Results

MOLECULAR MODELING & COMPUTATIONAL CHEMISTRY

Vol. 14, No. 7 **1 September 2005**

Coverage period: 1 July2005 through 31 August 2005

About xxx papers from xx journals are cited.

Editorial and News

In this issue, Qui and colleagues show how to use GBSP, a generalized surface potential that can be used to surround part of a protein, can be adapted for QM/MM studies of enzyme catalysis (see Methodology, QM/MM). With this approach, the MM portion can be constricted strongly because the GBSP does an excellent job of conveying the electric field from the outer protein and its solvation interface to the QM region.

Also, notice methodology articles about free energy perturbation using a nonphysical fourth dimension and addition of reaction field components to lattice sum calculations.

The august 1st issue of *Proteins* is entirely dedicated to the CAPRI (Competitive Assessment of PRedicted Interactions), introduced in the editorial (*Proteins* **60**, 149, 2005) by Joël Janin [CNRS], who is also one of the CAPRI organizers, and of the recent meeting in Gaeta, Italy. For the current rounds 3 to 5 a total of 10 targets were available and nearly 2000 models from 30 groups have been submitted. Relative to the rounds 1 and 2 (2001) progress is such that several classes of targets have migrated from 'difficult' to having obtained several excellent predictions. See **Journal Reviews** for a listing of titles.

David D. Busath, Editor

1. APPLICATIONS

1.1. *Small Molecules*

General and Model Systems

A Kirkwood-Buff derived force field for methanol and aqueous methanol solutions.

S. Weerasinghe and P. E. Smith* [Kansas State U]

J. Phys. Chem. B. **109,** 15080-15086 (2005)

A new mole-fraction consistent force field for methanol and aqueous methanol is developed and described.

Water and Solvation

Simulation of water cluster assembly on a graphite surface.

C. S. Lin, R. Q. Zhang* [City U Hong Kong], S. T. Lee, M. Elstner, T. Frauenheim, and L. J. Wan

J. Phys. Chem. B. **109,** 14183-14188 (2005)

DFT tight binding calculations supplemented by a van der Waals correction, confirmed by MP2 calculations, look at water on a graphite surface. The binding energy appears dependent on the number of waters that form hydrogen bonds rather than the water cluster size.

Diffusion at the liquid-vapor interface of an aqueous ionic solution utilizing a dual simulation technique.

C. D. Wick* [PNL] and L. X. Dang

J. Phys. Chem. B. **109,** 15574-15579 (2005)

Diffusion coefficients over various regions of a 2.2 M NaCl solution at the vapor-liquid interface are calculated in MD simulation. The results, requiring a polarizable model, display the unexpected behavior of ions at interfaces.

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Water and Solvation (cont'd)

Local density profiles are coupled to solute size and attractive potential for nanoscopic hydrophobic solutes.

N. Choudhury* [U Houston] and B.M. Pettitt

Mol. Sim. **31**, 457-463 (2005)

The density of water in the first solvation shell of a Lennard-Jones solute is much higher than that of bulk water. Solute hydration behavior showed marked solute size dependence for a purely repulsive analogue of the above model.

Structure and dynamics of hydrated NH_4^+: An *ab initio* QM/MM molecular dynamics simulation.

P. Intharathep, A. Tongraar* [Suranaree U Tech], and K. Sagarik

J. Comp. Chem. **26,** 1329-1338 (2005)

With ammonium and its inner hydration shell treated with QM and using a switching scheme to compensate for inner shell exchanges, it is found that ammonium rotates and translates rapidly in water due high flexibility in the inner shell composition and structure-breaking character of the ion. I was unable to find any mention of H exchange between ion and water.

Medicinal Chemistry and Drug Design

Cytochrome P450 in silico: An integrative modeling approach.

C. de Graaf, N.P.E. Vermeulen* [Vrije U], and K.A. Feenstra

J. Med. Chem. **48**, 2725-2755 (2005)

A review of Cytochrome P450 modeling.

Identification of novel extracellular signal-regulated kinase docking domain inhibitors.

C.N. Hancock, A. Macias, E.K. Lee, S.Y. Yu, A.D. MacKerell, Jr.* [U Maryland], and P. Shapiro* [U Maryland]

J. Med. Chem. **48**, 4586-4595 (2005)

Docking followed by experimental testing of compounds finds non-ATP competitive 5-10 μM inhibitors of ERK2 that appear to bind to the CD and ED docking domain region.

A rapid computational filter for cytochrome P450 1A2 inhibition potential of compound libraries.

K.K. Chohan* [AstraZeneca], S.W. Paine* [AstraZeneca], J. Mistry, P. Barton, and A.M. Davis

J. Med. Chem. **48**, 5154-5161 (2005)

QSAR models are built using a diverse set of CYP1A2 inhibitors and four different statistical approaches. The models consistently suggest that the important features for CYP1A2 inhbition are: lipophilicity, aromaticity, charge, and the HOMO/LUMO energies.

Enhanced virtual screening by combined use of two docking methods: Getting the most on a limited budget.

V. Maiorov* [Merck] and R.P. Sheridan

J. Chem. Inf. Model. **45**, 1017-1023 (2005)

When docking over 100k compounds, the user may be limited by the number of licenses for a commercial docking software. To overcome this, the authors suggest an obvious scheme of using free docking programs as a rough filter to generate a small set of ~1k compounds for screening using expensive, potentially more accurate, programs.

Medicinal Chemistry and Drug Design (cont'd)

Design of cyclic and other templates for potent and selective peptide α-MSH analogues.

S. Fung and V.J. Hruby* [U Arizona]

Curr. Opi. Chem. Biol. **9**,352-358 (2005)

Ligand-based drug design is useful for cyclization of linear peptides to rigidify peptide structure, to limit its conformational possibilities, and to find key pharmacophore elements in 3-D space.. SAR and MM studies of MT-II and SHU-9119, potent cyclic analogues for α-MSH, are useful for generating pharmacophore templates.

Predictive, non-GLP models of secondary pharmacodynamics: Putting the best compounds forward.

G.A. Reinhart* [Abbott Labs], R.M. Fryer, M.A. Osinski, J.S. Polakowski, B.F. Cox, and G.A. Gintant

Curr. Opi. Chem. Biol. **9**,392-399 (2005)

Secondary pharmacodynamic studies of new chemical entities play an important role in support of efficient drug discovery. "Non-good laboratory practices" secondary pharmacodynamic studies can eliminate compounds or structural series with undesirable profiles early, and useful in defining structure-activity relationships with regards to off-target effects.

Systems modeling: A pathway to drug discovery.

R. Priyamvada, S.J. Vayttaden, and U.S. Bhalla* [Tata Inst Fund Res]

Curr. Opi. Chem. Biol. **9**,400-406 (2005)

Systems' modeling is an emerging tool in therapeutics and is helpful to understand the effects of pharmacological intervention at receptor, intracellular and intercellular communication stages of cell signaling.

Chiral recognition of aromatic compounds by β-cyclodextrin based on bimodal complexation.

W. Cai* [U Sci & Tech China], Y. Yu, and X. Shao

J. Mol. Mod. **11,** 186-193 (2005)

A flexible docking algorithm FDOCK is used to study the chiral recognition of the selected aromatic chiral compounds by native β-cyclodextrin (β-CD) based on bimodal complexation. The complex stability constants and the preferred binding modes were well predicted with a quantitative empirical free energy relationship model.

A study on the influence of molecular properties in the psychoactivity of cannabinoid compounds.

K.M. Honório and A.B.F. da Silva* [U Sao Paulo]

J. Mol. Mod. **11,** 200-209 (2005)

Several molecular properties are calculated with AM1 for a set of 26 cannabinoid compounds with the goal of correlating the psychoactivity of the compounds with an appropriate set of calculated properties.

Recent advances in small molecule drug delivery.

A. Kidane and P.P. Bhatt* [Shire Labs Inc]

Curr. Opi. Chem. Biol. **9**, 347-351 (2005)

More specialized and rationalized products are developed to overcome the physicochemical, physiological and pharmacological challenges inherent with drugs, and to improve the treatment regimens for the patients.

A

Virtual screening to enrich a compound collection with CDK2 inhibitors using docking, scoring, and composite scoring models

S. Cotesta, F. Giordanetto, J.Y. Trosset, P. Crivori, R.T. Kroemer, P.F. Stouten, and A. Vulpetti* [Nerviano]

Proteins **60***,* 629-643 (2005)

QXP predicts poses more accurately, but GOLD and QXP are roughly equal in predicting affinity, and GOLD is the faster (with the 'library screening' settings used). Re-scoring with single or combined scoring functions can improve predictions, but which is best depends on the range of activities considered, the docking program, and the availability of a-priori data.

Quantitative Structure-Activity Relations

Structure-based validation of the 3D-QSAR technique MaP.

N. Stiefl and K. Baumann* [U Wuerzburg]

J. Chem. Inf. Model. **45**, 739-749 (2005)

A rotationally invariant 3D-QSAR model called MaP is performed on test compound sets, and the predicted fields are found to be good predictions of the known crystal structures of the binding sites. The study uses 49 AchE, 44 NNRT, and 46 PARP-1 inhibitors.

Interpreting computational neural network quantitative structure-activity relationship models: A detailed interpretation of the weights and biases.

R. Guha, D.T. Stanton, and P.C. Jurs* [Penn State]

J. Chem. Inf. Model. **45**, 1109-1121 (2005)

Neural networks have a reputation of being black boxes. Here, the authors develop an approach for interpreting neural networks in a physically relevant way.

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An approach toward the problem of outliers in QSAR.

R.P. Verma* [Pomona Coll] and C. Hansch

Bioorg. Med. Chem. **13**, 4579-4621 (2005)

Separating outliers from a main data set and formulating another QSAR showed that they can act by a different mechanism or binding mode.

