MMCC Results

MOLECULAR MODELING & COMPUTATIONAL CHEMISTRY

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About 126 papers from 11 journals are cited.

Editorial and News

The Biophysical Society meetings in Long Beach last month were stimulating and rewarding. The most influential presentation of the meeting, the National Lecture, was heavily dependent on molecular modeling. Joachim Frank (HHMI, Wadsworth Center) is an expert on ribosome function and gave a wonderful exposé on the inner ratchetings of the ribosome as it binds mRNA and the corresponding tRNA molecules, how the tRNA molecules undergo a conformational change, and how that leads to the addition of an amino acid to the nascent peptide chain. The streaming video of the lecture should soon be available at:

http://www.biophysics.org/meetings/lectures.htm

No other news this month. Enjoy!

David D. Busath, Editor

1. APPLICATIONS

1.1. *Small Molecules*

Water and Solvation

!

Physisorption of hydroxide ions from aqueous solution to a hydrophobic surface.

R. Zangi and J.B.F.N. Engberts* [U Groningen]

J. Amer. Chem. Soc. **127**, 2272-2276 (2005)

Atomistic MD simulations using PME and TIP5P water with hydroxide ions between two hydrophobic surfaces clearly demonstrate preferential association of the hydroxide ions within the first two water layers of the hydrophobic wall. The article claims that the driving force is the ordering of water molecules at the surface, which leads to a favorable dipole for the OH- or an apparent negatively charged nonionic surface (as seen experimentally).

Medicinal Chemistry and Drug Design

A

Comparison of automated docking programs as virtual screening tools.

M.D. Cummings* [Johnson & Johnson], R.L. DesJarlais, A.C. Gibbs, V. Mohan, and E.P. Jaeger

J. Med. Chem. **48**, 962-976 (2005)

Docking to five proteins of a compound set seeded with known actives using DOCK, DOCKVISION, GLIDE, and GOLD suggests that GLIDE and GOLD in general identify the most reasonable binding modes for known active compounds.

SARS-CoV protease inhibitors design using virtual screening method from natural products libraries.

B. Liu and J. Zhou* [Chinese Acad Sci]

J. Comput. Chem. **26,** 484-490 (2005)

Protease inhibitors were identified by virtual screening with statistical weighting to compensate for the natural selection for larger compounds. Lipinski's ROF and Xu's extension rules were used to screen the marine natural products and Chinese traditional medicines databases before the virtual screening.

MMCC Results
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Medicinal Chemistry and Drug Design (cont'd)

A new method for estimating the importance of hydrophobic groups in the binding site of a protein.

M.D. Kelly and R.L. Mancera* [De Novo]

J. Med. Chem. **48**, 1069-1078 (2005)

To estimate the relative importance of hydrophobic groups in a binding site with known structure, the group is represented as a dot surface, and then each dot is given a weighting depending on its local environment. A genetic algorithm is used to take the weighted dot information to predict the importance of the hydrophobic group, which may then be useful in guiding structure-based ligand design.

Atom, atom-type and total molecular linear indices as a promising approach for bioorganic and medicinal chemistry: Theoretical and experimental assessment of a novel method for virtual screening and rational design of new lead anthelmintic.

Y.M. Ponce* [Cent U Las Villas], J.A.C. Garit, E. Olazabal, H.S. Serrano, A. Morales, N. Castañedo, F.I. Velarde, A. H. Guillen, A.M. Sánchez, F. Torrens, and E.A. Castro

Bioorg. Med. Chem. **13,** 1005-1020 (2005)

Total and local linear indices and linear discriminant analysis were used to obtain a quantitative model that discriminates between anthelmintic and non-anthelmintic drug-like compounds. The results suggested that the proposed method is a good tool for studying the biological properties of drug candidates during the early state of the drug-development process.

A theoretical study on the structure-activity relationships of metabolites of folates as antioxidants and its implications for rational design of antioxidants.

H.F. Ji, G.Y. Tang and H.Y. Zhang* [Shandong U of Tech]

Bioorg. Med. Chem. **13,** 1031-1036 (2005)

DFT with B3LYP/6-31+G(,3pd) level is used to calculate the structure-activity relationships of metabolites of folates as antioxidants, the O–H bond dissociation enthalpies and ionization potentials. It was found that 4-HP and 5-HP held identical IPs, but the O–H BDE of the former was higher than that of the latter, which meant 4-HP was inert in H-atom donation. 4-HP is also a potential lead antioxidant and deserves attention in rational design of antioxidants.

Human telomerase inhibition and cytotoxicity of regioisomeric disubstituted amidoanthra-quinones and aminoanthraquinones.

H.-S. Huang* [Nat Def Med Cent], C.-L. Chou, C.-L. Guo, C.-L. Yuan, Y.-C. Lu, F.-Y. Shieh, and J.-J. Lin

Bioorg. Med. Chem. **13,** 1435-1444 (2005)

The effects on human telomerase of new classes of 1,4- and 1,5-difunctionalized tricyclic anthraquinone compounds were studied. Cytotoxicity assay, reporter SEAP assay to monitor the hTERT expression, and TRAP-G4 assay to measure the relative activity of these compounds are used and examined how the attached substituents affect their ability to influence telomerase.

Quantitative Structure-Activity Relations

TOMOCOMD-CARDD, a novel approach for computer-aided 'rational' drug design: I. Theoretical and experimental assessment of a promising method for computational screening and in silico design of new anthelmintic compounds

Y. Marrero-Ponce* [U Las Villas], J.A. Castillo-Garit, E. Olazabal, H.S. Serrano, A. Morales, N. Castañedo, F. Ibarra-Velarde, A. Huesca-Guillen, E. Jorge, A. del Valle, F. Torrens, and E.A. Castro

J. Comput.-Aid. Molec. Design **18**, 615–634 (2004)

A 3D-QSAR methodology based on quadratic indices of atoms and linear discriminants, is trained on 148 anthelmintic drugs and 143 non-active compounds and predicts 80% of a 127 compound test set correctly. Possibilities for application in large-scale (lead-finding) screening and in lead-development are investigated.

T

Molecular docking and 3D-QSAR studies of *Yersinia* protein tyrosine phosphatase YopH inhibitors.

X. Hu and C.E. Stebbins* [Rockefeller U]

Bioorg. Med. Chem. **13,** 1101-1109 (2005)

CoMFA and CoMSIA models were developed based on the docking conformations giving q^2 of 0.734 for CoMFA and 0.754 for CoMSIA respectively. The active site of YopH provides new insight into the protein-inhibitor interactions for this enzyme. The results are applicable to the prediction of the activities of new YopH inhibitors, providing structural implications for designing potent and selective YopH inhibitors as antiplague agents.

Predicting multiple drugs side effects with a general drug-target interaction thermodynamic Markov model.

H.G. Díaz, M.C. Monteagudo* [Cent U Las Villas], R. Molina, E. Tenorio, and E. Uriarte

Bioorg. Med. Chem. **13,** 1119-1129 (2005)

The target site or toxic effect is considered in addition to molecular structure for the use of Markov chain models to define novel molecular descriptors. A general Markov model is developed, which describes 39 different drugs side effects grouped in 11 affected systems for 301 drugs. This model encompasses a large number of side effects grouped in specific organ systems in a single stochastic framework for the first time.

Synthesis and structure-activity relationships of 6-4-[(3-fluorobenzyl)oxy]phenoxy nicotinamide derivatives as a novel class of NCX inhibitors: a QSAR study.

