Results

MOLECULAR MODELING & COMPUTATIONAL CHEMISTRY

Editorial and News

As mentioned last month, the majority of the journal reviews are now simply covered in the main section of the reviews.

I would call your attention on few highlighted articles, particularly in the Applications section related to Nucleic Acids and Methodology section related to Potentials and Parameters and QM/MM.

R.Nageswar, Editor

1. <u>APPLICATIONS</u>

1.1.   *Small Molecules*

General and Model Systems

Molecular modeling of noncovalent binding of homochiral (3*S*,3′*S*)-astaxanthin to matrix metalloproteinase-13 (MMP-13).

Zsolt Bikádi, Eszter Hazai, Ferenc Zsila and Samuel F. Lockwood* [Hawaii Biotech, Inc.]

Bioorg. Med. Chem. **14**, 5451-5458 (2006)

The geometry and energetics of Homochiral astaxanthin (3*S*,3′*S*-AST; 3*S*,3′*S*-dihydroxy-β,β-carotene-4,4′-dione), an important antioxidant and anti-inflammatory xanthophyll carotenoid to human MMP-13 is studied. The whole protein target is used in Blind docking in order to identify the possible binding sites of AST. AST is predicted to bind at several sites in close proximity to the active center. The results suggested that AST could bind to MMP-13 with high affinity and favorable energetics and predicts potential direct enzyme-inhibitory activity of AST against MMP-13.

Streamlining lead discovery by aligning *in silico* and high-throughput screening.

J.W. Davies* [Novartis Inst. for Biomed. Res. Inc.], M. Glick and J.L. Jenkins

Curr.Opi.Stru.Biol. **10**, 343-351 (2006)

In silico screening is now incorporated in all areas of lead discovery; from target identification and library design, to hit analysis and compound profiling. In silico screening plays an important role and evolved over the past few years in the lead discovery.

How good is your screening library?

J.J. Irwin* [UCSF]

Curr.Opi.Stru.Biol. **10**, 352-356 (2006)

Small molecules have lower affinities and screened at high concentration, larger compounds will often more closely resemble final drugs. The best general-purpose screening libraries may well be those of intermediate complexity that are free of artifact-causing nuisance compounds.

A practical view of 'druggability'.

T.H. Keller* [NITD], A. Pichota and Zheng Yin

Curr.Opi.Stru.Biol. **10**, 357-361 (2006)

Drug-likeness and druggability is extended to proteins and genes for target identification and selection. This article focusing on the recent advances in the field and examines the usefulness of 'the rules of the game' in practice from a point of view for medicinal chemist's.

Water and Solvation

Molecular dynamics simulations of liquid methanol and methanol-water mixtures with polarizable models.

Haibo Yu, Daan P. Geerke, Haiyan Liu, Wilfred F. van Gunsteren[*] [Swiss Federal Inst. of Tech. Zurich]

J. Comp.Chem. **27**, 1494-1504, 2006.

The Charge-on-Spring (COS) technique is used to develop a polarizable model for simulation of liquid methanol, compatible with the COS/G2 water model. The energies of various methanol dimers in the gas phase are examined and compared them with *ab initio* calculations values. The model is used to study the thermodynamic, dynamic, structural, and dielectric properties of liquid methanol as well as of a methanol-water mixture.

Molecular studies of the structural properties of hydrogen gas in bulk water.

D. Sabo* [Sandia Nat. Labs.], S.B. Rempe, J.A. Greathouse, and M.G. Martin

Mol. Sim. **110**, 269-278, 2006.

The structural properties of a hydrogen molecule dissolved in liquid water are studied. MD, MC and ab initio molecular dynamics (AIMD) simulations are used to calculate the radial distribution function, coordination number and coordination number distribution. The results are agreed well with the average and most probable number of water molecules occupying the inner hydration sphere around hydrogen is 16.

Medicinal Chemistry and Drug Design

Trypanocidal agents with low cytotoxicity to mammalian cell line: A comparison of the theoretical and biological features of lapachone derivatives.

V.F. Ferreira* [Univ. of Federal Fluminense], A. Jorqueira, A.M.T. Souza, M.N. da Silva, M.C.B.V. de Souza, R.M. Gouvêa, C.R. Rodrigues, A.V. Pinto, H.C. Castro, D.O. Santos, H.P. Araújo and S.C. Bourguignon

Bioorg. Med. Chem. **14**, 5459-5466 (2006)

Molecular Modeling studies are used to analyze the C-ring moiety and the redox center of β-lapachone molecule. The computational methods are used to delineate the structural requirements for the trypanocidal profile pointed out that the transposition of the C-ring moiety of β-lapachone, combined with its oxyran ring, electrostatic potential map, dipole moment vector, and calculated log *P* parameter. This study could lead to the development of new antichagasic medicines based on α-lapachone analogs.

The application of systems biology to drug discovery.

C.R. Cho, M. Labow, M. Reinhardt, Jan van Oostrum and M.C. Peitsch* [Novartis Inst. of Biomed. Res.]

Curr.Op.Stru.Biol. **10**, 294-302 (2006)

Recent advances in scientific computing and mathematical modeling of biological processes are useful to the development of genome-scale functional screens, large collections of reagents, protein microarrays, databases and algorithms for data and text mining. The advanced methods and tools are useful to test the complex biological systems by mathematical modeling and simulation.

Genomic approaches to drug discovery.

Darrell O Ricke, Shaowen Wang, Richard Cai and Dalia Cohen* [Novartis Inst. for BioMed.Res.]

Curr.Opi.Stru.Biol. **10**, 303-308 (2006)

New tools are developed for gene expression data mining to reflect differences in pathways in normal and disease states. In addition, forward and reverse genetics used in a high-throughput mode with full-length cDNA and RNAi libraries enable the direct identification of components of signaling pathways. The discovery of the regulatory function of microRNAs highlights the importance of continuing the investigation of the genome with sophisticated tools.

1 August 2006

Medicinal Chemistry and Drug Design (cont'd)

Functional role of P-glycoprotein in limiting peroral drug absorption: Optimizing drug delivery.

M.V.S. Varma, O.P. Perumal and RameshPanchagnula*[Univ. of Ulster]

Curr.Opi.Stru.Biol. **10**, 367-373 (2006)

Advanced techniques in molecular biology and biochemical characterization methodologies have helped in identification of various transporters involved in absorption or secretion of drugs. P-gp and its functional role in limiting drug absorption is critical to improve predictability of dynamic absorption models and aid in selection of new candidates for development, and also widen the scope of peroral delivery for 'challenging' molecules.

Computational approaches for modeling human intestinal absorption and permeability.

G. Subramanian* [Albany Mol. Res., Inc.,] and D.B. Kitchen

*J.Mol.Mod.***12***,* 577-589 (2006)

Computational models are developed to predict the absorption of drugs by the human intestine and the permeability through human Caco-2 cells. The results are compared with the other models derived by other methods and found the similar statistical quality. It is concluded that the results showed that the qualitative predictions could be obtained with close to a 70% success rate.

Computational approaches for predicting CYP-related metabolism properties in the screening of new drugs.

P. Crivori and I. Poggesi* [Nerviano Med. Sci.]

Euro.J.Med.Chem. **41**, 795-808 (2006)

Advanced computational approaches are currently available for predicting different cytochrome P450 (CYP)-related metabolism endpoints. The present article describes the different approaches and their impact on drug development process. An indication on the available software for the implementation is also described.

A molecular design approach to peptide drug stabilization.

S. M. Thompson* [Univ. of Kansas], S. Sinha, E. M. Topp, K. V. Camarda

Mol. Sim. **110**, 291-295, 2006.

MD simulations are used to study the polymer's stabilizing effect. The system AcVYGNGA, a model peptide, is studied, and is explored both alone in various forms and complexed with poly(vinylpyrrolidone) (PVP). The results suggested that the peptide-polymer complex must have a secondary structure. The results are useful to develop a set of structure-property relations which could be included within an optimization framework to design new polymers for peptide stabilization.

Quantitative Structure-Activity Relations

QSAR for non-nucleoside inhibitors of HIV-1 reverse transcriptase.

 P.R. Duchowicz* [Univ. National de La Plata], M. Fernández, Julio Caballero, E.A. Castro and F.M. Fernández.

Bioorg. Med. Chem. **14**, 5876-5889 (2006)

QSAR models are developed for the potency pIC_{90} of 154 non-nucleoside reverse transcriptase inhibitors (NNRTI) of the wild-type HIV-1 virus, considered as the second generation analogues of Efavirenz. Dragon 5 software is used by selection of the variables like forward stepwise regression, the replacement method, and the genetic algorithm approach.

Quantitative Structure-Activity Relationships (cont'd)

T!
CoMFA and CoMSIA investigations of dopamine D3 receptor ligands leading to the prediction, synthesis, and evaluation of rigidized FAUC 365 analogues.

I. Salama, K. Schlotter, W. Utz, H. Hübner,
P. Gmeiner and F. Boeckler* [Friedrich Alexander Univ.]

Bioorg. Med. Chem. **14**, 5898-5912 (2006)

CoMFA and CoMSIA are used to develop the 3D-QSAR models for dopamine D3 descriptors and investigated to assure their stability and predictivity.

Unify QSAR approach to antimicrobials. Part 1: Predicting antifungal activity against different species.

H. González-Díaz* [Univ. of Santiago de Compostela], F.J. Prado-Prado, L. Santana and
E. Uriarte

Bioorg. Med. Chem. **14**, 5973-5990 (2006)

The present work unify the Markov model to describe a single linear equation of the biological activity of 74 drugs tested against some of the fungi species selected from a list of 87 species. The data is processed by linear discriminant analysis classifying drugs as active or non-active against the different tested fungi species. The model correctly classifies 338 out of 368 active compounds and 89 out of 123 non-active compounds. Validation of the model is carried out by means of leave-species-out (LSO) procedure.

QSAR analysis of antimicrobial and haemolytic effects of cyclic cationic antimicrobial peptides derived from protegrin-1.

Vladimir Frecer* [Slovak Academy of Sciences]

Bioorg. Med. Chem. **14**, 6065-6074 (2006)

QSAR models are developed through genetic function approximation algorithm for antimicrobial and haemolytic activities of porcine protegrin-1 (PG-1) mimetics-cyclic cationic peptides with β-hairpin fold. The results are correlated with the antimicrobial potencies to the peptide's charge and amphipathicity index, while the haemolytic effect correlates well with the lipophilicity of residues forming the nonpolar face of the β-hairpin.

A QCAR-approach to materials modeling.

S. Sieg, B. Stutz, T. Schmidt, F. Hamprecht and W.F. Maier* [Univ. des Saarlandes]

*J.Mol.Mod.***12**, 609-619 (2006)

Support Vector Machines, multilevel B-splines approximation and Kriging approaches are applied to model the complete composition space of the mixed oxides of Ni-Cr-Mn and of Ni-Co-Mo-Mn for the oxidation of propene to acroleine. The results, that correlate chemical composition with function of heterogeneous catalysts. These approximation techniques are useful to predict the composition of the most active catalysts.

Investigation of substituent effect of 1-(3,3-diphenylpropyl)-piperidinyl phenylacetamides on CCR5 binding affinity using QSAR and virtual screening techniques.

A. Afantitis, G. Melagraki, Haralambos Sarimveis* [Nat.Tech.Univ. of Athens], P.A. Koutentis, J. Markopoulos and O. Igglessi-Markopoulou

J. Comp.-Aided Mol. Design. **20**, 83-95 (2006)

Multiple linear regression analysis is used to develop a linear quantitative-structure activity relationship model for a series of 1-(3,3-diphenylpropyl)-piperidinyl phenylacetamides derivatives with CCR5 binding affinity. Elimination Selection-Stepwise Regression Method (ES-SWR) is used for the selection of the best variables and the predictive ability of the model is evaluated against a set of 13 compounds. The results leads to a number of guanidine derivatives with significantly improved predicted activities.

Quantitative Structure-Activity Relationships (cont'd)

QSAR models based on quantum topological molecular similarity.

P.L.A. Popelier* [Univ. of Manchester] and P.J. Smith

Euro.J.Med.Chem. 41, 862-873 (2006)

Quantum topological molecular similarity (QTMS) is proposed to construct a variety of medicinal, ecological and physical organic QSAR/QSPRs. QTMS method uses quantum chemical topology (QCT) to define electronic descriptors drawn from modern *ab initio* wave functions of geometry-optimised molecules. The best models are obtained through a partial least square analysis in conjunction with a genetic algorithm. They are also able to highlight the active site, of the ligand or the molecule whose structure determines the activity.

Highly predictive CoMFA and CoMSIA models for two series of stromelysin-1 (MMP-3) inhibitors elucidate S1' and S1-S2' binding modes.

Elizabeth A. Amin* [Univ. of Minnesota] and William J. Welsh.

J. Chem. Inf. Model. **46** (4), 1775 -1783, 2006.

CoMFA and CoMSIA are performed to derive 3D-QSAR models for two training sets of arylsulfonyl isoquinoline-based and thazine/thiazepine-based matrix metalloproteinase inhibitors (MMPIs). Stromelysin-1 (MMP-3) crystal structure is used to pinpoint areas on the ligands and receptors.

Host-Guest Systems

Structural and quantum chemical studies of 8-aryl-sulfanyl adenine class Hsp90 inhibitors.

R.M. Immormino,Y. Kang, G. Chiosis, and D.T. Gewirth* [Memorial Sloan-Kettering Cancer Cent.]

J. Med. Chem., **49** (16), 4953 -4960, 2006

The structures of the water soluble 8-aryl-sulfanyl adenine class Hsp90 inhibitors, PU-H71 and PU-H64, in complex with the *N*-terminal domain of human Hsp90α is reported. Quantum chemical calculations of PU-H64 and its analogues that illuminate their basis for Hsp90 inhibition is presented.

