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OpenTox

OpenTox Euro 2013

Chemical decision support in toxicology and pharmacology

Ola Spjuth

ola.spjuth@farmbio.uu.se

Department of Pharmaceutical Biosciences

Faculty of Pharmacy, Uppsala University

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Open standards facilitates integration

- Aim: Take advantage of the OpenTox infrastructure in Bioclipse
  - Look up services (e.g. data and models)
  - Consume services (download, upload, run predictions)
  - Create nice GUI for OpenTox infrastructure
  - Integrate with Bioclipse offline capabilities

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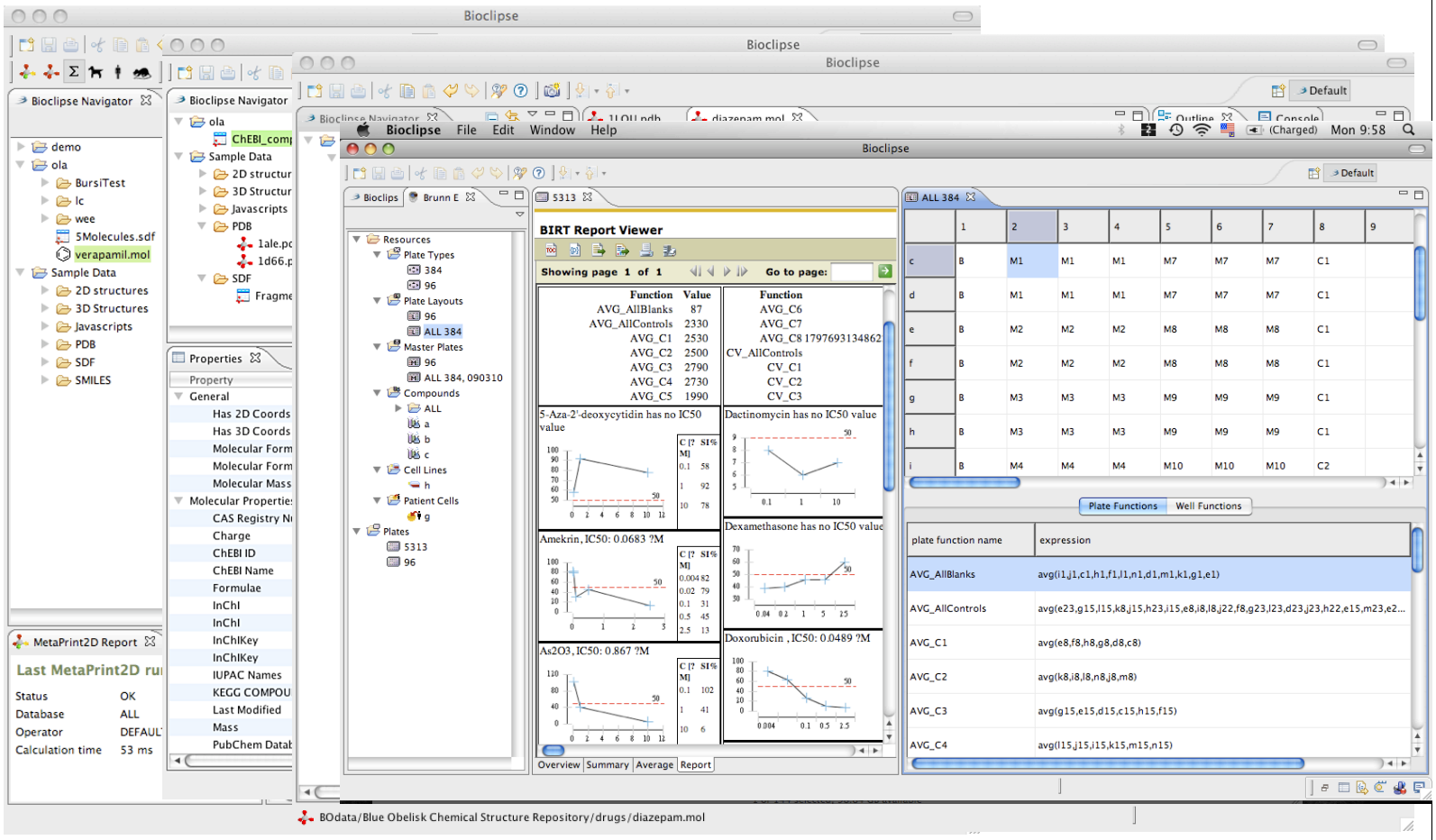
Bioclipse – an open source workbench for the life sciences



O. Spjuth, J. Alvarsson, A. Berg, M. Eklund, S. Kuhn, C. Mäsak, G. Torrance, J. Wagener, E.L. Willighagen, C. Steinbeck, and J.E.S. Wikberg. *Bioclipse 2: A scriptable integration platform for the life sciences*. BMC Bioinformatics 2009, **10**:397

Spjuth O, Helmus T, Willighagen EL, Kuhn S, Eklund M, Wagener J, Murray-Rust P, Steinbeck C, Wikberg JES: *Bioclipse: an open source workbench for chemo- and bioinformatics*. BMC Bioinformatics 2007, **8**:59.

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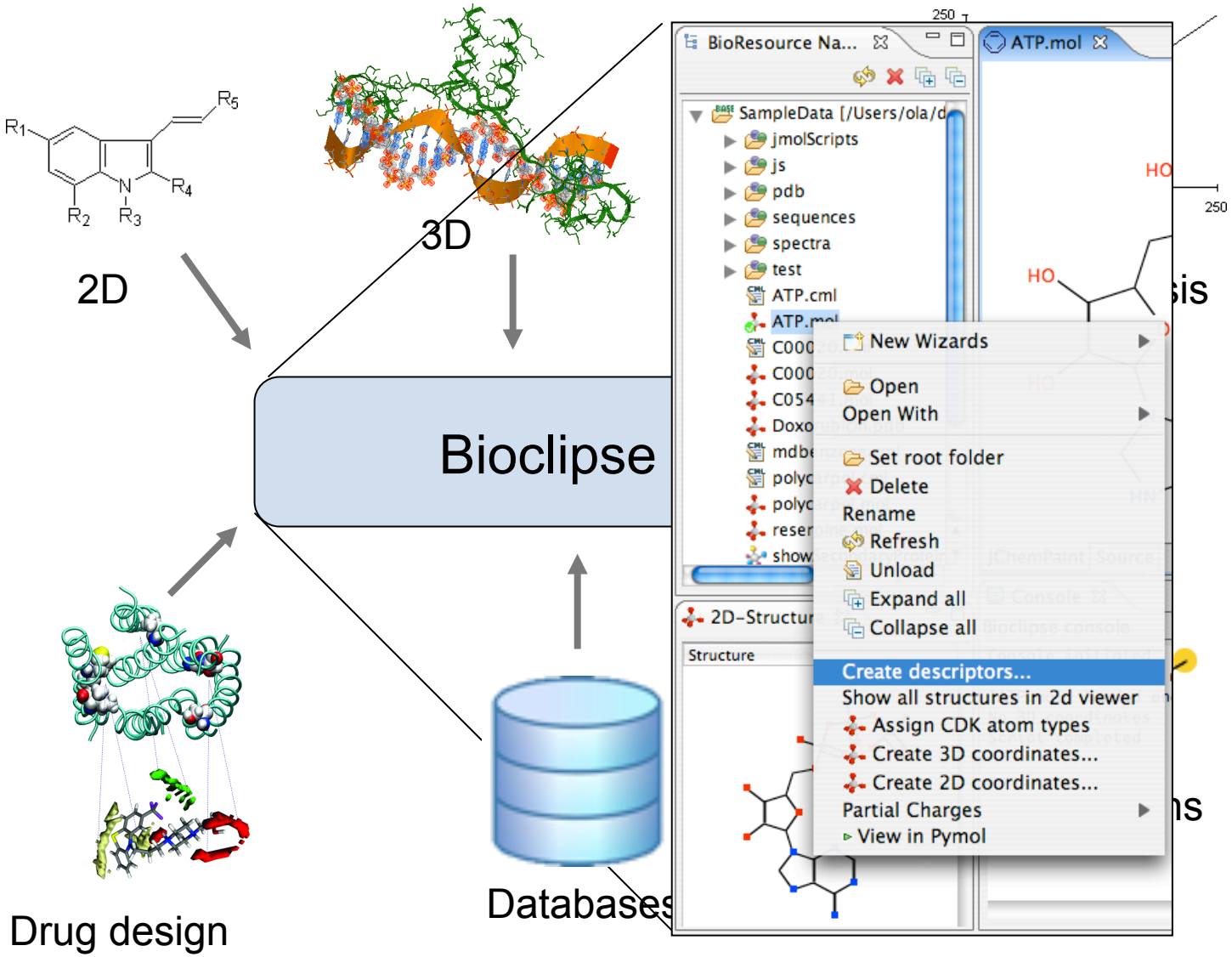
Component-based architecture