T. Kuramochi* [Yamanouchi Pharma Co Ltd], A. Kakefuda, I. Sato, I. Tsukamoto, T. Taguchi, and S. Sakamoto

Bioorg. Med. Chem. **13,** 717-724 (2005)

QSAR studies showed the inhibition of reverse sodium–calcium exchanger (NCX) activity by 6-4-[(3-fluorobenzyl)oxy]phenoxy nicotinamide derivatives is multiply dependent on the hydrophobicity (π) and the shape (B_{iv}) of the substituent at the 3-position of the phenyl ring.

Understanding topoisomerase I and II in terms of QSAR.

R.P. Verma* [Pomona Coll]

Bioorg. Med. Chem. **13,** 1059-1067 (2005)

16 QSAR models were developed for different sets of compounds that are camptothecin analogs, 1,4-naphthoquinones,unsaturated acids, benzimidazoles, quinolones, and miscellaneous fused heterocycles to understand chemical-biological interactions governing their inhibitory activities toward topoisomerase I and II.

Quantitative Structure-Activity Relationships (cont'd)

Exploring QSAR of thiazole and thiadiazole derivatives as potent and selective human adenosine A_3 receptor antagonists using FA and GFA techniques.

P. Bhattacharya, J.T. Leonard and K. Roy* [Jadavpur U]

Bioorg. Med. Chem. **13,** 1159-1165 (2005)

Quantum chemical and hydrophobicity parameters are used in QSAR studies. The derived equations of Genetic function approximation (GFA) showed the importance of Wang-Ford charges of different atoms of the thiazole/thiadiazole nucleus and phenyl ring along with similar impact of lipophilicity and R group on the binding affinity as in the component factor analysis (FA).

QSAR studies on some thiophene analogs as anti-inflammatory agents: enhancement of activity by electronic parameters and its utilization for chemical lead optimization.

A.D. Pillai, S. Rani, P.D. Rathod, F.P. Xavier, K.K. Vasu* [BV Patel Pharm Edn & Res Dev Cent], H. Padh, and V. Sudarsanam

Bioorg. Med. Chem. **13,** 1275-1283 (2005)

A series of 43 thiophene analogs are used. The clusters were individually taken up for a Hansch type of QSAR study with 10 molecular descriptors. The dominant role played by electronic properties and dipole moment in modulating the anti-inflammatory activity. A three point pharmacophore is established from these studies for designing novel anti-inflammatory molecules.

Exploring QSAR of thiazole and thiadiazole derivatives as potent and selective human adenosine A_3 receptor antagonists using FA and GFA techniques.

G. Ghosh and K. Roy* [Jadavpur U]

Bioorg. Med. Chem. **13,** 1185-1194 (2005)

ETA parameters are sufficiently rich in chemical information to encode the structural features contributing significantly to the acute toxicity of phenylsulfonyl carboxylates to *V. fischeri*.

Classical and three-dimensional QSAR for the inhibition of [^{3}H]ponasterone A binding by diacylhydrazine-type ecdysone agonists to insect Sf-9 cells.

Y. Nakagawa* [Kyoto U], K. Takahashi, H. Kishikawa, T. Ogura, C. Minakuchi, and H. Miyagawa

Bioorg. Med. Chem. **13,** 1333-1340 (2005)

3D-QSAR results were consistent with those obtained from the previously reported classical QSAR for 2-chlorobenzoyl analogs containing various *para*-substituents. The high activities of potent insecticides, such as tebufenozide and chromafenozide, were rationalized by CoMFA. CoMFA results are useful in the design of new compounds and in understanding the molecular mechanism of the ligand-receptor interactions.

Quantitative structure and aldose reductase inhibitory activity relationship of 1,2,3,4-tetrahydropyrrolo[1,2-*a*]pyrazine-4-spiro-3′-pyrrolidine-1,2′,3,5′-tetrone derivatives.

K. Ko and Y. Won* [Hanyang U]

Bioorg. Med. Chem. **13,** 1445-1452 (2005)

QSAR of spirosuccinimide-fused tetrahydropyrrolo-[1,2-*a*]pyrazine-1,3-dione derivatives acting as aldose reductase inhibitors contain a chiral center was investigated. QSAR model showed the hydrophobic character of the benzyl moiety is the major contributing factor to the aldose reductase inhibitory activity and the polar surface area descriptors modulate the inhibitory activity.

T

Quantitative Structure-Activity Relationships (cont'd)

Topological models for the prediction of anti-HIV activity of dihydro (alkylthio) (naphthylmethyl) oxopyrimidines.

V. Lather and A.K. Madan* [MD U]

Bioorg. Med. Chem. **13,** 1599-1604 (2005)

Three topological indices: Wiener's index, molecular connectivity index and eccentric connectivity index were used to investigate the relationship between the topological indices and anti-HIV activity of Dihydro (alkylthio) (naphthylmethyl) oxopyrimidines. These models were used to compare the biological activity with the reported anti-HIV activity.

QSAR treatment of drugs transfer into human breast milk.

A.R. Katritzky* [U Florida], D.A. Dobchev, E. Hür, D.C. Fara, and M. Karelson

Bioorg. Med. Chem. **13,** 1623-1632 (2005)

CODESSA PRO is used to generate a model for the correlation and prediction of milk to plasma concentration ratios (*M/P* ratio) for diverse pharmaceuticals. Based on the data set, a seven-parameter QSAR model was derived that shows a satisfactory correlation between predicted and observed values of log (M/P) ratio.

Antimalarial activity of thioacridone compounds related to the acronycine alkaloid.

J.P. Dheyongera, W.J. Geldenhuys, T.G. Dekker, M.G. Matsabisa, and C.J. Van der Schyf* [North West U]

Bioorg. Med. Chem. **13,** 1653-1659 (2005)

QSAR studies were performed for a series of thioacridone compounds. The most potent compound, 1-(2-dimethylaminoethylamino)-9(10*H*)-thioacridone, was docked into the chloroquine binding site of PfLDH. The slightly lower activity of this compound, compared with chloroquine, is due to steric interference within a restricted binding pocket.

QSAR studies-potent benzodiazepine γ-secretase inhibitors.

A.R. Keerti* [Nizam Coll], B.A. Kumar, V. Uma, and T. Parthasarathy

Bioorg. Med. Chem. **13**, 1873-1878 (2005)

A correlation was obtained between the physicochemical properties QlogP, SMR and the inhibitory activity. A model equation was generated to predict the best possible pharmacophore for treating Alzheimer's disease. The inhibitory activity of the compound depends on the lipophilicity positively and is sensitive to small changes in its SMR.

Cluster analysis and three-dimensional QSAR studies of HIV-1 integrase inhibitors.

H. Yuan and A. Parrill* [U Memphis]

J. Mol. Graph. Mod. **23**, 317-328 (2005)

3D-QSAR and cluster analysis were applied to a variety of HIV-1 integrase inhibitors. The 11 classes of inhibitors were classified into two groups. The MFA models for these two clusters had r^2 values of 0.90 and 0.95 and q^2 values of 0.85 and 0.91 that were noticeably enhanced from those of conventional QSAR models.

Topological models for the prediction of HIV-protease inhibitory activity of tetrahydropyrimidin-2-ones.

V. Lather and A.K. Madan* [MD U]

J. Mol. Graph. Mod. **23**, 339-345 (2005)

Wiener's index, Zagreb group parameter and eccentric connectivity index were used to findout the relationship between the topological indices and HIV-protease inhibitory activity of tetrahydropyrimidine-2-ones. A dataset comprising of 80 substituted tetrahydropyrimidine -2-one analogues was selected. The accuracy prediction of these models was varied from minimum 86% to maximum 88%.

T

Comparative molecular field analysis and comparative molecular similarity indices analysis of human thymidine kinase 1 substrates.