Evidence for a synergistic salt-protein interaction-complex pattern of activation vs. inhibition of nitrogenase by salt.

P.E. Wilson, A.C. Nyborg, J.Kenealey, T.J. Lowery, K. Crawford, C.R. King, A.J. Engan, J.L. Johnson and G.D. Watt* [Brigham Young Univ.]

*Biophysical J.***122**, 184-194 (2006)

Interactions between MoFe and the Fe proteins and between Fe protein and nucleotides (MgADP and MgATP) are important to catalysis. The salt effects are investigated for nitrogenase interactions to offer an in-depth analysis of the sources of salt inhibition and underlying apparent cooperativity. It is observed that charge screening of MoFe protein–Fe protein interactions in the nitrogenase complex accelerates the rate of nitrogenase complex dissociation.

Molecular modeling the reaction mechanism of serine-carboxyl peptidases.

Ksenia Bravaya, A. Bochenkova, B. Grigorenko, I. Topol, Stanley Burt, and A. Nemukhin* [Russian Acad. of Sci.]

J. Chem. Theory and Comp. **2**, 1168-1175, 2006.

The structure of the sedolisin-inhibitor complex designed the model enzyme-substrate complex and QM-MM calculations are performed to calculate the energy of the acylenzyme complex. The PBE0 exchange-correlation functional and the basis set 6-31+G** in the quantum part and the AMBER force field parameters in the molecular mechanical part are used to calculate the energies and forces. The reaction mechanism of serine-carboxyl peptidases should be viewed as a special case of carboxyl proteases, with the nucleophilic water molecule being replaced by the Ser residue.

Host-Guest Systems (cont'd)

Minimizing false positives in kinase virtual screens

Emanuele Perola*[Vertex Pharm.]

Proteins: Stru. Fun. and Bioinfo. **64**, 422-435, 2006.

The distinctive features of false positives in kinase virtual screens are investigated. A series of retrospective virtual screens on kinase targets is performed on specifically designed test sets, each combining true ligands. Docking studies generated for the top-ranking compounds highlighted key aspects differentiating true hits from false positives. The false-positive rates are significantly reduced and the enrichment factors increased by an average of twofold. The results suggested a generalized two-step protocol for virtual screening on kinase targets.

Carbon Nanoparticles

Pt-Ru supported on double-walled carbon nanotubes as high-performance anode catalysts for direct methanol fuel cells.

Wenzhen Li, Xin Wang, Z. Chen, Mahesh Waje, and Yushan Yan* [Nanyang Tech. Univ.]

J. Phys. Chem. B. **110**, 15353 -15358, 2006.

Ethylene glycol method is used to prepare the Pt-Ru supported carbon nanotubes catalysts. The Pt-Ru/DWNTs catalyst shows the highest specific activity for methanol oxidation reaction and the highest performance as an anode catalyst in direct methanol fuel cell single cell tests. The DMFC single cell with Pt-Ru/DWNTs produces a 68% enhancement of power density, and at the same time, an 83% reduction of Pt-Ru electrode loading when compared to Pt-Ru/C.

Surface segregation phenomena in Pt-Pd nanoparticles: Dependence on nanocluster size.

G. E. Ramirez Caballero* [Texas A&M Univ.] and P. B. Balbuena

Mol. Sim. **110**, 297-303, 2006.

MD simulations are used to investigate the effect of the nanocluster size on surface segregation phenomena of Pt alloys. The percent of the surface enriched either in Pt or Pd at a given concentration depends on the cluster size. The results suggested that surface segregation behavior in Pt-Pd supported nanoclusters is influenced by: differences in surface energies, interaction of the clusters with the substrate, and probably most importantly by the fabrication protocol.

1.2. *Biopolymers*

Comparative or Homology Modeling

Homology model of RSK2 N-terminal kinase domain, structure-based identification of novel RSK2 inhibitors, and preliminary common pharmacophore.

T. Luong Nguyen* [SAIC-Frederick, Inc.], R. Gussio, J.A. Smith, D.A. Lannigan, S.M. Hecht, D.A. Scudiero, R.H. Shoemaker and and D.W. Zaharevitz
Bioorg. Med. Chem. **14**, 6097-6105 (2006)

An atomic model of the RSK2 NTD (residues 68–323), which was built to simultaneously bind the distinctive molecular scaffolds of SL0101, Ro31-8220, and GF109203X. The RSK2 NTD model is used to identify two novel RSK2 inhibitors from the National Cancer Institute open chemical repository and to develop a preliminary structure-based pharmacophore model.

Comparative or Homology modeling (cont'd)

Comparison of a homology model and the crystallographic structure of human 11β-hydroxysteroid dehydrogenase type 1 (11βHSD1) in a structure-based identification of inhibitors

L. Miguet, Z. Zhang, M. Barbier and M.G. Grigorov* [Nestlé Res. Cent.]

J. Comp.-Aided Mol. Design. **20**, 67-81(2006)

Homology modeling is employed to build the 3D structure of 11βHSD1. Molecular docking is used to validate the predicted model by showing that it is able to discriminate between known 11βHSD1 inhibitors or substrates and non-inhibitors. Structure-based virtual screening experiments are carried out on both the homology model and the crystallographic structure with a database of 114'000 natural molecules. 15 molecules are consistently selected as inhibitors based on both the homology model and crystal structures of the enzyme.

A!
Comparative model of EutB from coenzyme B_{12}-dependent ethanolamine ammonia-lyase reveals a $\beta_8\alpha_8$, TIM-barrel fold and radical catalytic site structural features.

Li Sun, Kurt Warncke* [Emory Univ.]

Proteins: Stru. Fun. and Bioinfo. **64**, 308-319, 2006.

MODELLER is used to construct the structure of the EutB protein from Salmonella typhimurium, contains the active site of the coenzyme B_{12}. PROCHECK and VERIFY3D.are used to evaluate the model. The results identify a $\beta_8\alpha_8$, TIM-barrel fold for EutB, is consistent with a central role of the α/β-barrel structures in radical catalysis conducted by the coenzyme B_{12}- and S-adenosylmethionine-dependent enzyme superfamilies.

Protein Folding

Amino acid substitutions affecting protein dynamics in eglin C do not affect heat capacity change upon unfolding.

A.V. Gribenko, T.R. Keiffer, G.I. Makhatadze* [Penn State Univ. Coll. of Med.]

Proteins: Stru. Fun. and Bioinfo. **64**, 295-300, 2006.

Empirical surface area-based calculations could predict heat capacity changes reasonably well, and suggested that changes in hydration of those surfaces is not the only parameter contributing to the observed heat capacity changes upon unfolding. Protein dynamics changes resulting in increased rigidity of the protein structure might contribute to the observed heat capacity change upon unfolding.

Protein Dynamics

Topological and dynamical properties of Azurin anchored to a gold substrate as investigated by molecular dynamics simulation.

A. Rita Bizzarri* [Univ. della Tuscia]

Biophysical J. **122**, 206-214 (2006)

MD simulations are performed to study the electron transfer of the azurin, covalently bound to a gold substrate through its native disulphide group. Simulations and electric field are applied on neutral, positively and negatively charged substrates to investigate the effects on the protein structure and dynamics. The orientation, the height and the size of the protein with respect to the substrate are compared with the experimental data.

Structural stability and dynamics of an amyloid-forming peptide GNNQQNY from the yeast prion sup-35.

J. Zheng, B. Ma, Chung-Jung Tsai and R. Nussinov*[NCI-Frederick]

Biophysical J. **91**, 824-833 (2006)

All-atom explicit solvent MD simulations of various sizes and arrangements of oligomer seeds of the wild-type and its mutants to study its stability and dynamics. The results suggested that within the sheet, the driving forces to associate and stabilize are interstrand backbone-backbone and side chain-side chain hydrogen bonds, whereas between the sheets, shape-complementary by the dry polar steric zipper via the side chains of Asn-2, Gln-4, and Asn-6 holds the sheets together.

Protein-Dynamics (cont'd)

Dynamics of the WPD loop of the yersinia protein tyrosine phosphatase.

Xin Hu and C. Erec Stebbins* [The Rockefeller Univ.]

Biophysical J. **91**, 948-956 (2006)

MD simulations are used to investigate the conformational changes and dynamics of the WPD loop. The results are correlated with the experimental observations, showed that the WPD loop of YopH is intrinsically flexible and fluctuates between the open and closed conformation. The dynamic behavior of the WPD loop for the C403S mutant differs from the wild-type YopH. The results showed the role of the WPD loop in PTPase-mediated catalysis, and are useful in structure-based design for novel, selective YopH inhibitors as antibacterial drugs.

Adhesive dynamics simulation of neutrophil arrest with deterministic activation.

E.F. Krasik, K. Lai Yee and D.A. Hammer* [Univ. of Pennsylvania]

Biophysical J. 91, 1145-1155 (2006)

The ligation of E-selectin could stimulate the firm adhesion of neutrophils via a MAP-kinase cascade. An integrated model by combining two methodologies: a mechanics-based modeling of leukocyte adhesion (adhesive dynamics) and signal transduction pathway modeling is developed to study the possible mechanism by which neutrophil arrest could occur. This model is allowed to understand how intracellular signaling activity could set the timescale of neutrophil activation, adhesion, and diapedesis.

Molecular dynamics simulation of Leishmania major surface metalloprotease GP63 (leishmanolysin).

G. Bianchini , A. Bocedi , P. Ascenzi , E. Gavuzzo, F. Mazza, Massimiliano Aschi**** [Univ. L'Aquila]

Proteins: Stru. Fun. and Bioinfo. **64**, 385-390, 2006.

MD simulation of Leishmania major GP63 in water at pH 7 is reported. Upon solvation, GP63 undergoes a sharp structural relaxation with respect to the crystal structure. The results suggested that the N-terminal domain of GP63 is activating the proenzyme and the residues involved in the interdomain bending result highly conserved.

Local feature analysis: A statistical theory for reproducible essential dynamics of large macromolecules

Zhiyong Zhang, Willy Wriggers[*] [Univ. of Texas Health Sci.Cent. at Houston]

Proteins: Stru. Fun. and Bioinfo. **64**, 391-403, 2006.

The application of local feature analysis (LFA) to construct a topographic representation of functional dynamics is described. The LFA representations are low dimensional, and like PCA provide a reduced basis set for collective motions. The results are more reliable assignment of essential dynamics modes across different MD time windows. The intrinsic dynamics of local domains is more extensively sampled than that of globally coherent PCA modes.

Nucleic Acids

Collective dynamics of EcoRI-DNA complex by elastic network model and molecular dynamics simulations.

P. Doruker* [Bogazici Univ.], L. Nilsson and O. Kurkcuoglu

J. Biomol. Stru. and Dynamics. **10**, 1-6 (2006)

Anisotropic network model (ANM) is used to analyze the collective motions of restriction enzyme *Eco*RI in free form and in complex with DNA. Three independent MD simulations are performed for the *Eco*RI-DNA complex in explicit water to compare the analyzed results. The results indicated that the stems of the inner loops are quite immobile even in the free enzyme and form a large, almost fixed, pocket for DNA binding.

Nucleic Acids (cont'd)

Shape similarity measures for the design of small RNA switches.

Assaf Avihoo, Danny Barash* [Univ. of Haifa]

J. Biomol. Stru. and Dynamics. **10**, 17-24 (2006)

The aim is to computationally design small RNA switches that rely on the riboswitches. MD simulations utilize a variety of different similarity measures to assess the distances between an initial state and triggered states. These combined similarity measures that rely on both coarse-grained and fine-grained graph representations of the RNA secondary structure are described.

Possible inhibition of group-I intron RNA by resveratrol and genistein.

S. Usha, I.M. Johnson and R. Malathi* [Univ. of Madras]

J. Biomol. Stru. and Dynamics. **10**, 17-24 (2006)

Group I intron RNA is a unique class of RNA molecule that undergoes self-catalytic activity due to its unique folded structure that catalyze number of cellular reactions. The binding efficacy of resveratrol and genistein to group I intron RNA transcript and circular-intervening sequences of *Tetrahymena thermophila* and the binding efficacy of resveratrol and genistein to 25S rRNA of *C. albicans* is measured by quantification of the RNA using densitometric method. The results suggested that these natural compounds might bind with intron RNA and act as an potential target and modulates the cellular process during therapeutic intervention.

Sequence structure of human nucleosome DNA.

S.B. Kogan, M. Kato, R. Kiyama and E.N. Trifonov* [Univ. of Haifa].

J. Biomol. Stru. and Dynamics. **10**, 43-48 (2006)

The dominance of oscillating GG and CC dinucleotides in human nucleosomes and the contribution of AG(CT), GA(TC), and AA(TT) suggested a general nucleosome DNA sequence pattern -counterphase oscillation of RR and YY dinucleotides. AA and TT dinucleotides, commonly accepted as major players, are only weak contributors in the case of human nucleosomes.

Probing the nature of hydrogen bonds in DNA base pairs.

Yirong Mo* [Western Michigan Univ.]

*J.Mol.Mod.***12***,* 665-672 (2006)

Energy decomposition analyses based on the block-localized wave-function (BLW-ED) method are used to investigate the nature of the hydrogen bonds in DNA base pairs in terms of deformation, Heitler-London, polarization, electron-transfer and dispersion-energy terms. A modest electron-transfer effect is found in the Watson-Crick adenine-thymine (AT), guanine-cytosine (GC) and Hoogsteen adenine-thymine (H-AT) pairs, confirming the weak covalence in the hydrogen bonds. Theoretical and experimental results showed that the GC pair has a binding energy twice that of the AT and H-AT pairs, compared with three conventional N-H···O(N) hydrogen bonds in the GC pair and two in the AT or H-AT pair.

