CLiCC (Chemical Life Cycle Collaborative)

Network for Rapid Assessment of Chemical Life Cycle Impact

UCSB

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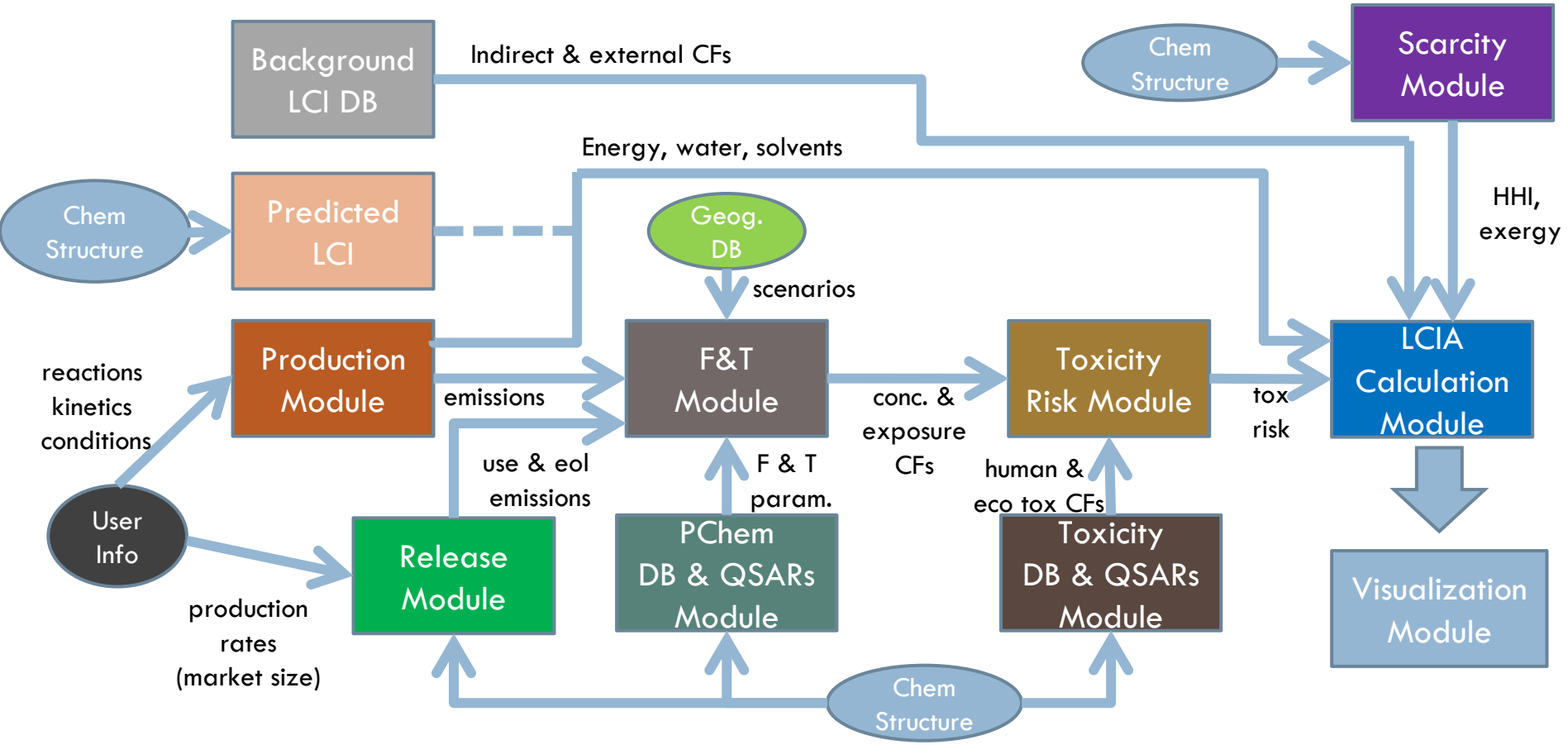
Internal Tool Workflow



CHEMICAL LIFE CYCLE COLLABORATIVE: CHEMICAL PROPERTIES MODULE

Mengya Tao, Runsheng Song, Jaye Harada, Kristin Denault

Chemical Properties Module

- Extending search of QSARs to more endpoints:
  - Carcinogenicity (more quantitative)
  - Developmental toxicity
  - Reproductive toxicity
  - Cardiovascular toxicity
  - Dermatotoxicity
  - Endocrine toxicity
  - Epigenetic toxicity
  - Genotoxicity
  - Hematotoxicity
  - Hepatotoxicity
  - Immunotoxicity
  - Musculoskeletal toxicity
  - Neurodevelopmental toxicity
  - Neurotoxicity
  - Ocular toxicity
  - Respiratory toxicity
  - Skin sensitization

Scarcity & Exergy

Evaluating proxies for natural resource and economic considerations

Jaye Harada

Scarcity module: abiotic depletion methods applied to new inorganics

- Current abiotic resource depletion methods do not evaluate all aspects of scarcity
  - supply risk
  - depletion rate
  - ore grade decrease
- Three goals for module:
  - Calculation of existing abiotic resource depletion characterization factors for new inorganic materials
    - **User can choose which method(s) to use** to evaluate a material's scarcity
  - Integration of future resource demand and production scenarios to calculate **future-oriented characterization factors**
    - These factors will be limited to reserve-based and production-based methods
  - **Evaluate uncertainty** in USGS production and reserves data
    - Consider year-to-year variance in USGS assessments

Potential exposure models at different levels

Dr. Dingsheng Li (new CLiCC project member)