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Bioclipse Scripting Language

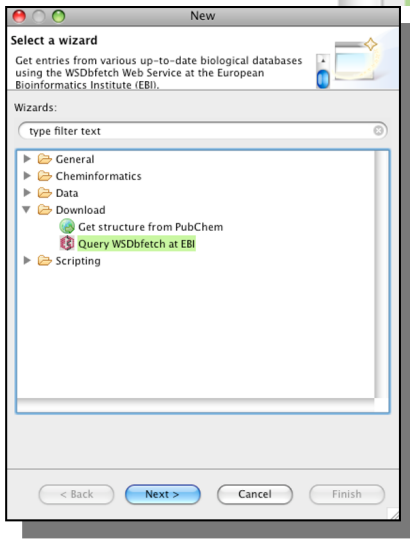
Properties | Progress | Javascript Console

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

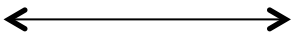
(a)

```
seqs = biows.queryEMBL("X56734,X56735");
aln = kalignws.alignDNA(seqs);
biojava.sequencesToFASTAfile(aln, "save here");
```

(b)



(c)



gist.github

my experiment

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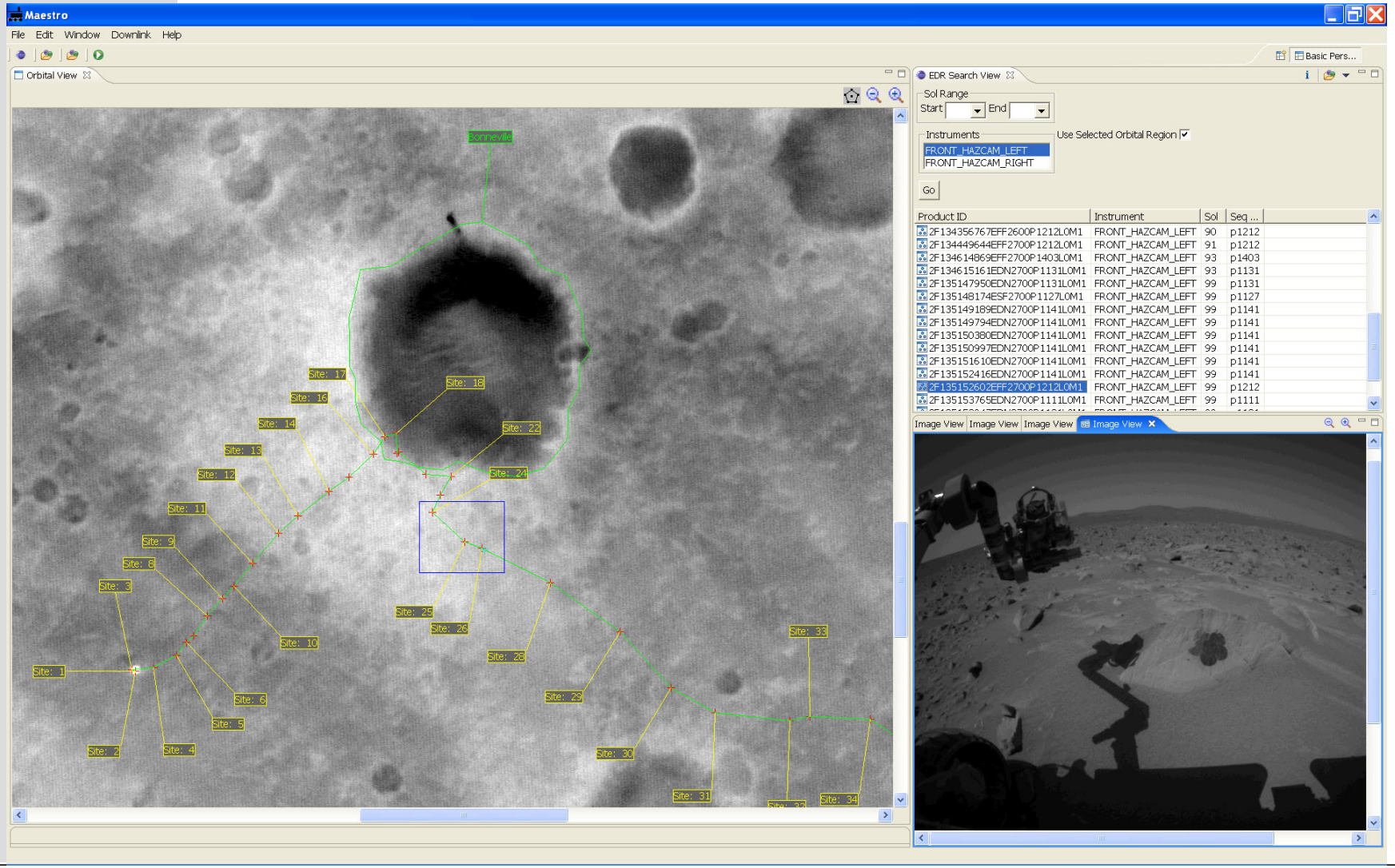
Eclipse: Proven technology