A.K. Bandyopadhyaya, J. Johnsamuel, A.S. Al-Madhoun, S. Eriksson, and W. Tjarks* [Ohio State U]

Bioorg. Med. Chem. **13**, 1681-1689 (2005)

CoMFA and CoMSIA were applied to analyze the phosphorylation capacity of a series of 31 TK1 substrates. The predictive capacity of both models was validated by calculating the known phosphorylation rates of five TK1 substrates that were not included in the training set. CoMFA and CoMSIA models contour maps are correlated with the experimentally developed SAR.

Crystal Growth

Understanding the barriers to crystal growth: Dynamical simulation of the dissolution and growth of urea from aqueous solution.

S. Piana and J.D. Gale* [Curtin U Tech]

J. Amer. Chem. Soc. **127**, 1975-1982 (2005)

MD and kinetic Monte Carlo modeling of surface growth and dissolution of urea [001] crystals is performed. The face grows with a rough surface topology rather than as a clean layer-by-layer mechanism, although the roughness is only the scale of a few molecules.

1.2. *Biopolymers*

Protein Sequence Analysis and Alignment

FAST: A novel protein structure alignment algorithm

J. Zhu and Z. Weng* [Boston U]

Proteins **58**, 618-627 (2004)

A novel sequence alignment method using clique detection in pair graphs pruned by empirical rules is shown to agree to 96% with HOMSTRAD with higher sensitivity (up to 93% at 80% specificity, in ~20% of the time) than DaliLite, K2 and CE. A detailed comparison of alignments for 11 example protein-pairs by HOMSTRAD, FATCAT, DALI and FAST is discussed.

Protein Structure Prediction

The protein structure prediction problem could be solved using the current PDB library.

Y. Zhang and J. Skolnick* [U Buffalo]

PNAS **102**, 1029-1034 (2005)

The TASSER algorithm is applied to build full-length models, where continuous fragments are excised from the top-scoring templates and reassembled under the guide of an optimized force field. The results suggested that the protein-folding problem can be solved based on the current PDB library by developing efficient fold recognition algorithms.

Comparative or Homology Modeling

Mechanistic study of proton transfer and hysteresis in catalytic antibody 16E7 by site-directed mutagenesis and homology modeling.

L. Zheng, R. Manetsch, W.D. Woggon, U. Baumann, and J.-L. Reymond* [U Berne]

Bioorg. Med. Chem. **13,** 1021-1029 (2005)

A 3D-structure model is developed by homology modeling and is used for docking procedure to obtain models for antibody-ligand complexes. This model suggested that substrate access to the catalytic site might be hindered by a flexible HCDR3 loop held in closed position by a hydrogen bond between Ser^{H99} and Glu^{L39}, explained the observed hysteresis effect.

Homology modelling of RNA polymerase and associated transcription factors from *Bacillus subtilis.*

I.J.A. MacDougall, P.J. Lewis, and R. Griffith* [U. Newcastle]

J. Mol. Graph. Mod. **23**, 297-303 (2005)

Homology model is developed for Gram positive organism *Bacillus subtilis* RNA polymerase in the core and holoenzyme forms. Interactions between RNA polymerase and the transcription factor σ^A were investigated in order to design peptide mimics of the major interactions.

Comparative protein modeling of methionine *S*-adenosyltransferase (MAT) enzyme from *Mycobacterium tuberculosis*: a potential target for antituberculosis drug discovery.

S.A. Khedkar, A.K. Malde, and E.C. Coutinho* [Bombay Coll Pharm]

J. Mol. Graph. Mod. **23**, 355-366 (2005)

The structures of *E. coli* MAT (PDB code: 1MXA) and rat MAT (PDB code: 1QM4) templates are used to construct a homology model of MAT by comparative protein modeling principles. The resulting model has the correct stereochemistry as gauged from the Ramachandran plot and good 3D structure compatibility as assessed by the *Profiles-3D* score. This model conserves the topological and active site features of the MAT family of proteins.

A

Construction of a 3D model of nattokinase, a novel fibrinolytic enzyme from *Bacillus natto:* A novel nucleophilic catalytic mechanism for nattokinase.

Z. Zheng, Z. Zuo, Z. Liu, K. Tsai, A. Liu, and G. Zou* [Wuhan U]

J. Mol. Graph. Mod. **23**, 373-380 (2005)

Homology modeling is used to construct a 3D-structural model of nattokinase (NK) from *Bacillus natto.* MODELLER program is used to build the initial models of NK and the refined model NKC1 was analysed by PROCHECK for the evaluation of Ramachandran plot quality, PROSA for testing interaction energies and WHATIF for the calculation of packing quality.

Peptide Conformational Analysis

Theoretical study of intramolecular interaction energies during dynamics simulations of oligopeptides by the fragment molecular orbital-Hamiltonian algorithm method.

T. Ishimoto* [Japan Sci Tech Agency], H.i Tokiwa, H. Teramae, and U.Nagashima

J. Chem. Phys. **122**, 09490501-09490509 (2005)

Gly_5 and Gly_{10} both have a propensity towards β-sheet structure when simulated *ab initio* with a helical starting structure. Fragment interaction energy decomposition shows that the hydrogen bonds in the helix weaken during the simulation.

Protein Structure Analysis

Lattice models, packing density, and Boltzmann-like distribution of cavities in proteins

A.A. Rashin* [BioChemComp] and A.H. Rashin

Proteins **58***,* 547-559 (2004)

Cavity formation is reproduced by random mutations in a lattice model, suggesting that random processes under constraints of packing density and protein stability can lead to the experimentally found Boltzmann distribution of cavity size.

!

An analysis of core deformations in protein superfamilies.

A. Leo-Macias, P. Lopez-Romero, D. Lupyan, D. Zerbino, and A.R. Ortiz* [CSIC-UAM]

Biophys. J. **88,** 1291-1299 (2005)

Analysis of the normal modes of 35 well-populated protein families suggests that successful mutations often affect the lowest frequency vibrations and that 4-5 dimensions in principle components analysis of normal mode effects are sufficient to represent evolutionary changes. This is pertinent to homology modeling.

The ConSurf-HSSP database: The mapping of evolutionary conservation among homologs onto PDB structures

F. Glaser, Y. Rosenberg, A. Kessel, T. Pupko, and N. Ben-Tal* [Tel Aviv U]

Proteins **58***,* 610-617 (2004)

Mapping phylogenetic conservation from the HSSP database onto protein structures, in a 'ConSurf' score, reveals functional residues and regions including those from HSSP, and other, novel, functional sites for the rabbit muscle pyruvate kinase. General application for function assignment is discussed.

Structure Conservation in Cytochromes P450

J. Mestres* [U Barcelona]

Proteins **58***,* 596-609 (2004)

A thorough structural comparison of 12 Cyt.P450 structures confirms in detail the well-known high structural conservation in spite of low sequence identities of 10-30%, and a very high structural similarity in the core around the heme co-factor. A new multiple-structure sequence alignment and local sequence entropies are presented and discussed.

Conservation of cis prolyl bonds in proteins during evolution

S. Lorenzen* [Charité Berlin], B. Peters, A. Goede, R. Preissner, and C. Frommel

Proteins **58***,* 589-595 (2004)

A detailed analysis of evolutionary relationships between 1729 sequences/structures in the PDB shows cis-prolyl to be more conserved than trans-prolyl, more than surrounding residues, and to persist in distant homologues down to 20% sequence identity. Interestingly, cis-prolyl was markedly underrepresented in low-resolution X-ray structures

Protein Folding

Misfolding pathways of the prion protein probed by molecular dynamics simulations.