Bioactive principles in the bark of Pilidiostigma tropicum.

W.N. Setzer* [Univ. of Alabama in Huntsville], G.F. Rozmus, M.C. Setzer, J.M. Schmidt, B. Vogler, Sabine Reeb, B.R. Jackes and A.K. Irvine

*J.Mol.Mod.***12***,* 665-672 (2006)

Molecular mechanics and *ab initio* molecular-orbital techniques are used to investigate the intercalation interaction of rhodomyrtoxin B with DNA. A favorable π-π interaction between rhodomyrtoxin B and the cytosine-guanine base pair is predicted, but the orientation of the interaction cannot be predicted based on frontier molecular orbitals.

Nucleic Acids (cont'd)

Mutagenic nucleotide incorporation and hindered translocation by a food carcinogen C8-dG adduct in *Sulfolobus solfataricus* P2 DNA polymerase IV (Dpo4): Modeling and dynamics studies.

L. Zhang, O. Rechkoblit, Lihua Wang, D.J. Patel, R. Shapiro and Suse Broyde* [New York Univ.]

Nucleic Acids Research. 34, 3326-3337 (2006)

MD simulations are used to investigate the nucleotide incorporation opposite the major adduct of 2-amino-1-methyl-6-phenylimidazo[4,5-*b*]-pyridine in the DinB family polymerase, Dpo4. The simulations indicated that dATP and dTTP are better incorporated in the damaged system than in their respective mismatches. Bulky C8-dG adducts, situated in the major groove are likely to impede translocation in this polymerase.

A!
Three-dimensional modeling of cytomegalovirus DNA polymerase and preliminary analysis of drug resistance.

Rong Shi , Arezki Azzi, Christian Gilbert , Guy Boivin**
[CHUL Hospital and Laval Univ.], Sheng-Xiang Lin

Proteins: Stru. Fun. and Bioinfo. **64**, 301-307, 2006.

3D-Jury Meta server and the program MODELLER are used to build the 3D models of closed and open conformations for CMV DNA polymerase based on the crystal structures of bacteriophage RB69 DNA polymerase. The results are useful to understand drug resistance mechanisms for CMV and the interpretation of novel viral mutations.

Free Energy

Minor groove deformability of DNA: A molecular dynamics free energy simulation study.

Martin Zacharias* [International University Bremen]

Biophysical J. **91**, 882-891 (2006)

An explicit solvent MD simulation in combination with the umbrella sampling approach is used to investigate the molecular mechanism of DNA minor groove deformations and the indirect energetic contribution to protein binding. The resulting deformed structures showed close agreement with experimental DNA structures in complex with minor groove-binding proteins.

Predicting RNA secondary structure by free energy minimization.

David H. Mathews*[Univ. of Rochester Med. Cent.]

Theor.Chem.Accounts., **116***, 160-168 (2006)

The stability of a given RNA secondary structure could be quantified using nearest neighbor free energy parameters. These parameters are the basis of a number of free energy minimization algorithms that predict RNA secondary structure for either a single sequence or multiple sequences. The progress of RNA secondary structure prediction by free energy minimization and the developed algorithms are reviewed.

Membrane Proteins and Lipid-Peptide Interactions

Cholesterol inhibits the insertion of the Alzheimer's peptide Aβ(25–35) in lipid bilayers.

Silvia Dante* [Darmstadt Univ. of Tech.], Thomas Hauß and N.A. Dencher

J. Europ.Biophys. **35**, 523 -531, 2006.

Cholesterol alters the capability of Aβ(25–35) to penetrate into the lipid bilayers at the molecular level. At very low cholesterol content, the location of the C-terminal part of Aβ(25–35) is unequivocally established in the hydrocarbon region of the membrane, correlated with the previous results on pure phospholipids membrane. The results link a structural property to a physiological and functional behavior and point to a therapeutical approach to prevent the AD by modulation of membrane properties.

Membrane Proteins and Lipid-Peptide Interactions (cont'd)

Interaction of the sugars trehalose, maltose and glucose with a phospholipid bilayer: A comparative molecular dynamics study.

C.S. Pereira and P.H. Hünenberger* [ETH-Hönggerberg]

J. Phys. Chem. B. **110**, 15572 -15581, 2006.

MD simulations are used to investigate the interaction of the sugars trehalose, maltose, and glucose with a phospholipid bilayer at atomic resolution. The three sugars are interact directly with the lipid headgroups through hydrogen bonds, replacing water at about one-fifth to one-quarter of the hydrogen-bonding sites provided by the membrane at 325 K.

Molecular investigation of the interactions of trehalose with lipid bilayers of DPPC, DPPE and their mixture.

S. Leekumjorn* [Virginia Polytechnic Inst. and State Univ.], and A. K. Sum.

Mol. Sim. **110**, 219-230, 2006.

MD simulations are performed to study structural and dynamic properties of fully hydrated pure and mixed bilayers of 1,2-dipalmitoyl-*sn*-glycero-3-phosphocholine (DPPC) and 1,2-dipalmitoyl-*sn*-glycero-3-phosphoethanolamine (DPPE) in the presence of trehalose. For the pure DPPE bilayer, an excess of hydrogen-donors create a competitive hydrogen bonding environment that weakens lipid–lipid interactions and favors hydration of the amine groups, which enhances the binding of trehalose with the bilayer.

Interactions of the C2 domain of human factor V with a model membrane.

Luca Mollica, F. Fraternali, Giovanna Musco* [Dulbecco Telethon Inst.], Giovanna Musco.

Proteins: Stru. Fun. and Bioinfo. **64**, 363-375, 2006.

MD simulations are performed on the open and closed conformers of domain C2 of coagulation Factor V (FaVC2) in water and in the presence of a neutral phospholipids bilayer model to investigate the mechanism, the dynamics and the energetics of the binding process. The results are consistent with the experimental values and suggested PS interaction site. The structural data is further useful to the design of potential inhibitors able to disrupt membrane association.

Delineating common molecular mechanisms in Alzheimer's and prion diseases.

K.J. Barnham, R. Cappai, K. Beyreuther, C.L. Masters and A.F. Hill* [The Univ. of Melbourne]

Trends in Biochem. Sci. **31**, 465-472 (2006)

The mechanism of Aβ toxicity is mediated through the coordination of redox-active transition-metal ions such as copper leading to the generation of reactive oxygen species, coupled with the propensity to interact with lipid bilayers. Key sequence and chemical similarities between prion protein (PrP) and Aβ indicate that similar therapeutic strategies might be applicable for the treatment of Alzheimer's and prion diseases.

Ligand Binding

The binding of 3′-*N*-piperidine-4-carboxyl-3′-deoxy-*ara*-uridine to ribonuclease A in the crystal.

D.D. Leonidas* [The Nati. Hellenic Res. Found.], T. Kanti Maiti, A. Samanta, S. Dasgupta, T. Pathak, S.E. Zographos and N.G. Oikonomakos.

Bioorg. Med. Chem. **14**, 6055-6064 (2006)

The binding mode of the inhibitor, 3′-*N*-piperidine-4-carboxyl-3′-deoxy-*ara*-uridine, to ribonuclease A is studied. Two inhibitors are bound in the central RNA binding cavity of RNase A exploiting interactions with residues from peripheral binding sites. The first inhibitor molecule occupies the purine-preferring site of RNase A, the rest of the molecule projects to the solvent. The second inhibitor molecule binds with the carboxyl group at the pyrimidine recognition site and the uridine moiety exploits interactions with RNase A residues Lys66, His119 and Asp121.

Ligand Binding (cont'd)

Novel potent and selective α_vβ_3/α_vβ_5 integrin dual antagonists with reduced binding affinity for human serum albumin.

P. Raboisson, C.L. Manthey, M. Chaikin, J. Lattanze, C. Crysler, K. Leonard, W. Pan, B.E. Tomczuk and J.J. Marugán* [Johnson & Johnson Pharm.Res. & Develop.]

Euro.J.Med.Chem. **41**, 847-861 (2006)

Structure-activity HSA binding data of organic acids have demonstrated that the incorporation of polar groups into a given molecule can dramatically decrease the affinity toward HSA. This strategy is applied by examining the effects of such modifications in both the central core constrain and the substituent-β to the carboxylate. The results lead with improved drug-like properties for further evaluations in the field of oncology and osteoporosis.

Synthesis of anthranylaldoxime derivatives as estrogen receptor ligands and computational prediction of binding modes.

T. Tuccinardi, S. Bertini, A. Martinelli, F. Minutolo* [Univ. of Pisa], G. Ortore, G. Placanica, G. Prota, S. Rapposelli, K.E. Carlson, J.A. Katzenellenbogen, and M. Macchia.

J. Med. Chem., **49** (16), 5001 -5012, 2006

Ligand docking followed by molecular mechanics Poisson-Boltzmann/surface area (MM-PBSA) studies suggested a molecular basis for the interaction of 3-and 4-phenyl rings of the *N*-Me-anthranylaldoximes compounds with the ERs and enabled the development of models able to predict the mode of ligand binding.

Computational characterization of metal binding groups for metalloenzyme inhibitors.

K.D. Dobbs, A.M. Rinehart, M.H. Howard, Ya-Jun Zheng, and D.A. Kleier* [Stine-Haskell Res. Cent.]

J. Chem. Theory and Comp. **2**, 990-996, 2006.

Electronic structure calculations are performed to characterize the binding ability of various metal binding groups on ligand displacement reactions in a model system related to the metalloenzyme, peptide deformylase. Qualitative considerations of electronic structure inspired by the calculations provide an understanding of binding energy trends across a variety of ligands for a given metal and across a variety of metals for a given ligand.

Structures of N-acetylornithine transcarbamoylase from Xanthomonas campestris complexed with substrates and substrate analogs imply mechanisms for substrate binding and catalysis.

Dashuang Shi * [Children's Nati. Med. Cent.], Xiaolin Yu, Lauren Roth, H. Morizono, M. Tuchman, N.M. Allewell

Proteins: Stru. Fun. and Bioinfo. **64**, 532-542, 2006.

Crystal structures of the binary complexes of AOTCase with its substrates, carbamoyl phosphate (CP) or *N*-acetyl-L-ornithine (AORN), and the ternary complex with CP and *N*-acetyl-L-norvaline are reported. The structures are compared resulting the substrate-binding mechanism of this novel transcarbamoylase is different from those of aspartate and ornithine transcarbamoylases, both of which show ordered substrate binding with large domain movements.

Enzyme Catalysis

Quantum chemistry applied to the mechanisms of transition metal containing enzymes - Cytochrome *c* oxidase, a particularly challenging case.

M.R. A. Blomberg* [AlbaNova Univ. Cent. Stockholm Univ.], Per E. M. Siegbahn

J. Comp.Chem. **27**, 1373-1384, 2006.

DFT with B3LYP basis set is used to study the mechanisms of O-O bond cleavage and proton pumping in cytochrome c oxidase. Models are designed to understand how the energy from the exergonic reduction of molecular oxygen is used to pump the protons across the mitochondrial membrane.

Protein-Protein Interactions

Development of small molecules designed to modulate protein-protein interactions.

Ye Che*[NIH], B.R. Brooks and G.R. Marshall

J. Comp.-Aided Mol. Design. **20**, 109-130 (2006)

A general approach is described based on the "privileged-structure hypothesis" – that any organic templates capable of mimicking surfaces of protein-recognition motifs are potential privileged scaffolds as protein-complex antagonists - to address the challenges inherent in the discovery of small-molecule inhibitors of protein-protein interactions.

Molecular dynamics with quantum statistics: Time correlation functions and weakly bound nano-clusters.

Pierre-Nicholas Roy* [Univ. of Alberta]

Trends in Biochem. Sci. **31**, 436-444 (2006)

Protein complexes are involving in the binding of linear motifs in one of the binding partners. An emerging mechanism of such non-covalent peptide–surface interaction involves the donation or addition of a β strand in the ligand to a β sheet or a β strand in the receptor. β-sheet augmentation, β-strand insertion and fold complementation, and β-strand zippering are the main classes for protein-protein contacts.

Lipids and Surfactants

Effects of mutations on the C-terminus of protegrin-1: A molecular dynamics simulation study.

A. A. Langham* [Univ. of Minnesota] and Y. N. Kansas.

Mol. Sim. **110**, 193 -201, 2006.

MD simulations are performed in sodium dodecylsulphate and dodecylphosphocholine micelles, bacterial and mammalian membrane mimics to study the effects of the charge of the C-terminus of protein-like peptides on activity and toxicity. Three protegrin mutants are examined and observed that while the peptides interact in different ways, the peptides all insert into the SDS micelles equally as deep, in agreement with their equal activities.

1.3.   *Surfaces, Catalysts, and Material Subjects*

Self-assembly of peptide scaffolds in biosilica formation: Computer simulations of a coarse-grained model.

Leonardo Lenoci and Philip J. Camp* [Univ. of Edinburgh]

J. Am. Chem. Soc. **128**, 10111 -10117, 2006.

Brownian dynamics simulations are used to design a coarse-grained, bead-spring model to mimic silaffins and to promote the formation of amorphous silica nanospheres. The results indicated that over a broad range of volume fractions, the characteristic structural lengthscales fall in the range 12-45 nm. The results suggested that self-assembled structures act as either nucleation points or scaffolds for the deposition of 10-100 nm silica-peptide building blocks from which diatom skeletons and synthetic nanospheres are constructed.

Mechanistic study of the electrochemical oxygen reduction reaction on Pt(111) using density functional theory.