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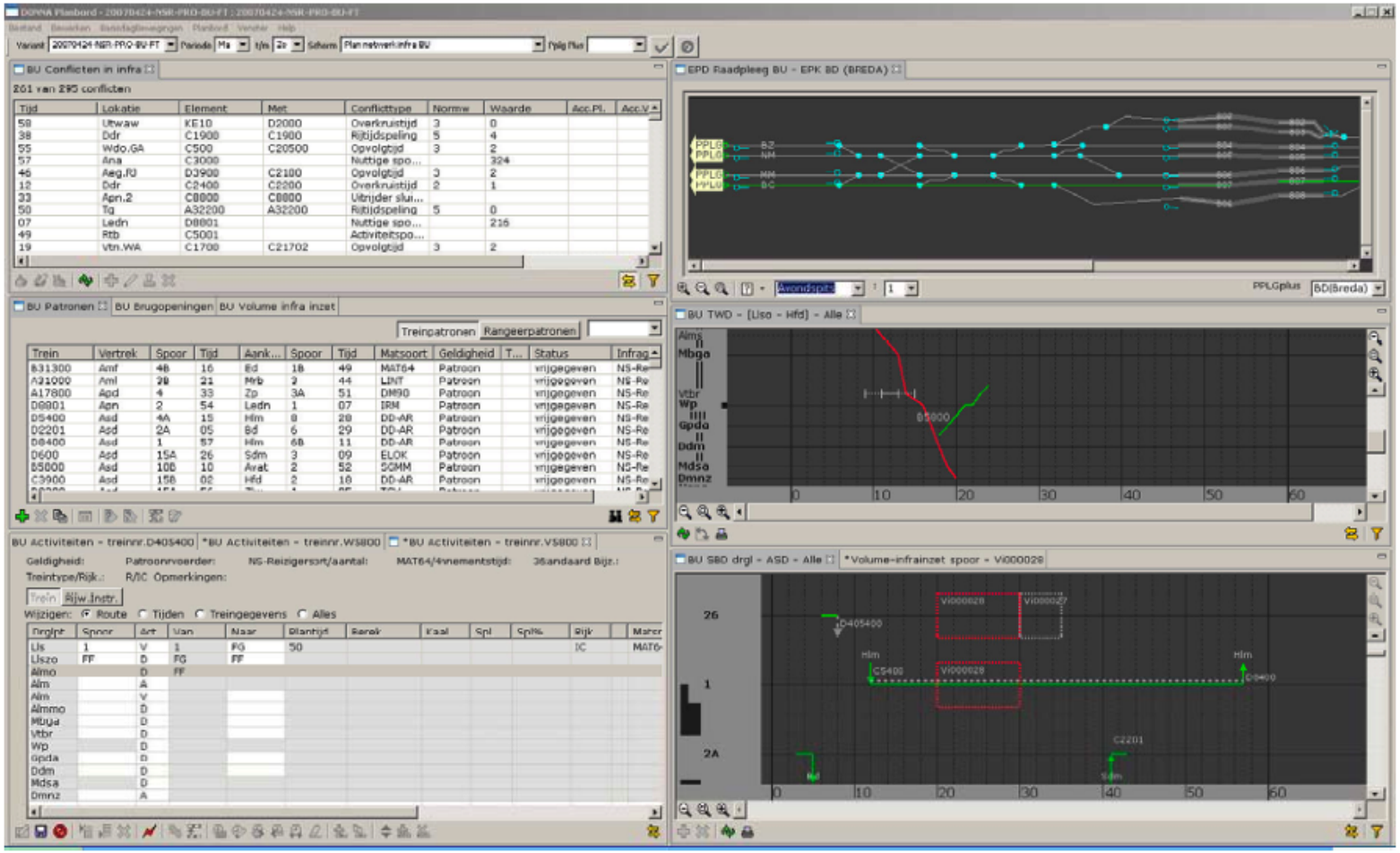
Example: Dutch railways



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From data to predictions

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

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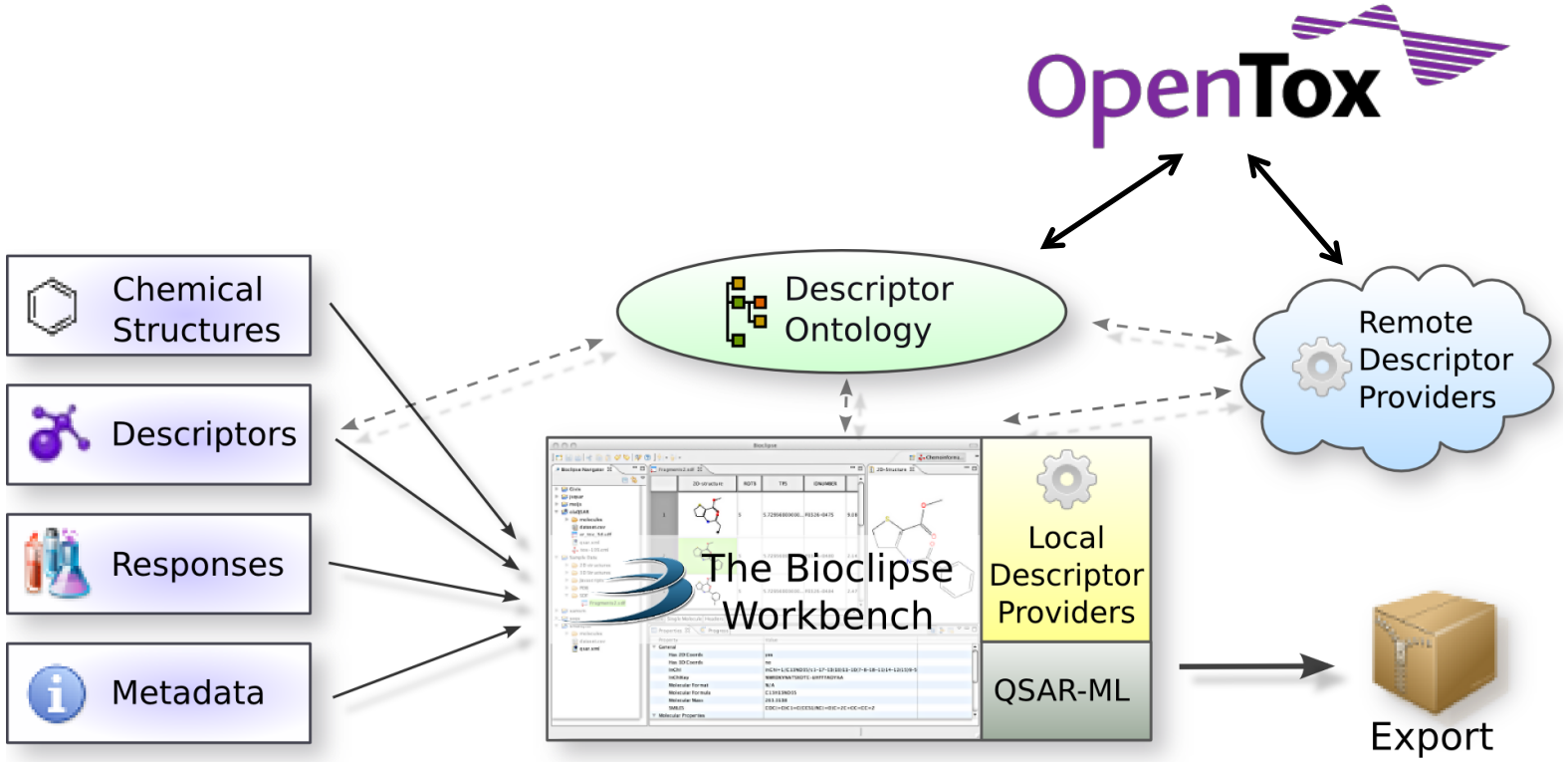
Bioclipse-QSAR: Reproducible QSAR datasets



O. Spjuth, E.L. Willighagen, R. Guha, M. Eklund, and J.E.S. Wikberg. *Towards interoperable and reproducible QSAR analyses: Exchange of data sets*. Journal of Cheminformatics 2010, **2**:5

