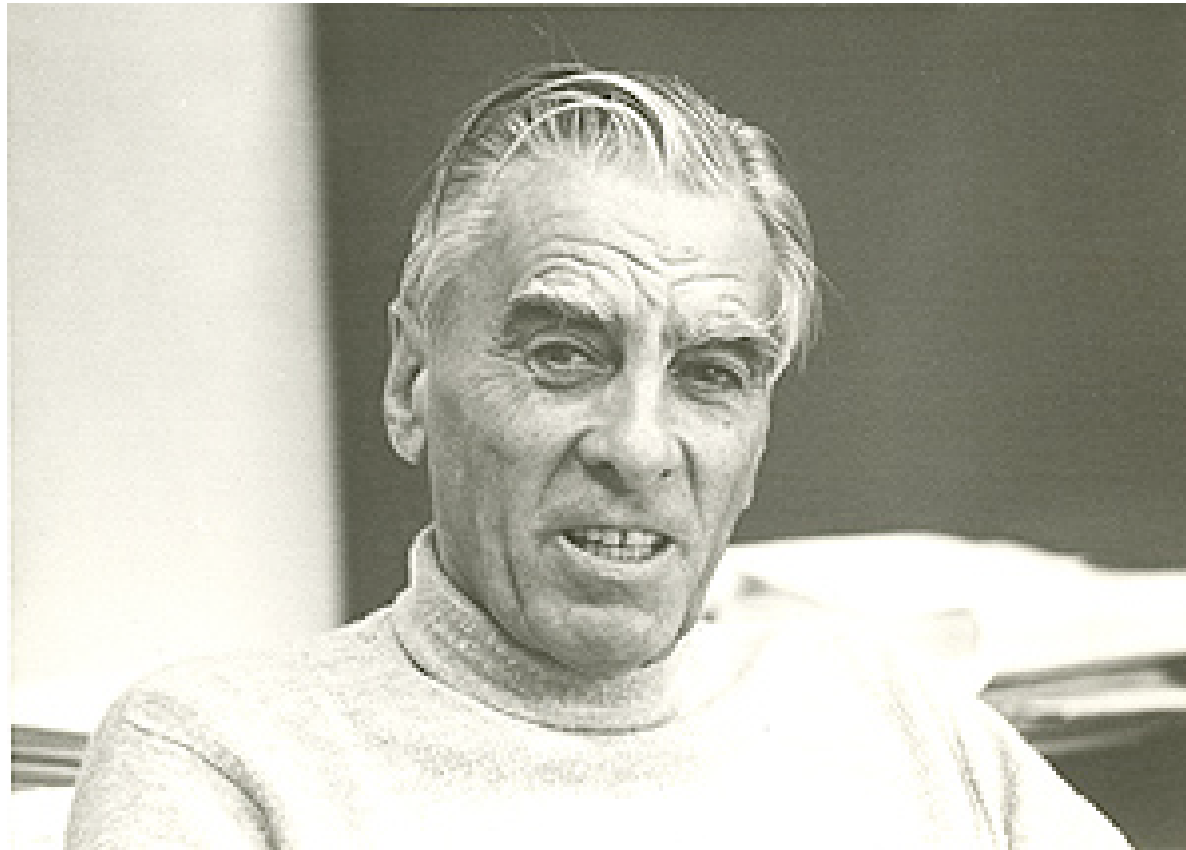


Perspiration, Inspiration, and Happenstance in Scientific Discoveries

Yvonne Connolly Martin

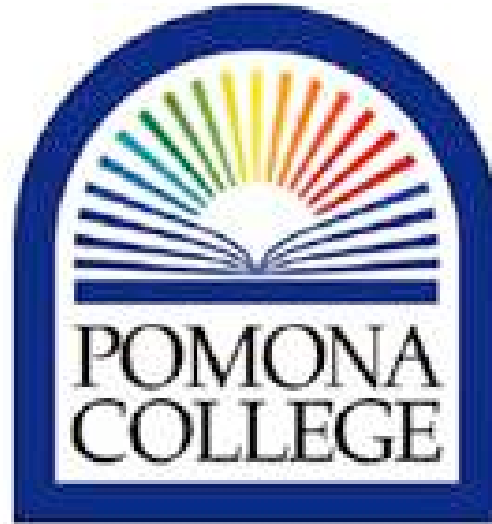
yvonnecmartin@comcast.net



Corwin Hansch 1919 - 2011

Photo curtesy of Cynthia Selassie

The Invention of QSAR



Robert M. Muir

The Relationship of Growth
Hormones and Fruit Development

PNAS (US) 33:312 (1948)

C. Hansch and R. M. Muir

“The Ortho Effect in Plant
Growth Regulators”

Plant Physiology 25: 389 (1950)

Hans H. Jaffé

A Reexamination of the
Hammett Equation

Chemical Reviews 53:191
(1953)

E. Havinga and H. Veldstra

Researches on Plant Growth
Regulators XIV. The Influence of
Synthetic Plant Growth Substances
on Lipoid Monolayers

Recueil des Travaux Chimiques des
Pays-Bas 67:855–863 (1948)

Annual Review of Plant Physiology
(1953)

Veldstra 4:151

The Relation of Chemical Structure to
Biological Activity in Growth Substances

Muir and Hansch 4:157

Chemical Constitution as Related to
Growth Regulator Action



T. Mitsui and T. Fujita

Surface Activity of the Plant Hormones

Jour. Agr. Chem. Soc. Japan 26:3 (1952)

“It was during a reflective period of a sabbatical leave in 1960 in Professor Huisgen’s laboratory in Munich that it finally became apparent to me that a study of partition coefficients of the phenoxyacetic acid growth regulators might be helpful in assigning relative lipophilic character to the different members of the series.”

Donald McIntyre at the Clarey Computer

http://www.electricscotland.com/mcintyre/index_f/menu_f/vitae_f/clary.jpg