Past work and ideas for the future

Introduction

- Why do we need exposure models

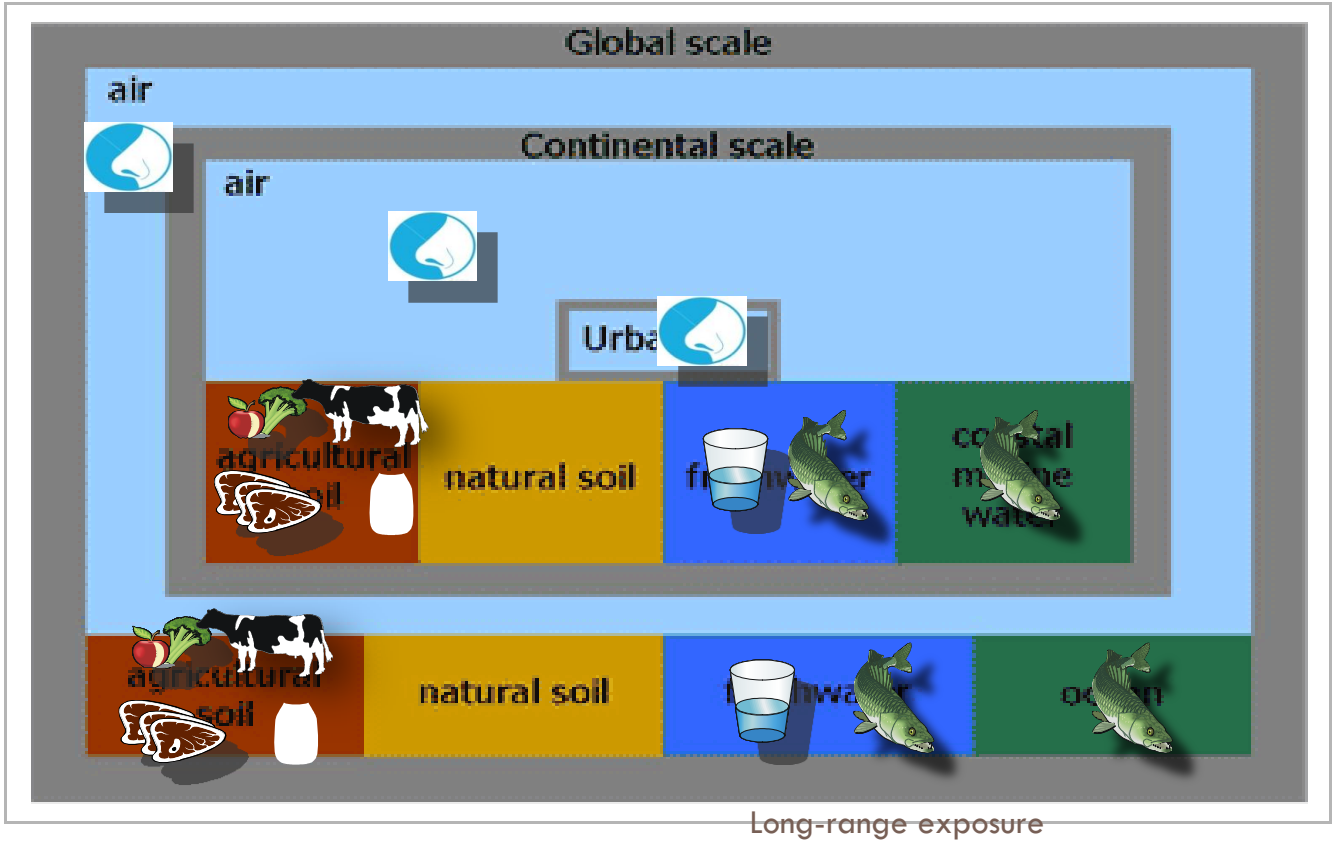
Environmental fate of chemicals

Human health impact assessment

Models at different levels

- **Long-range exposure models**
  - Traditionally employed in life cycle impact assessment (LCIA)
  - Can be improved for specific categories of chemicals
- **Close-range exposure models**
  - Indoor exposure
  - Personal care products
- **Internal organ specific exposure model**
  - Potential use of physiologically based toxicokinetic (PBTK) model
  - Linking target organs with toxic effects of chemicals
  - Much more complex than the other two

Long-range exposure



Long-range exposure

Input parameters

- **Inhalation:**
  - Concentration of chemical in the air (from Fate & Transport module)
  - Inhalation rate of the population (from EPA exposure handbook, can be adjusted for sensitive population)
  - Population size (pre-defined, scenarios)
- **Ingestion from water:**
  - Concentration of chemical in the water (from Fate & Transport module)
  - Ingestion rate of water (from EPA exposure handbook, can be adjusted for sensitive population)
  - Population size (pre-defined, scenarios)
- **Ingestion from food:**
  - Concentration of chemical in the water and agricultural soil (from Fate & Transport module)
  - Bioconcentration factors, biotransfer factors, etc. (from previous empirical models, need support from QSAR for calculations)
  - Ingestion rate of different produces (from established databases, can be differentiated to different age groups)
  - Population size (pre-defined, scenarios)

Output parameters

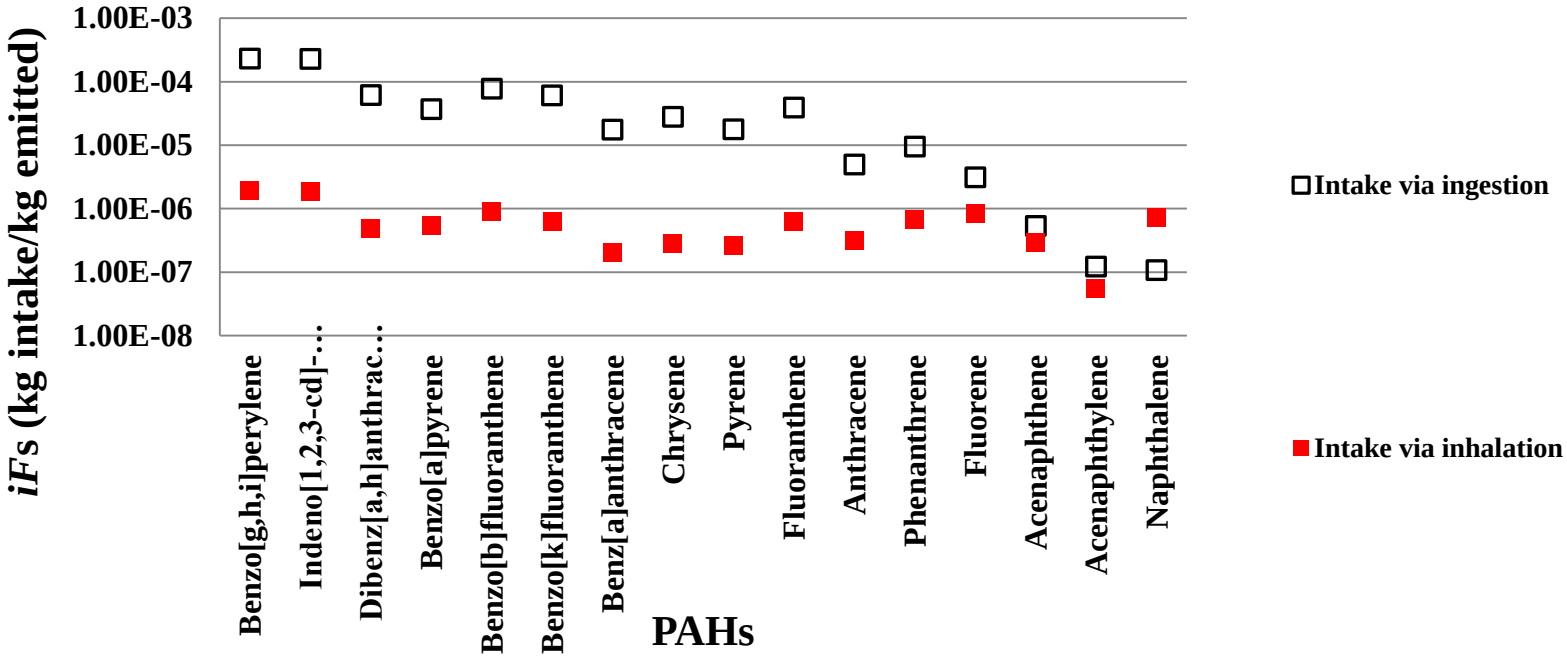
- **Intake amount**
  - Expressed in mass (kg) or dose (mg/kg-day)
  - Can be converted to intake fractions ($kg_{intake}/kg_{emitted}$)
  - Used to estimate human toxicity impact
  - Requires either epidemiology data or chronic *in vivo* animal toxicity data, which can be supported by QSAR module

