community
• Encouraging and constructive feedback
Bioclipse on desktop, web, and mobile
Acknowledgement: The Chemistry Development Kit (CDK)

- Most prominent open source Java library for cheminformatics, 10 year anniversary!
- Coordinated from Uppsala/Stockholm (Egon Willighagen) and EBI (Christoph Steinbeck)
- ~150 citations
- Widely Used in academia and pharma industry
  - AstraZeneca, Bayer, Merck-Serono, Sanofi Aventis, Eli Lilly, Novartis
• Providing commercial support around the topics of Bioclipse and statistical modeling.
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• www.genettasoft.com
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