OLEG A. RAEVSKY - SCIENTIST, TEACHER, PERSON

V.Y. Grigorev[1], O.V. Tinkov[2], V.P. Kazachenko[1]

[1]Institute of Physiologically Active Compounds at Federal Research Center of Problems of Chemical Physics and Medicinal Chemistry, Russian Academy of Sciences, Chernogolovka, Russia;

[2]Shevchenko Transnistria State University, Tiraspol, Moldova

Moscow, 2024

The activity of a scientist

Meeting of the International QSAR and Molecular Modeling Society Board, Boston (USA), August 1995.
Left to right: Prof. King (USA), Prof. Charton (USA), Dr. Magi (USA), Prof. Raevsky (Russia), Prof. Block (USA).

The activity of a scientist

Meeting on the Rhine (July 1993).
Seminar on Hydrogen Bonding. Left to right: Prof. Lawrence (France), Prof. Kerry (USA), Prof. Schneider (Germany), Prof. Abraham (UK), Prof. Raevsky (Russia).

The activity of a scientist

Final meeting of project leaders and collaborators of the International Science and Technology Center project, Liverpool, England, August 2010.
Standing left to right: Dr. A. Worth (Joint Research Center of the European Union, Italy), Prof. J.C. Dearden (John Moores University, Liverpool), and Prof. V.V. Poroikov (Institute of Biomedical Chemistry, Moscow).

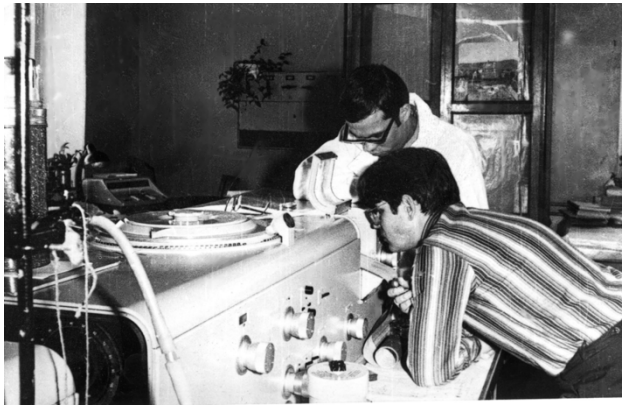
Foreign colleagues/co-authors

- Prof. Dr. H.-J. Schneider, University of Saarbrucken, Germany
- Dr. K.-J. Shaper, Research Center Borstel, Germany
- Prof. Dr. J.R. Chretien, University of Orleans, France
- Dr. H. Van de Waterbeemd, F. Hoffmann-La Roche Ltd, Switzerland
- Prof. Dr. J.C. Dearden, University John Moore, Liverpool, England
- Dr. J. McFarland, Pfizer, Groton, USA
- Dr. E.E. Weber Environmental Protection Agency (EPA), USA
- Prof. Dr. R. Mannhold, University of Dussedorf, Germany
- Dr. A. Worth, EU Joint Research Centre, Ispra, Italy

Education. The beginning of scientific work.

