NICEATM Computational Tools and Resources Supporting Alternative Test Method Development and Evaluation

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Abstract 2542

Highlights

- Development, evaluation, and implementation of new methods for chemical evaluation require access to reliable data and tools.
- NICEATM provides access to reliable data and tools via easy-to-use graphical web interfaces and open-source software.
- NICEATM resources apply FAIR data principles to improve utility of these data and tools to evaluate alternative test methods.

FAIR Data – What and Why?

FAIR data (https://www.go-fair.org/fair-principles/) are:

- **Findable:** data and associated metadata are easy for humans and machines to find.
  - § Relevant data for assessments can be readily identified.
  - § Experimental details necessary for interpretation are clear.
- **Accessible:** data and associated metadata are easy to access.
  - § Authentication and authorization are apparent.
  - § Common, standard identifiers and universal (open) platforms facilitate acquiring data and documenting sources.
- **Interoperable:** data can be used with other data.
  - § Data can be combined and used in workflows without the need for intensive manual manipulation.
- **Reusable:** data and data objects such as protocols and code can be reused.
  - § Enables metanalysis and inferencing.

The implementation of FAIR principles within NICEATM resources allows our stakeholders to easily use data from ICE and OPERA with other data and systems.

More Information

- Learn more about NICEATM tools at SOT:
  - § **Abstract 2958**: Daniel et al. Updates to the Integrated Chemical Environment: Expanding Tools and Data to Support Toxicity Assessments
    Biological Models for In Vitro-In Vivo Extrapolation platform session
    Tuesday, March 23, 2:45-4:15 p.m.

- Subscribe to the NICEATM News email list:
  https://list.nih.gov/cgi-bin/wa.exe?SUBED1=niceatm-l&A=1

Visit ICE
https://ice.ntp.niehs.nih.gov/

https://ntp.niehs.nih.gov/go/opera

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The Integrated Chemical Environment (ICE)

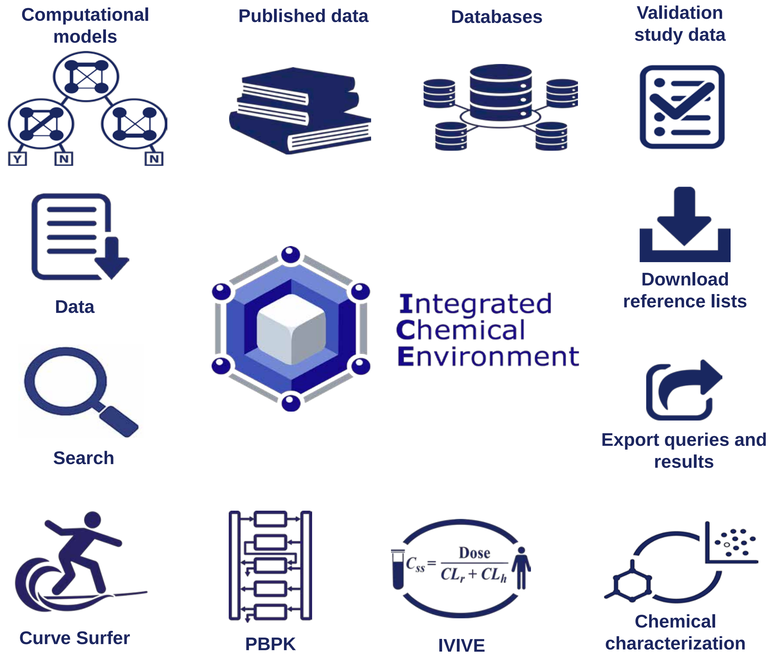
ICE is an access point for NICEATM data and tools. Organized around toxicity testing endpoints, ICE aims to advance non-animal approaches by simplifying the identification of useful data and democratizing the use and application of computational tools.

ICE provides free online access to:

- Curated in vivo and in vitro toxicity testing data.
- In silico toxicity and parameter predictions and chemical property data.
- Curated lists of chemicals with well-characterized toxic effects (reference chemical lists).
- Interactive computational tools that can characterize and predict toxicity for user-defined chemicals.

ICE supports:

- Data integration: brings together available data for chemicals and formulations from multiple sources.
- Results exploration: enables dynamic, graphical exploration with publication-quality graphics.
- Data analysis: allows characterization of data using online workflows.
- Data portability: connect with the U.S. Environmental Protection Agency's CompTox Chemicals Dashboard and the National Toxicology Programs Chemical Effects in Biological Systems (CEBS) database.



Open Structure-Activity/Property Relationship App (OPERA)

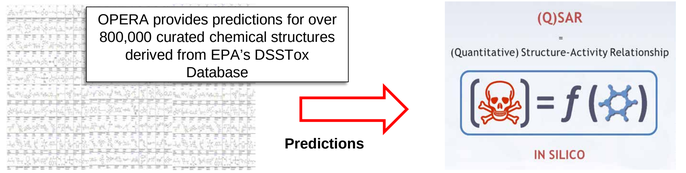
OPERA is a free and open-source quantitative structure-activity relationship (QSAR) tool. OPERA can predict both a long list of physio-chemical and absorption, distribution, metabolism, and excretion (ADME) properties as well as toxicity models targeting androgen and estrogen receptor and acute oral lethality that describe how a chemical interacts with its environment.

OPERA generates predictions of:

- Physicochemical properties
  - § Structural properties
  - § Environmental fate parameters
- ADME properties
  - § Plasma fraction unbound (Fu)
  - § Intrinsic clearance (CLint)
- Toxicity endpoints
  - § Estrogenic activity (models from CERAPP: **C**ollaborative **E**strogen **R**eceptor **A**ctivity **P**rediction **P**roject)
  - § Androgenic activity (models from CoMPARA: **C**ollaborative **M**odeling **P**roject for **A**ndrogen **R**eceptor **A**ctivity)
  - § Acute oral toxicity (models from CATMoS: **C**ollaborative **A**cute **T**oxicity **M**odeling **S**uite)

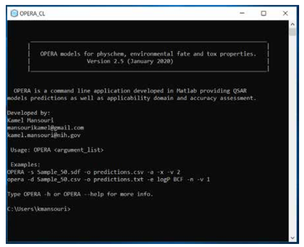
OPERA Predictions Available in ICE

Model	Description
CATMoS	Acute oral toxicity (five endpoints)
CERAPP	Estrogen pathway activity
CoMPARA	Androgen pathway activity
BP	Boiling point
CLint	Human hepatic intrinsic clearance
Fu	Human plasma fraction unbound
HL	Henry's Law constant
KOA	Octanol/air partition coefficient
LogD	Octanol-water distribution coefficient
LogP	Octanol-water partition coefficient
MP	Melting point
pKa	Acidic dissociation constant
VP	Vapor pressure
WS	Water solubility at 25º C

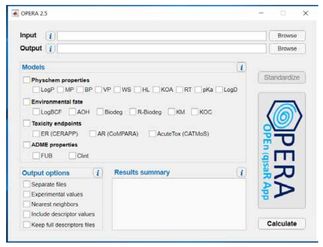


OPERA Standalone App

Command-line Interface



Graphical User Interface



- Free, open-source and open-data
- Single chemical and batch mode
- Multiple platforms (Windows and Linux)
- Embeddable libraries (java, C, C++, Python)