M.P. Hyman and J.W. Medlin* [Univ. of Colorado]

J. Phys. Chem. B. **110**, 15338 -15344, 2006.

DFT is used to study the electrolyte solution effects on the oxygen reduction reaction on Pt(111). $H_5O_2^+$ cluster is used to model the acid electrolyte. The results suggested that O_2 protonation precedes dissociation in the oxygen reduction reaction.

Surfaces, Catalysts, and Material Subjects (cont'd)

Simulations of glasses: Multiscale modeling and density of states Monte-Carlo simulations. J. Ghosh* [UC Davis], B.Y. Wong, Q. Sun, F.R. Pon, and R. Faller *Mol. Sim.* **110**, 175 -184, 2006.	Density of states (DOS), Monte-Carlo and multiscale modeling techniques are used to study the glass transition. DOS Monte-Carlo using the two-dimensional Ising model without external field on lattices of varying size is reviewed and the results of a model binary glass former are well compared. Self-consistent systematic mapping procedure for molecular models from the atomistic to the mesoscale is presented.
Molecular simulation of the thermophysical properties of fluids: Phase behaviour and transport properties. R. J. Sadus* [Swinburne Univ. of Tech.] *Mol. Sim.* **110**, 185 -189, 2006.	The application of molecular simulation to the prediction of the thermophysical properties of fluids relevant to chemical engineering applications is studied. The role of three-body interactions on the vapour-liquid coexistence of fluids is illustrated and compared with the experimental results. Molecular simulations are used to compare the viscosities of dendrimer fluids with linear polymers of equivalent molecular weight.
Molecular dynamics with quantum statistics: Time correlation functions and weakly bound nano-clusters. Pierre-Nicholas Roy* [Univ. of Alberta] *Theor.Chem.Accounts.,* **116***, 274-280 (2006)	The exact basis set techniques could be used to perform highly accurate calculations, complex bosonic systems such as doped helium clusters, Quantum Monte Carlo techniques could be used for the calculation of quantities of experimental interest. A perspective on future prospects for the calculation of real time correlation functions of bosonic nano-scale systems is presented.

2. <u>METHODOLOGY</u>

Quantitative Structure-Activity Relations

Structural insights into monoamine oxidase inhibitory potency and selectivity of 7-substituted coumarins from ligand- and target-based approaches. Marco Catto, Orazio Nicolotti, Francesco Leonetti, Andrea Carotti, Angelo Danilo Favia, Ramón Soto-Otero, Estefanía Méndez-Álvarez, and Angelo Carotti* [Univ. de Santiago de Compostela] *J. Med. Chem.,* **49** (16), 4912 -4925, 2006	CoMFA-GOLPE and docking studies are performed to derive the structure-affinity and structure-selectivity relationships for a series 3-, 4-, 7-polysubstituted coumarins. The physico-chemical properties of the monoamine oxidase A and monoamine oxidase B inhibitory potency and suggested the main structural determinants for high selectivity toward one of the two enzymatic forms. The predictive power of the derived model is proved with the design of a new inhibitor provide the MAO-B affinity and the highest MAO-B selectivity within the entire series of examined ligands.
A steroids QSAR approach based on approximate similarity measurements. M. Urbano Cuadrado, I. Luque Ruiz* [Inst. of Chem. Res. of Catalonia ICIQ], and M.A. Gómez-Nieto. *J. Chem. Inf. Model.* **46** (4), 1678 -1686, 2006.	A new QSAR method is developed based on the approximate similarity is applied to predict the steroids binding mode to the corticosteroid globulin receptor. The proposed model allowed to obtain valuable external predictions after training the model by cross-validation.

Quantitative Structure-Activity Relationships (cont'd)

A!
Exploration of a binding mode of benzothiazol-2-yl acetonitrile pyrimidine core based derivatives as potent c-Jun N-terminal kinase-3 inhibitors and 3D-QSAR analyses.

Pooja Sharma and Nanda Ghoshal* [Indian Inst. of Chem. Biol.]

J. Chem. Inf. Model. **46** (4), 1763 -1774, 2006.

Molecular docking and 3D-QSAR studies are performed on a set of 44 compounds of benzothiazol-2-yl acetonitrile derivatives. Ligand Fit module of Cerius2 is employed to locate the binding orientations of all the compounds within the JNK-3 ATP binding site. The calculated binding free energies suggested the identified binding conformations of potential inhibitors are reliable. The developed models are useful to design a novel inhibitor based on the benzothiazole derivatives against JNK-3 for the treatment of inflammatory disorders.

A structure-based 3D-QSAR study of anthrapyrazole analogues of the anticancer agents Losoxantrone and Piroxantrone.

H. Liang, X. Wu, L.J. Guziec, F.S. Guziec, Jr., K.K. Larson, J. Lang, J.C. Yalowich, and B. B. Hasinoff* [Univ. of Pittsburgh Sch. of Med.]

J. Chem. Inf. Model. **46** (4), 1827 -1835, 2006.

CoMFA and CoMSIA were carried out on the aligned structures of the anthrapyrazoles docked into DNA in 3D-QSAR models. Both CoMFA and CoMSIA yielded statistically significant models upon partial least-squares analyses. The 3D-QSAR analyses showed that hydrogen-bond donor interactions and electrostatic interactions with the protonated amino side chains of the anthrapyrazoles led to high cell growth inhibitory activity.

Local lazy regression: Making use of the neighborhood to improve QSAR predictions.

Rajarshi Guha* [Pennsylvania State Univ.], Debojyoti Dutta, Peter C. Jurs, and Ting Chen

J. Chem. Inf. Model. **46** (4), 1836 -1847, 2006.

The use of local lazy regression (LLR) is investigated, obtains a prediction for a query molecule using its local neighborhood, rather than considering the whole data set. This approach is especially useful for very large data sets and is applied to three biological data sets. In all cases, LLR led to a few observations being poorly predicted compared to the global model.

Development of a general quantum-chemical descriptor for steric effects: Density functional theory based QSAR study of herbicidal sulfonylurea analogues.

Zhen Xi* [Nankai Univ.], Zhihong Yu, Congwei Niu, Shurong Ban, Guangfu Yang

J. Comp.Chem. **27**, 1571-1576, 2006.

DFT is used to describe a general quantum-chemical descriptor by characterizing the volume of electron cloud for specific substituent. The application of the defined steric descriptors in the QSAR analysis of sulfonylurea analogues resulted in four QSAR models indicated that this descriptor could provide an effective way for solving the problem how to directly describe steric effect in quantum chemistry-based QSAR studies.

Conformational Search and Analysis

Computational analysis of Aza analogues of [2',5'-Bis-*O*-(*tert*-butyldimethylsilyl)-β-D-ribofuranose]-3'-spiro-5''-(4''-amino-1'',2''-oxathiole-2'',2''-dioxide) (TSAO) as HIV-1 reverse transcriptase inhibitors: Relevance of conformational properties on the inhibitory activity.

Elena Soriano* [CSIC], J. Marco-Contelles, C. Tomassi, A.N. Van Nhien, and D. Postel.

J. Chem. Inf. Model. **46** (4), 1666 -1677, 2006.

Computational tools are used to study the effect of the endocyclic amino moiety *N*-2'' on the inhibitory activity against HIV-1.Docking studies suggested that compounds substituted at the *N*-3 and *N*-2'' positions showed the same binding mode, where the endocyclic amino group remains mostly exposed to the solvent. MM and QM calculations are used for the conformational analysis provides a rationalization based on conformational preferences.

Conformational Search and Analysis (cont'd)

Simulation of conformational transitions.

Arjan van der Vaart* [Harvard Univ.]

Theor.Chem.Accounts., **116**, 183-193 (2006)

Computer simulations are playing an important role to understand the dynamical behavior into how the conformational changes are induced, propagated and used. Recent methods for the simulation of conformational transitions are reviewed, with a focus on atomistic molecular dynamics techniques for the calculation of transition pathways.

A!
Comparative performance assessment of the conformational model generators omega and catalyst: A large-scale survey on the retrieval of protein-bound ligand conformations.

 J. Kirchmair, G. Wolber, C. Laggner, and Thieny Langer* [Inte:Ligand Software and Consul. GmbH]

J. Chem. Inf. Model. **46** (4), 1848 -1861, 2006.

The present study is based on an enhanced test set of 778 drug molecules and pharmacologically relevant compounds from the PDB. The protocols are applied to both programs: (i) high-throughput settings for processing large databases and (ii) high-quality settings for binding site exploration or lead structure refinement. The results showed that Catalyst is faster in the first case, Omega 2.0 better reproduces the bound ligand conformations from the PDB in less time for the latter case.

Genetic algorithms for protein conformation sampling and optimization in a discrete backbone dihedral angle space.

Yuedong Yang, Haiyan Liu**** [Univ. of Sci. and Tech. of China]

J. Comp.Chem. **27**, 1593-1602, 2006.

Protein conformation sampling and optimization is investigated based on the genetic algorithm and discrete main chain dihedral state model. An efficient approach combining the genetic algorithm with local minimization and with a niche technique based on the sharing function is proposed. The importance of local minimization and population diversity in protein conformation optimization with genetic algorithms is demonstrated.

Comparative or Homology Modeling

A!
Structure of the virus capsid protein VP1 of enterovirus 71 predicted by some homology modeling and molecular docking studies.

Yi-Yu Ke, Yun-Chu Chen, Thy-Hou Lin[*] [National Tsing Hua Univ.]

J. Comp.Chem. **27**, 1556-1570, 2006.

Insight II/Homology program is used to construct the structure of enterovirus 71 (EV 71) capsid protein VP1 and is refined by energy minimization and MD simulations. ERRAT, PROCHECK, PROVE, and PROSA2003 programs are used to validate the model. Docking is used to check the inconsistency between the docking scores and the measured activity is observed for a series of EV 71 VP1 inhibitor. GRID-VOLSURF programs are used to develop the QSAR models for the ligand-protein model system.

Interactions of Aryloxyphenoxypropionic acids with sensitive and resistant acetyl-coenzyme A carboxylase by homology modeling and molecular dynamic simulations.

Xiao-Lei Zhu, Li Zhang, Qiong Chen, Jian Wan, and Guang-Fu Yang* [Central China Normal Univ.]

J. Chem. Inf. Model. **46** (4), 1819 -1826, 2006.

Homology models are constructed for carboxyl-transferase (CT) domain of ACCase, and are used as templates to study the molecular mechanism of herbicide resistance and stereochemistry-activity relationships of aryloxyphenoxypropionates (APPs). Docking analysis indicated that the binding model of high-active compounds is similar to that in the crystal structure of the enzyme-ligand complex. The results provided a new starting point for the identification of more potent inhibitors against both sensitive and resistant ACCase.

Potentials and Parameters

Molecular dynamics simulation of argon, krypton, and xenon using two-body and three-body intermolecular potentials.

E.K. Goharshadi* [Ferdowsi Univ.] and
M. Abbaspour.
J. Chem. Theory and Comp. **2**, 920-926, 2006.

MD simulations are performed to obtain energy and pressure of argon, krypton, and xenon at different temperatures using a HFD-like potential. The simple three-body potential is originally used in conjunction with the BFW potential, is also validated when used with the HFD-like potential. The results are compared with HMSA and ODS integral equation.

AM1/d parameters for magnesium in metalloenzymes.

Petra Imhof, Frank Noé, Stefan Fischer, and Jeremy C. Smith* [IWR Univ. of Heidelberg].

J. Chem. Theory and Comp. **2**, 1050-1056, 2006.

Monte Carlo simulations are used to derive the AM1/d parameters for magnesium and DFT is used to reproduce the geometries and energies of a training set, optimized for modeling reactions in metalloenzymes. The new AM1/d parameters provide an improvement in accuracy compared to the standard semiempirical methods AM1 and MNDO/d and are particularly useful for modeling reactions in large biological systems at low computational cost.

Development of a parametrized force field to reproduce semiempirical geometries.

A.M. Wollacott and K.M. Merz, Jr.* [The Pennsylvania State Univ.]

J. Chem. Theory and Comp. **2**, 1070-1077, 2006.

A new force field parameter is developed to reproduce the geometry of proteins minimized at the semiempicarical quantum mechanical level. This method will provide the geometries that are more consistent with a semiempirical treatment of protein structures. This force field allows rapid and stable geometry optimizations at the semiempirical level and could useful in the adoption of QM calculations for large biological systems.

Atomic charge parameters for the finite difference Poisson-Boltzmann method using electronegativity neutralization.

Qingyi Yang and Kim A. Sharp* [Univ.of Pennsylvania, Philadelphia]

J. Chem. Theory and Comp. **2**, 1152-1167, 2006.

Rappe and Goddard's charge equilibration (QEq) method is used to assigning atomic partial charges. Finite difference Poisson-Boltzmann (FDPB) method is used to calculate the solvation free energies and the results are correlated with the experimental results. The different contributions to the energy surface of the dipeptide are examined and compared with the results from fixed CHARMm charge potential, which is widely used for molecular dynamics studies.

Fluctuating charge force fields: Recent developments and applications from small molecules to macromolecular biological systems.

Sandeep Patel and Charles L. Brooks* [The Scripps Res.Inst.]

Mol. Sim. **110**, 231-249, 2006.

Recent development and application efforts of a polarizable biomolecular force field based on the fluctuating charge formalism and founded on the CHARMM non-polarizable force field is presented.
The parameterization, recent applications of chemical and biological systems such as small-molecule liquid-vapor interfaces, solvated proteins/peptides, and physiological membrane systems are discussed.

Solvation Energy

Increasing the efficiency of free energy calculations using parallel tempering and histogram reweighting.