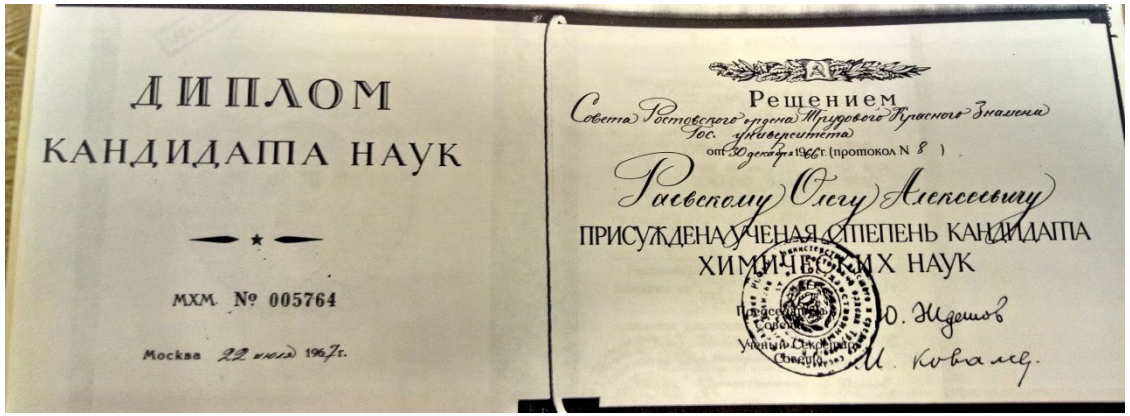
School, 1947-1957

Rostov State University, 1957-1962



Institute of Organic and Physical Chemistry, 1962-1979

Education



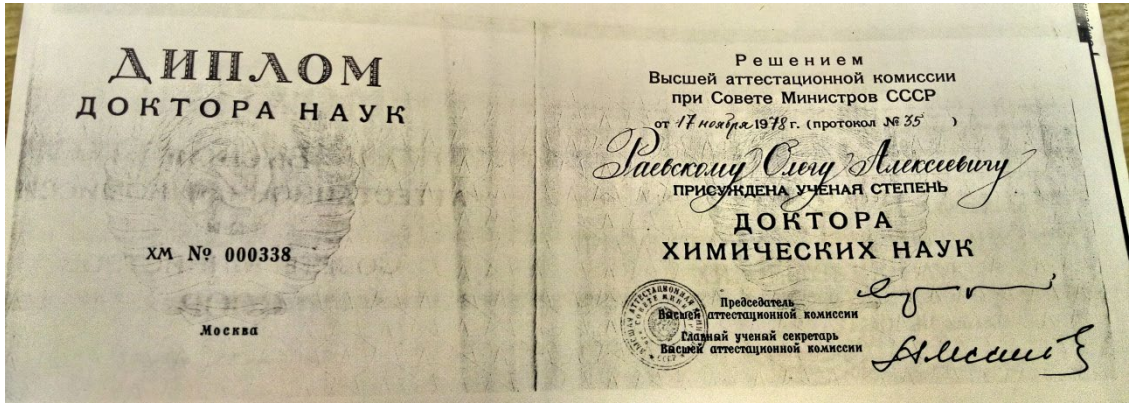
ДИПЛОМ
КАНДИДАТА НАУК

МХМ № 005764

Москва 22 июня 1967 г.

Решением
Совета Ростовского ордена Трудового Красного Знамени Гос. университета
от 30 декабря 1966 г. (протокол N 8)
Раевскому Олегу Алексеевичу
ПРИСУЖДЕНА УЧЕНАЯ СТЕПЕНЬ КАНДИДАТА ХИМИЧЕСКИХ НАУК

PhD thesis (1966): "Physicochemical properties and structure of semithiosemicarbazones"



ДИПЛОМ
ДОКТОРА НАУК

ХМ № 000338

Москва

Решением
Высшей аттестационной комиссии
при Совете Министров СССР
от 17 ноября 1978 г. (протокол № 35)
Раевскому Олегу Алексеевичу
ПРИСУЖДЕНА УЧЕНАЯ СТЕПЕНЬ
ДОКТОРА
ХИМИЧЕСКИХ НАУК

Председатель Высшей аттестационной комиссии

Главный ученый секретарь Высшей аттестационной комиссии

Doctoral dissertation (1978): "Spatial structure and intramolecular interactions in a series of acyclic organophosphorus compounds".

Work

Laboratory of Physico-Chemical Research (1983)

Department of Computer Aided Molecular Design (1991)

Department of Computer Aided Molecular Design (2015)