3D-QSAR studies on c-Src kinase inhibitors and docking analyses of a potent dual kinase inhibitor of c-Src and c-Abl kinases.

R. Thaimattam* [Dr Reddy's Labs], P.R. Daga, R. Banerjee, and J. Iqbal

Bioorg. Med. Chem. **13**, 4704-4712 (2005)

CoMFA and CoMSIA models were developed for quinazoline, quinoline, and cyanoquinoline derivatives inhibiting c-Src kinase and the r^2 values are 0.93 and 0.89 respectively. A homology model of c-Src kinase with the activation loop resembling the active conformation was constructed using the crystal structure of the kinase domain of Lck. The results of 3D-QSAR analyses and structure based studies are useful for the design of novel c-Src and c-Abl dual kinase inhibitors.

Relationships between structure and high-throughput screening permeability of diverse drugs with artificial membranes: Application to prediction of Caco-2 cell permeability.

M. Fujikawa, R. Ano, K. Nakao, R. Shimizu, and M. Akamatsu* [Kyoto U]

Bioorg. Med. Chem. **13**, 4721-4732 (2005)

The permeability coefficients obtained by parallel artificial membrane permeation assay were analyzed using a classical QSAR approach with simple physicochemical parameters and 3D-QSAR. Based on these results, an in silico good prediction model for the passive transcellular permeability of diverse structural compounds was obtained.

Design, modelling, synthesis and biological evaluation of peptidomimetic phosphinates as inhibitors of matrix metalloproteinases MMP-2 and MMP-8.

G. Bianchini, M. Aschi, G. Cavicchio, M. Crucianelli, S. Preziuso, C. Gallina, A. Nastari, E. Gavuzzo, and F. Mazza* [U dell'Aquila]

Bioorg. Med. Chem. **13**, 4740-4749 (2005)

Three novel peptidomimetic phosphinate inhibitors are evaluated as inhibitors of matrix metalloproteinases MMP-2 and MMP-8. The differences in binding affinities for MMP-2 and MMP-8 of the three phosphinates are rationalized by means of modelling studies and MD simulations.

Quantititative Structure-Activity Relations (cont'd)

Insight into 2-phenylpyrazolo [1,5-*a*]pyrimidin-3-yl acetamides as peripheral benzodiazepine receptor ligands: Synthesis, biological evaluation and 3D-QSAR investigation.

S. Selleri, P. Gratteri* [U Firenze], C. Costagli, C. Bonaccini, A. Costanzo, F. Melani, G. Guerrini, G. Ciciani, B. Costa, F. Spinetti, C. Martini, and F. Bruni

Bioorg. Med. Chem. **13**, 4821-4834 (2005)

Binding studies of new 2-phenylpyrazolo[1,5-*a*]pyrimidin-3-yl acetamides as selective peripheral benzodiazepine receptor ligands are presented. The variability of substituents at the 3-position was investigated. 3D-QSAR model was proposed to evaluate the effect of different substitutions on the acetamide moiety.

Carbon Nanoparticles

Engineering nanocrystals of silicon.

J.C.L. Cornish* [Murdoch U] , E. Mohamed, and R. Abdelaal

*Mol. Sim.***31**, 405-410 (2005)

The production of nanocrystals of silicon embedded in an amorphous silicon matrix is described. The contribution of the nanocrystals to the properties of the amorphous silicon matrix depends on their size, shape, orientation, distribution and volume fraction are investigated and modified. The effect of deposition conditions like filament temperature, substrate temperature, silane flow rate, pressure, and time are investigated.

Simulating nano-carbon materials.

I. Snook* [RMIT U], A. Barnard, S. Russo, R. Springal, and J. Srbinovsky

*Mol. Sim.***31**, 495-504 (2005)

Ab initio DFT based simulations are applied to study the structure and properties of graphene layers and graphene tubes to compare and contrast some of their properties such as energy, interconversion and X-ray spectra.

Size-dependent mobility of platinum cluster on a graphite surface.

J. Chen* [U Hong Kong] and K.-Y. Chan

Mol. Sim. **31**, 527-533 (2005)

MD simulations are used to study platinum clusters on a graphite surface diffusion and aggregation. The Sutton-Chen many-body potential was used for the Pt–Pt interaction and Steele potential was used to calculate the interaction between Pt atoms and carbon atoms of graphite. The results showed that the Pt clusters with less than 40 atoms are very mobile with a two-dimensional diffusion coefficient that is higher than $10^{-11}m^2s^{-1}$ at room temperature but that decreases rapidly with size.

Explosives

Atomistic-scale simulations of the initial chemical events in the thermal initiation of triacetonetriperoxide.

A. C. van Duin* [Cal Tech], Y. Zeiri, F. Dubnikova, R. Kosloff, and W. A. Goddard, III

J. Am. Chem. Soc. **127,** 11053-11062 (2005)

After parameterization of the ReaxFF reactive force field to match relative QM energies of the reactants, products, intermediates, and transition states, 100 independent unimolecular MD "cookoff" (i.e. rapid heating) simulations were performed. These compared favorably to similar simulations in the condensed-phase.

Crystal Growth

Energy ranking of molecular crystals using density functional theory calculations and an empirical van der Waals correction.

M. A. Neumann* [SARL] and M.-A. Perrin

J. Phys. Chem. B. **109,** 15531-15541 (2005)

DFT calculations with VASP, adding in an empirical van der Waals correction, are shown to well optimize and energy rank a variety of molecular crystals ranging from ethane, ethylene, and acetylene to methanol, acetic acid and urea.

Empirical molecular modelling of crystal growth modifiers.

F. Jones* [Curtin U Tech] and A.L. Rohl

Mol. Sim. **31**, 393-398 (2005)

Molecular modelling is used to interpret the effect of two molecules on the crystal growth of barium sulfate and is able to predict the preferred barium sulfate face for adsorption of ethylenediamine-tetramethylenephosphonic acid and ethylene-diaminetetraacetic acid.

1.2. *Biopolymers*

Bioinformatics

How well are protein structures annotated in secondary databases?

K. Rother* [Humboldt U], E. Michalsky, and U. Leser

Proteins **60***,* 571-576 (2005)

Cross-links from several sequence, classification, and functional databases to PDB entries are analyzed in detail. Manually curated databases suffer from an increasing lag due to the recent rapid growth of the PDB. In general, a bias can be introduced by selecting PDB entries from data available in such other databases.

Comparison of sequence and structure-based datasets for nonredundant structural data mining

C.K. Chu, L.L. Feng, and M.A. Wouters* [Victor Chang CRI]

Proteins **60***,* 577-583 (2005)

A comparison of relative over- and under representation of protein families in the sequence-based curated PDB_SELECT versus the structure-based SCOP and HSSP is presented. Structure-based selection of family representatives is preferable, but should be much more automated to be able to keep up with increasing database growth and ensure consistent classifications.

Comparative analysis of amino acid distributions in integral membrane proteins from 107 genomes

J. Nilsson, B. Persson, and G. von Heijne* [Stockholm U]

Proteins **60***,* 606-616 (2005)

The notion of Arg and Lys being strongly represented in the terminal parts of trans-membrane helices is confirmed by first identifying putative TMH's from hydrophobicity analysis on several genomes, and then determining the terminal residue bias.

Protein Sequence Analysis and Alignment

Armadillo: Domain boundary prediction by amino acid composition.

M. Dumontier, R. Yao, H.J. Feldman, and C.W.V. Hogue* [Mt Sinai Hospital]

J. Mol. Biol. **350**, 1061-1073 (2005)

A sequence-based domain predictor available at http://armadillo.blueprint.org achieves 37% sensitivity for multi-domain proteins and 56% sensitivity for two domain proteins, which is better than most other prediction methods.

Protein Secondary Structure

Structural determinants of transmembrane β-barrels.

T. Lazaridis* [City Coll New York]

J. Chem. Theory and Comput. **1**, 716-722 (2005)

The IMM1 implicit membrane model is extended, which allows the modeling of membrane proteins with an internal aqueous pore. The new model IMM1-pore gives stable MD trajectories for three β-barrel membrane proteins of different sizes and negative water-to-membrane transfer energies of reasonable magnitude and discriminates the correct fold for pairs of 10-stranded and 12-stranded transmembrane β-barrels.

Protein Structure Prediction

Structural and functional characterization of AtPTR3, a stress-induced peptide transporter of *Arabidopsis.*

S. Karim, D. Lundh, K.-Ove Holmström, A. Mandal, and M. Pirhonen* [U Helsinki]

J. Mol. Mod. **11,** 226-236 (2005)

Molecular modeling of the protein with fold recognition identified 12 transmembrane spanning regions and a large loop between the sixth and seventh helices.

Comparative or Homology Modeling

Structure of glutathione *S*-transferase of the filarial parasite *Wuchereria bancrofti*: A target for drug development against adult worm.

S.T. Nathan, N. Mathew* [ICMR], M. Kalyanasundaram, and K. Balaraman

J. Mol. Mod. **11,** 194-199 (2005)

Homology modeling is used to construct a 3D- structure of Glutathione-*S*-transferase (GST) of the lymphatic filarial parasite *Wuchereria bancrofti*. The model of *wb*GST built by MODELLER6v2 was analyzed by the PROCHECK programs. 1SFM is used for docking with GST inhibitors by Hex4.2 macromolecular docking using spherical polar fourier correlations.

Domain-based homology modeling and mapping of the conformational epitopes of envelope glycoprotein of west nile virus.

S. Vijayasri and S. Agarwal* [Indian Inst Info Tech]

J. Mol. Mod. **11,** 248-255 (2005)

Epitopes are mapped from the 3D structure of envelope glycoprotein of west nile virus and modeled using the concept of an antigenic domain. Also, dimerization, central and immunological domains, proposed as the binding sites for HLA proteins/B-cell receptors, were identified.

Protein Structure Analysis

A fourier fingerprint-based method for protein surface representation.

