Prescreening for environmentally-important properties through computational chemistry

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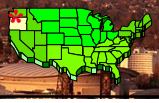
March, 2005



review - sw & methods to predict env. properties, directly and indirectly

Abstract

The ability to pre-screen for environmentally-important properties of candidate compounds and products, particularly before they are synthesized, can save significant laboratory time and expense. Although, R&D cost savings are important, the associated benefits of shortening time to market and minimizing environmental risk, offer the greatest potential for long-term profitability. Many environmentally-important properties are closely related to physical and chemical properties that can be predicted from just molecular structure information using quantum chemistry calculations. The latest generation of computational tools now makes it relatively simple to pre-screen large libraries of hypothetical candidate compounds for environmentally-important properties, using a regular Windows-based computer.

The author will review various approaches to the prediction of environmentally-important properties with examples covering aquatic fate, persistence, atmospheric fate, atmospheric lifetimes of halocarbons, soil remediation rates, and the design of ionic liquids for greener processes, using readily available tools based on quantum chemistry, statistical thermodynamics and related methods.

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Topics

1. Benefits of computation versus experiment
2. Environmental fate in aquatic ecosystems
3. Soil remediation of organochlorines
4. Atmospheric life-times of refrigerants
5. Vapor pressure and atmospheric fate
6. Designing ionic liquids for greener processes
7. Conclusions

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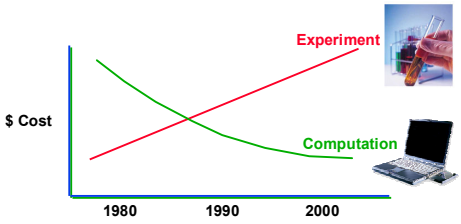
Computation versus Experiment

- Cost of lab. work rising: salaries, services, disposal costs, etc.
- Cost of computation falling (& getting faster) & often underutilized
- Now cheaper & faster to do some experiments on computer*



*IBM Almaden Research Lab. estimate based on *ab initio*

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EPA

"Recent trends in environmental regulatory strategies dictate that EPA will rely heavily on predictive modeling to carry out the increasingly complex array of exposure and risk assessments necessary to develop scientifically defensible regulations....."

Rosemarie C. Russo, Ph.D.
Director
Ecosystems Research Division
Athens, Georgia
EPA/600/R-03/030
March 2003

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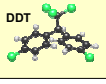
Transport Fate

Transport Fate* ~ f (water solubility) ?

> 1,000 PPM:	biodegradation, dissipation, metabolism, mobility
10-1,000 PPM:	uncertain, correlate with different property
< 10 PPM:	accumulation, adsorption, persistence, food-chain contamination



Water solubility of DDT ~ 0.003ppm
Persistent!

*Fate & Transport of Organic Chemicals in the Environment, Ronald E. Ney, Government Institutes, Inc., ISBN: 0-86587-470-0

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How to Predict Water Solubility?

1. Buy an off-the-shelf solubility predictor

   a) **Fragment-based,** e.g. ACD/Solubility DB

   b) ***QSPR-based,** e.g. QikProp, SPARC

   c) **Statistical thermodynamics-based,** e.g. COSMO*therm*

2. Use a Quantitative Structure-Property Relationship (QSPR) tool

   **e.g. Codessa, Adapt, CACheWorkSystem

*Quantitative Structure-Property Relationship
** Katritsky, Florida; Jurs, Penn State; Fujitsu

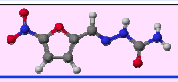
SPARC from EPA

http://ibmlc2.chem.uga.edu/sparc/

Structure-Property Relationships

Property (e.g. solubility)

p = *f*(s)



	A	B
	Chemical Sample	Experimental logW
128	*128-anisole*	-1.727
129	*129-phenetole*	-1.742
130	*130-acetonitrile*	0.530
131	*131-propionitrile*	0.330
132	*132-butyronitrile*	-0.330
133	*133-isoamyl bromide*	-2.880
134	*134-propyl acetate*	-0.730
135	*135-isobutyl formate*	-1.000

Sheet 1

Your experimental data

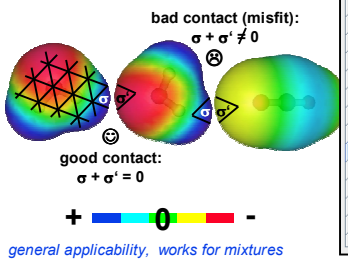
regression analysis to find the best correlation

Calculate 'Descriptors'
Mol. Wt., Vol.
# of O, N, atoms etc.
group counts
Kier & Hall indices
HOMO energy
electrophilicity
dipole moment
ionization potential
etc.

Computer can automate this part

Statistical Thermodynamics

1. Compute electrostatics on surface of molecule using QM DFT*
2. Calculate interaction energies between all segments
   published method: COSMO-RS**

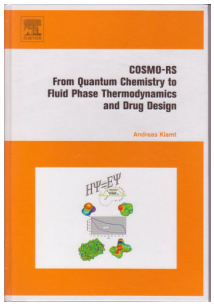


general applicability, works for mixtures

- Vapor Pressure
- Boiling Point
- Activity Coeff.
- Henry Const.
- Gas-Solubility
- Solubility
- LogP
- pKa
- VLE/LLE
- SLE
- Flatsurf
- Density
- Viscosity
- Mix-QSPR

* e.g. Turbomole (DFT) ** e.g. COSMO*therm*

COSMO-RS References



IBSN: 0 444 51994 7

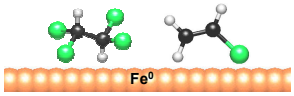
COSMO-RS: A novel and efficient method for the a priori prediction of thermophysical data of liquids,
A. Klamt & F Eckert,
Fluid Phase Equilib., 172 (2000) 43