Most suitable for

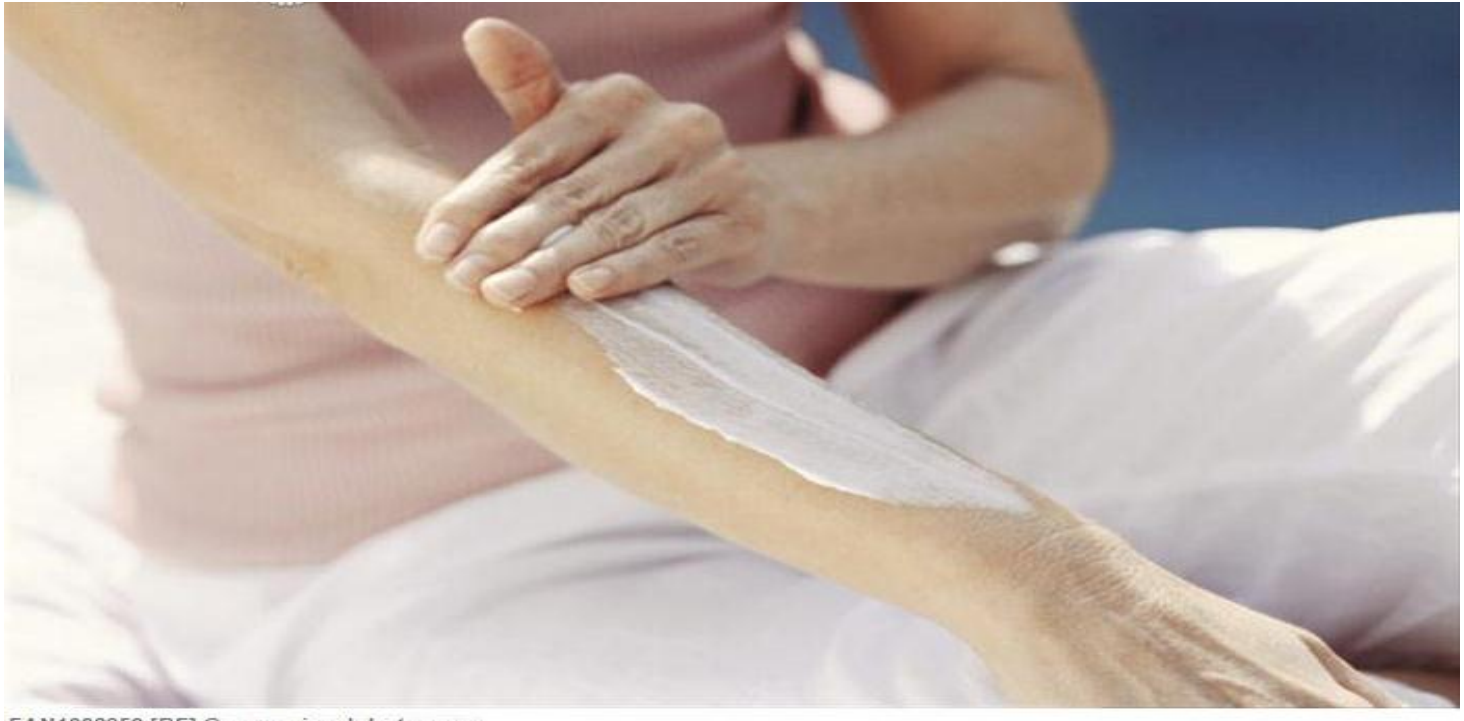
- **Chemicals emitted to the general environment**
  - Byproducts, pollutants, pesticides, etc.
  - No need to address indoor exposure/dermal exposure
- **For chemicals with relatively limited physico-chemical data**
  - Missing data can be generated from the QSAR module or Fate & Transport module

Long-range exposure

Example


iFs (kg intake/kg emitted)
1.00E-03
1.00E-04
1.00E-05
1.00E-06
1.00E-07
1.00E-08
Benzo[g,h,i]perylene
Indeno[1,2,3-cd]-…
Dibenz[a,h]anthrac…
Benzo[a]pyrene
Benzo[b]fluoranthene
Benzo[k]fluoranthene
Benz[a]anthracene
Chrysene
Pyrene
Fluoranthene
Anthracene
Phenanthrene
Fluorene
Acenaphthene
Acenaphthylene
Naphthalene
PAHs
Intake via ingestion
Intake via inhalation