M.J. Bayley, E.J. Gardiner, P. Willett, and P.J. Artymiuk* [U Sheffield]

J. Chem. Inf. Model. **45**, 696-707 (2005)

Of three methods for comparing protein surface patches by shape, one is shown to work reasonably on a 366-protein test set. The shape comparison algorithm uses fingerprints that are based on fourier analysis of the distribution of surface curvatures around surface points.

Quantititative Structure-Activity Relations (cont'd)

Protein function prediction using local 3D templates.

R.A. Laskowski, J.D. Watson, and J.M. Thornton* [EBI]

J. Mol. Biol. **351**, 614-626 (2005)

Four types of 3D templates (enzyme active sites, ligand-binding residues, DNA-binding residues, and reverse templates) are applied towards predicting function for proteins with known structure, such as those from structural genomics. The reverse template approach involves using a template generated from the target structure itself and scanned against a diverse set of protein with known structure and function.

The limit of accuracy of protein modeling: Influence of crystal packing on protein structure.

E. Eyal* [Weizmann], S. Gerzon, V. Potapov, M. Edelman, and V. Sobolev* [Weizmann]

J. Mol. Biol. **351**, 431-442 (2005)

An analysis of the PDB for structural effects of crystal packing found that crystal packing contributes to limiting of the practical accuracy of a protein model by a RMSD to 0.5-0.6Å in secondary elements, and 1.0 Å for loops or protein surface residues. A web-based tool is available at http://ligin.weizmann.ac.il/cryco.

!

Main-chain conformational tendencies of amino acids

R.J. Anderson, Z. Weng, R.K. Campbell, and X. Jiang* [Serono]

Proteins **60***,* 679-689 (2005)

Clustering residue conformational tendencies from pairwise distances of main-chain conformations of residues, is used to help settle the decades-old discrepancies between different 'standard' Ramachandran distributions, as used by e.g. What_Check and ProCheck. Surprising similarities and differences in tendency are found between residue pairs.

Statistical characterization of salt bridges in proteins

J.N. Sarakatsannis and Y. Duan* [UC Davis]

Proteins **60***,* 732-739 (2005)

Revisited analysis of 10370 salt-bridges in 2017 proteins reveals, in addition to earlier noted trends, preferences for α-helices, and for areas with between 0 and 50% solvent accessibility, with the maximum around 30%.

New method for protein secondary structure assignment based on a simple topological descriptor

T. Taylor, M. Rivera, G. Wilson, and I.I. Vaisman* [George Mason U]

Proteins **60***,* 513-524 (2005)

Analysis of simplex structures in Delauney-tesselation of Cα coordinates only, provides the basis of a fast secondary structure classification algorithm. Substantial correlation with existing 'explicit' methods (like DSSP) is shown, and comparisons with other 'fast' methods are made.

Hybrid native partitioning of interactions among nonconserved residues in chimeric proteins

G. Hernandez and D.M. Lemaster* [SUNY]

Proteins **60***,* 723-731 (2005)

Simultaneous exchange of clusters of mutually non-interacting residues between homologous proteins, is used as a bases for predicting structural integrity, and shown to correlate well with known gene-shuffling patterns for several examples.

Quantititative Structure-Activity Relations (cont'd)

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Dynamic mechanism for the autophosphorylation of CheA histidine kinase: molecular dynamics simulations.

J. Zhang, Y. Xu, J. Shen, X. Luo, J. Chen, K. Chen, W. Zhu* [Chinese Acad Sci], and H. Jiang* [Chinese Acad Sci]

J. Am. Chem. Soc. **127,** 11709-11719 (2005)

Homology modeling with Sybyl, ligand-protein docking, and MD simulation with GROMACS are applied to the chemotaxis protein CheA providing insight into the two-component signaling (autophosphorylation) pathway.

Protein Folding

Self-organization in protein folding and the hydrophobic interaction.

B.S. Gerstman* [Florida Int U] and P.P. Chapagain

J. Chem. Phys. **123**, 05490101-05490106 (2005)

Favorable interactions between hydrophobic side chains in the molten globular state stabilize a folding protein, as demonstrated with four-helix bundle simulations.

A toy model for predicting the rate of amyloid formation from unfolded protein.

D. Hall* [U Cambridge], N. Hirota, and C.M. Dobson

J. Mol. Biol. **350**, 195-205 (2005)

A proposed model uses a "conceptually transparent" collision-encounter formalism to empirically predict the rate of amyloid formation for a given protein as a function of the types of interacting residues.

The Go model revisited: Native structure and the geometric coupling between local and long-range contacts

P.F. Faisca* [U Lisboa], M.M. Telo da Gama, and A. Nunes

Proteins **60***,* 712-722 (2005)

Folding times of 48-mer 3D-lattice polymers depend strongly on the long-range interactions for two target geometries, but for one other geometry the formation of local contacts drives the formation of long-range interactions.

Loop-closure events during protein folding: Rationalizing the shape of Phi-value distributions

T.R. Weikl* [MPI-KG]

Proteins **60***,* 701-711 (2005)

Analysis of ϕ value distributions of fifteen proteins in terms of 'effective contact order' (from path lengths including previously formed contacts), reveals plausible folding pathways governed by the entropic cost of loop closure. Differences related to 'polar' versus 'diffuse' ϕ value distributions are discussed.

Ø values in protein-folding kinetics have energetic and structural components.

C. Merlo, K.A. Dill, and T.R. Weikl* [U Calif]

PNAS **101**, 10171-10175 (2005)

A simple analytical model is described for the folding kinetics in terms of the formation of protein substructures. The model shows that **Ø** values have both structural and energetic components. It also provides a natural and general interpretation of "nonclassical" **Ø** values. The model reproduces the **Ø** values for 20 single-residue mutations in the **α**-helix of the protein CI2, including several nonclassical **Ø** values, in good agreement with experiments.

Protein Design and Engineering

Design of amino acid sequences to fold into C_α-model proteins.

A. Amatori, G. Tiana* [U Milano, INFN], L. Sutto, J. Ferkinghoff-Borg, A. Trovato, and R. A. Broglia

J. Chem. Phys. **123**, 05490401-05490407 (2005)

Using featureless residues with contact potential controlled by a 20×20 quenched random matrix, several sequences were defined that would fold to within 2.6-4.0 Å of the SH3 conformation, a 60-residue recognition domain common to many regulatory proteins.

Protein Hydration

Molecular dynamics of a protein surface: Ion-residues interactions.

R. Friedman, E.Nachliel, and M. Gutman* [Tel Aviv U]

Biophys. J. **89,** 768-781 (2005)

Na^+ and Cl^- are detained electrostatically near charged surfaces of the bacterial ribosome S6 globular protein in simulations, which is taken as a model of how protons would behave. During detainment, they can shuttle rapidly from one area to another.

Effect of urea on peptide conformation in water: Molecular dynamics and experimental characterization.

A. Caballero-Herrera, K. Nordstrand, K.D. Berndt, and L. Nilsson* [Karolinska Inst]

Biophys. J. **89,** 842-857 (2005)

Urea denaturation is due both to increased hydrogen bonding with water and significant hydrogen bonding with urea, according to simulations with the ribonuclease A C-peptide analog and a sequence variant.

Osmolyte trimethylamine-*N*-oxide does not affect the strength of hydrophobic interactions: Origin of osmolyte compatibility.

M.V. Athawale, J.S. Dordick, and S. Garde* [Rensselaer Polytech Inst]

Biophys. J. **89,** 858-866 (2005)

Simulations yield no effects of trimethylamine-oxide on folding and unfolding of a hydrophobic polymer, so it must stabilize proteins by indirect (water-mediated) mechanisms.

Molecular dynamics study of water penetration in staphylococcal nuclease

A. Damjanovic* [JHU], B. Garcia-Moreno, E.E. Lattman, and A.E. Garcia

Proteins **60**, 433-449 (2005)

Water hydration lifetimes and patterns, and electrostatic properties of SN WT, V66E and V66K are compared, and explain titration properties of buried Lys and Glu residues as well as observed crystal waters.

Statistical and molecular dynamics studies of buried waters in globular proteins

S. Park and J.G. Saven* [U Penn]

Proteins **60**, 450-463 (2005)

Analysis of the structural roles of buried water molecules in X-ray structures show that H-bonding patterns between water and protein vary with the simultaneous intra-protein H-bonding, and important correlations with B-factors are present. A more detailed structural and dynamical analysis from MD simulations FKBP12 WT and several mutants is presented as well.

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Protein Electrostatics and Titration

On the use of different dielectric constants for computing individual and pairwise terms in Poisson-Boltzmann studies of protein ionization equilibrium.

V. H. Teixeira, C. A. Cunha, M. Machuqueiro, A. S. F. Oliveira, B. L. Victor, C. M. Soares, and A. M. Baptista* [UN Lisboa]

J. Phys. Chem. B. **109,** 14691-14706 (2005)

Poisson-Boltzmann calculations are applied to understand protein ionization states and test the hypothesis that different dielectrics are required for various regions. The current results suggest that for prediction of pKa values no real advantage is obtained by chosing different dielectric regions even for sites that are buried. Instead it is suggested that a dielectric constant ~20 is reasonable.

Protein Dynamics

Exploring the common dynamics of homologous proteins. Application to the globin family.

S. Maguid, S. Fernandez-Alberti* [U Nacional Quilmes], L. Ferrelli, and J. Echave

Biophys. J. **89,** 3-13 (2005)

Gaussian network model analysis can be used to ask whether global dynamics are conserved within a protein family. The lowest mode of vibration is conserved in the hemoglobin family, suggesting that dynamics may be an important factor in protein evolution.

Functional dynamics of PDZ binding domains: A normal-mode analysis.