A. Barducci, R. Chelli* [U Florence], P. Procacci, and V. Schettino

Biophys. J. **88,** 1334-1343 (2005)

In CCl_4 and, to a lesser extent, in water, the pathogenic mutant, D178N, of the prion protein, PrP^{Sc}, shows a weakening of the antiparallel β-sheet and an increase in β-structure during few-ns MD. The β-sheet weakening is not observed in the wild type protein.

Protein Folding (cont'd)

A detailed unfolding pathway of a β/α(8)-barrel protein as studied by molecular dynamics simulations

S. Akanuma, H. Miyagawa, K. Kitamura, and A. Yamagishi* [Tokyo U]

Proteins **58**, 538-546 (2004)

Analysis of room-, intermediate- and high-T unfolding simulations of a β/α(8) protein, shows a possible nucleation site and a larger folding scaffold that showed most resistance to unfolding throughout.

Protein conformational transitions coupled to binding in molecular recognition of unstructured proteins: Deciphering the effect of intermolecular interactions on computational structure prediction of the p27(Kip1) protein bound to the cyclin A-cyclin-dependent kinase 2 complex.

G.M. Verkhivker* [Pfizer]

Proteins **58**, 706-716 (2004)

From simulated annealing simulations with restrained secondary structure elements it is found that over-stabilization of these elements hinders the rapid formation of overall native-state structure of the protein.

***N,N'*-linked oligoureas as foldamers: Chain length requirements for helix formation in protic solvent investigated by circular dichroism, NMR spectroscopy, and molecular dynamics.**

A. Violette, M.C. Averlant-Petit, V. Semetey, C. Hemmerlin, R. Casimer, R. Graff, M. Marraud, J.-P. Briand, D. Rognan, and G. Guichard* [CNRS]

J. Amer. Chem. Soc. **127**, 2126-2164 (2005)

MD simulation, coupled with NMR and CD experiment, investigate the folding of linked ureas. A 2.5 helical fold is found in methanol beyond four residues and is stabilized by the removal of unfavorable amino terminal electrostatic interactions.

***Ab initio* simulations of protein-folding pathways by molecular dynamics with the united-residue model of polypeptide chains.**

A. Liwo, M. Khalili, and H.A. Scheraga* [Cornell U]

PNAS **102**, 2362-2367 (2005)

The united-residue (UNRES) force field was developed to obtain a hierarchical structure of the energy landscape. This is used to explore thousands of folding pathways and to predict not only the native structure but also the folding scenario of a protein together with its quantitative kinetic and thermodynamic characteristics.

Protein Design and Engineering

Ab initio prediction of the three-dimensional structure of a de novo designed protein: A double-blind case study

J.L. Klepeis, Y. Wei, M.H. Hecht, and C.A. Floudas* [Princeton]

Proteins **58**, 560-570 (2004)

A novel de-novo structure prediction method is shown to reproduce the designed structure of a designed 4-helix bundle protein (RMSD ~5 Å), and to agree with NMR data.

Computational de novo design and characterization of a four-helix bundle protein that selectively binds a nonbiological cofactor.

F.V. Cochran, S.P. Wu, W. Wang, V. Nanda, J.G. Saven* [U Penn, M.J. Therien, and W.F. DeGrado* [U Penn]

J. Amer. Chem. Soc. **127**, 1346-1347 (2005)

Using a computational design methodology described in previously published work, a novel four-helix bundle protein was designed and built around nonbiological cofactors. This communication discusses not the computational part, but the experimental characterization of the protein.

Protein Hydration

Water dynamics simulation as a tool for probing proton transfer pathways in a heptahelical membrane protein.

C. Kandt, K. Gerwert*, and J. Schlitter* [Ruhr-U Bochum]

Proteins **58***,* 528-537 (2004)

Analysis of water densities from MD simulations confirms known residues involved in proton conduction in bacteriorhodopsin and agrees with TR-FIR data. Entrance and exit pathways and involvement of additional residues are predicted.

Refinement of X-ray data on dual cosubstrate specificity of CK2 kinase by free energy calculations based on molecular dynamics simulation.

P. Setny* [Warsaw U] and M. Geller

Proteins **58***,* 511-517 (2004)

The relative free energies for binding of GTP and ATP to CK2 are calculated from TI with CHARMM confirm water-mediated binding, and identify a new water molecule not in the X-ray structure to be crucial in reproducing all the other water positions.

Protein Dynamics

Structural dynamics of nucleosome core particle: Comparison with nucleosomes containing histone variants.

A. Ramaswamy, I. Bahar, and I. Ioshikhes* [Ohio U]

Proteins **58***,* 683-696 (2004)

Normal modes analysis of an elastic network representation of nucleosomes shows less correlation and higher mobility for H2A.Z- or H2A.1/H2B.2-containing nucleosomes compared to the regular histones

Phosphorylation effects on cis/trans isomerization and the backbone conformation of serine-proline motifs: Accelerated molecular dynamics analysis.

D. Hamelberg* [UCSD], T. Shen, and J.A. McCammon

J. Amer. Chem. Soc. **127**, 1969-1974 (2005)

Accelerated MD, a technique which boosts the potential energy of lower lying states proportional to a Boltzman factor, is applied to cis/trans isomerization phosphorylated Ser/Thr proline motifs and shown to significantly increase the samping.

Protein Dynamics (cont'd)

Protein dynamics in solution and powder measured by incoherent elastic neutron scattering: the influence of Q-range and energy resolution.

F. Gabel* [Inst de Biol Stru]

*Eur.J.Biophys.***34**, 1-9 (2005)

The elastic intensity for several simple scattering functions was calculated to investigate the contributions of diffusive motions to intramolecular atomic mean square displacements. The concepts developed in this method are applied to interpret experimental data from H_2O- and D_2O-hydrated proteins. The analogies between the Gaussian approximation in incoherent elastic neutron scattering and the Guinier approximation in small-angle scattering are discussed.

Ligand Binding

Insights into saquinavir resistance in the G48V HIV-1 protease: Quantum calculations and molecular dynamic simulations.

K. Wittayanarakul, O. Aruksakunwong, S. Saen-oon, W. Chantratita, V. Parasuk, P. Sompornpisut* [Chulalongkorn U], and S. Hannongbua

Biophys. J. **88,** 867-879 (2005)

According to MD, combined with PB and QM analysis of the active site, indicate that the G48V mutation does not modify the binding mode of saquinavir, nor its interaction with the active site. However, by pressure on the drug from the Val side chain, it compromises the structure of the P2 binding site. Drugs that could avoid this effect may recover efficacy.

CH···O and CH···N hydrogen bonds in ligand design: A novel quinazolin-4-ylthiazol-2-ylamine protein kinase inhibitor.

A.C. Pierce* [Vertex], E. ter Haar, H.M. Binch, D.P. Kay, S.R. Patel, and P. Li

J. Med. Chem. **48**, 1278-1281 (2005)

Crystal structures and quantum mechanics conformational analysis is used to understand and suggest a possible role for an aryl CH--O hydrogen bond in a series of GSK3 inhibitors.

Unsupervised guided docking of covalently bound ligands.

X. Fradera* [Organon], J. Kaur, and J. Mestres

J. Comput.-Aid. Molec. Design **18**, 635–650 (2004)

A new module in MacDock is presented that allows prediction of covalent binding by docking, tested by reproducing six known covalent complexes and shown to recover known thrombin inhibitors in 5% of a 100.000 compound database.

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Docking studies on PARP-1 inhibitors: insights into the role of a binding pocket water molecule.