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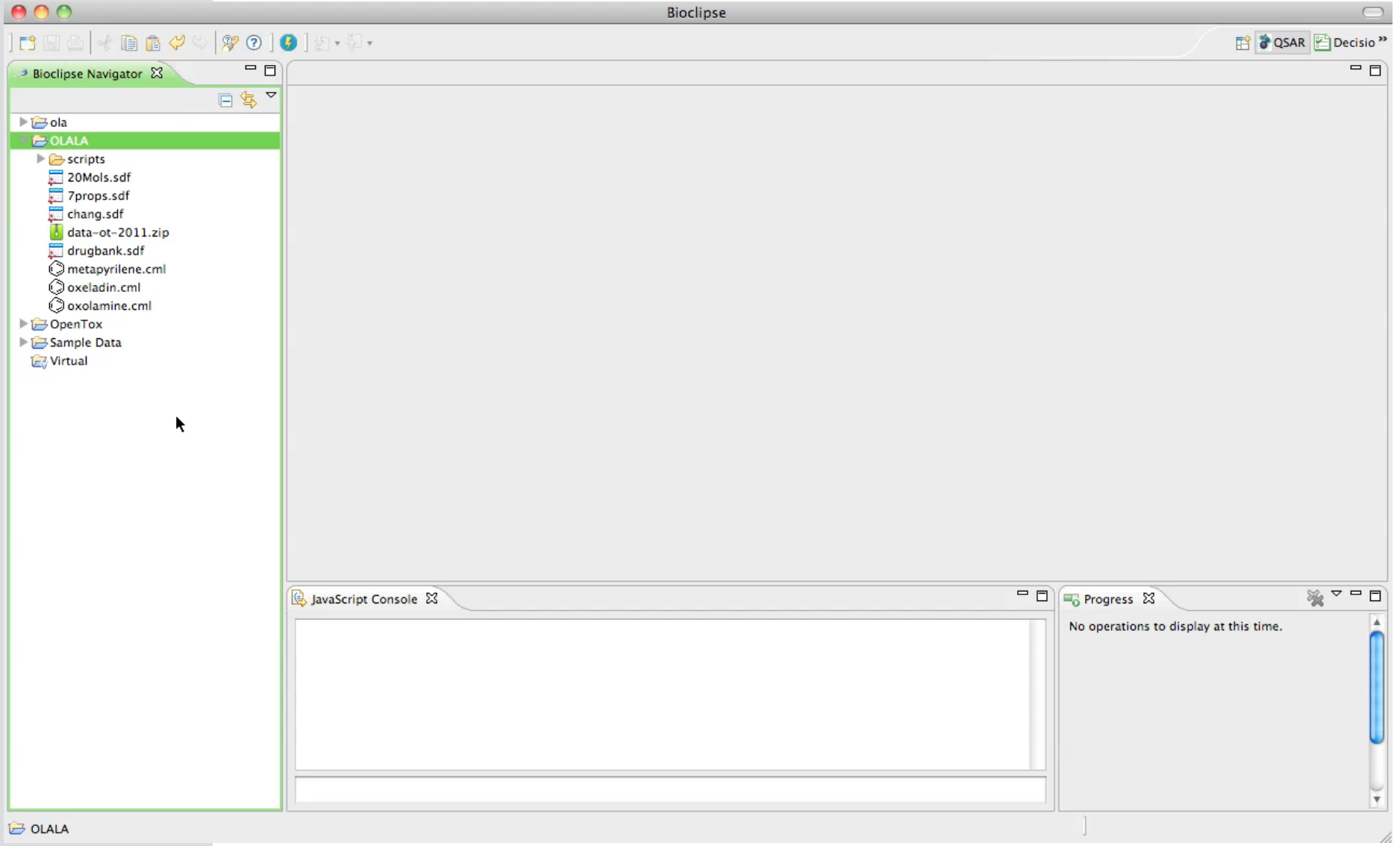
Bioclipse-QSAR with OpenTox



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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)

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Chemical Decision Support for safety assessment

- Integrate various predictive models
  - Similarity searches (InChi, signatures, fingerprints)
  - Structural alerts (toxicophores)
  - QSAR models (classification, regression)
- Demonstrated on drug safety endpoints:
  - Mutagenicity (AMES)
  - Carcinogenicity (CPDB)
  - AHR inhibition (PubChem BioAssay 2796)

O. Spjuth, L. Carlsson, M. Eklund, E. Ahlberg Helgee, and Scott Boyer.
Integrated decision support for assessing chemical liabilities.
J. Chem. Inf. Model, 2011, 51 (8), pp 1840-1847

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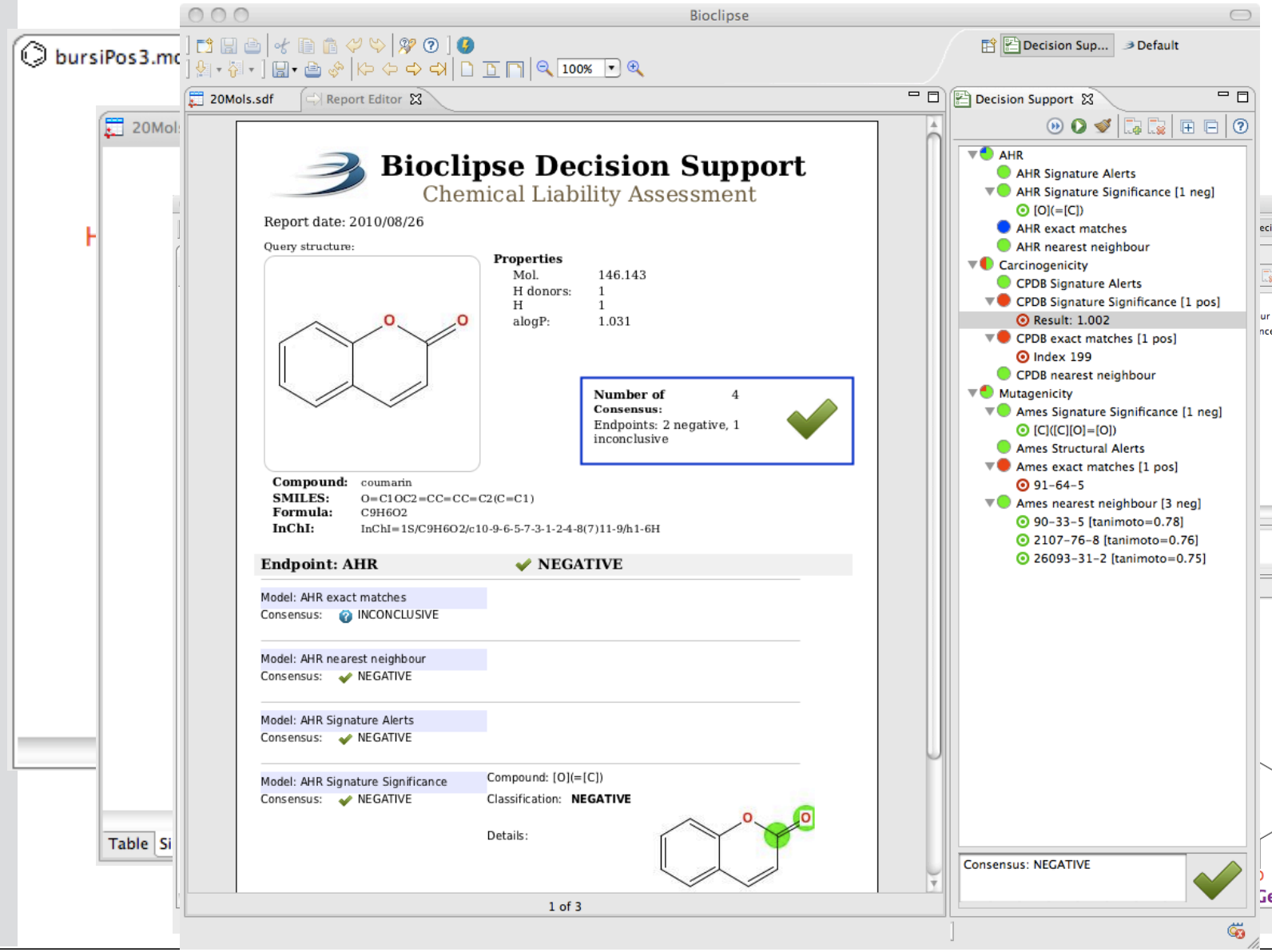
Bioclipse Decision Support