P. De Los Rios, F. Cecconi, A. Pretre, G. Dietler, O. Michielin, F. Piazza, and B. Juanico

Biophys. J. **89,** 14-21 (2005)

When the PDZ domain binds the C-terminal residues of proteins together in the cytoskeleton, one of the slow normal modes, representing collective vibrations of secondary structure elements, is modified. Binding modifies the conformational distribution.

Probing the local dynamics of nucleotide-binding pocket coupled to the global dynamics: Myosin versus kinesin.

W. Zheng* [NIH] and B.R. Brooks

Biophys. J. **89,** 167-178 (2005)

With the elastic network model, the myosin nucleotide binding pocket undergoes structural changes associated with the lowest normal mode (involving both switch I and switch II) when the conformation changes from the transition state to the rigorlike state. "structural changes in the nucleotide-pocket from the transition state to the rigorlike state. The same is true of kinesin, but the lowest mode only involves movements in switch I.

Molecular dynamics simulation of sperm whale myoglobin: Effects of mutations and trapped CO on the structure and dynamics of cavities.

C. Bossa* [U Roma "La Sapienza"], A. Amadei, I. Daidone, M. Anselmi, B. Vallone, M. Brunori, and A. Di Nola

Biophys. J. **89,** 465-474 (2005)

Opening and closure between preexisting pathways differ between three versions of sperm whale myogloblin, the deoxy native, a version recently dissociated from CO, and the YQR triple mutant.

Protein Dynamics (cont'd)

Intramolecular signaling pathways revealed by modeling anisotropic thermal diffusion.

N. Ota and D.A. Agard* [UC San Francisco]

J. Mol. Biol. **351**, 345-354 (2005)

A non-equilibrium molecular dynamics simulation method, anisotropic thermal diffusion, is applied to the PDZ domain PSD-95, resulting in observed long-distance correlations that are consistent with previous results of a sequence-based study.

Evidence of a double-lid movement in *Pseudomonas aeruginosa* lipase: Insights from molecular dynamics simulations.

S.L. Cherukuvada1, A.S.N. Seshasayee, K. Raghunathan, S. Anishetty, and G. Pennathur* [Madras Instit. Tech.]

PLoS Comp. Biol. **1**, e28 (2005)

Molecular dynamics of the 29 kD lipase, which have traditionally been thought to have one lid domain, results in a proposal that a second lid exists in the lipase and that it is important in the activation of the enzyme.

Gating charge displacement in voltage-gated ion channels involves limited transmembrane movement.

B. Chanda, O.K. Asamoah, R. Blunck, B. Roux, and F. Bezanilla* [UCLA]

Nature **436**, 852-856 (2005)

FRET measurements, molecular dynamics simulations, and Poisson-Boltzmann charge calculations applied to understand the movement of the S4 voltage-sensing helix suggests that there is limited movement and a transporter-like mechanism is used to move charge across the channel without the S4 segment being translocated across the membrane.

Ligand Binding

Loop conformation and dynamics of the *Escherichia coli* HPPK apo-enzyme and its binary complex with MgATP.

R. Yang, M.C. Lee, H. Yan, and Y. Duan* [U Calif Davis]

Biophys. J. **89,** 95-106 (2005)

Loops 2 and 3 are strongly constrained by crystal packing forces, according to MD simulations. Loop 3 flexibility participates heavily in ATP binding.

Molecular dynamics simulation studies of the wild-type, I21V, and I16T mutants of isoniazid-resistant *Mycobacterium tuberculosis* enoyl reductase (InhA) in complex with NADH: Toward the understanding of NADH-InhA different affinities.

E.K. Schroeder, L.A. Basso, D.S. Santos, and O.N. de Souza* [PUCRS]

Biophys. J. **89,** 876-884 (2005)

Isoniazid is modified and then binds covalently to nicotine in enoyl reductase cofactor, NADH, inhibiting mycolic acid synthesis. MD simulations indicate that resistance conferring mutations, known experimentally to reduce NADH affinity, reduce the NADH pyrophosphate binding. Apparently isoniazid, NADH, and the enzyme interact in a fairly complex manner. Perhaps the enzyme functions fine without the cofactor. Then if the cofactor can bind tightly at the pyrophosphate end with isoniazid attached to nicotine end, the isoniazid is then positioned to inhibit the enzyme. If the pyrophosphate will not bind, the NADH falls off easily and the enzyme functions normally.

Ligand Binding (cont'd)

Looking at enzymes from the inside out: The proximity of catalytic residues to the molecular centroid can be used for detection of active sites and enzyme–ligand interfaces.

A. Ben-Shimon and M. Eisenstein* [Weizmann]

J. Mol. Biol. **351**, 309-326 (2005)

A new enzyme active site prediction method based on available crystal structure is called EnSite and uses the finding that catalytic residues are often found in the 5% of residues closest to the enzyme centroid. Sorting unbound enzyme-inhibitor docking results based on distance to the centroid of the enzyme is useful in selecting the correct solution from a set of nearly correct solutions.

Computational and conformational evaluation of FTase alternative substrates: Insight into a novel enzyme binding pocket.

B.S. Henriksen, T.J. Zahn, J.D. Evanseck, S.M. Firestine* [Duquesne U], and R.A. Gibbs* [Purdue U]

J. Chem. Inf. Model. **45**, 1047-1052 (2005)

Docking and pharmacophore models developed in conjunction with available FTase crystal structures suggest a new hydrophobic binding pocket. Small molecule NMR studies confirm the computationally predicted favored conformation of the small molecule.

Molecular dynamics simulations of the endocannabinoid N-arachidonoylethanolamine (anandamide) in a phospholipid bilayer: Probing structure and dynamics.

D.L. Lynch and P.H. Reggio* [UNC Greensboro]

J. Med. Chem. **48**, 4824-4833 (2005)

A molecular dynamics simulation of anandamide, an important biological signaling molecule, in the lipid bilayer is used to characterize the molecule's preferential conformations, hydrogen bonding interactions, and C-H bond order parameters.

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Improving binding mode predictions by docking into protein-specifically adapted potential fields.

S. Radestock, M. Böhm, and H. Gohlke* [JW Goethe U]

J. Med. Chem. **48**, 5466-5479 (2005)

A general docking scoring function, DrugScore, is made specific for a particular target by a "reverse", protein-based CoMFA-type approach (called AFMoC) based on ligand information. Application of the method to HIV-1 protease results in significant improved binding mode predictions compared to unadapted DrugScore results, and in particular more than 75% of the 48 ligands binding modes were predicted within 2 Å RMSD.

Discovery of cell-permeable non-peptide inhibitors of β-secretase by high-throughput docking and continuum electrostatics calculations.

D. Huang, U. Lüthi, P. Kolb, K. Edler, M. Cecchini, S. Audetat, A. Barberis, and A. Caflisch* [U Zurich]

J. Med. Chem. **48**, 5108-5111 (2005)

Sets of protease-focused compounds were docked against a known BACE-1 co-crystal structure, and the top poses were energy minimized and scored using a LIE plus GB scoring function. Of the 72 compounds manually selected for testing, 12 are reported to inhibit, with almost all measured cell-based EC50 values falling within 1 kcal/mol of the computational binding affinity (from the isolated docked complex).

Ligand Binding (cont'd)

A combination of docking, QM/MM methods, and MD simulation for binding affinity estimation of metalloprotein ligands.

A. Khandelwal, V. Lukacova, D. Comez, D.M. Kroll, S. Raha, and S. Balaz* [N Dakota State U]

J. Med. Chem. **48**, 5437-5447 (2005)

A combination computational approach applied to prediction of MMP-9 inhibition by 28 hydroxamates resulted in a strong correlation (r^2=0.90) between experimental and calculated values. The QM/MM term significantly improves the root mean squared error.

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Virtual screening of biogenic amine-binding G-protein coupled receptors: Comparative evaluation of protein- and ligand-based virtual screening protocols.

A. Evers* [Aventis], G. Hessler, H. Matter, and T. Klabunde

J. Med. Chem. **48**, 5448-5465 (2005)

Comparison of several methods in their ability to retrieve known biogenic amine GPCR antagonists from virtual libraries suggests that ligand-based pharmacophore models, feature tree models, and 2D QSAR models perform substantially better than structure-based docking to homology models.

Combination of molecular modeling, site-directed mutagenesis, and SAR studies to delineate the binding site of pyridopyrimidine antagonists on the human CCK1 receptor.

M. Martín-Martínez* [CSIC], A. Marty, M. Jourdan, C. Escrieut, E. Archer, R. González-Muñiz, M.T. García-López, B. Maigret, R. Herranz, and D. Fourmy* [INSERM]

J. Med. Chem. **48**, 4842-4850 (2005)

Mutagenesis, antagonist SAR, and modeling are used to produce CCK1 homology models complexed with pyridopyrimidine compounds.

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A computational tool to optimize ligand selectivity between two similar biomacromolecular targets

D.L. Chen and G.E. Kellogg* [Virginia Commonw U]

J. Comput.-Aid. Molec. Design **19**, 69–82 (2005)

A simple steric and two ``HINT'' functional group scoring functions on a grid are combined in a 'trial-and-error' algorithm to elminiate unfavourable and introduce strong favourable interactions of ligands of L. casei thymidylate synthase and a mutant, and of to plant and mammalian 4-hydroxyphenylpyruvate dioxygenase are presented.

Multiple ligand-binding modes in bacterial R67 dihydrofolate reductase

H. Alonsoa, M.B. Gilliesa, P.L. Cumminsa, A.A. Bliznyuk, and Jill E. Gready* [Australian Natl U]

J. Comput.-Aid. Molec. Design **19**, 165–187 (2005)

Prediction of DHFR ligand binding by docking (AutoDock, FlexX) and MD simulations (Gromacs) and very thorough analysis of the highly variable binding modes and the binding dynamics, including water and water-mediated interactions, are presented.

