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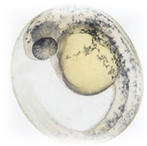
A Bayesian Network tool for Predicting Fish Acute Toxicity Based on Fish Embryo Toxicity test data



Introduction

- The **fish embryo toxicity test** (**FET**; OECD TG 236) has been proposed as an animal **alternative** to the **acute fish toxicity test** (AFT; OECD TG 203).
- The European Chemicals Agency has recommended the development of a **Weight-of-Evidence (WoE)** approach for using FET data to predict AFT.
- To this end, we have developed **a Bayesian network (BN)** model (Fig. 1) for using FET data in a **probabilistic** (Fig. 2) WoE approach [1, 2, 3] (Lillicrap et al. 2020, Moe et al. 2020, Belanger et al. 2022).

Data & methods

- Chemical and toxicological data from >4000 substances were used for parametrization of the BN (priors and conditional probability tables)
- A subset of 155 substances were used for **calibrating the weight** of the three **Lines of Evidence (LoE)** (Fig. 2) by cross-validation.
- Details of the model development and evaluation are given in previous presentations, available from www.niva.no/swift.

Example of model predictions

Prediction of AFT for the pharmaceutical substance **carbamazepine** is shown in Fig. 2.

- Contributions from **individual lines of evidence**:
  1) Fish embryo:
     - Most probable toxicity is 10-100 mg/L, alternatively 100-1000 mg/L
     - Consistent with observations for juvenile fish
  2) Algae & daphnids:
     - Inconsistent evidence results in higher uncertainty
     - Lower weight of evidence
  1) Fish gill cytotoxicity:
     - Indicates the possibility of **higher toxicity** (1-10 mg/L)
     - Also consistent with observations for juvenile fish
- Integrated prediction from all lines of evidence:
  - Correct predicted toxicity interval means high **accuracy**
  - Low **precision** reflects **inconsistencies** in evidence within and across LoEs

Model evaluation

- The **accuracy** of BN model predictions is evaluated by comparing **predicted vs. measured toxicity** to juvenile fish (Table 1)
- The BN predicts **correct or protective** toxicity levels for **86%** of the test substances
- Only **4%** of the substances have **underestimated toxicity** level AND fish embryo as the **most sensitive endpoint**

Table 1. Comparison of most probable posterior states for predicted vs. measured toxicity to juvenile fish, grouped by the most sensitive endpoint. The compared LC50 intervals are <1, 1-10 and >10 mg/L. Numbers show the percentage of test substances in each outcome class (total n = 155).

	Most sensitive endpoint			
Predicted toxicity level	**Algae**	**Daphnids**	**Embryo**	**Sum**
Too low (non-protective)	2%	8%	4%	**14%**
Accurate	19%	32%	12%	**63%**
Too high (protective)	10%	12%	2%	**23%**
Sum	**31%**	**51%**	**18%**	**100%**

Future perspectives

- The SWiFT BN model can contribute to using FET data in a WoE approach
- Remaining work includes further evaluation of the applicability domain, i.e. the types of substances for which the model performs well
- The SWiFT BN offers an objective method for estimating weights, both within and across lines of evidence
- A full WoE approach will need additional expert-based evaluations