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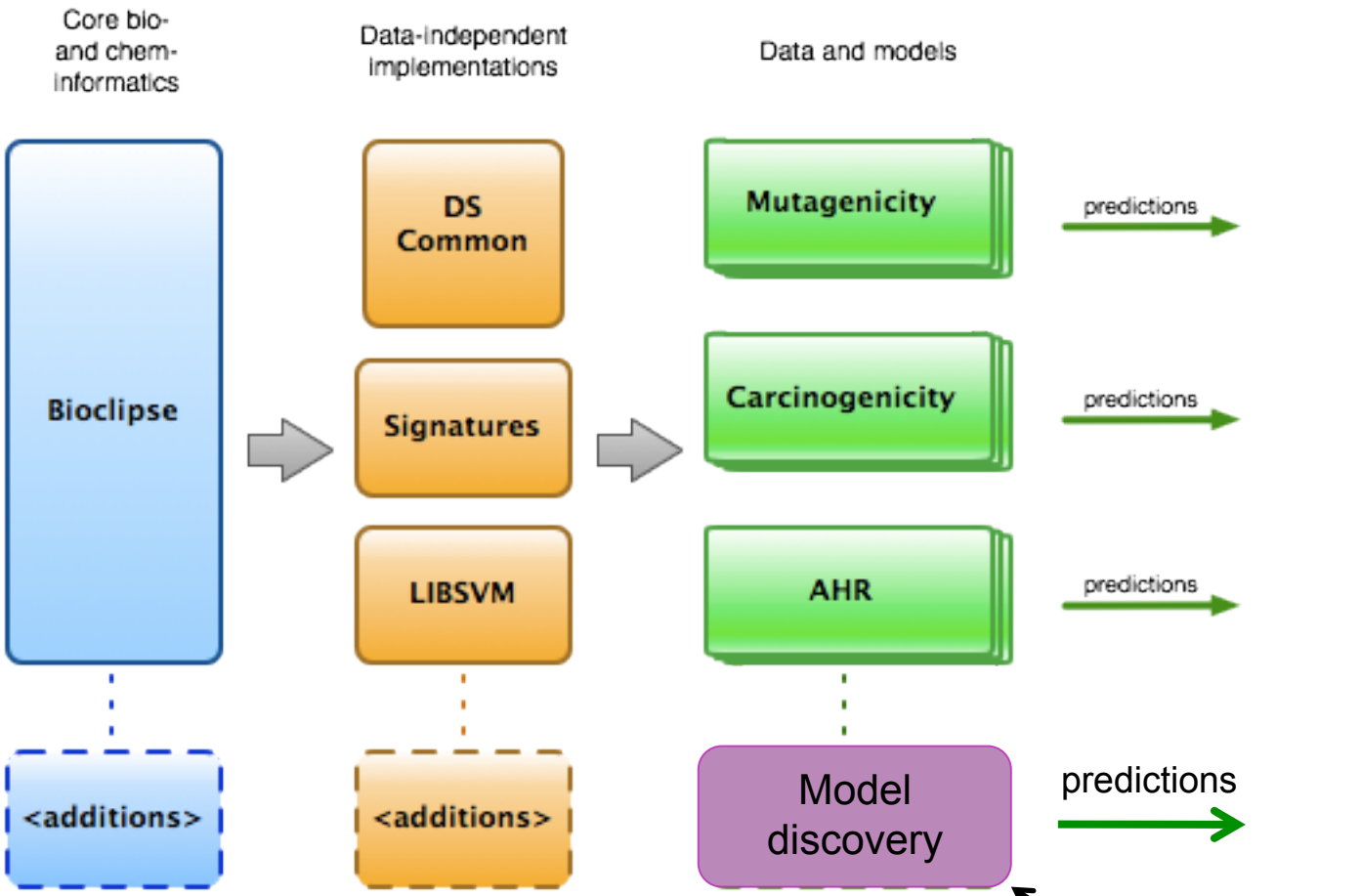
Bioclipse Decision Support



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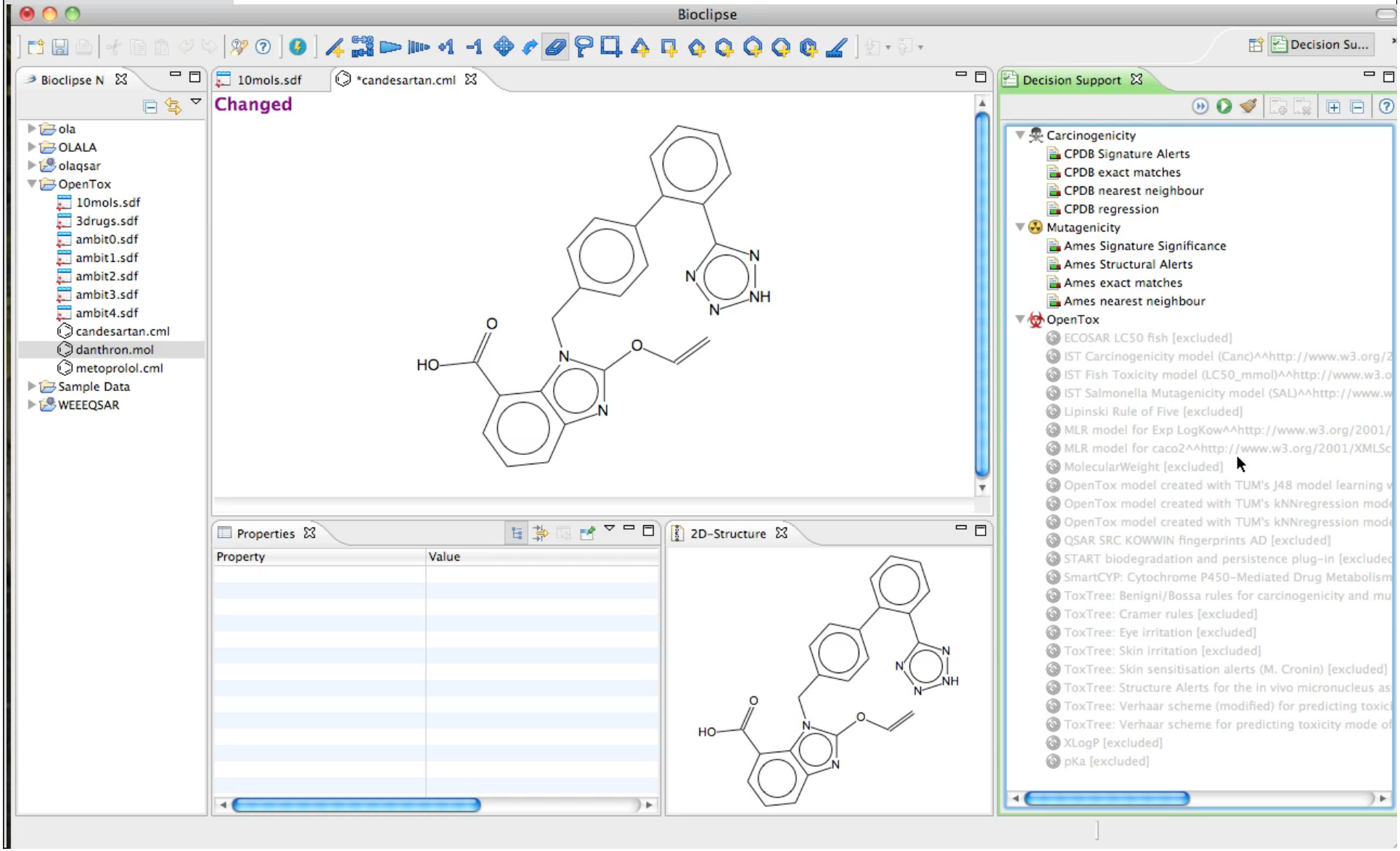
Rich GUI for predictions



