

The QSAR and Modelling Society

Chair: Yvonne Martin

Officers: Hugo Kubinyi (advisor to the chair), Stefan Balaz (treasurer)
Han van de Waterbeemd (secretary/editor)

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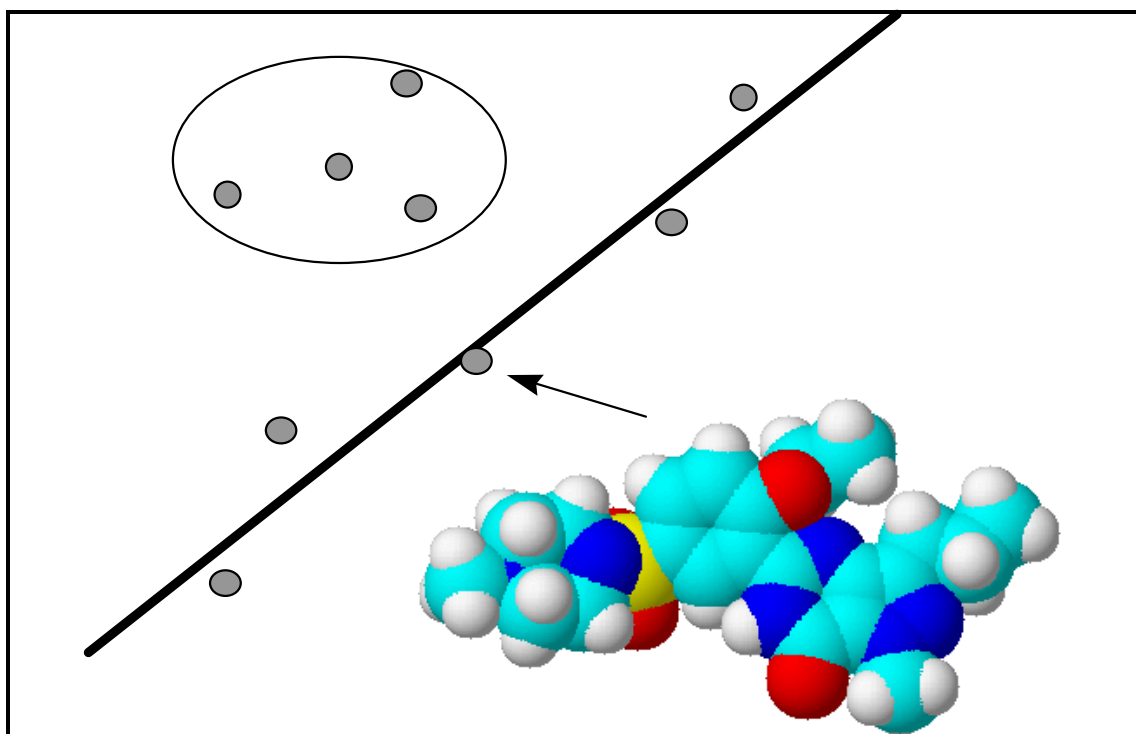
Honorary chair: Corwin Hansch *Past chairs:* Phil Magee, Hugo Kubinyi

NEWSLETTER

<http://www.qsar.org>

Issue No. 12

October 2001



Editorial

Report of the Chair

Membership:

We continue to grow! Current membership is now 777, representing 52 countries on every continent except Antarctica. This is a fantastic representation of the power of science to unite people of disparate backgrounds and experiences.

Finances:

James King has served the society as treasurer since its inception more than a decade ago. We all appreciate his careful management of our finances and wish him well in his retirement from this duty. Stefan Balaz has agreed to take over the treasurer duties.

The financial state of the Society is good. We currently have a balance of \$7204.79 plus the balance of the bank account in the UK kept for the Society by Han van de Waterbeemd per 10 September is £ 1324.85.

Our typical expenses include the Hansch award and support of students to attend the European QSAR meeting. Usually the QSAR Gordon Conference does not need our support.

Are there other ways that we could use our funds to foster the development or recognition of QSAR and Modelling? Send me e-mail and I will follow from there with a discussion with the board or the whole society as seems fit.

Some members aren't paying their dues! Please pay your dues of \$10.00/year, preferably for multiple years. Send either US cash or a check drawn on a US bank to

Stefan Balaz
North Dakota State University
College of Pharmacy
Department of Pharmaceutical Sciences
Sudro Hall, Room 108
Fargo, ND 58105
USA

We will also collect dues at the European Symposium on Quantitative Structure-Activity Relationships and at any ACS meetings that one of the officers attends (usually all of them). As has been our policy, members in developing countries may use their dues to support local meetings. Please tell Stefan if you are doing this so that we can credit your members.

The Society E-mail List

Osman Güner deserves a big vote of thanks for his work in overseeing the mailing list. He convinced Accelrys to provide the infrastructure and has worked diligently to solve the problems that have arisen. Although his work is in the background, we all appreciate the smooth way that the list operates.

Now it is up to us to use this list! Prof. Kubinyi called this society “the Quiet Society”. Let’s prove him wrong. Although sometimes there has been an active discussion, I am sure that there are more issues that the group could discuss.

The Hansch Award

It is not too late to start thinking of a nominee for the Hansch Award, which recognizes a young investigator in QSAR for their past contributions and expectations of their continued development of the field. As the time for nominations approaches, an e-mail reminder will be sent.

The Society Web Site:

Stefan Balaz also deserves a big vote of thanks for convincing the University of North Dakota to host our web site and for working very hard to update and expand it with interesting facts and links. If you haven’t looked at it lately, you will be surprised at how much is there.

We now have our own domain: www.qsar.org! Update your bookmarks/favorites so that if the site moves you will still get the current one.

Please check that your contact information on the Society web site is current. Are we sending e-mail to the best long-term address? Is your telephone number correct? Corrections should be sent to Han van de Waterbeemd who keeps very accurate records.

We currently have only 15 datasets on the QSAR web page. Haven’t you published a QSAR for which you would like to share your data? This is a good way to allow others to compare their “new and improved” methods against a published one. The officers, board, and Society would appreciate any other contributions that you would like to make to this site: meetings, links, additions to the history of QSAR, etc.

Upcoming Meetings of Special Note:

(see the Meeting section of the newsletter for others)

The next **QSAR Gordon Research Conference** will take place in Tilton, NH, U.S.A., 2003,

Chair: John van Drie (vandrie@mindspring.com)

Programme Chair: Peter Jurs (pcj@psu.edu)

The **14th European QSAR Conference** will be organised from 8-13 September 2002 by Martyn Ford, University of Portsmouth. The venue is Bournemouth on the attractive English south coast. The program promises to be even more attractive!!

See <http://www.euro-qsar.org> for detailed information.

Journals associated with the Society:

QSAR and the Journal of Computer Aided Molecular Design offer a special subscription rate to members of the Society: Elsewhere in this Newsletter are more detailed announcements relating to these journals.