Steven W. Rick* [Univ. of New Orleans]

J. Chem. Theory and Comp. **2**, 939-946, 2006.

Parallel tempering (PT) Monte Carlo and weighted histogram analysis method (WHAM) is used to improve the efficiency of free energy calculations. The aqueous solvation of *n*-butane and methane showed noticeable improvement in the precision of the free energy and entropy changes. The methods are an efficient to calculate the free energy, entropy, and enthalpy changes, which are performed in parallel for a number of closely spaced temperatures, and WHAM is used to enhance the data at each temperature.

Minimalist explicit solvation models for surface loops in proteins.

R.P. White and H. Meirovitch* [Univ. of Pittsburgh Sch. of Med.]

J. Chem. Theory and Comp. **2**, 1135-1151, 2006.

MD simulations are applied with explicit water to study the protein surface loops and the protein surface coverage. The results are compared to much larger, fully solvated systems and to results for the generalized Born surface area implicit solvation model. The importance of protein loop modeling and other loop models, along with other challenges including the relevance of an appropriate free-energy simulation methodology for the assessment of conformational stability is described.

Time dependent solvation: A new frontier for quantum mechanical continuum models.

B. Mennucci* [Univ. of Pisa]

Theor.Chem.Accounts., **116***, 31-42 (2006)

The improved versions and developments of the continuum theories are indeed able to qualitatively monitor the same picture of polar solvent dynamics like molecular theories are showed.

Molecular Dynamics

TRAJELIX: A computational tool for the geometric characterization of protein helices during molecular dynamics simulations.

Mihaly Mezei* [New York Univ.] and M. Filizola.

J. Comp.-Aided Mol. Design. **20**, 97-107 (2006)

A computer program is developed with the necessary mathematical formalism for the geometric characterization of distorted conformations of alpha-helices proteins. This formalism is incorporated into TRAJELIX, a new module within the SIMULAID framework that is capable of monitoring distortions of alpha-helices in terms of their displacement, global and local tilting, rotation around their axes, compression/extension, winding/unwinding, and bending.

Bayesian model based clustering analysis: Application to a molecular dynamics trajectory of the HIV-1 integrase catalytic core.

Yan Li* [Ocean Univ. of China]

J. Chem. Inf. Model. **46** (4), 1742 -1750, 2006.

Bayesian method is applied for clustering protein conformations sampled during a MD simulation of the HIV-1 integrase catalytic core. The results are useful to identifying transitions between conformational ensembles. The dihedral angles involved in such transitions are examined. The conformations in high dimensional space are projected into 3D space employing a multidimensional scaling technique to provide a visual inspection.

Molecular Dynamics (cont'd)

Ligand coordinate analysis of SC-558 from the active site to the surface of COX-2: A molecular dynamics study.

K. V. V. M. Sai Ram, G. Rambabu, J. A. R. P. Sarma, and G. R. Desiraju* [Univ. of Hyderabad]

J. Chem. Inf. Model. **46** (4), 1784 -1794, 2006.

MD simulations are used, and the results provided a confirmation for the existence of a shallow cavity near the protein surface in which the ligand is bound reversibly. The residues that show maximum mobility, one obtains an idea of the gating mechanism that governs the entry and exit of the protein into or from the deep pocket that contains the active site. The results provided an energy profile of the ligand during its entry/exit into/from the protein and could enable one to assess the residence time, which in turn may be associated or indirectly correlated with adverse cardiovascular side effects of non-steroidal anti-inflammatory drugs.

PROFASI: A Monte Carlo simulation package for protein folding and aggregation.

Anders Irbäck[*] [Lund Univ.], Sandipan Mohanty

J. Comp.Chem. **27**, 1548-1555, 2006.

PROFASI is an efficient program for simulating protein folding and aggregation. The systems are modeled using an all-atom description of the protein chains with only torsional degrees of freedom, and implicit water. The simulation methods implemented in PROFASI are Monte Carlo-based and include a semilocal move and simulated tempering.

QM/MM

Quantum mechanical and molecular dynamics simulations of ureases and Zn β-lactamases.

G. Estiu, D. Suárez, K.M. Merz, Jr* [Univ. of Florida]

J. Comp.Chem. **27**, 1240 -1262, 2006.

Different methodologies, quantum chemical calculations, molecular dynamic simulations, as well as mixed QM/MM approaches are described to understand the structure and function of metallo-β-lactamases and ureases.

A comparative QM/MM simulation study of the reaction mechanisms of human and plasmodium falciparum HG(X)PRTases.

Aline Thomas* [Inst. of Biol. Stru.-Jean-Pierre Ebel] and Martin J. Field

J. Am. Chem. Soc. **128**, 10096 -10102, 2006.

QM/MM hybrid potential free-energy simulations are performed to compare the reaction mechanisms of human hypoxanthine guanine phosphoribosyl transferase (HGPRTase) and the corresponding enyzme from Plasmodium falciparum (Pf), HGXPRTase. These enzymes share 44% of sequence identity but display very different affinities for xanthine. The results showed that in both enzymes phosphoribosyl transfer proceeds *via* a dissociative mechanism from an anionic form of the substrate.

A density functional theory study on the role of His-107 in arylamine *N*-acetyltransferase 2 acetylation.

Qing-An Qiao* [Yantai Normal Univ.], Chuanlu Yang, Rongjun Qu, Yueqing Jin, Meishan Wang, Zhihong Zhang, Qi Xu and Zhongxi Yu

*Biophysical J.***122**, 215-220 (2006)

The acetyl group is transferred directly from the donor, *p*-nitrophenyl acetate, to the acceptor, cysteine, the high activation energy. These energies have dropped a little in a range of 20–25 kJ/mol when His-107 is assisting the transfer process. When protonated His-107 is mediating the reaction, the activation energies have dropped about 70–85 kJ/mol. The resulting calculations strongly support an enzymatic acetylation mechanism that experiences a thiolate-imidazolium pair.

QM/MM (cont'd)

Systematic QM/MM investigation of factors that affect the cytochrome P450-catalyzed hydrogen abstraction of camphor.

Ahmet Altun, Sason Shaik, Walter Thiel***** [Max-Planck-Inst. for Kohlenforschung]

J. Comp.Chem. **27**, 1324 -1337, 2006.

Combined QM/MM calculations in the native enzyme environment and DFT in the gas phase are used to investigate the hydrogen abstraction reaction of camphor in cytochrome $P450_{cam}$. It is found that the ChemShell and QSite programs used in the QM/MM calculations got the same results at given geometries. The results gave an appropriate environment close to the X-ray structure only for protonated Asp-297.

QM/MM modeling of compound I active species in cytochrome P450, cytochrome C peroxidase, and ascorbate peroxidase.

J.N. Harvey***** [Univ. of Bristol], C.M. Bathelt, A.J. Mulholland

J. Comp.Chem. **27**, 1352-1362, 2006.

QM/MM calculations are used to predict the electronic structure of the metal center in metalloproteins, Cytochrome *c* Peroxidase (CcP) and Ascorbate Peroxidase (APX). The results are well agreed with the experimental values, and suggested that the difference in electronic structure is due to a large number of small differences in structure from one protein to another.

Performance of DFT in modeling electronic and structural properties of cobalamins.

Jadwiga Kuta , S. Patchkovskii, M.Z. Zgierski, P. M. Kozlowski[*] [Univ. of Louisville]

J. Comp.Chem. **27**, 1429-1437, 2006.

Three different functionals including B3LYP, BP86, and revPBE are performed to develop the models for a systematic analysis of the electronic and structural properties of coenzyme B_{12}. The results of B3LYP significantly underestimate the strength of the Co-C bond while the nonhybrid BP86 functional produces the consistent results in comparison with the experimental data.

Assigning the protonation states of the key aspartates in β-secretase using QM/MM X-ray structure refinement.

Ning Yu, S.A. Hayik, Bing Wang, Ning Liao, C.H. Reynolds, and K.M. Merz, Jr.***** [Johnson & Johnson Pharm. Res. and Develop.]

J. Chem. Theory and Comp. **2**, 1057-1069, 2006.

An energy function is introduced to the refinement where the atoms in the active site are modeled by QM and the surrounding atoms are by MM. A total number of 8 protonation configurations of the aspartyl dyad are considered, and QM/MM X-ray refinements are performed for all of them. The resulting structures are a consensus of theoretical and experimental data and remark on the significance of our results in structure based drug design and mechanistic studies.

Symbolic algebra in quantum chemistry.

So Hirata* [Univ. of Florida]

Theor.Chem.Accounts., **116***,* 2-17 (2006)

New algorithms, which automate the algebraic transformation and computer implementation of many-body quantum-mechanical methods for electron correlation is reviewed. These are enable a whole new class of highly complex but vastly accurate methods, the manual development of which is no longer practical.

Pseudobond ab initio QM/MM approach and its applications to enzyme reactions.

Yingkai Zhang* [New York Univ.]

Theor.Chem.Accounts., **116***,* 43-50 (2006)

The methodology and development approaches of QM/MM covalent boundary problem, an efficient iterative optimization procedure, the methods to determine enzyme reaction paths, and the approaches to calculate free energy change in enzyme reactions are discussed. The methods are examined to know the efficiency with several examples and future directions are also discussed.

QM/MM (cont'd)

Quantum chemical modeling of enzyme active sites and reaction mechanisms.

Fahmi Himo* [Royal Inst. of Tech.]

Theor.Chem.Accounts., **116***, 232-240 (2006)*

DFT methods with B3LYP function methods and models are used to study the enzyme active sites and their reaction mechanisms using quantum chemical methods are reviewed with recent examples.

Ligand Docking

Molecular docking study and development of an empirical binding free energy model for phosphodiesterase 4 inhibitors.

F.G. Oliveira, C.M.R. Sant'Anna, E.R. Caffarena, L.E. Dardenne and E.J. Barreiro* [Univ. Federal do Rio de Janeiro]

Bioorg. Med. Chem. **14**, 6001-6011 (2006)

Computational methods are combined to develop a model for the prediction of PDE4B inhibitors activity. An exhaustive docking procedure is performed to identify the most probable binding modes of the ligands to the enzyme, including the active site metal ions and the surrounding structural water molecules. The results showed that both the inclusion of the structural water molecules close to the ions in the binding site and the use of a free energy model with a quadratic dependency on the ligand free energy of solvation are important aspects for molecular docking investigations involving the PDE4 enzyme family.

Information-driven protein-DNA docking using HADDOCK: It is a matter of flexibility.

Marc van Dijk, Aalt D. J. van Dijk, Victor Hsu, Rolf Boelens and Alexandre M. J. J. Bonvin* [Utrecht Univ.]

Nucleic Acids Research. **34,** 3317-3325 (2006)

High Ambiguity Driven DOCKing (HADDOCK) is extensively used to study the DNA flexibility. HADDOCK uses non-structural experimental data to drive the docking during a rigid-body energy minimization, and semi-flexible and water refinement stages. This approach is used on the monomeric repressor-DNA complexes formed by bacteriophage 434 Cro, the *Escherichia coli* Lac headpiece and bacteriophage P22 Arc. The results are further used to generate a library of pre-bent and twisted DNA structures that served as input for a second docking round.

S!
Accurate prediction of the relative potencies of members of a series of kinase inhibitors using molecular docking and MM-GBSA scoring.

P.D. Lyne* [AstraZeneca R&D], M.L. Lamb, and J.C. Saeh.

J. Med. Chem., **49** (16), 4805 -4808, 2006

Glide and an MM-GBSA postdocking scoring protocol is used to correctly rank a number of congeneric kinase inhibitors is assessed. The approach is successful for the cases considered and suggests that this may be useful for the design of inhibitors in the lead optimization phase of drug discovery.

SLICK - Scoring and energy functions for protein-carbohydrate interactions.

A. Kerzmann* [Univ. of Tubingen], D. Neumann, and O. Kohlbacher

J. Chem. Inf. Model. **46** (4), 1635 -1642, 2006.

SLICK, a new package containing a scoring and an energy function to predict binding modes and free energies of sugars and sugarlike compounds to proteins. SLICK accounts for van der Waals interactions, solvation effects, electrostatics, hydrogen bonds, and CH⋯π interactions, protein-carbohydrate interactions. SLICK predicts the binding free energies of predicted complexes with high accuracy.

Ligand Docking (Cont'd)

Flexible docking of ligands into synthetic receptors using a two-sided incremental construction algorithm.

A. Steffen* [Max-Planck-Inst. for Informatics], A. Kämper, and T. Lengauer.

J. Chem. Inf. Model. **46** (4), 1695 -1703, 2006.

A new algorithm is developed based on the protein-ligand docking program FlexX and extends this program to the docking technique FlexR. A novel docking strategy is applied that uses an adaptive two-sided incremental construction algorithm which incorporates the structural flexibility of both the ligand and synthetic receptor. This method promising results on a test data set comprising 10 complexes of synthetic receptors and ligands.

GFscore: A general nonlinear consensus scoring function for high-throughput docking.

S. Betzi, K. Suhre, B. Chétrit, F. Guerlesquin, and Xavier Morelli* [Parc Sci. de Luminy]

J. Chem. Inf. Model. **46** (4), 1704 -1712, 2006.

A methodology for High Throughput Screening (HTS) process is presented, by allowing focused screens or for hitlist triaging when a prohibitively large number of hits is identified in the primary screen. A non-linear Generalist scoring function, GFscore, is trained to discriminate true positives from false positives in a data set of diverse chemical compounds. GFscore eliminates up to 75% of molecules, with a confidence rate of 90% and therefore GFscore is a powerful tool for the biologist, saving both time and money.

A!
Ensemble docking into flexible active sites. Critical evaluation of FlexE against JNK-3 and β-secretase.