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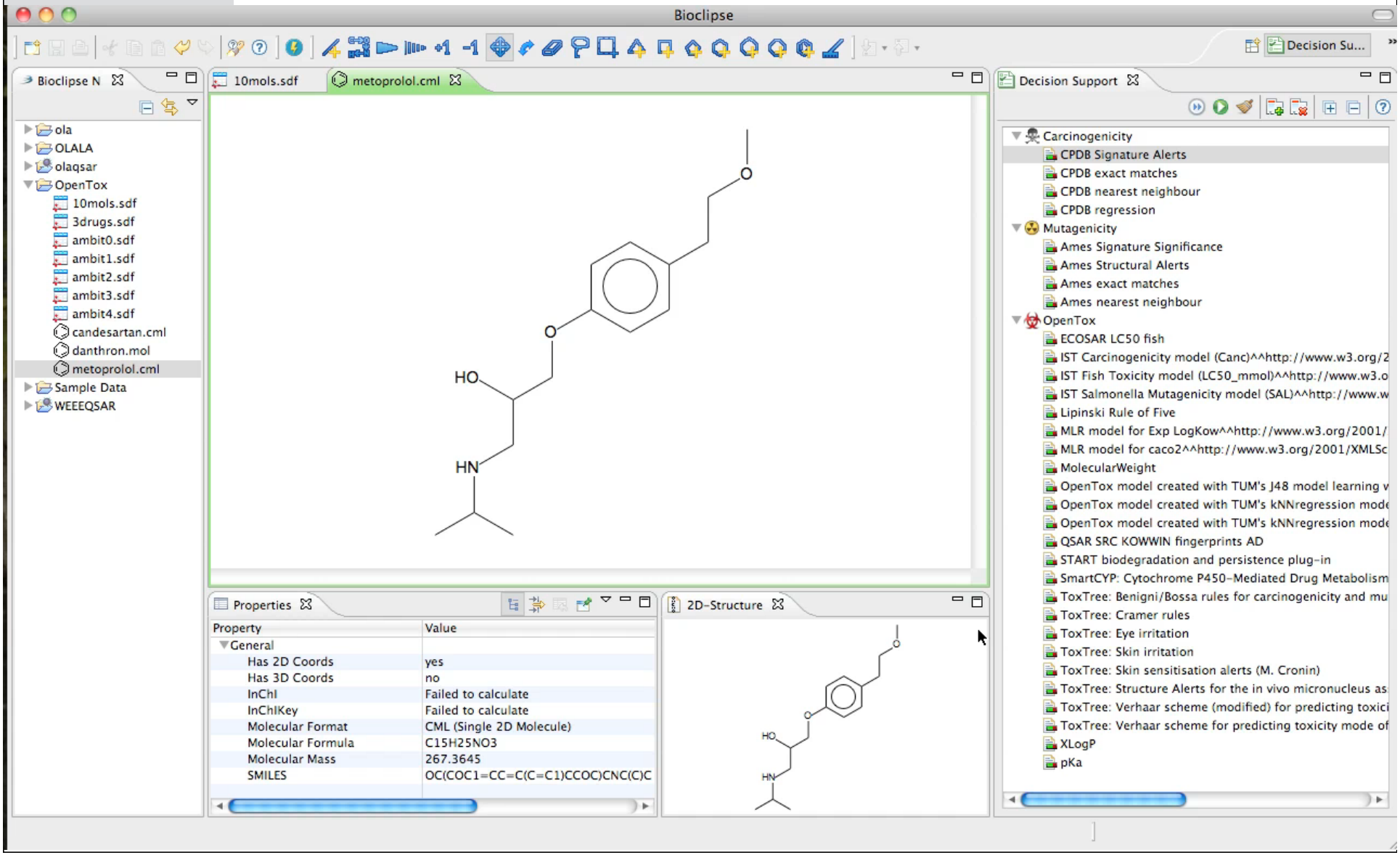
OpenTox in Bioclipse



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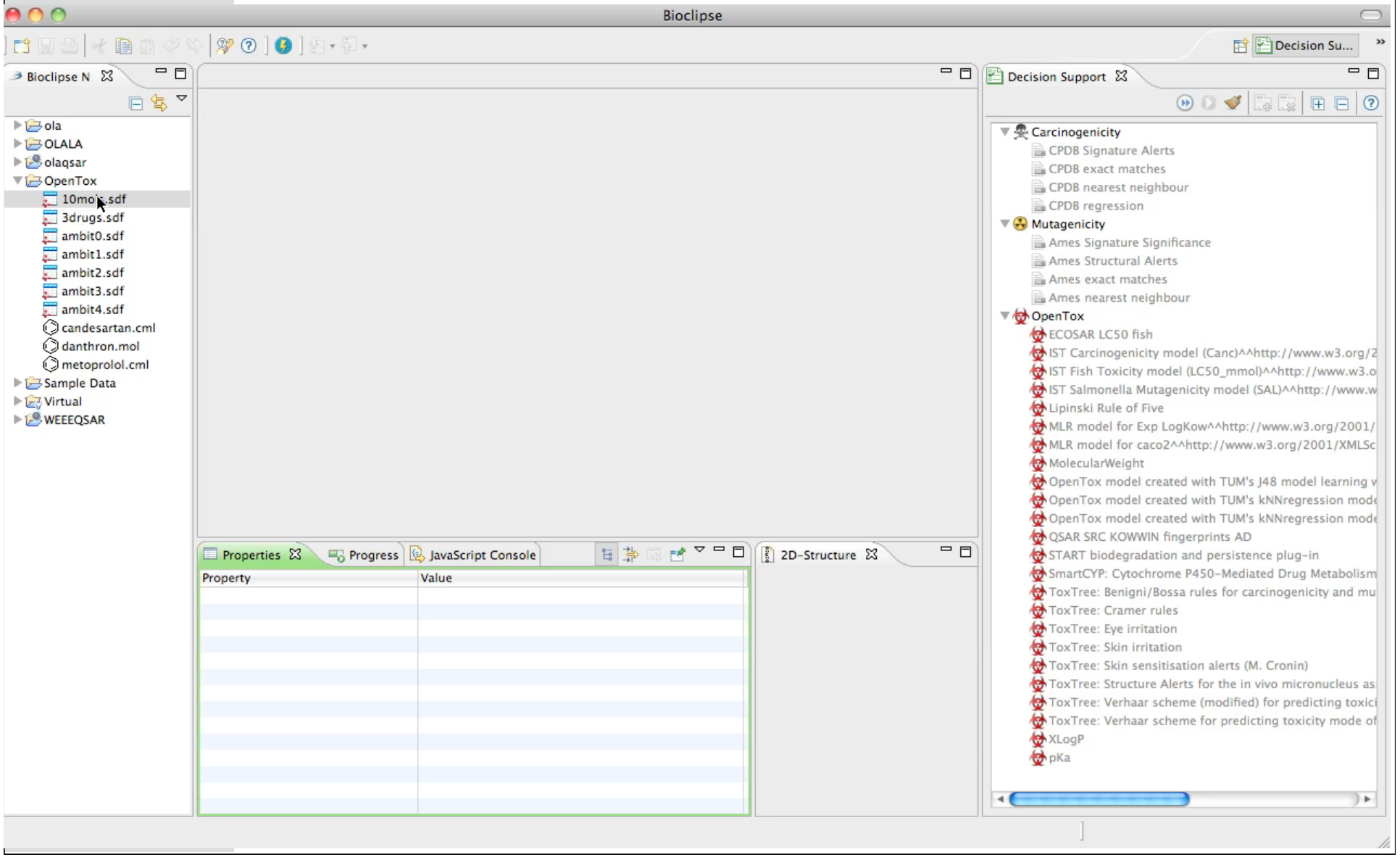
OpenTox in Bioclipse (2)