Visibility of the Society by Promoting Other Meetings:

Because not everyone can attend the European QSAR Symposia and the QSAR Gordon Conference, we are working to expand the number of meetings at which QSAR and Modelling Society members can present their latest work and talk with colleagues. In this respect the Society is organizing a multiple day symposium for the Computers in Chemistry Division at the ACS Meeting in Boston, August 18-22, 2002. We hope to organize a social event at this meeting as well. Information will be provided by e-mail. More details on this symposium are elsewhere in the newsletter, but think now about submitting a talk or poster.

Please suggest other opportunities to increase the visibility of the society. I would especially like to see us help with meetings in places other than the US and Western Europe.

Yvonne Martin,
Chair 2000-2005

The Corwin Hansch AWARD

I am pleased to announce that the 2001 Hansch Award of the QSAR and Modelling Society has been presented to Gabriele Cruciani, of the Dipartimento di Chimica, Università di Perugia, Italy. This award recognizes the work of a young investigator in QSAR and modelling with the expectation that they will continue to advance the field for many years to come. Dr. Cruciani was chosen from a field of very able researchers.

Dr. Cruciani has published extensively in three broad areas: chemometrics as a tool to improve the predictivity of QSAR models, applications of QSAR, and novel molecular descriptors. He showed the utility of D-optimal design for variable selection in 3D QSAR and produced GOLPE, a program that provides this utility to scientists. He also proposed Smart Region Definition for CoMFA, and GRID/PCA to design selective inhibitors. His work has been applied, for example, to inhibitors of glycogen phosphorylase, quinolone antibacterials, antileishmanial chalcones, monoamine oxidase inhibitors and a variety of ADME properties. Novel QSAR descriptors proposed by Dr. Cruciani include GRIND, VolSurf, and ALMOND approaches. All of this work is characterized by careful thinking and enthusiasm for the field.

Please join me in congratulating Dr. Cruciani on this recognition of his work.

Yvonne Martin, Chair, QSAR and Modelling Society



From the Secretary



In the past years, the number of our **members** increased from

August 1995	346 members
August 1996	463 members
July 1997	549 members
July 1998	599 members
July 1999	660 members
August 2000	725 members
October 2001	780 members

Distribution of the Newsletter

An alert will be send to all members via our Mailbox that the Newsletter is available in pdf format at our web site. No printed copies will be sent to save costs.

Update of e-mail addresses

Please support our work, especially for the distribution of messages, by regularly updating e-mail addresses. If you detect a wrong address in the members list in our Web page, please inform han_waterbeemd@sandwich.pfizer.com

Lost members

We have no address of the following members. Does anyone know where these people are now?

Bradley	Prudence K.	USA
Dietrich	Stephen	USA
Gange	David	USA
Gohda	Keigo	JAPAN
Jonsson	Jörgen	SWEDEN
Namboodiri	Krishnan	USA
Olsen	Erik	
Robson	Barry	UNITED KINGDOM
Sapegin	Alexey M.	RUSSIA
Sauchet	Michael	
Shimomura	Satoshi	JAPAN
Space	Brian	USA
Spears	Colin P. / Lucy Ann	
Wohl	Ronald	USA

Lost email addresses

Although we all work with computers, still some email addresses are missing. Can you help finding them? Let me know so that we can get these folks back on line.

Allen	Mark
Araki	Koichi
Ashman	William P.
Ashton	Michael
Barlett	Bob
Basak	Subjash C.
Bauman	Norman
Bellott	Emile M.
Berner	Heinz
Biagi	Gian Luigi
Blaschke	Heinz
Blum	Diane J. W.
Bolton	Evan
Boxall	Alistair
Bradley	Prudence K.
Brannigan	Lawrence H.
Burgot	Jean Louis
Burgot	Gwenola
Cativiela Marin	Carlos
Cato	Stephen, J.
Caumel	Yves
Chau	Pak-Lee
Cholinski	Jacek
Cipriano	Robyn
Coats	Joel
Coe	Chris
Colombo	Lino
Cossement	E. R.
Csorvasi	Istvan
De Paulis	Tomas
Dietrich	Stephen
Donescu	Alexandrina
Dragos	Dan
Dross	Karl
Elenes	Florin
Eng	George
Engle	Thomas
Escobar	Jose-Luis
Evans	Suzanne
Fadhil	G. F.
Farahi	Asgar Kh.
Fisanick	William
Fukami	Harukazu

Gange	David
Gao	Ying-Duo
Geiss	Kevin T.
Golender	Valery
Gorbunov	Sergey
Govers	H.
Hadzi	Dusan
Helmes	C. Tucker
Hillenbrand	Mihaela
Hoeschele	James D.
Holzgrabe	Ulrike
Howe	W. Jeffrey
Izumi	Keiichi
Jerman-Blazic	Borka
Jonsson	Jörgen
Kamoshita	Katsuzo
Khambay	B. P. S.
Kido	Masaru
Kint	Saima
Knjasev	Boris Ananjevich
Kuchar	Miroslav
Kuchcaev	Boris Irikovich
Kumita	Izumi
Kurbatova	Svetlana
Kuyper	Lee
Ladner	David W.
Lämmerhofer	Michael
Lau	Wan
Lee	On
Lehmann	Pedro A.
Leonardi	A.
Luca	Costantino
Mager	Harry
Makino	Kenzi
Martin	Fernando
Mattie	Renee
Miller	Joseph
Moser	Peter
Moyer-Zirpoli	Susan
Mracec	Mioara
Murcko	Mark
Mutsukado	Motoo
Namboodiri	Krishnan
Naylor	Adel
Negrié	Cristina
Nurgabylova	Aigul
O'Connor	Mary V.
Oda	Kengo
Ohtaka	Hiroshi

Olsen	Erik
Omata	Kenzo
Ordukhanian	A. Ashot
Pallakoff	Pamela A.
Pankkioyj	Leonia
Parodi	Silvio
Parton	Richard
Phillips	Richard B.
Pillan	Antonio
Potashnikov	Piotr
Pouplana Sole	Ramon
Profeta, Jr.	Salvatore
Ramsden	C. A.
Rejholec	Valcav
Ren	Shijng
Robson	Barry
Roy	Timothy
Rozenblit	Anatoly
Sahini	Victor Emanuel
Salama	Zoser
Sapegin	Alexey M.
Sauchet	Michael
Seclaman	Eduard
Shimomura	Satoshi
Shorter	John
Siegel	Sidney
Singh	Bupinder
Singh	Suresh B.
Smith	Eric W.
Southwick	Rett
Spears	Colin P. / Lucy Ann
Speece	R. E.
Stein	Mark M.
Stein	Reinhardt
Szabadai	Zoltan
Szalkowski	Mary B.
Tosato	Maria Livia
Turner	James E.
Umeda	Yoshihisa
Volanschi	Elena
Vorpagel	Erich, R.
Weber	Hans-Peter
Weinberg	Josette
Wipf	Hans-Kaspar
Wohl	Ronald
Wolters	Fred
Wong	Rosalind Y.
Xie	Qian
Yamakawa	Masumi



Yoshimura
Yoshioka
Yuta

Yoshinobu
Hirosuke
Kohtaro



Webmaster

The webmaster is Stefan Balaz at North Dakota University (stefan_balaz@ndsu.nodak.edu). The Societies' URL is in the heading of this Newsletter.

