

ToxPredict Exercises

Predict the toxicity of a compound

OpenTox Workshop, February 2011

ToxPredict

Objective

To demonstrate and evaluate a prototype OpenTox application (ToxPredict) that accepts chemical structures and names as input and automatically generates a toxicity report based on various pre-calibrated toxicity models.

Description of ToxPredict

ToxPredict is a web-based interface for predicting toxicity of individual chemicals. Users can either search for a compound in the OpenTox prototype database, which currently includes quality labeled data for 163,122 chemicals (including all chemicals currently registered with REACH) grouped in 2,409 datasets, or upload their own chemical structure in the SDF format. It runs the selected calculations automatically using a collection of distributed computational services. ToxPredict currently includes eighteen validated models addressing 15 different endpoints, and is extensible.

Prerequisites: A computer with browser (Internet Explorer or Firefox) and fast internet connection.

Note: any compounds not found in the OpenTox database, must be uploaded as SDF or MOL files.

Exercise A. Predict the toxicity of a chemical in the database, by name

ToxPredict searches its database for chemical structures entered as chemical names, SMILES strings, CAS number or via an integrated 2D chemical drawing editor. The steps below illustrate using the chemical name:

1. Open a Browser window (Internet Explorer or FireFox are recommended)
2. Type in "toxpredict.org" (without the quotation marks) and press "Enter" on the keyboard

ToxPredict
OpenTox demo application

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ToxPredict estimates the chemical hazard of chemical structures. It relies on **OpenTox API-v1.1** compliant **RESTful webservices**. Users can either search the OpenTox prototype database, which includes currently quality labeled data for 168053 chemicals (521189 structures), grouped in 3906 datasets, or upload their own chemical structure data. ToxPredict provides access to **18 ready to use models**, addressing 15 different endpoints. The **ToxCreate** sister application allows more advanced users to train new OpenTox models. Press **NEXT** to enter your ToxPredict workflow.

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Estimate toxicological hazard of a chemical structure

1. Select structure(s) 2. Verify structure(s) 3. Select model(s) 4. Run prediction(s) 5. Display result(s)

NEXT

Figure 1.

3. Click "NEXT", after the screen has loaded (see figure 1 above).
4. Type a chemical name in the text box, e.g. "benzene" (or CAS number, SMILES string...) (see figure 2 below)



Free text search
(Enter chemical name, registry identifier, SMILES, InChI, any keywords)★

benzene

Number of hits: 1



Figure 2.

- Click "NEXT" to start the search, (if the error message "not found" is displayed, then the name could not be found in the database, so you will need to try a different name or upload the structure as an SDF file)
- Click "NEXT" again to view the list of endpoints (see Figure 3 below)



Model	Endpoint	Algorithm	Validation
<input type="checkbox"/> MolecularWeight		MolecularWeight	
<input type="checkbox"/> ToxTree: Michael acceptors		ToxTree: Michael acceptors	
<input type="checkbox"/> QSAR SRC KOWWIN fingerprints AD		Applicability domain: Fingerprints, Tanimoto distance to a consensus fingerprints	
<input type="checkbox"/> ECOSAR LC50 fish	Acute toxicity to fish (lethality)	Regression: Linear regression	
<input type="checkbox"/> ToxTree: Verhaar scheme for predicting toxicity mode of action	Acute toxicity to fish (lethality)	ToxTree: Verhaar scheme for predicting toxicity mode of action	
<input type="checkbox"/> ToxTree: Benigni/Bossa rules for carcinogenicity and mutagenicity	Carcinogenicity	ToxTree: Benigni/Bossa rules for carcinogenicity and mutagenicity	
<input type="checkbox"/> pKa	Dissociation constant (pKa)	pKa	
<input type="checkbox"/> ToxTree: Structure Alerts for the in vivo micronucleus assay in rodents	Endpoints	ToxTree: Structure Alerts for the in vivo micronucleus assay in rodents	
<input type="checkbox"/> ToxTree: Eye irritation	Eye irritation/corrosion	ToxTree: Eye irritation	
<input type="checkbox"/> OpenTox model created with TUM's kNNregression model learning web service.	Gastrointestinal absorption	http://opentox.informatik.tu-muenchen.de:3080/OpenTox-dev/algorithm/kNNregression	
<input type="checkbox"/> Lipinski Rule of Five	Human health effects	Lipinski Rule of Five	
<input type="checkbox"/> ToxTree: Cramer rules	Human health effects	ToxTree: Cramer rules	

Figure 3.

- Click to select each of the 18 boxes in the left column (you must click each box)
- Click "NEXT" to start the calculations
- Click "NEXT" again (to view the results)

Exercise B. Predict the toxicity of a chemical in the database, by structure

ToxPredict searches its database for chemical structures entered as chemical names, SMILES strings, CAS number or via an integrated 2D chemical drawing editor. The steps below illustrate using the integrated drawing editor to sketch a structure:

- Open a Browser window (Internet Explorer or FireFox are recommended)
- Type in "toxpredict.org" (without the quotation marks) and press "Enter" on the keyboard
- Click "NEXT", after the screen has loaded (see figure 1 above).
- Click the "Draw" tab (see Figure 4 below)

Figure 4.

- Use the drawing tools to sketch a molecule structure
- Click "NEXT" (if the error message "not found" is displayed, then the structure could not be found in the database, so you will need to try a different structure or upload the structure as an SDF file)
- Click "NEXT" again (to view the list of endpoints)
- Click to select each of the 18 boxes in the left column (you must click each box)
- Click "NEXT" to start the calculations
- Click "NEXT" again (to view the results)

Exercise C. Predict the toxicity of a chemical not in the database, by upload

To predict the toxicity of a new chemical that is not in the current ToxPredict database, you will need to upload the structure file as an "SD" or "SDF" file as follows (please ask if you need some sample SD files to try):

1. Open a Browser window (Internet Explorer or FireFox are recommended)
 2. Type in "toxpredict.org" (without the quotation marks), then press "Enter" on the keyboard
 3. Click "NEXT", after the screen has loaded (see figure 1 below).
 4. Click the "Upload" tab
 5. Click "Browse..."
 6. Navigate to and select your SDF file (example SD files are available)
 7. Click "Open"
 8. Click "NEXT"
 9. Click "NEXT" again (to view the list of endpoints)
 10. Click to select each of the 18 boxes in the left column (you must click each box)
 11. Click "NEXT"
 12. Click "NEXT" again (to view the results)
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