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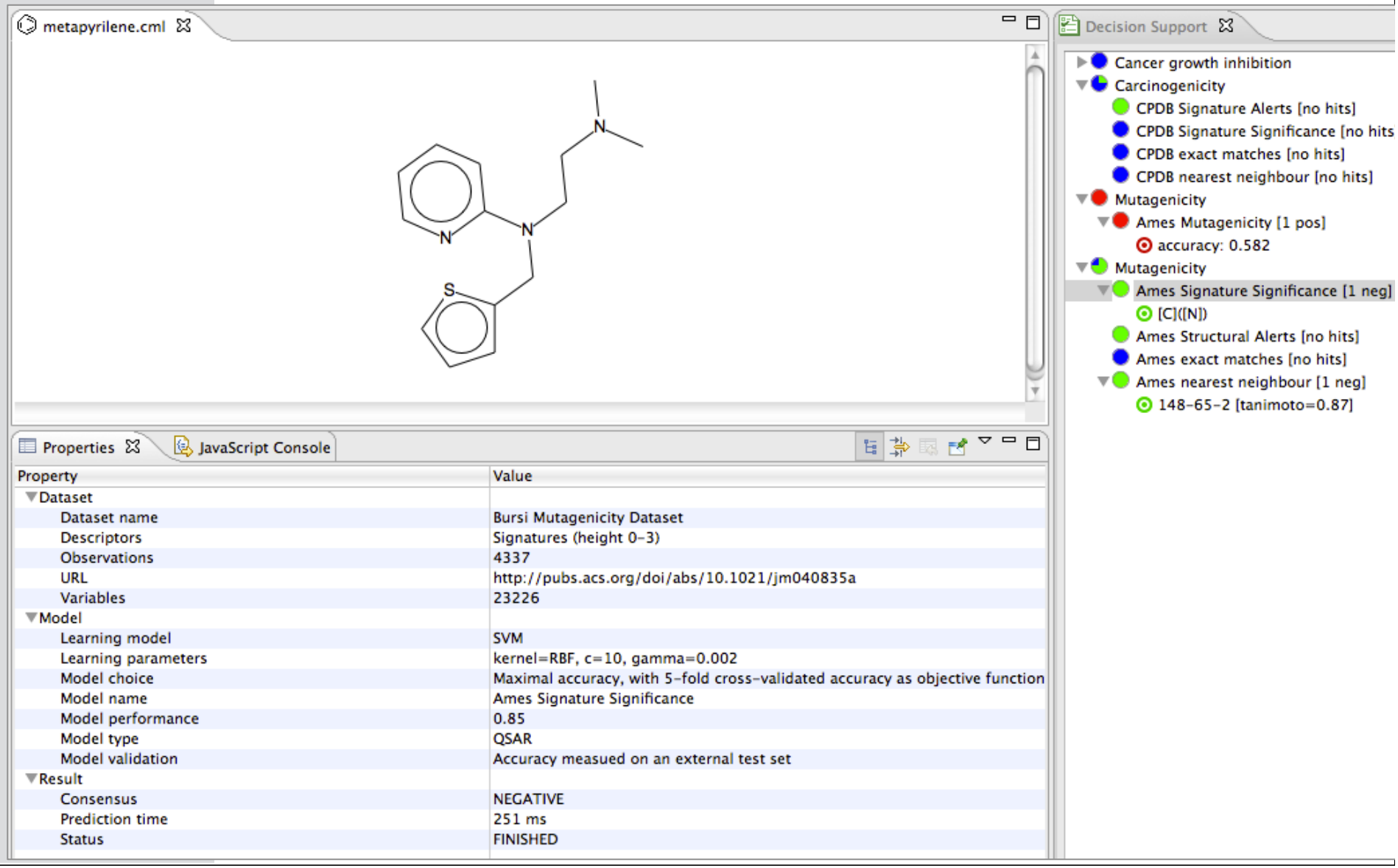
Report model validation



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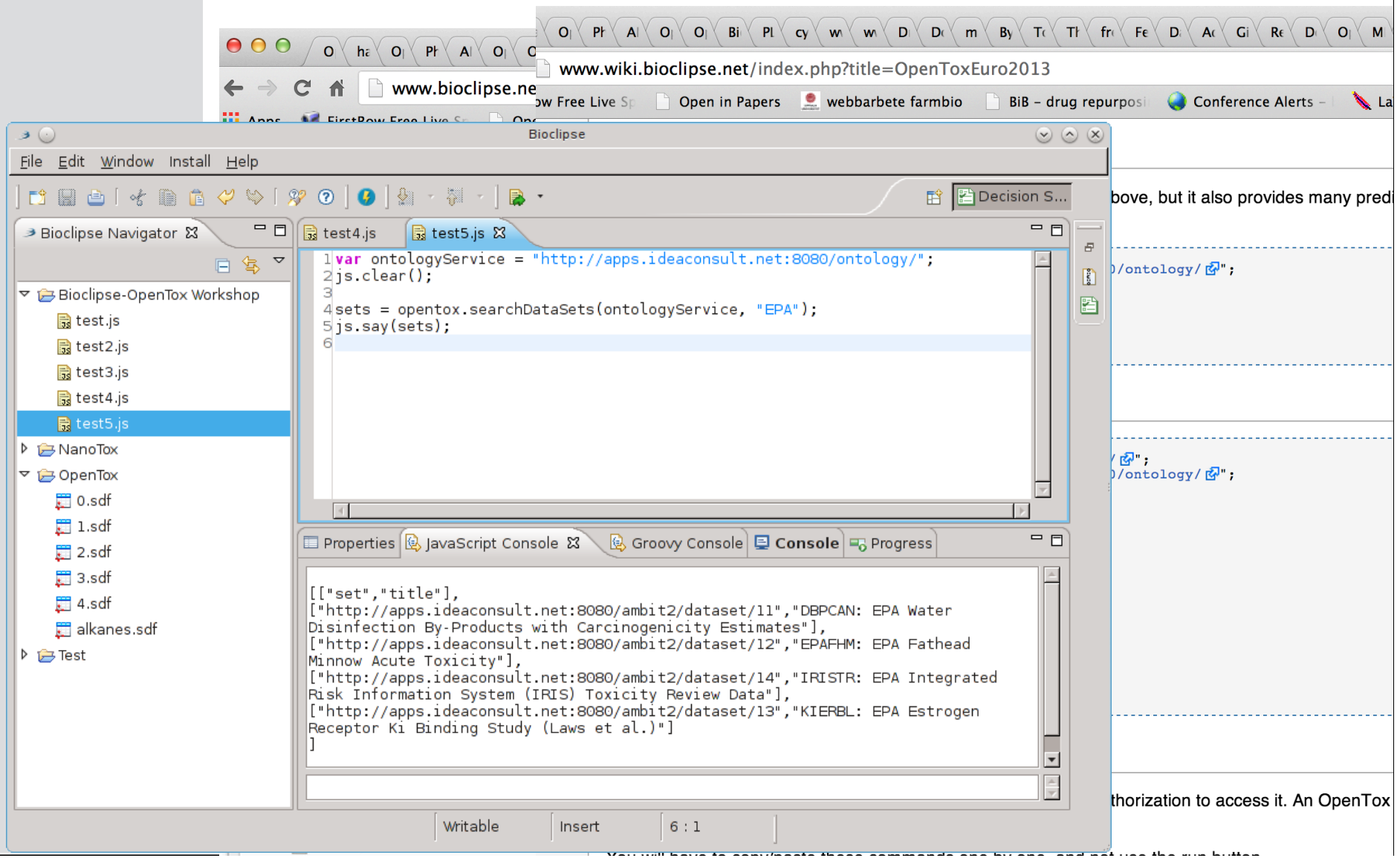
Scripting OpenTox in Bioclipse