D. Bellocchi, A. Macchiarulo, G. Costantino* [U of Perugia], and R. Pellicciari

Bioorg. Med. Chem. **13,** 1151-1157 (2005)

Autodock 3.0 is used to investigate the binding mode of a series of competitive PARP-1 inhibitors. The calculated binding energies and experimental inhibitory activities were in good agreement either by including or not the structural water molecule. The results suggested that the water molecule should be considered part of the hydration shell of polar inhibitors and not as structural water.

Enzyme Catalysis

Molecular dynamics simulations of the TEM-1β-lactamase complexed with cephalothin.

N. Díaz, D. Suárez, K.M. Merz, Jr.* [Penn State], and T.L. Sordo [U Oviedo]

J. Med. Chem. **48**, 780-791 (2005)

MM/PBSA and quantum chemical PBSA schemes applied to TEM-1b-lactamase complexed with cephalothin suggests that the kinetic preference of the enzyme for penicillins over cephalosprins is due to the lower efficacy of cephalosporins in simultaneously binding the "carboxylate pocket" and the "anion hole" at the active site.

How does the cAMP-dependent protein kinase catalyze the phosphorylation reaction: An ab initio QM/MM study.

Y. Cheng* [UCSF], Y. Zhang, and J.A. McCammon

J. Amer. Chem. Soc. **127**, 1553-1562 (2005)

QM/MM calculations with a DFT treatment of the active site probe the mainly dissociative phosphorylation reaction of cAMP-dependent protein kinase.

Protein-Protein Interactions

Analysis of sequence-reactivity space for protein-protein interactions.

J. Li, Z. Yi, M.C. Laskowski, M. Laskowski, Jr., and C. Bailey-Kellogg* [Sudikoff]

Proteins **58**, 661-671 (2004)

A thorough statistical analysis of predictions of binding affinity of Kazal serine proteases to ligand proteins, with a sampling-based scheme to cover sequence space of both partners, is presented. Implications for protein design are discussed.

Prediction of interfaces for oligomerizations of G-protein coupled receptors.

W. Nemoto* [Kyoto U] and H. Toh

Proteins **58**, 644-660 (2004)

Analysis of the distribution of conserved surface residues from projections of the coordinates in the membrane plane, enables prediction of established interfaces in rhodopsin and rhodopsin-based models of D2 dopamine and β2 adrenergic receptors. Possible implication in diseases, as well as shortcomings of the method, is discussed.

Small-world network approach to identify key residues in protein–protein interaction.

A. del Sol* [Fujirebio] and P. O'Meara

Proteins **58**, 672–682 (2004)

Highly central residues in the interaction network of protein interfaces are shown to correlate well with known so-called 'hot-spots' for 50 interfaces. The possibility for prediction from non-complexed structures is discussed.

Membrane Proteins and Lipid-Peptide Interactions

Subunit rotation models activation of serotonin 5-HT3AB receptors by agonists

G. Maksay, M. Simonyi, and Z. Bikádi* [Hungarian Ac Sci]

J. Comput.-Aid. Molec. Design **18**, 651–664 (2004)

Antagonist binding modes from docking in a 5-HT3AB model (based on AchBP) with clock- and counter-clockwise subunit rotations and without rotation show distinctly different interaction patterns. Implications for possible receptor activation mechanisms are discussed.

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

Implicit solvent simulations of peptide interactions with anionic lipid membranes

T. Lazaridis* [City College NY]

Proteins **58***,* 518-527 (2004)

An 'implicit solvent' membrane model using relatively simple linear dielectric screening is presented, using a non-polar core and optional anionic head group region. The model reproduces well the binding characteristics of 5-Lys, *n*-(Phe,Lys), mellitin, magainin 2, penetratin and cardiotoxin peptides.

The transmembrane domain of the acetylcholine receptor: Insights from simulations on synthetic peptide models.

L. Saiz* [U Pennsylvania] and M.L. Klein

Biophys. J. **88,** 959-970 (2005)

Simulations with DMPC show that the M2 helix of the δ subunit of the NAChR aggregate to form a channel, as had been found previously with planar bilayer and NMR studies. In the simulations, the C-terminus forms salt bridges with Arg side chains, dehydrating the extracellular end of the channel.

Penetratin-membrane association: W48/R52/W56 shield the peptide from the aqueous phase.

M.F. Lensink* [U Libre Bruxelles], B. Christiaens, J. Vandekerckhove, A. Prochiantz, and M. Rosseneu

Biophys. J. **88,** 939-952 (2005)

Peptides associate with the bilayer surface without significant aggregation, according to MD. The process is facilitated by three positive side chains, which interact with negatively charged lipid molecules. Sweeping by the side chains open defects in the bilayer were the peptide inserts. Effects on lipid molecule structure are primarily local.

Homology modeling and molecular dynamics simulations of transmembrane domain structure of human neuronal nicotinic acetylcholine receptor.

A.C. Saladino, Y. Xu, and P. Tang* [U Pittsburgh]

Biophys. J. **88,** 1009-1017 (2005)

A simulation of an homology model of the neuronal NAChR TM region in a DMPC bilayer showed an extra constricting salt bridge, compared to the muscle protein. However, it is a hydrophobic ring, rather than this steric occlusion, that appears to constrict water flow.

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The transmembrane oligomers of coronavirus protein E.

J. Torres* [Nanyang Tech U], J. Wang, K. Parthasarathy, and D.X. Liu

Biophys. J. **88,** 1283-1290 (2005)

Exhaustive *in vacuo* global searching MD simulations of aggregation possibilities for 13 subtypes of the 1-TM protein from SARS indicate that it is prone to form dimers, trimers, and two types of pentamers in lipid bilayers. This result is consistent with the experimentally observed oligomerization and is dependent upon highly conserved N15.

Molecular modeling of nearly full-length ErbB2 receptor.

P. Bagossi* [U Debrecen], G. Horváth, G. Vereb, J. Szöllösi, and J. Tözsér

Biophys. J. **88,** 1354-1363 (2005)

A model of epidermal growth factor, a tyrosine kinase, constructred from experimentally determined extracellular, kinase domain, and transmembrane structures and positioned according to FRET analysis, shows favorable dimerization contacts at all three levels.

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

Investigation into the interaction of the bacterial protease OmpT with outer membrane lipids and biological activity of OmpT:lipopolysaccharide complexes.

K. Brandenburg* [Leibniz Inst Med & Biochem] ,
P. Garidel, A.B. Schromm, J. Andrä, A. Kramer, M. Egmond, and A. Wiese

Eur. J. Biophys. **34**, 28-41 (2005)

The activities of outer-membrane proteases T (OmpT) and lipopolysaccharide (LPS):OmpT complexes were investigated in biological test systems and with phospholipid model membranes. The results showed that a strong influence of OmpT on the mobility of the lipids leading to a considerable fluidization of the acyl chains of the phospholipids as well as LPS, and a rigidification of the phospholipids.

Proteins and Surfaces

Mechanically induced titin kinase activation studied by force-probe molecular dynamics simulations.

F. Gräter, .J. Shen, H. Jiang, M. Gautel, and H. Grubmüller* [Max-Planck Inst]

Biophys. J. **88,** 790-804 (2005)

MD simulations in which titin kinase is pulled apart to expose the active site give evidence that the enzyme serves as a biochemical stress sensor. First, N- and C-terminal beta sheets are ruptured. This leads to rearrangement of the autoinhibitory tail.

Systematic size study of an insect antifreeze protein and its interaction with ice.

K. Liu, Z. Jia, G. Chen* [Beijing Normal U], C. Tung, and R. Liu

Biophys. J. **88,** 953-958 (2005)

Semiempirical and QM simulations of insect antifreeze protein, which is a very requlr coil with the sequence in each turn being TCTxSxxCxxAx, has increasing synergy of interaction with ice for the first five turns. The synergy then declines for further coils.