Close-range exposure



Close-range exposure

Input parameters

- **Inhalation:**
  - Removal and degradation rates (from indoor air model [Wenger et al., 2012])
  - Inhalation rate of the population (from EPA exposure handbook, can be differentiated to different age groups)
  - Indoor room descriptions: ventilation rate, volume, occupants, temperature, etc. (pre-defined, scenarios)
- **Dermal exposure:**
  - Contact duration (pre-defined, scenarios, data from industry)
  - A series of permeability and transfer rates (QSAR, Berg 2009)

Output parameters

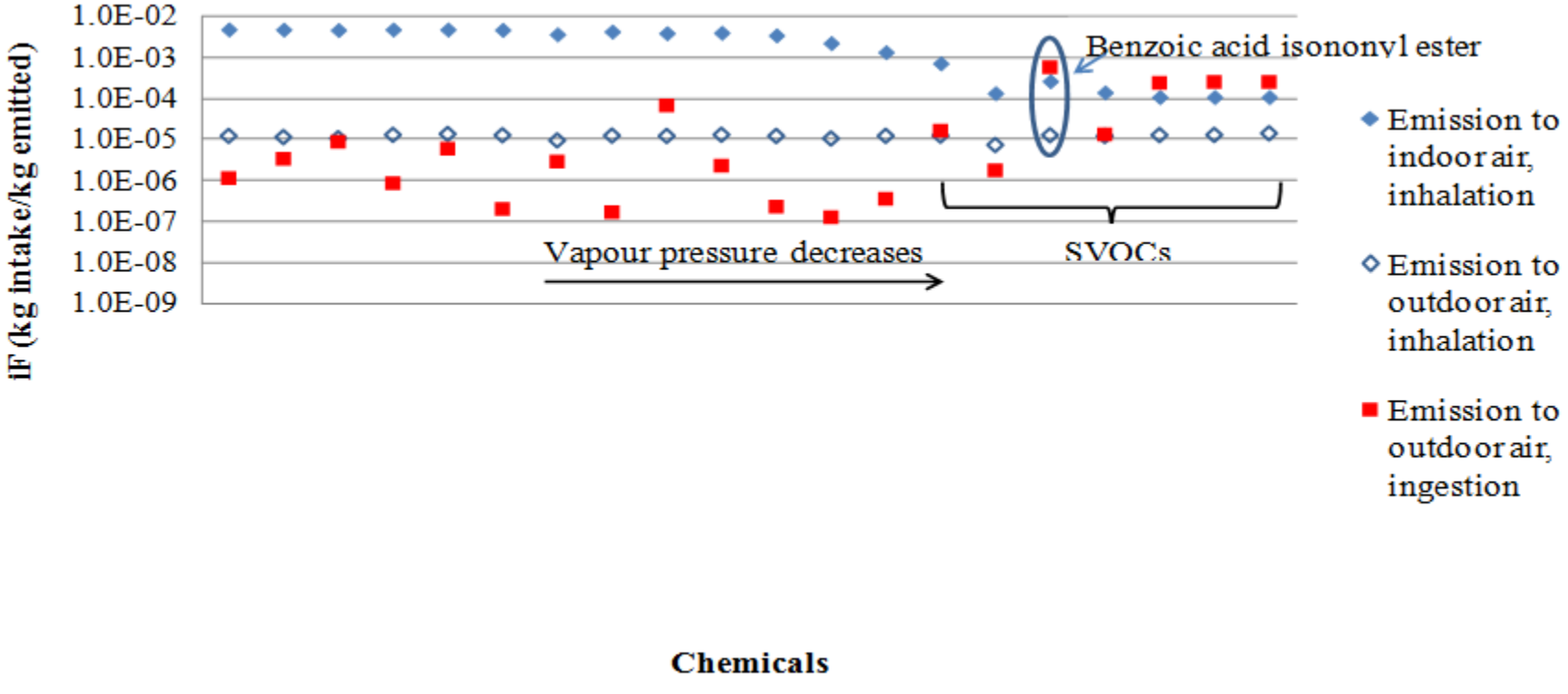
- **Intake fractions**
  - Expressed in fractions ($kg_{intake}/kg_{emitted}$)
  - Usually orders of magnitude higher than iF of the same chemicals released to the general environment
  - Used to estimate human toxicity impact, with support of emitted/applied mass (user input)
  - Requires either epidemiology data or chronic *in vivo* animal toxicity data, which can be supported by QSAR module

Most suitable for

- **Chemicals emitted to the indoor environment**
  - VOCs that are released from products used indoors
  - Occupational setting
- **Chemicals used in personal care products**
  - Directly applied to skins such as shampoo, lipsticks, lotions, etc.
  - Data about how the products are used is essential

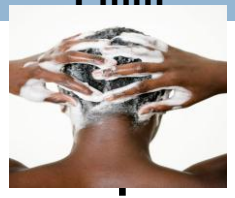
Close-range exposure

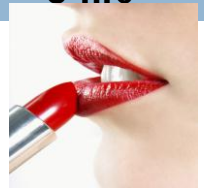
Example



Close-range exposure

Example





Time [hr]