Remediation Rate Prediction

- **Persistent Organic Pollutants Treaty (Sept 1999)***
  Aldrin, Endrin, Toxaphene, Chlordane, Dieldrin, Heptachlor, Mirex, Hexachlorobenzene, DDT, PCBs, Dioxins, Furans
  (immune, reproductive, development disorders)
- **New "safer" agrochemicals implicated in amphibian decline****
  atrazine, metolachlor, chlorpyrifos, etc

Remediation rate predictions could be used to "develop scientifically defensible regulations"

chlorinated alkanes and alkenes with granular zero-valent iron

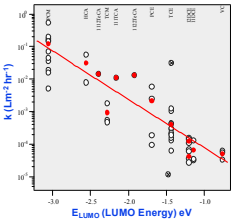


* Chemical & Engineering News, September 20, 1999, p. 9
** Chemical & Engineering News, March 29, 1999, p. 22; www.frogweb.gov

Dechlorination Rate QSPR

E_{LUMO} MOPAC AM1 COSMO	$r^2 = 0.85$

LUMO = Lowest Unoccupied Molecular Orbital



First reliable QSPR for remediation of chlorinated organics

Correlation Analysis of Rate Constants for Dechlorination by Zero-Valent Iron, Environmental Science and Technology, 1998, 32, 3026-3033; M.Scherer, B.Balko, D.Gallagher, P.Tratnyek

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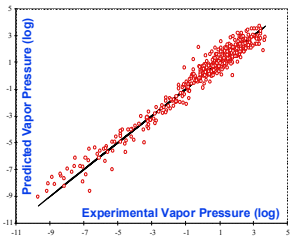
Vapor Pressure (QSPR)

- 479 compounds.
- Polarizability descriptor
  dispersion forces, van der Waals
- 6 polar group descriptors
  dipole interactions, H-bonding
- Regression:
  $r^2 = 0.960$
  $r_{CV}^2 = 0.957$
  avg. error = 0.396



$\log VP = -0.432\alpha - 1.382(OH) - 0.482(CO) - 0.416(NH) - 2.197(COOH) - 1.383(NO_2) - 1.101(CN) + 4.610$

*D. Gallagher & C. Liang, *J. Chem. Inf. Comput. Sci,* 1998, 38(2), 321.

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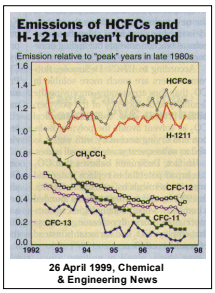
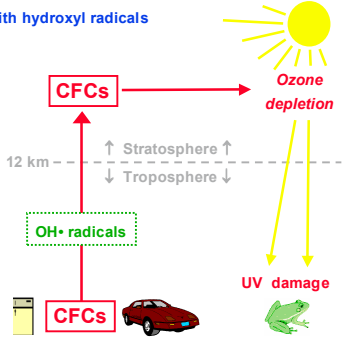
Atmospheric Life-times of Refrigerants

CFCs react too slowly with hydroxyl radicals





CFC = chlorofluorocarbon

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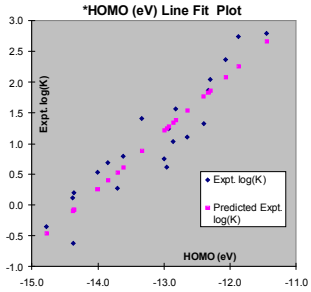
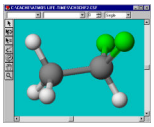
HFC Reaction Rate with OH•





$\text{Log(K)} = 0.939 \times {}^*E_{HOMO} + 13.409$

$r^2 = 0.863$

*E_{HOMO} calculated with MOPAC AM1

*HOMO: Highest Occupied Molecular Orbital

Percival et al, 1995 *Atmos. Environ.* 29: 305-311
Barlotti & Edney, 1994. Int J. Chem. Kinet, 26: 913-920
Cooper, Pot. CFC replacements, 1993 *Atmos. Environ.* 27A: 117-119

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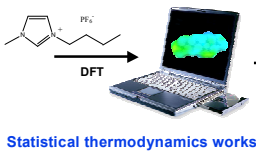
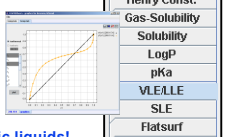
Green Chemistry & Ionic Liquids

- Extremely low of vapor pressure prevents escape into environment
- Improved safety because sudden pressure surges are not possible

"Designer Solvents", often developed for specific synthetic problems





- Vapor Pressure
- Boiling Point
- Activity Coeff.
- Henry Const.
- Gas-Solubility
- Solubility
- LogP
- pKa
- VLE/LLE
- SLE
- Flatsurf
- Density
- Viscosity
- Mix-QSPR

Statistical thermodynamics works for ionic liquids! COSMO*therm* includes a library of anions, cations & common compounds. Add more with DFT*.

* DFT e.g. Turbomole

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Conclusions

Computational methods are faster & cheaper than experiment, and can identify environmental issues earlier in the development cycle

A wide range of environmentally -important properties can be predicted using commercial and free computer software*

*e.g. quantum chemistry, stat. therm., QSPR, 'off-the-shelf' predictors,

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"MasterCard Advertisement"

New laptop computer	**$500**
COSMO*therm* (Group license, per user)*	**$300**
Codessa QSAR (1 user)	**$975**
SPARC (EPA)	**FREE**
MOPAC 2007*	**FREE**
Saving the environment	**Priceless !** 

Presentation handouts available

***See COSMO*therm* & MOPAC at Booth 1114**

Academic prices

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