Nucleic Acids

Interaction of sodium and potassium ions with sandwiched cytosine-, guanine-, thymine-, and uracil-base tetrads.

M. Meyer* [Revotar Biopharm], A. Hocquet, and J. Sühnel

J. Comput. Chem. **26,** 352-364 (2005)

DFT with microsolvation indicates that metal ions would bind at the center of all four homotetrads (in which the bases essentially form a ring with an electronegative hole in the center), with K^+ being more favored than Na^+. Such tetrads appear occacionally in association with loops.

A computer-generated supercoiled model of the pUC19 plasmid.

E.A. Kümmerle* [Geschäftsbereich Sicherheit & Strahlenschutz] and E. Pomplun

Eur. J. Biophys. 34, 13-18 (2005)

A computer code was developed to calculate the coordinates of individual atoms in supercoiled plasmid DNA. In this study, the known base-pair sequence of the pUC19 plasmid is utilized and this model was built in a three-step process.

Nucleic Acids (cont'd)

Probing counterion modulated repulsion and attraction between nucleic acid duplexes in solution.

Y. Bai, R. Das, I.S. Millett, D. Herschlag* [Stanford U] and S. Doniach

PNAS **102,** 1035-1040 (2005)

A simple model DNA system is used to determine how the ion atmosphere modulates interactions between duplexes in the absence of specific metal ion-binding sites. Especially, it was tested whether the Coulomb repulsion between nucleic acids is reversed by counterions to give a net attraction. The results indicated that a counterion-induced attractive force between nucleic acid duplexes is not significant under physiological conditions.

Lipids and Surfactants

Experimental validation of molecular dynamics simulations of lipid bilayers: A new approach.

R.W. Benz, F. Castro-Román, D.J. Tobias* [U Calif Irvine], and S.H. White* [U Calif Irvine]

Biophys. J. **88,** 805-817 (2005)

The simulated structure of a DOPC bilayer with 5.4 water molecules per lipid molecule using charm and GROMOS force fields based on system structure factors and Fourier analysis was not consistent with experimental results to within experimental uncertainties. The width of the terminal methyl distribution was especially erroneous and the bilayer width was ~4 Å too great. The charmm27 force field performed better than charmm22, but GROMOS is much better than both.

The dynamic stress responses to area change in planar lipid bilayer membranes.

J. Jeon and G.A. Voth* [U Utah]

Biophys. J. **88,** 1104-1119 (2005)

The DMPC bilayer was subjected to step and oscillating pressure fluctuations using NEMD to evaluate dynamic viscosity properties. Responses are linear for changes of 6-20%, depending on the visoelastic property involved.

Phosphatidylethanolamine-phosphatidylglycerol bilayer as a model of the inner bacterial membrane.

K. Murzyn, T. Róg, and M. Pasenkiewicz-Gierula* [Jagiellonian U]

Biophys. J. **88,** 1091-1103 (2005)

MD with POPE:POPG (3:1) in Na^+ electrolyte show that PE H-bonds more with PG than PE, that PG rarely H-bonds with PG, that PG sits deeper in the membrane and is more ordered, and occupies a larger area. Na^+ interactions with the lipid head groups are rare. Bacterial regulations of the ratio are probably adaptive.

1.3. Polymers

A molecular dynamics study on universal properties of polymer chains in different solvent qualities. Part I. A review of linear chain properties.

M.O. Steinhauser* [Fraunhofer Ernst-Mach-Inst]

J. Chem. Phys. **122**, 09490101-09490113 (2005)

Polymer simulations with linear polymers were analyzed for typical properties in the evaluation of "triple-MD," an algorithm that utilized MD for fast relaxations and MC pivots to explore slower structural changes efficiently. The program has been parallelized for massive linux cluster usage.

1.4. Surfaces, Catalysts, and Material Subjects

A molecular dynamics simulation of the adsorption of water molecules surrounding an Au nanoparticle.

S-P. Ju* [National Sun Yat-Sen U]

J. Chem. Phys. **122**, 09471801-09471806 (2005)

MD shows that water molecules form two shells around a gold particle with stronger interactions and shell structures for smaller particles. Hydrogen bonds with other water molecules are sacrificed.

2. METHODOLOGY

Quantitative Structure-Activity Relations

Heuristic molecular lipophilicity potential (HMLP): A 2D-QSAR study to LADH of molecular family pyrazole and derivatives.

Q. Du, P.G. Mezey, and K.-C. Chou* [Gordon Life Sci Inst]

J. Comput. Chem. **26,** 461-470 (2005)

VDW radii are supplemented with molecular, fragment, and atomic hydrophilic and lipophilic indices based on QM and other studies to create a simple 2D QSAR approach, which is tested successfully with the liver alcohol dehyrdrogenase system.

Non-stochastic and stochastic linear indices of the 'molecular pseudograph's atom adjacency matrix': application to 'in silico' studies for the rational discovery of new antimalarial compounds.

Y.M. Ponce*[Cent U Las Villas], A.M. Torres, M.M. Peréz, C.R. Zaldivar, M.I. Veitía, and R.N.G. Sánchez

Bioorg. Med. Chem. **13,** 1293-1304 (2005)

The TOpological MOlecular COMputer Design strategy approach is introduced to obtain two quantitative models for the discrimination of antimalarials. The validated models, including non-stochastic and stochastic indices, classify more than 90% of compounds correctly in both training and external prediction data sets. These QSAR models are used in the identification of previously un-known antimalarials compounds.

Potentials and Parameters

Knowledge-based elastic potentials for docking drugs or proteins with nucleic acids.

W. Ge, B. Schneider, and W.K. Olson* [Rutger's State U NJ]

Biophys. J. **88**, 1166-1190 (2005)

The distribution of water molecules around the DNA helix was used to derive elastic ellipsoid functions for use with ligand docking in the helical grooves. Ligands appear to faithfully replace water molecules when binding. Steric hindrance and hydrogen bonding allow distinction between the minor and major groove sides of C-G and G-C pairs.

A scoring function for docking ligands to low-resolution protein structures.

E. Bindewald and J. Skolnick* [U Buffalo]

J. Comput. Chem. **26,** 374-383 (2005)

To predict lilgand-contact residues for low-resolution structures, the scoring feature must be tuned differently than for high-resolution structures. The current implementation does four-times better at predicting at least half of the contact residues than the Dolores method.

Potentials and Parameters (cont'd)

Comparative performance of MM3(92) and two TINKERTM MM3 versions for the modeling of carbohydrates.

C.A. Stortz* [Ciudad U]

J. Comput. Chem. **26,** 471-483 (2005)

Although TINKER versions of MM3 have some improvements in carbohydrate force field parameters, they lack anomeric effects on bond lengths, which can substantially distort structures and energies for some structures.

Transferability of parameters of strictly local geminals' wave function and possibility of sequential derivation of molecular mechanics.

A.M. Tokmachev* [RWTH Aachen] and A.L. Tchougréeff* [Karpov Inst]

J. Comput. Chem. **26,** 491-505 (2005)

The antisymmetrized product of strictly local geminals is examined as a basis for transferable potential functions that could be useful for building accurate molecular mechanics force fields. Density matrix elements and basis one-electron states (hybrid orbitals) are shown to be transferable under very nonrestrictive conditions.

Solvation Energy

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Incorporating variable dielectric environments into the generalized Born model.