Contributions to the Newsletter and our web site

All members are invited to contribute our Newsletter and to our web site. This Newsletter shall not be a one-man show, it gains from your experience. Our publishing policy will not allow us to accept scientific contributions which better should be sent to a reviewed journal. However, tips and tricks, key references, conferences, books, shareware, even the announcement of new commercial software, are welcome. We depend on your active participation!

Please send your comments and contributions to



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FROM OUR BRANCHES



Russia

Contact: Oleg Raevsky
<http://www.ibmh.msk.su/qsar/>

Italy

Contact: Sergio Clementi

UK

Contact: Iain McLay (chairman) or Patrick Barton (Newsletter)
<http://www.iaimn.demon.co.uk/>

Hungary

Contact Antal Lopata (lopata@chemicro.hu)

During the past year we organized two meetings. The first was held in Szeged on November 15-16, 2000 together with the Chemometrics Group of the Hungarian Chemical Society. Altogether 25 lectures were given, 12 in two chemometrics sessions and 13 in two QSAR sessions. The 13 QSAR lectures are as follows (titles are translated from Hungarian):

G. M. Keserű (Gedeon Richter Ltd.):

Methods of Molecular Design in Drug Research

Z. Bikádi, M. Simonyi (Chemical Research Center, Hung. Acad. Sci.):

A Pharmacophore Model of Cholinergic Agonists

A. P. Borosy (Institute of Drug Research):

Use of Mass Spectra to Calculate the Similarity of Drug Molecules

R. Vanyúr, K. Héberger, J. Jakus (Chemical Research Center, Hung. Acad. Sci.):

Prediction of the Accumulation and Tumoricidal Effect of Sensitizers Applied in Photodynamic Therapy Using Linear and Nonlinear Variable Selection Methods

I. Simon (Institute of Enzymology, Hung. Acad. Sci.):

Stability Centers of Proteins

I. Kolossváry (Novartis):

Modeling Biomolecules without Molecular Dynamics

G. Kiss, T. Körtvélyesi, S. Lovas, B. Penke (University of Szeged):
Investigation of the Structure of Amyloid Peptides and Their Fragments Using Molecular Dynamics

T. Veszprémi (Technical University of Budapest):
Recent Trends in Quantum Chemistry

I. Komáromi, L. Muszbek (University of Debrecen):
IMOMM Methods and Their Applications in Modeling Blood Coagulation Enzymes

G. G. Ferenczy (Chinoïn Ltd.):
An Efficient Calculation of Intermolecular Interactions in Condensed Phases

T. Körtvélyesi, K. Héberger, M. Görgényi (University of Szeged, Chemical Research Center, Hung. Acad. Sci.):
Investigation of Structure-Retention Relationships in Gas Chromatography Using Stationary Phases of Different Polarity

A. Lopata, Á. Fazekas, M. Simonyi (CheMicro Ltd., Chemical Research Center, Hung. Acad. Sci.):
Investigation of Hydrogen Atom Abstraction from Substituted Phenols by Polyvinyl Acetate Radicals Using CoMFA

I. Lukovits, E. Kálmán (Chemical Research Center, Hung. Acad. Sci.):
Relationship between the Structure and Efficiency of Aromatic Corrosion Inhibitors

Our second meeting was held in Budapest, on June 15, 2001 with the following lectures (titles are translated from Hungarian):

I. G. Csizmadia (University of Toronto):
Computational Molecular Medicine

G. Csonka (Technical University of Budapest):
Modeling Oligosaccharide Structures (ab initio)

A. Czajlik, Z. Gáspári, I. Hudáky, P. Hudáky, I. Jákl, T. Beke, A. Perczel (Eötvös University):
Peptide Folding in the View of Applied Quantum Chemistry: Why α - and not β -Amino Acids Form Proteins?

L. Nemes, F. Varga (Chemical Research Center, Hung. Acad. Sci.):
Calculation of the Geometry of C₆₀⁺ Cation Using Semiempirical and DFT methods

We are pleased to announce that the Hungarian QSAR Group has got a web site since last November (in Hungarian): www.qsar.mtesz.hu

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Contact: Zeno Simon & Tudor Oprea



MEETING REPORTS



QSAR and QSPR at the ACS Meeting, August 2001

OPINIONS 🟡🟡🟡🟡

None this time!



CONTRIBUTIONS



Beginnings of QSAR, CADD?

This turned out to be a more complex question than initially intended to be. It ventured us into the definition of QSAR and CADD, and then to the earlier (and very earlier) work leading to modern QSAR. The question still remains: While the transition from SAR to QSAR may have been “fuzzy,” is there a single event, a single paper that can be considered a milestone in this transition? And if so... which one is it?

As the members of the International QSAR Society, perhaps we should feel empowered to make a decision on this milestone. It will allow us to track the

evolution of the discipline going into future and use various anniversaries to highlight the contributions of QSAR to science and, ultimately, the well being of our species. Depending on whether this milestone is in the 50s or 60s, we are approaching either the 50th or 40th anniversary of QSAR... a critical date that provides us an opportunity review, document the history, and pave the road to future developments.

This discussion doesn't seem to be over. Votes were clustered around both 50s and 60s, and the specific milestone events that seemed to receive most attention were centered around papers from Hammett, Taft, Coulson, and Pullman on the 50s or Hansch-Fujita and Free-Wilson papers on the 60s. Hansch and Fujita received the clear majority of the votes. However, we should give the supporters of the 50s another chance to make a case. Ultimately, we should try to reach some sort of a consensus and move on.

Below is an organized summary of contributions to this discussion... the original question is posted at the very end. I apologize for the long message, but you will find this to be a very interesting reading.

Cheers...Osman

Definition of QSAR, CADD:

David LIVINGSTONE:

"This raises the question of the definition of QSAR, or what does the Q stand for? I think I've said this a few times (see *J. Chem. Inf. Comput. Sci.*, **40**, 195-209 (2000) for example) but I believe that the Q refers to the characterization of chemical structure (changes) in quantitative terms, not to "quantitative relationships". I think that Osman really means the latter as I quote from his posting:

- > Most of the earlier
- > work were, of course, qualitative. The quantitative SAR in which the
- > bioactivity is mathematically related to some set of parameters came
- > later on.

Thus, to my mind, the distinguishing difference between SAR and QSAR is the use of properties to define structure. You can have quantitative relationships in an SAR "model", since that is what the Free and Wilson (really the Bruice, Kharasch, and Winzler) method is. Thus, with this definition, QSAR doesn't need any data (like in set selection) but does need properties to characterize the structures."