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Ligand Binding (cont'd)

Hypocrea jecorina (Trichoderma reesei) Cel7A as a molecular machine: A docking study

C. Mulakala and P.J. Reilly* [Iowa SU]

Proteins **60**, 598-605 (2005)

A detailed analysis of the molecular mechanics underlying cellobiose binding and, particularly, forces and events associated with unbinding, to Cel7A cellulose hydrolase, is presented and leads to in-depth insights in a sophisticated molecular machine..

Modeling protein recognition of carbohydrates

A. Laederach and P.J. Reilly* [Iowa SU]

Proteins **60**, 591-597 (2005)

Recent advancements in methodology, notably forcefield development, for sugar-protein interactions are reviewed briefly. Due to the high internal flexibility, polarity and involvement of water, this remains a challenging and complex problem.

Binding MOAD (Mother Of All Databases)

L. Hu, M.L. Benson, R.D. Smith, M.G. Lerner, and H.A. Carlson * [U Mich]

Proteins **60**, 333-340 (2005)

The curating of the PDB (~14.000 protein structures, aug 2003) into a database of 5331 non-covalent protein-ligand complexes including the accompanied binding data for 1375 of those, is described. A non-redundant set of one complex for each of the 1780 protein families present in the database, is compiled, and comparisons with the recently updated PDBbind are made as well.

Van der waals interactions dominate ligand-protein association in a protein binding site occluded from solvent water.

E. Barratt, R. J. Bingham, D. J. Warner, C. A. Laughton, S. E. Phillips, and S. W. Homans* [U Leeds]

J. Am. Chem. Soc. **127,** 11827-11834 (2005)

MD simulations decomposing the van der Waals energy aid interpretation of experiment (isothermal titration calorimetry, crystallography and site-directed mutagenesis) in understanding the interaction of 2-methoxy-3-isobutylpyrazine with the mouse major urinary protein.

Computational prediction of native protein ligand-binding and enzyme active site sequences.

R. Chakrabarti, A.M. Klibanov, and R.A. Friesner* [Mass Inst Tech]

PNAS **101**, 10153-10158 (2005)

The sequences of protein ligand-binding and enzyme active sites are predicted by optimization of scoring functions based on protein ligand-binding affinity rather than structural stability. This method is applied to an identical algorithm to the active sites of diverse enzymes from the peptidase, β-gal, and nucleotide synthase families. The results suggested that simple selection pressures played a predominant role in determining the sequences of ligand-binding and active sites in proteins.

Evaluating molecular similarity using reduced representations of the electron density.

N. Meurice* [U Arizona], G.M. Maggiora, and D.P. Vercauteren

J. Mol. Mod. **11,** 237-247 (2005)

A genetic algorithm procedure is used to evaluate molecular similarity for a model system of four benzodiazepine-like ligands for the central benzodiazepine receptors and peripheral benzodiazepine receptors. Alignments were produced by MIMIC, a field-based superimposition method that matches both steric and electrostatic molecular fields.

Ligand Binding (cont'd)

A molecular dynamics simulation of the binding modes of D-glutamate and D-glutamine to glutamate racemase.

E. Puig, M. Garcia-Viloca, À. González-Lafont, I. López, X. Daura, and J.M. Lluch* [ICREA]

J. Chem. Theory and Comput. **1**, 737-749 (2005)

MD simulations gave an explanation for the apparent disagreement between the D-Gln bound MurI X-ray crystal structure and the expected position and orientation of the substrate D-Glu in order to make it possible for the assumed Cα deprotonation (by Cys70)/reprotonation (by Cys178) racemization mechanism.

Enzyme Catalysis

Water dependent properties of cutinase in nonaqueous solvents: A computational study of enantioselectivity.

N.M. Micaelo, V.H. Teixeira, A.M. Baptista, and C.M. Soares* [U Nova Lisboa]

Biophys. J. **89,** 999-1008 (2005)

Enantioselectivity for substrate is optimal at 10% water (in hexane) for explicitly solvated cutinase according to MD simulations with the tetrahedral intermediate.

Large-scale prediction of function shift in protein families with a focus on enzymatic function

S. Abhiman and E.L. Sonnhammer* [KI]

Proteins **60***,* 758-768 (2005)

Existing and new methods for function shift prediction are tested on a selected sub-set of 4225 Pfam protein families and 13,599 subfamilies and sub-divided based on EC classes. The best method predicted up to 71% accurate for an independent test-set. Detailed results for galactose-1-phosphate uridylyltransferases are presented.

Computational study of phosphatase activity in soluble epoxide hydrolase: High efficiency through a water bridge mediated proton shuttle.

M. De Vivo* [U Penn], B. Ensing, and M. L. Klein

J. Am. Chem. Soc. **127,** 11226-11227 (2005)

The phosphoryl transfer reaction in the first step of the catalytic cycle of expoxide hydrolase is probed in a Car-Parrinello QM/MM approach using a snapshot obtained from classical MD simulation.

Properties of the emitting state of the green fluorescent protein resolved at the CASPT2//CASSCF/CHARMM Level.

A. Sinicropi, T. Andruniow, N. Ferre, R. Basosi, and M. Olivucci* [U Siena]

J. Am. Chem. Soc. **127,** 11534-11535 (2005)

Ab initio QM/MM calculations are applied to a minimal model of the GFP including nearby residues to the *p*-hydrobenzilideneimidazolinone chromophore.

Enzyme Catalysis (cont'd)

On the nature of the transition state in catechol O-methyltransferase. A complementary study based on molecular dynamics and potential energy surface explorations.

M. Roca, J. Andres, V. Moliner* [U Jaume I], I. Tunon* [U Valencia], and J. Bertran

J. Am. Chem. Soc. **127,** 10648-10655 (2005)

QM/MM MD simulation and PMF calculations with DYNAMO aer performed on a model of SAM and catecholate (at the QM level) surrounded by the enzyme COMT inside a cubic solvated box.

Insight into the self-association of key enzymes from pathogenic species.

M.A. Perugini* [U Melbourne], M.D.W. Griffin, B.J. Smith, L.E. Webb, A.J. Davis, E. Handman, and J.A. Gerrard

Euro.Biophys. J. **34,** 469-476 (2005)

A 3-D model of the leishmaniasis GDP-MP hexamer is described based on homology with the uridyltransferase enzyme, Glmu. GDP-MP and DHDPS are only active in their oligomeric states so inhibition of self-association is a potential target.

Catalytic reaction mechanism of oxalate oxidase (Germin). A hybrid DFT study.

T. Borowski* [Stockholm U], A.B. Nigel, G.J. Richards, and P.E.M. Siegbahn

J. Chem. Theory and Comput. **1**, 686-693 (2005)

The hybrid DFT B3LYP method is used to investigate the mechanism of the catalytic reaction for oxalate oxidase. The enzyme-oxalate complex adopted two conformations, first one with bidentate oxalate and 6-coordinate manganese and the second one with monodentate substrate and coordinatively unsaturated Mn(II). The apparent mechanism provides an explanation for the coupling between the two-electron dioxygen reduction and oxalate oxidation.

Protein-Protein Interactions

Prediction of multimolecular assemblies by multiple docking.

Yuval Inbar* [Tel Aviv U], H. Benyamini, R. Nussinov and H.J. Wolfson

J. Mol. Biol. **349**, 435-447 (2005)

A protein docking algorithm for multi-protein complexes predicts at least one near-native solution and ranks it in the top ten, even when unbound conformations are used.

Assessment of CAPRI predictions in rounds 3-5 shows progress in docking procedures

R. Mendez, R. Leplae, M.F. Lensink, and S.J. Wodak* [U Libre Bruxelles]

Proteins **60***,* 150-169 (2005)

A detailed overview is presented of CAPRI targets, research groups, methods, software and results. An improvement of methodology and quality of results is noted, especially also in the difficult cases,.

Protein-Protein Interactions (cont'd)

Exploring the charge space of protein-protein association: A proteomic study

Y. Shaul and G. Schreiber* [Weizmann]

Proteins **60**, 341-352 (2005)

A meticulous analysis of residue interactions contributing to the on and off rates of protein-protein association is presented, and effects of mutations at different sites are predicted.

Various strategies of using residual dipolar couplings in NMR-driven protein docking: Application to Lys48-linked di-ubiquitin and validation against (15)N-relaxation data

A.D. van Dijk, D. Fushman, and A.M. Bonvin* [Utrecht U]

Proteins **60**, 367-381 (2005)

On the boundaries between protein-protein docking and NMR complex structure refinement, a comparison of several methods, extensions to the HADDOCK program, is presented. In the best one, NMR RDC data is used in a two stage method for protein-protein docking, first guiding the relative orientations and then directly restraining the complex structure.

Hydrogen-bonding interactions in the binding of loop 1 of fasciculin 2 to *Torpedo californica* acetylcholinesterase: A density functional theory study.

J. Wang, J. Gu* [MSU], and J. Leszczynski* [MSU]

J. Phys. Chem. B. **109,** 13761-13769 (2005)

DFT calculations are applied to model the interaction of model complexes representing the loop1 of Fas2 to AChE using the AIM approach to characterize the hydrogen bonds.

Free energy landscape of protein-protein encounter resulting from Brownian dynamics simulations of barnase: barstar.

A. Spaar and V. Helms* [Saarland U]

J. Chem. Theory and Comput. **1**, 723-736 (2005)

Brownian dynamics simulations are used, and the free energy landscape of a protein-protein encounter is obtained by summing the energy and entropy contributions.

Membrane Proteins and Lipid-Peptide Interactions

Modeling of an ion channel in its open conformation.

C. Domene* [U Oxford], D.A. Doyle, and C. Vénien-Bryan

Biophys. J. **89**, L1-L3 (2005)

With the crystal structure for a closed state and unpublished EM images of the putative open state for a homolog, MD simulations of KirBac1.1 were carried out to identify the conformational transition. Bending of outer helices at a Gly seems to be a key factor.