T. Polgár and G.M. Keserü* [Gedeon Richter Ltd.]

J. Chem. Inf. Model. **46** (4), 1795 -1805, 2006.

FlexE is tested against that of FlexX and FlexX-Pharm, by virtual screening experiments on two sets of the enzymes β-secretase (BACE), and c-jun N-terminal kinase 3 (JNK-3). The side-chain flexibility revealed that at the most FlexE could achieve the enrichment yielded by FlexX in JNK-3 but not in BACE. Although limited side-chain variations could be treated by FlexE, docking into protein ensembles remains a practical tool that decreases the average run time for a ligand.

Protein Folding

Protein folding simulations: Combining coarse-grained models and all-atom molecular dynamics.

Giorgio Colombo* [Inst. di Chem. del Riconoscimento Mol.] and Cristian Micheletti

Theor.Chem.Accounts., **116***, 75-86 (2006)

Different computational strategies are employed to understand the protein folding problem, based on the use of either coarse-grained or all-atom protein descriptions. Recent approach that allows to extending the ordinary folding simulations by using a simplified description of protein structures and energy functional in conjunction with all-atom molecular dynamics is described.

The thermodynamics of folding of a β- hairpin peptide probed through replica exchange molecular dynamics simulations.

Andrij Baumketner* [Inst. of Condensed Matter Phys.]

Theor.Chem.Accounts., **116***, 262-273 (2006)

A recent advance in sampling techniques, including replica exchange molecular dynamics, allows full characterization of the thermodynamics of folding of small peptides. MD simulation of a small β-hairpin peptide using the replica exchange algorithm and illustrate how this enhanced sampling scheme enables a thorough characterization of the native and unfolded states, and sheds new light into its folding mechanism is discussed.

Molecular Graphics

Molecular imaging strategies for drug discovery and development. S. Gross and D. Piwnica-Worms* [Washington Univ. Sch. of Medicine] *Curr.Opi.Stru.Biol.* **10**, 334-342 (2006)	Non-invasive molecular imaging advances are providing exciting opportunities for discovery, validation and development of novel therapeutics. Molecular imaging is an indispensable for drug discovery and development. They enable spatial and temporal monitoring of *in vivo* gene expression, signaling pathways, biochemical reactions and targets as they relate to the pharmacokinetics and pharmacodynamics of novel drugs.
Data visualization during the early stages of drug discovery. D.M. Maniyar*[Aston Univ.], I.T. Nabney, B.S. Williams, and A. Sewing *J. Chem. Inf. Model.* **46** (4), 1806 -1818, 2006.	Generative topographic mapping (GTM) and hierarchical GTM (HGTM) are applied to help the screening scientists, chemists, biologists, etc. to know and draw meaningful decisions. PCA, Sammon's mapping, and self-organizing maps, to demonstrate their enhanced power to help the user visualize the large multidimensional data sets during the early stages of the drug discovery process. GTM and HGTM algorithms allowed the user to cluster active compounds for different targets and understand them better than the benchmarks.

Structure Determination

Structural investigation of syringomycin-E using molecular dynamics simulation and NMR. E. Mátyus* [Semmelweis Univ.], L. Monticelli, K.E. Kövér, Z. Xu, K. Blaskó, J. Fidy and D.P. Tieleman. *J. Europ.Biophys.* **35**, 459 -467, 2006.	MD simulations are used for the molecular features of syringomycin-E (SR-E) in water and octane. A peptide model was built and examined its structure in water and octane. The results are useful to understand the antifungal and antibacterial activity of the peptide.
Energy minimization of crystal structures containing flexible molecules. P.G. Karamertzanis and S.L. Price* [Univ. College London] *J. Chem. Theory and Comp.* **2**, 1184-1199, 2006.	A new methodology is proposed for the accurate minimization of crystal structures of flexible molecules and is validated and tested by minimizing the experimental crystal structures of a set of flexible molecules. This method is used to refine the low-energy structures found in rigid-body crystal structure prediction studies of the diastereomeric salt pair (*R*)-1-phenylethylammonium (*R/S*)-2-phenylpropanoate and the antiepileptic drug carbamazepine.
Theoretical and computational studies of vectorial processes in biomolecular systems. Q. Cui*[Univ. of Wisconsin] *Theor.Chem.Accounts.,* **116***,* 51-59 (2006)	Recent developments in biophysical and biochemical techniques have provided new information about the structure, dynamics and interaction of biomolecules involved in vectorial life processes at multiple length and temporal scales. Vectorial biomolecular machines, myosin and cytochrome c oxidase are used for the identification of interesting and biologically relevant questions that require thorough theoretical analysis.

3. J O U R N A L   R E V I E W S

Journal of Computational Chemistry 27(12), September, 2006

1223-1239 **Spin states in polynuclear clusters: The [Fe2O2] core of the methane monooxygenase active site,**
Carmen Herrmann, Lian Yu, Markus Reiher* [Lab. for Phys.Chem., ETH Zurich]

>   The energetics of different total and local spin states of a dinuclear oxygen-bridged iron(IV) model for the intermediate **Q** of the hydroxylase component of methane monooxygenase by means of spin-unrestricted Kohn-Sham density functional theory is studied.

1240-1262 **Quantum mechanical and molecular dynamics simulations of ureases and Zn β-lactamases,**
Guillermina Estiu, D. Suárez, K.M. Merz, Jr* [Univ. of Florida]

>   **See Methodology, QM/MM**

1263-1277 **DFT models for copper(II) bispidine complexes: Structures, stabilities, isomerism, spin distribution, and spectroscopy,** M. Atanasov, Peter Comba* [Univ. Heidelberg], B. Martin, V. Müller, G. Rajaraman, H. Rohwer, S. Wunderlich

>   DFT and *ab initio* methods are used to compute the structures, relative stabilities, spin density distributions, and spectroscopic properties of the two possible isomers of the copper(II) complexes with derivatives of a rigid tetradentate bispidine ligand with two pyridine and two tertiary amine donors, and a chloride ion.

1278-1291 **Theoretical, spectroscopic, and mechanistic studies on transition-metal dinitrogen complexes: Implications to reactivity and relevance to the nitrogenase problem,** Felix Studt, Felix Tuczek* **[**Christian-Albrechts-Univ. Kiel]

>   DFT calculations are used to investigate the electronic structure and eactivity of dinitrogen complexes of transition metals exhibit different binding geometries of N_2.

1292-1306 **DFT calculations of ^{57}Fe Mössbauer isomer shifts and quadrupole splittings for iron complexes in polar dielectric media: Applications to methane monooxygenase and ribonucleotide reductase,** Wen-Ge Han, Tiqing Liu, Timothy Lovell, Louis Noodleman* [The Scripps Res. Inst.]

>   Linear regression between the measured isomer shifts and DFT calculated to predict the isomer shifts of Fe complexes in different oxidation and spin states.

1307-1323 **Can the semiempirical PM3 scheme describe iron-containing bioinorganic molecules?,** Jonathan P. McNamara, M. Sundararajan, I.H. Hillier* [Univ. of Manchester], Jun Ge, A. Campbell, Claudio Morgado

>   Semiempirical PM3 method is used to develop a set of iron parameters to allow the structure and redox properties of the active sites of iron-containing proteins to be accurately modeled, focussing on iron-sulfur, iron-heme, and iron-only hydrogenases.

1324-1337 **Systematic QM/MM investigation of factors that affect the cytochrome P450-catalyzed hydrogen abstraction of camphor,** Ahmet Altun, Sason Shaik, Walter Thiel* [Max-Planck-Inst. fo Kohlenforschung]

>   **See Methodology, QM/MM.**

1338-1351 **Electronic structure of iron(II)-porphyrin nitroxyl complexes: Molecular mechanism of fungal nitric oxide reductase (P450nor),** Nicolai Lehnert* [Christian-Albrechts-Univ. Kiel], V. K. K. Praneeth, F. Paulat

    DFT calculations are used to investigate key intermediates of the catalytic cycle of fungal nitric oxide reductase (P450nor).

1352-1362 **QM/MM modeling of compound I active species in cytochrome P450, cytochrome C peroxidase, and ascorbate peroxidase,** J.N. Harvey* [Univ. of Bristol], C.M. Bathelt, A.J. Mulholland.

    See Methodology, QM/MM

1363-1372 **On the O_2 binding of Fe-porphyrin, Fe-porphycene, and Fe-corrphycene complexes,** H. Nakashima, Jun-ya Hasegawa, Hiroshi Nakatsuji* [Kyoto Univ.]

    The present investigates the O_2 binding mechanism in the Fe-porphyrin isomers, Fe-porphycene (FePc), and Fe-corrphycene (FeCor) complexes.

1373-1384 **Quantum chemistry applied to the mechanisms of transition metal containing enzymes – Cytochrome *c* oxidase, a particularly challenging case,** M.R. A. Blomberg* [AlbaNova Univ. Cent. Stockholm Univ.], Per E. M. Siegbahn.

    See Methodology, QM/MM

1385-1397 **On the accuracy of density functional theory for iron - sulfur clusters,** Robert K. Szilagyi* [Montana State Univ.], Mark A. Winslow.

    A wave function manipulation method is introduced for developing ground state electronic wave function for [2Fe-2S] and [Mo-3Fe-4S] clusters.

1398-1414 **The reaction mechanism of iron and manganese superoxide dismutases studied by theoretical calculations,** Lubomír Rulíšek, Kasper P. Jensen, Kristoffer Lundgren, Ulf Ryde* [Lund Univ.]

    DFT is applied to study the reaction mechanism of iron and manganese superoxide dismutase on realistic active-site models, with large basis sets and including solvation, zero-point, and thermal effects.

1415-1428 **Metal-thiolate bonds in bioinorganic chemistry,** Edward I. Solomon* [Stanford Univ.], Serge I. Gorelsky, Abhishek Dey.

    H-bonding is significantly affecting the covalency of the metal-thiolate bond and contribute to redox tuning by the protein environment.

1429-1437 **Performance of DFT in modeling electronic and structural properties of cobalamins,** Jadwiga Kuta, S. Patchkovskii, M.Z. Zgierski, P. M. Kozlowski*[Univ. of Louisville]

    See Methodology, QM/MM

1438-1445 **A DFT study of the mechanism of Ni superoxide dismutase (NiSOD): Role of the active site cysteine-6 residue in the oxidative half-reaction,** R. Prabhakar, Keiji Morokuma* [Emori Univ.], D.G. Musaev.

    DFT is used to investigate the catalytic mechanism of H_2O_2 formation in the oxidative half-reaction of NiSOD, E-Ni(II) + O_2^- + 2H$^+$ ⟶ E-Ni(III) + H_2O_2.

1446-1453 **A DFT study on the relative affinity for oxygen of the α and β subunits of hemoglobin,** Jean-Didier Maréchal, Feliu Maseras* [Univ. Autònoma de Barcelona], Agustí Lledós, Liliane Mouawad, David Perahia

DFT calculations are performed to generate the computational models of the active center of the α- and β-subunits of hemoglobin in both its oxygenated (R) and deoxygenated (T) states.

1454-1462 **Correlation between computed gas-phase and experimentally determined solution-phase infrared spectra: Models of the iron-iron hydrogenase enzyme active site,** Jesse W. Tye, M.Y. Darensbourg, and Michael B. Hall* [Teas A&M Univ.]

Gas-phase DFT calculations with B3LYP, double zeta plus polarization basis sets are used to predict the solution-phase infrared spectra for a series of CO- and CN-containing iron complexes.

1463-1475 **QM/MM calculations with DFT for taking into account protein effects on the EPR and optical spectra of metalloproteins. Plastocyanin as a case study,** Sebastian Sinnecker, Frank Neese* [Max-Planck-Inst. for Bioorg. Chem.]

QM/MM approach is used to study the influence of the surrounding protein on magnetic and optical spectra of metalloproteins.

Journal of Computational Chemistry 27(13), October, 2006

1477-1485 **Kirkwood-Buff derived force field for amides**, Myungshim Kang, Paul E. Smith* [Kansas State Univ.]

A force field for the computer simulation of aqueous solutions of amides is presented and is designed to reproduce the experimentally observed density and Kirkwood-Buff integrals for N-methylacetamide, allowing for an accurate description of the NMA activity.

1486-1493 **Proton affinities of maingroup-element hydrides and noble gases: Trends across the periodic table, structural effects, and DFT validation,** Marcel Swart, Ernst Rösler, F. Matthias Bickelhaupt* [Scheikundig Laboratorium der Vrije Univ.]

Generalized gradient approximation (GGA) of the DFT at BP86/QZ4P//BP86/TZ2P is used to investigate the proton affinities at 298 K of the neutral bases constituted by all maingroup-element hydrides of groups 15-17 and the noble gases.

1494-1504 **Molecular dynamics simulations of liquid methanol and methanol-water mixtures with polarizable models.**

See Applications,Water and Solvation.

1505-1516 **A general efficient implementation of the BSSE-free SCF and MP2 methods based on the chemical Hamiltonian approach,** P. Salvador* [Univ. of Girona], D. Asturiol, I. Mayer.

A new, general, and efficient implementation of the BSSE-free SCF and second-order Møller-Plesset perturbation theories of intermolecular interactions, based on the "Chemical Hamiltonian Approach" is applicable for both open-shell and closed-shell systems and for an arbitrary number of interacting subsystems.

1517-1533 **The tetracycline: Mg^{2+} complex: A molecular mechanics force field,** Alexey Aleksandrov, Thomas Simonson* [Ecole Polytech.]

A molecular mechanics force field model of Tc (Tetracycline) is developed, which is consistent with the CHARMM force field for proteins and nucleic acids.

1534-1547 **Energy barriers of proton transfer reactions between amino acid side chain analogs and water from *ab initio* calculations,** Elena Herzog, Tomaso Frigato, Volkhard Helms, C. Roy D. Lancaster* [Max Planck Inst. of Biophys.]

Energy barriers for shifting the proton from donor to acceptor atom were calculated by electronic structure methods at the MP2/6-31++G(d,p) level, and the well-known double-well potentials are characterized.

