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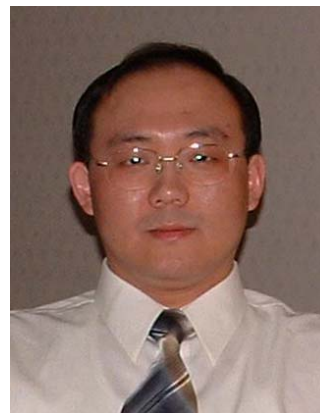
B.S. & M.S. (Nankai University, China)

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Major Research Interest: **Computational Biology;**
Molecular Biology

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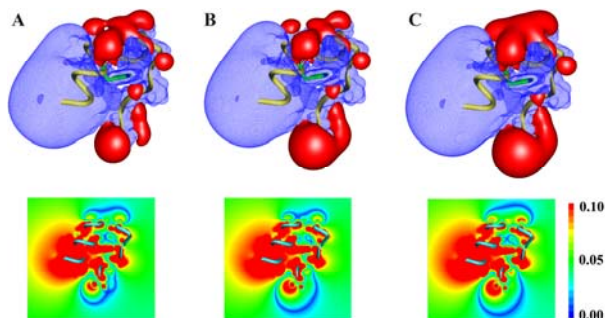
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The Dawei research group has two key research interests involving computational biology and molecular biology.

(1) Development of Force Field

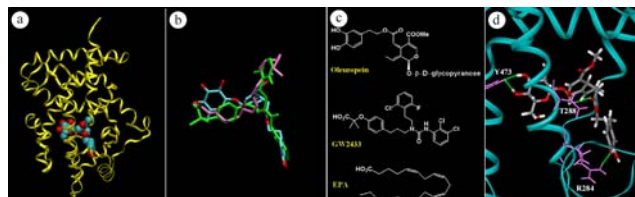
We are collaborating with Prof. John Zhang's group at New York University to develop new force field containing polarized protein-specific charges (PPC) for molecular dynamics simulation of proteins by combining a recently developed fragment-based scheme, molecular fractionation with conjugate caps (MFCC), with continuum solvent model. Since the PPC is derived from first principal quantum solvation calculation of protein in a native (or a given) structure and thus correctly represents electronically polarized state of the protein and therefore provides accurate electrostatic interaction near the native structure. Extensive researches will be carried out to investigate the effects of PPC on protein folding, protein-protein interaction, protein-ligand interaction, protein-ligand docking and structure-based virtual screening.



Trp-cage protein. *Upper panel*: ESP contour surfaces drawn at ± 15 kT/e (blue for positive and red for negative charge) and *Lower panel*: ESP color-filled contour maps (color gradient from red to blue) from (A) full system calculation, (B) MFCC calculation in gas phase, and (C) MFCC-PB in water solution respectively

(2) Structure-Function of CAM

Structure-based virtual ligand screening computation is performed on a natural compound library to discover novel classes of PPAR δ agonists. The free energies of binding with PPAR δ will be predicted by using linear interaction energy (LIE) method. The real binding affinity values of putative candidates will be measured by adipogenesis assay and whether they are agonists or antagonists or partial agonists will be determined by measuring the expression of PPAR δ during adipocyte differentiation. After confirming the validity of the predicted binding energy values and also their binding conformations by comparing the predicted values with the experimental data, we will then further analyze the binding conformations of PPAR δ agonists to identify important structural determinants that would favour PPAR δ binding. The goal of our research in the field of complementary and alternative medicine (CAM) is to identify novel natural PPAR δ agonists as promising new drugs in the fight against obesity.



The predicted PPAR δ -oleuropein binding structure (a) the final snapshot of the 3-ns MD simulation of PPAR δ -oleuropein complex. The PPAR δ backbone is represented by the yellow ribbon, and oleuropein is represented with vdW and is color coded as follows: carbon, cyan and oxygen, red. (b) Superposition of the structures of GW2433 (green) and EPA (mauve) bound to PPAR δ . (c) Chemical structures of the compounds described as in (b). (d) Hydrogen bonds formed by the oleuropein and the surroundings are indicated as green dotted lines.

Selected Publications

Da W. Zhang and J. Z. H. Zhang, Molecular fractionation with conjugate caps for full quantum mechanical calculation of protein-molecule interaction energy. *J. Chem. Phys.*, 119, 3599 (2003).

Da W. Zhang, Yun Xiang, and J. Z. H. Zhang, New advance in computational chemistry: full quantum mechanical *ab initio* computation of streptavidin-biotin interaction energy. *J. Phys. Chem. B.*, 107, 12039 (2003).

Da W. Zhang, Yun Xiang, Ai M. Gao, and John Z.H. Zhang, Quantum mechanical map for protein-ligand binding with application to beta-trypsin/benzamidine complex. *J. Chem. Phys.*, 120, 1145 (2004).

Yun Xiang, Da. W. Zhang, and John Z. H. Zhang, Full quantum mechanical energy optimization for protein-ligand structure. *J. Comput. Chem.*, 25, 1431-1437 (2004)

Sylvia Lee-Huang, Philip Lin Huang, Dawei Zhang, et al. Discovery of small-molecule HIV-1 fusion and integrase inhibitors: Oleuropein and Hydroxytyrosol: 1. fusion inhibition. *Biochem. Biophys. Res. Commun.* 354, 872-878 (2007).

Sylvia Lee-Huang, Philip Lin Huang, Dawei Zhang, et al. Discovery of small-molecule HIV-1 fusion and integrase inhibitors: Oleuropein and Hydroxytyrosol: 2. integrase inhibition. *Biochem. Biophys. Res. Commun.* 354, 879-884 (2007).

Patent

Compositions and methods for treating obesity, obesity related disorders and for inhibiting the infectivity of HIV, Sylvia Lee-Huang, Paul L. Huang, Philip Lin Huang, Da W. Zhang, John Z.H. Zhang, et al. US patent application number: 11/827135, 2007.