The fast gating mechanism in ClC-0 channels.

D. Bisset, B. Corry* [U Western Australia], and S.-H. Chung

Biophys. J. **89,** 179-186 (2005)

Factors that could affect the putative gate to chloride channels, a glutamate side chain, include pressure on the side chain by the transported Cl^- ion, titration, membrane potential, and external ionic strength.

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

A homology model of the pore region of HCN channels.

A. Giorgetti, P. Carloni, P. Mistrik, and V. Torre* [SISSA]

Biophys. J. **89,** 932-944 (2005)

Modeled after KcsA and KirBac1.1, the filter region of the cyclonucleotide-gated channel is more flexible and probably for this reason, less selective. Also, the S6 gating bending amplitude in the closed state appears to be lower than for MthK. A Cys near the intracellular end may act as a cell redox state sensor.

KvAP-Based model of the pore region of *Shaker* potassium channel is consistent with cadmium- and ligand-binding experiments.

I. Bruhova and B.S. Zhorov* [McMaster U]

Biophys. J. **89,** 1020-1029 (2005)

Molecular modeling of the *Shaker* channel, based on the KvAP crystal structure, indicate that *Shaker's* Cd^{++}-and correolide-binding characteristics require the openness of the KvAP pore.

Molecular dynamics simulations of the helical antimicrobial peptide Ovispirin-1 in a zwitterionic dodecylphosphocholine micelle: Insights into host-cell toxicity.

H. Khandelia, and Y. N. Kaznessis* [U Minn]

J. Phys. Chem. B. **109,** 12990-12996 (2005)

MD simulations are applied to understand the interaction of an antimicrobial peptide with a DPC micelle model. The simulations tend towards agreement with experiment despite initial conditions that are somewhat distinct and despite the fact that no special enhanced sampling methods are applied.

Molecular dynamics simulations of proteins in lipid bilayers.

J. Gumbart, Y. Wang, A. Aksimentiev, E. Tajkhorshid, and K. Schulten* [U Illinois Urbana-Champaign]

Curr. Opi. Stru. Biol. **15**, 423-431 (2005)

MD simulations of any structurally known membrane protein in its native environment are now routinely covering the 100 ns timescale.

Protein-Nucleic Acid Interactions

Interfacial water as a "hydration fingerprint" in the noncognate complex of *Bam*HI.

M. Fuxreiter* [Inst Enzymology], M. Mezei, I. Simon, and R. Osman

Biophys. J. 2005 89: 903-911

Cavity-biased grand canonical MC simulations with full hydration suggest that loose binding of the transcription factor to DNA is replaced by tight binding with release of water molecules trapped in the complex upon site recognition.

Electrostatic potential of aminoacyl-tRNA synthetase navigates tRNA on its pathway to the binding site.

D. Tworowski, A.V. Feldman, and M.G. Safro* [Weizmann]

J. Mol. Biol. **350**, 866-882 (2005)

The domain composition of aaRS and non-conserved subset of charged residues that are unique to a given aaRS type are the most important contributors to specificity of long-range electrostatic potentials of aaRS and their cognate tRNA, according to Poisson-Boltzmann computational studies.

Protein-Nucleic Acid Interactions (cont'd)

Exploring assembly energetics of the 30S ribosomal subunit using an implicit solvent approach.

J. Trylska* [UCSD], C. L. Brooks, III, and J. A. McCammon

J. Am. Chem. Soc. **127,** 11125-11133 (2005)

A continuum PB method including a solvent accessible surface area term and molecular mechanics are applied to estimate the relative binding free energies of the twenty subunit protein components of the 30S ribosomal subunit coming together.

Proteins and Surfaces

Strong repulsive forces between protein and oligo (ethylene glycol) self-assembled monolayers: A molecular simulation study.

J. Zheng, L. Li, H.-K. Tsao, Y.-J. Sheng, S. Chen, and S. Jiang* [U Washington]

Biophys. J. **89,** 158-166 (2005)

A layer of water molecules tightly bound to the polymer monolayer inhibits protein binding, according to mean force calculations using rigid protein molecules. The repulsivity sequence for the self-assembled monolayers was $S(CH_2)_4(EG)_4OH > S(CH_2)_{11}OH > S(CH_2)_{11}CH_3$.

Nucleic Acids

Nature of minor-groove binders-DNA complexes in the gas phase.

M. Rueda, F. J. Luque* [U Barcelona], and M. Orozco* [U Barcelona]

J. Am. Chem. Soc. **127,** 11690-11698 (2005)

MD simulations of DNA duplexes in complex with minor groove binders in the gas phase are reported to better understand the effect of extreme dehydration and partial neutralization of the complexes occurring during ES mass spectrometry. In each case, although the DNA distorts, the drugs remain bound.

Graphical approach to analyzing DNA sequences.

B. Liao* [Hunan U] and K. Ding

J. Comp. Chem. **26,** 1519-1523 (2005)

A 2D graphical approach is developed to determine optimal alignment between two sequences and the effect of mutations.

Lipids and Surfactants

Surface viscosity, diffusion, and intermonolayer friction: Simulating sheared amphiphilic bilayers.

S. A. Shkulipa, W. K. den Otter* [U Twente], and W. J. Briels

Biophys. J. **89,** 823-829 (2005)

Course-grained bilayers were exposed to shear fields either parallel or perpendicular to the bilayer. In the first case, molecular diffusion could be compared to expectations from the Saffman-Einstein expression. In the second case, the intermonolayer friction could be computed.

Lipids and Surfactants (cont'd)

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Self-consistent mean-field model based on molecular dynamics: Application to lipid-cholesterol bilayers.

G.A. Khelashvili, S.A. Pandit, and H.L. Scott*
[Illinois Inst Tech]

J. Chem. Phys. **123**, 03491001-03491013 (2005)

Representing cholesterol as a rod and diglyceride molecules as a two-dimension lattice field in the lipid chain order parameters, 20 μs simulations of 500 nm lateral size bilayers are possible. At low cholesterol density (2-4%, 50º C), cholesterol molecules cluster and order surrounding lipids. Ordered regions overlap at 11% cholesterol. No cholesterol-rich/cholesterol-poor regions or superlattice structures are observed.

Effect of the choice of the pressure coupling method on the spontaneous aggregation of DPPC molecules.

R.Y. Patel and P.V. Balaji* [IIT]

J. Phys. Chem. B. **109,** 14667-14674 (2005)

Self-assembly of DPPC molecules has been shown in MD simulation. This study probes the effect of pressure coupling algorithm on this process. Of some concern is that the algorithm choice seems to influence the process (although less so if the bilayer is already formed).

Role of lipid charge in organization of water/lipid bilayer interface: Insights via computer simulations.

A.A. Polyansky* [Moscow State U], P.E. Volynsky, D.E. Nolde, A.S. Arseniev, and R.G. Efremov

J. Phys. Chem. B. **109,** 15052-15059 (2005)

MD simulation of fully hydrated DOPS (1,2-dioleoyl-*sn*-glycerol-3-phosphoserine) and DOPC confirm that a proper treatment of the long-range electrostatics is necessary (comparing cutoff to PME) and suggest that the lipid-water interface is looser in DOPC than DOPS.

Implicit solvent simulations of DPC micelle formation.

T. Lazaridis* [CCNY], B. Mallik, and Y. Chen

J. Phys. Chem. B. **109,** 15098-15106 (2005)

DPC micelle formation in an implicit solvent is monitored in MD simulation. The formed micelles appear more irregular than micelles in explicit water, however the calculations are significantly faster and allow study of larger micelles over longer time periods.

Carbohydrates

Neutron diffraction and computer simulation studies of D-xylose.

P.E. Mason, G.W. Neilson, J.E. Enderby, M.L. Saboungi, and J.W. Brady* [Cornell U]

J. Am. Chem. Soc. **127,** 10991-10998 (2005)

Neutron diffraction with isotopic substitution (NDIS) and MD simulation are paired to provide insight into the structure of D-xylose in aqueous solution representing the first time NDIS experiments have been applied to sugar solutions.

Structure of aqueous glucose solutions as determined by neutron diffraction with isotopic substitution experiments and molecular dynamics calculations.

P.E. Mason, G.W. Neilson, J.E. Enderby, M.-L. Saboungi, and J.W. Brady* [Cornell U]

J. Phys. Chem. B. **109,** 13104-13111 (2005)

D-glucose is studied instead of D-xylose using NDIS and MD simulation as in the previous review. This paper notes deficiencies in the underlying force field and suggest the use of QM methods to improve the force field which can be checked by comparison to the diffraction data.

1.4. Surfaces, Catalysts, and Material Subjects

Can the π-facial selectivity of solvation be predicted by atomistic simulation?

R. Berardi, G. Cainelli* [U Bologna], P. Galletti, D. Giacomini, A. Gualandi, L. Muccioli, and C. Zannoni* [U Bologna]

J. Am. Chem. Soc. **127,** 10699-10706 (2005)

In order to better understand the solvent-dependent face selectivity (or diastereoselectivity in reaction), MD simulations of (R)-2-phenyl-propionaldehyde in *n*-pentane and *n*-octane was performed over different temperature ranges. This approach may prove useful for predicting inversion temperatures and reproducing subtle solvent effects.

DFT study of hydrogen adsorption on Al13 clusters.

I. Yarovsky and A. Goldberg* [Accelrys]

Mol. Sim. **31**, 475-481 (2005)

DFT approach is used to investigate the adsorption of hydrogen on A113. The calculated dissociation-adsorption barrier for the hydrogen molecule of ~14 kcal/mol and a desorption barrier of ~19 kcal/mol together with a high theoretical storage capacity of Al13 clusters suggested further investigations of Al nanostructures for application in hydrogen storage.

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2. METHODOLOGY

Quantitative Structure-Activity Relations

Development of a quasi-dynamic pharmacophore model for anti-complement peptide analogues.