G. Sigalov* [Virginia Tech], P. Scheffel, and A. Onufriev

J. Chem. Phys. **122,** 09451101-09451115 (2005)

The Generalized Born model of Still (1990) is improved by solving the electrostatics within a sphere of one dielectric surrounded by a sphere of another. The result is as efficient as the standard approach, but more accurate, as demonstrated by comparison with PB results.

Free Energy Methods

Elucidating protein thermodynamics from the three-dimensional structure of the native state using network rigidity.

D.J. Jacobs* [Calif State U] and S. Dallakyan

Biophys. J. **88,** 903-915 (2005)

Enthalpy and entropy are deduced from a distance constraints network. Five parameters are required, two of which can be determined by fitting heat capacity curves. Ubiquitin and histidine binding protein curves at different pHs provided these parameters. Cooperativity and folding are influenced most by hydrogen bond network topology.

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Alchemical free energy calculations and multiple conformational substates.

M. Leitgeb* [U Vienna], C. Schröder, and S. Boresch

J. Chem. Phys. **122**, 08410901-08410915 (2005)

A Non-Boltzmann TI (NBTI) approach to FEP simulations is introduced in which thermodynamic integration is accompanied by adaptive umbrella sampling. Convergence and accuracy are dramatically improved. A method of obtaining the FEP energy from numerically integrated partition functions at the endpoints is also presented.

Protein Structure Prediction

Improved greedy algorithm for protein structure reconstruction.

P. Tuffery* [U Paris 7], F. Guyon, and P. Derreumaux.

J. Comput. Chem. **26,** 506-513 (2005)

In a greedy algorithm, you start with at the N-terminus and add building blocks piecewise, retaining up to, say, 3000 conformations for each 3-to-9-residue building block. The millions of structures are then scored, perhaps with a Go-potential, which rewards native contacts as deduced from xray or NMR data. Here the algorithm is improved for use with the minimalistic Go-potential.

Surface and Volume Determination

A new analytical method for computing solvent-accessible surface area of macromolecules and its gradients.

S. Hayryan, C.-K. Hu* [Academia Sinica], J. Skivánek, E. Hayryane, and I. Pokorný

J. Comput. Chem. **26,** 334-343 (2003)

Line integrals along circular curves are used to determine the molecular surface in a general way.

Ligand Docking

Flexible docking in solution using metadynamics.

F.L. Gervasio* [ETH], A. Laio, and M. Parrinello

J. Amer. Chem. Soc. **127**, 2600-2607 (2005)

Their new metadynamics method—a method that supplements restrained MD with a history dependent potential—is applied to docking to flexible receptors in solution allowing construction of the free energy path of drug association and dissociation. The docked geometry is reproduced along with the free energy of docking.

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

Journal of Computational Chemistry 26(4), March, 2005

325-333 **Characterization of molecular orbitals by counting nodal regions.** Y. Hatano, S. Yamamoto* [Chukyo U], and H. Tatewaki

Molecular orbitals can be characterized according to nodal regions, even during conformational changes.

334-343 **A new analytical method for computing solvent-accessible surface area of macromolecules and its gradients.** S. Hayryan, C.-K. Hu* [Academia Sinica], J. Skivánek, E. Hayryane, and I. Pokorný. See **Methodology, Surface and Volume Determination.**

344-351 **Two-electron integrations in the quantum theory of Atoms in Molecules with correlated wave functions.** A. Martín Pendás* [U Oviedo], E. Francisco, M. A. Blanco.

A monadic factorization of the second-order reduced density matrix is used to compute the two-electron integral.

352-364 **Interaction of sodium and potassium ions with sandwiched cytosine-, guanine-, thymine-, and uracil-base tetrads.** M. Meyer* [Revotar Biopharm], A. Hocquet, and J. Sühnel. See **Applications, Nucleic Acids.**

365-373 **Stereodynamics of bond rotation in tertiary 1-naphthoic acid amides: A computational study.** P. Campomanes, M. I. Menéndez, R. López, and T.L. Sordo* [U Oviedo]

The N-CO bond cannot rotate independently of the Ar-CO bond and an ethyl torsion. Gibbs free energies for concerted rotations agree with experiment.

374-383 **A scoring function for docking ligands to low-resolution protein structures.** E. Bindewald and J. Skolnick. See **Methodology, Potentials and Parameters.**

384-388 **Vibrational computations beyond the harmonic approximation: Performances of the B3LYP density functional for semirigid molecules.** P. Carbonniere, T. Lucca, C. Pouchan, N. Rega, and V. Barone* [U Federico II].

"The study reveals that the relatively cheap 6-31+G(d,p) basis set performs a very good job for harmonic frequency calculations" whereas "B3LYP anharmonicities are in close agreement with the reference values irrespective of the basis set used." Therefore, a hybrid force is recommended.

389-398 **Quantum vs. classical models of the nitro group for proton chemical shift calculations and conformational analysis.** M. Mobli* [U Liverpool], and R.J. Abraham

"The most accurate results" for chemical shift calculations in sterically crowded organic molecules with nitro groups "are found when the structures are calculated using B3LYP/6-311++G(2d,p) level of theory, and the chemical shifts are calculated using the CHARGE program" with classical models.

399-409 **Continuous medium theory for nonequilibrium solvation: III. Solvation shift by monopole approximation and multipole expansion in spherical cavity.** Q. Zhu, K.-X. Fu, X.-Y. Li* [Sichuan U], Z. Gong, and J.-Y. Ma

The role of solvation electrostatics in fluorescence depolarization and photoionization is explored in the context of the "spring" decomposition construct presented for *ab initio* calculations previously.

Journal of Computational Chemistry 26(5), April 15, 2005

v **Announcements**

Nominations for the International Academy of Quantum Molecular Science young investigator award for molecular quantum mechanics research publications can be entered at http://www.iaqms.org/.

411-435 **Structures and electron affinities of the di-arsenic fluorides As2Fn/As2Fn- (n = 1-8).** V. Kasalová and H.F. Schaefer III* [U Georgia]

Structures and electronic behaviors of fluorinated As-As compounds were evaluated with DFT.

436-442 **Short-time Fourier transform analysis of ab initio molecular dynamics simulation: Collision reaction between CN and C4H6.** M. Tamaoki, Y. Yamauchi, and H. Nakai* [Waseda U]

The vibrational dynamics during the cyanide collision with dimethylacetylene, common in the Titan atomosphere, were illucidated with AIMD.

443-446 **A comparative study of various computational approaches in calculating the structure of pyridoxal 5-phosphate (PLP)-dependent -lyase protein. The importance of protein environment.** R. Prabhakar, K. Morokuma, and D.G. Musaev* [Emory U]

The protein environment is critical for maintaining active site structure, according to large scale ONIOM calculations.

447-454 **Chemical structures from the analysis of domain-averaged fermi holes. Nature of the MnMn bond in bis(pentacarbonylmanganese).** R. Ponec* [Czech Acad Sci], G. Yuzhakov, and M.R. Sundberg

Based on domain-averaged Fermi holes, subtleties in the Mn-Mn bond were illucidated.

455-460 **Maximal probability domains in linear molecules.** A. Gallegos, R. Carbó-Dorca, F. Lodier, E. Cancès, and A. Savin* [U Paris VI]

Identification of the volume with maximal probability of holding a specific number of atoms was used to evaluate electronic structures of LiH, BH, N_2, CO, CS, C_2H_2, and C_4H_2 and compared to electron localization functions.