Richard CRAMER:

"To me it is difficult to address this question without at least a working definition of QSAR --

- If the definition emphasizes the use of transferable (or "universal") parameters ("substituent constants"), whose values are themselves derived from experiment, then
-

Hammett is a key pioneer (the Hammett equation of course consists of two such transferable parameters). CoMFA is not really a QSAR method [by this definition] (btw, my impression is that this would indeed be the position of Hansch and probably others)

- If the definition further emphasizes a transferable parameter in which the defining experiments are biological, then -- as previously noted we must look to Collander and Overton as originators of partition coefficients
- If the definition instead emphasizes an empirical search among multiple descriptors and data analysis methods for predictive regularities, then -- in my personal view to deal with the complexity of actual biological systems, anything less seems to me unrealistically simplistic this is what most of we do today for beginnings, we cannot go back before the computer when the only tool was graph paper and only one- and two-dimensional systems could be examined, larger number of variables required postulating a relationship, then graphing to validate the postulated relation
- by this definition Hansch et al. would clearly be the pioneers”

Alan SHUSTERMAN:

“Some of the answers to this question are citing dates well before the invention of automatic computers. Certainly these answers cannot represent the start of CADD. I wonder about Osman's intent in asking this question. Does he simply want the earliest examples of these types of activities, or does he want to know when people began to pay attention to a particular style of research activity? I'm sure we can go back a long ways if we are only interested in examples of activities that involved quantitative relationships (especially if one loosens the definition of "structure"). These are interesting, but I think a genuine history of the subject should focus on the papers that got modern QSAR going.”

Early history (really... very early history):

David LIVINGSTONE:

“I believe the beginnings are due to the inspirational paper of Crum-Brown and Frazer (*Trans. Roy. Soc. Edinburgh*, 1868-- 9; **25**, 151-203). They proposed an equation linking changes in biological activity to changes in chemical structure but they didn't show a way to characterize chemical structure in quantitative terms.

If you prefer to see chemical structure expressed as physicochemical parameters then how about solubility (B.J. Richardson, *Medical Times and Gazette*, 1868, **2**, 703), molecular weight (C.Richet, *C.R. Seances Soc. Biol.*, 1893, **9**, 775) or partition coefficient (E. Overton, *Z Physik. Chem.*, 1897, **22**, 189, H. Meyer, *Arch. Experim. Pathol. und Pharmakol.*, 1899, **42**, 109)”

Tudor OPREA:

“If it comes to priority, Crum-Brown and Frazer should be mentioned their paper does indeed suggest that biological activity is a function of chemical structure. This laid the foundation for all QSAR. Whether people were aware of this paper in particular or not is irrelevant, since it must have permeated the scientific process from different directions. - Thanks to Dave L. for all the clarifications.”

John DEARDEN:

“If QSAR is taken to include QSPR (which I believe it should), or rather QSPR can be taken to include QSAR, then its origins do indeed go back to the 1800s. In 1884 or 1885, E.J.Mills developed a QSPR for prediction of melting points and boiling points of homologous series, which was accurate to better than 1 degree. I'll post the full

reference when I get back to the office. It's listed in my recent review on the prediction of melting point.”

Follow-up posting:

“If we accept that QSAR is a part of QSPR (an activity is a property), the earliest proper QSPR that I've come across is one published in 1884 for predicting the melting points and boiling points of homologous series. Predictions were generally within 1°, and the QSPR was capable of predicting mps and bps of infinite members of a series (i.e. polymers). The reference is: Mills E.J. Philosophical Magazine, Series 5, vol. 17, pp. 173-187.”

Klaus KAISER:

“If I may suggest, Dmitri Mendelejeff [German spelling of his name], is certainly a contender, predicting new elements and their properties in 1869.”

Han WATERBEEMD:

“What would you think of Collander who did work in the 1930s?”

50's

Hugo KUBINYI:

“The only remarkable event close to 1954 seems to be the publication by Bruice, T. C., Kharasch, N., and Winzler, R. J., Arch. Biochem. Biophys. 62, 305 - 317 (1956), which is the first application of a Free-Wilson type analysis (properly defined 8 years later, in Free Jr., S. M., and Wilson, J. W., J. Med. Chem. 7, 395 - 399 (1964)).”

Lemont B. KIER:

“In the middle 50's, centering on the year 1954, the work from several laboratories came together to offer a quantitative explanation and relationship to a biological activity. That work focused on the carcinogenicity of polycyclic aromatic hydrocarbons. The players were the Daudels, the Pullmans, Coulson and some others. The studies were done using valence bond theory and molecular orbital theory to quantify the involvement of certain bonds in an event initiating the onset of a carcinogenic outcome. Out of this came a possible mechanism involving the "K" and the "L" regions of the hydrocarbons. Tables and plots were published revealing the definition of limiting structures on the bases of theoretical structure descriptors. Articles by Coulson (Advances in Cancer Res., 1953) and by the Pullmans (Advances in Cancer Res., 1955) lay out the model quantitating this activity and the structures producing it.”

Steve CABANISS:

“Based on my understanding, QSAR has its roots in linear free energy relationships- i.e., Taft, Hammett and others in the 50's. Certainly, a history of QSAR should not begin _after_ that period, although earlier papers may be pertinent.”

Donald B. BOYD:

“Of the choices you give, the earliest date (1950s) seems most appropriate for CADD.”

Lemont B. KIER:

"I vote for the mid-50's"

Roger LAHANA:

"I would definitely vote for Early 50's. Papers published by the Pullmans and Coulson are indeed about establishing quantitative structure-activity relationships. And how could we discount the pioneering publications of Taft and Hammett?"

60's

Hugo KUBINYI:

"From my point of view, the real start of QSAR were the simultaneous publications of the Free-Wilson model (Free Jr., S. M., and Wilson, J. W., J. Med. Chem. 7, 395 - 399 (1964)) and the Hansch model (Hansch, C., and Fujita, T., J. Am. Chem. Soc. 86, 1616 - 1626 (1964)).

By looking for "Oldies" from these early QSAR years, you might also consider Rudolf Zahradnik (see e.g. Zahradnik, R., and Chvapil, M., Experientia 16, 511 - 512 (1960); Zahradnik, R., Arch. Int. Pharmacodyn. Ther. 135, 311 - 329 (1962); Zahradnik, R., Experientia 18, 534 - 536 (1962)), who formulated Hansch-type relationships relatively early and who is, like Corwin, still active."

Donald B. BOYD:

"The concepts of CADD started gradually and occurred to a lot of people independently. QSAR does not equal CADD. Pullmans' Quantum Biochemistry book (1963) was an important milestone for those interested in CADD.

The beginnings of QSAR are more definable. Your email mentions several important milestones. Another one includes the start of the QSAR GRC (which I think was 1973). Hansch and Fujita's 1964 paper may be most often pointed to as a formal beginning for QSAR as practiced today."

Karel WAISSER:

"I have printed (Chem. Listy, 92, 867-869, 1998) a review "The Predecessor of Hansch" with 38 references. I think, that really founder of QSAR is Corwin Hansch, because he has shown, that QSAR is a new discipline of science."

Tudor OPREA:

"If it comes to the modern day foundations of QSAR, no doubt that Hansch and Fujita deserve the credit for opening this new field, that in spite of the phys-chem work by Hammett and Taft."