B. Mallik and D. Morikis* [UC Riverside]

J. Am. Chem. Soc. **127,** 10967-10976 (2005)

MD simulation is applied to the complement inhibitor (13-residue cyclic) peptide compstatin (including four active and four inactive analogues) in order to develop a quasi-dynamic pharmacophore model that describes the spatial arrangement of the physicochemical properties and accounts for the flexibility.

Potentials and Parameters

A fast, scalable method for the parallel evaluation of distance-limited pairwise particle interactions.

D.E. Shaw* [Columbia U]

J. Comp. Chem. **26,** 1318-1328 (2005)

Parallelization of nonbonded interactions can be dramatically improved with a new algorithm "that significantly reduces the amount of data transferred between processors by comparison with traditional methods. Specifically, the amount of data transferred into and out of a given processor scales as $O(R^{3/2}p^{-1/2})$, where p is the number of processors" and R is the cutoff distance, "and with constant factors that should yield a substantial performance advantage in practice."

Test of molecular dynamics force fields in gramicidin A.

T. Bastug* [U Sydney] and S. Kuyucak

Euro.Biophys. J. **34,** 377-382 (2005)

Ion permeation in the gramicidin A channel is considered as a test of the AMBER force field in a membrane environment. The potentials of mean force for potassium ions are calculated along the channel axis and compared with that deduced from the experimental data. The results indicate a rather large central barrier similar to those obtained from other force fields, suggesting that lack of polarizability is the most likely cause of this problem.

Potentials and Parameters (cont'd)

Force field impact and spin-probe modeling in molecular dynamics simulations of spin-labeled T4 lysozyme.

I. Stoica* [NRC Canada]

J. Mol. Mod. **11,** 210-225 (2005)

A comparative study of the effect of the MD force field on conformational sampling and equilibration in two spin-labeled T4 lysozyme variants, N40C and K48C is reported. Ensembles of 10 x 3 ns-trajectories per variant and per force field OPLS/AMBER and AMBER99 are analyzed for a reliable assessment of convergence and sampling. It was found that subtle site-dependent differences in spin-probe rotations and torsions are more readily captured in the AMBER99 trajectories than in the OPLS/AMBER simulations.

Prediction of water and metal binding sites and their affinities by using the Fold-X force field.

J.W. H. Schymkowitz, F. Rousseau, I.C. Martins,
J. F. Borg, F. Stricher, and L. Serrano* [Euro Mol Biol Lab]

PNAS **101**, 10147-10152 (2005)

An enhanced version of the empirical force field Fold-X allows prediction of the position of structural water molecules and metal ions. Fold-X picks up 76% of water molecules found to interact with two or more polar atoms of proteins in high-resolution crystal structures and predicts their position to within 0.8 Å on average. The Mg^{2+}, Ca^{2+}, Zn^{2+}, Mn^{2+}, and Cu^{2+} metals were included in the force field. The free energy of binding of Ca^{2+} and Zn^{2+} and its dependence on ionic strength well agreed with the experimental data, allowing one to discriminate between high- and low-affinity binding sites.

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A polarizable force field and continuum solvations methodology for modeling of protein-ligand interactions.

J.R. Maple* [Schrodinger], Y. Cao, W. Damm,
T.A. Halgren, G.A. Kaminski, L.Y. Zhang, and R.A. Friesner

J. Chem. Theory and Comput. **1**, 694 -715 (2005)

A polarizable force field (PFF), and associated continuum solvation model is developed to study the energetics and structural features of protein binding to the wide range of ligands with potential for medicinal applications. PFF parameters are derived from gas-phase *ab initio* calculations.

Nonuniform charge scaling (NUCS): A practical approximation of solvent electrostatic screening in proteins.

S.M. Schwarzl, D. Huang, J.C. Smith, and S. Fischer*
[U Heidelberg]

J. Comp. Chem. **26,** 1359-1371 (2005)

An initial PB analysis is used to estimate screening factors for the atomic charges in a protein. The scaled charges can then be used in a simulation.

A molecular mechanics force field for biologically important sterols.

Z. Cournia, J.C. Smith, and G.M. Ullmann* [U Heidelberg]

J. Comp. Chem. **26,** 1383-1399 (2005)

Charmm27 force field parameters for bonds and atomic charges were developed for cholesterol, ergosterol, and lanosterol using quantum chemical analysis.

Potentials and Parameters (cont'd)

A new GROMOS force field for hexopyranose-based carbohydrates.

R.D. Lins and P.H. Hünenberger* [ETH]

J. Comp. Chem. **26,** 1400-1412 (2005)

A 45A4 force field for use with sugars based on quantum chemical calculations. "The new set is general enough to define parameters for any (unbranched) hexopyranose-based mono-, di-, oligo- or polysaccharide."

CH/π interactions involving aromatic amino acids: Refinement of the CHARMM tryptophan force field.

A.T. Macias and A.D. MacKerell Jr.* [U Maryland]

J. Comp. Chem. **26,** 1452-1463 (2005)

The CH-π interactions in CHARMM22 were checked and found to be quite reasonable. Trp side chain parameters were tuned slightly and then produced experimental heats of sublimation for indole and free energies of aqueous solvation for methylindole.

Boundary Conditions

Combining the lattice-sum and reaction-field approaches for evaluating long-range electrostatic interactions in molecular simulations.

T.N. Heinz and P.H. Hünenberger*
[Hochschule Hönggerberg]

J. Chem. Phys. **123**, 03410701-03410719 (2005)

A few equations can be changed in the lattice sum code to incorporate a reaction field in addition to usual Coulombic interactions in the Ewald sum. The computational cost is small. The periodicity artifacts must be balanced against the dielectric heterogeneity artifacts.

!

Nonperiodic boundary conditions for solvated systems.

G. Petraglio* [ETH Zürich], M. Ceccarelli, and M. Parrinello

J. Chem. Phys. **123**, 04410301-04410307 (2005)

Rather than periodic boundaries, one may prefer to use a spherical system with a reaction field based on the method of images. This concept is a bit old hat, and the interested reader would want to compare the approach to SSBP and GSBP approaches.

Solvation Energy

Long dynamics simulations of proteins using atomistic force fields and a continuum representation of solvent effects: Calculation of structural and dynamic properties

X. Li, S.A. Hassan* [NIH], and E.L. Mehler

Proteins **60**, 464-484 (2005)

A lengthy but thorough derivation of a continuum solvent model for MD simulations of proteins in water is presented. For ProtG and BPTI, multi-ns simulations in explicit (PAR22) and continuum solvent (PAR22 and CMAP) in CHARMM are compared with structural, dynamic and electrostatic experimental data.

Limitations of atom-centered dielectric functions in implicit solvent models.

J. M. J. Swanson* [UCSD], J. Mongan, and J. A. McCammon

J. Phys. Chem. B. **109,** 14769-14772 (2005)

The use of an atomic surface is shown to be problematic in continuum calculations due to the presence of interstitial high dielectric regions.

Solvation Energy (cont'd)

Detailed considerations for a balanced and broadly applicable force field: A study of substituted benzenes modeled with OPLS-AA.

D.J. Price and C.L. Brooks III* [Scripps]

J. Comp. Chem. **26,** 1529-1541 (2005)

GB is correlated well enough with explicit solvent simulations that GB-FEP estimates of hydration energy can be used as a guide for tuning the force field errors for alkyl-, nitro-, and thiobenzenes functional groups for use on mono- and disubstituted benzenes with OPLS-AA.

Electrostatics and Titration

Constant pH molecular dynamics with proton tautomerism.

J. Khandogin* [Scripps] and C.L. Brooks, III

Biophys. J. **89,** 141-157 (2005)

Two-dimensional λ-dynamics allows inclusion of tautomerism for imidazole and carboxylate groups, yielding improved accuracy in pK shift, structure, and tautomeric state estimates. The method is illustrated using ovomucoid third domain and ribonuclease A.

Global Energy Minimization

Deterministic global optimization of molecular structures using interval analysis.

Y. Lin and M.A. Stadtherr* [U Notre Dame]

J. Comp. Chem. **26,** 1413-1420 (2005)

The deterministic approach using interval analysis guarantees detection of the global minimum. The approach is illustrated using a 40-atom system in a simple potential and an 11-atom system in a more typical complex potential.

Protein structure prediction with the UNRES force-field using Replica-Exchange Monte Carlo-with-Minimization; Comparison with MCM, CSA, and CFMC.

M. Nanias, M. Chinchio, S. Oldziej, C. Czaplewski, and H.A. Scheraga* [Cornell U]

J. Comp. Chem. **26,** 1472-1486 (2005)

"REMCM located global minima for four proteins faster and more consistently than either MCM or CFMC, and it converged faster than CSA for three of the five proteins tested" and was easy to implement.

Normal Modes Analysis

Normal mode calculations of icosahedral viruses with full dihedral flexibility by use of molecular symmetry.

H.W.T. van Vlijmen and M. Karplus* [Harvard]

J. Mol. Biol. **350**, 528-542 (2005)

Group theoretical methods allow full normal mode calculations on virus capsids of greater than 50,000 residues.

Molecular Dynamics

Molecular dynamics with the united-residue model of polypeptide chains. I. Lagrange equations of motion and tests of numerical stability in the microcanonical mode.

M. Khalili, A. Liwo, F. Rakowski, P. Grochowski, and H. A. Scheraga* [Cornell U]

J. Phys. Chem. B. **109,** 13785-13797 (2005)

An integrator for MD simulation with the UNIRES (united atom) force field utilized by the Scheraga group is developed and discussed.

Effects of solute-solvent proton exchange on polypeptide chain dynamics: A constant-pH molecular dynamics study.

M. Dlugosz and J. M. Antosiewicz* [Warsaw U]

J. Phys. Chem. B. **109,** 13777-13784 (2005)

MD simulations coupled with Poisson-Boltzmann calculations using multiple reference states in implicit solvent calculations provide insight into peptide structure and dynamics at a given pH.