“It was a complicated process in which three ‘boards’ full of holes were wired to carry out three steps. One first entered the data using board one, then with the second board the data matrix was inverted, and with the third board the results were printed out. As chance would have it, MacIntyre’s help in writing our first program was crucial, as I had had no thought of ever needing a computer. The limit of the Clarey was to deal with three terms, which were all that we needed at this time.”

Corwin Hansch *J. Med. Chem.*, 1976, 19 (1), pp 1-6. DOI: 10.1021/jm00223a001

C. Hansch, P. Mahoney, T. Fujita,
R. Muir

Correlation of Biological Activity of
Phenoxyacetic Acids with Hammett
Substituent Constants and Partition
Coefficients

Nature 194:182 (1962)

C. Hansch, R. Muir, T. Fujita, P.
Mahoney, F. Geiger, M. Streich

The Correlation of Biological Activity of
Plant Growth Regulators and
Chloromycetin Analogues with
Hammett Constants and Partition
Coefficients

JACS 85:2817 (1963)

C. Hansch and T. Fujita

ρ - σ - π Analysis. A Method for
the Correlation of Biological
Activity and Chemical
Structure

JACS 86:1616 (1964)

T. Fujita, J. Iwasa, C. Hansch

A New Substituent Constant,
 π , Derived from Partition
Coefficients

JACS 86:5175 (1964)

Invention of QSAR: Persistence, Inspiration, and Luck

SMILES

Photo of Dave Weininger

http://www.daylight.com/meetings/mugshots/muggers/weininger_dave.html

Weininger, D. 1978.

Accumulation of PCBs by Lake Trout
in Lake Michigan.

Department of Water Chemistry,
University of Wisconsin, Madison,
Wisconsin. 232 pp.