Richard CRAMER:

"If the definition instead emphasizes an empirical search among multiple descriptors and data analysis methods for predictive regularities... by this definition Hansch et al. would clearly be the pioneers"

Yvonne MARTIN:

"I'm just back from a vacation and so am late in adding my comments. I would vote that QSAR began with Hansch and Fujita. They added two things to what had been done before: (1) the recognition that one can use calculated properties to correlate

with biological activities and (2) the recognition that because multiple properties may influence biological activity it is necessary to use the computer to fit the equation. My recollection is that Corwin said that it took two weeks to calculate the regression equation in the phenoxyacetic acid paper. By chance Pomona College had been given a computer and he decided to give it a try. They had to swap boards in and out to do various parts of the calculation.”

Anecdotes, memories, other references, and still more interesting reading:

Richard L. WOOD:

”I suppose that you could see Chapter 3 of the book *Intermolecular Interactions and Biomolecular Organization* by A. J. Hopfinger. It gives a description of the development of structure and activity relationships as far as drug design goes.”

Robert LIPNICK:

“I have written a series of feature articles in *Trends in Pharmacological Sciences* on the historical origins of QSAR, and have covered some other aspects in some other papers of mine. The first was on Overton. When I sent this to Corwin Hansch many years ago, he thanked me, and wanted to know when I would do a similar article on Meyer (as in Meyer-Overton theory correlating partition coefficients with anesthetic potency). The 3rd TIPS article is on Nikolai Vasilyevich Lazarev, who continued where Overton and Meyer left off, applying partition coefficients to development of industrial hygiene standards. Lazarev reported correlations on a log log scale, and developed a system for estimating partition coefficients from chemical structure (Overton in an early paper had already determined which functional groups increase or decrease partition coefficients!). Also, I edited the first English translation of Overton's classic work "Studien uber die Narkose".

Papers listed below. In some other papers I have traced the even earlier correlation of water solubility with toxicity.

R.L. Lipnick. Charles Ernest Overton: Narcosis studies and a contribution to general pharmacology. *Trends Pharmacol. Sci.*, **7**, 161-164 (1986)

R.L. Lipnick. Hans Horst Meyer and the lipid theory of narcosis, *Trends Pharmacol. Sci.*, **10** (7) July, 265-269 (1989); Erratum: **11** (1) Jan (1990), p. 44.

R.L. Lipnick and V.A. Filov. Nikolai Vasilyevich Lazarev, toxicologist and pharmacologist, comes in from the cold, *Trends Pharmacol. Sci.*, **13** (1992), 56-60.

R.L. Lipnick (ed.) *Charles Ernest Overton: Studies of Narcosis and a Contribution to General Pharmacology*, Chapman and Hall, London, and Wood Library-Museum of Anesthesiology, 1991.”

Srinivasan PARTHIBAN:

“While I strongly agree with many of the QSAR-ians that Hansch and Fujita deserve the credit for opening this new field. I notice that some try to dig the history of science and come up with few references in the 19th century. This reminds me something, which I read long back. Since the topic is "Beginning" I would like to share this well-known info with you.

About 2500 years ago, Plato described a "gasification" (!) reaction as a transformation of fire into air in an aqueous solution:

aqueous

2 Fire ----- > 1 Air

solution

Assuming

Fire = Pyramid structure

Water= Icosahedron

Air = Octahedron

Fire is not tetrahedral, water is not icosahedral and air is not octahedral, but the great adventure- the attempt to correlate properties (chemical and physical behavior) and structure-had begun 2500 years ago!!!!”

Richard CRAMER:

“If this question interests you, perhaps some personal reminiscences about less well known QSAR pioneers will also:

Free-Wilson. Mike Free and Jim Wilson became my colleagues when I joined SK&F in 1971. Mike Free was the head of Biostatistics and had custody of the only R&D computer, an IBM 1130 (on which btw I developed a very early substructural analysis after 5 PM on weekdays, see a 1973 publication). Free-Wilson analysis was clearly Mike's baby, as he told me, "I put Jim Wilson's name on the manuscript because he was Alfred Burger's student, Burger was J.Med.Chem's creator and editor, ..". Like many other statisticians, Mike had been trained as an (analytical) chemist. Mike was a restless and outspoken man, whom I admired as much as any scientist at the Philadelphia site, and who encouraged my own beginning efforts and promoted them to others. He had talked the antibiotic screening team into cassette dosing (in infected whole animals), because as he said "Most compounds to most organisms are just sawdust" -- of course meaning sources of metabolic energy. On another occasion I heard him advise a group of senior managers "don't piss down your leg" if their scheduling goals proved unrealistically. Perhaps no one with big pharma experience will be surprised to learn that soon after that, Mike left SK&F, to begin a very successful career consulting on the interpretation of clinical data. I also liked Jim Wilson very much, especially for his unfailing courtesy and graceful Southern manner (while Tom Spurling of CSIRO Australia was a visiting scientist with me, Jim stopped by for a chat -- when he left Tom said, "you know, I couldn't understand a word that man said other than 'dopamine'", to which I tongue in cheek replied "that's strange, because you're both from the south"). Jim was still at SKF/B when I left in 1983, hosting the lunchtime MedChem departmental bridge games attended by about half the PhD staff (btw, just wondering who out there under the age of 40 plays bridge? it was not so long ago a universal social skill acquired in college.)

Swain-Lupton. Lupton was a pre-med undergrad at MIT doing a research project with Prof. (Gardner) Swain while Stefan Unger (who remembers Stefan Unger?) and I were Swain graduate students. The long-term project was of course Swain's, Lupton just happened to be the guy who performed what proved to be the breakthrough calculation.

I have almost no personal recollection of him. Gardner Swain and I did not have the best of relations. But he had a creative mind, and was perhaps the only professor then at MIT who accepted female graduate students. (He was very close to his wife Margaret (also scientifically trained I believe), he was proud to say that they had together climbed every recognized mountain in New England.)”

Peter GUND:

“My view is that Louis P. Hammett of Columbia University was the father of Linear Free Energy Relationships (LFER); as an undergraduate, I learned physical chemistry (not very well) from him in 1961. Hammett's sigma-pi correlation work was instrumental to the derivation of QSAR as a discipline by Hansch and his colleagues in the late 1960s. My impression is that the term QSPR came later.

A comment on an earlier discussion:

Computer Aided Drug Design/Discovery (CADD) certainly could not pre-date the computer, by definition. However, early LFERs were derived by hand or by calculator; and, as pointed out already, other calculational disciplines such as quantum mechanics, vibrational/rotational theory, and molecular mechanics predated the computer. (Wayne Hendrickson computed low energy conformations for most common ring systems by calculator, Ken Wiberg published the first general purpose computer program for conformational energy of hydrocarbons). The computer simply allowed the theory to be extended, generalized, and applied to larger systems with fewer simplifications - and for heroic calculations to be done much faster and without arithmetic errors!”