References

Belanger et al. 2022. IEAM. https://doi.org/10.1002/ieam.4581
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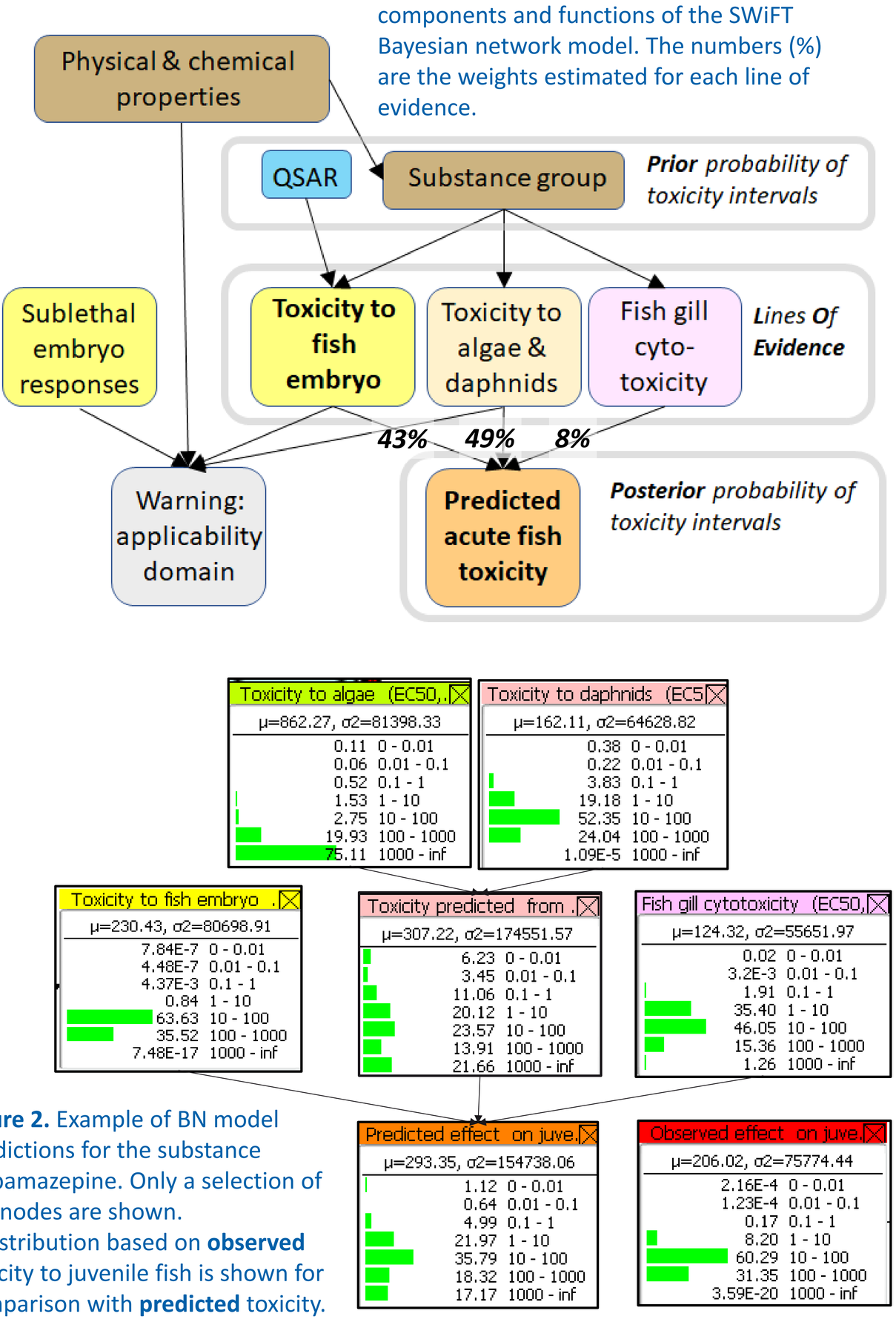

Figure 1. Schematic diagram of the main components and functions of the SWiFT Bayesian network model. The numbers (%) are the weights estimated for each line of evidence.

Figure 2. Example of BN model predictions for the substance carbamazepine. Only a selection of the nodes are shown. A distribution based on **observed** toxicity to juvenile fish is shown for comparison with **predicted** toxicity.

Web user interface

- The model is publicly available from a web user interface (Fig. 3)
- URL: swift.hugin.com/models/FET
- Values can be entered by:
  - manual input
  - uploading excel tables
- Predicted toxicities are given as:
  - probability distributions for all endpoints (cf. Fig. 2)
  - additional conclusion statements
- Also available from the web site:
  - Input and output values (.txt)
  - Summary report (.pdf)
- Interested in a demonstration?
  - Visit NIVA's exhibition
  - Contact the authors

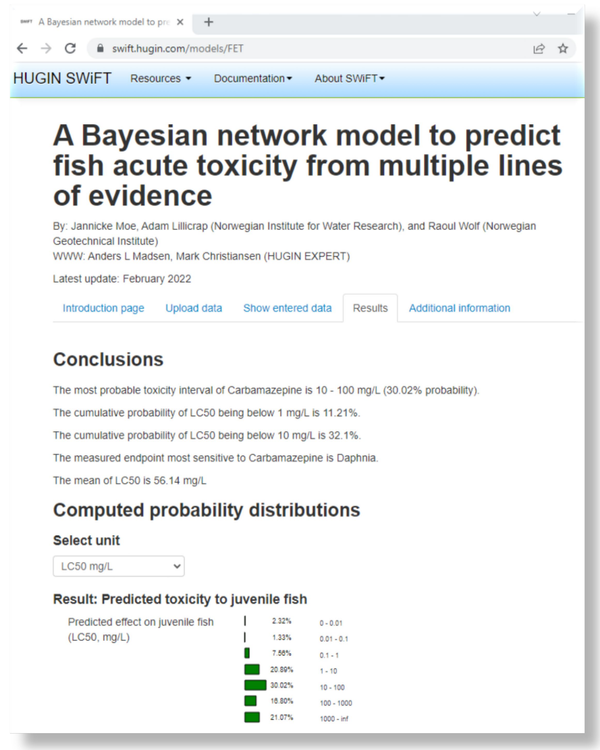

Figure 3. Web user interface to the SWiFT BN model: extract of the Results page

Acknowledgements

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