0.0001 0.001 0.01 0.1 1 10

iF

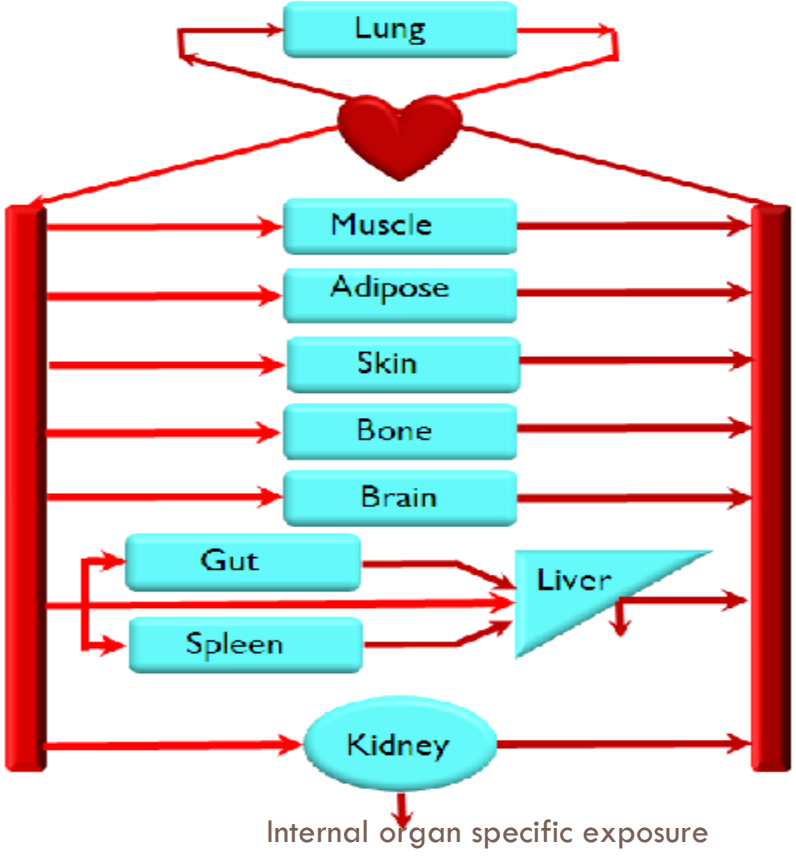
1 0.1 0.01 0.001 0.0001 0.00001

high volatility, high skin permeability

low volatility, low skin permeability

Close-range exposure

Internal organ specific exposure



Input parameters

- **Human physiology data:**
  - Body weight, organ weights, cardiac output, etc.
  - Existing literature, can be adjusted for sensitive population
- **Exposed amounts:**
  - Concentration of chemical in air/food (from Fate & Transport module)
  - Inhalation rate and ingestion rates (from USEtox refs, EPA exposure handbook)
- **Inside body kinetics (most challenging):**
  - Adsorption (from existing QSAR type models: Caco-2, PAMPA, etc.)
  - Distribution (from existing database, potential QSAR models)
  - Metabolism (from existing database)
  - Excretion (from existing models)

Output parameters

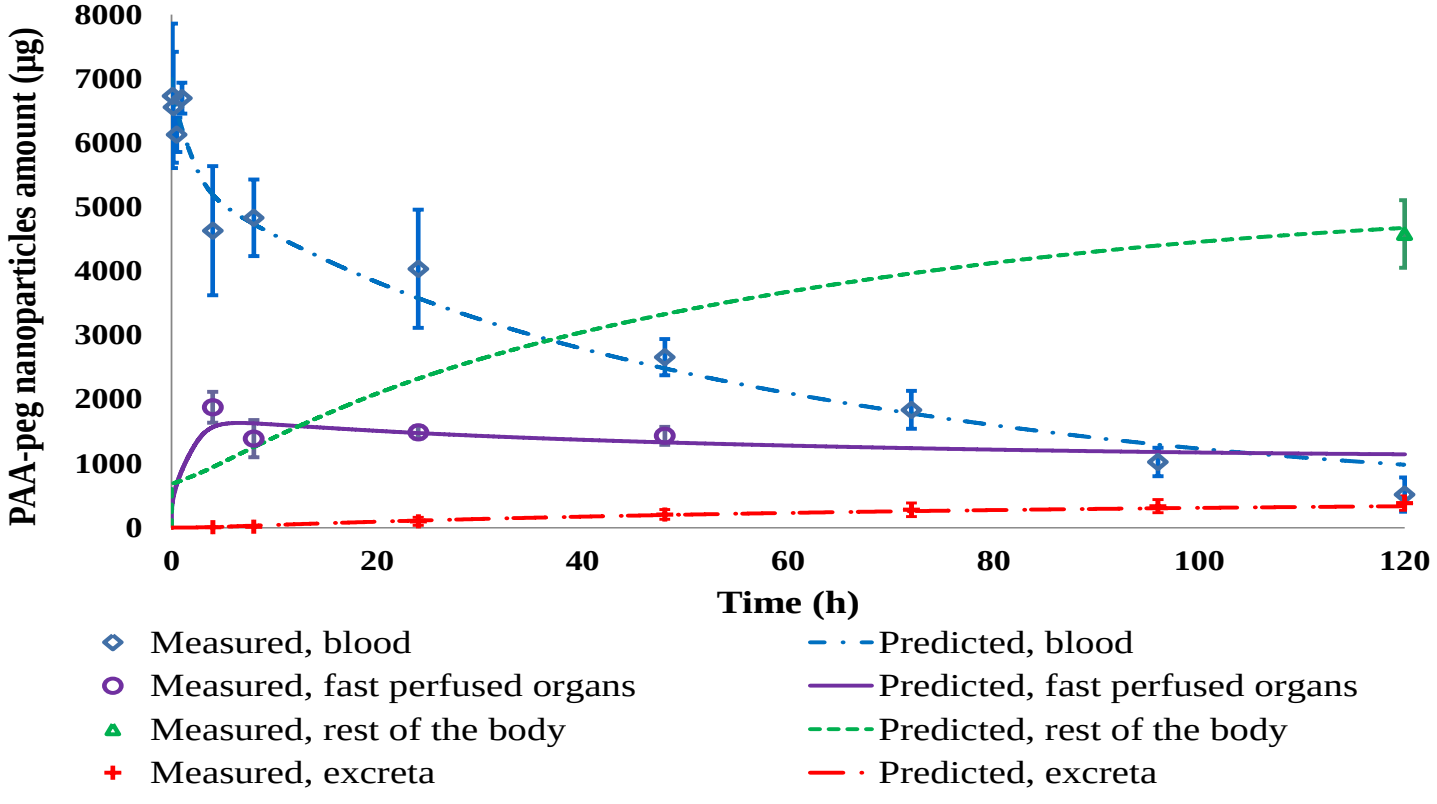
- **Concentrations in blood and various organs**
  - Can be converted to cumulative amounts in blood and various organs over time
  - Compare with high throughput *in vitro* toxicity tests
  - Can be independent on epidemiology/animal tests, opening up much wider toxicity dataset
  - More accurate representation of internal dose – given the data and model are good (otherwise, garbage in garbage out)

Most suitable for

- **Chemicals that require higher accuracy or dynamic of exposure**
  - Can predict doses in sensitive organs at different ages
- **Chemicals without epidemiology/animal toxicity data**
  - Can use other data sources for human health impact assessment
- **Chemicals with richer physiological kinetic data**
  - Linked with QSAR models, the data gap in the ADME parameters may be closed