461-470 **Heuristic molecular lipophilicity potential (HMLP): A 2D-QSAR study to LADH of molecular family pyrazole and derivatives.** Q. Du, P.G. Mezey, and K.-C. Chou* [Gordon Life Sci Inst]. See **Methodology, Quantitative Structure Activity Relationships.**

471-483 **Comparative performance of MM3(92) and two TINKERTM MM3 versions for the modeling of carbohydrates.** C.A. Stortz* [Ciudad U]. See **Methodology, Potentials and Parameters.**

484-490 **SARS-CoV protease inhibitors design using virtual screening method from natural products libraries.** B. Liu and J. Zhou* [Chinese Acad Sci]. See **Applications, Medicinal Chemistry and Drug Design.**

491-505 **Transferability of parameters of strictly local geminals' wave function and possibility of sequential derivation of molecular mechanics.** A.M. Tokmachev* [RWTH Aachen] and A.L. Tchougréeff* [Karpov Inst]. See **Methodology, Potentials and Parameters.**

506-513 **Improved greedy algorithm for protein structure reconstruction.** P. Tuffery* [U Paris 7], F. Guyon, and P. Derreumaux. See **Methodology, Protein Structure Prediction.**

Software News & Updates

514-521 **XMVB: A program for ab initio nonorthogonal valence bond computations.** L. Song, Y. Mo, Q. Zhang, and W. Wu

This program, which is based on Heitler-London-Slater-Pauling state functions, has been parallelized for use with the MPI library. "XMVB contains the capabilities of valence bond self-consistent field (VBSCF), breathing orbital valence bond (BOVB), and valence bond configuration interaction (VBCI) computations. The VB orbitals, used to construct VB functions, can be defined flexibly in the calculations depending on particular applications and focused problems, and they may be strictly localized, delocalized, or bonded-distorted (semidelocalized)."

Journal of the American Chemical Society 127(5-9), 2005

1364-1365 **Face-integrated Fukui function: Understanding wettability anisotropy of molecular crystals from density functional theory**, T. Li* [U Ky], S. Liu, S. Feng, and C.E. Aubrey, [DFT is applied to understand wettability or relative softness of different crystal faces]

1368-1369 **Ab initio calculation of optical rotation in (P)-(+)-[4]triangulane**, T.D. Crawford* [Virginia Tech], L.S. Owens, M.C. Tam, P.R. Schreiner, and H. Koch, [CCSD-LR calculations applied to estimate specific rotation of a chiral nonane]

1438-1445 **Spectroscopy and quantum chemical modeling reveal a predominant contribution of excitonic interactions to the bathochromic shift in α-crystacyanin, the blue caratenoprotein in the carapace of the lobser *Homaus gammarus***, A.A.C. van Wijk, A. Spaans, N. Uzunbajakava, C. Otto, H.J.M. de Goot, J. Lugtenburg, and F. Buda* [Leiden U], [Spectroscopy and TDDFT on astaxanthin]

1563-1575 **Structures and properties of self-assembled monolayers of bistable [2]rotaxanes on Au (111) surfaces from molecular dynamics simulations validated with experiment**, S.S. Jang, Y.H. Jang, Y.-H. Kim, W.A Goddard III* [Calif Tech], A.H. Flood, B.W. Laursen, H.-R. Tseng, J.F. Stoddart, J.O. Jeppesen, J.W. Choi, D.W. Steuerman, E. Delonno, and J.R. Heath, [MD using a DFT optimized force field and experiment combine to study nanotech of switchable rotaxanes]

1658-1659 **Origins of the activity of PAL and LAP enzyme inhibitors: Toward ab initio binding affinity prediction**, E. Dyguda, J. Grembecka, W.A. Sokalski* [Wroclaw U Tech], and J. Leszczynski, [Ab initio calculations probe the active sites of phenylalanine ammonia-lyase and bovine lens leucine aminopeptidase]

1675-1689 **Synthesis, structure determination, and spectroscopic/computational characterization of a series of Fe(II)-thiolate model complexes: Implications for Fe-S bonding in superoxide reductases**, A.T. Fiedler, H.L. Halfen, J.A. Halfen* [U Wisc], and T.C. Brunold* [U Wisc], [DFT and semi-empirical calculations complement experiment on iron-thiolate complexes]

2218-2230 **Correlations between ^{31}P chemical shift anisotropy and molecular structure in polycrystalline *O,O'*-dialkyldithiophosphate zinc(II) and nickel(II) complexes: ^{31}P CP/MAS NMR and ab initio quantum mechanical calculation studies**, A.-C. Larsson, A.V. Ivanov, W. Forsling, O.N. Antzutkin* [Lulea U Tech], A.E. Abraham, and A.C. de Dios, [Gaussian98 is used to estimate shift tensors]

2238-2248 **Interaction with glycine increases stability of a mutagenic tautomer of uracil. A density function theory study**, I. Dablowska, M. Gutowski* [PNL], and J. Rak* [U Gdansk], [UG tautomers studied by DFT]

2249-2255 **A computational study of the effect of bending on secondary kinetic isotope effects in S_N2 transition states**, F. Hasanayn* [American U Beirut], A. Streitwieser* [UCB], and R. Al-Rifai, [KIE's with Gaussian03]

2324-2333 **Identity hydride-ion transfer from C-H donors to C acceptor sites. Enthalpies of hydride addition and enthalpies of activation. Comparison with C-H-C proton transfer. An ab initio study**, S. Gronert* [SF State] and J.R. Keeffe* [SF State], [Hydride addition to X-CHO and other model compounds at MP2 level]

2370-2371 **^{67}Zn NMR chemical shifts and electric field gradients in zinc complexes: A quantum chemical investigation,** Y. Zhang, S. Mukherjee, and E. Oldfield* [U Il], [hybrid DFT to calculation chemical shifts]

2580-2590 **Simulation of the embryonic stage of ZnS formation from aqueous solution,** S. Hamad* [Royal Inst GB], S. Cristol, and C.R.A. Catlow, [DL_POLY of solvated Zn2+ S2- ions placed in periodic boxes]

2608-2614 **Balancing dynamics and nondynamic correlation for diradical and aromatic transition states: A renormalized coupled-cluster study of the cope rearrangement of 1,5-hexadiene**, M.J. McGuire and P. Piecuch* [Mich State U], [High level calculations examine the cope rearrangement]

2615-2619 **Unexpectedly strong energy stabilization inside the hydrophobic core of small protein rubredoxin mediates by aromatic residues: Correlated ab initio quantum chemical calculations**, J. Vondrasek, L. Bendova, V. Klusak, and P. Hobza* [Czech Acad Sci], [High level ab initio calculations on a protein core]

2620-2627 **New selective haloform-type reaction yielding 3-hydroxy-2,2-difluoroacids: Theoretical study of the mechanism,** S. Olivella [CSIC], A. Sole, O. Jimenez, M.P. Bosch, and A. Guerrero, [DFT calculations of cleavage of a CO-CF_3 bond]

2677-2685 **Elucidation of the thermochemical properties of tripenyl- or tributyl-substituted Si-, Ge-, and Sn-centered radicals by means of electrochemical approaches and computations**, A. Hjarbaek Holm, T. Brinck* [Swedish RIT], and K. Daasbjerg* [U Aarhus], [DFT with LanL2DZ basis]

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305-313 **Ptuba: a tool for the visualization of helix surfaces in proteins.** J.A. Lopera* [Inst. Biol.Stru. & Microbiol.], J.N. Sturgis and J.P. Duneau

A Uniform B-spline algorithm is a tool for the visualization of interactions between helices in membrane proteins to generate projections of 3D helices.

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329-337 **Structure-activity study of thiazides by magnetic resonance methods (NQR, NMR, EPR) and DFT calculations.** J.N. Latosińska* [Mickiewicz Univ.]

A comprehensive analysis of the relationship between the electronic structures of thiazides and their biological activity was described.

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