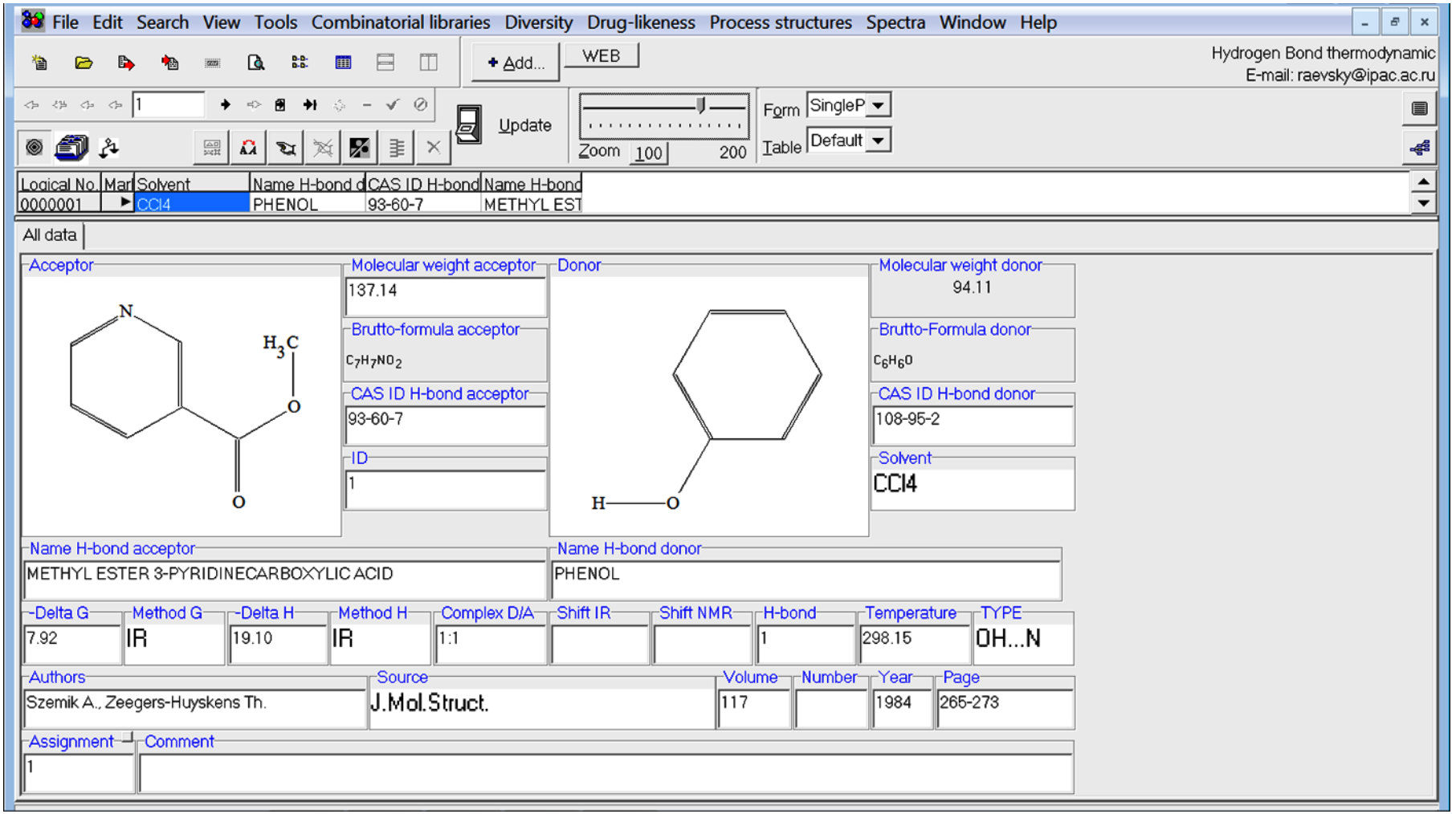
Deputy Director of the IPAS RAS for research(2006)

Work

Research interests:

- Physical chemistry
- Spectroscopy
- Molecular modeling
- Study of the structure-property relationship
- Design and computer search for new physiologically active compounds
- Development of computer programs and creation of databases

Parameterization of H-bond (database)



Parameterization of H-bond (model/scale)

Database : (CCl_4; 1:1; 163 H-donor; 195 H-acceptors; N=936)

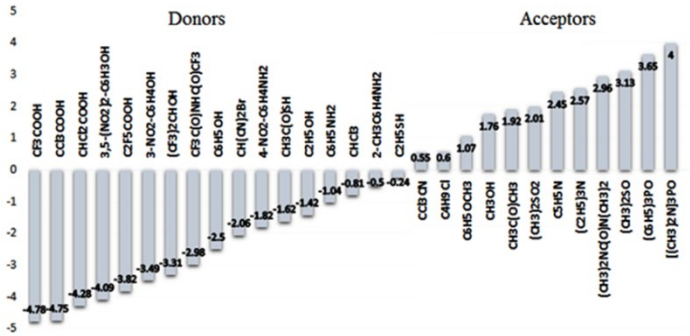
Additive-multiplicative model:

E_a – enthalpy H-acceptor descriptor
E_d – enthalpy H-donor descriptor
C_a – free energy H-acceptor descriptor
C_d – free energy H-donor descriptor