1548-1555 **PROFASI: A Monte Carlo simulation package for protein folding and aggregation**, Anders Irbäck[*] [Lund Univ.], Sandipan Mohanty.

See Methodology, Molecular Dynamics.

1556-1570 **Structure of the virus capsid protein VP1 of enterovirus 71 predicted by some homology modeling and molecular docking studies,** Yi-Yu Ke, Yun-Chu Chen, Thy-Hou Lin[*] [National Tsing Hua Univ.]

See Methodology, Comparative or Homology Modeling.

1571-1576 **Development of a general quantum-chemical descriptor for steric effects: Density functional theory based QSAR study of herbicidal sulfonylurea analogues,** Zhen Xi***** [Nankai Univ.], Zhihong Yu, Congwei Niu, Shurong Ban, Guangfu Yang.

See Methodology, QSAR.

1577-1592 **Assessment of the performance of density-functional methods for calculations on iron porphyrins and related compounds,** Meng-Sheng Liao, John D. Watts, Ming-Ju Huang* [Jackson State Univ.]

The behaviors of a large number of GGA, meta-GGA, and hybrid-GGA density functionals in describing the spin-state energetics of iron porphyrins and related compounds are investigated.

1593-1602 **Genetic algorithms for protein conformation sampling and optimization in a discrete backbone dihedral angle space**, Yuedong Yang, Haiyan Liu* [Univ. of Sci. & Tech. of China]

See Methodology, Conformational Search and Analysis.

1603-1619 **Efficiency and accuracy of the elongation method as applied to the electronic structures of large systems,** Marcin Makowski* [Kyushu Univ.], Jacek Korchowiec, Feng Long Gu, Yuriko Aoki.

Recent development of the elongation method proposed by Imamura is presented and including geometry optimization and employment of the fast multiple method, is highlighted.

✳✳✳

4. <u>A D D R E S S E S   O F   P R I N C I P A L   A U T H O R S</u>

The production sites for the corresponding or principal authors are given in brackets in the citations. When not designated by the publisher, the first author is assumed to be the principal. Current addresses are listed here.

Angelo Carotti
Dept. de Bioquím. & Biol. Mol.
Facu. de Med., Univ. de Santiago de Compostela
Santiago de Compostela, Spain

A. Rita Bizzarri
Biophys. and Nanosci. Cent., CNISM
Dept. di Sci. Ambientali
Univ. della Tuscia, I-01100
Viterbo, Italy

Andreas Kerzmann
Div. for Simul. of Biol. Systems
Cent. for Bioinformatics
Univ. of Tübingen
Sand 14, 72076 Tübingen, Germany

Andreas Steffen
Max-Planck-Inst. for Informatik
Stuhlsatzenhausweg 85
D-66123 Saarbrücken
Germany

Aline Thomas
aline.thomas@ibs.fr
Lab. de Dynamique Mol.
Inst. de Biol. Structu.- Jean-Pierre Ebel (CEA/CNRS/UJF)
41 rue Jules Horowitz, 38027
Grenoble Cedex 1
France

Anders Irbäck
anders@thep.lu.se
Complex Systems Division
Dept. of Theor.Phys.
Lund Univ.
Sölvegatan 14A, SE-223 62 Lund, Sweden

Alexander Nemukhin
Inst. of Biochem. Phys.
Russian Acad. of Sci.
Moscow 119997, Russian Federation
Russia.

A. A. Langham
Univ. of Minnesota
Dept. of Chem. Engg. & Mat. Sci.
421 Washington Avenue SE
Minneapolis, MN, 55455, USA

Arjan van der Vaart
vaart@fas.harvard.edu
Dept. of Chem. and Chem. Biol.
Harvard Univ.
12 Oxford Street
Cambridge, MA 02138, USA

Andrij Baumketner
andrij@icmp.lviv.ua
Inst. for Condensed Matter Phys.
1 Svientsitsky Str., Lviv, 79011
Ukraine

Andrew F. Hill
Dept. of Biochem. and Mol.Biol. & Bio21 Mol. Sci. and Biotech. Inst.
The Univ. of Melbourne
VIC 3010, Australia

Brian B. Hasinoff
Dept. of Pharmacology
Univ. of Pittsburgh Sch. of Med.
Pittsburgh, Pennsylvania 15261
USA.

Benedetta Mennucci
bene@dcci.unipi.it
Dept. di chimica e chimica Indust.
Univ. di Pisa
Via Risorgimento 35, 56126 Pisa, Italy

C. Erec Stebbins
stebbins@rockefeller.edu
Lab. of Stru. Microbiol.
The Rockefeller Univ.
New York, New York 10021
USA

Charles L. Brooks
Dept. of Mol. Biol.
TPC-6, The Scripps Res. Inst.
10550 N. Torrey Pines Road
La Jolla, CA, 92037, USA

Daniel A. Hammer
hammer@seas.upenn.edu
Dept. of Bioengg.
Univ. of Pennsylvania
120 Hayden Hall, 3320 Smith Walk
Philadelphia, PA 19104, USA.

D.M. Maniyar
Neural Comp. Res. Group, Inform. Engg.
Aston Univ.
Birmingham, B4 7ET
United Kingdom

Daniel A. Kleier
DuPont Crop Protection
Stine-Haskell Research Center,
P.O. Box 30
Newark, Delaware 19714

D. Sabo
Comp. Biosci.
Sandia National Labs
MS 1413 & 0310
Albuquerque
New Mexico, 87185
USA

Dashuang Shi
dshi@cnmcresearch.org
Children's Res.Inst.
Children's Nati.Med.Cent.
111 Michigan Avenue, N.W.
Washington, DC 20010-2970

David H. Mathews
David_Mathews@urmc.rochester.edu
Dept. of Biochem. and Biophys.
Univ. of Rochester Med. Cent.
601 Elmwood Avenue
Box 712, Rochester, NY 14642, USA

Dalia Cohen
Novartis Inst. for BioMed. Res. Inc.
250 Massachusetts Avenue
Cambridge, MA 02139, USA

David Piwnica-Worms
Mol. Imaging Cent.
Mallinckrodt Inst. of Radiology
Washington Univ. Sch. of Med.
Box 8225, 510 S. Kingshighway Blvd.
St Louis, MO 63110, USA

D.D. Leonidas
Inst. of Org. and Pharm. Chem.
The Nat. Hellenic Res. Foundation
48 Vas. Constantinou Avenue
11635 Athens, Greece

Danny Barash
dbarash@cs.bgu.ac.il
Genome Diversity Cent.
Inst. of Evolution
Univ. of Haifa
Haifa 31905, Israel

Daniel T. Gewirth
Dept. of Med.
Program in Mol. Pharm. and Chem.
Memorial Sloan-Kettering Cancer Cent.
New York, New York 10021, USA.

Elena Soriano
Lab. de Resonancia Magnética
Inst. de Invest. Biomédicas (CSIC)
C/ Arturo Duperier 4, 28029
Madrid, Spain

Elizabeth A. Amin
Dept. of Chem. and Minnesota Supercomp. Inst.
Univ. of Minnesota
207 Pleasant St. SE
Minneapolis, Minnesota 55455

Emanuele Perola
emanuele_perola@vrtx.com
Vertex Pharmaceuticals
130 Waverly Street, Cambridge, MA 02139

E. Mátyus
szedit@puskin.sote.hu
Inst. of Biophys. & Radiation Biol.
Semmelweis Univ.
P.O. Box 263, 1444 Budapest
Hungary

E.K. Goharshadi
Dept. of Chem.
Ferdowsi Univ.
Mashhad 91779, Iran

Edward I. Solomon
Edward.Solomon@stanford.edu
Dept. of Chem.
Stanford Univ.
333 Campus Drive, Stanford, California 94305

Eliezer J. Barreiro
LASSBio, Lab. de Avaliação e Síntese de Substâncias Bioativas
Facu. de Farmácia and Inst. de Química
Univ. Federal do Rio de Janeiro
PO Box 68006, Rio de Janeiro
RJ 21944-910, Brazil

E.N. Trifonov
trifonov@research.haifa.ac.il
Genome Diversity Cent.
Inst. of Evolution
Univ. of Haifa
Mount Carmel, Haifa 31905, Israel

Frank Neese
theochem@thch.uni-bonn.de
Max-Planck-Inst. for Bioanorg. Chem.
Stiftstrasse 34-36, D-45470
Mülheim an der Ruhr, Germany

Feliu Maseras
fmaseras@iciq.es
Unitat de Química Física, Edifici
Cn
Univ. Autònoma de Barcelona
08193 Bellaterra, Catalonia, Spain

Frank Boeckler
Dept. of Med. Chem.
Emil Fischer Center
Friedrich Alexander Univ.
Schuhstraße 19
D-91052 Erlangen, Germany

Felix Tuczek
ftuczek@ac.uni-kiel.de
Inst. for Anorganische Chem.
Christian-Albrechts-Univ. Kiel
Otto Hahn Platz 6/7, 24098 Kiel
Germany

Fahmi Himo
himo@theochem.kth.se
Theor.Chem., Dept. of Biotech.
Royal Inst. of Tech.
Albanova Univ. Cent.
SE-106 91 Stockholm
Sweden

Filippo Minutolo
Dept. di Sci. Farmaceutiche
Univ. di Pisa
Via Bonanno 6, 56126 Pisa, Italy

Govindan Subramanian
gsubramanian@ttpharma.com
Computer-Aided Drug Discovery
Dept.
Albany Mol. Res., Inc.,
21 Corporate Circle
P.O. Box 15098, Albany
NY 12212-5098, USA

Gerald D. Watt
Dept. of Chem. and Biochem.
Brigham Young Univ.
Provo, UT 84602, USA

G. R. Desiraju
Sch. of Chem.
Univ. of Hyderabad
Hyderabad 500 046, India

György M. Keserü
CADD&HTS, Gedeon Richter Ltd.
P.O. Box 27, H-1475 Budapest
Hungary

Guang-Fu Yang
Key Laboratory of Pesticide &
Chemical Biology of Ministry of
Education
Coll. of Chem.
Cent. China Normal Univ.
Wuhan 430079
PR China

G. E. Ramirez Caballero
Dept. of Chem. Engg.
Texas A&M Univ.
College Station, TX, 77843, USA

George I. Makhatadze
Makhatadze@psu.edu
Dept. of Biochem. and Mol. Biol.
Penn State Univ. Coll. of Med.
500 University Drive
H171, Hershey, PA 17033

Guy Boivin
guy.boivin@crchul.ulaval
Res. Cent. in Infectious Disease
Cent. Hospital Univ. de Québec
(CHUL hospital) and Laval Univ.
Québec City, Canada

Giovanna Musco
musco.giovanna@hsr.it
Dulbecco Telethon Inst.
Biomolecular NMR Laboratory
c/o S. Raffaele Scientific Inst.
Via Olgettina 58, Milan 20132,
Italy

Giorgio Colombo
giorgio.colombo@icrm.cnr.it
Inst. di Chem. del Riconoscimento
Mol.
CNR, via Mario Bianco, 9,
20131 Milano, Italy

Gabriel Waksman
Inst. of Stru. Mol. Biol.
Sch. of Crystallography
Birkbeck Coll.
Univ. Coll. London
London, WC1E 7HX, UK

Hiroshi Nakatsuji
hiroshi@sbchem.kyoto-u.ac.jp
Dept. of Synthetic Chem. and
Biol.Chem.
Graduate Sch. of Engg.
Kyoto Univ.
Katsura, Nishikyo-ku,
Kyoto 615-8510, Japan

Haiyan Liu
hyliu@ustc.edu.cn
Hefei Nati. Lab. for Phys.Sci.
Key Lab. of Stru.Biol.
School of Life Sci.
Univ. of Sci. and Tech. of China
Hefei, Anhui 230026, PR China

Haralambos Sarimveis
hsarimv@central.ntua.gr
Sch. of Chem. Engg.
Nati. Tech. Univ. of Athens
Athens, Greece

Humberto González-Díaz
Dept. of Org. Chem.
Univ. of Santiago de Compostela
15782
Spain

Hagai Meirovitch
Dept. of Comp. Biol.
Univ. of Pittsburgh Sch. of
Medicine
3064 Biomedical Sci. Tower 3
Pittsburgh, Pennsylvania 15260
USA.