Yvonne MARTIN:

“It is interesting that MedLine goes back only to 1966. No wonder no one knows the past!

I certainly didn't mean to imply that our early monoamine oxidase inhibitor work was a beginning of QSAR--we attempted to do QSAR, but weren't smart enough to do it until I learned from Hansch that I could calculate partition coefficients and that relationships might be parabolic. We had actually measured pKa's and some chloroform-buffer logP's in 1960, but couldn't make anything of the data.

I won't make any claim that some of my favorite early papers are the beginnings of QSAR and, especially CADD, but highly recommend them if you haven't read them. They deal with the relationships between physical properties, usually measured, and biological activity. (However, Fieser realized that one can calculate logP, although he used olive oil I think.) I was aware of the Brodie and Bell and Roblin papers by the time I met Corwin in 1967, but not the Fieser ones.

- Shore, P. A., B. B. Brodie, et al. (1957). The gastric secretion of drugs: a pH partition hypothesis. *Journal of Pharmacology & Experimental Therapeutics* 119: 361.

- Hogben, C. A. M., D. J. Tocco, et al. (1959). On the mechanism of intestinal absorption of drugs. *Journal of Pharmacology & Experimental Therapeutics* 125: 275.

- Bell, P. H & R. O. Roblin, (1942) *J. Amer. Chem. Soc.* 64: 2905. I don't have the title, but it has to do with an optimum pKa for antibacterial activity of sulfonamides.

- Fieser, L. F. et al. (1948) *J. Amer. Chem. Soc.* 70: 3151. Fieser, L. F., M. G. Ettlinger, & G. Fawaz, *ibid* 3228. Fieser, L. F., & A. P. Richardson, *ibid* 3156. I don't have the titles, but these articles have to do with lipophilicity and antimalarial activity of naphthoquinones. If you haven't read this series of articles, do so. (There are ~16 in the series, detailing work done during WWII.) They detail exquisite insight into the factors and data that need to be considered in designing a biologically active compound. All of their analysis was qualitative, graphical, as I remember. (We analyzed this data in 1973. Martin, Y. C., T. M. Bustard, et al. (1973). Relationship between Physical Properties and Antimalarial Activities of 1,4-Naphthoquinones. *Journal of Medicinal Chemistry* 16: 1089-1093.)

- E. J. Ariens has an interesting chapter: Ariens, E. J. (1971). A General Introduction

to the Field of Drug Design. Drug Design. E. J. Ariens. New York NY, Academic. I: 1-270. He cites Traube (1904), Warburg (1921), Mullins (1955) as well as Pauling. Just before Hansch & Fujita, and Free and Wilson, bioisosterism was in the air (Friedman, 1951 & 1954).”

The original question:

“When can be considered the starting dates of QSAR or more generally Computer-Aided Drug Design?

So far, there are several papers of Hansch and Fujita in the early 60's that are heavily cited for QSAR. However, are there any work earlier that can be considered as the beginning? How do you define the "beginning". If we have to draw the line somewhere, one way of defining the "beginning" is the point we have transitioned from more empirical research into "scientific" research. Hence, the early SAR papers may not necessarily qualify unless there are some statistical (or quantitative) considerations.

Given the above constraints, I had a fairly clear view of the "beginnings" but after starting asking around, I am not so sure anymore. Let me share what I have found out so far, then I would like to hear from you of your opinions/suggestions.

Hugo Kubinyi proposes 1964 paper by Free and Wilson (Free-Wilson model), and 1964 papers by Hansch and Fujita (Hansch model). However he also notes that a Bruice, Kharasch, and Winzler paper in 1956 with a first application of Free-Wilson type analysis. Also a paper by Zahrandic on 1960-62 with Hansch-type relationships.

Yvonne Martin proposes a 1960 paper in Nature by Taylor and Wykes on MAO inhibitors. Another paper by Swett and Martin in 1963 involves Pargyline Series.

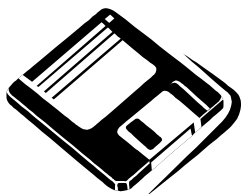
Lemont Kier proposes early 1950's with articles by Coulson (1953) and by the Pullmans (1955) laying out some quantitating carcinogenic activity via valence bond and molecular orbital computations.

Then I received a 17 page manuscript from Barbara and Marvin Charton's that detail the history of QSAR all the way back to 1800's. Most of the earlier work were, of course, qualitative. The quantitative SAR in which the bioactivity is mathematically related to some set of parameters came later on. The earliest mathematical formulations, according to Charton's, were Ferguson principle (started at 1939 but mostly at around 1950s) for toxicity; Hammett equation (1953); Taft equation (1956); Hansch-Fujita model (1962).

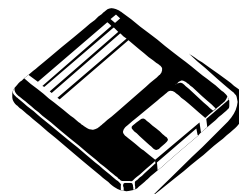
So... any suggestions from here on? Are there any other references that I am missing? If not, based on the above what would be your vote for the beginnings of CADD (note I am not limiting to QSAR alone):

- 1- Early 50's: [Hammett, Taft, Coulson, Pullman, Ferguson]
- 2- Early 60's: [Hansch-Fujita; Free-Wilson; Zahrandic; Taylor]
- 3- Any other suggestions?”

Compiled by Osman F. Güner



SOFTWARE



- **TRITON release announcement**

The graphical program TRITON has been developed for modelling protein mutants and assessment of their activities. Protein mutants are modelled from the wild type structure by homology modelling using the external program Modeller. Chemical reactions taking place in the mutants active site are modelled using the semi-empirical quantum mechanic program MOPAC. Semi-quantitative predictions of mutants activities can be achieved by evaluating the changes in energies of the system and partial atomic charges of active site residues during the reaction. The program TRITON offers graphical tools for the preparation of the input data files, for calculation and for the analysis of the generated output data. Implementation ensures the overall integrity of consecutive steps in the modelling of mutants and calculation of reaction coordinates, but the program can also be used simply for combinatorial generation of multiple mutants by homology modelling. The program functionality has been validated by the modelling of activities of haloalkane dehalogenase mutants.

Availability: The program TRITON can run under operating systems IRIX, Linux and NetBSD. The software is FREE for academic users and is available at <http://www.chemi.muni.cz/lbsd/triton.html>.

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<http://www.chemi.muni.cz/~jiri/index.html>



PARM1.3 SYBYL INTERFACED VERSION

We are pleased to announce the release of the new PARM (PseudoAtomic Receptor Model) (see NEWS LETTERS, Issue No. 9 October 1998) SYBYL interfaced version (1.3), a very user friendly one that just needs the user to be familiar with SYBYL MSS(Molecular Spreadsheet).

The detailed principle of the PARM program may be found in J. Chem. Inf. Comput. Sci., 1998, 38, 243-250.

Software applications may be found in:

1)M. Santagati, A. Doweyko, A. Santagati, M. Modica, S. Guccione, H.M. Chen , G. Uccello Barretta , F. Balzano,

5-HT_{1A} receptors mapping by conformational analysis (2D NOESY/MM) and "three way modelling" (HASL, CoMFA, PARM),

Molecular Modelling and Prediction of Bioactivity, K. Gundertoft & F.S. Jorgensen Eds. Proceedings of the 12th European Symposium on Quantitative Structure-Activity Relationships, Copenhagen, Denmark , August 23-28, 1998.