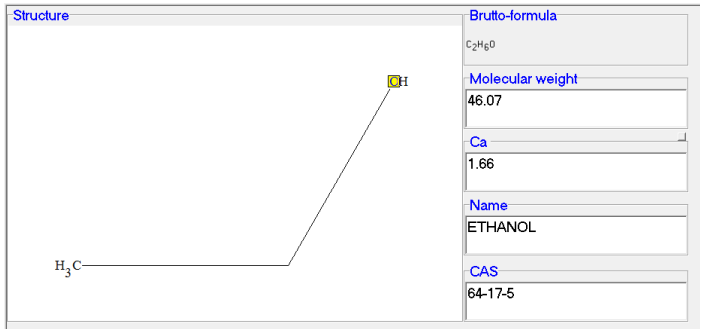
Standard H-donor: phenol (E_d=-2.50; C_d=-2.50)
Standard H-acceptor : HMPA (E_a=2.50; C_a=4.00)

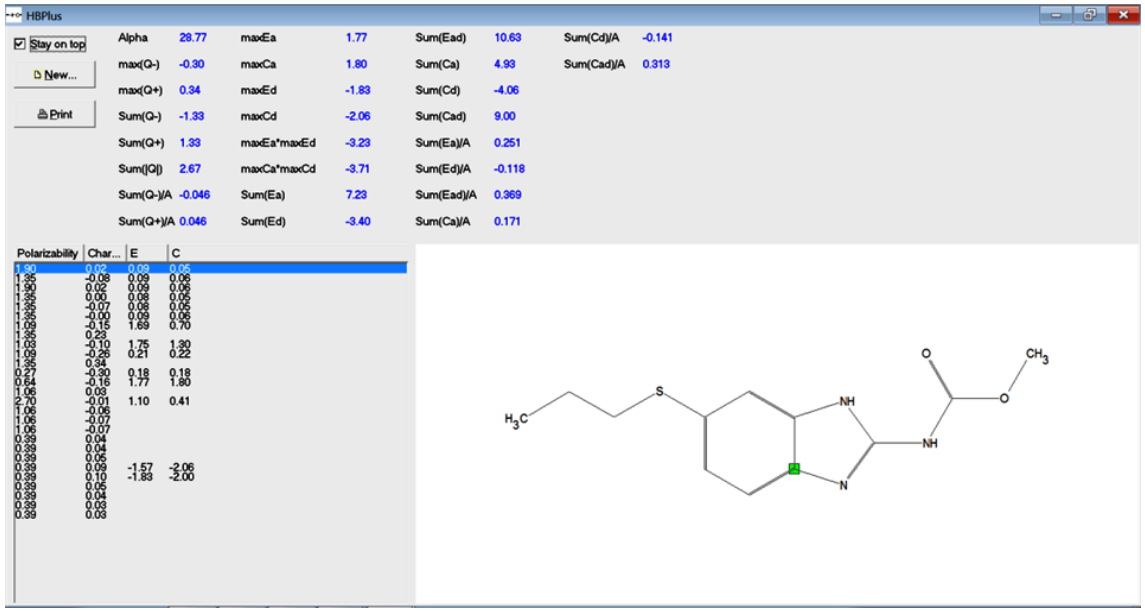
$\Delta H(kJ/mol) = k_1 * E_a E_d + k_2$; k_1=4.96; k_2=0.00

$\Delta G(kJ/mol) = k_3 * E_a E_d + k_4$; k_3=2.43; k_4=5.70



Parameterization of H-bond (HBPLUS)





Local Descriptors	Molecular Descriptors	Composed Descriptors
$C_D^{\max}$	$\sum C_D$	$\sum C_D / MW$
$E_D^{\max}$	$\sum E_D$	$\sum E_D / MW$
$C_A^{\max}$	$\sum C_A$	$\sum C_A / MW$
$C_D^i E_D^i C_A^i E_A^i$	$\sum C_A + \sum C_D$	$(\sum C_A + \sum C_D) / MW$

Parameterization of H-bond (QSAR)

Water solubility:

$\log S = 0.43(\pm 0.12) - 0.298(\pm 0.009)\alpha + 1.09(\pm 0.05)\Sigma C_a - 0.30(\pm 0.05)\Sigma C_d$

$n=630;\ r^2=0.90;\ s=0.54$

Acute toxicity (*Guppy*):

$\log LC_{50} = 5.14(\pm 0.12) - 0.259(\pm 0.008)\alpha + 0.79(\pm 0.03)\Sigma C_a$

$n=90;\ r^2=0.95;\ s=0.32$

Blood-brain barrier penetration:

