Cyberinfrastructure for Next-Generation Biomolecular Modeling

Teresa Head-Gordon and Martin Head-Gordon, University of California, Berkeley

Vijay Pande, Stanford University and Jay Ponder, Washington University, St. Louis

CHE-0535710

Recent efforts –

- A first draft of a complete set of force field parameters for nucleic acids is in place, and is now undergoing initial testing in TINKER.
- A variety of implicit solvation models for use with the AMOEBA force field and non-polarizable force fields have been implemented in TINKER (Figure 1).
- New sampling methods for thermodynamics calculations via a series of new enhancements to simulated tempering (ST) methodology.Using a Bayseian framework, a method to iteratively and adaptively calculate the needed weights for ST extremely rapidly, as well as new implementations to use a WHAM-like method to combine distributed computing trajectories to calculate the needed weights.
- Development of basis set pairs that can reproduce the MP2 basis set limit to high accuracy while offering approximately 10-fold decrease in computation time are now published and in the public domain to facilitate widespread adoption of dual basis techniques.
- This absolutely localized molecular orbitals (ALMO's) electronic structure method developed for molecular clusters and liquids has the physical interpretation of restricting intermolecular interactions to exclude partial charge transfer. We have used this approach as the basis for a new energy decomposition analysis (EDA) of intermolecular interaction energies (Figure 2).

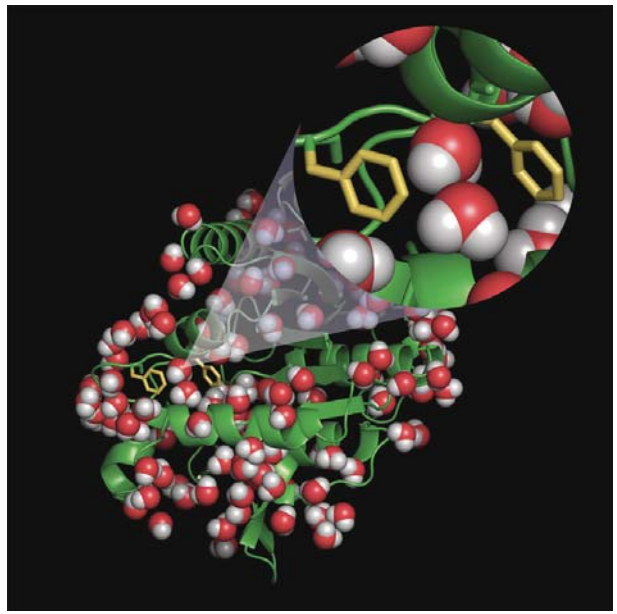

Figure 1. A new solvation function has been implemented in TINKER that outperforms other reported scoring functions in terms of correct native ranking and low Z-scores for a variety of decoy sets. This work shows that the stabilizing effect of hydrophobic exposure to aqueous solvent is a major improvement over solvent accessible surface area models that penalize hydrophobic exposure.

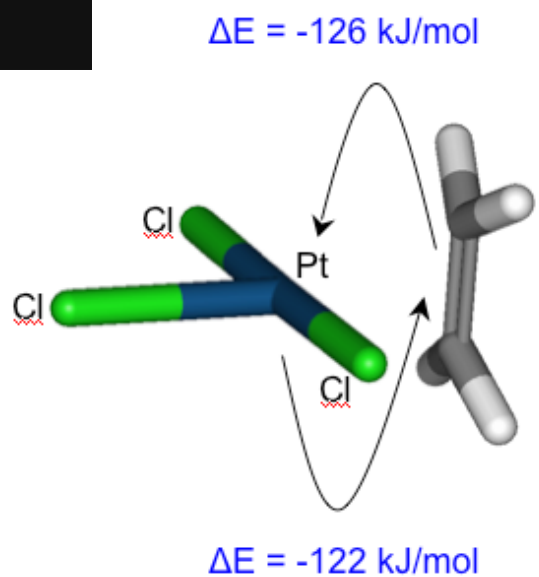

Figure 2. *A new approach to analyzing intermolecular interaction energies.* This approach gives well-defined values that quantify traditiona chemical concepts such as forward an back donation in transition metal complexes (Zeiss' salt is shown). This information can be used to tune intermolecular binding energies via substituent effects, for practical purposes.