DEC GT40 Graphic Display Terminal

<http://www.brouhaha.com/~eric/retrocomputing/dec/gt40/>

Invention of SMILES: Insight, Inspiration

Photo of Al Leo

http://www.daylight.com/meetings/mugshots/muggers/leo_al.html

Problem of Calculating log P

http://www.daylight.com/meetings/mug98/Leo/clogp_history.html

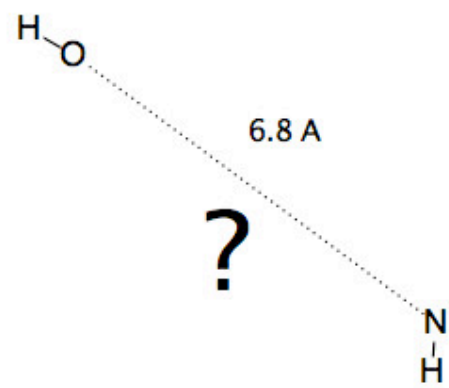
Invention of CLOGP: Perspiration and Inspiration



BioByte



DAYLIGHT
Chemical Information Systems, Inc.



Y. Martin, E. Danaher, C. May, D.
Weininger

Menthor, a Database System for Three-
dimensional Structures Searchable by
Substructure Alone or Combined with
Geometric Properties

JCAMD 2:15 (1988)

John H. Van Drie

Novartis photo

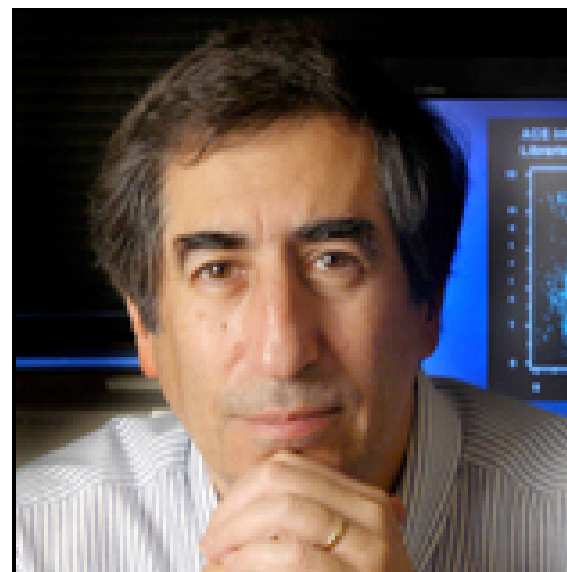
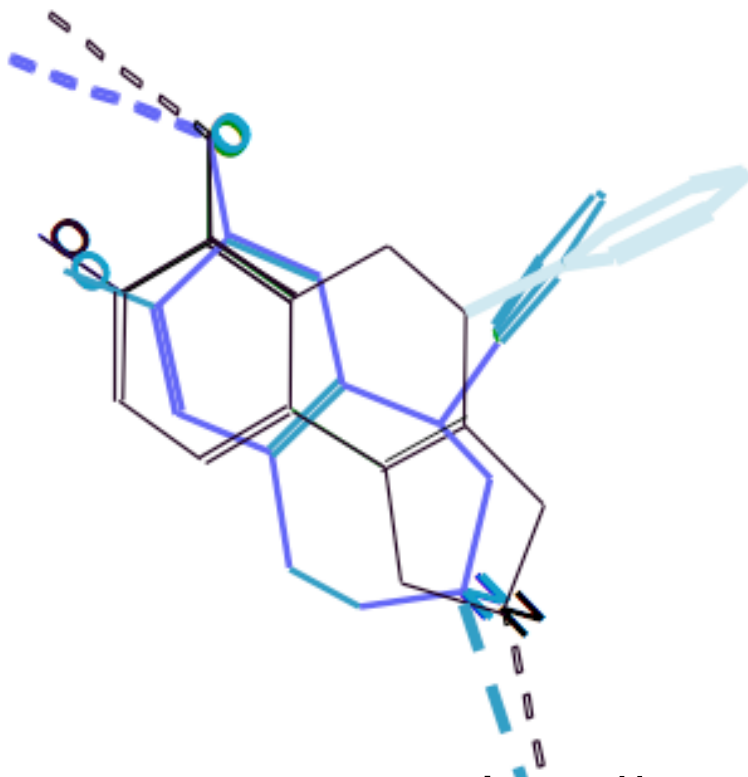
<http://pubs.acs.org/cen/employment/83/8316employment.html>