RF_cv: n=1000; SN=0.824; SP=0.756; ACC=0.790

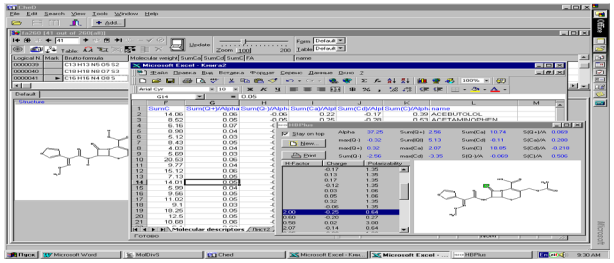
RF_test: n=100; SN=0.940; SP=0.700; ACC=0.820

Computer programs

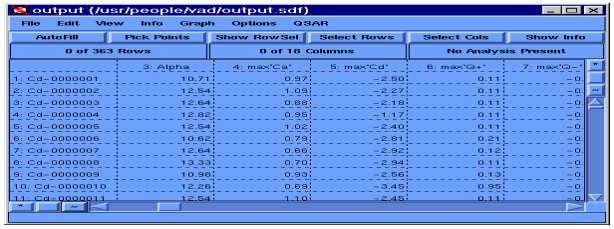
HBPLUS (Hydrogen Bond PLUS): 2D H-bond descriptors
DNESTR (Design New Effective STRuctures): 2D molecular descriptors
MOLTRA (MOLecular TRansform Analysis): 3D H-bond descriptors
SLIPPER (Solubility LIPophilicity, PERmeability): solubility, lipophilicity, permeability
MOLDIVS (MOLecular DIVersity and Similarity): molecular similarity and diversity
DISCON (DISsociation CONstants): pKa
AMP (Arithmetic Mean Property)
LOREP (LOcal REgression Property)
SOCR (Super Overlapping Cluster Regression)

HYBOT (HYdrogen BOnd Thermodynamics)

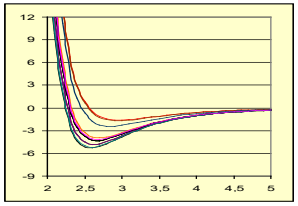
Complete description of hydrogen bonding for QSAR, Molecular Modelling and Drug Design on your desk!

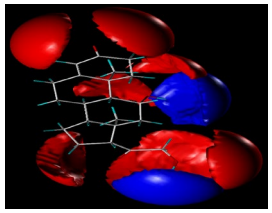


Program package HYBOT under Windows, UNIX, LINUX contains vast databases of thermodynamics parameters of H-bonding (15000 complexes), enthalpy and free energy factors (34000), the program for calculation of enthalpy and free energy of H-bonding as well as 16 two and 10 three dimensional original descriptor.

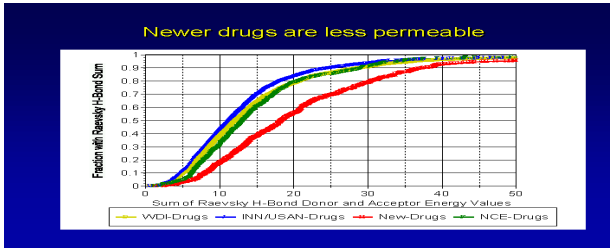


«Calculation of many different descriptors is possoble using a range of commercially available software packages, such as Sybyl, Cerius2, Tsar, Malconn-Z, HYBOT etc.» (H. Waterbeemd, D.S. Smith, K. Beaumont, D.K. Walker. *J. Med. Chem.,* 44, 1313-1333 (2001)).



