

Computational Toxicology

The application of computer technology and mathematical / computational models to analyze, model and/or predict potential toxicological effects from:

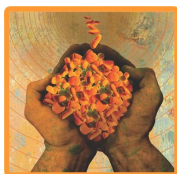
- Chemical structure (parent compound or metabolites)
- Inference from similar compounds
- Exposure, bioaccumulation, persistence (biomonitoring data)
- Differential indicators or patterns related to exposure
- Networks of biological pathways affected by the chemical



Environmental Pollutants



Therapeutics



To further understand mechanisms of toxicity: by organ, organism, and/or disease specific relationship

To explain why certain individuals are more susceptible to toxic insults

Highlight points:

1. 150 students – over 5 years
2. 4 hr credit course
3. Individual projects
4. Independent study
5. Honors research
6. Internships at FDA

Key methods

- Chemical fragment or structural similarities (structural alerts)
- Categorization or grouping
 - Analogs, categories based on mechanism, mode of action
- QSARs
- Biological pathway perturbations



UC BERKELEY

Green Chemistry Teaching Postcard



DTCS

Information about the curriculum:

• Tool Box Creation

- A combination of free on-line resources and commercial software
- Converting chemical and biologic data into usable formats
- Student proficiency exercises

• Environmental or therapeutic challenge

2010 student example

- Create *in silico* methods to identify and prioritize chemicals of concern that may increase the risk of human breast cancer
- Solve chemical disease-related issues in new ways

• Tutorials and resources

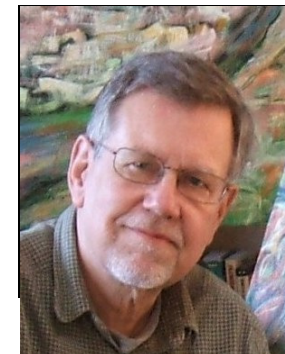
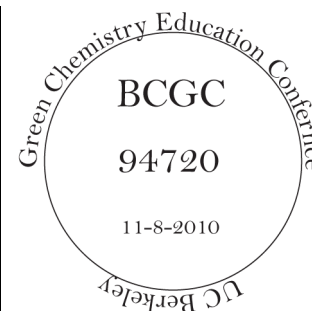
- Toxicology tutorials for non-toxicology majors
- Software tutorials and user manuals
- Extensive links to software, datasets, environmental and chemical information

• UC Berkeley computer laboratory

- College of Natural Resources; Geospatial Innovation Facility (GIF); Mulford Hall
- Full administrative and technical support

Notes

- Current developing practices for filling data gaps has long history with validation
- Physico-chemical properties accurately predicted
- Databases linking chem-biol interactions are limited in scope and size
 - Genotoxicity linked to carcinogenicity generally accurate predictions
 - Non-genotoxic carcinogenicity more complex
- QSARs always limited by applicability domain (chemical space) of training sets
- Interactions with bio-pathways important to identify targets and mechanisms



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Where to find resources:

Toxicology Tutorials

<http://sis.nlm.nih.gov/enviro/toxtutor.html>

National Center Comp Tox

<http://www.epa.gov/ncct/>

European Comp Tox

<http://ecb.jrc.ec.europa.eu/qsar/>