Internal organ specific exposure

Example



Internal organ specific exposure

More of a field of research

- **No "generic" PBTK model exist yet**
  - The community in toxicology is still working on this topic
  - Mostly due to the complexity of different chemicals kinetics inside the body
- **No attempt to link PBTK with LCIA has been made**
  - Cross disciplinary may LCIA be, PBTK is still untouched by LCIA researchers
- **More complex model, more computation time**
  - Even the most basic PBTK model is much more complex than the other exposure models
  - Complexity similar to multimedia environmental fate models
  - Therefore takes more computation power
  - More complexity usually leads to more uncertainty, too

Summary

- Three models addressing different scales of exposure/output are being considered for further development and integration into CLiCC framework
- User would have the option to determine which one to use based on their need
- Ranking of readiness:
  - Long-range exposure models (easy after F&T model fully developed)
  - Close-range exposure models (relatively easy after F&T model fully developed)
  - Internal organ specific models (requires more complex PBTK modeling & QSARs for internal body parameters)

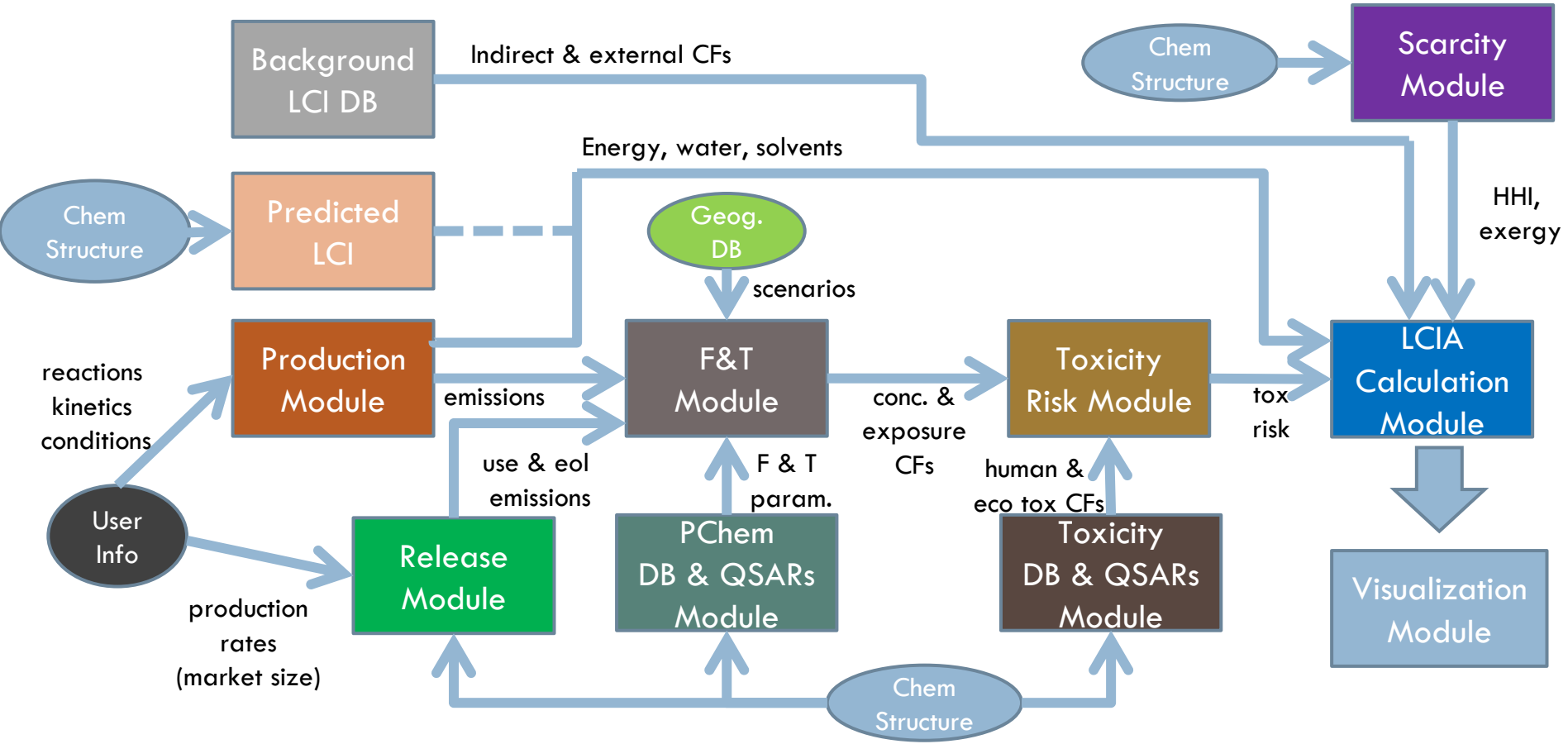
APPLICATION OF THE CLiCC TOOL

USES FOR DECISION MAKERS

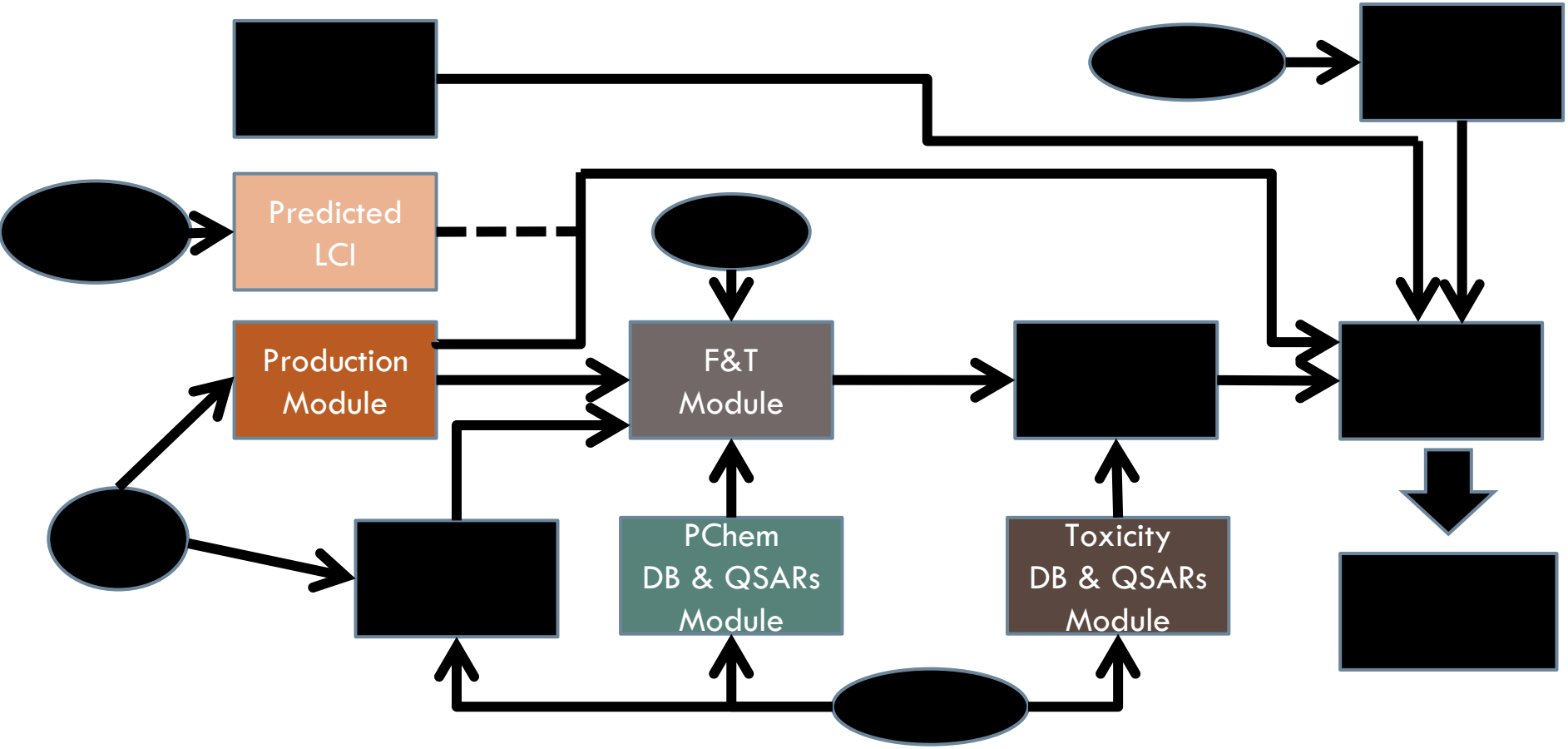
Industry Partner Guidance

- Characterization of uncertainty is very important
  - Identification of uncertainty "hotspots"
  - Stochastic representation (probability distributions)
- Outputs provided for individual modules (not just entire CLiCC Tool results)
  - First round of case studies: individual modules to determine feasibility and guide output visualization
- Most users will be relatively technical and LCA literate
- Need to be transparent about data sources
  - Will provide output identifying the data sources used in each module for a given chemical run through the CLiCC tool

CLiCC Tool Architecture



Modules for Case Studies



Reaction kinetics

Chemical formula

Operating ranges

Scale

Upper/lower flammability limits

Any other process constraints

Chemical Synthesis & Production Module

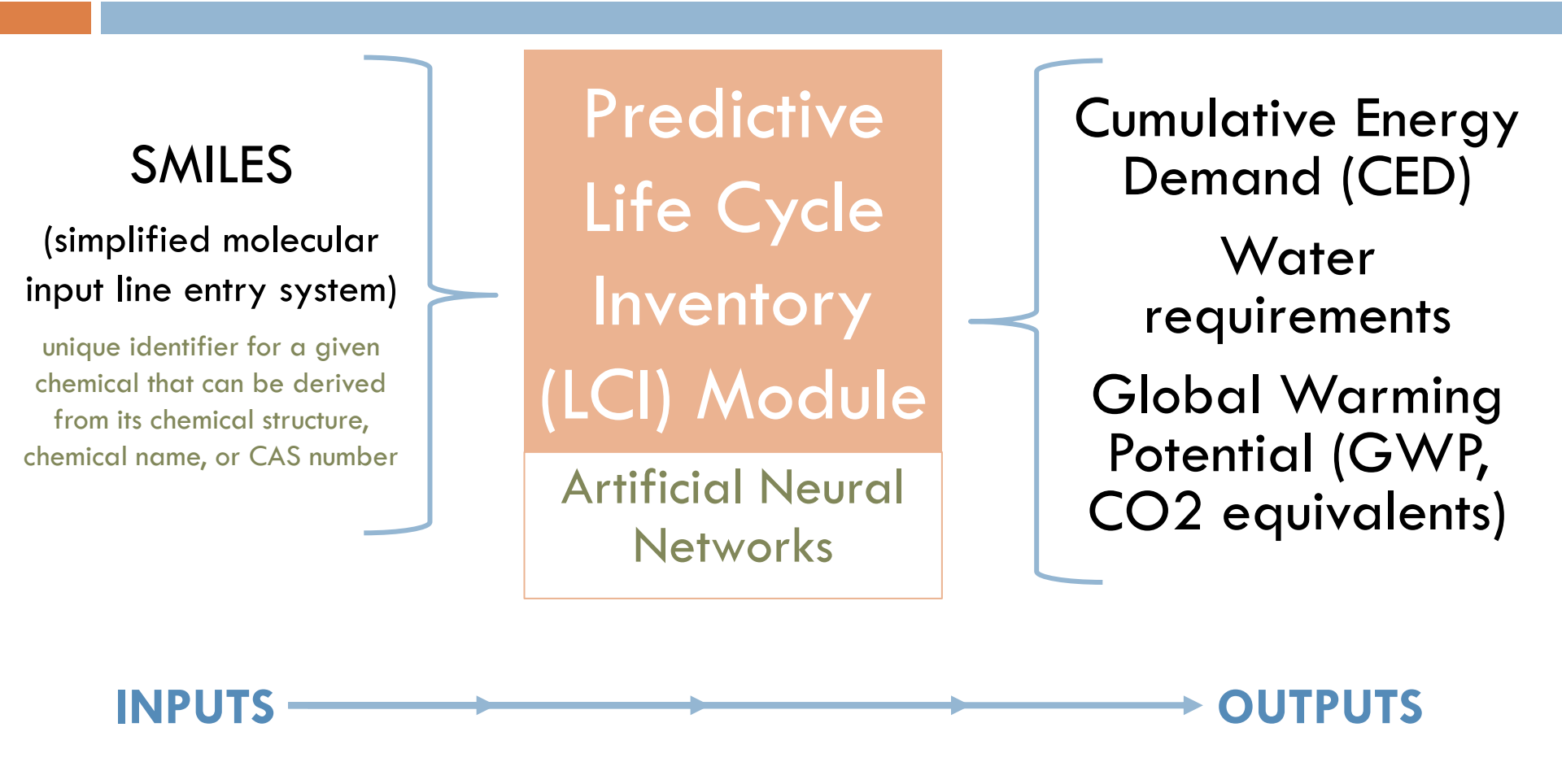
Raw material requirements (molar or mass)