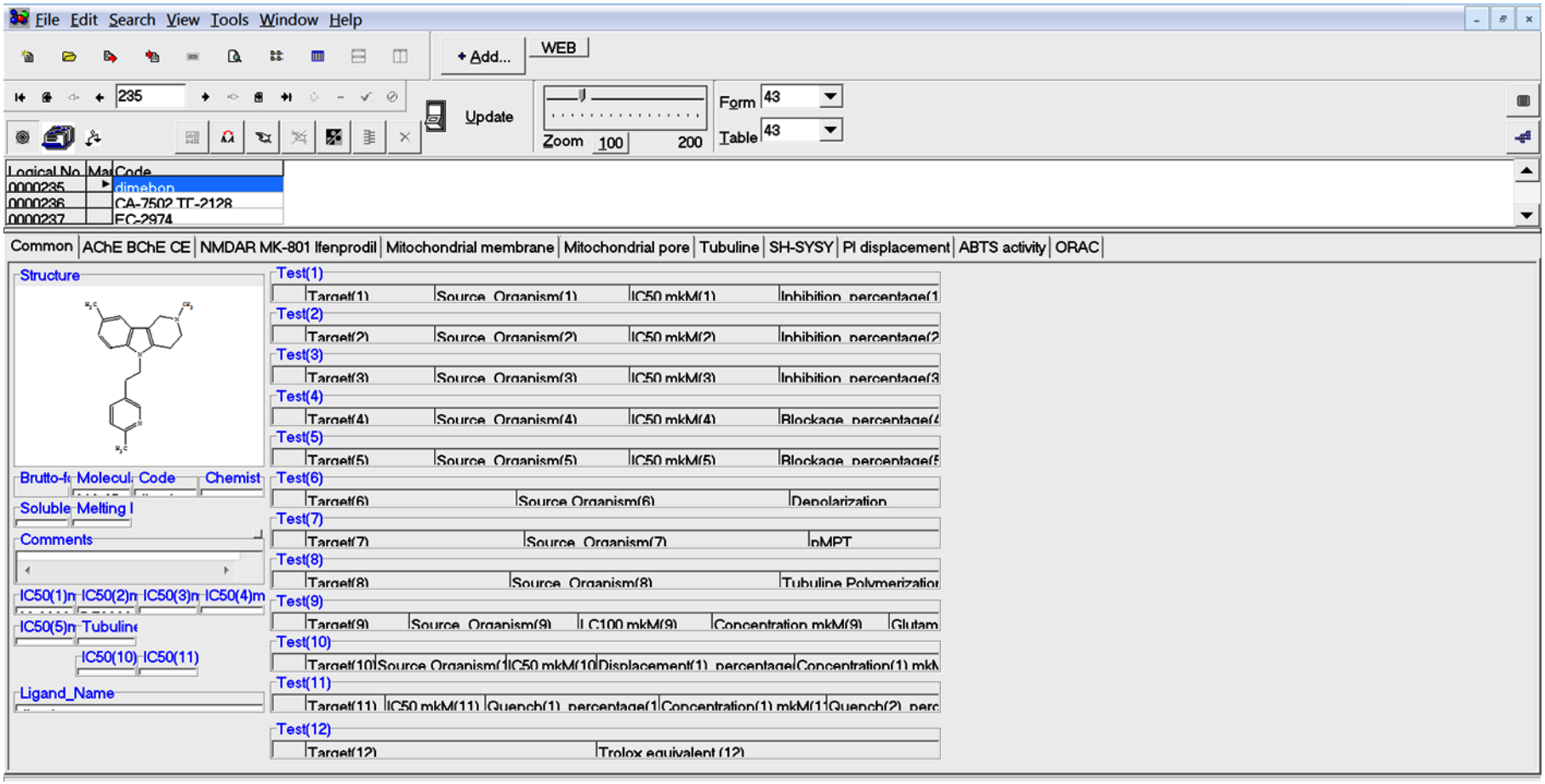


«We have used ABSOLV and three other commercial software packages (HYBOT-PLUS, Molecular modeling Pro and QsarIS) that calculate descriptors of similar classes, to model partitioning in the four solvent-water systems. Overall, HYBOT-PLUS gave the best results.» (J.C. Dearden, D. Bentley. *SAR QSAR Environ Res*., 13, 185–197 (2002)).



C.A. Lipinski (Pfizer, Groton, USA) used the HYBOT descriptor ∑Cad as global measure of permeability for analysis of four data bases (WDI, INN/USAN0DRUGS, NSE DRUGS and New Drugs) and estimated that the "newer drugs are less permeable". This declaration had essential influence on Drug Development projects of not only this company but also many others.

Database of the Institute of Physiologically Active Compounds (IPAC) of the Russian Academy of Sciences