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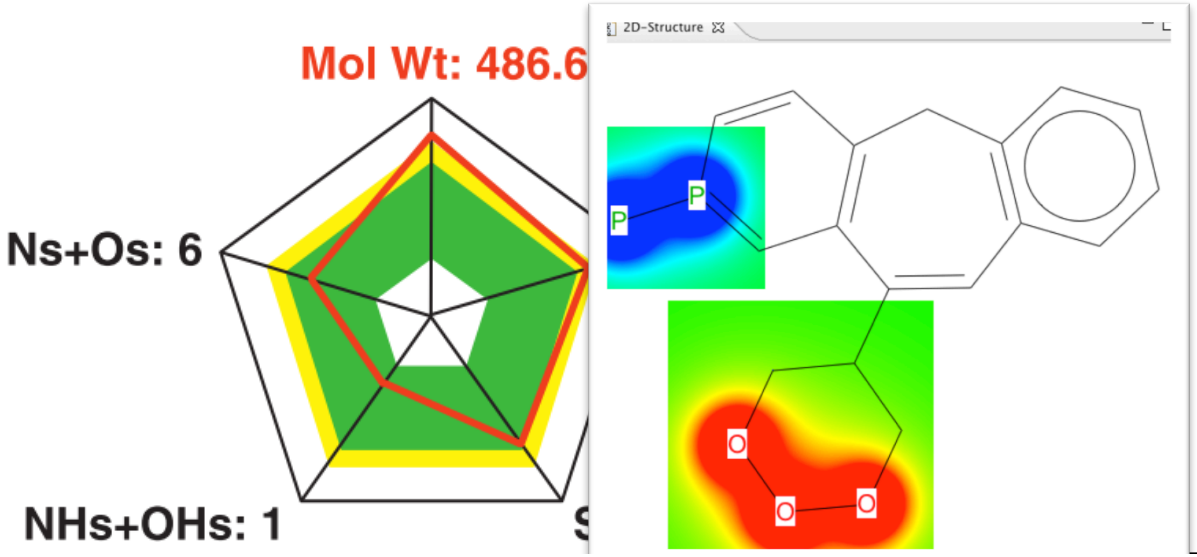
Related work

- Modeling in Bioclipse
  - Integrated solutions (e.g. libsvm)
  - Modeling with R
- Publish Bioclipse models using p2
- Visualizations



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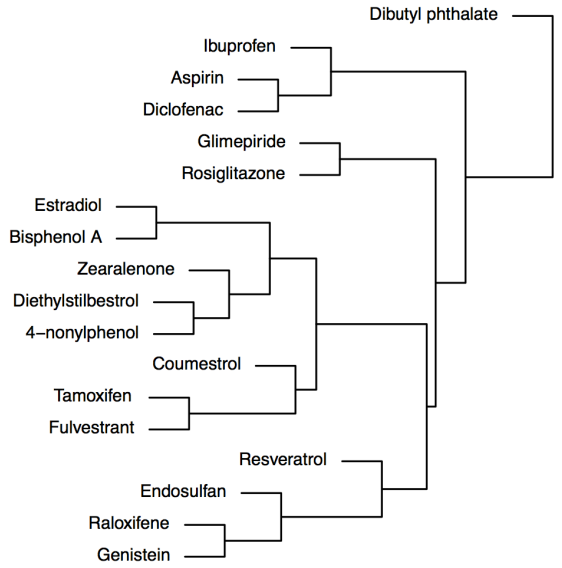
Related work 2

- Secure provisioning of offline models
- Model building on HPC/cloud resources
- Secondary pharmacology predictions
- Biological similarity: QuantMap



Schaal W, Hammerling U, Gustafsson MG, Spjuth O.
Automated QuantMap for rapid quantitative molecular network topology analysis.
Bioinformatics. 2013 Sep 15;29(18):2369-70.

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Next steps: Bioclipse-OpenTox

- Better indication of AA, status, classification, and confidence of results (API improvements?)
- Distinguish local and remote services better
- Highlight OpenTox substructure results
- Categorization of models

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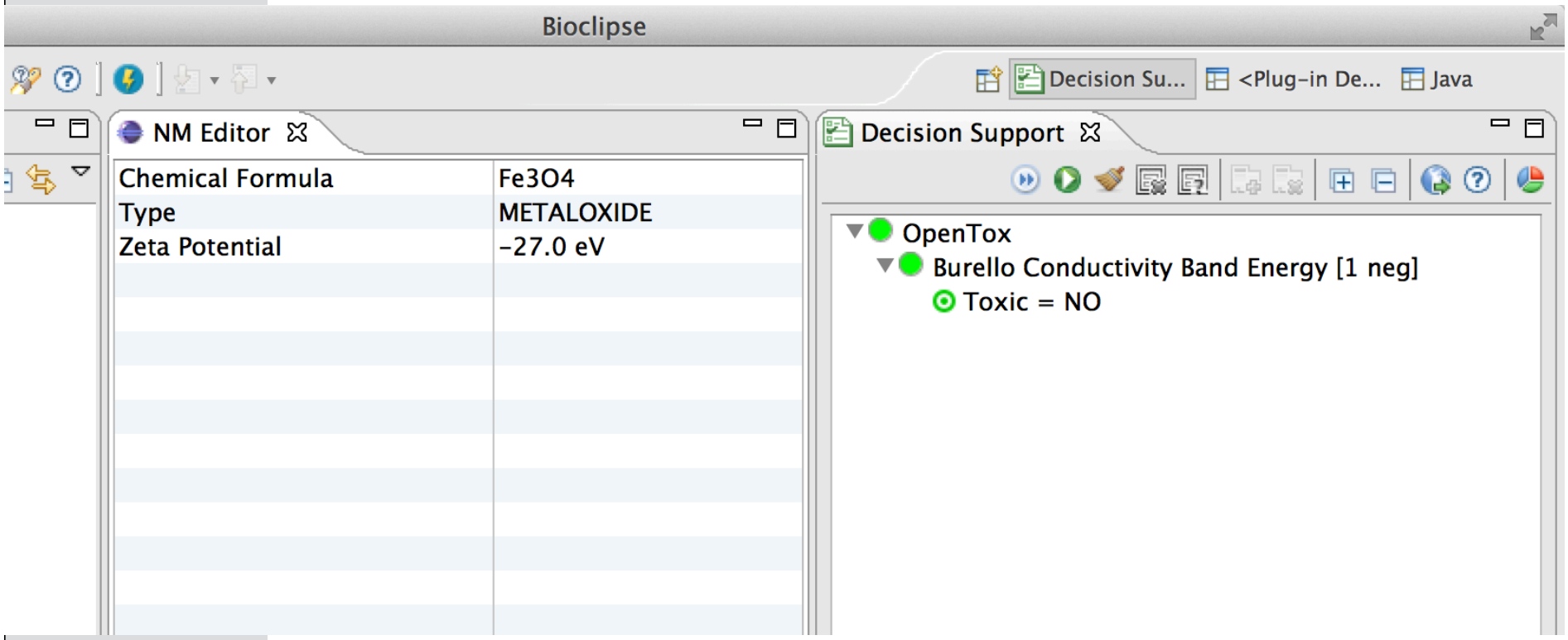
Predicting nanotoxicity using OpenTox from Bioclipse



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Acknowledgement: The Chemistry Development Kit (CDK)

- Most prominent open source Java library for cheminformatics
- Coordinated from Maastricht University (Egon Willighagen) and EBI (Christoph Steinbeck)
- ~200 citations
- Widely Used in academia and pharma industry
  - AstraZeneca, Bayer, Merck-Serono, Sanofi Aventis, Eli Lilly, Novartis

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Genetta SOFT

- Providing commercial support around the topics of Bioclipse and statistical modeling.
- Research, implementations, education, branding/deployment
- www.genettasoft.com

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OpenTox

OpenTox 2011

- Thank you -

Ola Spjuth

ola.spjuth@farmbio.uu.se

Department of Pharmaceutical Biosciences

Faculty of Pharmacy, Uppsala University