2000 Kluwer Academic/Plenum Publishers, New York, 183-194.

2)M. Santagati, H. M. Chen , A. Santagati, M. Modica, S. Guccione, G. Uccello Barretta, F. Balzano,

Application of PARM to constructing and comparing 5-HT_{1A} and α_1 receptor models, Molecular Modelling and Prediction of Bioactivity, K. Gundertoft & F.S. Jorgensen Eds. Proceedings of the 12th European Symposium on Quantitative Structure-Activity Relationships, Copenhagen, Denmark , August 23-28, 1998.

2000 Kluwer Academic/Plenum Publishers, New York, 433-439.

3) S. Guccione,

Combining different 3D-QSAR methodologies in a multiconformer context: a new approach to map not X-ray determined targets of pharmaceutical interest overcoming alignment problems.

Proceedings of the conference "Crystallography and Drug Design '99" (CDD 99), Lodz (Poland), May 20th-22nd 1999, 85-93.

4)S. Guccione, M. Modica, A. M. Doweyko, M. Santagati, A. B. Nordquist, J. R. Torrente, H. M. Chen, and R. J. Mattson,

PARM Mapping of Rat and Human Serotonin 1A (5-HT_{1A}) Receptor,

13th European Symposium on Quantitative Structure-Activity Relationships, Rational Approaches to Drug Design.

QSAR 2000 Düsseldorf, Heinrich-Heine-Universität, Düsseldorf, Germany, 27 August-1 September, 2000. Abstract book P.12

System Requirements : IRIX 6.0 (or higher).

For more informations:

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MULTIGEN (Multiconformer Generation)

Lowest energy conformers are usually assumed in 3D-QSAR studies as the active form of a drug molecule but more and more evidences clearly show that a minimum conformation is not critical for bioactivity.

MULTIGEN (shortcut for Multiconformer Generation) is a new algorithmic innovation working under WINDOWS (95 or +) or LINUX environment developed by the collaborative work of the V. Potemkin and S. Guccione groups at the Chelyabinsk State University (Russian Federation) and the University of Catania (Italy), respectively.

MULTIGEN allows to define *multiconformational* models of a molecular dataset¹⁻⁴. Starting from the geometry of the lowest energy conformer, the approach can be decomposed into 4 steps: 1) the normal vibrational (or internal rotational) modes (directions of vibrations) are defined for the lowest energy conformer; 2) the atoms of the molecule are moved along each mode until the nearest maximum of energy is overcome; 3) the new probable conformer is defined using a local minimum search; 4) the geometry of the new conformer is saved when its energy is less than an accepted value with respect to the low energy conformer. The process is iteratively carried out for each of the newly defined conformers. The conformational search is ended when the iteration doesn't lead to any new conformer, then a multiconformers based model is created by the BiS⁵ superimposing of the generated conformers. The model includes the cartesian coordinates of the atoms of all the conformers and the probabilities of their location in each point of this space .

The biological activity of a compound (A) is defined as the sum of the conformers activities :

$A = a + b \sum p_i A_i$ (where A_i = partial activity of the conformer i ; p_i = statistical probability of a conformation to exist; a and b = parameters which are function of units of activity but independent from the dataset itself.

The proposed method has been benchmarked using the recently reported multiconformer data on a dataset of 5-HT_{1A} receptor ligands⁶. The MultiGen results are generally in agreement with Guccione *et al.*⁶ and allowed to pick up the most active conformer for each structure in the dataset when used as input for BiS⁵ and HASL⁶ calculations.

Software applications can be found in:

1) V.A. Potemkin, R.M. Arslambekov, E.V. Bartashevich, M.A. Grishina, A.V. Belik, S. Perspicace, S. Guccione,

MULTIGEN: A NEW PARADIGM FOR "Multiconformational" Alignment of Molecular Structures IN 3D-QSAR STUDIES.

COMPUTER ASSISTANCE TO CHEMICAL RESEARCH-2001, International Symposium

Zelinsky Institute of Organic Chemistry of Russian Academy of Sciences, Moscow, Russia, May 22-23, 2001.

2) <http://195.90.164.41/Fock/proceedings/3/440>

3) V.A.Potemkin, R.M.Arslambekov, E.V. Bartashevich, M.A. Grishina, A.V.Belik, S.Perspicace, S.Guccione,

Multi-Conformational Method of Analysis of Biological Activity of Molecules, Russ. J. Struct. Chem J.Struct.Chem. (Engl.Transl.), *in press* .

4) E.V. Bartashevich, V.A.Potemkin, M.A. Grishina, A.V.Belik,

A Method for Multi-Conformational Modelling of Spatial Form of Molecules, Russ. J. Struct. Chem, *in press*.

5) V. A. Potemkin, E. V. Bartashevich, M. A. Grishina and Salvatore Guccione,

An Alternative Method for 3D-QSAR and the Alignment of Molecular Structures: BiS (Biological Substrate Search),

Rational Approaches to Drug Design. H-D. Holtje&W. Sippl Eds. Proceedings of the 13th European Symposium on Quantitative Structure-Activity Relationships, QSAR 2000 Düsseldorf. Düsseldorf, Heinrich-Heine-Universität, Düsseldorf, Germany, 27 August-1 September, 2000. 2001 Prous Science Publishers, 349-353 and references therein enclosed.

6) S. Guccione, A. M. Doweyko, H.M. Chen, G. Uccello Barretta, F. Balzano,

3D-QSAR Using "Multiconformer" Alignment: The Use of HASL in the Analysis of 5-HT_{1A} Thienopyrimidinone Ligands, J. Comput.-Aided Mol. Des., 14 (2000), 647-657 and references therein enclosed.

MINIMUM PC Requirements: Intel Pentium, 150 MHz, RAM 16 MB.

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Russian Federation.

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NEW BOOKS



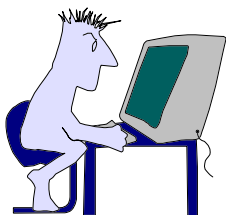
Pharmacokinetic Optimization in Drug Research. Biological, Physicochemical, and Computational Strategies. Bernard Testa, Han van de Waterbeemd, Gerd Folkers and Richard Guy (Eds.), Wiley-VCH (2001). ISBN 3-906390-22-5.



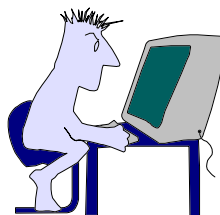
BOOK REVIEW



none



POSITIONS



none



JOURNALS



- **Quantitative Structure-Activity Relationships**

This VCH journal is considered to be the "home" journal of THE QSAR AND MODELLING SOCIETY. Editors are Prof. Michael Wiese, University of Bonn, and Prof. Gerd Folkers, ETH Zurich.