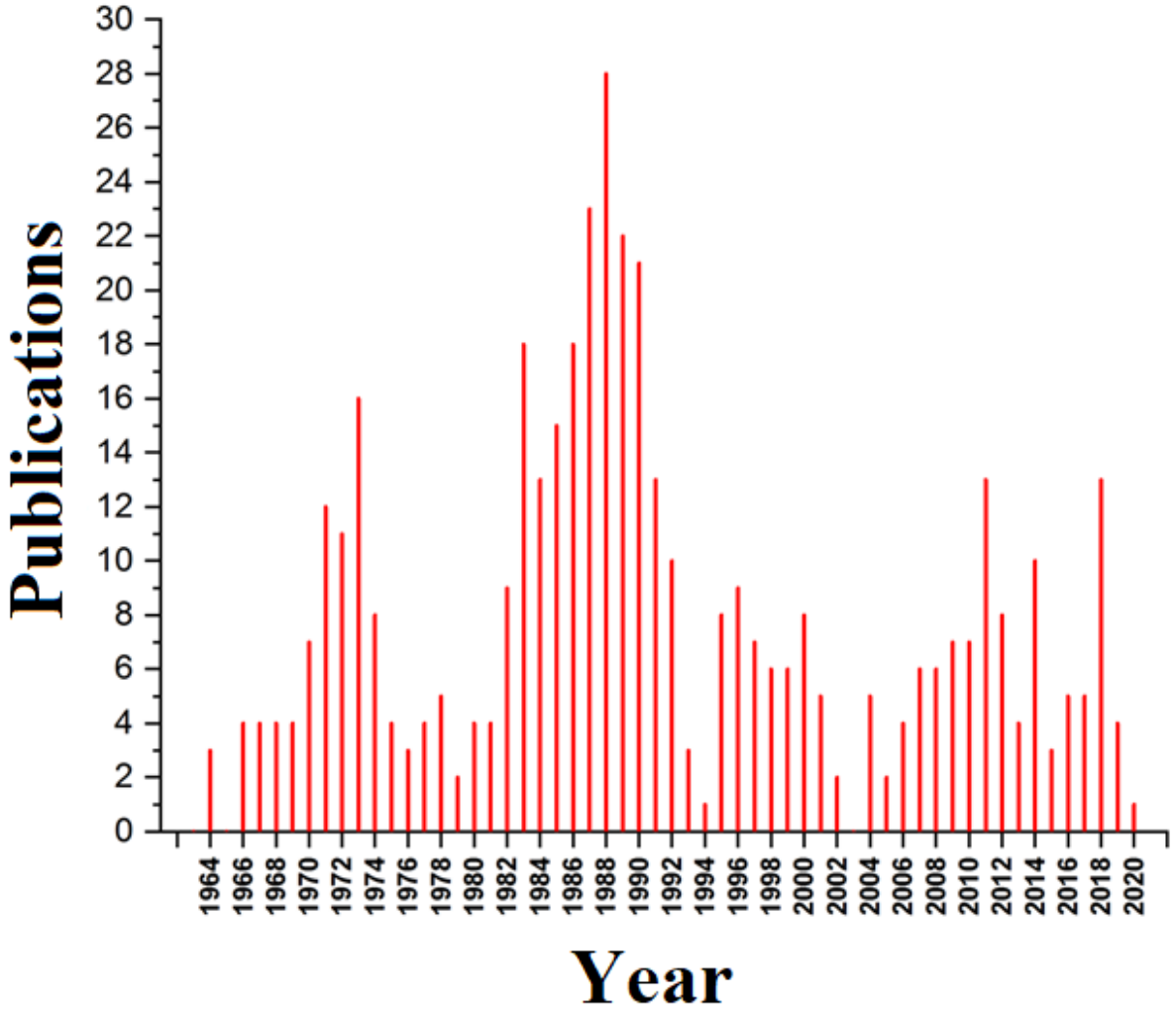


Database of IPAC RAS (tests)

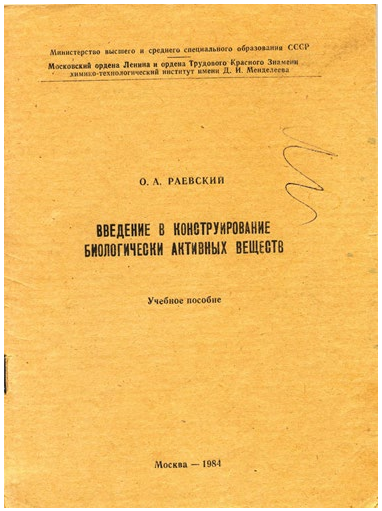
- acetylcholinesterase (AChE)inhibition
- butyrylcholinesterase (BChE) inhibition
- carboxylesterase (CE) inhibition
- N-methyl-D-aspartate (NMDA) receptor blockade, [3H]MK-801 binding site
- NMDA receptor blockade, [3H]ifenprodil binding site
- mitochondrial potential
- effect on opening of non-specific mitochondrial pore MPT (Mitochondrial permeability transition)
- tubulin polymerization
- cytotoxicity and protection from glutamate-induced toxicity
- inhibition of AChE-induced beta-amyloid aggregation
- antioxidant activity, ABTS test
- antioxidant activity, ORAC test