I. Poggesi
Prediction and Modeling
Nerviano Med. Sci. S.r.l.
Viale Pasteur 10, 20014 Nerviano
(MI), Italy

Irene Luque Ruiz
Inst. of Chem. Res. of Catalonia
ICIQ
Avinguda Països Catalans 16
E-43007 Tarragona, Spain

Ian H. Hillier
Ian.Hillier@manchester.ac.uk
Sch. of Chem.
Univ. of Manchester
Manchester, M13 9PL
United Kingdom

John W Davies
Lead Discovery Center
Novartis Inst. for Biomed.Res.Inc,
250 Massachusetts Avenue
Cambridge, MA 02139, USA

J. Will Medlin
Dept. of Chem. and Biol. Engg.
Univ. of Colorado
Boulder, Colorado 80309

Juan José Marugán
Depts. of Med. Chem., Stru.Biol.
and Mol. Design and Informatics,
Drug Discovery
Johnson & Johnson Pharm. Res.
and Develop., L.L.C., 665 Stockton
Drive, Exton, PA 19341, USA

Jeremy C. Smith
Comp. Mol. Biophys. & Comp.
Biochem.
IWR Univ. of Heidelberg
Im Neuenheimer Feld 368
69120 Heidelberg, Germany

J.J. Irwin
Dept. of Pharm. Chem.
Univ. of California San Francisco
1700 4th St, San Francisco
CA 94143-2550, USA

Jeremy N. Harvey
Jeremy.Harvey@bristol.ac.uk
Sch. of Chem. & Cent. for
Comp.Chem.
Univ. of Bristol
Cantock's Close, Bristol BS8 1TS
United Kingdom

J. Ghosh
UC Davis
Dept. of Chem. Engg. & Mat. Sci.
Davis, CA, 95616, USA

Keiji Morokuma
morokuma@emory.edu
Cherry L. Emerson Cent. for
Sci.Comp. and Dept. of Chem.
Emory Univ.
1515 Dickey Dr., Atlanta, Georgia
30322

Kurt Warncke
Dept. of Phys.
N201 Mathematics and Sci. Cent.
400 Dowman Drive
Emory Univ.
Atlanta, GA 30322-2430

Kenneth M. Merz, Jr.
Johnson & Johnson Pharm. Res.
and Development
L.L.C., P.O. Box 776
Welsh and McKean Roads
Spring House, Pennsylvania
19477-0776

K.M. Merz, Jr.
Dept. of Chemistry
The Pennsylvania State Univ.
Univ. Park
Pennsylvania 16802

Kim A. Sharp
Johnson Res. Found. and Dept. of
Biochem. and Biophys.
Univ. of Pennsylvania
Philadelphia, Pennsylvania 19104

Kenneth M. Merz, Jr.
merz@qtp.ufl.edu
Dept. of Chem., Quantum Theory
Project
Univ. of Florida
2328 New Physics Building
P.O. Box 118435, Gainesville
Florida 32611-8435
U.S.A.

Louis Noodleman
lou@scripps.edu
Dept. of Mol.Biol.
TPC15, The Scripps Res.Inst.
10550 N. Torrey Pines Road
La Jolla, California 92037, USA.

Michael B. Hall
mbhall@tamu.edu
Dept. of Chem.
Texas A&M Univ.
College Station, Texas 77843-3255
USA.

Manuel C Peitsch
Dept. of Systems Biology
Genome and Proteome Sciences
Novartis Inst. of Biomed. Res.
Novartis AG, CH-4002 Basel
Switzerland

Martin G. Grigorov,
Analytical Science
Nestlé Res. Cent.
Nestec Ltd, CH-1000 Lausanne 26
Switzerland

Mihaly Mezei
mezei@inka.mssm.edu
Dept. of Physiol. and Biophys.
Mount Sinai Sch. of Med.
NYU, One Gustave L. Levy Place
Box 1218, New York, NY 10029,
USA

Marcin Makowski
makowskm@chemia.uj.edu.pl
Dept. of Mol. and Mat. Sci.
Interdisciplinary Grad. Sch. of
Engg. Sci.
Kyushu Univ.
Fukuoka 816-8580, Japan.

Martin Zacharias
m.zacharias@iu-bremen.de
Sch. of Engg. and Sci.
International Univ. Bremen
Campus Ring 6, D-28759 Bremen
Germany

Massimiliano Aschi
aschi@caspur.it
Dept. of Chimica, Ingegneria
Chimica e Materiali
Univ. L'Aquila, Via Vetoio,
Coppito, 67100 L'Aquila, Italy

Markus Reiher
markus.reiher@phys.chem.ethz.ch
Lab. for Phys.Chem.
ETH Zurich, Hoenggerberg
Wolfgang-Pauli-Str. 10
CH 8093 Zurich, Switzerland

M.R. A. Blomberg
mb@physto.se
Dept. of Physics
AlbaNova Univ. Cent.
Stockholm Univ.
S-106 91 Stockholm, Sweden

F. Matthias Bickelhaupt
FM.Bickelhaupt@few.vu.nl
Theor. Chem.
Scheikundig Lab. Vrije Univ.
De Boelelaan 1083
NL-1081 HV Amsterdam
The Netherlands

Ming-Ju Huang
mhuang@chem.jsums.edu
Dept. of Chem.
P.O. Box 17910, Jackson State
Univ.
Jackson, Mississippi 39217

Nanda Ghoshal
Drug Design, Development and
Molecular Modeling Division
Indian Inst. of Chem. Biol. (CSIR)
4 Raja S.C.Mullick Road
Jadavpur, Kolkata -700032, India

Nicolai Lehnert
nlehnert@ac.uni-kiel.de
Inst. for Anorganische Chem.
Christian-Albrechts-Univ. Kiel
Olshausenstrasse 40, D-24098 Kiel
Germany

Qing-An Qiao
Sch. of Chem. and Mat. Sci.
Yantai Normal Uni.
Yantai 264025, China

Vladimir Frecer
Cancer Res. Inst.
Slovak Acad. of Sci.
Bratislava SK-83391, Slovakia

Paul E. Smith
pesmith@ksu.edu
Dept. of Chem.
Kansas State Univ.
111 Willard Hall
Manhattan, Kansas 66506-3701

Pawel M. Kozlowski
pawel@louisville.edu
Dept. of Chem.
Univ. of Louisville
2320 S. Brook Street
Louisville, Kentucky 40292

Pemra Doruker
doruker@boun.edu.tr
Dept. of Chem. Engg. and Polymer
Res.Cent.
Bogazici Univ.
Bebek 34342, Istanbul, Turkey

Philippe H. Hünenberger
Lab. of Phys. Chem.
ETH-Hönggerberg, HCI
CH-8093 Zürich, Switzerland

P.L.A. Popelier
School of Chem.
Sackville Site, North Campus
Univ. of Manchester,
Manchester M60 1QD, UK

Pierre-Nicholas Roy
pn.roy@ualberta.ca

Dept. of Chem.
Univ. of Alberta, Edmonton
AB, T6G 2G2, Canada

Peter Comba
peter.comba@aci.uni-heidelberg.de
Univ. Heidelberg
Anorganisch-Chem. Inst.
Im Neuenheimer Feld 270
D-69120 Heidelberg, Germany

Pablo R. Duchowicz
INIFTA, Div. Química Teórica
Dept. de Química, Facu. de
Ciencias Exactas
Univ. Nacional de La Plata
Diag. 113 y 64, Suc. 4
C.C. 16, (1900) La Plata
Argentina

Paul D. Lyne
Cancer Discovery
AstraZeneca R&D Boston
35 Gatehouse Drive
Waltham Massachusetts 02451
USA

Philip J. Camp
philip.camp@ed.ac.uk
Sch. of Chem.
Univ. of Edinburgh
West Mains Road
Edinburgh EH9 3JJ
United Kingdom

Q. Cui
cui@chem.wisc.edu
Dept. of Chem. and Theor. Chem.
Inst.
Univ. of Wisconsin
Madison 1101 Univ. Avenue
Madison, WI 53706, USA

Robert K. Szilagyi
Szilagy@Montana.edu
Dept. of Chem. and Biochem.
Montana State Univ.
223 Gaines Hall, Bozeman,
Montana 59717

R. J. Sadus
Centre for Mol. Sim.
Swinburne Univ. of Tech.
PO Box 218, Hawthorn
Victoria, 3122, Australia

Rajarshi Guha
Dept. of Chem.
Pennsylvania State Univ.
Univ. Park, Pennsylvania 16802
USA

R. Nussinov
ruthn@ncifcrf.gov
NCI-Frederick, 469-151 CCRNP
Frederick, MD 21702.

R. Malathi
r_malathi@hotmail.com

Department of Genetics
Dr. ALM Post Grad. Inst. of Basic
Med. Sci.
University of Madras
Taramani, Chennai - 600 113, India

Ramesh Panchagnula
Sch. of Biomed. Sci.
Univ. of Ulster
Cromore Road
Coleraine, BT52 1SA, UK

C. Roy D. Lancaster
volkhard.helms@bioinformatik.uni
saarland.de
Dept. of Mol. Membrane Biol.
Max Planck Inst. of Biophys.
Max-von-Laue Strasse 3
60438 Frankfurt am Main
Germany

Samuel F. Lockwood
Hawaii Biotech, Inc.,
99-193 Aiea Heights Drive
Suite 200, Aiea, HI 96701, USA

Suse Broyde
broyde@nyu.edu
Dept. of Biology
New York Univ.
New York, NY, USA

Silvia Dante
silvia.dante@hmi.de
Phys. Biochem.
Darmstadt Univ. of Tech.
Petersenstrasse 22
64287 Darmstadt
Germany

So Hirata
hirata@qtp.ufl.edu
Quantum Theory Project
Dept. of Chem.
Univ. of Florida
Gainesville, FL 32611-8435
USA

S. M. Thompson
Dept. of Chem. and Petroleum
Engg.
Univ. of Kansas
Lawrence, KS, 66045, USA

S. Leekumjorn
Virginia Polytech. Inst. and State
Univ.
Dept. of Chem. Engg.
Blacksburg 24061, VA
USA

P. Salvador
pedro.salvador@udg.es
Dept. of Chem. and Inst. of Comp.
Chem.
Univ. of Girona
17071 Girona, Spain

Sarah L. Price

Dept. of Chem.
Univ. College London
20 Gordon Street
London, United Kingdom WC1H
0AJ

Steven W. Rick
Dept. of Chem.
Univ. of New Orleans
New Orleans, Louisiana 70148

Samuel F. Lockwood
Hawaii Biotech, Inc.,
99-193 Aiea Heights Drive
Suite 200, Aiea, HI 96701, USA

Thierry Langer
Inte:Ligand Software-
Entwicklungs- und Consulting
GmbH
Clemens Maria Hofbauer-Gasse 6
A-2344 Maria Enzersdorf
Austria

Thy-Hou Lin
thlin@life.nthu.edu.tw
Dept. of Life Science
Inst. of Molecular Medicine
National Tsing Hua Univ.
Hsinchu 30043, Taiwan

Tam Luong Nguyen
Target Structure-based Drug
Discovery Group
SAIC-Frederick, Inc.
NCI Frederick
Frederick, MD 21702, USA

Thomas H Keller
Novartis Inst. for Tropical Diseases
(NITD)
10 Biopolis Road, #05-01 Chromos
138670 Singapore

Thomas Simonson
thomas.simonson@polytechnique.f
r
Lab. de Biochimie (CNRS
UMR7654)
Dept. of Biol.
Ecole Polytechnique
91128 Palaiseau, France

Ulf Ryde
Ulf.Ryde@teokem.lu.se
Dept. of Theor. Chem.
Chemical Centre, P.O. Box 124, x,
Lund S 221 00, Sweden
Vitor F. Ferreira
Dept. de Química Orgânica
Inst. de Química
Univ. Federal Fluminense
24020-150 Niterói, Rio de Janeiro,
Brazil
Vitor F. Ferreira

Dept. de Química Orgânica
Inst. de Química
Univ. Federal Fluminense
24020-150 Niterói, Rio de Janeiro,
Brazil

Vladimir Frecer
Cancer Res. Inst.
Slovak Acad. of Sci.
Bratislava SK-83391, Slovakia

Walter Thiel
thiel@mpi-muelheim.mpg.de
Max-Planck-Institut für
Kohlenforschung
Kaiser-Wilhelm-Platz 1
D-45470 Mülheim an der Ruhr,
Germany

Willy Wriggers
wriggers@biomachina.org
Lab. for Biocomp. & Imaging
Sch. of Health Info. Sci. & Inst. of
Mol.Med.
Univ. of Texas Health Sci. Cent.at
Houston
7000 Fannin St., Suite 600,
Houston, TX 77030

William N. Setzer
wsetzer@chemistry.uah.edu
Dept. of Chem.
Univ. of Alabama in Huntsville
Huntsville,
AL 35899, USA

Wilfred F. van Gunsteren
wfvgn@igc.phys.chem.ethz.ch
Lab. of Phys.Chem.
Swiss Federal Inst. of Tech. Zurich
ETH Hönggerberg, 8093 Zürich,
Switzerland

Wilhelm F. Maier
w.f.maier@mx.uni-saarland.de
Lehrstuhl für Technische Chemie
Univ. des Saarlandes
66123 Saarbrücken, Germany

Xavier Morelli
Parc Sci. de Luminy
163 Avenue de Luminy
FR-13288, Marseille Cedex 09
France

Yirong Mo
yirong.mo@wmich.edu
Dept. of Chem.
Western Michigan Univ.
Kalamazoo, MI 49008, USA

Yingkai Zhang

yingkai.zhang@nyu.edu
Dept. of Chem.
New York Univ.
New York, NY 10003, USA

Ye Che
chey@nhlbi.nih.gov
Lab. of Comp. Biol.
Nati. Heart, Lung and Blood Inst.
Nati. Inst. of Health
Bethesda, MD 20892, USA

Yushan Yan
Div. of Chem. and Biomol. Engg.
Nanyang Tech. Univ.
Singapore 637722
Singapore

Yan Li
Dept. of Appl. Chem.
Ocean Univ. of China
Qingdao 266003, P. R. China

Zhen Xi
zhenxi@nankai.edu.cn
State Key Lab. of Elemento-
Organic Chem. & Dept. of Chem.
Biol.
Nankai Univ.
Tianjin-300071, PR China.

5. DISCLAIMER, COPYRIGHT, AND PUBLISHER INFORMATION

Editor:
> R.Nageswar Ph.D.   Tel. (858) 663-0162
>   MMCC Results   E-mail: drnageswar@yahoo.com
> RR Labs Inc.,
> 8013 Los Sabalos Street
> San Diego, CA 92126

Bruce Gelin, founder and editor of MMCC Results Volumes 1-6, is Editor Emeritus.
David Busath, editor of MMCC Results Volumes 7-14, is Editor Emeritus.

Assistant Editors:
Anston Feenstra, Vrije Univ., Amsterdam, Netherlands
Naresh Aerra, Rational Labs, Hyderabad, India.
R.Mutyala, RR Labs Inc., San Diego, CA.