J. Van Drie, Y. Martin, D. Weininger

ALADDIN: An Integrated Tool for
Computer-Assisted Molecular Design and
Pharmacophore Recognition from
Geometric, Steric, and Substructure
Searching of Three-Dimensional
Molecular Structures

JCAMD 2:225 (1989)

Invention of Aladdin: Inspiration and Happenstance



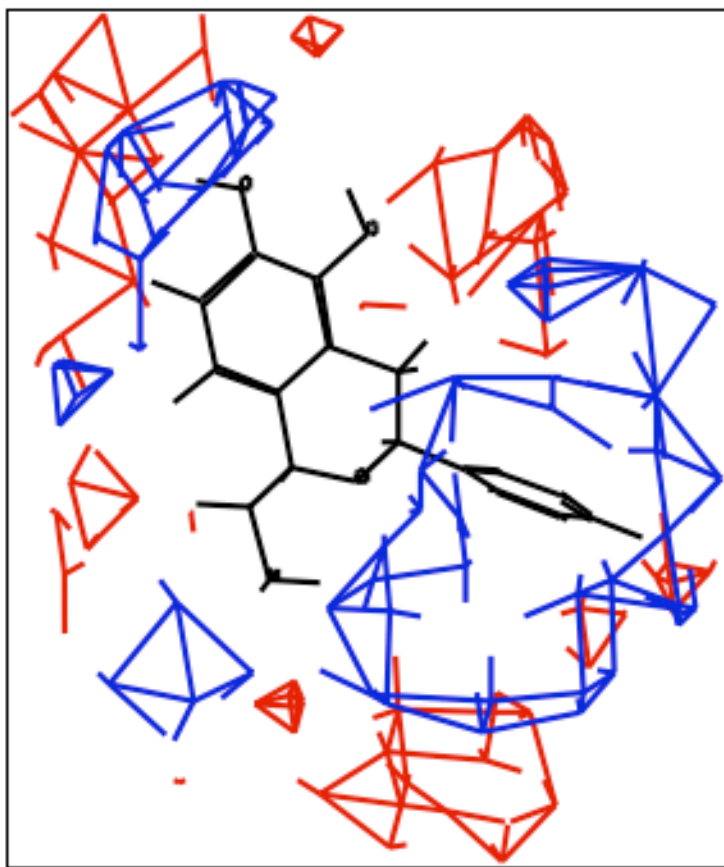
Robert Pearlman

[http://www.utexas.edu/pharmacy/divisions/
pharmaceutics/faculty/pearlman.html](http://www.utexas.edu/pharmacy/divisions/pharmaceutics/faculty/pearlman.html)

Marriage of CONCORD and
ALADDIN:
A Happy Happenstance

D1 CoMFA Model on 61 Compounds

Positive & negative
steric CoMFA contours



61 full agonists and antagonists
of very diverse structures: CH₃
probe, 2A spacing.

Leave-one-out cross-validation
 $Q^2 = 0.51$
RMSE = 0.79



Peter Willett

<http://www.sheffield.ac.uk/is/about/usdis/issue45/hodcorner.html>

A. Brint and P. Willett

Algorithms for the Identification
of Three-Dimensional Maximal
Common Substructures

JCICS 27: 152 (1987)

YC Martin, MG Bures, EA Danaher, J
DeLazzer, I Lico, PA Pavlik

A Fast New Approach to Pharmacophore
Mapping and its Application to
Dopaminergic and Benzodiazepine
Agonists.

JCAMD 7: 83. (1993)

Invention of DISCO: Inspiration and Happenstance

<i>Invention</i>	<i>Sweat</i>	<i>Insight</i>	<i>Luck</i>
QSAR	X	X	X
SMILES		X	X
CLOGP	X	X	
ALADDIN		X	X
CONCORD	X		X
DISCO		X	X