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Of course, Ferenc Darvas remains the Editor of the Abstracts Section. Please consider also to subscribe personally to the QSAR journal. It's good and it's cheap, extremely cheap for members of our Society (call VCH, phone +49-6201-6060, for the current price).

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Preview Quantitative Structure-Activity Relationships, issue 3&4 (2001)

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S.P. Niculescu, K.L.E. Kaiser

Use of Support Vector Machine in pattern classification: application to QSAR studies

R. Czerminski, A. Yasri, D. Hartsough

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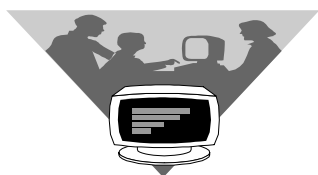
Pharmacophore Identification and Bioactivity Prediction for Group I Metabotropic Glutamate Receptor Agonists by the Electron-Conformational QSAR Method

E. Rosines, I.B. Bersuker, J.E. Boggs

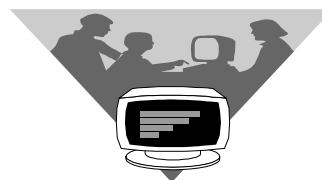
- **Journal of Computer-Aided Molecular Design (JCAMD) incorporating Perspectives in Drug Discovery and Design (PD3)**

<http://www.wkap.nl/journals/jcamd>

Kluwer Academic Publishers is pleased to announce that members of the QSAR and Modelling Society are able to subscribe to JCAMD Volume 16 (12 issues) 2002, at the special rate (paper version only) of:



Meetings /Courses



2001

- ADME: Perspectives in high-throughput and in silico approaches, London, December 4th, 2001. Contact: Han van de Waterbeemd (han_waterbeemd@sandwich.pfizer.com).

2002

- ACS, Spring Meeting, Orlando, 7-11 April 2002.

ADME/TOX INFORMATICS

At Spring ACS meeting in Orlando (April 7-11, 2002)

Sponsored by the Chemical Information Division (CINF)
Co-sponsored by Division of Medicinal Chemistry (MEDI),
Division of Chemical Toxicology (TOXI),
and Division of Computers in Chemistry (COMP)

The symposium will be on the informatics challenges faced with the increasing contribution of ADME/Tox studies in the early drug discovery. If you are working on predictive ADME/Tox in lead discovery, lead optimization, or combinatorial library design and analysis, you may want to share your views and results with the scientific community by contributing to this symposium. How are you managing the information flow? How is information captured and made available to scientists in a multi-disciplinary set up? Are there examples of increased quality of candidates through use of predictive ADME/Tox in early discovery?

Please use the OASys to submit your abstract. You can access the CINF symposia at OASys via <http://oasys.acs.org/oasys.htm>. The deadline for submitting abstracts is November 1st.

"Near-Neighbor Searching for Lead Follow-up: Algorithms and Descriptors"

The November 12th deadline for submitting papers to the April 2002 ACS Symposium on "Near-Neighbor Searching for Lead Follow-up: Algorithms and Descriptors" is rapidly approaching. I have already accepted some excellent abstracts and am eager to accept more. However, we only have room in the Symposium for a limited number of presentations. Thus, I suspect that I will be forced to make some difficult choices about which abstracts to include in the Symposium and which to recommend for general podium presentation. At some point, the date an abstract is submitted will become a factor in this decision-making process so I encourage you to submit your abstract as soon as possible.

A copy of the original call-for-papers is appended below but please note the NEW 2-STEP INSTRUCTIONS FOR SUBMITTING AN ABSTRACT:

1. Please submit your abstract through the OASYS facility. Point your browser to: <http://oasys.acs.org/acs/223nm/comp/papers/index.cgi> and click the button for the "Near-neighbor searching ..." Symposium. Please be sure to follow the formatting instructions provided by OASYS.
2. Please e-mail a copy of your abstract to me at pearlman@list.phr.utexas.edu.

CALL-FOR-PAPERS:

April 2002 ACS Symposium on "Near-Neighbor Searching for Lead Follow-up: Algorithms and Descriptors" As its name suggests this symposium will address: (1) novel algorithms or methods related to near-neighbor searching in the context of lead follow-up and (2) molecular descriptors useful for near-neighbor searching in the context of lead follow-up. In addition (and if space on the program permits), the symposium will also address: (3) "success stories" in using near-neighbor searching in the context of lead follow-up. The deadline for submitting abstracts is November 12th. I'm looking forward to seeing you in Orlando in April.

Best wishes,

-- Bob Pearlman

- 14th European Symposium on QSAR, 8-13 September 2002, Bournemouth, UK. Chairman: Martyn Ford (email: martyn.ford@port.ac.uk), <http://www.euro-qsar.org>.
- The Eighth Chemometrics in Analytical Chemistry Conference will be held in Seattle, USA, Sept. 22-26, 2002, at the Washington Athletic Club (www.wac.net). The conference is organized under the auspices of the North American/International Chemometrics Society (NAMICS). Following the tradition of the preceding CAC conferences, emphasis will be on new developments and applications of chemometrics in analytical chemistry. Specific topics will include:
 - * Combinatorial Chemistry, Genomics and Proteomics
 - * Bioinformatics
 - * High Throughput Screening
 - * Spectroscopic Imaging
 - * Handling of missing data, robust estimation
 - * Method validation and metrology
 - * Experimental design
 - * Pattern recognition, classification, multi-way analysis
 - * Process analytical chemistry
 - * Multivariate modelling and calibration
 - * Genetic algorithms, neural networks, data mining
 - * Chemometrics in environmental and industrial problems
 - * Graphical communications
 - * Chemometrics in low-dimensional spaces

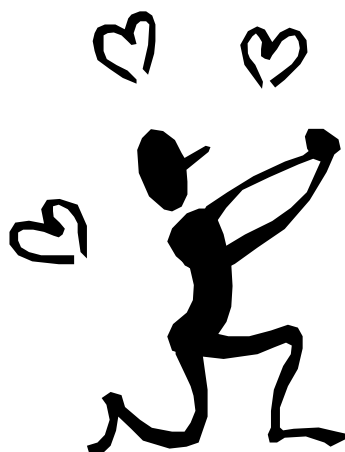
In addition to the technical sessions, a number of short courses will be offered on Sept. 21 and 22, prior to the conference.

Barry M. Wise, Ph.D.
CAC-2002 Chair
Eigenvector Research, Inc.

830 Wapato Lake Road
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USA

phone: (509)687-2022
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e-mail: bmw@eigenvector.com
web: www.eigenvector.com

- 5th Swiss School on Medicinal Chemistry, October 2002, Leysin, Switzerland.
Contact: Gerd Folkers, Bernard Testa, Han van de Waterbeemd.



Please send annual fees of **\$10** to Stefan Balaz.

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Or to Han van de Waterbeemd in the UK (Eurocheques should be drafted in £).



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WWW HOMEPAGE



The best source for current information is our Web Home Page. You are encouraged to participate actively in improving and updating this site by sending us information and suggestions.

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