Molecular simulations of aqueous electrolyte solubility: 1. The expanded-ensemble osmotic molecular dynamics method for the solution phase.

M. Lisal* [Czech Acad Sci], W. R. Smith, and J. Kolafa

J. Phys. Chem. B. **109,** 12956-12965 (2005)

The expanded-ensemble osmotic molecular dynamics (EEOMD) method is described applicable to electrolyte solutions. The method uses a fixed number of solvent molecules, pressure, temperature, and overall electrolyte chemical potential in CPT MD simulations within an expanded grand canonical Monte Carlo ensemble

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Thermal conductivities of molecular liquids by reverse nonequilibrium molecular dynamics.

M. Zhang* [Intl U Bremen], E. Lussetti, L. E. S. deSouza, and F. Muller-Plathe

J. Phys. Chem. B. **109,** 15060-15067 (2005)

RNEMD (reverse non-equilibrium molecular dynamics) is adapted for molecular fluids. The method applies a heat flux and monitors the resulting temperature gradient allowing estimation of the thermal conductivity. A large force field dependence is observed.

Computer simulation of electrodeposition: Hybrid of molecular dynamics and Monte Carlo.

Y. Kaneko* [Kyoto U], T. Mikami, Y. Hiwatari, and K. Ohara

Mol. Sim. **31**, 429-433 (2005)

A hybrid method of MD and MC is proposed for the simulation of thin film growth with electrodeposition. The dynamics of particles by the MD method is simulated, while the reactions of the deposition are realized by the MC method. The correlation between the surface structure and the deposition condition is investigated.

Free Energy Methods

Absolute free energy calculations by thermodynamic integration in four spatial dimensions.

T. Rodinger, P.L. Howell, and R. Pomès* [Hosp Sick Children, U Toronto]

J. Chem. Phys. **123**, 03410401-03410411 (2005)

Using a nonphysical fourth dimension, *w*, it is convenient to compute the free energy of insertion or extraction of small solutes in dense fluid with TI, moreso than with umbrella sampling. Examples of ions and methanol in water are used to evaluate Coulombic force errors for a droplet system.

!

Solvation Energy (cont'd)

Unprejudiced identification of reaction mechanisms from biased transition path sampling.

D. Zahn* [Max Planck Inst]

J. Chem. Phys. **123**, 04410401-04410407 (2005)

A method for distinguishing mechanisms for transition state crossings with a somewhat complex manifold was developed. Effectiveness is demonstrated with a simple particle on a 2D manifold and then with pressure-induced insertion of helium into a C_{60} buckyball.

Phase-space overlap measures. I. Fail-safe bias detection in free energies calculated by molecular simulation.

D. Wu and D.A. Kofke* [U Buffalo]

J. Chem. Phys. **123**, 05410301-05410310 (2005)

In free energy computations, assessing the adequacy of sampling is a challenge. A heuristic based on phase-space overlap integrals is useful for determining whether the work-based free energy is bias-free.

QM/MM

Reliable treatment of electrostatics in combined QM/MM simulation of macromolecules.

P. Schaefer, D. Riccardi, and Q. Cui* [U Wisconsin]

J. Chem. Phys. **123**, 01490501-01490514 (2005)

The GBSP (generalized boundary solvent potential) can be applied to QM/MM with good effect at both QM and MM levels. The long range electrostatic component from beyond the MM region has an important impact on the QM structure. The method was illustrated with carbonic anhydrase.

Dual-topology/dual-coordinate free-energy simulation using QM/MM force field.

H. Hu* [Duke U] and W. Yang

J. Chem. Phys. **123**, 04110201-04110204 (2005)

By computing the QM component for two environments simultaneously, one can get $\Delta\Delta G$ in about half the time.

On possible pitfalls in ab initio quantum mechanics/molecular mechanics minimization approaches for studies of enzymatic reactions.

M. Klahn, S. Braun-Sand, E. Rosta, and A. Warshel* [USC]

J. Phys. Chem. B. **109,** 15645-15650 (2005)

Warshel and co-workers examine the limitations of QM/MM minimization approaches using the hypothetical reaction of a metaphosphate ion with water in the Ras-GAP complex. Using various snapshots from MD simulation as starting points, large differences in the resulting minima on the QM/MM PES were observed. The work highlights the importance of sampling the protein configurational states.

A QM/MM exploration of the potential energy surface of pyruvate to lactate transformation catalyzed by LDH. Improving the accuracy of semiempirical descriptions.

S. Ferrer, J.J. Ruiz-Pernía, I. Tuñón* [U Valencia], V. Moliner, M. Garcia-Viloca, A. González-Lafont, and J.M. Lluch

J. Chem. Theory Comput. **1**, 750-761 (2005)

A QM/MM study of the potential energy surface of the pyruvate to lactate transformation catalyzed by L-lactate dehydrogenase is presented. The transformation involves a hydride and a proton transfer, which are followed by means of the corresponding antisymmetric combination of the distances from the hydrogen atom to the donor and the acceptor atoms.

Protein Structure Prediction

Determining protein topology from skeletons of secondary structures.

Y. Wu, M. Chen, M. Lu, Q. Wang, and J. Ma* [Rice U]

J. Mol. Biol. **350**, 571-586 (2005)

A new method for deducing protein folds based on low-resolution data, such as cro-EM data, uses a knowledge-based geometry filter followed by an energetics-based evaluation. Interestingly, validation results suggest that in general among possible topology candidates the native topology is the one that can accommodate the largest structural variations.

Rigid Cluster Dynamics

Rigid-cluster models of conformational transitions in macromolecular machines and assemblies.

M.K. Kim, R.L. Jernigan, and
G.S. Chirikjian* [Johns Hopkins U]

Biophys. J. **89,** 43-55 (2005)

Constraints for the elastic network interpolation used to represent rigid-body interactions can be obtained using atomistic modeling. The approach can turn the $300{,}000^2$-cell Hessian matrix virus capsid problem into an 84^2-cell Hessian matrix problem. Reduction depends only on the amount of the cluster that can be assumed to be rigid-body.

Protein Folding

Orientation-dependent potential of mean force for protein folding.

A. Mukherjee* [Indian Inst Sci], P. Bhimalapuram, and
B. Bagchi

J. Chem. Phys. **123**, 01490101-01490111 (2005)

Ellipsoidal side chains with orientation-dependent interactions were parameterized from PDB structures with implicit solvation. Hydrophobic side chain interactions proved to have deeper wells than polar side interactions.

Ligand Docking

Optimal clustering for detecting near-native conformations in protein docking.

D. Kozakov, K.H. Clodfelter, S. Vajda, and
C.J. Camacho* [Boston U and U Pittsburgh]

Biophys. J. **89,** 867-875 (2005)

Small ligands dock to proteins because of VDW forces and form clusters <2Å in radius, whereas proteins dock because of long-range dehydration and electrostatic forces in the 4-9 Å range. Near-native conformations can be found by clustering analysis.

Large-scale validation of a quantum mechanics based scoring function: Predicting the binding affinity and the binding mode of a diverse set of protein-ligand complexes.

Kaushik Raha and Kenneth M. Merz, Jr.* [Penn State]

J. Med. Chem. **48**, 4558-4575 (2005)

A QM-based scoring function has the advantage of being able to predict free energies of binding without fitting of parameters, and one implementation is demonstrated here on a large docking test set. Additional advantages include accounting for charge interactions more accurately and the ability to include effects such as polarization and charge transfer in metalloenzymes.

Ligand Docking (cont'd)

Comparing protein-ligand docking programs is difficult

J.C. Cole, C.W. Murray, J.W. Nissink, R.D. Taylor, and R. Taylor* [CCDC]

Proteins **60**, 325-332 (2005)

A detailed and thorough analysis is presented of methodological issues in recent published comparisons of different docking programs. Seemingly innocuous details, like different implementations of the same algorithm, different program versions, generation of (3D) starting conformations, choice of measure of success, can have dramatic effects.

Structure Determination

A new molecular-dynamics based approach for molecular crystal structure search.

V. Buch* [Hebrew U], R. Martoňák, and M. Parrinello

J. Chem. Phys. **123**, 05110801-05110804 (2005)

Searching for transitions from disorder to order with a small, periodically bounded system allows for automatic identification of possible crystal forms. These can be useful for interpretation of low quality or complex diffraction patterns.

Toward direct determination of conformations of protein building units from multidimensional NMR experiments VI. Chemical shift analysis of his to gain 3D structure and protonation state information.

P. Hudáky and A. Perczel* [Eötvös University]

J. Comp. Chem. **26,** 1307-1317 (2005)

Chemical shifts of His protons allow assignment of secondary structure with 80% accuracy.

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

Proteins 60, August 1, 2005

170-175 **The targets of CAPRI rounds 3-5**. J. Janin

176-180 **Classification of protein complexes based on docking difficulty**. S. Vajda

181-186 **CAPRI rounds 3-5 reveal promising successes and future challenges for RosettaDock**. M.D. Daily, D. Masica, A. Sivasubramanian, S. Somarouthu, and J.J. Gray

187-194 **Progress in protein-protein docking: atomic resolution predictions in the CAPRI experiment using RosettaDock with an improved treatment of side-chain flexibility.** O. Schueler-Furman, C. Wang, and D. Baker

195-201 **Docking to single-domain and multiple-domain proteins: old and new challenges.** E. Ben-Zeev, N. Kowalsman, A. Ben-Shimon, D. Segal, T. Atarot, O. Noivirt, T. Shay, and M. Eisenstein

202-206 **Modeling oligomers with Cn or Dn symmetry: application to CAPRI target 10.** A. Berchanski, D. Segal, and M. Eisenstein

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MMCC Results is published ten times per year, at the beginning of each month except January and August. For subscription information, please contact MMCC Publishing:

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