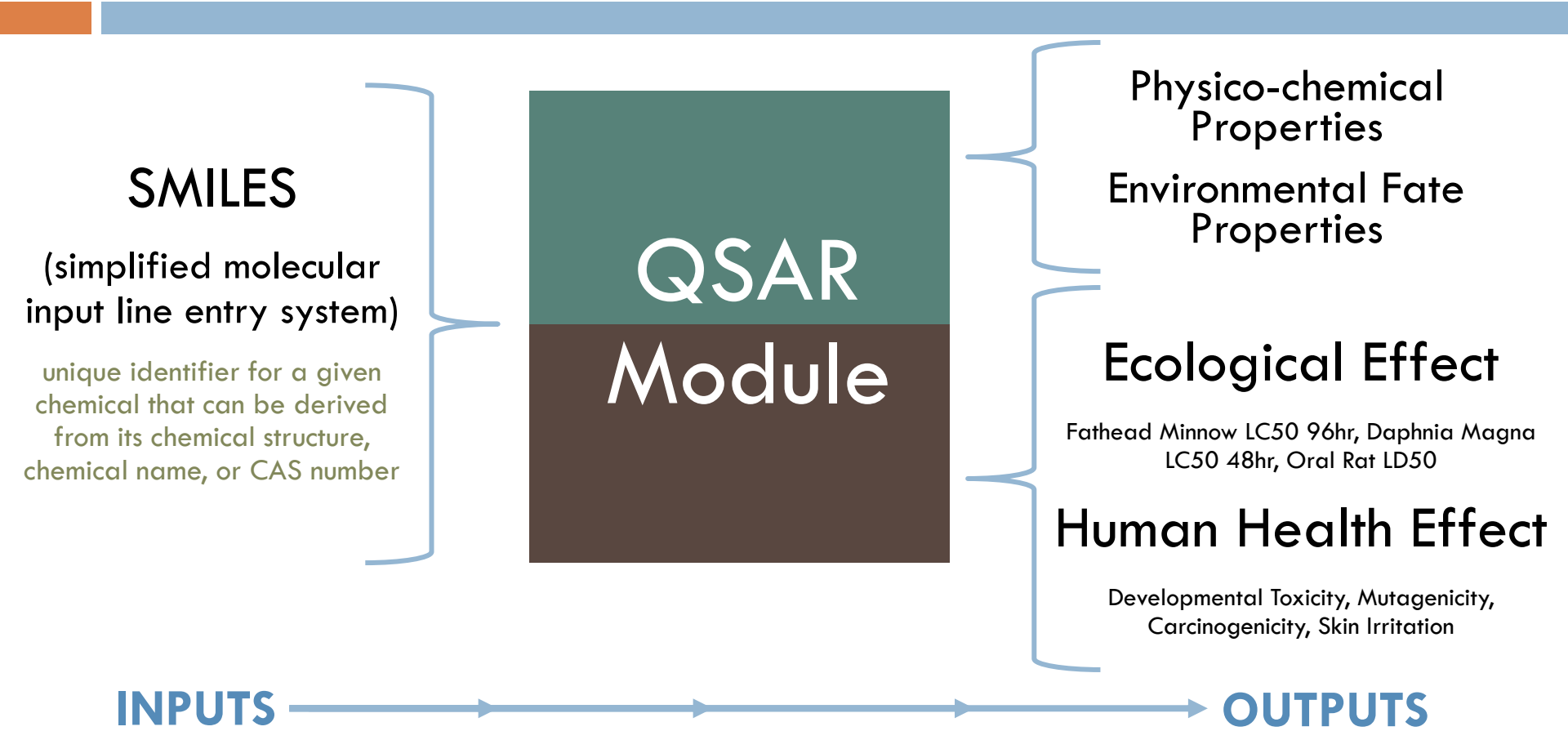
Production rates for product, by-product, waste

Upper bound on selectivity

Minimum energy requirements (next step in module development)

INPUTS → **OUTPUTS**


SMILES
(simplified molecular input line entry system)
unique identifier for a given chemical that can be derived from its chemical structure, chemical name, or CAS number
Predictive Life Cycle Inventory (LCI) Module
Artificial Neural Networks
Cumulative Energy Demand (CED)
Water requirements
Global Warming Potential (GWP, CO2 equivalents)
INPUTS
OUTPUTS


SMILES
(simplified molecular input line entry system)
unique identifier for a given chemical that can be derived from its chemical structure, chemical name, or CAS number
QSAR Module
Physico-chemical Properties
Environmental Fate Properties
Ecological Effect
Fathead Minnow LC50 96hr, Daphnia Magna LC50 48hr, Oral Rat LD50
Human Health Effect
Developmental Toxicity, Mutagenicity, Carcinogenicity, Skin Irritation
INPUTS
OUTPUTS

Chemical name/identifier

physico-chemical properties and environmental fate properties from QSAR module

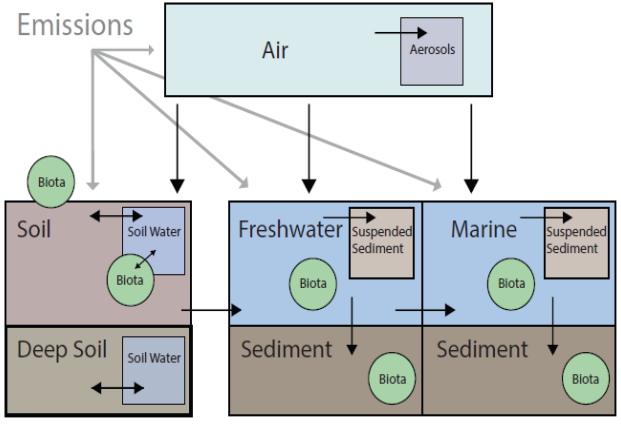
Geographical Information

Emissions
(rate of release over time)

Fate & Transport Module

Fate Factors

(FF, concentration and mass by compartment over time)



INPUTS → **OUTPUTS**

Thank you!