Publication activity (Russian Science Citation Index)

Number of publications : 454 (1964-2020)
Number of citations : 4687
***h*-index** : 27

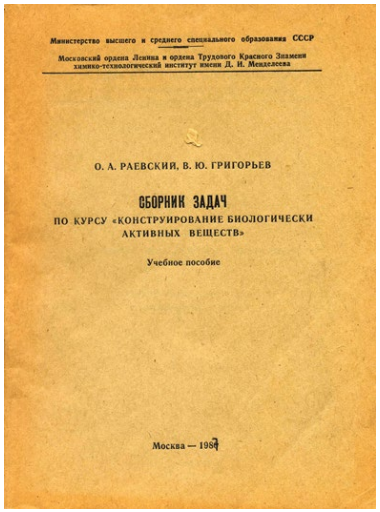


Publication activity

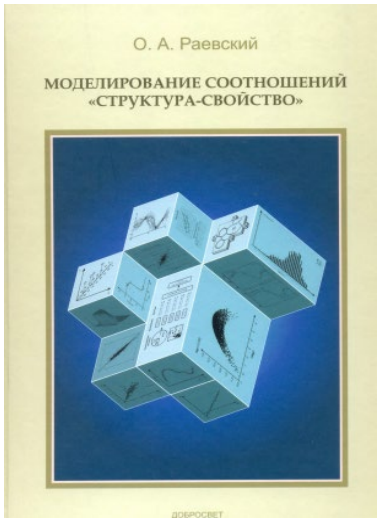


1984

2013



1987



2015

Most cited works (Russian Science Citation Index)

1. Van De Waterbeemd H., Camenisch G., Folkers G., Chretien J.R., Raevsky O.A. ESTIMATION OF BLOOD-BRAIN BARRIER CROSSING OF DRUGS USING MOLECULAR SIZE AND SHAPE, AND H-BONDING DESCRIPTORS // J. Drug Target. 1998. Vol. 6. P. 151-165.

2. Van Waterbeemd H.D., Camenisch G., Folkers G., Raevsky O.A. ESTIMATION OF CACO-2 CELL PERMEABILITY USING CALCULATED MOLECULAR DESCRIPTORS // Quant. Struct.-Act. Relat. 1996. Vol. 15. P. 480-490.

3. Raevsky O.A., Grigor'ev V., Kireev D., Zefirov N. COMPLETE THERMODYNAMIC DESCRIPTION OF H-BONDING IN THE FRAMEWORK OF MULTIPLICATIVE APPROACH // Quant. Struct. –Act. Relat. 1992. Vol. 11. P. 49-63.

4. Raevsky O.A. MOLECULAR STRUCTURE DESCRIPTORS IN THE COMPUTER-AIDED DESIGN OF BIOLOGICALLY ACTIVE COMPOUNDS // Russ. Chem. Rev. 1999. Vol. 68. P. 505-524.

5. McFarland J.W., Avdeef A., Berger C.M., Raevsky O.A. ESTIMATING THE WATER SOLUBILITIES OF CRYSTALLINE COMPOUNDS FROM THEIR CHEMICAL STRUCTURES ALONE // J. Chem. Inf. Comput. Sci. 2001. Vol. 41. P. 1355-1359.

Selected works of O.A. Raevsky in the field of computer molecular design in Russian can be downloaded from the link :
https://new.ras.ru/upload/iblock/e23/ss3xm4zb5kbnioockwj3z72smie071j0.pdf?ysclid=m0f1jizolk18528432

The Laboratory of Quantitative Structure-Activity Relationships (QSAR)

Main research areas:

- experimental study of the physicochemical properties of physiologically active compounds
- study of the relationship between the structure and biological activity of chemical compounds based on machine learning
- creation of new approaches to studying the “structure – property” relationship using fractal geometry and nonlinear dynamics methods

Interests, hobbies, travels

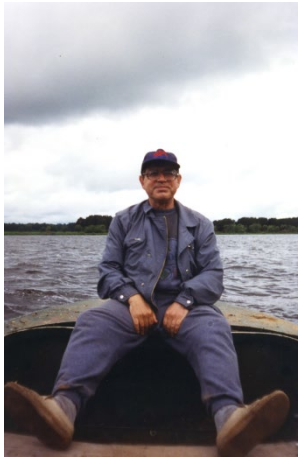
Chernogolovka, 2007

New York, 1995

Venice, 2007

Chernogolovka, 1991

Uglich, 1997



Thank you for your attention!